

ANNUAL REPORT | 2020-21



INDIAN COUNCIL OF MEDICAL RESEARCH
NEW DELHI



icmr
INDIAN COUNCIL OF
MEDICAL RESEARCH
Serving the nation since 1911

Annual Report

2020-21



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PREFACE

It gives me immense pleasure to present the Annual Report of the Indian Council of Medical Research (ICMR) for the year 2020-21. ICMR scientists worked as a team to achieve the goals in sync with government policies and programmes in the field of biomedical research. An unprecedented worldwide spread of the SARS-CoV-2 started in January, 2020 when severe challenges on India's healthcare facilities and medical infrastructure were faced. ICMR-National Institute of Virology (NIV), Pune, the standalone lab for COVID testing then, standardized the rRT-PCR based diagnostic test. On January 30, 2020, ICMR-NIV, Pune reported first case of COVID-19. The capacity for COVID-19 testing was exponentially increased across the country reaching to 2435 laboratories by March, 2021. Immense efforts were put in to establish labs in difficult terrains like Ladakh, Sikkim, Arunachal Pradesh, Nagaland, other NER states and islands like Lakshwadeep and Andaman & Nicobar.



Multiple mentor institutes (institutes of national standing like AIIMS and PGIMER) were roped in to train and hand-hold multiple government labs to enable them to start COVID-19 testing. As a result, a COVID-19 testing lab was made operational in all the medical colleges of the country. A common sample referral form (SRF) was developed and deployed with the help of National Information Centre (NIC) through the RTPCR application. To understand the disease trend in a real time manner, ICMR developed nation wide COVID-19 testing data portal which facilitated the COVID-19 testing data entry across the country. Apart from deploying infrastructure for COVID-19 testing and implementation of technologies, a systematic platform for validation of diagnostic commodities was developed by setting up of 24 validation centres. Taking India's agenda forward of self-reliant India, ICMR approved 72% of the indigenous test kits which resulted in cost reduction of single rRT-PCR test.

Ten COVID-19 biorepositories for helping industry/academia with appropriate samples of SARS-CoV-2 for developing indigenous diagnostics etc. have been established. The National Task Force (NTF) on COVID-19 was constituted to guide the Ministry of Health & Family Welfare, Government of India in prevention and control activities for COVID-19 in the country. A rapid response team of ICMR was formed to formulate public health response for combating COVID-19 pandemic.

ICMR-NIV, Pune and Bharat Biotech International Pvt. Ltd jointly developed India's first inactivated whole-virus COVID-19 vaccine (COVAXIN). The vaccine has been approved by DCGI for human use and is being used in the national immunization program.

ICMR initiated a National Clinical Registry for COVID-19 (NCRC) in collaboration with Ministry of Health & Family Welfare (MOHFW), All India Institute of Medical Sciences, Delhi (AIIMS) and ICMR- National Institute of Medical Statistics (ICMR-NIMS) with an objective to collect data regarding clinical and laboratory features, treatments, and outcomes of hospitalized COVID-19 patients in 42 hospitals, spread across all geographical zones of the country. Daily testing scaled up tremendously to the extent that by Mar 2021, 244 Million samples were tested.

ICMR-NIV developed the first indigenous SARS-CoV-2 IgG ELISA kit 'KAVACH' for detection of antibodies in human serum with 92.37% and 97.9% sensitivity and specificity respectively. The technology has been transferred to 07 companies for scale-up and commercialization.

Under the Atmanirbhar Bharat program, ICMR-NIV evaluated 168 real time RT-PCR kits, 164 RNA extraction kits, 99 VTMs & swabs; validated Truenat Beta CoV E-gene screening assay and Truenat SARS-CoV-2 RdRp gene-confirmatory assay (Molbio Diagnostics, India); evaluated 225 commercial serodiagnostic kits (Rapid Diagnostic Test, ELISA & CLIA) for SARS-CoV-2 and validated forty-six products; validated two out of three commercial technologies based on ozone and negative ion generation systems for surface decontamination of SARS-CoV-2 virus.

A high throughput COBAS8800 automated system in the COVID-19 testing facility was inaugurated by Hon'ble Prime Minister of India that tremendously boosted the capacity of screening samples for SARS-CoV-2. ICMR coordinated COVID-19 testing of the members of Parliament of India during all three sessions.

India also developed National Guidelines for Ethics Committees reviewing research during COVID-19 pandemic along with SOP's for emergency review. Guidance document for appropriate recording of COVID-19 related deaths in India was developed to ensure the correct reporting of deaths due to COVID-19.

ICMR has been playing a pivotal role in testing, treatment, and aggressive research into drugs and vaccination to fight the Coronavirus pandemic. A total of 5 technologies related to COVID -19 viz. Kavach ELISA, Equine Anti Serum against SARS COV-2, COVID-19 rapid antibody detection kit, RT-LAMP assay for detection of SARS-COV-2 and Development of TaqMan SARS COV-2 multiplex RT PCR has been transferred to companies on non-exclusive basis.

To monitor the quality of testing for COVID-19 test done by the approved laboratories, ICMR has followed inter-laboratory comparison i.e. random rechecking of the samples tested by these labs (ILQC). The Covid-19 Data APIs were developed to handle the challenge of the huge testing database and were provided to different organisations (NDMA, NHA, Aarogya Setu App etc.), states and city administration for real-time monitoring of the situation.

ICMR in partnership with WHO, developed a film on India's response to Covid-19. IJMR published Four special issues on COVID-19 in February & March 2020, May 2020, July & August 2020 and January & February 2021; and one special issue on 'One Health' in March 2021. The special issue on 'One Health' was released by Dr. Harsh Vardhan, Honourable Minister of Health and Family Welfare, Government of India.

During this period, ICMR also initiated a Centre for Innovation and Bio-Design (CIBioD) at PGIMER, Chandigarh, which will create a platform for collaboration of clinicians and domain experts to share the idea and evolve the innovative and patent-oriented research. The centre has started a Promotion of Innovation & Entrepreneurship (PIE) programme and a Journal named 'E-Avishkar'. ICMR has done an agreement with Federation of Indian Chambers of Commerce and Industry (FICCI) for both national and international commercialization of health technologies under HTAC program. HTAC program has three components viz. Commercialization component, training component and exposition components.

(Dr. Balram Bhargava)

Secretary, DHR & DG, ICMR

New Delhi

EDITOR'S DESK

The Indian Council of Medical Research (ICMR) is today the apex and premier medical research organization in the country which spearheads planning, formulation, coordination, implementation and promotion of biomedical research. It is one of the oldest medical research bodies in the world. In 1911, Government of India made a historic decision to establish Indian Research Fund Association (IRFA) with the specific objectives of sponsoring and coordinating medical research in the country. After Independence, in 1949, the IRFA was re-designated as the Indian Council of Medical Research (ICMR) with considerable expansion in its functions and activities.

ICMR played a pivotal role at each step during COVID 19 pandemic, right from isolating virus, diagnostic labs establishment, development & validation of kits, policy framing, data collection & maintenance, formulating guidelines for prevention & treatment for all age groups, vaccine development and scientific knowledge publication.

ICMR-NIMR established a biorepository of COVID-19 positive blood in which blood samples of COVID-19 patients admitted to various hospitals are collected. Blood samples are aliquoted and stored in -80C freezers. They can be used for validation of antibody kits, developing new diagnostics, therapeutics, vaccine research, immunological response, to understand the host-pathogen dynamics and disease pathogenesis etc. These samples in the biorepository will support the current and the future research projects on COVID-19 in India.

The COVID-19 testing facility at ICMR-NICED is a 24x7 working lab that tested more than 2.15 lakh samples from the hospitals and other health facilities of Kolkata and different districts of West Bengal. The institute has acted as depot for supplying kits to the North Eastern States.

ICMR-NIE conducted three rounds (round 1: Apr - May 2020; round 2: Aug – Sept 2020; round 3: Dec 2020 - Jan 2021) of nationwide community based serosurveys between April 2020 and Jan 2021, to measure the extent of SARS-CoV-2 infection and track the progress of pandemic in India.

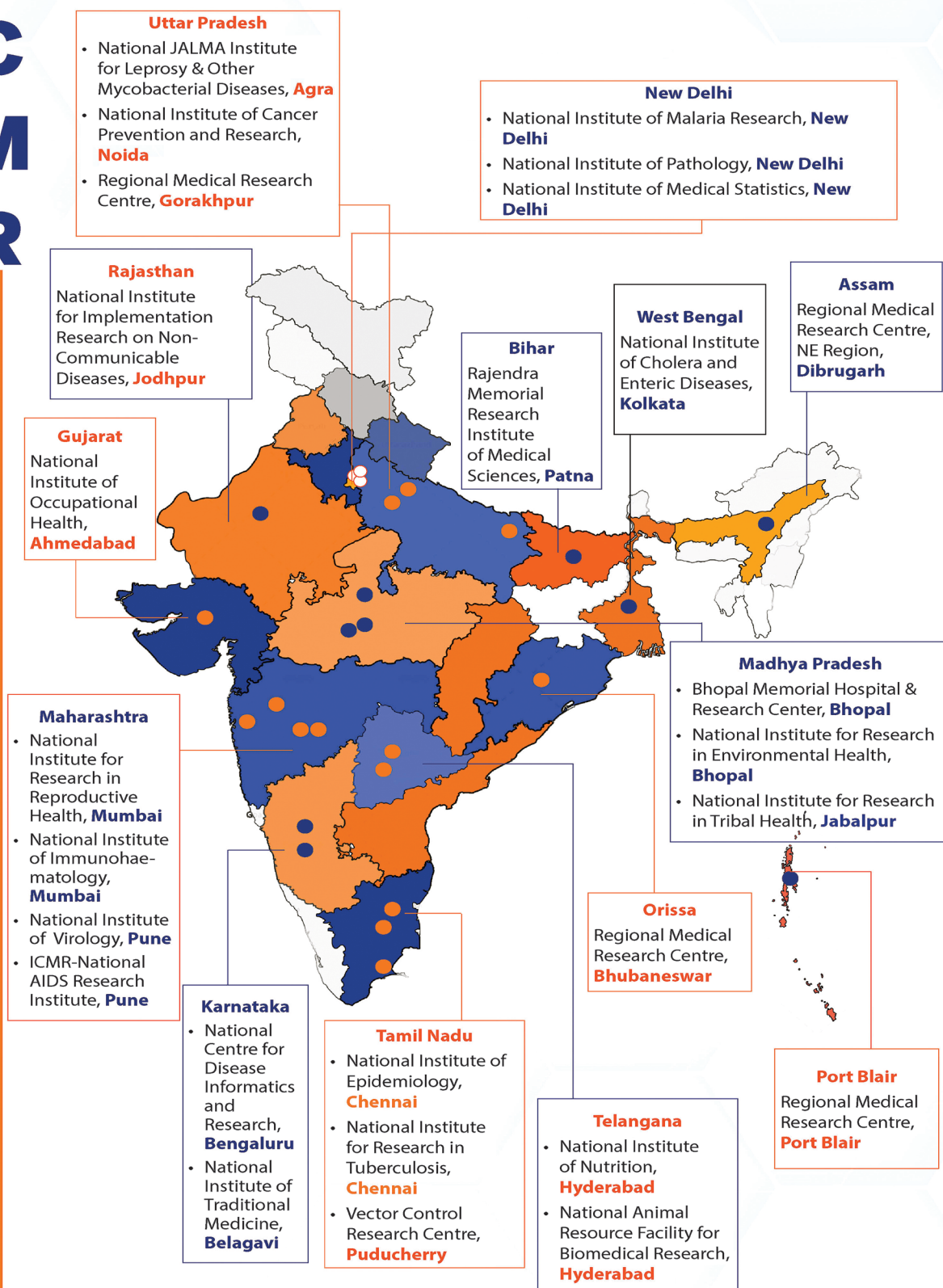
ICMR-NICED established the interchangeability of currently available two rotavirus vaccines (Rotasil & Rotavac) in India. The centre received SKOCH Award (Gold) for multi-component efforts in combatting COVID-19. An e book on “Framework for Telemedicine use in Management of Cancer, Diabetes, Cardiovascular Diseases, and Stroke” was released on 25th January 2021 to mark the Foundation Day of ICMR-NCDIR, Bengaluru.

Lieutenant Governors commendation certificate was awarded to ICMR-RMRCPB in view of exceptional contributions provided to the whole Islands - diagnosis , contact screening and Identification of hot spots - SARS COV 2 / COVID 19.



INSTITUTES/REGIONAL MEDICAL RESEARCH CENTRES

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Anticipating a high workload and scarce availability of resources in the islands as well as the difficulties in procuring diagnostic kits and consumables, that have to be imported from Mainland- India, which was difficult in particular during the lockdown, a cost-effective pool testing technique was introduced for the first time in India at Andaman & Nicobar Islands by ICMR-RMRCBPB. The centre is also working on control of Tuberculosis among the Nicobarese Tribe of Car Nicobar. A Truenat - micro real time-PCR for rapid diagnosis of leptospirosis at minimal resource settings was evaluated. The centre also demonstrated the advantage of novel strategy that supplementing MDA with mass double fortified salt (DEC+iodine) for eliminating diurnally sub-periodic *Wuchereria bancrofti* in two Islands.

An Epidemiological Investigation of an Acute Neurological Outbreak in Eluru, Andhra Pradesh was conducted by ICMR-NIN. From the investigations, it was reported that the outbreak was due to pesticide organophosphate (Triazophos) contamination of water. Nutritional status of below 12 years Children during an outbreak of Acute Encephalitis Syndrome (AES) hit Muzaffarpur district, Bihar was assessed through a rapid survey. Studies on the Particularly Vulnerable Tribal Groups (PVTGs) Chenchu and Kolam tribes and their food habits has shown that the resource base of indigenous foods used by the tribe is slowly dwindling and there is a need to conserve and mainstream the important nutritious indigenous foods. An animal study on the impact of vitamin D insufficiency on muscle metabolism showed impaired functional parameters in muscle such as contraction, energy metabolism and mitochondrial biogenesis; thereby indicating that subclinical deficiency as seen in humans may impair muscle function. There was development of E-module to facilitate the training for trainers who are involved in implementation of Anemia *Mukt Bharat* programme.

Ministry of Health and Family Welfare, Govt. of India launched a scheme “Strengthening of Intersectoral Coordination for Prevention and Control of Zoonotic Diseases” with an objective to strengthen Intersectoral coordination between the different sectors. ICMR-NIN Released the latest Nutrient Requirements for Indians and Recommended Dietary Allowances. For the first time, the report includes the Estimated Average Requirements (EAR) and Tolerable Upper Limits (TUL) of nutrients alongside RDAs. What India Eats? Report, for the first time, analyzed the data from earlier diet surveys and provided an overview of the dietary patterns across the country projected based on food groups. This report gives details of Regional Dietary Pattern of Indian Population. A contextually relevant methodology to assess dimensions of the rural food environment using a novel 5A’s approach i.e., availability, affordability, accessibility, acceptability and accommodation was formulated. A Diet Diversity Score was developed and validated. E-learning Modules on nutrition were developed and POSHAN Abhiyaan has become highly popular with 73,315 (27,059 females and 46,162 males) registrations.

A total 773 Adhoc proposals, 815 Fellowships, and 237 DHR-GIA proposals were processed.

A total of 21 Scientists and young researchers were awarded in 14 different ICMR Awards/Prizes categories in the field of biomedical research. A special edition on ICMR Women warriors was published. The history timeline of ICMR depicting 108 year journey of the Council since the day of its inception in 1911, was developed.

As the government is moving ahead with the mantra of “monetize and modernize”, ICMR has formulated “Technology Transfer and Revenue sharing guidelines”. These guidelines endeavour to disseminate ICMR technologies through a framework that ensures seamless transfer of technology to industry(ies) leading to indigenous product development and commercialization as per Make-in-India initiative of the Government.

Leprosy Data Management System (Nikusht) has been handed over to National Leprosy Eradication Program (NLEP). The web-base and mobile app solution for Jal Jeevan Mission is being implemented

in partnership with States, to enable every household in villages to have functional household tap connection by 2024. A centre for rabies diagnosis and research was established at ICMR-NIV, Pune.

ICMR has formulated “Policy document for Innovation and Entrepreneurship for Medical Professionals, Scientists and technologist at Medical /Dental/ Para Medical Institutes/ Colleges and allied Biomedical Research and Academic Institutions”. This initiative will promote Medical Device Innovations in the Country and thus promoting Make-in-India, Skill India and Start-up-India initiatives of the Government of India.

A total of 15 patents applications were filed, 4 Indian patents and 2 foreign patents have been granted. A total of 36 patents were maintained. ICMR has established “Medical Device and Diagnostics Mission Secretariat (MDMS)”. This will promote innovative technology development, skill development and will foster indigenous manufacturing of medical devices to decrease import dependency of India. Two biodesign programs were initiated at IIT Kharagpur and IIT Hyderabad.

In view of the increasing danger of COVID-19 pandemic the WHO FCTC Global Knowledge Hub on Smokeless Tobacco at ICMR-NICPR issued an appeal for tobacco control and prohibiting public spitting, due to which MoHFW, GoI has issued an advisory to control tobacco and prohibit spitting in public places. ICMR-NICPR played a pivotal role in the establishment of Covid-19 testing laboratory at Leh.

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COMMUNICABLE DISEASES

Communicable and infectious diseases pose serious public health problems. ICMR's research efforts in the area of communicable diseases were made by 16 institutes/centres including Regional Medical Research Centres (RMRCs) and their field stations located in different parts of the country as well as by granting adhoc projects in extramural mode in universities/medical colleges and other organizations. The research activities carried out by different ICMR Institutes and their outcome for the year 2020-21 are detailed in this chapter.

INTRAMURAL RESEARCH

ICMR-NATIONAL INSTITUTE OF VIROLOGY, PUNE (ICMR-NIV)

SARS-COV-2

Optimization and supply of diagnostic real-time RT-PCR for screening of samples

To enhance the testing capacity of India, ICMR-NIV optimized/standardised real-time PCR assay targeting E, RdRp, ORF and RNasP genes shared by WHO for screening and confirmation of probable COVID-19 cases. It also acted as the central hub and distributed ~57 lakh real-time RT-PCR reactions alongwith required reagents (VTM, extraction kit etc) to 1200 Government laboratories as on 31st March 2021. The Institute also provided training to scientific and technical staff of COVID-19 testing laboratories and conducted QA/

QC at regular intervals. In addition, the following achievements were also made.

- ICMR-NIV, Pune, along with its peripheral units at Mumbai, Bengaluru and Kerala together screened 795,678 samples and detected 113,665 positives as on 31st March 2021.
- Indigenously developed and standardized a one-tube SARS-COV-2 assay and supplied to >1200 government labs in the country.
- Developed and standardized a one-tube combo kit for simultaneous testing of SARS-COV-2 and influenza viruses.
- An RT-LAMP assay for detection of SARS-COV-2 virus has been standardized.
- ICMR-NIV has achieved a major feat by qualifying the WHO-EQAS panel in 2020 and 2021 with 100% concordance. ICMR has established a three-tier system for quality control and evaluated performance of 108 laboratories.

Molecular epidemiological analysis of SARS-COV-2 virus circulating in different parts of India

Next-generation sequence analysis of 696 SARS-COV-2 genomic sequences procured from different parts of India during January to August 2020 revealed predominance of 'G' clade and its variants (GH and GR) (Fig 1). Mixed SARS-COV-2 clade variants (G-S, GR-GV, and GH-GR) and a unique

variant identified by amino acid changes in the ORF1ab region (B.4 variant) were also identified.

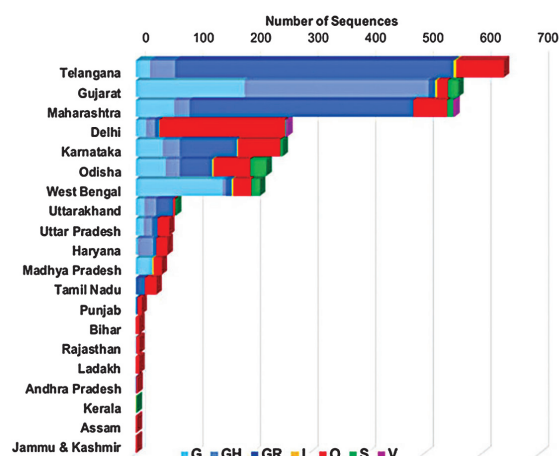


Fig. 1: State-wise distribution of SARS-CoV-2 sequences deposited from India to GISAID from January to September 2020. The colours denote the GISAID clades.

Isolation and characterization of new SARS-CoV-2 strains (Variant of Concern 202012/01 UK)

Whole-genome analysis of 942 (out of 2196) positive samples retrieved from international travellers identified 103 samples as UK variant (B.1.1.7), 05 as South African (B.1.351) and one as Brazilian variant (P2 lineage).

The UK variant was successfully isolated in cell culture in December 2020 (Fig 2) and studies in Syrian hamsters demonstrated significantly higher viral RNA shedding in comparison to the strain existing in India. South African (B.1.351) and Brazilian (B.1.1.28.2) were also isolated and characterized. Analysis of 44 gene sequences from Maharashtra showed amino acid mutations in the spike protein at positions G142D, E154K, L452R, E484Q, P681R, and Q1071H in 14 sequences.

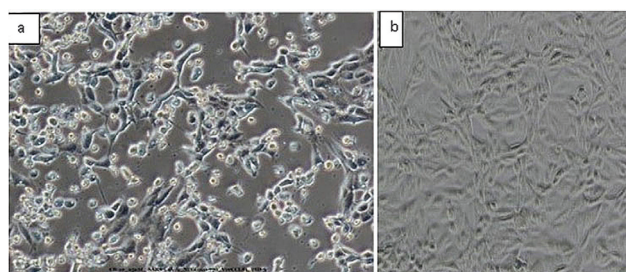


Fig. 2: Virus isolation (a) VERO CCL-81 cell line showing CPE (b) Negative cell control.

Bio-banking of SARS-CoV-2 samples and Development of Anti-SARS-CoV-2 IgG ELISA

ICMR-NIV indigenously developed an anti-SARS-CoV-2 human IgG ELISA (KAVACH) to study the sero-prevalence in humans. A bio-repository of >3000 sera samples (acute and convalescent) of patients with COVID-19 was established at ICMR-NIV. Well-characterized samples from the repository were used to prepare serum panel for validation of anti-SARS IgG ELISA. The assay showed 92.37% sensitivity, 97.9% specificity and was reproducible with positive and negative predictive values of 94.44% and 98.14%, respectively.

An attempt was also made to develop an ELISA using spike and nucleocapsid proteins to assess antibody response. SARS-CoV-2 nucleocapsid protein was cloned, expressed in a bacterial system and the purified protein was used as coating antigen to develop indirect ELISA. Further standardization is in progress.

Evaluation of susceptibility of mice (C57BL/6, Balb/c) and Syrian hamsters to SARS-CoV-2 virus

Syrian hamsters were found susceptible to the virus as virus replication was observed in the respiratory tract. Weight loss followed by induction of anti-SARS COV-2 antibodies was also observed in infected hamsters. However, both mouse species (adults) were found refractory to the virus.

Development of the inactivated SARS-CoV-2 vaccine "COVAXIN"

ICMR-NIV and Bharat Biotech International Pvt. Ltd (BBIL), Hyderabad jointly developed the first indigenous inactivated, whole-virion SARS-CoV-2 vaccine (COVAXIN). ICMR-NIV contributed in the following ways:

- Mass production of the virus in cell culture (VERO-CCL-81).
- Inactivation of the virus using β -propiolactone and confirmation of inactivation.

- (iii) Evaluation of immunogenicity and protective efficiency of vaccine candidates in Syrian hamster and rhesus monkey models (the vaccine candidate induced significant titers of SARS-COV-2 specific IgG and neutralizing antibody).
- (iv) Live virus challenge in vaccinated animal models. Study showed rapid virus clearance from the lower and upper respiratory tracts, absence of lung pathology and enhanced

humoral immune response. Study design and time line is given in Fig 3.

- (v) In human trials BBV152 vaccine candidate showed high immunogenicity and enhanced humoral and cell-mediated immune responses. In the Phase III field trial 81% efficacy was detected.
- (vi) Neutralization studies with heterologous strains: Serum collected from recipients of COVAXIN demonstrated neutralization of UK variant by PRNT.

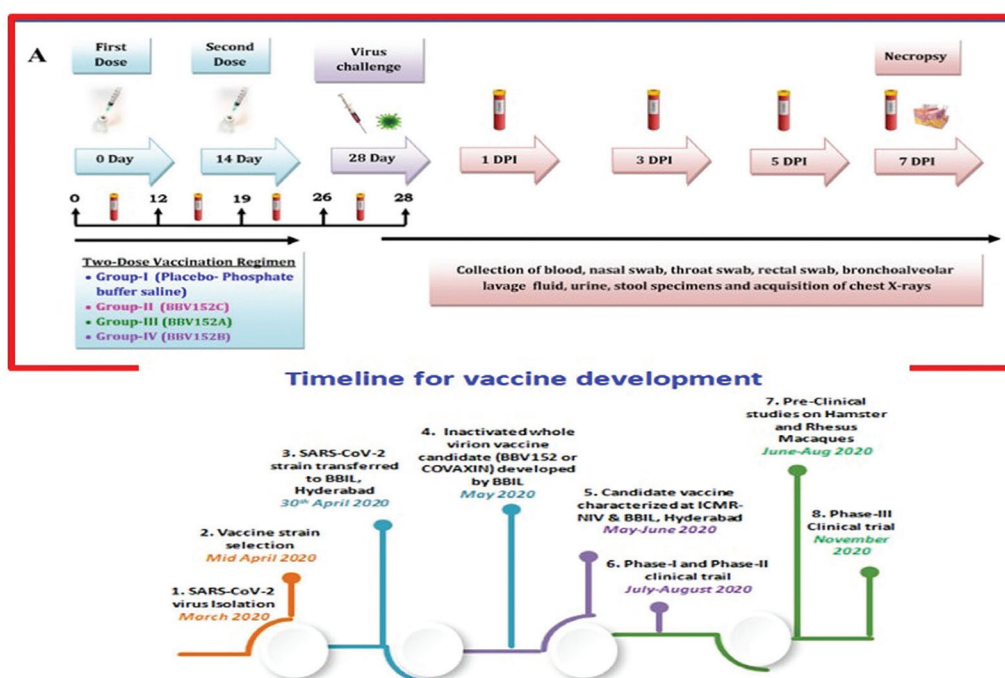


Fig. 3: Study design and time line for vaccine development and pre-clinical studies for India's indigenous SARS-COV-2 vaccine (COVAXIN).

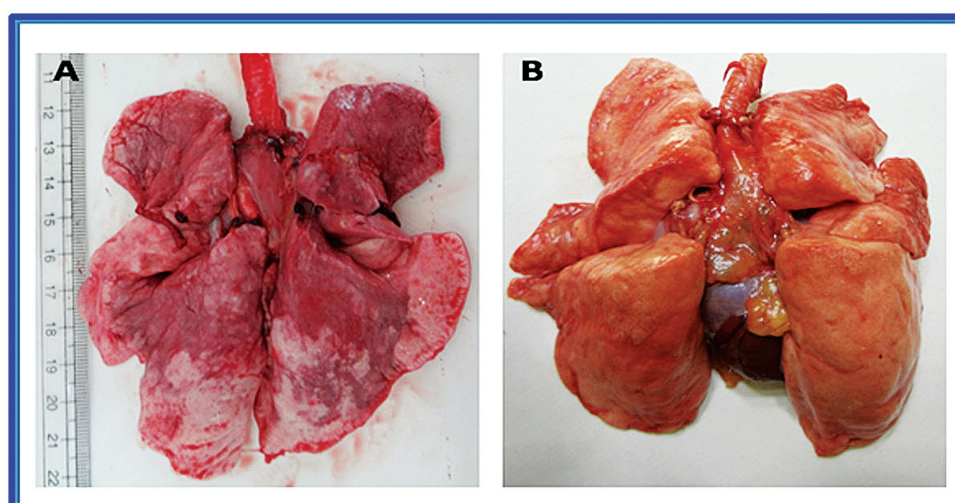


Fig. 4: Lungs showing gross pathology in lung tissues (A: infected, B: Normal lung).

Histopathology and Immunohistochemistry

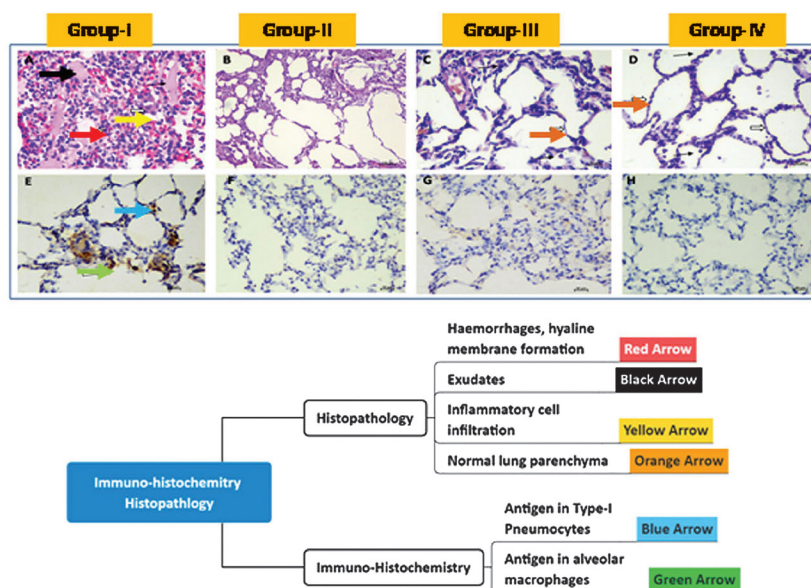


Fig. 5: Histopathology and Immunohistochemistry studies in lung tissues showing gross changes.

Evaluation of immunogenicity and protective Efficacy of ZyCOV-D DNA Vaccine

ICMR-NIV evaluated the immunogenicity and protective efficacy of a DNA vaccine candidate (ZyCOV-D) developed by Cadila Healthcare Ltd., in rhesus macaques. The vaccine candidate in a dose of 2mg administered through needle-free injection system elicited significant levels of SARS-COV-2 S1 spike region-specific IgG and neutralizing antibody. Protective response was demonstrated by viral load reduction in vaccinated animals in comparison to the placebo group.

Evaluation of SHPL RBD-VLP display COVID-19 vaccine

Immunogenicity and protective efficacy of six formulations of a VLP based vaccine candidate of SARS-COV-2 developed by Serum Institute of India were evaluated in the Syrian hamster model. Despite administering two doses, none of the combinations elicited significant neutralizing antibody titre.

Evaluation of Convalescent plasma therapy: (PLACID Trial)

ICMR-NIV participated in an open-label, parallel-arm, phase II, multicentric, randomized controlled human trial evaluating convalescent plasma therapy in COVID-19 patients. As part of the team, the Institute performed micro-neutralization assay and cytokine analysis (IL-6) of over 1500 sera and 800 plasma samples respectively. No therapeutic effect of the plasma therapy could be detected in COVID-19 patients.

Evaluation of therapeutic efficacy products in Syrian hamster model

- ICMR NIV has evaluated the therapeutic efficacy of SARS-COV-2 human antiserum immunoglobulin [Purified F(ab')₂ fragments] developed by Biological E Ltd., Hyderabad in Syrian hamsters. However, no protective efficacy could be detected.
- ICMR NIV also evaluated a COVID-19 equine antiserum developed by Serum Institute of India Pvt. Ltd., for its therapeutic effect in Syrian hamsters. Neither reduction in viral RNA load in target organs nor reduction in lung pathology could be detected.

Antiviral screening of potential repurposed/ novel drugs for SARS COV-2

- Antiviral assays based on plaque assay and TCID₅₀ assay demonstrated anti-SARS-COV-2 activity in 22 of 101 drugs/compounds screened.
- Using computational docking studies, the binding potential of natural compounds of marine origin against the main protease (3CLpro) of SARS-COV-2 was analyzed. Comparison of docking with the 3CLpro of SARS-COV-1 was also undertaken. Among the four phlorotannin compounds, *i.e.*, Triphlorethol A, Dieckol, Fucodiphloroethol G, and Phlorofucofuroeckol A, only Dieckol bound to SARS-COV-2 3CLpro with better site complementarity and binding affinity as compared to SARS-COV-1 3CLpro. However, bioavailability of phlorotannins and their conformational isomers is a concern.

Detection of SARS-COV-2 in faecal matter of positive patients

ICMR-NIV successfully designed a technique to detect SARS-COV-2 virus in sewage samples. SARS-COV-2 viral RNA was detected in 64 of 217 stool samples (29.5%) collected from COVID-19 patients in Pune by real-time RT-PCR and Next-generation sequencing.

Assessment of the role of host immune response in COVID-19 infection

High levels of pro-inflammatory cytokines *viz.*, CXCL-10, TNF- α , IL-1 β and IL-6 and lower levels of anti inflammatory cytokines could be put forward as biomarkers of recent SARS-COV-2 infection. Higher number of Th, Tc cells and lower numbers of NK cells correlate with resolving mild SARS-COV-2 infection. SARS-COV-2 specific T cell response in the recovered individuals at 48-60 days post recovery suggested protection from re infection.

Innate immune receptors in upper airway cells as biomarkers for COVID-19 have revealed increased MDA-5 and TLR-2 in asymptomatic positive cases

than symptomatic patients. Asymptomatic children suffering from primary immunodeficiency (PID) harboured SARS-COV-2 in the gastrointestinal tract for a prolonged period posing the risk of faeco-oral transmission. Co-infection of SARS-COV-2 with enterovirus, noroviruses and human adenoviruses was observed in asymptomatic PID patients.

Validation of products and techniques under the Atmanirbhar Bharat program

(i) Performance evaluation of Truenat TM BETA COV test on TruelabTM workstation

Three technologies by Molbio Diagnostics, India, *viz.*, Truenat Beta COV E-gene screening assay, Truenat SARS-COV-2 RdRp gene-confirmatory assay and a multiplex assay combining E-gene screening and Orfla-gene were validated for their sensitivity and specificity by ICMR-NIV.

(ii) Real-time RT-PCR kits, RNA extraction kits and VTMs

Evaluated 168 RT-PCR kits, 164 RNA extraction kits and 99 VTMs and swabs.

(iii) Serological test kit Validation (Rapid Antibody Test, ELISA & CLIA)

Validated 46 out of 225 commercial serodiagnostic kits (Rapid Antibody Test, ELISA & CLIA) and approved for commercial production.

(iv) Validation of commercial technologies for surface decontamination

Two of three commercial technologies based on ozone and negative ion generation for surface decontamination of SARS COV-2 from PPE were validated.

Establishment of a facility for production of SARS-COV-2 positive controls

SARS-COV-2, being a BSL-3 agent, ICMR-NIV has undertaken the task of production and supply of positive controls to government as well as private testing centres. During the year, live virus, as well as inactivated virus, was supplied to commercial

partners for vaccine development and IgG ELISA kit development. SARS-COV-2 antigen was also shared with a few institutes for research activities after procuring MoU.

ZOONOTIC VIRUSES

Development of Serodiagnostic assays for Nipah virus

ICMR-NIV has developed and standardized anti-NiV human IgM and IgG ELISA using indigenous technology using the virus isolated during the 2018 outbreak in Kerala. The assays had 90% and 93.9% sensitivity and specificity for IgM ELISA and 91% and 99.25% for IgG ELISA in comparison to CDC (USA) ELISAs. Similarly, anti-NiV bat IgG ELISA was also optimized with sensitivity and specificity of 100% and 83.3% respectively in comparison to CDC ELISA. External validation at two labs has shown 99.3% to 100% concordance.

Evaluation of an RT-LAMP for Rapid and Real-Time Detection of Kyasanur Forest Disease Virus (in collaboration with DRDE, Gwalior)

Evaluated a sensitive RT-LAMP assay for rapid, detection method for KFD virus.

Evaluation of double antibody sandwich ELISA for detection of Crimean-Congo hemorrhagic fever virus (in collaboration with DRDE, Gwalior)

A rapid and sensitive double antibody-based antigen capture ELISA with a detection limit of 1000 genome equivalents was evaluated. The assay was compared with a commercial kit employing γ -irradiated CCHFV, revealing 100% sensitivity and specificity.

OUTBREAK INVESTIGATIONS

Avian Influenza: Clinical samples from 155 poultry workers and cullers collected from outbreak areas were screened for H5N1 and H5N8 virus by real time RT-PCR, but none tested positive.

Investigations on AES outbreak in Andhra Pradesh: An idiopathic disease broke out in Eluru, Andhra Pradesh, involving people of all age groups with clinical symptoms *viz.*, headache, back pain, vomiting, dizziness, convulsions and other neurological symptoms. Though anti-IgM antibodies to dengue and chikungunya were detected, no viral agent that associated to the symptoms could be identified.

Influenza activity during COVID-19 Pandemic: Screening of 9068 referred clinical samples fulfilling SARI and ILI case definition had detected 67 cases of A(H3N2) and 06 cases of A(H1N1) pdm09. HA and NA gene sequencing of 13 A(H3N2) conducted showed clustering of Indian isolates (Fig 6). Sixteen isolates of Influenza A(H1N1) pdm09-12, two isolates each of Influenza B and Influenza A(H3N2) were found susceptible to Oseltamivir.

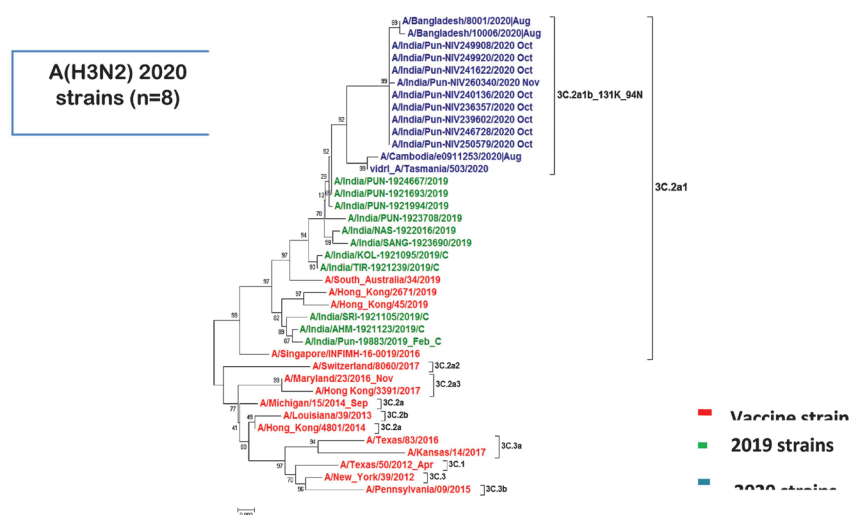


Fig. 6: Phylogenetic analysis of HA and NA genes of Influenza A (H3N2) virus.

EM STUDIES

In-vitro studies to examine the possible role of myristoylation of DENV2 NS1 protein (as predicted from *in-silico* studies) in the biology of the virus and on host-virus interactions was carried out. The effect of inhibition of cellular myristoylation with hydroxymyristic acid treatment showed reduction in DENV virus negative strand copy numbers. In addition, transfection studies using a deletion mutant of NS1 also showed significant difference in the cellular expression and localization profiles (Fig 7). At this phase of the study, team could establish the proof-of-principle that myristoylation of DENV NS1 may have an important role in both virus biology and host interaction events.

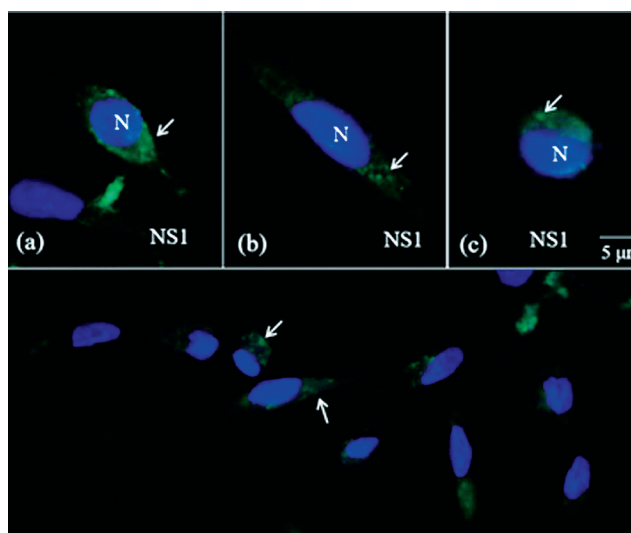


Fig. 7: Effect of inhibition of myristoylation on DENV replication. Representative IFA images of NS1 localization pattern in DENV2 infected SK Hep1 cells treated with 2-OHM. (a, c) Single cells showing perinuclear punctate NS1 expression in infected cells not treated with 2-OHM and probed with anti-NS1 monoclonal and anti-DENV polyclonal primary antibody, respectively. (b,e) Distribution of DENV2 antigens in infected cells treated with 2-OHM and labeled with anti-NS1 monoclonal and anti-DENV polyclonal antibody, respectively. (d) A wide-angle large field showing overall staining pattern in infected, untreated cells. (f) Uninfected control.

ARBOVIRUSES

Apex referral laboratory activity for Dengue and Chikungunya

During 2020-2021, 83 out of 400 samples referred from Maharashtra tested positive for dengue (31) and chikungunya (52). Serotyping of dengue

positive samples revealed of 23 DEN-1, 7 DENV-2 and 1 DENV-3 serotypes. Of the 40 samples referred from Goa, 17 tested positive for dengue (03 DENV-1, 10 DENV-2, and 04 DENV-3). Out of 56 samples from Patna, Bihar, 36 tested positive for dengue which constituted 35 DENV-1 and 01 DENV-2 serotypes.

Repurposing of drugs towards anti-Dengue and Chikungunya viruses using systems biology approach

Using “Multi-omics” data and bioinformatics techniques, identified 1585 signature genes of DENV and 18 CHIKV based on the transcriptome data. Based on inverse gene signature analysis of the transcriptome data using ‘CMap’, drug candidates, viz., staurosporine, vorinostat, wortmannin, doxorubicin and triptolide for DENV and Ibuprofen, tosyl-phenylalanyl-chloromethylketone and PKC beta-inhibitor for CHIKV were identified.

Japanese encephalitis epidemiology in Central India: enhanced sentinel surveillance for etiological contribution and burden following vaccination in Maharashtra and Telangana

AES-related hospitalizations in Maharashtra and Telangana together accounted for 8.4% (32/604) and 1.3% (50/372) in children and adults respectively. JE contributed to 9.3% among children and 8% in adults despite having JE child immunization coverage of 91.9% in Maharashtra and 94.3% in Telangana. Dengue (27) and HSV (11) were the other viral agents detected while Scrub typhus (4), leptospirosis (3) and typhoid (2) contributed to non-viral etiologies. However, investigation of 851 referred clinical specimens (CSF=418; sera=433) from 534 AES cases from different parts of the country revealed anti-JEV and anti-dengue IgM antibodies in 5% and 14% samples respectively. Samples from Maharashtra and Gujarat showed Chandipura virus activity in 0.7% cases.

Expression of Japanese encephalitis virus-genotype 1 envelope and non-structural proteins to explore in early diagnosis

To enhance the specificity of the existing JE MAC-ELISA kits, studies were initiated to replace the whole virus with purified envelope (E) protein. Evaluation of purified JEV GI envelope glycoprotein showed a correlation coefficient of 0.91 suggestive of better specificity.

Development of an indirect ELISA for surveillance of Japanese encephalitis

Evaluation of an indirect ELISA developed using recombinant JEV envelope glycoprotein to detect IgG antibodies in convalescent sera of JE patients found results at par with PRNT results and could be used as a surveillance tool.

Structure-based design and evaluation of lead compounds targeting Chikungunya virus nsP3 RNA binding site

In vitro antiviral studies revealed 14 compounds belonging to Benzothiazole and benzoxazole groups having inhibitory activity against chikungunya virus either as prophylactic or therapeutic potential. Molecular docking analysis of two benzothiazole derivatives showed effective binding affinity and significant interactions with CHIKV RNA dependent RNA polymerase enzyme while two benzoxazole derivatives showed significant interactions with CHIKV nsP2 protease.

Use of lipid nanoparticles for effective delivery of siRNA in Chikungunya virus

siRNA loaded in stearylamine based solid lipid nanoparticle (SLN) delivery system induced strong cationic charge on SLN that aided in highest complexation with siRNA in comparison to other delivery systems developed using different cationic lipids/ polymers. Stearylamine based SLN delivery system exerted strong inhibition against CHIKV in Vero cells and *in vivo* studies in infant mice.

Antiviral screening of natural products against dengue

Among the several natural products screened for anti-dengue activity, α -Mangostein, a xanthanoid

demonstrated anti-dengue activity under *in vitro* conditions. However, five commercial drugs containing papaya as an active ingredient *i.e.* Papayen, Tcyte, Platenza, Platex, and Reditus, were found to have no anti-dengue activity.

Antiviral activity of approved drugs and natural peptides against dengue and chikungunya

In vitro screening of 32 natural compounds (obtained from NITM, Belagavi) revealed seven compounds with anti-dengue virus activity and two with moderate anti-chikungunya activity.

Antiviral activity of Remdesivir and Galidesivir against Chandipura virus

In vitro (Vero cells) studies with Galidesivir, at 300 μ M concentration have shown 50% reduction in plaque size and plaque number. However, Remdesivir did not show any anti-CHPV effect.

Metagenomic analysis of viromes of Aedes mosquitoes in India

Two pools of *Ae. aegypti* mosquitoes comprising 50 male and 50 female mosquitoes were processed to standardize the cDNA preparation protocol. RNA was extracted from the mosquitoes using QIAAMP viral RNA mini kit. cDNA synthesis for the mosquito pools was carried out using random anchored primers. The cDNA library preparation using ligation Sequencing Kit (SQK-LSK109) from ONT is being optimized. A nanopore sequencer, MinION Mk1B (ONT, UK), was installed and a control lambda phage sequencing was carried out to evaluate the instrument.

Study of cross-neutralization of neonatal G12P[11] strain against convalescent-phase sera from children vaccinated with rotavirus vaccines

Neutralizing antibody (NAb) response to G1–G4, G9 and G12P[11] rotavirus types were studied among ROTAVAC® and ROTASIIL® vaccinated infants. A higher proportion of serum NAb against G1P[8], G3P[8], G4P[6] and G9P[8] were detected

in subjects receiving RotaSIIL. Both the vaccines failed to induce NABs against G12P[11].

Studies on measles and rubella

Surveillance of measles and rubella and strengthening laboratory capacity for confirmation of outbreaks as part of the National elimination program has been initiated.

Genetic and antigenic characterization of measles, mumps and rubella virus isolates

Complete genome sequencing of 15 MeV isolates obtained from Maharashtra, Uttarakhand, Odisha, Gujarat, Tamil Nadu and Union territory of Dadra and Nagar Haveli showed 12 as D8 and 3 as D4 genotypes.

Genetic and antigenic characterization of rubella virus isolates

Comparative analysis of Indian Rubella viruses (2B) with global isolates and vaccine strain RA 27/3 (1a) revealed that the observed mutations in structural proteins have no major impact on the 3D structure, function and antigenicity thereby substantiating the use of current vaccines.

Seroepidemiology, maternal immune status and missed diagnosis of pertussis among young infants in India - a multicentric study

A study of 284 infant-mother pairs showed protection against pertussis in infants is low in mothers immunized during childhood (12.63%) as compared to women who availed acellular pertussis vaccine during pregnancy (54.26%).

Preparatory steps for establishing diagnostics and research capabilities on rabies

A new laboratory for rabies virus studies was established in the Pashan Campus of ICMR-NIV. Staff was given pre-exposure rabies vaccination and sero-conversion was verified. Virus strain was procured from Central Research Institute, Kasauli and is in the process of adaptation to cell culture. Immunofluorescent antibody technique, hemi-

nested reverse transcriptase PCR and real-time RT-PCR were optimized for detection of nucleoprotein and large (polymerase) genes of rabies virus.

Establishment of Poliovirus Essential Facility at ICMR-NIV, Pune as per the global action plan-III (GAP-III)

This facility gratifies the need for safe storage and essential research activities as part of preparedness to tackle polio virus-related emergencies arising in post-eradication time. The global containment commission has awarded Certification of Participation for development of the PEF at ICMR-NIV, Pune. Cross-sectional serologic assessment of immunity to polioviruses post-tOPV-bOPV switch period, *In-vivo* potency evaluation for the hexavalent IPV vaccine formulation etc have been initiated.

MAC ELISA KITS

ICMR-NIV supplied 5886 MAC-ELISA kits comprising 3666 DEN, 1577 chikungunya and 213 JE for detection of IgM antibodies, to national laboratories under the NVBDCP and DHR-VRDLs.

Mobile application for immunization data in India (MAIDI) (BIRAC-DBT project)

Field testing of MAIDI was initiated with the involvement of eight ASHAs and four ANMs in Pune. Since November 2020, 448 children were vaccinated and the operational feasibility is being studied.

Health Technology Assessment Resource Centre/hub

Cost-analysis of diagnostic tests for COVID-19 at ICMR-NIV was conducted and estimated to be Rs 574/- and Rs 340/- for per unit of SARS-COV-2 real time RT-PCR and COVID-19 Kavach IgG ELISA respectively.

Launch of a database

A database of arboviral proteins reported from the Indian subcontinent has been launched as

‘ArVirInd’. A database to retrieve information of arboviral strains reported from Indian subcontinent has been launched. The unique database provides information on amino acid sequence, epitopes and functional sites of dengue, Chikungunya, Chandipura, West Nile and Japanese encephalitis viruses originating from India, Bhutan, Nepal, Bangladesh, Sri Lanka, Maldives and Pakistan. ArVirInd is available at www.arvirind.co.in.

ICMR-NATIONAL INSTITUTE FOR RESEARCH IN TUBERCULOSIS, CHENNAI (ICMR-NIRT)

CLINICAL RESEARCH

This diligent division had been the origin of many guidelines both nationally and internationally. Two landmark trials funded by ICMR that finished enrolment promptly despite the odds of COVID-19 pandemic were i) Effectiveness of BCG vaccine in SARS COV2, and ii) the Tuberculosis (TB) vaccine study. With shortening of TB treatment being a global priority, the clinic geared up to tread on these programmatic priorities for formulating newer regimens. In this regard, a pragmatic trial of Moxifloxacin containing 4- months’ ATT regimen would soon be evaluated under field conditions among drug sensitive TB for feasibility of translating it into TB programme. The TB lymphadenitis study (biopsy confirmed) had already shown favourable trends towards shortening of TB regimens.

ICMR-NIRT provided technical support for the COVID-19 vaccine trials in collaboration with Tamil Nadu Government that had ultimately expedited vaccine approval, saving many a lives. A Vaccine control room was established in NIRT premises under the guidance of ICMR to supervise as well as allay anxiety among health care professionals during the initial period of vaccine roll-out. The ongoing multi-national multi-centric studies like the STREAM study stage 2 in MDR-TB and the BEAT Study in pre-XDR and XDR-

TB continued their vigilant supervision using mobile units without a single day of treatment default, mitigating the effect of COVID-19 induced lockdown on TB care in ICMR-NIRT. The analysis of data from MET-RIF study using metformin as an adjuvant in TB therapy and HICON-R using high dose rifampicin are underway. Other studies from this department included airborne infection control, predictors of emergence of additional TB drug resistance and predictors of mortality among hospitalised COVID -19 patients.

BACTERIOLOGY

Being a Supranational reference laboratory for SAARC countries, actively supporting the National TB Elimination programme including EQA testing for DST for labs under the national TB programme, the bacteriology laboratory has been ably supporting clinical trials conducted at NIRT, and has developed the state of the art technology, to perform drug susceptibility testing for newer anti-TB drugs like Bedaquiline and Delamanid. The other major achievements had been validation of True-Nat kit for TB diagnosis, Multi-centric validation of indigenous kit ‘TB-Detect’ for the diagnosis of TB, preclinical trials for testing of newer molecules and compounds for anti-tubercular activity and Whole Genome Sequencing for potential mutations and detecting true relapses. Alternative novel diagnostic strategies had been conceptualised like the use of stool and urine for TB detection in children, Luciferase reported phage assay for drug resistance and exploring efflux pump inhibitors for drug resistance. The department has successfully completed the drug resistance surveillance during the present year.

BIOCHEMISTRY

Apart from providing fully automated systems supporting trials, the studies recently initiated in the department include 1) Evaluation and characterization of potential therapeutic leads from AYUSH system of medicine for adjuvant therapy

during ATT, ii) Point of care estimation of Vitamin D and C-Reactive Protein for TB screening in household contacts of active pulmonary TB patients in Chennai, India: A pilot study and development and iii) Characterization of a novel nano-peptide system for therapeutic application in residual lung injury caused by Pulmonary TB.

EDP & EPIDEMIOLOGY STATISTICS

The major projects under fray from this department were 1) Development of a quantitative tool to assess barriers and facilitators to completion of TB treatment ii) Application of multiple imputation approaches to the prevalence estimation in large scale tuberculosis prevalence surveys and iii) Use of Artificial Intelligence aided diagnosis of Pulmonary Tuberculosis among Indian population using chest X-ray images.

HEALTH ECONOMICS

Established recently as a regional hub of DHR for Health care cost evaluation, the departments' scientific work focussed on a diversity of ailments like TB, Hepatitis B and C and dengue. The other studies carried out were 1) The Evaluation of a Standardized Treatment Regimen of Anti-Tuberculosis Drugs for Patients with MDR-TB – Health Economics Component – India, 2) Social

network analysis as a tool to improve active case finding at community level in Chennai, south India 3) Measuring socio-economic risk-benefits and health related quality of life changes associated with tuberculosis disease disclosure in Tamil Nadu and 4) Exploring and understanding the psychosocial factors enabling drug resistant tuberculosis patients to achieve better treatment adherence and completion-A qualitative study in Bengaluru and Hyderabad.

HIV/AIDS

This department, internationally accredited for HIV load and CD4 cell count estimation, was involved in the following studies 1) National HIV Cohort Program – Cohorts of HIV Resistance and Progression in Indian Children and Adults (CoHRPICA), 2) Development and validation of a diagnostic kit for early detection of Human Papilloma Virus (HPV) infection in cervical cancer, 3) Impact of malnutrition on immune responses to tuberculosis in Indian children, 4) TB-induced alterations in neutrophil response during infection and treatment and 5) Identification of Biomarkers that can predict progression from Latent Tuberculosis Infection to Active Tuberculosis Disease. The department also hosted the COVID-19 testing centre in Chennai.



Fig. 8: Fully functional COVID-19 lab established in ICMR-NIRT.

ICER

Some of the flagship projects in ICER included 1) Probing into the clinical immunology of SARS – COV2 infection and Multisystem Inflammatory Syndrome in children and 2) Evaluating the role of neutralizing antibodies and inflammatory biomarkers in children in the same syndrome. The ICER department had also undertaken extensive research in evaluating the influence of parasitic infections on Latent TB and also provided sensitive markers for detecting presence of higher bacterial burden and inflammation among diabetics with TB disease. The other important studies that had been conducted were 1) a cross-sectional study to estimate the influence of malnutrition, diabetes mellitus and helminth infections on bio-signatures in latent tuberculosis in a South Indian population, 2) A pilot study of the effects of helminth infection and SARS-COV-2 Sero-positivity on immune response and the intestinal microbiota in India, 3) Regional Prospective Observational Research in Tuberculosis (RePORT)- Phase and 4) characterization of immune responses in tuberculous lymphadenitis.

EPIDEMIOLOGY

The National survey for state-wise prevalence of microbiologically confirmed pulmonary tuberculosis in India that commenced from September 2019, had expanded to involve all the

20 state groups in March 2020. After an initial hold up due to COVID-19 pandemic, the survey had covered over 250,000 as on date. The IGRA Lab was established at Tiruvallur sub-centre, with 2 automated DYNEX machines as part of the survey. The district wise prevalence survey was inaugurated on 24th February 2021 by Dr. Radhakrishnan, IAS, Principal Secretary (Health and Family Welfare Department), and Government of Tamil Nadu in Chennai (Fig. 9).

IMMUNOLOGY

The division of immunology contributed towards prevention of COVID-19 disease by evaluating the characterization and durability of COVID-19 vaccine induced immune responses in healthcare/ frontline workers and looking into humoral and cellular immune response among recovered COVID-19 patients. Similar studies of importance included 1) Systems biology and immunology of the effect of tuberculosis chemoprophylaxis in HIV infection, 2) Identification of *Mycobacterium tuberculosis* complex (MTBC) organisms in the lymph node samples of slaughtered cattle in Chennai, 3) Genomic adaptation of *M. Tuberculosis* in cattle and 4) Immunomodulation of Autophagy by Vitamin D3 in macrophages Infected with *Mycobacterium tuberculosis*. The ARREST –TB project (Accurate, Rapid, and Robust & Economical Diagnostic Technologies for Tuberculosis) had been an international collaboration of significance incorporating a multidisciplinary approach.



Fig. 9: Tamil Nadu State TB Prevalence Survey Inauguration on 24th February 2021.

PHARMACOLOGY

To resolve the Abilene paradox of dosing in FDCs, the department conducted a crucial study to evaluate the bioavailability of first line anti-TB drugs in patients with pulmonary tuberculosis in both adult and paediatric age group, crucial for dose modifications wherever appropriate.

BIOSTATISTICS

The department recently initiated a study on “Latent class analysis of Health Related Quality of Life of TB patients during and post treatment in a Longitudinal Design” funded by ICMR. The department supports all the clinical trials of the institute in data management and the conduct of the trial. This department had started development of a database for converting Hard copy X-rays into DICOM images as part of Electronic Data capture system and archiving, providing a complete digital solution, with integration of trial data.

SOCIAL & BEHAVIOURAL RESEARCH

A selective glimpse of the projects undertaken by the department include 1) Patients’ Perception of Quality of Care in Tuberculosis Care settings in Chennai, 2) Utilization of School Students as Ambassadors in TB sensitization in Chennai

city, 3) Mental Health and Social Stigma among Healthcare Personnel Involved in the Management of COVID-19 Patients in India, 4) Factors Related To COVID-19 Stigma: A Mixed-Methods Study, 5) Study on Knowledge, Attitude, Practice towards Tuberculosis (TB) and Feasibility of TB Screening among Public and Private Drivers and Conductors in Tamil Nadu and 6) Health Systems Strengthening - Feasibility and effectiveness of Aadhar linked Electronic Medical Record (NIKSHAY) to minimize lost to follow-up and to promote treatment adherence.

PUBLIC HEALTH

- In collaboration with various ICMR institutes like NIE and state TB cells, repeat cross sectional surveys for SARS COV-2, were conducted nationally from May 11 – Jun 4, 2020, Aug 17 – Sep 22, 2020 and Dec 17, 2020 – Jan 8, 2021, which showed a sero prevalence of 0.73% (0.34-1.13), 7.1% (6.2-8.2) and 14.3% (13.5-15.1) respectively, with the sero-prevalence among health care workers being 25.7% (23.6-27.8) during the period of Dec 17, 2020 to Jan 8, 2021.
- NIRT, through its meticulously executed study using a 4 month Moxifloxacin containing



Fig. 10: SARS COV-2 Sero-surveillance study – Field photographs.

regimen, showed a 4% recurrence rate at 24 months follow up period. This was currently taken to the field, headed by Director, for its final lap of confirmation in a pragmatic way. If proved useful, this would substantially bring down cost and attrition rates for the TB programme to achieve its vision.

- The clinical division and ICER studied the effectiveness of BCG Vaccine in reducing morbidity and mortality in elderly Individuals in COVID-19 Hotspots in India.
- The High dose rifampicin study has shown promising results at phase II B levels, in concordance with other global studies that a higher dose of rifampicin is indeed a promising candidate to be used in future trials for shortening TB treatment.
- The STREAM study, aimed at shortening MDR-TB treatment, has the translational application of not only shortening MDR-TB treatment to 9 months, but has the dual advantage of offering a safe oral regimen to be used in this group, accelerating decentralisation to the masses. That all trials continued to run unabated in NIRT despite the lockdowns, was a big achievement in itself.
- Whole genome sequencing platform established deeper insights into mutated genes and their correlation with acquisition of drug resistance.
- The bacteriology department has started extension of True NAT technology to other ATT drugs including fluoroquinolones and BDQ and concentrated on estimation and establishment of critical concentration (CC) of Rifampicin, moxifloxacin, ethambutol and PAS.
- A Health Technology Assessment (HTA) of decentralized diagnostic program for Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) implemented in Tamil Nadu, found early diagnosis and treatment for HBV and HCV including vaccination for HBV negatives could save lives and reduce out-of-pocket expenditures.
- The health economics department had established an effective partnership with the state government of Tamil Nadu for conducting Health technology assessment studies in priority areas.
- The statistical division attempted to quantify growth rate of COVID-19 pandemic and assess the effect of controlling measures taken, using the data of the first 41 days of the outbreak started on March 7, 2020.
- HIV department, hosting the largest TB Biorepository in the country, extended its services to establish an ICMR approved COVID-19 testing lab and Central Depot for COVID-19 test kits and reagents. It is already a Regional Reference Laboratory for NACO for HIV-1 Viral Load Testing and HIV-1 DNA PCR and had been accredited by WHO as a Regional Reference Lab for *HIV-1* drug resistance genotyping.
- NIRT extended its work to include zoonotic TB as well; findings of *M. Tuberculosis* strain rather than *M. Bovis* affecting cattle was a definite public health concern in this region.
- Therapeutic drug monitoring, in ruling out malabsorption and cryptic non adherence, had been performed for patients referred from various hospitals, for suboptimal response to TB therapy. Standardisation of procedures for pharmacokinetic evaluation of newer drugs like BDQ and LZD had been initiated.
- The department of pharmacology performing drug level estimation using HPLC was one of the unique institutes in India, validating most of the anti-TB and anti-retroviral drugs in various biological fluids and had been part of the International Quality Assurance Program, Netherlands – (Proficiency Testing).
- EDP department developed “Household contact card and register” for screening

Household contacts of PTB patients. Digital display boards were erected in prominent places around the premise that gather crowd, to spread awareness to patients, attenders and general public.

- The immunological studies conducted in the department of Immunology and ICER had been helpful in confirming lineages in extra-pulmonary TB and the cytokines associated with lymphadenitis. The immunological cascade in TB and diabetes mellitus had been unravelled and more importantly, found to be reversible with ATT.
- Important immunological leads had been found in this institute that predisposed to poorer outcome and adverse reactions to TB treatment. These inputs would be further explored in due course, for translating them from “bench to bedside” to be utilised in patient care.
- In the social and behavioural context, the study tool on “Patients’ Perception of Quality of Care in TB care settings” was found to be feasible, ethical, useful, and appropriate in assessing the quality of TB care settings, enabling a more patient-centred approach.
- Incorporating younger generation in TB control, the research among school children as ambassadors against TB suggested that school children could be empowered to be torch-bearers in fighting against tuberculosis.
- On 24th March 2021, on the eve of World TB Day, NIRT disseminated the findings of the project - “Towards a TB Free Chennai initiative: an innovative Intersectoral partnership” (Fig. 11) project jointly implemented by ICMR-NIRT, Greater Chennai Corporation and REACH, an NGO funded by STOPTB Partnership/ UNOPS/USAID. The intended objective of the workshop was to broadly discuss the impact of TB-Free Chennai initiatives and its replication and scale-up other parts of the state and the country. The dissemination meeting also helped to better understand the limitations and gaps during implementation of the project

and the way forward to come up with similar initiatives to achieve the TB elimination goals.



Fig. 11: Workshop on “Towards a TB Free Chennai initiative: an innovative inter-sectoral partnership”.

ICMR-NATIONAL JALMA INSTITUTE FOR LEPROSY & OTHER MYCOBACTERIAL DISEASES, AGRA (ICMR-NJIL&OMD)

Studying the role of chemokines and chemokine receptors in the *Mycobacterium tuberculosis* induced angiogenesis in granuloma and role of solTNF in granuloma formation

Investigated the effect of angiogenic factors inhibition on mycobacterial survival in guinea pig model of tuberculosis and identified angiogenic factors which might be useful as biomarkers to monitor dissemination of tuberculosis, disease severity and bacterial burden. Studied the Development of combination therapy to regulate the dissemination of tuberculosis infection in guinea pigs.

Proteomic profiling of exosomes for the identification of potential biomarkers for tuberculosis in HIV patients

Investigated the proteomic content of serum derived exosomes of HIV patients with and without tuberculosis co-infection and identify significantly altered proteins which need to be included as target

in further validation studies to identify potential biomarker(s) for the development of newer diagnostic tests for early diagnosis of tuberculosis in HIV positive patients.

Established COVID-19 Diagnostic Laboratory

Approved for CB-NAAT and Real-Time PCR based diagnosis of Novel Coronavirus (2019-nCoV) infection. The testing capacity of the laboratory is about 1100 samples per day. During the period 2020-2021, a total of 1,74,806 samples were tested for SARS-COV-2 infection at newly established COVID-19 laboratory of the Institute. The COVID-19 laboratory has 100% concordance in the results of Quality control samples tested for the presence of SARS-COV-2 at the reference laboratories (NIV Pune and KGMU, Lucknow).

Multicentric trial to study the effect of early active mobilizations as compared two three weeks immobilization following tendon transfer procedures for claw hand

A total of 75 participants were recruited in the study. The duration between surgery and discharge was on the average 12 days shorter in the early mobilization group. The scores were comparable between the two arms at each follow-up time. The angles of deficit and the reductions in deficit were more in the Delayed arm, some of them being statistically significant. The proportion of cases with claw hand correction (all 4 fingers with 0° deficit) were statistically not different between the 2 arms. However, the non-inferiority of the early mobilization could not be established with 5% non-inferiority margin.

Analysis was focused on angles of deficit in unassisted open hand as they are directly relevant to the objectives. Almost all patients had zero deficit for all four fingers before surgery in unassisted & assisted closed fist. In view of this, the need and additional advantage of analysis on angles of deficit in assisted open hand, unassisted & assisted closed fist to be decided.

Novel static-progressive splint design for ulnar claw hand for pre-operative domiciliary mobilization – a pilot study

Specification planning, prototype design, final splints have been fabricated. The pilot trial has been registered prospectively with CTRI.

HIV/AIDS Unit, Integrated Counseling & Testing Centre (ICTC)

HIV testing and counselling is provided to all Clients, who come either voluntarily or referred from different Hospitals, and NGOs, Agra. Pre- and Post-Test Counselling is provided to each individual undergoing HIV testing after obtaining informed consent.

Characterization of drug resistant HIV-1 mutants of Agra region, India by genomic and proteomic approaches

A cohort study was focused on the first line ART patients who were recruited from the period of December 2009 to November 2016 at the ART centre, Sarojini Naidu Medical College, Agra, India. A total of 211 patients were selected based on CD4 counts <350 cubic/mm. Viral load was completed with all 211 patients' sample. The patients who were on first line anti-retroviral therapy (ART) with a falling CD4 count less than the CD4 count (<350) at baseline before the start of ART or CD4 count less than 50% of the highest CD4 count during the therapy for >1-2 Years, >3-4 years, >5-6 years and had a viral load >1000 RNA copies/mL were included in this period for genotypic assay.

The genotypic assay was formed with WHO dried blood spot protocol 2010 and the drug resistance mutations were analyzed by Stanford HIV drug resistance data base, USA. The NRTI mutation M184V and NNRTI mutation K103N was observed in highest frequency in >1-2 Years, >3-4 years, >5-6 years of patients. The proteomics approaches like MALDI-TOF/TOF and SWATH-MS was applied in the fourteen high viral load (treatment failure) plasma samples. A

total of eight significant differentially expressed proteins such as serotransferrin, Apolipoprotein-AI, complementC4-A, Immunoglobulin heavy variable 1-2, Carboxylic ester hydrolase, Fibulin-1, Immunoglobulin lambda constant 7, Secreted phosphoprotein 24 were identified and characterized in these high viral loads considered as drug resistant or treatment failure patients.

Drug resistance mutation M184V (ATG to GTA) (63.15%) associated with lamivudine and abacavir and K103N (AAG or AAA to AAU) (36.84%) associated with efavirenz and nevirapine were predominantly identified in first-line ART failure patients. During follow-up, it was observed that 3 out of 21 who were in second-line ART died, whereas 9 out of 36 died who were in the firstline ART. No mutation could be associated with mortality although TAM-2 mutations were absent in patients who died.

Development of mice models for amyloidosis: A rare disease

Institute has started to standardise ELISA and Congo red staining protocols for detection of Serum Amyloid A in serum and amyloid fibrils in different organs of MTB infected mice. The plasma SAA concentration was significantly higher (40µg/ml) in *Mycobacterium tuberculosis* (H37Rv) infected group as compared to naïve mice group (20µg/ml). Detection of amyloid deposition by Congo red staining in different organs is going on.

Study of TCR (T cell receptor) mediated T cell signalling events in systemic circulation and at the site of infection in TB pleurisy patients

Since there is no study of T cell activation mechanism of *M. tuberculosis* infection in any relevant physiological model. The team studied proximal and distal events of T cell signalling regulating IFN- γ and IL-2 production in blood and pleural fluid of same TB pleurisy patients in response to *M. tb* antigens (ESAT-6 and Ag85A). The study observed upregulated activation of Protein kinase C (PKC), Signal transducer and

activator of Transcription molecules 4 (STAT-4) and cAMP-response element binding protein (CREB) in *M. tuberculosis* antigens (ESAT-6 and Ag85A) stimulated cells in local disease site (pleural fluid) as compared to peripheral blood samples of TB pleurisy patients. Altered binding affinity of NFAT and NF κ B the transcription factors responsible for IFN- γ and IL-2 production was also observed in blood and pleural fluid of TB pleurisy patients.

In concordance of the above results, team observed significantly higher percentage of IFN- γ and IL-2 producing CD3+T cells in pleural fluid as compared to blood in TB pleurisy patients but not in matching disease controls/non-TB pleurisy patients. Altogether our result showed that the increased cytokine IFN- γ and IL-2 at local disease site is a result of up regulated TCR mediated activation mechanism at local disease site as compared to systemic circulation in TB pleurisy patients. This study would delineate the molecular mechanisms of T cell activation, to better understand interactions between *M. tuberculosis* and human immune system, and to facilitate development of better vaccine.

Characterization and clinical relevance of hypothetical proteins of aminoglycosides resistant isolates of *Mycobacterium tuberculosis*

Aminoglycosides are broad spectrum antibiotics and are an important component of any antituberculosis therapy regimen especially for category II patients. Kanamycin, amikacin and streptomycin are the key aminoglycosides against tuberculosis and resistance to them severely limits the options for treatment. The earlier findings revealed that hypothetical proteins were overexpressed in the cytosol and membrane of amikacin & kanamycin resistant *Mycobacterium tuberculosis* isolates. As cell wall is the outermost structure of *M. tuberculosis* and resists the diverse stress factors, it is important to identify these entities using two-dimensional gel electrophoresis and mass spectrometry approaches.

Amikacin & kanamycin resistant and susceptible *M. tuberculosis* isolates were grown and cell wall

proteins were extracted using detergent. With SDS-PAGE, the difference in protein profile was not significant however, on comparing two-dimensional gel profile by PDQuest Advanced software, thirteen cell wall proteins spots were found to be upregulated in resistant as compared to sensitive isolates. Identification of these proteins will be carried out by mass spectrometry.

ICMR-NATIONAL INSTITUTE OF CHOLERA AND ENTERIC DISEASES, KOLKATA (ICMR-NICED)

COMMUNITY / HOSPITAL BASED STUDIES

A Multicentre, Phase III, Double-Blind, Randomized, Placebo-Controlled Study to Evaluate the Efficacy of Recombinant BCG VPM 1002 In Reducing Infection Incidence and Disease Severity of SARS-COV-2/ COVID-19 Among High-Risk Subjects

This multi-centre study was conducted to evaluate the reduction in infection incidence and severity of COVID-19 infection among high-risk subjects by enhanced trained immune response through VPM1002 vaccine (recombinant *Mycobacterium bovis* BCGΔureC::Hly+).

An Event-Driven, Phase3, Randomized, Double-blind, Placebo-controlled, Multicentre Study to Evaluate the Efficacy, Safety, Immunogenicity, and Lot-to-Lot consistency of BBV152, a Whole-virion Inactivated SARS-COV-2 Vaccine in Adults ≥18 Years of Age

This is an ongoing multi-centric Phase III efficacy study, where 25,800 participants were enrolled in 1:1 ratio to evaluate the protective efficacy, immunogenicity, and safety of BBV152 - an indigenous whole virion inactivated COVID-19 vaccine developed by Bharat Biotech in partnership with ICMR and NIV.

SaniPath Typhoid - Assessment of Typhoid Exposure Pathways in Low-Income Urban Settings



Fig. 12: Field activities under SaniPath typhoid project.

The study was designed to address the causal pathways of Typhoid in low-income urban area in Kolkata where there is inadequate water and sanitation systems and young children are at risk of Typhoid fever. The major components of the research were Environmental Exposure Assessment through behavior study and Environmental Surveillance comprising of Moore swabs and Pooled latrine triggered samples.

Evaluation of Prescription Patterns of Drugs for Diarrhoeal Diseases and Acute Respiratory Infection in Medicine and Pediatrics OPDs of Tertiary Care Hospitals in West Bengal, India

The study revealed inappropriate prescription practices such as polypharmacy, brand names, FDC and overuse of antibiotics with non-adherence to standard guidelines related to Diarrhoea and ARI.

Evaluation of a Typhoid Conjugate Vaccine (TCV) Introduction Program - Navi Mumbai, India

This multi-component project comprises of hospital based prospective hybrid surveillance, supplemented by a continuous community assessment. Vaccine effectiveness is assessed through community based case-control method. Vaccine coverage, safety evaluation and economic

evaluations are also conducted in this study. The aim is to highlight disease burden, inform prevention and control interventions, and generate baseline evidence for policy translation.

LABORATORY BASED (BACTERIOLOGICAL) STUDIES

Estimation of *Vibrio cholerae* O1 infection in India: a step towards identification of cholera hotspot

This ongoing ICMR Task Force study is a sero-epidemiology study along with triangulation of data on cholera from available multiple sources. Vibriocidal assays on ~8000 sera samples have been completed so far.

The role of a single base mutation in *carR* in the emergence of polymyxin B sensitive *Vibrio cholerae* O1 El Tor biotype

Vibrio cholerae O1 classical biotype is polymyxin B (PB) sensitive and El Tor is resistant. The G265A mutation in *carR* is responsible for the emergence of PB-sensitive El Tor strains. This change in sensitivity is a major event in the history of cholera after 1961.

OXA-181-like carbapenemases in *Klebsiella pneumoniae* from septicemic neonates: co-existence with NDM-5, transmissibility, and genome diversity

Klebsiella pneumoniae possessing OXA-181-like carbapenemases (*bla*_{OXA-181} and *bla*_{OXA-232}) belonged to diverse sequence types (ST14, ST15, ST23, ST48, and ST231). *bla*_{OXA-181/OXA-232} & *bla*_{NDM-5} was found in a high-risk clone ST14. This study shows coexistence of *bla*_{OXA-181/232} and *bla*_{NDM-5} in isolates from neonatal sepsis.

Development and evaluation of a heat killed multi-serotype oral *Shigella* vaccine

A newly developed hexavalent heat killed oral *Shigella* immunogen (HKMS) was evaluated in rabbit, guinea-pig and mice models. Oral

immunization induced humoral, cell mediated and mucosal immune responses. Challenge studies revealed that HKMS immunization caused protection from lethal *Shigella* challenge in animal models. HKMS showed no reactogenicity in animal models.

Therapeutic intervention of *Shigella flexneri* host pathogen interaction by a herbal compound

Capsaicin (Caps), a herbal compound to intervene *S. flexneri* proliferation has been studied. Exploiting host autophagy machinery by Caps appears to be a promising therapeutic strategy in combating *S. flexneri* infection.

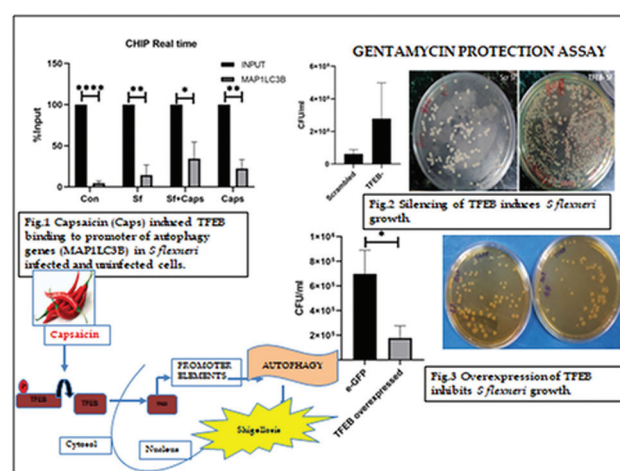


Fig. 13: Caps induced TFEB binding to promoter of autophagy genes and Silencing of TFEB inducing *S. flexneri* growth.

HIV/AIDS

ICMR-NICED being the Regional Institute of NACO for eastern and north eastern regions carried out several programmatic activities, service delivery and research studies on HIV/AIDS. The major efforts include HIV Sentinel Surveillance (HSS) among antenatal clinic attendees, high risk groups, bridge populations and prison inmates in the East and North Eastern states; (b) part of the Consortium of NRLs for Kit Quality for evaluation of diagnostic kits for transfusion transmitted infections; (c) Early Infant Diagnosis (EID) for molecular diagnosis of HIV among babies (up to 18 months) born to HIV infected mothers; (d) HIV viral load estimation for those under ART; (e)

external quality assessment of HIV testing; and (f) HIV counseling and testing services.(g) Support to PPTCT Program.

A facility based cross sectional study on status of nutrition, immunization and chemoprophylaxis in Children Living with HIV/ AIDS (CLHIV) aged 1- 14 years in a tertiary hospital, Kolkata, India

This study aims to generate evidence on nutritional, immunization and chemoprophylaxis status and adherence gap, if any, in reference to national guidelines for HIV infected children for further policy direction.

STUDIES ON OTHER VIRAL DISEASES

Comprehensive analysis of genomic diversity of SARS-COV-2 in different geographic regions of India

Sequence analysis of 837 SARS-COV-2 genomes revealed the occurrence of 33 different mutations, 18 being novel to India. Indian SARS-COV-2 isolates were classified into 22 groups based on co-existing mutations. Phylogenetic analysis revealed that the A2a clade was dominant in India (71.34%), followed by A3 (23.29%) and B (5.36%).

Developing a commercially viable multiplex-RT-PCR kit for diagnosis of viral gastroenteritis

An in-house, conventional, multiplex reverse-transcription PCR was developed for screening of major enteric viruses namely Group-A Human Rotavirus (GARV), Human Adenovirus species F serotype 40/41 (HAdVF), Astrovirus (AstV) and Norovirus Genogroup I and II (NoV GI/GII). The assay revealed >90% sensitivity and >95% specificity compared to the CE-IVD approved real time RT-PCR kit.

Studies on HCV drugs resistance in HCV infected patients in Eastern part of India

Direct acting antivirals (DAAs) are currently in use for HCV treatment. But the major obstacle for DAAs treatment is to develop HCV drug resistance

variant like other RNA virus. Comparative analysis indicated that HCV drug resistance was more common within genotype 3 than genotype 1 in eastern part of India.

Circulating Dengue Serotypes in 2020 in West Bengal

As a NBVDCP Apex Referral Laboratory, ICMR-NICED received 446 dengue NS1 sero-positive but COV-19 negative samples from Kolkata and its suburbs. Co-circulation of all four serotypes was observed, among them 47% were DENV4, followed by 34% DENV2, 12% DENV3 and 7% DENV1.

Virus Research and Diagnostic Laboratory (VRDL)

Apart from the diagnosis and research on common viruses and agents of public health importance, this is the first lab in eastern India to start routine testing of SARS-COV-2. Later, it also became the referral centre in the State for final confirmation of COVID-19 cases. This is an ICMR designated facility responsible for training, quality control, kit validation, and research on COVID-19 (Table 1).

Table. 1. The summary of the major findings of VRDL are presented in this table.

Investigations Performed	Total No. of Samples Tested in 2020-21	Positive Samples	Isolation Rate (%)
SARS-COV-2	215976	22834	10.57
Hepatitis A IgM ELISA	42	12	28.57
Hepatitis E IgM ELISA	36	3	8.33
Hepatitis B Surface Ag ELISA	25	1	4
Hepatitis C Ab ELISA	24	1	4
Scrub typhus IgM ELISA	50	12	24
Leptospira IgM ELISA	33	8	24.24
Respiratory RSV-A PCR	68	10	14.70
Respiratory hmpV-A1A2 PCR	68	1	1.47
Respiratory Adenovirus PCR	68	1	1.47
Respiratory Rhinovirus PCR	68	5	7.35

COVID-19 Biorepository at ICMR-NICED

This is a part of the network of ICMR biorepositories for COVID-19 across India with a mandate for collecting, storing, and maintaining clinical samples of COVID-19 cases. Such samples will be used to develop validated diagnostics, therapeutics, vaccines etc. Additionally, the samples will be a valuable resource for further research and development activities.

STUDIES ON PARASITIC DISEASES

State wise prevalence mapping of soil transmitted helminthes in Indian children to support health impact evaluation

The post-deworming follow up survey in Tripura and Chhattisgarh revealed that both STH incidence and intensity have drastically reduced as compared to the baseline prevalence among school going children; thus, the initiative has been highly successful.

Characterization of the Pathogenic Factors of Local Isolates of *Giardia lamblia*

The cathepsin B family of genes in *Giardia* are known virulence factors involved in processes like encystation and excystation. We noted that upregulation of a cathepsin cysteine protease gene occurred when the trophozoites entered the death phase; this was unique as upregulation occurred for other members of the cathepsin family mainly during encystation/excystation.

CAPACITY BUILDING

During 2020-21, 43 Ph.D. students were trained at ICMR-NICED and 3 students were awarded Ph.D. degree. During this period, 24 post graduate students were enrolled for summer internship.

Five hundred twelve participants including physicians and health care workers were trained through several workshops and training programs.

Five hands-on training workshops on laboratory detection of SARS-COV-2 by RT-PCR were

organized for healthcare professionals. Thirteen participants were from 5 different institutions.

Fifty two participants were trained on Biosafety and Biosecurity issues.

PUBLIC HEALTH

- Developed Loop Mediated Isothermal Amplification (LAMP) based assay to detect *Vibrio cholerae* O1 directly from diarrhoeal stool specimens.
- OXA-48-like carbapenemase - producing *Klebsiella pneumoniae* belonging to diverse sequence types were identified from neonatal septicemic cases. This study has reported the coexistence of *bla*_{OXA-181/232} and *bla*_{NDM-5} in isolates from neonatal sepsis challenging the treatment of these cases.
- Developed a non-typhoidal salmonella (NTS) OMVs based vaccine candidate and a natural NTS gastroenteritis model. NTS OMVs immunization induced adaptive immune responses in adult mice, T and B cell immune responses and found to be protective against experimental NTS infection in laboratory animal.
- Established the interchangeability between currently available rotavirus vaccines through randomized trial, which will enable rolling of rotavirus vaccination in India to a large extent.
- Reported the first case of pulmonary Paragonimiasis from West Bengal as well as newer species of sweet water crab for the first time identified.
- Post deworming follow up study revealed STH incidence and intensity were drastically reduced in the states of Tripura and Chhattisgarh suggesting that the deworming initiative was highly successful.
- New species of *E. moshkovskii* specific for India has been identified by high resolution sequencing. Almost half of positive samples had sole infection with *E. moshkovskii*.

- Identified two completely new *Cryptosporidium* species from human patients viz. *C. viatorum*, *C. rynae*. Isolates of *C. rynae* appeared to be highly zoonotic as the same species was identified from humans, cattle and environmental samples.
- ICMR-NICED Parasitology Lab received accreditation from NABL; this is the first NABL accredited lab in India for PCR identification of different enteric parasites.
- Development and validation of multiplex RT-PCR assay for rapid detection of enteric viruses.
- Whole genome sequencing (WGS) of SARS-COV-2 virus from clinical samples has been carried out in collaboration with NIBMG, Kalyani.
- Validation of various types of Make in India RNA isolation and real-time PCR kits for detection of SARS-COV-2.
- Explored the role of DDR pathway in RV infection. Chemical inhibitors targeting DDR components have anti rotaviral potential.
- HCV drug resistant strains against direct acting antivirals have evolved in Eastern India, specially within HCV genotype 3, the major circulating genotype in India.
- The COVID-19 testing facility at ICMR-NICED is a 24x7 working lab that tested more than 2.15 lakh samples from the hospitals and other health facilities of Kolkata and different districts of West Bengal. The automated and robotic PCR machine COBAS8800 further augmented the testing capacity. The institute has acted as depot for supplying kits to the North Eastern States.

ICMR-NATIONAL INSTITUTE OF MALARIA RESEARCH, NEW DELHI (ICMR-NIMR)

EPIDEMIOLOGY AND CLINICAL RESEARCH

Evaluation of the clinical performance of the STANDARD™ Q Malaria/CRP Duo Test (SD Biosensor, South Korea) for the diagnosis of malaria and the detection of C-reactive protein in finger prick blood of febrile patients

This study was a prospective clinical trial conducted in primary health care facilities located in a malaria endemic area to assess the clinical performance of the STANDARD™ Q Malaria/CRP Duo Test when in malaria endemic areas. Performance was assessed in comparison with expert microscopy as the reference test for malaria, and with a high quality, commercially available CRP test kit run on a laboratory machine as a reference test for CRP. A total of 1808 patients were enrolled, of which 9 patients had to be withdrawn or excluded, resulting in a total study population of 1799 patients included in the analysis. The sensitivity of the Malaria/CRP test for the diagnosis of malaria, *P. falciparum* and *P. vivax* was estimated to be 97.9%, 91.4% and 95.0% respectively.

National Malaria Slide Bank

This study aims to establish a Malaria Slide Bank at national level to impart the trainings and assessments for malaria microscopist at regular intervals and quality assurance. (Fig 14). NIMR has prepared around 25000 slides till date, supported training of malaria microscopists for detection and identification and counting of parasites and sent slide panels to states hospitals and Bhutan Government.



Fig. 14: Blood smear preparations and mass staining of smears at NIMR, Delhi.

Quality Assurance of Malaria Rapid Diagnostic Tests

This laboratory is recognized by WHO to assess the quality of malaria RDTs procured and supplied by NVBDCP in India. *P. vivax* and *P. falciparum* panels were prepared from the samples collected from malaria endemic regions of India. Panels were validated by at least two reference kits, before testing the RDTs every time. The post-dispatch RDTs received from the field were also tested for their quality.

This is the only lab of its kind in South East Asia, that performs RDTs lot testing to ensure distribution of quality diagnostics under programme.

Fever Clinic

At fever clinic, NIMR HQ, 23 malaria cases were diagnosed from January 2020 to December 2020. 65% were males while 35% were females and malaria cases were observed in the month of August and September. All the confirmed malaria cases were given treatment as per the national treatment guidelines.

Assessment of knowledge, attitude and practice of Mitanin's with respect to Malaria control in Chhattisgarh

This study was designed to find out the knowledge of mitanins about malaria and training need of mitanins to handle primaquine and reporting serious cases to higher centres. The first survey to find out the training needs of mitanins has been completed and Mitanin training module was developed based on the findings of the survey. Mitanin trainers were trained to impart the required training to mitanins.

Assessment of the coverage, use rate and physical integrity of Long Lasting Insecticide Net (LLN) after scaling up of their distribution in Gujarat, India

The objectives of the study is (i) To assess the distribution pattern, coverage and use rate of long lasting insecticide nets (LLNs) distributed in villages, (ii) To determine the physical condition and barrier of LLN use in community. The study

is conducted in four districts viz. Surendranagar, Anand, Kutch and Godhra. The state health programme has distributed 10 lakh LLNs during last one years in all the 33 districts of Gujarat. A standard WHO based performa developed to conduct the study. Total 4610 performa were filled from Surendranagar, Godhra, Kutch and Anand district. The outcome may provide guidance to strength the malaria control using LLNs in difficult areas and evidence to obtain better LLN product.

VECTOR CONTROL

Screening of novel compounds for insecticidal potential

Screening of novel compounds for ant larval activities and development of protocol for large scale screening for their larvicidal potential (Fig. 15). Larvicidal protocol was developed for high throughput to screen a large number of compounds. Tests were performed to evaluate the larvicidal potential; approx. 40 chemical compounds against *Anopheles* larvae were used. Taking this as platform, screening of non-biological synthetic compounds as candidate against mosquito vectors for their efficacy against mosquito immature and adult form is being planned and to estimate lethal concentrations of the candidate compounds so that such compounds which show anti-malarial potential might be useful in either killing mosquito larvae or can clear parasite from mosquitoes or may be targeted for shortening of lifespan of mosquitoes.

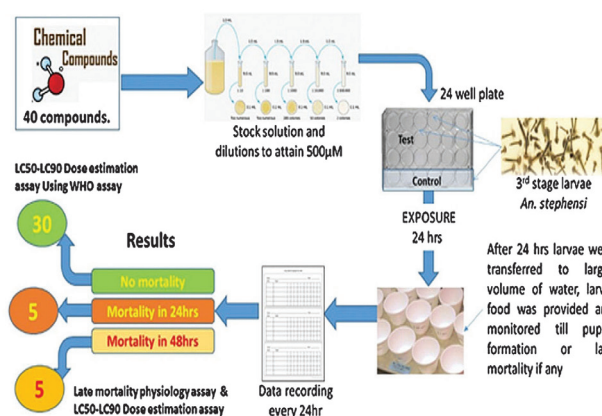


Fig. 15: Schematic representation of 40 compounds tested using high throughput bioassay.

PARASITE BIOLOGY AND DRUG DISCOVERY

Expression studies of *vir* genes in the clinical samples of *Plasmodium vivax*

Antigenic genes are present in malaria parasites, which encode the variant surface antigens (VSAs) providing protective immunity to the parasite against host/vector. Among these genes, the *vir* family of *P. vivax* is the largest subtelomeric multigene superfamily likely to be involved in antigenic variation and pathogenesis. A total 56 clinical samples of *Plasmodium vivax* were analysed for four *vir* genes (*vir*-12, *vir*-14 related, *vir*-10 and *vir*-17 like). The severe *P. vivax* cases showed higher expression levels of *vir* 12 gene and the drug resistance gene as compared to the non-severe *P. vivax* infections. The increased expression levels of these genes in severe infections indicates the role of *vir* genes in disease pathogenesis and might be responsible for the changing trends of complicated *P. vivax* (Fig. 16).

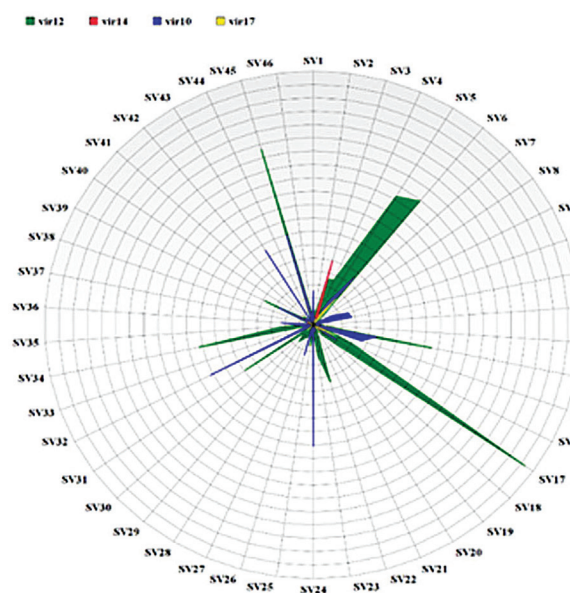
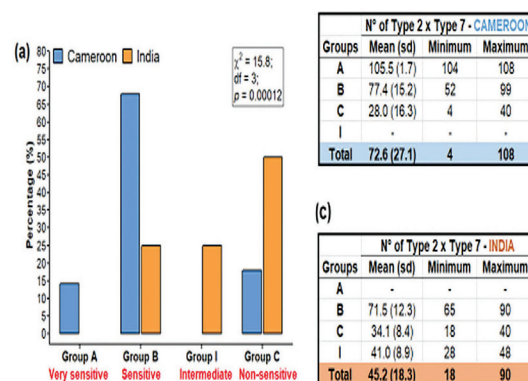


Fig. 16: Radar Graph representing the relative quantification of expression levels of *vir* genes analyzed in *Plasmodium vivax* clinical infections.

Comparative analysis of genetic diversity of histidine-rich protein 2 and 3 genes of *Plasmodium falciparum* field isolates

Several reasons can explain worryingly high statistics of malaria *viz.* i) the emergence and spread of parasites resistant to first-line treatment, ii) high genetic diversity of *Plasmodium falciparum* (*Pf*), the deadliest malaria species, iii) the high-rate emergence of non-falciparum species in sSA, iv) asymptomatic malaria, low (very low) malaria parasite density, and more recently v) the emergence of *Pf* parasites with deletions in the histidine-rich protein 2 gene (*pfhrp2*), coding the HRP2 protein which is largely used for designing *Pf*-detecting rapid diagnostic tests (RDTs). High rates of deletions were found to be present in *pfhrp2* gene in Africa and India field isolates leading to false negative PfHRP2-based RDT results (Fig 17).

Profile of RDT Sensitivity of isolates from Cameroon and India (b)



- The proportion of "non-sensitive" isolates to *Pfhrp2*-only RDTs was significantly ($p = 0.03$) higher in India as compared to Cameroon (17.9% vs 50.0%, $p = 0.00012$)

Fig. 17: Relation between PfHRP2 peptide chain reaction and RDT in Cameroon and India. (a) Proportion of different sensitivity groups; (b) Mean length of PfHRP2 sequences by sensitivity groups in Cameroon; (c) Mean length of PfHRP2 sequences by sensitivity groups in India.

Whole Genome sequencing (WGS) of the Indian field isolate of *Plasmodium falciparum*

WGS has been carried out successfully for an Indian field isolate of *P. falciparum*. More field samples are underway for the WGS and to be available as reference genome sequences in near future (Fig 18).

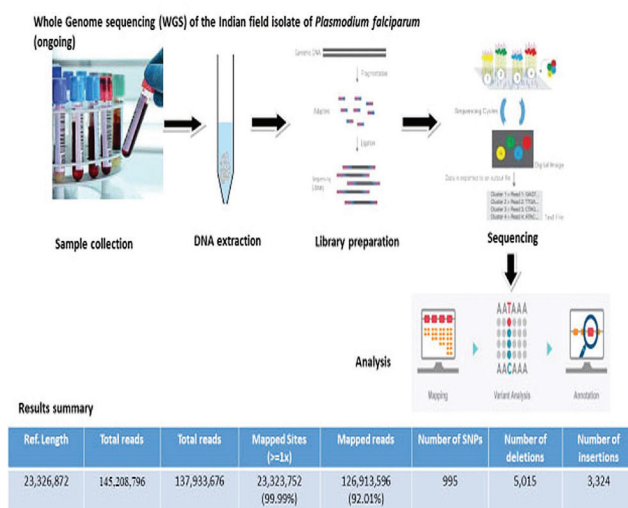


Fig. 18: Illustration of the methodology used in the WGS and the result summary of the data obtained.

A Phase-II interventional multicentre, randomized open label study to determine the effective and tolerable dose of KAF156 and Lumefantrine solid dispersion formulation in combination given once daily for 1, 2 and 3 days to adults and children with uncomplicated *Plasmodium falciparum* malaria

This study aims to establish 5-aminolevulinic acid hydrochloride salt and sodium ferrous citrate as combination for the treatment of malaria.

NFHS-5

It is an ICMR flagship project named “Establishing a pan-India landscape of human *Plasmodium* infections from dried blood spots collected under National Family Health Survey – 5 (NFHS – 5)” with main objectives of developing a pan-India cross-sectional landscape of:

- persons infected with one or more of the five *Plasmodium* species known to infect humans (*P. falciparum*, *P. vivax*, *P. malariae*, *P. ovale* & *P. knowlesi*).
- presence of molecular markers of anti-malarial drug resistance in *Plasmodium falciparum* & *Plasmodium vivax*.
- presence of *hrp2/hrp3* gene deletions in *Plasmodium falciparum*.

NFHS-5 is a multi-investigator project with stakeholders from ICMR headquarter, ICMR-NIMR, ICMR-NIMS and International Institute of Population Sciences, Mumbai. The project deals with ~90,000 dried blood samples that are mandated to be processed for a final outcome within a short span of 12 months.

Screening of potent inhibitors against novel cysteine protease, Metacaspase-2 of *P. falciparum* (PfMCA-2)

Metacaspases are cysteine-dependent proteases present in malaria parasite but absent in Human. Considering their role in *Plasmodium* pathogenesis, the team screened potent and specific inhibitors against PfMCA-2 based on structural modification of caspase inhibitor. C-532 and C-533 were found, which inhibited explicitly PfMCA-2 in nanomolar concentration and blocked the parasite with an IC₅₀ of 3.0 and 2.1 nM, respectively. Using the gene-knock out technique and specific inhibitors, MCA-2 is shown to play a significant role in controlling the number of oocysts, ookinete and sporozoites. Therefore, C-532 and C-533 can be used efficiently as transmission-blocking molecules.

VECTOR-PARASITE INTERACTION BIOLOGY

Decoding tissue specific molecular dynamics of mosquito-*Plasmodium vivax* parasite interaction in *Anopheles stephensi*

During its development inside the mosquito host *Plasmodium* needs to cross over several tissue-specific immune barriers, however, the molecular basis of this developmental complexity, is poorly known. Through comprehensive gut meta-transcriptomic, the team targeted to decode complexity of pre-invasive ~30 hours of tripartite gut-microbe-parasite interaction in gut-lumen, followed by post-gut invasive tissue specific direct interaction of (i) fast developing early & late oocysts in the gut, (ii) free circulatory sporozoites interaction with mosquito immune blood cells

i.e. hemocytes, and (iii) salivary interaction with invaded sporozoites, through multi-tissue RNAseq based transcriptomic studies.

In naïve mosquitoes, *Elizabethkingia meningitis* and *Pseudomonas* spp. are the dominant bacteria and blood-feeding leads to a heightened detection of *Elizabethkingia*, *Pseudomonas* and *Serratia* 16S rRNA. A parallel RNAseq analysis of blood-fed midguts also shows the presence of *Elizabethkingia*-related transcripts. After, *P. vivax* infected blood-meal, however, bacterial 16S rRNA were not detected until circa 36 h. Intriguingly, the transcriptional expression of a selected array of antimicrobial arsenal cecropins 1–2, defensin-1, and gambicin remained low during the first 36 h—a time frame when ookinetes/early oocysts invaded the gut. In conclusion, during the pre-invasive phase, *P. vivax* outcompetes midgut-microbiota. This microbial suppression likely negates the impact of mosquito immunity which in turn may enhance the survival of *P. vivax* (Fig. 19) in the mosquito gut lumen.

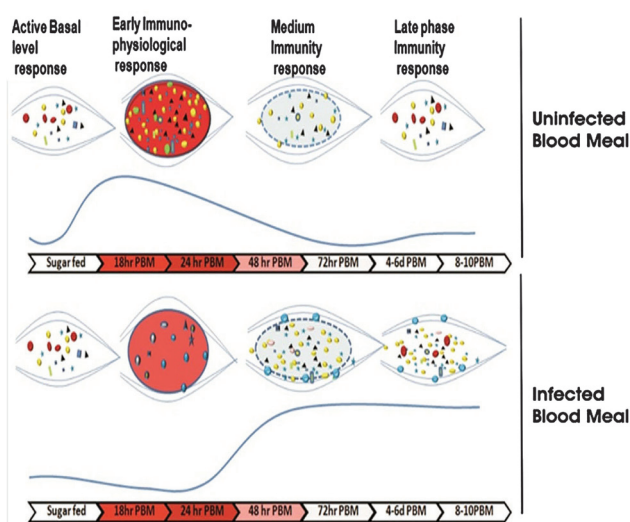


Fig. 19: Survival strategy model of *P. vivax* during pre-invasive phase of development inside the mosquito gut.

The team demonstrated that post gut invasion, a shrewd molecular relationship with individual tissues such as midgut, hemocyte, salivary glands, and strategic changes in the genetic makeup of *P. vivax* favors its survival in the mosquito host. A transient suppression of ‘metabolic machinery by early oocysts, and increased immunity’ against late oocysts suggested a

unique mechanism of gut homeostasis restoration and *Plasmodium* population regulation. Though a hyper immune response of hemocyte was a key to remove free circulating sporozoites, but a strong suppression of salivary metabolic activities, may favor successful survival of invaded sporozoites (Fig. 20).

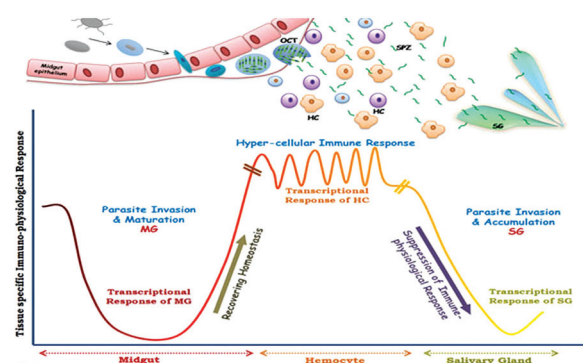


Fig. 20: Tissue specific molecular interactions during complete development of *P. vivax* in the mosquito host.

The above study allowed to identify novel molecular targets such as, *Fibrinogen Related Proteins* (FREPs), *Trehalase* and *heme-peroxidase* (HPX12) to disrupt the mosquito’s immunity, nutritional and reproductive physiologies. The pilot studies highlight their important role energy metabolism, and host-seeking as well as mating behavioral physiology, respectively.

Molecular forms of *Anopheles subpictus* and *Anopheles sundaicus* in Indian subcontinent

Anopheles subpictus and *Anopheles sundaicus* are closely related species, each comprising several sibling species. Ambiguities exist in the classification of these two nominal species and the specific status of members of these species complexes. In India, *An. sundaicus* is considered as a potent malaria vector, but *An. subpictus* has not been recognized yet as a malaria vector by the national malaria control programme. However, *An. subpictus* is considered a potential vector in Southeast Asian countries. In India, there are increasing evidences supporting the role of *An. subpictus* as a potential malaria vector, especially in coastal areas of India and Sri Lanka. The varying vectorial potential in different geographical areas is most likely due to the presence of different biological species (cryptic

species) present in *An. subpictus*. To resolve the taxonomic issues, sequencing was done for Internal Transcribed Spacer-2 (ITS2), 28S-rDNA (D1-to-D3 domains) and cytochrome oxidase-II (*COII*) of morphologically identified specimens of two nominal species, *An. subpictus sensu lato* (*s.l.*) and *An. sondaicus s.l.*, collected from the Indian subcontinent (Fig 21) and performed genetic distance and molecular phylogenetic analyses.

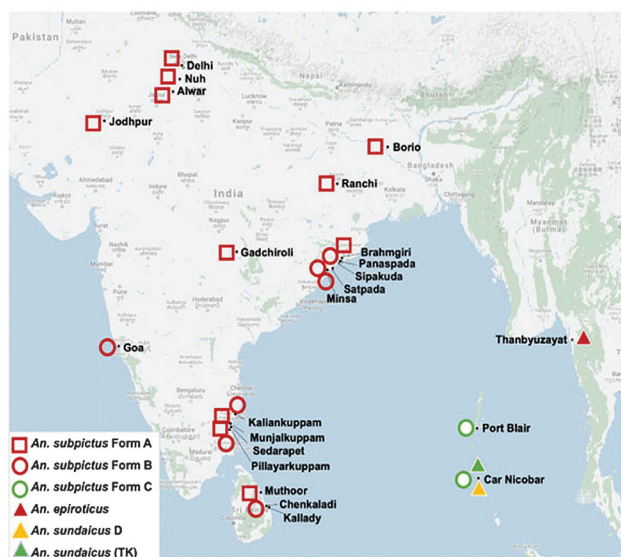


Fig. 21: Map showing geographical locations of study sites and distribution of different molecular forms of *An. subpictus s.l.* and *An. sondaicus s.l.*

Molecular characterization of mosquitoes for rDNA revealed the presence of two molecular forms of *An. sondaicus s.l.* and three molecular forms of *An. subpictus s.l.* (provisionally designated as Form A, B and C) in the Indian subcontinent. Phylogenetic analyses revealed two distinct clades: (i) subpictus clade, with a single molecular form of *An. subpictus* (Form A) prevalent in mainland India and Sri Lanka, and (ii) sondaicus clade, comprising of members of Sondaicus Complex, two molecular forms of *An. subpictus s.l.* (Form B and C), prevalent in coastal areas or islands in Indian subcontinent, and molecular forms of *An. subpictus s.l.* reported from Thailand and Indonesia. Based on the number of float-ridges on eggs, all *An. subpictus* molecular Form B were classified as Species B whereas majority (80%) of the molecular Form A were classified as sibling species C. Fixed intragenomic

sequence variation in ITS2 with the presence of two haplotypes was found in molecular Form A throughout its distribution (Fig 22).

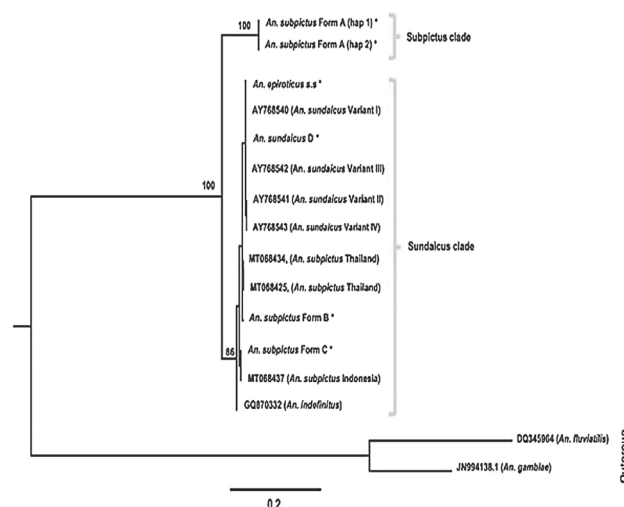


Fig. 22: Maximum Likelihood (ML) rooted tree of different molecular forms of *An. subpictus* and *An. sondaicus* complex based upon 28S-D2-D3 sequences. Numbers at nodes are ML bootstrap values (only > 80 are shown).

COVID-19

Central and Regional Depot for COVID-19 diagnostic reagents

ICMR-NIMR is functioning both as central depot and regional depot for storage and distribution of various reagents/kits required for COVID-19 diagnosis in the country (Fig. 23). As a central depot, NIMR, Delhi is currently catering to more than 500 COVID-19 testing labs across the country, through the networks of 18 regional depots NIMR has made initial guidelines for Institutes about facilities and manpower requirements for Depots and their management. NIMR is also involved in guiding the institutes to establish depots and specific guidelines for smooth distribution of COVID-19 testing kit supplies. NIMR has also prepared transportation and appropriate storage protocols (SOPs) for different temperature sensitive kits. Till date, the institute has managed the receipt / distribution of more than 4.7 million VTMs, 11.5 Lakh RT-PCR tests and more than 6.4 million viral RNA extraction kits. Maintaining and management of all necessary documents/ records related to receiving and distribution of kits to across the country.



Fig. 23: COVID-19 initiative at NIMR.

Quality Assurance of COVID-19 diagnostics

COVID-19 Quality Assurance Laboratory was established at ICMR-NIMR by modifying the existing laboratory in record time despite the lockdown. ICMR-NIMR also contributed in finalizing the uniform SOPs for Quality assurance and Lot testing. The institute is also providing technical support to the local vendors to develop their product for COVID-19 testing on large scale in India. New indigenous (make in India) testing products are being tested for their sensitivity and accuracy like Viral lysis buffers/ molecular Transport media which can reduce the risk of infection during sample transport as replacement of VTM.

Support to NIB-ICMR COVID-19 Lab

ICMR has also given responsibility to NIMR for setting up a NIB-ICMR COVID-19 Data Management Unit at National Institute of Biologicals (NIB), Noida. A team of 15 NIMR staff is working 24/7 to manage the data. The

machine release results for 96 reactions every 3 hours. NIB staff further share output to the data management team. Subsequently, the NIMR team A (molecular biologists and statisticians) enter the results to prepare the report, which is verified by team B (researchers) from the patient record forms to overcome all the possibilities of false reporting. Once verified, a clinician attests the report and dispatches to the concerned medical officials. Team C (researchers) maintains the record of all the reports and looks for any discrepancy and missing sample report. Furthermore, team D (data entry operators) submits the data on ICMR COVID-19 portal.

Biorepository of COVID-19 blood samples

NIMR is establishing a biorepository of COVID-19 positive blood samples. NIMR is collecting blood samples of COVID-19 patients admitted to various hospitals. Blood samples are aliquoted and stored in -80°C freezers. They can be used for validation of antibody kits, developing new diagnostics, therapeutics, vaccine research, immunological

response, to understand the host-pathogen dynamics and disease pathogenesis etc. These samples in the biorepository will support the current and the future research projects on COVID-19 in India.

COVID-19 testing for the Parliament of India, Rashtrapati Bhawan, PMO, Delhi Government

NIMR Coordinated COVID-19 Testing of the Parliament of India during all three sessions i.e. Monsoon session (July to August/September); Winter session: (November to December); Budget session: (January/February to May). NIMR has conducted RDTs for Rashtrapati Bhawan and has been testing regularly VIPS from PMO and Different Ministries. More than 28000 COVID-19 tests were conducted for Delhi Government.

Management of COVID-19 Vaccine follow-up

Management of follow up call management for the person taking COVAXIN vaccination against COVID-19.

ICMR-VECTOR CONTROL RESEARCH CENTRE, PUDUCHERRY(ICMR-VCRC)

LYMPHATIC FILARIASIS

Development of monitoring and evaluation protocol for accelerated MDA with IDA for lymphatic filariasis elimination programme

This study was proposed to develop appropriate monitoring and evaluation (M&E) protocol by generating evidence base to identify appropriate infection indicator(s) and target population that can be used to decide on stopping mass drug administration (MDA) with triple drugs (Ivermectin, DEC and albendazole). Following the Phase I study (i.e, baseline survey prior to MDA), one-year post MDA survey 1 (Phase - II) was undertaken in Simdega (Fig. 24) and this showed a significant reduction in circulating filarial antigen (CFA) prevalence among children but not among

adults compared to baseline. Further, there was no difference in the Mf -prevalence between baseline and 1- year post MDA. The survey in Yadgir was to be initiated in July 2020; but postponed due to COVID-19 pandemic. Soon after some relaxation in the lockdown rules, xeno-monitoring survey resumed in Yadgir.



Fig. 24: Blood samples collected in Simdega.

Adaptation, validation and application of LYMFASIM model to predict the risk of resurgence following stopping MDA based on transmission assessment survey (TAS)

The study initiated in 2015 was successfully completed. The outcome of this study included:

- (i) At least 6 rounds of MDA-IDA with 65% coverage is required to achieve >99% probability of elimination for settings with no previous MDA.
- (ii) Operational decision on stopping MDA based on TAS could be made 2-years post-6 rounds of MDA-IDA for settings with no previous MDA.
- (iii) Any age class could be targeted for assessing transmission interruption (stopping MDA).

Development of a Xenomonitoring protocol for monitoring and evaluation of *Brugia malayi* transmission

The preliminary observations of this study

suggested that there may be chances of resurgence of *B. malayi* and also co-infection of both *B. malayi* and *W. bancrofti* parasites in the vectors, long time after chemotherapeutic intervention to filariasis in Alappuzha district (Kerala) and Balasore district (Odisha). Adequate vector samples were planned to be collected during the time of peak density for further confirmation. However, only a limited number of samples were obtained due to unusual rains, and further on account of COVID-19 pandemic in the study areas.

Infrared thermograph (IRT) as a tool for the Diagnosis and prognosis of the lower extremity lymphoedema

The objective of this study was to find the temperature distribution over the lymphoedema in filariasis and to extract diagnostic and prognostic information. IR thermography was considered as an alternate to expensive lymphoscintigraphy in well-established lymphoedema cases, the precision was considered at 7.5% level and the sample size worked out. For the present study, considering the sensitivity as priority, it was planned to recruit a total of 88 unilateral lymphoedema patients. A total of 29 eligible participants were identified for the study which included 7 and 22 grade II and II LE patients respectively.

Development of Nano-formulations of repurposed drugs and in vitro and in vivo testing for antifilarial activity

In vitro antifilarial screening test results showed that out of 13 repurposed drug molecules screened, 4 molecules are macrofilaricidal at 0.1 mg mL⁻¹ with >50% reduction in formazan formation whereas the currently used drugs DEC, Albendazole and Ivermectin at the same test conditions showed <50% inhibition. Out of these molecules one was tested at lower concentration and found effective in killing the adult filarial worms. These molecules have to be screened at lower concentrations further to find out the medium lethal concentration.

MALARIA

Studies on behavioural change in anopheline vectors in areas of insecticidal nets (ITNs/LLINs) used in Odisha, a possible challenge to malaria elimination programme

The study was conducted in two southern districts (Koraput and Malkangiri) of Odisha State, where LLINs were in use for the last 4 years. After distribution of LLINs, the overall abundance of *An. fluviatilis* has been drastically reduced in two districts. The resting behaviour of this vector species has been shifted from human dwellings to cattle sheds in three terrains of Koraput district. The feeding behavior of *An. fluviatilis* has been shifted from anthropophagy to zoophagy. The distribution of LLINs has no impact on the resting behavior of *An. culicifacies*, as there was no change in the density of this species in human dwellings and cattle sheds in three terrains of both the districts.

The malaria in the study villages of both the districts was maintained at zero incidence during the study period, indicating the impact of LLINs on malaria transmission.

LEISHMANIASIS

Entomological and epidemiological investigations on leishmaniasis among the tribal populations in the Western Ghats, Kerala

A total of 996 tribal people from different tribal communities (Kaadar, Ulladan, Malayan, Mannan, Paniyaretc) in Malappuram and Thrissur districts were surveyed. Active CL (n=1) and VL (n=3) cases were recorded among a total of 15 suspected leishmaniasis cases identified from the tribal belt of Western Ghats in Kerala. Also, a total of 1358 sandflies constituting 14 different species were collected from the study area. *Phlebotomus argentipes* (77.10%) was identified to be the most predominant species followed by *Sergentomyia monticola* and *S. babu*. 215 specimens (10 species) have been barcoded, and 16 barcode sequences have been deposited to NCBI GenBank. However, none

of the 345 *P. argentipes* (101 pools) samples tested was positive for natural infection with *Leishmania* parasites.

Mathematical modelling: understanding and controlling the patterns of visceral leishmaniasis (VL) and transmission

The ICMR-VCRC has conducted a systematic review on the population dynamics of sandfly population. The findings of the review indicated that none of the existing VL transmission models have explicitly modelled both the sand fly population dynamics and transmission dynamics of VL due to paucity of data from field or experiments. Currently, as part of the SPEAK India project, the LSHTM in collaboration with RMRI, Patna is carrying out a molecular xeno-monitoring (MX) study to understand the dynamics of infection between human and vector. The data from this MX study as well as from literature will be utilized to arrive at a quantitative relationship between human and vector infection which will be plugged into the existing transmission models. The resulting model will be fitted and validated against available surveillance data.

Also, the Centre has completed extraction of covariates data on 19 bioclimatic (Jan 2013-Dec 2018) variables and 4 environmental (Jan 2013-Oct 2019) variables for all the blocks (endemic / non-endemic) in Bihar, Jharkhand, UP and West Bengal. Preliminary analyses of the monthly aggregated reported VL cases showed a seasonal cyclic pattern of VL incidence and declining trend over years. The patterns of monthly VL incidence and aggregated values of different environmental covariates were found to have significant positive correlations with minimum ($r_s=0.28$) and maximum temperature ($r_s=0.36$) and negative correlation with soil moisture ($r_s=-0.30$). Fitting of a variety of spatio-temporal models relating monthly VL incidence data at block level from 4 endemic states with environmental and bioclimatic variables are in progress.

Reported VL cases showed a seasonal cyclic pattern and a declining trend over years as observed in the climatic (minimum and maximum temperatures and environmental (soil moisture) covariates.

DENGUE/ ZIKA/ CHIKUNGUNYA

Role of immune cells in the pathogenesis of dengue virus disease

Assessment of cell morphology by bright field microscopy, cell viability by MTT assay, protein estimation by Bradford reagent were done in cells exposed to NS1 antigen in the presence and absence of paracetamol. Cytokines estimations were done by ELISA. Expressions profile of matrix metalloproteinase genes were done using real-time PCR and reverse-transcriptase PCR.

NS1 exposure of THP-1 monocytes cells, changed their cell morphology and activated them for release of proteins in 24 hours. Expressions of MMP-2, MMP-8, MMP-9 and MMP-14 genes were upregulated by NS1 exposure. Further, exposure of NS1 to THP-1 monocytes cells increased expression profile of MMP-10 and MMP-13 genes to a lesser extent. Treatment with paracetamol (1 mg/ml and 2 mg/ml), significantly down-regulated the expression profile of MMP-2, MMP-8, MMP-9 and 14 in dose dependent manner. NS1 exposure also increased the release of cytokines IL-4, IL-6, and IL-10 but decreased the release of TNF-alpha and IL-15. Interestingly, paracetamol reversed NS1 induced changes in the release of these cytokine in dose dependent manner. We also found that, HL-60 cells differentiated to eosinophils show upregulated expressions of MMP-2 when exposed to NS1 antigen of DENV-2.

Monocytes mediated MMPs expressions significantly participate in the development of dengue pathogenesis in the severe cases of disease and paracetamol has a protective effect in dengue viral disease.

Development of Artificial diet for female *Aedes aegypti* mosquitoes

In an attempt to replace using the animal blood as source of food for laboratory vector mosquitoes, the Centre embarked upon the preparation and use of artificial diet for dengue vector, *Aedes aegypti*. Mosquito diet (VCRCAeDiet) was prepared using the components such as vitamins, minerals and proteins. The mosquitoes were fed on the VCRCAeDiet. The fed mosquitoes were kept for egg laying. The laid eggs were kept for hatching. The hatched larvae were counted and allowed to pupate. The pupae emerged to F1 generation. The F1 generation was again fed on the prepared diet VCRCAeDiet and continued the process to get the F2 generation successfully.

HUMAN RESOURCE DEVELOPMENT

M.Sc. Public Health Entomology (PHE) course

Ninth batch of 12 students continued the program, affiliated to Pondicherry Central University. As a part of the course curriculum, M.Sc., students visited VCRC field stations at Koraput for Malaria study and Kottayam for Dengue and Chikungunya study. Students were unable to visit other National Institutes, owing to COVID-19 pandemic.

Ph.D. Programmes: Three full time (Chemistry – 1; Zoology – 2) and one part time (Zoology) candidates continue to pursue their Ph.D. programme.

Training on Vector Borne Disease epidemiology and control: A total of 104 students and Research Scholars from eight Institutions have been offered hands on / observational training.

RT-PCR based COVID-19 Testing Facility at ICMR-VCRC

Testing of COVID-19 samples by RT-PCR was initiated on 27th August, 2020 and presently the facility can test 540 samples per day. Samples were received from Indira Gandhi Medical College, Pondicherry from 27th August to 7th September,

2020 (n=475). From 8th September onwards, samples were received from Karaikal and PHCs of Puducherry. A total of 28, 905 samples were tested and 3,355 samples were positive for COVID-19.

PATENTS

- M. Manonmani, P. Jambulingam, S. Tamilselvan and M. Vairakkannu. Fly ash based mosquito larvicidal formulations of *Bacillus thuringiensis* var *israelensis* (Serotype H14). Indian Patent No. 347708/2020



Fig. 25: Catch the Rain- 2020.



Fig. 26: Jan Andolan Campaign on COVID- 19.

ICMR-NATIONAL AIDS RESEARCH INSTITUTE, PUNE (ICMR-NARI)

Impact Evaluation of Antiretroviral therapy (ART) program in India

This was the first national-level impact evaluation of the Government of India's free ART programme under the National AIDS Control program (NACP). It highlighted that over 90% persons taking ART and retained with the program had adequately suppressed the virus in their blood at 5 years.

Sustained and Timely AIDS Response (STAR): Community Engagement in Mizoram

A rapid situation and response assessment across 5 districts of Mizoram (Aizawl, Mamit, Champhai, Lunglei and Kolasib), highlighted the need for systematic approach in moving forward the community engagement agenda in the context of the Mizoram State Integrated Plan for HIV & AIDS. Action framework for the same was developed.

An indigenous in-house HIV drug resistance (HIV-DR) assay

ICMR-NARI is the first WHO certified Indian laboratory for 'Integrase' resistance genotyping using indigenous in-house assay. It successfully developed and validated an in-house assay for HIV-1 'Integrase' resistance genotyping. ICMR-NARI provided genotyping to Sri Lanka for their National primary drug resistance survey and for patients failing the ART regimens.

Estimation of seroprevalence for Hepatitis B and C among adults in India

Dried blood spot specimens from the National Family Health Survey-4, were tested for Hepatitis B and C. These first-ever national data showed seroprevalence of Hepatitis B and Hepatitis C as 0.95% and 0.32% respectively.

Psychosocial needs among HIV infected adolescents in India

Anger, body image issues and parental hyper-vigilance were significant mediators and moderators in the pathway leading to emotional distress among adolescent with HIV. The study recommends establishment of 'adolescent transition clinic' for all adolescents.

National TB Prevalence survey

ICMR-NARI screened 37321 individuals for TB in 46 clusters across Maharashtra. This generated baseline evidence on the prevalence of microbiologically confirmed pulmonary TB in Maharashtra to inform program, to help achieve the aim to 'End TB' by 2025.

Operational feasibility of DBS as a sample type for HIV-1 viral load assay

This was a pilot study to understand the feasibility of DBS as alternative of HIV-1 plasma viral load testing for the 'hard-to-reach' region of public sector laboratories in North-Eastern states and Andhra Pradesh.

Assessment of Experiential learning-based Community Engagement Tools to Enhance Research Literacy and Participation in HIV Biomedical Research in Rural Maharashtra

An intervention using 'Participatory theatre, gamification, the creative arts and behavioral science approaches was delivered among 381 FSW, MSM, TGW across Satara, Sangli and Kolhapur districts of Maharashtra, India. Subsequently, endline survey was conducted among 600 participants to study the acceptability of the intervention and data are being analysed.

Effects of Yoga and Naturopathy interventions in inflammatory status of obese patients. A pilot study

The project studied the gut microbiome changes among obese patients with routine naturopathic practices intervention.

Regulation of RNA interference during rotavirus infection and characterization of cellular miRNAs as novel antiviral therapeutics

Several miRNAs were identified as dysregulated during Rota Virus infections through the miRNA-Microarray and their functions in context to viral pathogenicity were analyzed.

SARS COV-2 / COVID-19

Validation of Dry swab RNA extraction free RT-PCR method for SARS COV-2 detection

Two validation protocols for dry swab method were conducted. The first validation revealed lower sensitivity and specificity as compared to the standard RT-PCR method; while a methodology modification showed improved performance. ICMR released an advisory for this variant method.

Panel development for validation of COVID-19 serological assays

ICMR-NARI was identified as one of the centre for validation of serological assays to detect the antibodies against SARS-COV-2. Eleven of 66 antibody kits showed satisfactory performance, using the well developed validation panel.

Diagnostic utility of oral swab as an alternative to nasopharyngeal swab (NPS) for detection of SARS COV-2

The acceptability and feasibility of self collected oral swab sampling for SARS-COV-2 testing, using both RT-PCR and Rapid Antigen Test (RAT) was demonstrated. A very good agreement between 'self-collected' oral swab specimen and 'health-care-worker collected' nasopharyngeal specimen was noted for RT-PCR while moderate agreement seen with RAT.

ICMR-WHO Solidarity Clinical Trial for treatment of hospitalised COVID-19 patients

The ICMR-WHO-INDIA Solidarity Trial, initiated during the strict lockdown period in 2020, tested

four drugs Remdesivir, Lopinavir/Ritonavir, Hydroxychloroquine, Interferon Beta1A along with local standard of care to see their effect on preventing death or progress to ventilation in hospitalised COVID-19 patients. ICMR-NARI coordinated the trial across 26 sites in India which randomised 1047 patients. None of the drugs was found to be useful in preventing death or need for ventilator. This helped provide information to prevent unnecessary use of these drugs.

Knowledge, Attitude and practices towards COVID-19 among People Living with HIV (PLHIV) attending ART centre at Pune, India: a cross-sectional study

Among 1175 PLHIV, average knowledge but correct attitude towards adherence to government prevention and control measures, and appropriate practices towards prevention of COVID-19 was noted. Counselling sessions at ART centres should include COVID-19 prevention information.

ICMR-Biotech COVAXIN protocol

Follow up telephonic calls to collect adverse event data following vaccination with COVAXIN was conducted among 5629 individuals as part of ICMR implementation protocol.

Social Drivers of acceptance and rejection of protective measures against COVID-19 infection in the community

A cross-sectional telephonic survey among 1,016 adults from randomly selected households in mid 2020 revealed that increase in "Knowledge score" facilitated protective behavior while "No source of income" was independently associated with not using protective measures against COVID-19. These data suggest that behavior change communication strategies should be specifically directed towards the low socio-economic populations through trusted sources only.

COVID-19 stigma study

The centre participated in a multi-centric mixed-method cross-sectional study, to assess stigma

during the COVID-19 pandemic in urban and rural settings. COVID-19 recovered individuals reported experiencing stigma and mental distress. Prevalent stigma led to non-disclosure of COVID-19 status, resulting in delayed access to treatment.

Population-based serosurvey to estimate the prevalence of SARS-COV-2 antibodies in India

ICMR-NARI participated in National serosurvey, completing the survey in six districts of Maharashtra. This helped generate evidence for policy decisions.

Phase II Clinical Trial of ICMR SII Covovax vaccine

The trial was initiated at six sites on 25th March 2021 after receiving all approvals. The initial seven-day safety data was presented to DSMB and received recommendations for proceeding to Phase III part of ICMR SII Covovax vaccine study.

PrEP demonstration study among MSM and TGW in Pune and Punjab

This demonstration study among MSM and Transgender Women was continued. Different service delivery models are under evaluation and during lock down. Dispensing of the tablets at the convenient locations and virtual meetings were some strategies used.

Probing the interaction between SARS-COV-2 Nsp13 and ALG-2 interacting protein-X(ALIX)

The role of Nsp13 protein of SARS COV-2 in virus release through its interaction with host protein ALIX is being explored. Initial docking and in-vitro experiments indicated the plausible interaction between SARS COV-2 Nsp13 and ALIX.

Study of genital Human papillomavirus (HPV) infection in men: type-specific distribution, risk determinants and natural history

This study will shed light on the type-specific HPV prevalence, the associated risk determinants and natural history of genital HPV infection in men from within India.

Host-pathogen interactions of HIV and associated common opportunistic infections: identification of important therapeutic targets and their modulators

System biological investigations of host-pathogen interaction (HPI) of HIV and other common opportunistic infections are planned. This project also involves the establishment of an animal-microbial co-culture setup for the evaluation of inhibitors against studied pathogens.

Diagnostic utility of buccal swab specimen as an alternative to sputum for molecular detection of pulmonary tuberculosis

The study explores the use of oral swab for diagnosis of bacteriologically confirmed TB. If useful it will be easier to detect TB.

endTB (Evaluating Newly approved Drugs for multidrug-resistant TB) & endTB-Q (Evaluating Newly Approved Drugs in Combination Regimens for Multidrug-Resistant TB with Fluoroquinolone Resistance (Q))

These two international, multi-country, phase III clinical trials for MDR TB patients evaluating efficacy and safety of new short, all oral novel regimens consisting of new and repurposed drugs have been initiated.

Estimating Incremental Cost of treating Antimicrobial Resistant infections in India

This is primarily a retrospective cohort study with data collection in process at 8 hospitals participating in the study from ICMR's Antimicrobial Resistance Surveillance Network.

Phase III double blind placebo control trial to study the efficacy and safety of two candidate TB vaccines

ICMR-NARI established two trial sites and randomized 1593 participants of the total 12,717 enrollment across 18 sites in India. Follow-up is ongoing.

Cohorts of HIV Resistance and Progression in Indian Children and Adults (CoHRPICA)

This multi-centric cohort of HIV infected and uninfected individuals and biorepository of their samples will act as a resource for answering questions on HIV prevention and disease progression.

Studies on mucosal immune response

Studies evaluate the role of TGF- β on HIV viral release as well as the cell signaling pathways on inflammation at the female mucosal sites. We established an *in-vitro* cell-associated model of HIV infection in cervical epithelial cells (CECs), where TGF- β was identified as negative regulator of HIV release in the infected CECs.

Studies on HIV latency and epigenetic aging

Role of innate immune modulators as latency reversal agents and associations of inflammatory markers on epigenetic aging in HIV infected patients are being explored. ADCC mediating antibodies generated from the memory B cells of Long Term Non Progressors (LTNPs) showed an ability to kill reactivated latent reservoirs. These studies have implications in formulating the immune therapeutic strategies.

Studies on matricellular protein galectin 9 (Gal-9)

After we reported strong correlation of plasma Galectin-9 levels with HIV viral load in ART failure patients, we are currently evaluating it as a surrogate marker for HIV viremia and possible role in monitoring anti-tubercular treatment response in HIV/TB co-infected patients.

MicroRNAs and Exosomes: The Key Players in Rotavirus Stability, Viral RNA transmission and Infection

This Ramanujan Fellowship grant seeks to elucidate the mechanism by which coordinated expression of cellular microRNAs regulate the innate immune response during Rotavirus infection.

Role of microRNAs in liver disease progression in HIV/HCV co-infected individuals

HIV/HCV co-infected cells display modulation of a group of miRNAs, in-vivo and in-vitro that plays a crucial role in liver disease progression and HIV pathogenicity. This study focused on the detection of miRNAs from patients sample as novel biomarker in liver fibrosis as well as their mechanistic role and regulation during HIV pathogenicity.

India Hypertension Control Initiative (IHCI)

Over the period of two years there was a significant increase in hypertension control from 5% to 16% in patients registered in 4 sentinel sites under India Hypertension Control Initiative. The IHCI model was adopted by Department of Health Services, NCD Division at 8 additional districts for improving control of BP.

Contribution to Government of India's National Programmes (NACP, NVHCP)

- External Quality Assurance (EQA) Programme for HIV serology, CD4 count estimation, confirmation of HIV-2 diagnosis were carried out by ICMR-NARI as crucial support to the National AIDS Control Program. Consortium activities of the National Reference Laboratories (NRLs) for Kit Quality Testing to support the National AIDS Control Programme and external quality assurance for HIV-1 viral load testing were also carried out.
- The 17th round of HSS Plus 2020-21 surveillance was successfully implemented among Antenatal Care Attendees (ANC), Prisoners, High Risk Group and Bridge population sites across five western Indian states. We covered 203 ANC (tertiary & district hospital) sites, 14 Central Prison sites, 81 HRG and 16 Bridge population targeted intervention sites in western India region (Maharashtra, Madhya Pradesh, Rajasthan, Goa, Gujarat, Dadra and Nagar Haveli and Daman and Diu)

- National AIDS Control Organization supported – Pune Municipal Corporation (PMC) - ART Centre was operated by the scientists of ICMR-NARI. A total of 3477 patients were under active care out of which 160 were newly enrolled and are alive on ART.

ICMR-NATIONAL INSTITUTE OF RESEARCH IN TRIBAL HEALTH, JABALPUR (ICMR- NIRTH)

Diagnosis Services of COVID-19 in the State of Madhya Pradesh

In view of declared pandemic of COVID-19 by WHO, preparedness for diagnosis for SARS COV-

2 at ICMR-NIRTH were started after brief training to the existing staff of the Virology laboratory. A capacity of about 60 samples per day was ramped up to 300 samples a day and as of now it is about 600 samples per day. More than 93,000 samples have been received and tested for SARS-COV-2 of which 4645 (positivity = 4.9%), were found positive up to March 2021. The laboratory is functioning in two different shifts every day. The turnaround time less than 24 hour was managed by laboratory despite of high sample load, in fact all attempts were made to provide diagnosis within 24 hours from the time of sample collection. This has helped public health authorities to track and treat the COVID-19 infected patients on time (Fig. 27).



Fig. 27: Lab Activities of COVID-19 diagnosis.

COVID-19 Sero-Surveillance Study in Madhya Pradesh

As a part of the nation-wide community based sero-surveillance activity, a 45-member team comprising scientists and technical staff of ICMR-NIRTH, Jabalpur has collected 1200 venous blood samples from 30 clusters of three different districts of Madhya Pradesh (Dewas, Gwalior and Ujjain). The study was done in three rounds (Fig. 28).

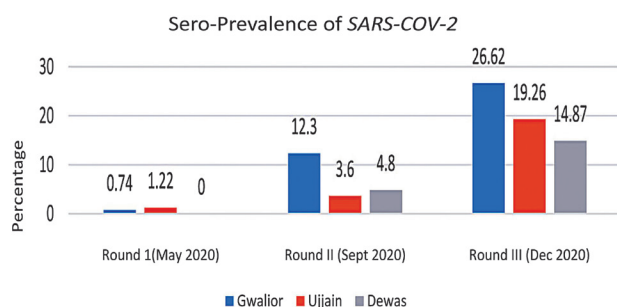


Fig. 28: Sero-Prevalence of SARS-COV-2 in different times in three districts of Madhya Pradesh.

Capacity Building for COVID-19 diagnosis in Government Medical Colleges, Madhya Pradesh

Diagnostic service of SARS COV-2 has been provided to about 20 districts of Madhya Pradesh. However, to build capacity in term of trained manpower for diagnosis, on request of the Government of Madhya Pradesh, Virology laboratory, ICMR-NIRTH, Jabalpur has provided hands on training to 38 medical, paramedical and technical staff from 08 government medical colleges on diagnosis of SARS COV-2 (Fig. 29).



Fig. 29: Training of state health officials for COVID-19 diagnosis.

Assessment of neonatal screening approaches for sickle cell disease and the effect of early intervention in management of the disease in tribal population

During the financial year, 1619 newborns in districts Mandla and Dindori were screened. Twenty-two sickle disease affected babies and 236 sickle carrier babies were identified. Regular clinical follow up and necessary care to all SCD and equal number of carrier babies is being provided (Fig. 30).



Fig. 30: Follow up of newborns SCD patients.

Impact of new, one-minute, sensitive diagnostic with innovative malaria elimination plan

The study is being conducted at three study sites viz; Sheopur (Madhya Pradesh), Udaipur (Rajasthan) and Jagdalpur (Chhattisgarh). The major objective of the project is the evaluation of new point of care malaria diagnostic device and its comparison with current gold standard tests to determine the accuracy. So, far 11,322 febrile patients have been screened on all three study sites. Out of which, a total of 1,699 were enrolled for the study. Screening by microscopy resulted in 345 malaria parasite positive cases. Screening of 1373 samples by PCR resulted in 509 malaria parasite positive cases [*Plasmodium falciparum* (321),

Plasmodium vivax (92), *Plasmodium malariae* (02), Pf+Pv (74), Pf+Pm (11), other mixed (9)]. So, far the performance of the device is very much comparable to RDT (Fig. 31).

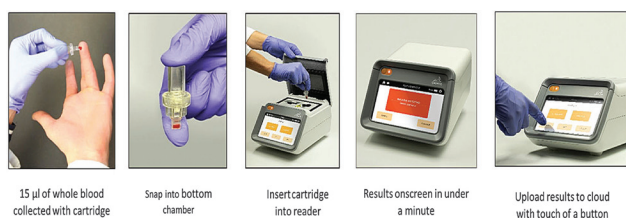


Fig. 31: Steps for Malaria diagnosis using point of care device.

Efficacy and safety of ACT for the treatment of uncomplicated *Plasmodium falciparum* malaria in India: Madhya Pradesh, Odisha, Rajasthan, Telangana and West Bengal

The objective of this project is to measure the clinical and parasitological efficacy of AS+SP in patients suffering from uncomplicated falciparum malaria. Therapeutic efficacy was determined in 151 (96.7%) patients who had completed their 28 days follow-up while 5 patients either withdrew from the study or lost to follow up due to various reasons. Adequate clinical and parasitological response (ACPR) was observed in 100% of cases. Neither early treatment failure (ETF) nor late clinical failure (LCF) was observed in this study.

Behavioral change in anopheline vectors in areas of insecticidal nets (ITNs/ LLINs) use in Madhya Pradesh and Chhattisgarh: a possible challenge to malaria elimination programme

The study is continuing in Dindori district of Madhya Pradesh and Korea district Chhattisgarh with the objective to generate data on the behavioural changes in anopheline vectors due to use of LLINs. Six villages of 2 CHCs in each of district were selected for study. Two known malaria vectors viz. *An. culicifacies* and *An. fluviatilis* were found prevalent in both districts. During the study, large number of unfed mosquitoes were found inside houses which may be due to the effect of LLINs being used by the households. Out of 1551 (1064 from Dindori and 487 from Korea) samples of *An. culicifacies*, only 2 samples from Dindori

district were detected sporozoite positive (*Pf* strain). Further, *An. culicifacies* was found to be resistant to DDT, malathion and two pyrethroids i.e. alphacypermethrin and deltamethrin as per WHO susceptibility tests carried out in both the districts.

Public Health

- **Control and management of TB among Saharia:** ICMR-NIRTH, Jabalpur continued its intensified tuberculosis control programme among Saharia PVTG of M.P where there is high prevalence of TB. During the period under report, a total of 31222 presumptive TB cases were identified and tested and 3250 TB cases were detected and put on treatment. The success rate of treatment continued to be more than 90%.
- **National serosurvey for SARS COV-2:** ICMR-NIRTH was part of ICMR's National serosurvey for SARS COV-2 conducted by ICMR. Three rounds of serosurvey were conducted in 3 districts of M.P., Gwalior, Ujjain and Dewas. Health care workers of these 3 districts were also screened during Round III in December. Serosurvey was also conducted in hotspot city Indore.
- A total of 1,45,702 patients have been registered under **India Hypertension Control Initiative in Madhya Pradesh**. Blood Pressure control rate was 37% for MP. Lowest in Sehore (25%) and highest in Chhindwara (41%).
- Centre achieved 91% reduction of indigenous cases of malaria in Mandla district during June 2017 to Sept 2020 through case management and conventional vector control strategies in malaria elimination demonstration project.

ICMR - NATIONAL INSTITUTE OF EPIDEMIOLOGY, CHENNAI (ICMR-NIE)

COVID-19 National Serosurveys

ICMR conducted three rounds (round 1: Apr - May 2020; round 2: Aug – Sept 2020; round 3: Dec

2020 - Jan 2021) of nationwide a community based serosurveys between April 2020 and Jan 2021, to measure the extent of SARS-COV-2 infection and track the progress of pandemic in India. These serosurveys were coordinated by ICMR-NIE and were conducted by different ICMR institutes.

For these surveys, 700 clusters (villages in rural areas and wards in urban areas) were selected from 70 districts across 21 states/Union Territory. From each district, a minimum of 400 individuals aged ≥ 10 years were selected through a probability sampling method. The serum samples were tested for the presence of IgG antibodies against S1-RBD and nucleocapsid protein of SARS-COV-2 using chemiluminescence immunoassay. The weighted and test adjusted seroprevalence of IgG antibodies against S1-RBD and/or nucleocapsid protein was estimated along with 95% CI. In each round of survey, a minimum of 28,000 participants were enrolled.

The seroprevalence of IgG antibodies during the Apr-May 2020 was less than 1% and increased to around 7% by Aug-Sept 2020. The seroprevalence by the end of December 2021 was 24%. The seroprevalence did not differ by sex and age groups. The seroprevalence was higher in urban slum and non-slum areas compared to rural areas (Table 2).

Table. 2. The estimated number of SARS-COV-2 infection and infection to case ratio at the three time-points.

	Serosurvey 1	Serosurvey 2	Serosurvey 3
Study period	April - May 2020	August - September 2020	December 2020 - January 2021
Study population	Individuals aged ≥ 18 years	Individuals aged ≥ 10 years	Individuals aged ≥ 10 years
Number of Individuals enrolled	28,000 (92.5)	29,082 (82.6)	28,598 (81.5)
Overall seroprevalence* (% , 95% CI)	0.73 (0.34-1.13)	7.1 (6.2-8.2)	24.1 (22.9 - 25.4)
Total infections (in million) (95% CI)	6.46 (3.82-11.1)	74.3 (65.3-83.3)	271.4 (259.0-284.9)
Infection to case ratio (infections/ COVID-19 case)	81.6 (48.3-141.4)	31.8 (27.9-35.6)	27.1 (25.8 - 28.4)

Persistence of humoral immune response to SARS-COV-2 up to 7 months post-infection

Information about longevity of antibody mediated immune response in convalescent COVID-19 patients is vital in understanding the duration of immunity. A study was conducted to determine the longevity of humoral antibody response among COVID-19 patients. Blood samples were collected from recovered COVID-19 patients at the following seven time-points (i.e. 15–30, 31–60, 61–90, 91–120, 121–150, 151–180 and 181–232 days) since their RT-PCR confirmation. The sera were tested for the presence of IgG antibodies against nucleocapsid (NC) and spike (S1-RBD) proteins using chemiluminescent immunoassays, and neutralizing antibodies (NAbs) using surrogate virus neutralization test (sVNT).

A total of 755 individuals (minimum 100 participants in each time-group) were enrolled in the study. Seropositivity for IgG against NC, S1-RBD and Nabs is summarized in (Fig. 32).

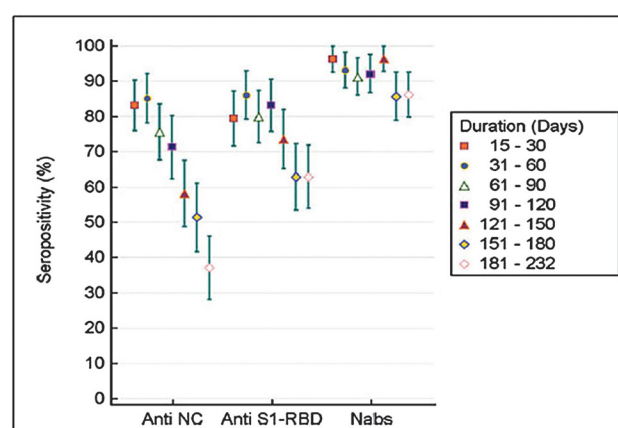


Fig. 32: SARS-COV-2 specific IgG seropositivity (%) with 95% CIs among recovered COVID-19 patients by duration since infection (N = 755).

The findings of the study indicated that IgG antibodies against NC and S1-RBD waned over time but the neutralization function of the antibody remained stable in majority of the COVID-19 infected patients till 7 months of post-infection. These findings suggested a lower possibility of reinfection by the same viral strain among infected individuals during the 7 month period.

COVID-19 testing, timeliness and positivity from ICMR's laboratory surveillance network in India: Profile of 176 million individuals tested and 188 million tests, March 2020 to January 2021

In early 2020, ICMR set up a national laboratory network for diagnosis of SARS-COV-2. By March 2021, 176 million individuals and 188 million tests were conducted in India. This database was analyzed to describe the epidemiology of the pandemic at national and sub-national levels. The following indicators were estimated: incidence of COVID-19 by age, gender and state and tests per 100,000 population, the proportion of symptomatic individuals among those tested, the proportion of repeat tests and test positivity.

The overall incidence of COVID-19 in India was 0.8% and 12,584 persons per 100,000 population underwent SARS-COV-2 testing. 6.1% of individuals tested had a positive result. 10 States/ Union Territories accounted for about 75.6% of the total cases (Fig. 33).

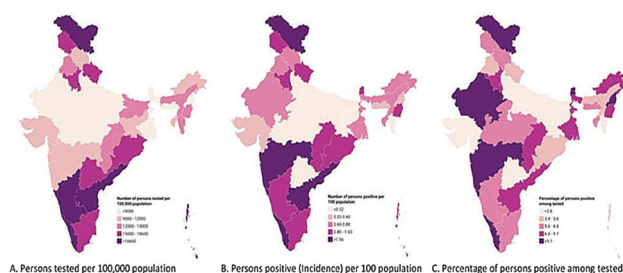


Fig. 33: State-wise distribution of COVID-19 testing, incidence and positivity among tested individuals, India (March 2020 to January 2021).

Daily testing scaled up from 40,000 initially to nearly one million in March 2021. The laboratory network set-up by ICMR was scaled up massively over a short period, which enabled testing a large section of the population. Timeliness between the various surveillance activities was acceptable, indicating good responsiveness of the surveillance system.

India Hypertension Control Initiative

At least one in three adults in India has hypertension. Still, only about 10% of them have their blood

pressure under control. To achieve India's target of a 25% relative reduction in the prevalence of raised blood pressure, approximately 4.5 crore additional people with hypertension need blood pressure control. To support the states in achieving the goal, the India Hypertension Control Initiative (IHCI) was launched in November 2017. The project is coordinated by ICMR-NIE and ICMR HQ. The project has five core strategies, namely standard treatment protocol, uninterrupted drugs supply up to the most peripheral level facilities, task sharing, decentralized care closer to patient's home and cohort based monitoring system using an app or card based system (Fig. 34). Between 2018-2021, 101 districts across 19 States enrolled more than 1.9 million patients in 12,300+ health facilities. Nearly half of the facilities where the project was implemented were Health Wellness Centres. In the 26 initial districts, almost one-fifth (22%) of the district's estimated total number of people with hypertension were enrolled. Among patients initiated on treatment, nearly half achieved control, and one-fourth did not visit regularly.



Fig. 34: Five core strategies of India hypertension Control Initiative

The project demonstrated the feasibility of hypertension management in primary care using standard treatment protocols with low-cost antihypertensive drugs. Supportive supervision was one of the project's important components, ensuring rapid feedback and response to various field-level challenges. The project strategies are being integrated with the national program in a phased manner.

Measles and rubella seroprevalence to evaluate the impact of the mass vaccination campaigns in India: Pre-and post- cross-sectional household serosurveys in four Indian districts, 2018-2020

India conducted phased measles-rubella supplementary immunization activities (MR-SIAs) targeting children aged 9 months to <15 years from 2017 to 2019, introducing rubella vaccine into the Universal Immunization Programme. Measles and rubella seroprevalence was measured before and after the MR-SIAs to estimate the impact of MR-SIAs.

Community-based, cross-sectional serosurveys were conducted in four districts in India before and after MR-SIAs. Thirty villages or wards were selected within each district and one census enumeration block from each of them was selected as the survey cluster. Households were enumerated and 13 children each in the age groups of 9 months to <5 years and 5 to <15 years were randomly selected. Socio-demographic characteristics, vaccination history, and venous blood were collected after obtaining consent. Serum samples were tested for IgG antibodies to measles and rubella viruses by enzyme immunoassay.

Specimens were collected from 2570 children before and 2619 children after the MR-SIA. Overall campaign coverage was 85.7% (range 74.3% to 93.6%). After the MR-SIA, measles seroprevalence among younger children increased to above 90% (range 91.5% to 96%) in all the districts except Kanpur Nagar where it remained unchanged (80.4%). Among older children, measles seroprevalence increased to above 90% (range 93.7% to 96.5%) in all the districts except Hoshiarpur (88.7%). A significant increase in rubella seroprevalence was observed in all districts in both age groups with the largest impact in Dibrugarh, where rubella seroprevalence increased from 10.6% to 96.5% among younger children.

The findings of the serosurveys indicated that measles and rubella seroprevalence had increased

significantly following the MR-SIAs, but population immunity appeared to be insufficient to achieve measles elimination goals.

Verification of sub-national claims for progress towards TB free status, India, 2020

Central TB Division (CTD) decided to incentivize the states/districts by giving monetary and non-monetary awards, based on the percentage reduction in TB incidence in 2020 compared to 2015. These achievements were considered under four categories: 20-39% (bronze), 40-59% (silver), 60-79% (gold), $\geq 80\%$ (TB free). During 2020, claims for reduction in TB incidence was submitted by 67 districts, 1 state and 2 UTs. CTD identified ICMR-NIE, Chennai, as the independent agency for verifying the claims submitted by States/districts. ICMR-NIE partnered with the Indian Association for Preventive and Social Medicine (IAPSM), World Health Organization (WHO) – Country office India and ICMR- NIRT for verifying the claims.

TB incidence for the year 2020 was estimated by the three methods (direct, indirect and drug data-based). In the direct method, incidence of TB was estimated based on incident cases of TB identified during the community-based survey conducted in each district. An underreporting factor was calculated for each district by matching the incident cases detected in the survey with the TB notification system. In the indirect method, incidence was calculated based on TB notification adjusted for under-reporting factor. TB incidence was also calculated from the drug sale data in the private sector and drug utilization data in the public sector. We compared the three estimates of TB incidence in 2020 with TB incidence in 2015. The decline in incidence was calculated by comparing the 2020 incidence, estimated by different methods with baseline incidence of 2015. We used predefined, standard criteria based on this decline to determine eligibility for awards. A combination of quantitative (survey and secondary data review) and qualitative techniques were used. Survey data were collected

using a mobile application developed by the WHO-India and the secondary data was captured in a web application developed by ICMR-NIE.

The community-based survey was conducted in 73 districts between 8 February and 12 March 2021 by 645 survey teams. Field teams contacted 355,171 households, interviewed 11,92,808 participants, and collected sputum samples from 24,886 eligible individuals. MTB was detected from 998 samples. TB incidence in Kerala, Lakshadweep, Puducherry, and 35 districts had declined by at least 20% since 2015. Budgam district and Lakshadweep in India were declared TB-free in 2020 (Table 3).

Table. 3. Summary of recommended awards for subnational progress towards TB Free status, 2020.	
Category	District/ State/ UT
TB free	2
Gold	1
Silver	4
Bronze	31
Not recommended	32

ICMR-NATIONAL INSTITUTE OF MEDICAL STATISTICS, NEW DELHI (ICMR-NIMS)

Clinical Trial Registry-India

CTRI is an online portal for registering Clinical Trials conducted in India and surrounding countries who do not have trial registry of their own. CTRI is coping with the voluminous amount of trials being submitted in the era of COVID-19 pandemic by working 24 X 7. It has implemented the Result Disclosure on its portal as per WHO recommendation. CTRI has also incorporated customized data set items from Ayurveda studies. Total number of trials registered in CTRI till March 2021 are 32470.

HIV Burden Estimation in India

The biennial HIV Estimation exercise is carried out in India by ICMR-NIMS in collaboration with National AIDS Control Organization (NACO),

Ministry of Health and Family Welfare (MoHFW), GOI since 2003. This round of HIV Estimation provided updates on the status of HIV epidemic in India at the national and State/UT level. The district level HIV estimates on key indicators have been generated to respond to the needs of the National AIDS Control Programme (NACP) of providing more nuanced epidemiological information on the HIV epidemic at the district level.

District-level HIV Burden Estimates (2019) corroborates the diversity of HIV/AIDS epidemic in India. The adult HIV prevalence in the districts of the country ranges between <0.10% and 4.00%. The number of people living with HIV (PLHIV) in the districts ranges between <100 and 57,000, with around 90% of infections in 360 districts. The annual new HIV infections (among people aged 15+ years) in the districts range between <50 and 2,600, with around 90% of the new infections in 340 districts. The annual prevention of mother-to-child transmission (PMTCT) needs in the districts ranges between <10 and 450, with 90% of the total PMTCT need in 400 districts (Fig. 35).

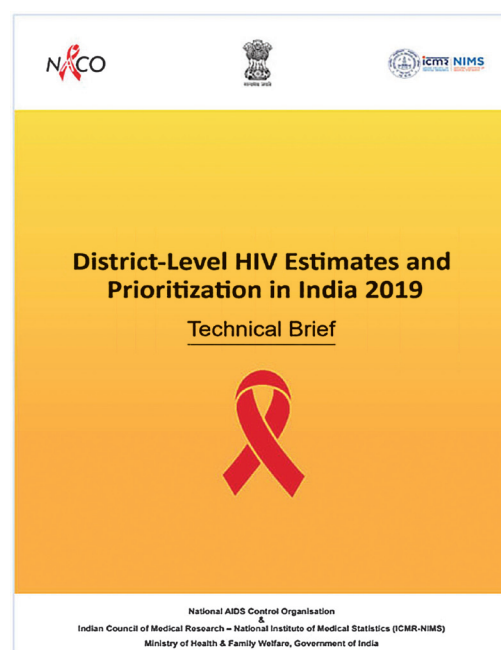


Fig. 35: HIV burden estimation in India.

National Data Quality Forum

The National Data Quality Forum (NDQF) is a multi-stakeholder, collaborative platform for a

sustained dialogue among the producers and users of demographic and health data in India on issues related to data quality and potential solutions, and for supporting institutionalization of promising solutions.

- **Data quality guideline:** Different sections of the “National data quality guidelines for surveys” were drafted. The guideline aims to educate the data producers and users on best practices and strategies to set up institutionalized and project-specific data quality assurance mechanisms and systems to ensure data quality in surveys.
- **Webinars:** To sustain and deepen interest on importance of data quality among producers and users of data, 10 webinars were conducted where experts were invited to share their experiences on importance of maintaining quality in various domains of survey, including phone surveys, anthropometric data, health and malnutrition and administrative data. Besides webinars, 2 blogs and 3 infographics were also developed.
- NDQF has collaborated with the Health Management Information System (HMIS) division, MOHFW, to improve the quality of HMIS data recording and reporting.

Spatio-Temporal Variations in Malnutrition among Children of Tribal and Non- Tribal Population of India: Level & Trends from various rounds of NFHS (1992-2016)

The study developed an online geo-referenced database on malnutrition among children for Tribal and Non-tribal populations for each state and district of India by using the data of three rounds of National Family Health Survey. The results shows that the burden of childhood undernutrition varied significantly across the social, economic, demographic and contextual factors in India. Maternal education status, wealth status, extended birth intervals and maternal body mass index (BMI) were significantly associated with anthropometric deprivation of children in India. Investing in

maternal education, improving nutritional status of mothers, focussing upon healthy birth spacing to increase the size of birth interval, six months of exclusive breastfeeding and more may also go a long way in improving childhood nutritional status in India. The findings underscore the need to devise targeted policy interventions to ameliorate nutritional deprivation among children, particularly from the tribal population with the most deprived socioeconomic characteristics.

Strengthen Research in Ayurveda by utilizing the CTRI Platform and Impart Capacity Building Program in Research Methodology

ICMR-NIMS has undertaken the task to utilize CTRI data to strengthen research in traditional medicines under the ICMR task force for leveraging Traditional System of Medicine. Under this project, the CTRI has undertaken to develop a distinct data set which is comprehensive, and tailor made for sharing research details of Ayurvedic studies. The health condition Section has been developed, with 3866 codes, using the classification coding from the NAMASTE Portal of Ministry of AYUSH. Intervention/comparator section has also been modified as per detailing of the Ayurveda trials in consultation with experts from Central Council for Research in Ayurvedic Sciences.

Evaluation of Impact of Antiretroviral Therapy under National AIDS Control Programme in India [The ART Impact Evaluation- India Study (ARTIE-India)-Northern Region

The study on Impact Evaluation of ART under NACP, shows that Government of India’s free antiretroviral treatment initiative has been a success story for the National AIDS Control Program (NACP) in terms of reducing mortality, improving survival and quality of life, achieving viral suppression and preventing TB among those who have been retained with the program. While the programme has shown overall impact in terms of survival benefits, to further improve upon these the focus needs to be on improving monitoring of PLHIV on ART and improving access to next-line ART.

Development and pilot testing of intervention strategies for smokeless tobacco and areca nut cessation among tribal women in Manipur

The overall objective is to develop culturally appropriate cessation strategies for smokeless tobacco and areca nut use among tribal women users in Manipur. Data collection for the study is in progress.

Investigating foetal and maternal factors for perinatal mortality in India- A systematic review and Meta-Analysis

The study aimed to identify maternal and fetal factors predicting perinatal mortality in India which will enable us to generate strong evidence and streamline future thrust areas for research. This systematic review suggested that maternal age, parity, higher birth order and maternal anaemia were major risk factors of perinatal mortality in India. Complications during pregnancy like antepartum haemorrhage, preeclampsia, obstructed labour, preterm labour were also documented as risk factors similar to those by other published studies. Fetal factors like gestational age and low birth weight were documented as risk factors for perinatal deaths. The results of this review will help in informing policy and further streamlining future thrust areas of research and assist policy makers in planning, developing, and implementing public health interventions which provide adequate antenatal and obstetric care services. This will ultimately lead to improvement in maternal health and reducing perinatal mortality at both the individual and community levels.

Gain in life expectancy by age after elimination of death due to specific cause in selected states of India using MCCD data

The study estimated the gain in life expectancy by sex and age after partial and complete elimination of ten leading causes of deaths viz., certain infectious and parasitic diseases (A00-A99); neoplasms (C00-D48); diseases of blood & blood forming organs & certain disorders involving the immune mechanism (D50-D89); endocrine,

nutritional and metabolic diseases (E00-E89); diseases of the nervous system (G00-G98); diseases of the circulatory system (I00-I99); diseases of the respiratory system (J00-J98); diseases of the digestive system (K00-K92); diseases of the genitourinary system (N00-N99); and injury, poisoning and certain other consequences of external causes (S00-T98) in India and 15 selected states using multiple decrement life tables and cause-eliminated life tables.

Results show that the maximum benefit in terms of gained years in life would be obtained after reducing mortality from diseases of the circulatory system which is a major public health problem and is leading to premature deaths and morbidity across all selected states of India. These findings may have implications for practical decision making in setting up health goals, allocating resources and launching tailor-made health care programmes. The reduction in mortality due to the causes and its effect on the changes in life expectancy at birth is a useful way to evaluate the impact of interventions on population health and setting priorities for health research.

Mental Health and social stigma among healthcare personnel involved in the management of COVID-19 patients in India- Data Management, Analysis and reporting unit

The aim of this study was to determine the burnout levels and factors associated with the risk of psychological distress among healthcare workers (HCW) engaged in the management of COVID-19 in India. The study showed that positive facilitators for coping include appreciation from the society, health authorities and feeling of being useful despite the risk. There was a need for psychological support services, a strong and vigilant health system to respond to the challenges that HCWs face and provide them with what they require such as health insurance, incentives and support to balance work and family. The role of media to promote right information and prevent misinformation as well the need for strong community engagement

in sensitization of communities through positive approaches was recommended.

Factors related to COVID-19 Stigma: A Mixed Methods Study

This study provided insights into the stigma associated with the COVID-19 and suggested potential strategies for mitigation of such stigmatization. Majority (80.5%) of COVID-19 recovered participants experienced at least one form of stigma and 51.3% of respondents from the community reported severe stigma attitudes towards those diagnosed with COVID-19. Fear of infection and lack of adequate knowledge were associated with stigma. Qualitative data analysis suggested that stigma, in few cases, resulted in non-disclosure of COVID-19 status and delayed treatment. Study highlighted the need for timely interventions to mitigate stigma by increasing awareness on the modes of transmission and measures of prevention of COVID-19 and misconceptions of risk that promote stigma through visual, print and social media. Additionally, psychosocial intervention strategies through trained counsellors should be provided for those quarantined, infected as well as recovered for better coping and acceptance in the community.

Impact of COVID-19 on maternal and child health services through the public health system in India

The study assessed the impact of the ongoing COVID-19 epidemic on the Maternal and Child health service in India. The immediate impact assessment was done via a two-pronged strategy, the rapid assessment survey with structured tools (questionnaires) through telephonic interviews of both the health care workers and MCH beneficiaries and analysed the data available through the Health Management Information System (HMIS).

The ANC registration in 2020 witnessed a decline in the month of March and April in all seven states compared to 2019. The major challenges faced by the beneficiaries were related to lack of transport facilities during the lockdown, interrupted hospital-based services both in public and private health

facilities, and disrupted outreach services like routine antenatal care and supplementary nutrition. As reported by health officials, the supply-side challenges were mainly linked to lack of infrastructural preparedness for outbreak situations and a shortage of human resources at health facilities. The quarantining of medical staff further lead to the shortage of staff at health facilities. The frontline workers of ASHA/ANM were diverted in COVID-19 duties, which reduced referral cases by ANM/ASHA. In order to maintain continuum of care during pandemic a holistic approach is required, which focusses on both preparedness and response to the outbreak as well as reassignment and reinforcement of health care professionals to cater to essential health care services.

National Clinical Registry for COVID-19

National Clinical Registry for COVID-19 is a comprehensive, systematically collected database covering different regions of the country allowing both researchers and policy makers to make relevant hypotheses, gain important insights into COVID-19, and trends in the pandemic process (Fig. 36).

A digital platform for collecting data was developed using the PHP language and mysql on the back end.

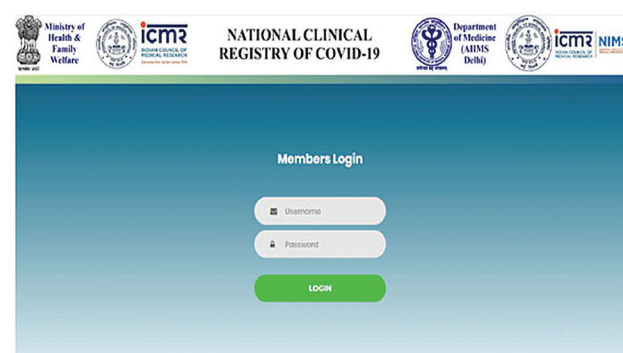


Fig. 36: National Clinical Registry for COVID-19.

Public Health

- Clinical trials registry India, a flagship programme of ICMR is hosted at the ICMR-NIMS and running successfully for the last 13 years and catering to the clinical research. In India and neighbouring countries where there

is no trial registry of their own. At present more than 32470 trials are registered and maintained in CTRI. Recently a separate data set items have been developed for registering Ayurveda studies. IPD sharing and result disclosure commitment has been incorporated in CTRI portal.

- National Data Quality Forum established at ICMR-NIMS to create ecosystem to ensure data quality. A draft guidelines entitled “National Data Quality Guidelines for Surveys” was prepared. Ten webinars were conducted.
- HIV 2019 estimates have been generated for all 735 district of India and the report is available on NACO website.
- The Institute conducted an Online Workshop on Introduction to Systematic Reviews and Meta-Analysis in health research (Fig. 37 & 38).



Fig. 37: Focus group discussion in Changangai Kabui village, Imphal West District.



Fig. 38: Online workshop on Introduction to Systematic Reviews and Meta-Analysis in Health Research.

EXTRAMURAL RESEARCH

Virology

An unprecedented worldwide spread of the SARS-COV-2 started in January, 2020 when severe challenges on India's healthcare facilities and medical infrastructure were faced. Indian Council of Medical Research (ICMR)-National Institute of Virology (NIV), Pune the standalone lab for COVID-19 testing then standardized the rRT-PCR based diagnostic test. On January 30, 2020, ICMR-NIV, Pune reported first case of COVID-19. The virology unit worked hand-in-hand with senior leadership at the ICMR HQ, NIV and other ICMR institutes to meet the challenges that arose in the wake of this pandemic. Key achievements are summarized below.

- The capacity for COVID-19 testing was exponentially increased across the country reaching to 2435 laboratories by March, 2021. Immense efforts were put in to establish labs in difficult terrains like Ladakh, Sikkim, Arunachal Pradesh, Nagaland, other NER states and islands like Lakshwadeep and Andaman & Nicobar.
- Multiple mentor institutes (institutes of national standing like AIIMS, PGI and PGIMER) were roped in to train and hand-hold multiple government labs to enable them to start COVID-19 testing. As a result, a COVID-19 testing lab was made operational in all the medical colleges of the country.
- A common sample referral form (SRF) was developed and deployed with the help of National Information Centre (NIC) through the RTPCR application.
- To understand the disease trend in a real time manner, a uniform data entry portal was developed with BMI division.
- To ascertain the quality of COVID-19 testing by these laboratories, a quarterly Quality Control program and external quality assurance program was implemented for rRTPCR laboratories.

- Apart from rRT-PCR technology, other different platforms – TrueNat, CBNAAT, high throughput machines (Cobas 6800 and 8800) were also roped in with help of manufacturers of these platforms.
- Validation of Rapid antigen test was done at three hospital locations across NCR and the test was rolled-out that helped ease load on rRT-PCR based testing and provided results in a quick turn-around time.
- Apart from deploying infrastructure for COVID-19 testing and implementation of technologies, a systematic platform for validation of diagnostic commodities was developed by setting up of 24 validation centres. Taking India's agenda forward of *self-reliant India*, ICMR approved 72% of the indigenous test kits which resulted in cost reduction of single rRT-PCR test. Moreover, to have an uninterrupted supply of diagnostic commodities across the country, 16 depots were set up by ICMR.
- Ten COVID-19 biorepositories for helping industry/academia with appropriate samples of SARS-COV-2 for developing indigenous diagnostics etc. have been established.
- The Virology unit co-ordinated multiple scientific studies done at NIV Pune to help
- Development of indigenous whole virion inactivated vaccine by Bharat Biotech International Ltd.
- Laboratory assays like the gold standard Plaque Reduction Neutralization Test (PRNT) was established.
- Animal challenge experiments were conducted to understand the efficacy of vaccines and therapeutics.

b) COVID-19 Vaccine Trials

- i. COVAXIN of Bharat Biotech International Ltd (BBIL).
- ii COVID-19 vaccines manufactured by Serum Institute of India.
- iii Pre-clinical studies of ZyCOV-D of Zydus Healthcare.

c) Other Activities

- Laboratory studies for development of monoclonal antibodies for COVID-19 prophylaxis and treatment have been successfully completed. Clinical evaluation and next steps are being taken up.

India TB Research Consortium

- India TB Research Consortium (ITRC) is a flagship programme of ICMR and DHR to tackle TB in a mission mode. The significant achievements of the programme are development of the New indigenous cost effective molecular Point of care (POC) diagnostics for detection of TB/MDR-TB and also paediatric and extrapulmonary TB which has been successfully adopted by National Programme after recommendations of ICMR. Three new kits for improved smear microscopy at peripheral level and a simple bio-safe sputum transportation and DNA extraction kits have also been validated by ICMR and recommended to NTEP.
- ICMR completed multicentric validation of the new skin test C-Tb in 6 states and the sensitivity

a) Virus Isolation

Three different strains of SARS-COV-2 were isolated and cultured at ICMR-NIV, Pune – original, UK variant and Brazilian variant. Virus isolation paved the way for development of following technologies:

- Indigenous ELISA IgG kit by NIV, Pune. Technology was transferred to 7 Indian companies.
- Hyper-immune horse serum, which offers a promising tool for prophylaxis and treatment of SARS-COV-2 exposed/ infected individuals. ICMR has provided the virus and is working closely with three companies for clinical development of this product.

of C-TB is higher in General population, high risk population in adults and Children above 6 yrs. (although the number of children were less) as compared to TST while the specificity is comparable. The safety of C-Tb and TST at 48 hrs and at 28 days is comparable. The C-TB can be used for detection of latent TB in adult population under the NTEP.

- The ICMR also recommended high dose rifampicin (25mg/kg BW) for Drug sensitive TB in the standard treatment for improved treatment outcomes, to the national programme. The all oral 6-9 months shorter regimen with 4 drugs i.e Bedaquiline, Delamanid, Clofazimine and Linezolid were also found to be effective for treatment of XDR-TB and has been recommended to National Programme.
- A Phase III regulatory clinical trial for evaluating the safety and efficacy of two TB vaccines: VPM1002 and MIP (indigenous vaccine), as against Placebo is ongoing at 8 main sites with 10 sub-sites. The trial completed enrolment of 12717 participants in December 2020, who are under different stages of follow-up. The safety analysis has shown that both the vaccines are safe and acceptable. The follow-up for efficacy is ongoing.
- A recently concluded study by ICMR, revealed that routine screening for symptoms & Chest X-testing for high risk groups (all patients aged 60 years or more, all diabetics, all people living with HIV and all patients admitted to medical wards) visiting health care facilities for any reason to increase TB case detection. The study showed that current diagnostic algorithm (2 spot and one overnight sputum sample) can be simplified by limiting sputum collection to a single spot sample only.
- Under the implementation research, active case finding in severely malnourished children admitted to nutritional rehabilitation centres has shown very high (5%) incidence of TB and the case detection can be improved with proper training and providing point of care diagnostic tests under national Programme. Interim results

of a Cluster randomized trial of nutritional support to TB patients and their HH contacts in communities with high prevalence of under nutrition in Jharkhand has shown significantly lower mortality rates in the patients and reduction in TB incidence in HHCs.

- **National TB Prevalence Survey:** National TB prevalence survey for prevalence of national and state-wise data on TB and latent TB along with health seeking behaviour has been concluded by ICMR and the report shared with CTD. This mega survey is a significant contribution and will help immensely in tackling TB elimination of India.

Tribal Health Research

- Under an implementation research project entitled, “Prevention and Management of Snake Bite and Scorpion Bite envenomation including complications within primary health care system in tribal block of Dahanu, Palghar, Maharashtra”, a situation analysis of the Dahanu block to assess the local disease burden suggested that snake bite envenomation and scorpion sting is one of the most common public health problems in this tribal region. 394 scorpion sting cases and unknown bite as 4259 was recorded. The 3 year average incidence rate of snake bite has been reported to be 121 per 100,000, ranging from 104 to 147 per 100,000 when the entire population was assumed to be at risk, with a peak in the month of July. IEC materials, training manuals were distributed in the community and primary health care system alongwith ASHA, ANM and MPW to empower them on prevention, diagnosis and management of snakebite envenomation. Based on the study’s findings, a multisectoral model is developed to reduce mortality and morbidity due to snakebite envenomation. ICMR National Task Force on snakebite recommended scaling up the study at the National level. The study is being implemented in Maharashtra and Odisha states in Phase I. Technical support has been provided by ICMR-NIRRH, Mumbai, to the

Government of Maharashtra for capacity building of medical officers for snakebite management as per the national protocol (STG, 2017).

- During a field study of environmental reservoirs of *Vibrio cholerae* serogroups in the tribal areas of Odisha, efforts were done to isolate different serogroups of *V. cholerae* from water bodies like river, nala, chua from the study blocks. The *V. cholerae* O139 strains from river water and reports were submitted to the concerned health authorities. People were made aware not to use the river water for cooking and washing utensils, as a result of which, a possible cholera outbreak was averted. 18 *V. cholerae* O1 strains were detected from the planktons and stool samples, which showed close similarity among themselves through multiplex PCR assays. The major reservoirs of *V. cholerae* in the flowing water bodies like river, stream was detected in the partial stagnant condition of water and also in the water bodies which is a major breakthrough of this study.
- On the basis of a letter received from Ministry of Environment, Forest and Climate change, on the directives of National ST Commission, health assessment and projection of health of people living in 33 villages of Tamnar block, district Raigarh, Chhattisgarh was undertaken by ICMR-NIRTH, Jabalpur. The study assessed the health & nutritional status and cause of deaths among tribes residing in Tamnar. The investigation included collection of data on demographic and socio-economic particulars of the households, anthropometry; clinical examination for general morbidity and nutritional deficiency disorders. Since this was the first such study undertaken in this area, it helped the local government in planning specific health programmes in this area. The conclusion report along with major recommendations for taking further action was submitted to the Ministry of Environment, Forest and Climate change.
- Under an ongoing Task Force study entitled, “Assessment of neonatal screening approaches

for Sickle Cell Disease (SCD) and effect of early intervention in management of the disease in tribal populations”, which is ongoing and being coordinated by ICMR-Hqrs. at 7 centres in 6 states, a total of 7708 newborns were screened during the reported, of which 6493 (84.2%) samples showed AA pattern, 1131 (14.7%) showed AS pattern and 66 (0.9%) newborns showed SS pattern. 0.2% newborn samples showed presence of other variant hemoglobins. A caste-wise analysis was available in 67 out of 68 SCD newborns (66: HbS homozygous, 2: HbS- β -thalassemia) identified. All together, 40.2 % of the newborns were detected in Vasava caste, followed by Gond tribe (7.5%). A total of 197 newborns SCD newborns were followed up. It was observed that 14.7% babies had pallor, 5.6% had acute respiratory infections, 4.6% of the babies presented with acute pain crisis, 3% newborns showed acute febrile illness. 2% newborns needed blood transfusion. Further study is in progress.

North-East Region Research

- Under the project entitled, “Effectiveness of Single Dose of live attenuated SA 14-14-2 Vaccine against Japanese encephalitis (JE) in adults over a period of three years in two districts of Assam, India”, which was conducted by ICMR-RMRC-NE, Dibrugarh, a single dose of live attenuated SA 14-14-2 JE vaccine was administered among adults (15-65 years) in Sivasagar and Dibrugarh districts of Assam. The study, which aimed to assess long-term effectiveness of the single dose of the vaccine, showed that despite the decline in effectiveness over seven years in two highly endemic areas of Assam, the vaccine provided ample protection for the endemic regions for ~6 years post-vaccination. In the seventh-year, effectiveness of the vaccine is seen to reduce to statistically insignificant levels. However, it is worth mentioning that there has been an appreciable reduction in number of JE cases. The incidence rate (per 1 lakh population) dropped from around 12 during the pre-

vaccination years to around 5 in the post-vaccination years and was maintained at the same level in the seventh year too. Furthermore, it was found that the vaccine effectiveness fell from 91% (first year post vaccination) to 72% (7th year post vaccination). The fall through the years has been gradual and steady. The findings suggest that along with routine immunization programs in children, a single dose of the vaccine administered to the adults in JE endemic areas could provide the desired protection against the disease. The study also highlighted the actual vaccine coverage among various age groups in the study population.

- Sporadic epidemics due to fermented foods consumption are occasionally reported from different regions of NE India. Therefore, five fermented foods of Manipur were intervened and assessed for microbial safety using cultivation independent molecular analysis in a completed study entitled, “Quantifying the microbial risk in protein-rich fermented foods of Manipur to identify the critical control points and development of LAMP-based rapid diagnosis kit for major foodborne pathogens”. The study revealed a dominant presence of potential foodborne pathogens namely *Proteus mirabilis*, *Bacillus cereus*, *S. aureus*, *Clostridium spp.* and *Enterococcus faecalis* in the marketed protein-rich (soybean, meat, milk and fish) fermented foods of Manipur. The study reported a high presence of antibiotic resistance genes, which supported the risk associated with these foodborne pathogens. The study optimised the LAMP reactions for 10 WHO prioritised foodborne pathogens commonly present in the fermented foods of Manipur. A simplified version of LAMP reaction-based diagnostic kit in 96 well microtiter plate was achieved from this study.
- Apart from 3 ongoing multicentric Task Force studies on Paragonimiasis, Viral Hepatitis, Operational feasibility study on Malaria, which are being executed in all the North-East states of India, another Task Force study on HPV has been initiated during the reported period under

the North-East research programme of the Division. Persistence of high-risk oncogenic human papilloma virus (hr-HPV) infection, which occurs in minority of infections, is required for development of cervical neoplasia. The cause of persistence of HPV infection is still elusive. Sensitive markers to predict the subjects prone for persistence of infections is also elusive. Further, HPV prevalence data is not available for the eight Northeastern states of India and there are no data on the HLA polymorphism and epigenetic association studies with HPV infection from Northeast India. Thus, a multicentric project entitled, “Study on persistence of high-risk HPV infection and its association with specific epigenetic markers and HLA-class-II gene polymorphism among adult females from Northeast India” has been initiated to be carried out at 8 tertiary care hospitals in the NE India, which proposes to estimate prevalence of HPV infection and involves HPV genotyping in women attending gynecology OPDs in the collaborating centres located in different Northeastern India states, with an aim to explore persistence of HPC infection, which plays an essential causative role in the development of cervical cancer. In addition, the project will simultaneously address host factors including specific epigenetic changes in a set of genes and examine association of persistent HPV infection with specific polymorphism at the HLA Class II loci.

Antimicrobial resistance

The Indian Council of Medical Research (ICMR) has been supporting research on antimicrobial resistance through the Antimicrobial Resistance Research & Surveillance Network (AMRSN) since 2013. The data collected from the network has enabled compilation of drug resistance data on six pathogenic ie (i) *Enterobacteriales* causing sepsis (ii) Gram-negative non-fermenters (iii) Typhoidal *Salmonella* (iv) Diarrhoeagenic bacterial organisms, (v) Gram-positives: staphylococci and *enterococci*, and (vi) Fungal pathogens from thirty tertiary care hospitals/laboratories

across the country. Data collected from the network is used to track resistance trends and to better understand mechanisms of resistance in the key priority pathogens using genomics and whole genome sequencing (WGS). From the data collected through this network, *Escherichia coli* is most commonly isolated followed by the *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and *Staphylococcus aureus*. Imipenem susceptibility of *E. coli* has dropped steadily from 86% in 2016 to 63% in 2019 and showed slight recovery to 72% in 2020 and that of *Klebsiella pneumoniae* dropped steadily from 65% in 2016 to 46% in 2019 and remained at 45% in 2020. In *A. baumannii*, reduced susceptibility of 10-20% was observed against cephalosporins, carbapenems, monobactams and β -lactam- β -lactamase inhibitors. Among *Staphylococcus aureus* isolates, susceptibility to erythromycin, clindamycin, ciprofloxacin, co-trimoxazole and high level mupirocin was more evident in Methicillin sensitive *S. aureus* (MSSA) when compared to Methicillin resistant *S. aureus* (MRSA). The anti MRSA antibiotics such as vancomycin and tigecycline showed excellent in vitro activity (100% against MRSA isolates). Teicoplanin and linezolid resistance was encountered in MRSA isolates albeit at very low rates of 0.5 and 1 %, respectively. Fungal infections among hospitalized patients are significantly increasing. Majority of the fungal infections are caused by few common fungal agents nevertheless rare species are also increasing requiring newer treatment strategies. *C. auris*, multidrug resistant yeast known to cause hospital outbreaks has been consistently isolated from regional centres across India.

Based on the laboratory evidence and the inputs of clinicians, ID physicians and clinical microbiologists, the drug resistant difficult to pathogens can be classified into three groups (Table 4). The infections caused by the pathogens listed under Group I and II have been documented to be associated with high rates of mortality and morbidity, both in India and globally. Additionally, they increase hospital lengths of stay and result in major increase in healthcare expenditure and healthcare resource utilization.

For the first time in the history of ICMR, a structured program to strengthen antimicrobial stewardship programs in tertiary care hospitals of India has been initiated in Indian tertiary care hospitals. Through this program, the multidisciplinary teams in these hospitals were trained on AMSP and the hospitals were supported to establish a structure and framework of AMSP. This included setting up hospital AMSP committees, hospital antibiotic policy and establish framework to implement some of the practices of AMSP including the education and awareness activities on AMSP. Development of treatment guidelines and antimicrobial stewardship documents by ICMR and helped creating a national resource guidance document which formed foundation for launching this very important endeavour. The data collection from these hospitals show that broad spectrum antimicrobials, from Watch and Reserve list of WHO-AWARE classification are extensively used in tertiary care hospitals. There are increasing trends for MDR pathogens post COVID-19 pandemic.

Table 4. Difficult to treat drug resistant pathogens in Indian hospitals.

	Group I	Group II	Group III
Pathogens	- Carbapenem Resistant Enterobacterales - Carbapenem Resistant <i>A. baumannii</i> - Drug resistant <i>Salmonella</i> Typhi <i>Candida auris</i>	- ESBL producing Enterobacterales - Multidrug resistant <i>P. aeruginosa</i> - Vancomycin-resistant enterococci, - Azole Resistant <i>Candida</i> spp	- Methicillin Resistant <i>Staphylococcus aureus</i> - Azole resistant <i>Aspergillus fumigatus</i> - Amphotericin B resistant <i>Aspergillus flavus</i> - Drug-resistant <i>Stenotrophomonas maltophilia</i> - Colistin Resistant Enterobacterales - Colistin resistant <i>Acinetobacter</i> spp.
Action required for containment	Aggressive action	Sustained action	Continuous monitoring and prevention efforts

- **Group I pathogens** include pathogens that have become resistant to last-resort antibiotics including carbapenems, the best available antibiotics for treating multi-drug resistant bacteria and pose a high risk to patients. They can cause severe and often deadly infections such as ventilator-associated or hospital-acquired pneumonia, bloodstream infections and urinary tract infections. *Candida auris*, pathogenic yeast has also been included under urgent threat that causes bloodstream and other invasive infections and is resistant to most of the antifungal drugs.
- **Group II pathogens** include multi drug resistant bacteria, conferring high risk to patients, mainly prevalent in hospital acquired infections and is associated with serious multidrug-resistant infections and ventilator associated pneumonia, complicated urinary tract infections and surgical site.
- **Group III pathogens** include drug resistant bacteria that are responsible for only a small number of infections but detection and early prevention of such infections can have significant impact on public health and need to be carefully watched in future.

Vector Borne Disease & Zoonosis

Malaria Elimination Research Alliance-India, launched in 2019, had floated its first call for proposals. In year 2020-21, more than 40 projects have been formulated under Task Force multi-centre themes format. These projects are directed towards malaria elimination strategies and acceleration of malaria elimination. The ICMR Malaria Mission was announced, which is a step toward combining research efforts and bringing together research expertise from all the ICMR Institutes that work on malaria. ICMR-NIMR is coordinating the program.

In India, data in the health system is a major problem because it is often fragmented and not updated on a timely basis, discouraging young

people from doing analyses or planning research initiatives. From 2020 through 2030, India has pledged to eliminate malaria. In the view of this commitment, the ICMR-NIMR proposed a study to develop a district-level malaria dashboard application. The protocol for the study is now being reviewed.

It was decided to form a Task Force to continue the work on measuring vector resistance in the field. The ICMR scientists and professionals in the area have amended the common standard protocol considering the recent advancements and changes in methodology. In September 2020, a call for research proposals on Kala azar was announced, which will encourage interdisciplinary, innovative, close to practice research in the field of Leishmaniasis.

One Health

ICMR has been working in areas of zoonosis to strengthen its footprint and also taken initiatives to take forward research focused on One Health. It has supported extramural ad-hoc and task force studies which has been carried out on diseases like bovine tuberculosis, leptospirosis, coxiellosis, rabies, scrub typhus and anthrax which have been carried out at various in key institutes of human and animal research. A task force study involving 8 institutes was funded to determine the presence of Lyme disease causing agents and status of controversial Tick-borne LD in India. A nationwide multi-centric representative community survey has been carried out by ICMR-NIE Chennai to estimate the incidence of human rabies deaths and animal bite burden, a first of its kind in India. A Task force study under ICMR-RMRC, Bhubaneswar has been carried out across 14 blocks in Odisha's Koraput, an endemic tribal district for coordinated interventions to check animal-to-human transmission of anthrax. This is a first study applying One Health concept for the elimination of human anthrax in India. A policy brief document has also been developed under this study. An ICMR ICAR collaborative

study involving 4 sites have been carried out in Northeast region to investigate the prevalence of selected zoonotic pathogens in livestock and the status of intermingled ecological niche including environment and farm workers.

The construction work of the proposed ICMR-NIV Satellite Centre of One Health at Nagpur is under progress. To adopt a holistic and integrated approach towards solving health issues and developing a roadmap to steer One Health approach in the country a High Level Inter-Ministerial Steering Committee was constituted by DHR, and a meeting was held on 26th March 2021 which was chaired by Hon'ble Union Minister for Health and Family Welfare. The committee has also committed to support and guide the establishment of the National Institute of One Health at Nagpur as a knowledge centre for Eco Health in the country. A special issue of ICMR's Indian Journal of Medical Research dedicated on One Health has been published, which is serving as a useful resource for researchers, policy makers and program planners alike.

FOODBORNE & MYCOLOGY

Surveillance of foodborne Pathogens (FBP) from North-East India

This study will estimate the burden of food borne diseases so that risk of acquisition of infection from food can be assessed, which may provide a foundation for food safety policy and prevention efforts. The project consists of market survey, hospital survey, community survey and outbreak investigations. A staff training workshop was held from 1st to 3rd Dec 2020 at ICMR-RMRC, Dibrugarh. To maintain the uniformity across the centres, a Standard Operating Procedures (SOPs) for bacteriology and virology was developed and finalized for ICMR foodborne pathogens survey. MOU signed and 'Annual Monitoring indicators' developed to monitor the progress of the project.

Estimation of *Vibrio Cholerae* O1 infection in India: a step toward identification of cholera hotspots

This study will estimate incidence of *V. cholerae* O1 infections across 5 regions of India using sero epidemiological methods along with triangulation of data on cholera from available multiple sources (a) published literature and grey literature archives (b) program data like Integrated Disease Surveillance Program (IDSP), Field Epidemiology Training Program (FETP) reports, National Health Profile (NHP) maintained by Central Bureau of Health Intelligence (CBHI) and data on Swachh Bharat initiated sanitation drive (c) information from annual reports and (d) serological testing (vibriocidal) for cholera markers on stored samples collected during Dengue National serosurvey. Cholera Hotspot mapping of 15 states was done based on the composite score. Karnataka ranked the highest with a score of 170.8, followed by Madhya Pradesh, West Bengal, Odisha and Maharashtra with a score of 169.4, 168.8, 161.1, and 138.7, respectively. The results show Karnataka is more vulnerable to Cholera outbreaks based on IDSP and serological data in comparison to other states.

Network of advanced mycology laboratory and research centres

These are established in different geographical region of the country to provide diagnostic facility for patient care, create awareness and to establish a strong platform for fungal research to map the fungal infections in the country. These laboratories will provide a quality and range of services to public health not only in their hospitals but will cover the complete region. A 'Mycology unit' was developed to support the establishment of Advanced Mycology Diagnostic and Research Centre (AMDRC). Five centres initiated i.e AIIMS Bhopal, AIIMS Bhubaneswar, KGMU, Lucknow, PD Hinduja, Pune, Assam Medical College. MOU signed and 'Annual Monitoring indicators' developed to monitor the progress of the project. AIIMS Bhopal inaugurated 'ICMR Mycology Advanced Resource Centre' (iMARC) in the presence of Honorable Health and Union minister Dr. Harsh Vardhan and DG, ICMR on 13th Mar 2021.

Validation of a dry swab RNA-extraction-free method based diagnostic test for SARS-COV-2 compared with the standard VTM based swab collection method: A multicentric study

The RNA extraction free method of diagnostic test for SARS-COV-2 was validated in clinical setting. The aforementioned validation was implemented independently by two organizations namely the ICMR-NARI, Pune (n=584) and the School of Tropical Medicine, Kolkata (n=554). The overall sensitivity and specificity of the dry swab variant method (tested in 1138 samples) were found to be 78.9 % (95% CI 71% to 86%) and specificity was 99 % (95% CI 98% to 99.6%) respectively. The positive predictive value was 92 (95% CI 85% to 96%) and the negative predictive value was 97 (95% CI 96% to 98%). The overall concordance between VTM swab and dry swab method based output was 96.8 % and the discordance between the two methods was 3.2 %. The agreement between the tests was 96.8 % and the kappa value is 0.83 (0.77 to 0.89, SE=0.03).

Community voices for vaccines in India: A Rapid appraisal focusing on COVID-19

This qualitative study was a community consultation-based inquiry to explore the perception around COVID-19 vaccines among community members to understand their concerns and assess their readiness to accept COVID-19 vaccine. The study was conducted during January and February 2021, when the vaccine roll-out had not gained pace in three States viz. Tamilnadu, Kerala and Karnataka. Around 15- 18 interviews per state were conducted using pre-determined domains. Expression of hope and eagerness to receive COVID-19 vaccines was found in most of the respondents for reinstating the impact of the pandemic and resuming normalcy. Safety concerns and fear of side effects were found to be the major cause for vaccine hesitancy. Apprehensions around vaccines in the wake of rapid development and complacency following the declining trend of disease were identified

as other determinants of vaccine hesitancy. The community leaders indicated that safety concerns should be addressed effectively through responsive communication strategies.

HIV/AIDS & STIS

Collaboration with external agencies were formed for epidemiological and health system research projects as part of the National Task force on HIV related research. Projects related to psychosocial aspects such as stigma, mental health and psychological health of various population groups in India due to stigmatisation of their STI/HIV status were carried out.

Tool Development

In COVID-19 Operational Research project, ICMR developed tools for assessment of stigma among COVID-19 recovered and community individuals for assessment of experienced and perceived stigma. The team coordinated the validation of an artificial intelligence based tool for detection of Chest X-Rays of COVID-19 patients with respiratory symptoms. ICMR got involved in the development of the Indian Novel Claim Portal inovecop.

i-DRONE

ICMR participated in drone based vaccine delivery project in which the phase I study at IIT Kanpur was conducted in the first half of 2021 for the limited efficacy trials.

MRU & MRHRU Network

In the year 2020-21, a rapid response team of ICMR was formed to formulate public health response for combating COVID-19 pandemic. The National Task Force (NTF) on COVID-19 was constituted to guide the Ministry of Health & Family Welfare, Government of India in prevention and control activities for COVID-19 in the country. A total of 35 NTF Meetings were held during the year and treatment protocol for COVID-19,

an advisory on appropriate use of convalescent plasma in COVID-19 management and 6 versions of testing strategy in the pandemic were developed. Epidemiology & Surveillance Working Group on COVID-19 was also constituted to advise NTF on public health research priorities and develop research protocols. Three rounds of serosurvey on COVID-19 and 2 epidemiological studies were guided by ESG of NTF on COVID-19. The group also developed protocol for facility-based surveillance of the disease very early on in the pandemic.

The COVID-19 testing capacity was to be enhanced. The ICMR/DHR research network of Multidisciplinary Research Units (MRUs) and Model Rural Health Research Units (MRHRUs) were mentored to support the cause. 8 MRUs and 1 MRHRU initiated COVID-19 testing and 44 MRUs supported Viral Research & Diagnostic Laboratories (VRDLs) in terms of human resource and infrastructure. 16 Regional Distribution Depots were also established by ICMR for coordinating distribution of RT-PCR Test kits and reagents to all government laboratories in their respective regions.

Covaxin was given Emergency Use Authorization and was administered under Clinical Trial mode w.e.f 16th Jan, 2021. The monitoring of adverse effects due to the vaccine was undertaken by ICMR.

The Department of Health Research constituted a Core Committee and a Working Group to draft the new Health Research Policy considering the current national health priorities of health sector.

COVID-19 Registry

In April, 2020, ICMR initiated a Randomized Clinical Trial, to assess the role of convalescent plasma in moderate COVID-19 adult patients. Thirty-nine hospitals across the country participated in the trial. The trial concluded that Convalescent plasma was not associated with a reduction in progression to severe COVID-19 or all-cause mortality. This also led to update the treatment

protocol subsequently. The trial was also included in a metanalysis “Continuous Monitoring of Pooled International Trials of Convalescent Plasma for COVID-19 Hospitalized Patients (COMPILE)”.

In September 2020, ICMR initiated a National Clinical Registry for COVID-19 (NCRC) in collaboration with Ministry of Health & Family Welfare (MOHFW), All India Institute of Medical Sciences, Delhi (AIIMS) and ICMR- National Institute of Medical Statistics (ICMR-NIMS). The observational study has an objective to develop a digital COVID-19 registry to collect data regarding clinical and laboratory features, treatments, and outcomes of hospitalized COVID-19 patients in India, and 42 hospitals, spread across all geographical zones of the country are a part of this registry. The project is still ongoing, and the data from the registry is often used for programmatic interventions in COVID-19 pandemic.

LEPROSY

Programmatic implementation and Comparison of MIP Vaccine Immunoprophylaxis and Rifampicin Chemoprophylaxis under the National Leprosy Eradication Programme (NLEP) in High Endemic Settings

The project was initiated in 2017 in four districts of Gujarat; Navsari- both Rifampicin and MIP vaccine used, Narmada - MIP vaccine only, Tapi- Rifampicin only and Bharuch- no intervention done. Currently, in the NLEP, single dose Rifampicin (600mg) used as chemoprophylaxis, for leprosy contacts, however it can increase Rifampicin resistance in the community and may cause severe problem for TB control program. MIP vaccine was introduced in 2016. MIP vaccine improves the immunity and resists the *M.leprae* to progress into clinical disease among contacts of Leprosy cases. MIP vaccine is the only indigenous vaccine approved and licensed by DCGI and programmatic implementation as immunoprophylaxis to control Leprosy transmission and could help to achieve

elimination goal at state and district level. It is proposed for programmatic introduction of MIP vaccine to Bihar and Chhattisgarh as soon as possible.

Multicentric trial to study the effect of early active mobilizations as compared two three weeks immobilization following tendon transfer procedures for claw hand

Six centres were involved in this project i.e (a) Karigiri, Tamil Nadu, (b)Kolkata, (c)Purulia, West Bengal, (d) Allahabad, (e) JALMA, Agra, (f) AIIMS, New Delhi. It was a non-inferiority trial but non-inferiority of the early mobilization could not be established, due to lack of adequate sample size.

REPRODUCTIVE, CHILD & NUTRITION HEALTH

ICMR is undertaking research in the field of reproductive, child and Nutrition health through its research institutes viz. National Institute of Research in Reproductive Health, Mumbai, National Institute of Nutrition, Hyderabad as well as extramural research projects. These studies are aimed to protect and enhance the reproductive and nutritional health of people through research and development of technologies and programmes for field applications which can be incorporated into National Programmes.

INTRAMURAL RESEARCH

ICMR - NATIONAL INSTITUTE FOR RESEARCH IN REPRODUCTIVE HEALTH, MUMBAI (ICMR-NIRRH)

FEMALE INFERTILITY AND ASSOCIATED REPRODUCTIVE DISORDERS

Deciphering the Putative Epigenetic Mechanisms Pertaining to Polycystic Ovary Syndrome (PCOS)

Evidence of the involvement of tissue-specific epigenetic changes in development of complex diseases prompted us to investigate the involvement of epigenetic changes in ovarian granulosa cells from women with PCOS. The transcript expression and methylation status of physiologically important differentially methylated genes (DMGs) identified in our NGS study such as AR, LHCGR, FSHR,

FST, AMH, AMHR2, AKR1C3, CASR, GHRHR, OLR1, MAMLD1, RETN, TF, TNF, HAPLN1, PTGER1 and LIF were investigated. We were able to dissect some novel molecular mechanisms that trigger hyperandrogenemia, defects in oocyte development, cumulus-oophorus-complex (COC) expansion, luteal maintenance, angiogenesis and redox homeostasis. Comparing our NGS dataset with different PCOS and ovarian databases, we have identified 49 common genes whose expression must be regulated by methylation and play key roles in PCOS pathophysiology. Other epigenetic changes including DNA-5hmC profiling and RNA methylation mapping has been planned for future studies in granulosa cells of PCOS women.

PON1 Expression, Activity and its Relationship with Oocyte and Embryo Quality in Women with PCOS undergoing Assisted Reproductive Technique

PCOS is associated with suboptimal oocyte quality and poor outcomes of ART treatment. We observed an imbalance of oxidative stress markers in the follicular fluid of PCOS with particular emphasis on components of glutathione system and paraoxonase1 activity. These alterations can cause detrimental issues, such as poor oocyte and embryo development, and pregnancy outcome. Not only do these serve as non-invasive biomarkers to comprehend the redox status in oocyte microenvironment, but treatment directed towards correcting redox imbalance may possess potential to improve oocyte/embryo quality in

ART settings. Our data suggest that granulosa cells may play crucial role in maintaining follicular redox homeostasis. Oxidative stress is a significant contributor to PCOS pathophysiology. We plan to study glucose metabolism pathways in granulosa cells which play an important role in the supply of glucose to oocytes.

Understanding Follicular Angiogenesis in Women with PCOS

The cyclic growth and regression of the ovarian follicles depend on the balance of vasculature formation and regression around the follicle. In women with PCOS the arrest of follicular growth and compromised corpus luteum (CL) may be attributed to defects in vascularization around the follicle. Previously, we reported decreased angiogenic capacity of follicular fluid (FF) and altered expression of angiogenic factors in FF and granulosa-lutein cells (GLCs). Further, GLCs showed reduced tube forming ability in PCOS compared to controls, when cultured in presence of their corresponding FFs. Also, the tube formation capacity was significantly low when GLCs from controls were cultured in presence of FF from women with PCOS. Our results suggested that the endothelial cell-like properties and angiogenic potential of GLCs is compromised in PCOS. This may affect the vasculature development in CL leading to compromised CL formation and its function in women with PCOS, and thus may lead to luteal phase insufficiency and frequent miscarriages observed in these women.

Unraveling Pathogenetic Mechanisms of PCOS by Whole Exome Sequencing

Due to variations of phenotype, ethnicity and geography; polymorphisms-based studies show differing association with PCOS risk in various populations. To study the genetic predisposition in PCOS, we have been investigating the polymorphisms reported in GWAS of other populations for their association with PCOS risk in Indian population. We have completed genotyping of intronic variants in LHCGR,

THADA and DENND1A. We found no association of rs13429438 of THADA and rs13405728 of LHCGR and rs10818854 of DENND1A with PCOS susceptibility. The genotyping of rs10818854 of DENND1A and rs4385527, rs3802457 and rs72748550 polymorphisms of C9orf3 were continued and no significant association was found with PCOS. Additionally, investigation of the European cohort variants - rs1894116 of YAP1 gene has been initiated which is the key transcriptional target of hippo pathway and rs705702 of RAB5B gene which affects the glucose and androgen levels in Han Chinese and European women. Preliminary results show that rs1894116 of YAP1 is significantly associated with PCOS risk. An exome sequencing study has been initiated to find novel and/or rare causative mutations for PCOS risk and elucidate their relationships with reproductive and metabolic phenotypes.

Evaluation of Prevalence, Regional Phenotypic Variation, Comorbidities, Risk Factors and the Variations in Response to Different Therapeutic Modalities among Indian Women with Polycystic Ovary Syndrome (PCOS): A Multicentre Study across India

This multicentric study initiated in 2018 intends to enrol 1000 participants at each site divided equally between urban and rural to estimate prevalence of PCOS. At NIRRH, rural enrollment target of 500 participants is completed, while 424 are enrolled in urban group. Due to COVID-19 pandemic, 21 enrolled participants in urban and 20 in rural group have either refused to participate further in study or lost to follow up. 93 (32P + 61C) participants in rural and 75 (21P + 08K + 46C) in urban group have completed all investigations as per protocol. On the basis of complete evaluation of participant profiles, 11 in rural and 11 in urban groups are confirmed PCOS cases. Thus the prevalence is noted to be 11.82% in rural and 14.66% in urban groups (out of those investigated). Reports were distributed to participants, and the ones needing expert help were referred accordingly. The study is ongoing.

Clinical Phenotypes and Genetic Regulation of Endometriosis in Indian Women

Large scale, standardized, Indian population data on different endometriosis phenotypes and genotypes will be generated through ECGRI study. This will be the first evidence on clinical phenotypes and GWAS identified risk factors for endometriosis in India. Endometriosis clinical database (<http://app.ecgri.in/login>) was launched and biorepository has been established. In spite of the disruptions due to COVID-19 pandemic, we were able to recruit more than 300 participants. Amongst the endometriosis cases (n=153), 21.6% were superficial peritoneal (SUP), 62.7% ovarian endometrioma (OMA) and 14.4 % deep infiltrating endometriosis (DIE). We also observed 1.3% of scar endometriosis. Isolated (53.6%) and overlap of endometriosis sub-phenotypes (46.4%) was observed in Indian women. Regional data on endometriosis sub-phenotypes will be useful in developing the strategies and policies to address the endometriosis associated morbidity in India.

Pregnancy Outcomes in Indian Women with Endometriosis and Biomarker Correlation: A Cohort Study

A total of 248 women with endometriosis were recruited at six study sites all over India. Out of these 17% of women (41/248) conceived either naturally or with the use of assisted reproductive technologies. The detailed clinical and surgical phenotype analysis of 204 women with endometriosis was carried out. Endometriosis was classified as minimal, mild, moderate and severe disease as per rASRM endometriosis classification: stage I (n=77/204, 38%), stage II (n=22/204, 11%), stage III (n=21/204, 10%) and stage IV (n=84/204, 41%). Regional differences in endometriosis subtypes [superficial peritoneal endometriosis (SUP), ovarian endometrioma (OMA) and deep infiltrating endometriosis (DIE)] were observed. Women with endometriosis recruited from eastern region reported higher frequency of SUP (42%, 53/127), whereas women with endometriosis

recruited from southern and northern regions reported higher frequencies of OMA (54%, 26/48) and DIE (62%, 18/29) respectively ($p<0.001$). Comorbidities were reported in 34% (69/204) of women with endometriosis. Recurrent endometriosis was observed in 12.3% (25/204) of women in the present cohort. The biomarker analysis and correlation with endometriosis is ongoing.

Pathways to Oncogenesis in the Pathophysiology of Endometriosis

Endometriosis is defined by the presence of tissue resembling endometrium at sites outside the uterine cavity. Although considered benign, endometriosis shares certain features such as adhesion to heterotypic tissues, invasion, increased proliferation and angiogenesis with cancerous cells. Cancerous cells are also known to have a dysregulated DNA Damage Response (DDR). We previously demonstrated increased DDR accompanied by higher DNA damage in the mid-proliferative phase eutopic endometrium of women with endometriosis. Higher DNA damage, arising due to either replicative stress or exposure to genotoxic agents, may cause genomic insults in a cell, if left unrepaired. These genomic insults are repaired via different pathways, including an error-prone non homologous end-joining pathway (NHEJ). Polymorphisms in X-Ray Repair Cross Complementing 4 (XRCC4) gene, a key player in the canonical NHEJ pathway, are reported to be associated with increased susceptibility to endometriosis. However, there exists no information on the endometrial levels of XRCC4 protein in endometriosis. Studies carried out during the reporting year demonstrated a significant reduction in the levels of XRCC4 protein in the mid-proliferative phase eutopic endometrium of women with endometriosis, compared to women without endometriosis. Further, in vitro studies using endometrial stromal (ThESC) and epithelial (Ishikawa) cells were carried out to assess the effect of higher oxidative stress on XRCC4 protein expression. Higher immunolocalization of DNA

damage markers (γ -H2AFX and 8-OHdG) was observed in ThESCs and Ishikawa cells exposed to higher oxidative stress, compared to unexposed cells. XRCC4 expression at protein level was found reduced in both cell types exposed to higher oxidative stress. Overall, our study suggests that higher oxidative stress affects endometrial expression of XRCC4 in women with endometriosis.

Studies to Evaluate the Effect of Metformin on Endometrial Functions

Metformin is an established first line anti-diabetic drug. Apart from its effects on glucose metabolism, metformin is known to be effective against various reproductive dysfunctions in women with PCOS. Metformin is known to regularize menstrual cycles, increase pregnancy rates and reduce early pregnancy losses in PCOS women. However, studies demonstrating the direct effects of metformin on endometrium are limited and hence, this study was undertaken to decipher whether metformin elicits direct effects on endometrium. We previously showed that metformin at low dose induces proliferation of endometrial cells. Further, to understand the mechanism of metformin action on endometrial cells, microarray was performed. Microarray analysis revealed activation of mitochondrial function related genes in cells treated with lower dose of metformin (0.05mM) compared to HEC-1A cells which were either untreated or treated with high dose of metformin (10mM). In cells treated with low dose of metformin the number of mitochondria were found to be more whereas in the cells treated with high dose of metformin the number of mitochondria was found reduced. However, high dose of metformin led to a reduction in the number of mitochondria in endometrial cells. Increased mitochondrial function may have a role in the proliferation of endometrial cells at lower concentration of metformin. Studies are ongoing to understand the effects of the low dose of metformin on mitochondrial functions in endometrial cells.

Uterine Alarmins and their Relevance in Implantation

Alarmins or Damage-Associated Molecular Patterns (DAMPs) are constitutively expressed endogenous molecules which are released in response to tissue damage or immune induction in the absence of an infection, a phenomenon known as sterile inflammation. High-mobility group box-1 (HMGB1), S100 proteins, heat shock proteins, IL-1 α , and IL-33 are known to act like alarmins. Our group previously demonstrated the presence of the alarmins HMGB1 and S100A8 in the uterine fluid of healthy women. We also demonstrated menstrual cycle-dependent changes in the uterine fluid levels of these two alarmins. The present study was undertaken to determine the physiological role of alarmins HMGB1 and S100A8 in implantation in rats. Studies conducted so far demonstrated that the physiological levels of S100A8 in the uterine fluid are higher in the metestrus phase, compared to proestrus phase. Further, we created an excess of HMGB1 in the uterine fluid by intrauterine administration of recombinant HMGB1 (rHMGB1) in the uterine horns of pregnant rats. Initial analyses of the uterine fluid using multiplex cytokine array showed alterations in the levels of pro-inflammatory and anti-inflammatory cytokines in rHMGB1-treated animals, compared to saline-treated animals. Efforts will be undertaken to determine whether these alterations are caused by rHMGB1-induced modulation in the frequency or phenotype of immune cells. These studies may further our understanding of the role of DAMPs in implantation or implantation failure.

Damage Associated Molecular Patterns (DAMPs) and their Receptors in Endometrial Repair

Endometrial repair post-menstruation is highly efficient and scar-free process. Impairment in the endometrial repair causes conditions such as heavy menstrual bleeding or menorrhagia. In India, menorrhagia is responsible for 56% of hysterectomies in a women aged between 30-49 years. There exist reports indicating higher abundance of Damage Associated Molecular Patterns (DAMPs) in human menstrual fluid. Our

previous study reported expression of DAMPs and their receptor in endometrium. The present study is undertaken to investigate the role of DAMPs in endometrial repair. We developed a rat model of endometrial breakdown and repair by inducing menstrual cycle in an ovariectomized rat through sequential administrations of estrogen and progesterone followed by withdrawal of progesterone. Histological analysis showed breakdown and repair of endometrium within 48 hours post progesterone withdrawal. Studies are underway to investigate role of DAMPs in endometrial repair.

Identification of FSHR Antagonist and Agonist Modulators

With the help of *in-silico*, *in-vitro* and *in-vivo* studies, we identified few peptides, small molecules and peptidomimetics with FSHR modulatory activity. A 9-mer (FSH β 89-97) peptide within seat-belt loop of FSH β along with its analogue (Δ FSH β 89-97(91STDC94/AAAA)) generated by replacing central non-critical residues with alanine behaved as FSHR antagonist by inhibiting FSH-FSHR interaction *in-vivo*. Another peptide (FSHR(271-275)) derived from hinge region of FSHR stimulated FSH-FSHR interaction acting as positive allosteric modulator. A small molecule identified for FSHR(TMD) inhibited binding of [¹²⁵I]-FSH to rat FSHR and FSH-induced cAMP production. Through extensive docking studies performed with modeled structure of full-length FSHR and experimentally-validated low molecular weight compounds, we mapped the FSHR binding sites for known agonists and antagonists. This study identified few peptidomimetics with positive and negative allosteric activity *in-vitro*. FSHR modulators also have potential as therapeutic agents for ovarian cancer.

MALE INFERTILITY AND ASSOCIATED REPRODUCTIVE DISORDERS

Identification of New Male Infertility Genes in Obstructive Azoospermic Men with Congenital Bilateral Absence of Vas Deferens

Based on whole exome sequencing (WES) analysis of 16 men with congenital bilateral absence of vas deferens (CBAVD), 141,405 variants were retrieved. After further extensive analysis of exome data, we prioritized missense and loss of function (LoF) variants using various disease models and variant prioritization tools. A total of 16 rare variants (gnomAD/ExAC minor allele frequency < 0.01) from 16 genes, that were mostly stop gain, frameshift indels and missense were identified. Currently, we are validating the prioritized variants in patient samples by Sanger sequencing. This study will be useful for development of mutation panel for screening Indian men with CBAVD opting for ICSI.

Studying Sperm Chemotactic Behaviour using a Microfluidic Chip

Chemotaxis, as a mechanism for sperm guidance although known, has been difficult to demonstrate *in-vitro*. Consequently, very few chemoattractants have been identified till date. Using the chemotaxis device developed by us we investigated sperm motility behaviour in response to ovulatory (OV) and preovulatory (preOV) oviductal fluid (OF) and identified potential chemotactic metabolites. Hydrophilic metabolites extracted from the OF of both the phases were resolved and identified by LC-MS/MS, followed by data analysis using XCMS and Metaboanalyst software, and chemotactic potential of the most promising compound was validated using the microfluidic device. LC-MS/MS of the OFs demonstrates 5 and 4 metabolites to be exclusive to the OV-OF and preOV-OF, respectively, and 25 metabolites common to both, of which 14 metabolites including N-formyl L-aspartate (NFA) are increased in OV-OF; NFA, tested for its ability to influence sperm movement, shows chemotaxis potential. It remains to be seen whether NFA is present in the follicular fluid of infertile women, and whether it may likely be a reason for the failure of natural conception in idiopathic infertile women.

Genome-wide Mapping of Androgen and Estrogen Receptor Binding Sites in Adult Rat Seminiferous Epithelium

Sertoli cells are crucial for spermatogenesis. Adult rat Sertoli cell expresses estrogen receptor beta (ER β) and androgen receptor (AR). The study aimed to acquire a genome-wide map of estrogen- and androgen-regulated genes in adult Sertoli cells. 30,859 peaks in ER β and 9,594 peaks in AR were identified with a fold enrichment >2 fold. Pathway analysis of the genes enriched by ER β and AR demonstrated significant enrichment of genes involved in lipid metabolism which was further validated. Treatment with 17 β -estradiol and DHT in *in-vitro* adult Sertoli cell culture showed significant alterations in the expression of genes involved in lipid metabolism, thereby functionally validating the binding sites obtained by ChIP-Seq. The study elucidates a mechanism by which sex hormones regulate lipid metabolism in Sertoli cells.

Identification and Characterization of Sertoli and Leydig Cell Homing Peptides

Homing peptides are potential molecules as ligands for targeted drug delivery and diagnosis. In this study, Sertoli cell and Leydig cell homing peptides were identified using a phage display peptide library. Previously we identified Sertoli cell homing peptides. During the period of this report, *in-vitro* and *in-vivo* biopanning was performed to identify Leydig cell homing peptides. The phage pool from final round was subjected to amplicon NGS and data analysis is in process. In an attempt to identify the target of the Sertoli cell homing peptides we have performed affinity purification with the help of identified peptide. We are able to find the three proteins, Stress-70 protein, mitochondrial (73.4 kDa), Endoplasmic reticulum chaperone BiP (72.4 kDa) and Heat shock cognate 71 kDa protein (70.9 kDa).

Idiopathic Recurrent Pregnancy Loss: Possible association with Paternal Exposure to Endocrine Disruptors and Epigenetic Modifications in Sperm

Whole-Genome bisulfite sequencing of both healthy fertile and iRPL group sperm DNA was done and Differentially Methylated Cytosines (DMCs) were identified with >25% methylation change and with a Q-value <0.05. A total of 9498 DMCs were obtained among which 4610 DMCs were hypomethylated and 4889 DMCs were hypermethylated. A total of 2087 genes were found to be differentially methylated. Upon pathway analysis using KEGG mapper, crucial signaling pathways involved in development such as Wnt, Hippo, Notch, PPAR were found to be affected. Based on the DMCs, 28 differentially methylated imprinted genes were observed. Among the imprinted and non-imprinted genes implicated in embryogenesis and placentation, few genes (*Kcnq1*, *Esr1*, *Pparg*) have been successfully validated by pyrosequencing in these groups. These findings suggest that aberrant methylation of sperm DNA affecting imprinted and other developmental genes could be responsible for embryo loss in the first trimester of pregnancy.

Role of Testis Specific Histone H2B Variant (TH2B) in Sperm Function and Early Embryo Development

Biological relevance of the major testis specific histone H2B variant (TH2B) in sperm is not fully understood. Given that mature human sperm are transcriptionally and translationally inactive, the presence of TH2B is intriguing. To address its role in sperm, the genomewide localization of TH2B was investigated in sperm of fertile men by ChIP-seq analysis and the genomic loci associated with TH2B has been identified. Bioinformatic analysis revealed ~5% sperm genome and 5527 genes to be associated with TH2B. Out of these, 105 (1.9%) and 144 (2.6%) genes showed a direct involvement in sperm function and early embryogenesis, respectively. TH2B enrichment was more in promoter and gene body region. Enrichment of TH2B was also observed at developmentally important loci such as HOXA and HOXD and on genes required for normal sperm function, few of which were validated by ChIP-qPCR. The relative expression of these genes was altered in particular

subgroup of infertile men showing abnormal chromatin packaging. This altered transcriptome may be a consequence or cause of abnormal nuclear remodeling during spermiogenesis. Studies are ongoing to determine the influence of TH2B on early embryo development.

RTI/ STIS/HIV/ MICROBICIDES

Development of a Multi strain Probiotic *Lactobacillus* Formulation Effective Against Reproductive Tract Infections

Vaginal microbial architecture of women with asymptomatic BV (n=21) and normal microbiota (n=19) was investigated using 16s rRNA V3-V4 region sequencing (HiSeq Illumina). Beta diversity comparison using Bray Curtis indicated distinct microbial communities clustering between normal and BV samples. Firmicutes were the major phyla observed in vaginal specimens of normal microbiota whereas Actinobacteria, Fusobacteria, Bacteroidetes were significantly abundant in BV samples. *L.fermentum*, *L.gasseri*, *L.iners*, *L.jensenii*, *L.mucosae*, *L.ruminis*, *L.salivarius*, *L.coleohominis* were exclusively present in normal microbiota. Predicted functional analysis indicated differences in the functional profiles between BV and normal microbiota. Normal microbiota utilized pathways essential for adhesion, cell wall synthesis and utilization of lactose; whereas amino acid catabolism for polyamine synthesis, sialic acid utilization, LPS and exopolysaccharide biosynthesis pathways were noted in BV samples. The study provides insights into the vaginal microbial structure of Indian women that will enable to explore probiotic candidates for the maintenance of vaginal microbiota.

In-vitro Evaluation of Vaginal Lactobacilli Isolated from Indian Women for Potential Anti-cervical Cancer Activity and Elucidating its Possible Mechanism of Action

Anticancer mechanism of cell free supernatants (CFCs) of selected lactobacilli (M54A, M92B, M118, M129 and M269A) was studied on

cervical cancer cell lines (HeLa, SiHa and C33A). Lactobacilli CFCs repressed E6 and E7 oncogenes in HPV18 integrated HeLa and HPV16 integrated SiHa cells; whilst CFCs of pathogens (*G. vaginalis*, *E. coli*, *S. aureus*) upregulated the expression of E6 and E7 oncogenes in both cell lines. Additionally, *Lactobacillus* CFCs exerted their cytotoxic activities against cervical cells by downregulating cyclin dependent kinase (CDK2) and cyclin A and upregulating p21 levels. However, treatment with CFCs of pathogens upregulated CDK2, cyclin A and downregulated p21 levels. Lactobacilli CFCs promoted apoptosis by upregulation of BAX, BAD, bcl-2, caspase 3, caspase 8 and caspase 9 except bcl2 gene which showed downregulation; whereas pathogen CFCs downregulated apoptosis genes in cervical cancer cells. Thus selected lactobacilli could be used as therapeutics to target HPV-associated cervical cancer.

Identification and Validation of Potential Drug Targets *Candida* spp. using *In Silico* and Wet Lab Methods

Candida albicans and non-albicans *Candida* spp. are a major cause of systemic mycoses with an attributable mortality rate of 10-49%. A few antifungal drugs available such as azoles and polyenes are not efficient to successfully eradicate *Candida* infection. There is an urgent need to expand the druggable space of *Candida* spp. A comprehensive computational workflow has been adopted to identify novel targets that includes: (i) identification of essential drug-target candidates using comparative sequence analysis and protein interaction network analysis; and (ii) system biology-based flux variability analysis approach to predict the metabolic reactions and genes essential for growth of the pathogen. The most promising drug targets identified were 54S and 34S mitochondrial ribosome proteins, of which 54S ribosomal protein YmL9 was validated by drug inhibition assay. The computational workflow used in this study has been integrated into an offline platform for escalating the discovery of drug targets by screening pathogenic proteomes. The offline tool can be downloaded from <http://www.pbit.bicnirrh.res.in/offline.php>.

Demonstration of Vaginal Epithelium as Transient Reservoir Facilitating HIV-1 Transmission

To understand the role of vaginal epithelium in facilitating viral acquisition, we examined the interaction of HIV-1 with vaginal epithelial cells using Vk2/E6E7, an established cell line exhibiting an HIV-binding receptor phenotype (CD4-CCR5-CD206+) similar to primary cells. Our results showed rapid viral sequestration, as a metabolically active process that was dose-dependent. Sequestered virus demonstrated monophasic decay after 6 hours with a half-life of 22.435 hours, though residual virus was detectable 48 hours' post-exposure; (ii) Infection *in trans* of FACS sorted CD4+ T lymphocyte subsets expressing co-receptors CCR5 and CXCR4 and, for the first time, potentially gut homing CD4+ T cell subsets co-expressing integrin $\alpha 4\beta 7$ and CCR5; and (iii) a hitherto unexplored role for the vaginal epithelium as a transient viral reservoir enabling infection of susceptible cell types.

MATERNAL AND CHILD HEALTH

Enhancing Male Participation in Interventions to Prevent Unintended Pregnancy

The objectives of the study are to: (i) develop and implement the intervention [Counselling Husbands and Wives to Achieve Reproductive Health and Marital Equity (CHARM2)]; (ii) evaluate the impact of CHARM2 on spacing contraceptive use; and (iii) assess the quality, scalability, replicability and sustainability of CHARM2. A total of 1200 women aged 18-29 and their husbands; not using permanent contraceptive methods and not willing to have child in the next one year were randomly selected from villages and baseline, 9 months follow up and 18 months follow up survey was conducted after obtaining the informed consent. The preliminary analysis showed that there was increased in family planning use from 37.6% to 53.1% over the follow up survey. The study is ongoing.

Maternal Near Miss (MNM) Review and Corrective Measures at Selected Tertiary Hospitals in Maharashtra

This study was implemented by ICMR-NIRRH at two hospitals Lokmanya Tilak Municipal General Hospital (LTMGH), Sion, Mumbai and Government Medical College, Nagpur. The main objective was to operationalize the MNM-R guidelines developed by the Government of India (GOI) at these two hospitals in Maharashtra. All MNM cases were reviewed and discussed in monthly MNM meetings and corrective measures were recommended based on the three delay model. A total of 228 women with MNM events were identified. Leading causes of MNM were hemorrhage (36.4%) and hypertensive disorders of pregnancy (30.3%). Level one and two delay was reported by 52.6% and 32.5% women respectively. Level three delay at referral centres and at tertiary hospitals was reported by 69.7% and 48.2% women respectively. The study identified challenges in the process of implementation and provided feedback to state and central Government for improving quality of care in maternal health services during pregnancy and childbirth.

Maternal Near Miss Review and Corrective Measures at District and Women's Hospitals in Maharashtra

The project was implemented by ICMR-NIRRH in collaboration with MGIMS, Sewagram for the year 2020-21 at five district/women's hospitals in Maharashtra- (Nasik, Parbhani, Ratnagiri, Nanded and Akola). It is funded by the Programme Implementation Plan of Government of Maharashtra. The overall objective is to implement the Maternal Near Miss Review (MNM-R) Guidelines and take corrective measures at the district and women's hospitals in Maharashtra. MNM cases are identified at each hospital and facility based MNM form is filled as per the Operational guidelines. The total number of MNM cases identified at all District/ Women's Hospital during the reporting year April 2020-March 2021 was 131 (Akola - 38, Nanded - 17, Nashik - 49 Parbhani - 13 and Ratnagiri - 17). Data analysis is ongoing. The cases are discussed in detail and gaps are identified based on the three-delay model. Based on the recommendations of the MNM committee, corrective actions were taken at all the five hospitals accordingly.

Strengthening Maternal and Perinatal Death Surveillance and Response (MPDSR) Action in Tribal Blocks of Palghar District in Maharashtra

The overall objective of the project is to strengthen MPDSR action in two tribal blocks (Dahanu and Jawhar) in Palghar district of Maharashtra. The main activities of the formative phase for 6 months are FGD conduction, review of maternal and perinatal death forms, key informant interviews with the state officials and training of the service providers (Medical Officers, ANMs and ASHAs). Ten FGDs have been conducted in five PHCs of Dahanu block (5 -ASHAs and 5- women of reproductive age group). The expected outcome of the formative phase will be: (i) the status of MPDSR review mechanism will be understood, perceptions of women about MPDSR will be known; (ii) background information regarding MPDSR from ASHAs and ANMs will be gained and service providers will be trained. The findings of the formative phase will be submitted to the ICMR and based on them; the implementation phase for the next one year will be planned.

Involvement of Paternal Imprinting at microRNA Clusters of Chromosomes 14 and 19 in Recurrent Spontaneous Abortions (RSA)

Genomic imprinting is important for embryogenesis and the paternal genome contributes towards placental development. Two large imprinted miRNA clusters: on chromosome-14 (C14MC) and Chromosome-19 (C19MC) are known to regulate the trophoblast cell proliferation, migration; and invasion. Altered expression of miRNAs of these clusters may dysregulate these processes resulting in RSA. Since C14MC and C19 MC are imprinted, altered expression of miRNAs of the two imprinted cluster could be due to changes in their DMR methylation status in the gametes. The methylation at DMRs of these clusters was studied in the spermatozoa of partners of women experiencing RSA. The results obtained till date showed that the paternally expressed C19MC DMR showed

significant hypermethylation in the study group. The study indicated aberrant paternal imprinting to be associated with RSA. Studies are on to investigate if aberrant methylation in spermatozoa correlates with the expression of the miRNAs of these clusters in the chorionic villi.

Aberrant Paternal Imprinting: A Risk Factor for Preeclampsia

Abnormal placentation due to shallow invasion of maternal spiral arteries by the cytotrophoblasts results in poor placental perfusion causing preeclampsia. Several imprinted genes have been found to be implicated in its pathogenesis. Since paternal genome is involved in placental development, the present study aimed to determine if paternal imprinting could be a risk factor for preeclampsia. The methylation of imprinted gene DMRs were studied in the spermatozoa of partners of healthy women and those experiencing preeclampsia. The methylation of the paternally unmethylated KvDMR and PEG 10 DMR was significantly higher in the cases. KvDMR regulates the expression of the imprinted genes, PHLDA2 and CDKN1C. The expression of these genes is affected in placenta of preeclampsia women and the paternally methylated DLK1-GTL2 IG-DMR was hypomethylated. Studies are going on to investigate if aberrant methylation in spermatozoa correlates with the expression of these imprinted genes in term placenta.

Development of Database of Genes, Pathways and Networks Associated with Precocious Puberty

Precocious puberty (PP) is an important endocrine disorder affecting children globally. We developed PrecocityDB, the first online database that catalogues genetic and polymorphism data associated with PP along with relevant reference literature. It is a systematic collation and analysis of shared genes and biochemical pathways associated with PP that can be used to comprehend comorbidity risks. Pathway enrichment analysis using PrecocityDB gene-set indicated that individuals with PP are at higher risk of developing reproductive and

metabolic disorders. Pathways related to prostate cancer, breast, endometrial and hormone-dependent neoplasms were found to be enriched in the PP gene-set. These hypotheses generated based on enrichment analysis are consistent with existing clinical observations. Precocity DB is freely accessible at <http://www.precocity.bicnirrh.res.in>.

Community Based Screening and Management of Latent TB among under-Five Children from Urban Slums in Mumbai

The present study is a community based study in urban slums is in collaboration with Tertiary Hospital and Health post (MCGM), aiming to screen under-five children at risk for LTBI as per WHO guidelines. The study also aims to assess acceptability of testing and adherence to treatment of LTBI among parents. During the reporting year, 349 eligible children were enrolled and screened for LTBI using Tuberculin Skin Test (TST), CBC and IGRA by QuantiFERON-TB Gold Plus. It was observed that, total number of IGRA positives was 41(11.74%), out of which 35(10.02%) were TST positives and 6(1.71%) were TST negative. Total TST positives accounted to 74(21.20%) out of which children positive only for TST were 38(10.88%). IGRA results were indeterminate among 19(5.44%) children. Active tuberculosis was ruled out amongst children suspected for LTBI. Children confirmed with LTBI have been started on INH prophylaxis at BJ Wadia Hospital-TB Clinic as per the guidelines. Children with LTBI are being followed up at the clinic as per the protocol.

Population Based Birth Defect (BD) Surveillance in Linkage with Rashtriya Bal Swasthya Karyakram (RBSK) Programme in Rural Blocks of Palghar District in Maharashtra

This ongoing surveillance project is being implemented at MRHRU Dahanu to estimate prevalence of Birth Defects (BDs) upto 6 weeks age in seven rural blocks of Palghar district. At present, there is no database on BD except for screening done through RBSK Mobile Health

teams. Therefore, the project has been linked with RBSK to utilize existing resources and in turn strengthen the BD component of RBSK. Through this project, a BD registry will be developed and maintained at PHC, RH and SDH. To avoid missed diagnosis at community level, trainings are being conducted for ASHAs to identify BDs during HBNC visits. For training purpose IEC materials like information booklet, flyer and video have been developed. A total of 987 ASHAs have been trained in 19 of 38 PHCs. Post training data collection will begin in all public healthcare facilities for a period upto 24 months.

Development of a Non-Invasive Evaluation Protocol for Detection of Congenital Cytomegalovirus Infection in Newborns

Newborn screening programs facilitate early diagnosis and treatment of congenital diseases. Currently, there are no national newborn screening programs for congenital infections such as cytomegalovirus (CMV) infection, a leading cause of childhood mortality and morbidity. In view of this, we carried out non-invasive sampling followed by PCR based screening of 430 neonates from a tertiary care hospital, for congenital CMV infection. The results obtained indicate a high birth prevalence of CMV infection even among asymptomatic neonates. The feasibility of non-invasive sampling using saliva and stool samples also suggests that it could be used for scaling up the newborn screening program. This in turn could help in timely identification of neonates with symptomatic CMV infection resulting in prompt and effective disease management.

Assessment of Neonatal Screening Approaches for Sickle Cell Disease and the Effect of Early Intervention in Management of the Disease in Tribal Populations

The present study includes screening of newborns at birth to understand the magnitude of the problem to understand the barriers for undertaking such programme, to measure the benefit of early comprehensive care of affected babies. It also aims to evaluate the genotypic and phenotypic correlation

to understand role of genetic modifiers for disease severity. During the reporting year, out of total 2464 deliveries at SDH, 1001 newborns were screened for sickle cell disease. Amongst them, three babies were sickle cell homozygous (sickle cell Disease), one baby was HbS- beta thal heterozygous and 84 babies were sickle cell heterozygous (sickle cell trait). Five babies had other haemoglobinopathies of undermined significance. The babies are being followed up at 6 weeks for confirmation of diagnosis and for screening of family members as per the protocol followed by genetic counselling. Sickle cell homozygous babies were started on pneumococcal vaccinations and prophylactic antibiotics from 3 months as per standard of care and are being followed up to 3 years of life. The project was hampered due to ongoing COVID-19 pandemic. Recruitment was stopped for about three month period from 25th March 2020 which later resumed on 6th July 2020. The follow up during that period and after was delayed due to restriction in travel.

Study of Adverse Event Profiles of Copper Containing Intrauterine Contraceptive Devices (TCu 380 A and TCu 200B)

This retrospective cohort study is undertaken to compare adverse event rates associated with the use of two intrauterine contraceptive devices - TCu380A and TCu200B, to determine their continuation rate and to study the factors associated with discontinuation of their use during 5 years of use. Data records of 695 Copper T insertions among 437 women with either Copper T 200B (42.6%) or Copper T 380A (57.4%) was included. Number of devices (695 devices) that were inserted by women ranged from 1 (n=284), 2 (n= 85) 3 (n= 40), 4(n= 20), 5(n=7), 6(n=1). The frequently reported adverse events were accidental pregnancy (1.1%), complete expulsion (1.8%), partial expulsion (10.2%), menorrhagia (9.1%), abdominal pain (7.3%), infection (3.6%), low placement (2.5%), difficult removal (3.3%) and uterine perforation (0.4%). The study is ongoing.

GENETIC RESEARCH CENTRE

Functional Study of Voltage-Gated Calcium Channel Gene Mutations in Schizophrenia Using Induced Pluripotent Stem Cells (iPSCs): A New Approach for Developing a Cellular Model

Schizophrenia is a devastating mental disorder characterized by reality distortion. There are multitudes of factors that contribute towards the pathophysiology. With heritability as high as 80%, it is the most heritable among all common diseases. The aim of the study is to find such candidate genes to elucidate the genetics of Schizophrenia and further modelling it through iPSCs. Familial cases including affected first-degree relatives were analysed. Whole exome sequencing revealed a common pathway (glycosaminoglycan pathway) that was found affected. Further, microarray analysis identified the presence of copy number loss in 7q35-q36.1 region, encompassing the CNTNAP2 gene. The generation of iPSCs from the PBMCs from a control individual has been standardized. The well-characterized colonies were differentiated into cortical neurons from these iPSCs. Likewise, patient-specific iPSCs will be generated followed by differentiation to neurons. The functional activity of patients iPSCs derived neurons will be compared to the control neurons. Thus, the pathogenicity could be ascertained due to the genetic defect in cases of Schizophrenia.

Identifying Cytogenetic Abnormalities in Cases of Disorders of Sex Development

Disorders of sex development (DSD) arise due to congenital defects in chromosomal, gonadal, or anatomical sex development. Accurate molecular diagnosis is utmost important for assigning gender as well as multidisciplinary management of the newborn baby. The objective of this study was to screen the patients of DSD for SRD5A2 mutations. The spectrum of mutation in SRD5A2 gene was reported earlier. In this reporting period, 15 patients were analysed for AR gene mutation analysis. In a

case of complete androgen insensitivity syndrome, a novel nonsense mutation in AR gene was identified in this case. Further CAG repeat analysis have been carried out. It has been observed that the patients with high testosterone to DHT ratio showed an increase in number of CAG repeat in AR gene. Thus, the number of CAG repeat may have some effect in causation of the disorder.

STEM CELL BIOLOGY

Investigating the Effects of Neonatal Exposure to Estrogen and DES on Mouse Testicular Stem Cells

Earlier it was shown in centre's study that mouse testicular stem cells get affected by perinatal endocrine insults and carry the defect to adult life when their proliferation/differentiation is altered leading to reduced sperm count, infertility and testicular cancer-like changes. Testicular dysgenesis syndrome has a stem cell basis. In the reporting year we focused on developing reversal strategies whereby testicular stem cells biology could be normalized and hence the disease state. Firstly, bone marrow mesenchymal stromal cells were transplanted in the testes of mice neonatally exposed to endocrine disruption. Second approach was to treat with XAR (nano-formulation of resveratrol) which acts in multiple ways including reversal of epigenetic errors. Both approaches revealed improved spermatogenesis in the group neonatally exposed to estradiol but the reversal remained partial in the group exposed to DES. Also, tumor-like changes were not observed upon XAR treatment which were otherwise observed in 80% of mice neonatally exposed to DES.

Studies on Ovarian Stem Cells

Two population of stem cells exist in adult ovary including very small embryonic-like (VSELs) and ovarian stem cells (OSCs), which can differentiate into oocytes *in-vitro*. However, their function *in-vivo* under physiological conditions remains to be deciphered. In the reporting year, various events during oogenesis were deciphered for the first time

in adult mouse ovaries. Similar to PGCs in fetal ovaries, VSELs/OSCs clonally expand to form germ cell nests, which remain connected by ring canals. Cytoplasmic organelles get transported into one of the cells destined to become egg, resulting in the formation of Balbiani Body. Mitosis/meiosis were demonstrated by co-expression of BrdU uptake in MVH, DAZL and SCP-3 positive germ cells. The haploid oocyte later breaks away from the nest and gets assembled as a primordial follicle whereas rest of the nurse cells die by apoptosis. Various events involved in oogenesis from the stem cells under physiological conditions have been delineated for the first time.

Investigating the Effects of Follicle Stimulating Hormone and Steroid Hormone on Uterine Stem Cells

Various events including regular regeneration, growth and differentiation of uterine endometrium during normal menstrual/estrus cycles are closely regulated by the circulatory estradiol (E) and progesterone (P) and their dysregulation results in 'uteropathies' including non-receptive uterus, hyperplasia, adenomyosis, endometriosis, endometrial cancer and leiomyomata. Pluripotent very small embryonic-like stem cells (VSELs) were reported by us in adult mouse endometrium and myometrium. In the reporting year, studies were undertaken to evaluate whether uteropathies occur due to intrinsic changes in stem cells or changes in circulatory ovarian hormones. Despite similar hormonal treatment to bilaterally ovariectomized adult mice, neonatal endocrine disruption resulted in upregulation of stem cell markers and their blocked differentiation. This was associated with extensive proliferation and hyperplasia of endometrium (cancer) and myometrium (fibroids). Defective VSELs/EnSCs migrated into myometrium (adenomyosis) and into blood vessels (could initiate endometriosis). Being immortal, VSELs/EnSCs carry defects into adult life and lead to uteropathies.

Neonatal Exposure to Estrogen and its Effects on Adult Mouse Prostate Stem Cell Biology

A recent single-cell RNAseq study failed to detect stem cells in adult mouse and human prostate and it was suggested that adult cells dedifferentiate to stem-like state for regeneration after castration. In the reporting year we have studied prostate stem cells and their survival following castration. Understanding the tissue-resident stem cells will lead to better understanding of how their dysfunction could lead to prostate cancer. We are able to successfully enrich stem cells based on our ICMR patent that being quiescent and of very small size, tissue resident stem cells can be collected only when centrifuged at 3000 rpm. They get unknowingly discarded when cells are processed at 1000 rpm. Using similar method, stem cells were also enriched from adult mouse heart.

Evaluating the Role of Hypoxia in Human Embryonic Stem Cells (KIND1) Differentiation towards Trophoblast Lineage

Fetal growth is supported by placenta and failure of proper placental development can compromise embryonic development and lead to complications like miscarriages, still birth, pre-term labour, pre-eclampsia and intra uterine growth restriction. Early development of placental trophoblast cells is poorly studied due to limited sample availability and ethical concerns. Availability of a proper human model is highly warranted to investigate early trophoblast development. We have differentiated in-house derived hESC cell line KIND1 into trophectoderm lineage. Further studies are underway to obtain differentiation into syncytiotrophoblast cells. Following development of the *in-vitro* model, placental organoids will be developed and effect of hypoxia during differentiation would be determined.

NATIONAL CENTRE FOR PRECLINICAL REPRODUCTIVE AND GENETIC TOXICOLOGY

Deciphering the Molecular Mechanism of Triclosan on Hypothalamus Pituitary Gonadal Axis

The present study was undertaken to decipher the molecular mechanism of Triclosan (TCS), an antimicrobial agent, on hypothalamus-pituitary-gonadal axis and to investigate the effect of TCS exposure on male reproductive system through epigenetic mechanism. In the reporting year, expression of DNA methyltransferases at gene and protein level was studied upon perinatal exposure to TCS at different doses (0.1, 4, 40 and 150 mg/kg b.wt./day). Nearly two-fold significant decrease in the expression of Dnmt1 in animals treated with TCS at 4, 40 and 150 mg/kg b.wt./day was found. Further, a significant increase in the expression of Dnmt3a and Dnmt3b was observed in 0.1, 4, 40 and 150mg/kg b.wt./day and in 4, 40 and 150mg/kg b.wt./day treated animals respectively. Alteration in expression of Dnmts could be one of the possible mechanisms of triclosan mediated adverse effects on male germ line, leading to subfertility in F1 male rats.

An Endocrine Disrupter- Atrazine induced Epigenetic Regulations in the Male Germ Line Following Perinatal Exposure

Atrazine known to cause altered steroidogenesis and endocrine disruption in male. In the reporting year, F0 dams were treated with various doses of ATR (0, 2, 10, 70 and 100 mg/kg b.wt./day) subcutaneously from gestational and lactational periods. A delay in testicular descent was observed in male rats treated with 10, 70 and 100mg/kg b.wt. doses. To delineate the molecular mechanism expression of Steroidogenic genes (StAR and Aromatase) and INSL3 at the transcript level in F1 male rat testis was studied. The expression of steroidogenic genes StAR and Aromatase were upregulated significantly at all the tested ATR doses. A nearly 2.0-2.5-fold increase was seen in the INSL3 gene expression at doses 2, 10, 70, and 100 mg/kg b.wt./day as compared to vehicle control. Thus, the present study demonstrates that altered expression of steroidogenic genes may affect the process of steroidogenesis, leading to subfertility in F1 male rats exposed perinatally to ATR.

Cellular and Molecular Effects of Cypermethrin on Reproductive Functions of Male and Female Rats

The synthetic insecticide Cypermethrin (CYP) is a potent endocrine disruptor known to have estrogenic and anti-androgenic effects. Previously, we reported that perinatal exposure (GD 6 to PND 22) of pregnant rats to CYP (0, 10, 25 mg/kg b.wt./day) impairs reproductive functions of F1 male and female offspring. In F1 males, reduced sperm counts, motility and subfertility were observed. Further investigations on the mechanism of action of CYP on spermatogenesis of F1 males was done. The gene/protein expression profiles of different cell-type specific meiotic and mitotic markers were studied. The expression of markers such as *Pcna*, *Plzf* and *Sohlh2* was upregulated and of *Ccna1*, *Sycp1*, *Ccnb1*, *Acrv* and *Amh* was downregulated in all dose groups. These expression patterns indicated a population decline from the spermatocyte stage until the round spermatid stage. Further, these findings highlight the adverse effects of perinatal CYP exposure on the crucial process of spermatogenesis leading to a condition of subfertility in adulthood.

REPRODUCTIVE CANCERS

Immunogenetics of Natural Killer Cell Receptors in HPV Infected Women with or without Cervical Cancer

Polymorphism of genes encoding NK-killer cell immunoglobulin-like receptors (KIRs), natural killer group 2-member D (NKG2D) and NKG2A receptor and their expression were studied in 3 groups of participants; (i) with cervical cancers (n=148); (ii) HPV infected women with Pap normal cervix (n=111); and (iii) women without any infection as healthy controls (n=125). The study highlighted the association of NK cell receptor gene, specifically the activating KIR2DS5 with cervical cancer, whereas presence of high frequency of inhibitory KIR2L5B receptor among the healthy controls revealed its protective association. Presence of high frequency

of five activating KIR genes also indicated these as risk factors of cervical cancer. Absence of antibody against HPV or their polymorphism in more than 50% of cases further suggest that infected women with poor immune response have a higher chance of developing cancer if exposed to HPV infection. Reduced expression of NK cell receptors also indicated that low immune response is associated with cervical cancer.

Intervention to Increase Breast Cancer Awareness and Breast Self-Examination among Women in the Community- A Multiple Approach

The objective of the study was to assess the effect of health education on breast cancer awareness among 410 women aged 18-55 years living in low socio-economic area of Mumbai. It was found that only 51% of women had ever heard of breast cancer during the baseline survey whereas it improved to 100% after the interventions. Only 2.8% women were practicing breast self examination (BSE) before intervention and post intervention around two-thirds (65%) of the women reported practicing BSE. The reason for not practicing BSE was that they do not get time (55%) or they do not feel it is needed (32%). About 61 women went for clinical breast examination (CBE) after interventions. The women who have not done CBE believed it is not needed (46%) for them now. Around 13% of them told they are either scared or embarrassed to see a doctor for the CBE.

Role of Toll-like Receptors and TLR Agonists in Modulating Response to Chemotherapy in TNBC Patients

The objective of the study was to analyze the Toll Like Receptor (TLR) expression in triple-negative and identify the relevant TLRs associated with progression and prognosis of TNBC. The analysis of RNA sequence datasets of TNBC tumors in 'The Cancer Genome Atlas' showed a difference in expression of TLRs (TLR1-10) across different molecular subtypes of TNBC. A similar trend in

differential TLR expression was also observed in TNBC cell lines representing different molecular subtypes of TNBC. Also, a significant difference in TLR4 expression was observed in chemo-sensitive and chemo-resistant TNBC tumors and cell lines. Currently the status of TLR expression is being evaluated in PBMCs and tumor tissue samples collected from TNBC patients in collaboration with TMH, Mumbai.

Trop2 in Ovarian Cancer: Evaluating its Potential as Immunotherapeutic Target

Trop2 is an over-expressed tumor antigen reported to have a role in tumor cell proliferation and invasion. Anti-Trop2 monoclonal antibodies have got FDA approval as cancer therapeutics. Identification of immunodominant epitopes in the extracellular domain (ECD) of Trop2, a cell surface protein, would help in utilizing it for active immunotherapeutic approaches. Knowledge of regions/residues important for mediating its interaction with binding partners is also needed for its therapeutic utility. A part of Trop2ECD was cloned and expressed in large scale using 293 suspension culture. The partially purified Trop2ECD protein was used for immunization of rats. The sera collected from immunized rats are being investigated for the presence of anti-Trop2 antibodies. Parallely, site-directed mutagenesis approach was employed to change N-glycosylation sites in the Trop2 ECD. Loss of N-glycosylation at Asn120 or at Asn206 was found to affect its interaction with Claudin-7.

Deciphering the Role of PSP94 and CRISP Family Proteins in Ion-Channel Modulation

PSP94 and CRISP3 (cysteine-rich secretory protein 3) are interacting partners and are shown to be dysregulated in prostate cancer. Both these proteins are implicated as diagnostic and/or prognostic markers for prostate cancer. CRISP family proteins have an ion-channel regulatory domain at its C-terminus and interaction with PSP94 with CRISP is hypothesized to inhibit this

activity. Studies in rodents have identified certain ion-channels modulated by specific CRISP family proteins. However, channels regulated by human CRISPs are not yet known. To identify novel ion-channels regulated by CRISPs, membrane proteome of prostate cancer cell line LNCaP and total lysates from rat caudal sperm was subjected to immunoprecipitation (IP) using anti-CRISP3 and anti-Crisp4 antibody respectively. The IP samples were subjected to LC-MS to identify co-immunoprecipitated proteins. The list of proteins was obtained for CRISP3 IP and is being compared with the control IP reaction to identify the specific CRISP3 interacting membrane proteins.

Role of Kisspeptin Mediated Signaling in ONSET of Puberty

The neuropeptide kisspeptin-1 (KISS1) and its cognate G-protein coupled receptor, the kisspeptin-1 receptor (KISS1R), are central players in the induction of puberty. Activating mutations in KISS1/KISS1R can lead to idiopathic central precocious puberty (ICPP), whereas inactivating mutations can lead to idiopathic hypogonadotropic hypogonadism (IHH). Hence, identification and characterization of mutations in KISS1/KISS1R implicated in pubertal disorders is important to gain insights into the pathophysiology of these disorders. Three naturally occurring mutations in KISS1R reported in literature were generated *in-vitro* using site directed mutagenesis as a tool. The mutation P196H was causal for ICPP whereas the mutations S125L and R198G were responsible for IHH in the children harbouring these mutations. The effects of these mutations on KISS1R function are currently being investigated.

Improving Access for Screening of Common Cancers and Non-Communicable Diseases among Women in Tribal Block of Maharashtra: Challenges in Implementation

To understand the community perspectives and health seeking behaviour, FGDs of eligible women age 30-59 years was conducted. Findings of

formative research highlight that there is limited knowledge on non-communicable diseases (NCDs) and common cancers among tribals as literacy is also low. Women accessed the services of traditional healers like Bhagats. Barriers were transportation, time spent at the public health care facility and behaviour of the staff. ASHAs are key connecting link between women and health system. ASHAs needed incentives for transport and some financial remuneration. Hence, awareness and health seeking behaviour needs to be improved through health education activities involving the ASHA workers. ASHA workers need to be incentivised. Health care facilities need to be upgraded in terms of infrastructure, equipment and trained manpower to implement screening services. These research findings will help in effective implementation through health and wellness centres in tribal areas.

Exploring the Therapeutic Potential of Peptides Targeting Lysophosphatidic Acid Receptors in Ovarian Cancer

Ovarian cancer affects women health worldwide. Lysophosphatidic acid (LPA), an onco-lipid is elevated in ovarian cancer. LPA binds LPAR and activates growth signaling pathways leading to cell proliferation, migration and metastasis of ovarian cancer cells. LPAR2 and LPAR3 are overexpressed in ovarian cancer. We hypothesis that targeting LPAR3 with LPAR3 binding peptide may disturb LPA-LPAR interaction and might delay ovarian cancer metastasis. Therefore, the present study aims to identify the peptides targeting LPAR3 using phage display peptide library approach. In the reporting year, we studied the effect of LPA on expression of LPARs at mRNA level in human and mice ovarian cancer cell lines. Cells treated with 1 μ M LPA for 24 hours showed upregulation of LPARs compared to control cells. Studies will be undertaken to assess the relevance of increased LPAR expression in ovarian cancer cells.

Investigating the Key Elements in Estrogen Signaling and their Contribution to Prostate Cancer

Estrogen, a steroid hormone, is well known for its pathological contribution to cancers of different organs. Estrogen mediates its effect via two major receptors, ER α and ER β . These receptors exert their action either via the genomic pathway or through the non-genomic signaling which is activated by binding of estradiol to plasma membrane-localized receptors. We previously demonstrated the presence of plasma membrane localized estrogen binding sites in the prostatic cells of TRAMP (Transgenic Mouse Model of Prostate), a mouse model for prostate cancer. During the reporting year, studies were conducted to determine if the abundance of estrogen binding sites is altered in the plasma membrane (pmER) during the progression of PCa in TRAMP mice. A reduction in the abundance of pmER in the epithelial cells of prostates displaying well differentiated carcinoma (WDC) and poorly differentiated carcinoma (PDC), compared to control was observed. Interestingly, the expression pattern revealed by estradiol binding to the plasma membrane of prostatic cells of WDC/PDC was similar to the expression pattern of estrogen receptor alpha (ESR1) transcript in the epithelial cells of human prostate tumors of high grade, as apparent from the data available in the public domain. Thus, our investigation in TRAMP model coupled with data mining from human PCa studies suggest reduction in the epithelial levels of ESR1 transcript in prostate tumors compared to non-cancerous prostatic epithelial cells. In addition to this, we investigated whether prostate stem cells (pSCs) in TRAMP mice have estrogen binding sites on their plasma membrane. Flow cytometric analysis revealed binding of cell impermeable estradiol to the plasma membrane of stem cells (CD49f+Sca1+Trop2+Lin-). Our studies indicate that prostatic stem cells are also potential targets of estradiol. Studies will be undertaken to investigate the effect of androgen deprivation on the abundance of pmERs in the prostatic stem cells.

HEALTH TECHNOLOGY ASSESSMENT

Health Technology Assessment of Intravenous Tranexamic Acid Use in Management of Primary Post-Partum Haemorrhage in India

This project is undertaken as part of the HTA Resource Hub activity supported by DHR after technical approval from HTAIn. Intravenous Tranexemic Acid use in all women with primary PPH is recommended by the World Health organization based on results from the 2017 WOMAN trial. This is a HTA to answer the policy question of whether this recommendation should be made in the Indian public health system. A decision tree was constructed to answer this question. It was found from the model that the addition of I.V. TXA to public health system of India would be cost-effective as per current threshold of USD 2099.6. An Incremental cost per DALY averted from a health system perspective (INR 14,580) was found to be less than the per capita gross national income of India in 2020-21. The results of the model are robust as sensitivity analysis shows that 82% of the 1000 ICURs on PSA would be cost-effective. Based on these results it is recommended that all policy guidelines on PPH management, including DAKSHATA packages, training material etc. to be updated to reflect its use within three hours of birth.

COVID-19 RESEARCH

An Integrated approach towards delineating determinants of viral pathology and disease progression of SARS-COV-2 infection

Using an integrated approach of monitoring inflammatory and mucosal migratory markers together with kinetic of anti-viral antibody generation in a cohort (n=84) of SARS-COV-2 infected individuals, it was found that IL-6 and sMAdCAM levels among in-patients inversely correlated with one another. When expressed as a novel integrated marker –sMIL index (sMAdCAM/IL-6 ratio), these levels were incrementally and significantly higher in various disease states with convalescents exhibiting the highest values. Importantly, sMAdCAM levels as well as sMIL index (fold change) correlated with peak association rates of receptor binding domain and fold change in binding to spike respectively as measured by SPR. Our results highlight key systemic and gut-

associated parameters that need to be monitored and investigated further to optimally guide therapeutic and prophylactic interventions for COVID-19.

National Registry of Pregnant Women with COVID-19 in India (PregCovid Registry)

This program was initiated to generate evidence on clinical presentation, obstetric and neonatal outcomes and maternal child transmission of SARS-COV-2 in pregnant women. A registry of pregnant women with COVID-19 (PregCovid registry, www.pregcovid.com) was launched in April 2020 in collaboration with Medical Education and Drugs Department, Government of Maharashtra and Municipal Corporation of Greater Mumbai (MCGM). The data of pregnant and post-partum women with COVID-19 and their newborns is captured into electronic patient record system. A total of 4283 pregnant and post-partum women with confirmed diagnosis of COVID-19 were registered on PregCovid registry portal till 31st March 2021. A total of 3254 women have delivered. There are 78 spontaneous abortions, 15 ectopic pregnancies, 99 still births and 36 maternal deaths in our study cohort. Important observations related to public health policy such as impact of universal testing, co-infection of malaria & dengue, post-partum psychosis, delirium, twin gestation, tuberculosis, heart disease, etc. were published on priority. A detailed analysis of clinical, epidemiological characteristics, maternal and neonatal outcomes is ongoing.

Pregnancy, Placenta and COVID-19

Maternal infection during pregnancy is a matter of concern for the risk of mother-to-child transmission of the virus. The placenta protects the fetus from maternal infection and prevents congenital transmission of the virus. To address the possibility of congenital transmission of SARS-COV-2 virus, we determined if the placental cells express the necessary factors required for SARS-COV-2 infection. Our results showed that the SARS-COV-2 receptors (ACE2 and TMPRSS2) are co-expressed in the placental cells in all three trimesters. They also expressed genes involved in viral budding and

replication. Further, we could detect the persistent presence of SARS-COV-2 in the placenta and amniotic fluid from an asymptomatic woman with COVID-19 in the early first trimester. This is the first study to provide concrete evidence of persistent placental infection of SARS-COV-2 and its congenital transmission which was associated with hydrops fetalis and intrauterine fetal demise in early pregnancy. Studies are ongoing to determine the incidence of mother-to-child transmission of SARS-COV-2 and its effects on the placenta.

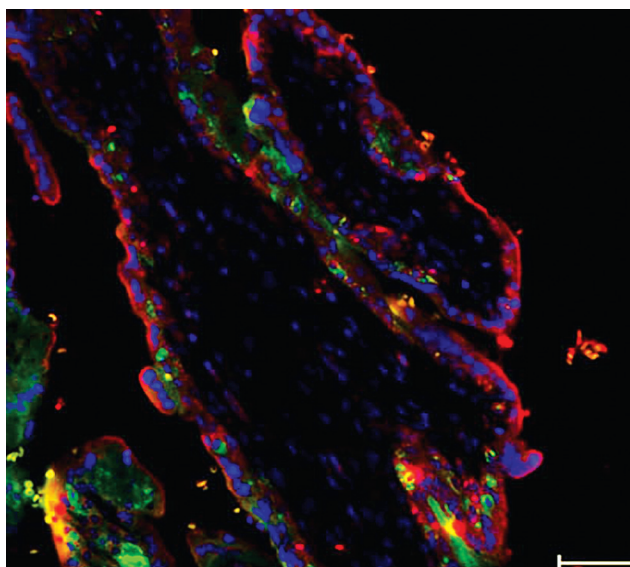


Fig. 1: SARS-COV-2 in the first-trimester placenta. Green is ACE2 (receptor for SARS-COV-2) and Red is SARS-COV-2 (NS protein). Blue are cell nuclei.

A Recombinant Fragment of Human Surfactant Protein D binds SPIKE Protein and Inhibits Infectivity and Replication of SARS-COV-2 in Clinical Samples

COVID-19 is an acute infectious disease caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-COV-2). Human surfactant protein D (SP-D) is known to interact with spike protein of SARS-COV. The study aimed to examine the potential of a recombinant fragment of human SP-D (rfhSP-D) as an inhibitor of replication and infection of SARS-COV-2. The interaction of rfhSP-D with spike protein of SARS-COV-2 and hACE-2 receptor was predicted via docking analysis. The inhibition of interaction between spike protein and ACE-2 by rfhSP-D was confirmed using direct and indirect ELISA. The effect of rfhSP-D

on replication and infectivity of SARS-COV-2 from clinical samples was studied by measuring the expression of RdRp gene of the virus using qPCR. *In-silico* interaction studies indicated that three amino acid residues in the RBD of spike of SARS-COV-2 were commonly involved in interacting with rfhSP-D and ACE-2. Studies at the BSL-3 facility of ILBS, Delhi, using clinical samples of SARS-COV-2 positive cases (asymptomatic, n=7 and symptomatic, n=8 and negative controls n=15) demonstrated that treatment with rfhSP-D inhibited viral replication by ~5.5 fold and was more efficient than Remdesivir. Approximately, a 2-fold reduction in viral infectivity was also observed after treatment with rfhSP-D. These results conclusively demonstrate that the calcium independent rfhSP-D mediated inhibition of binding between the receptor binding domain of the S1 subunit of the SARS-COV-2 spike protein and human ACE-2, its host cell receptor, and a significant reduction in SARS-COV-2 infection and replication *in-vitro*.

PUBLIC HEALTH

- Health education on breast cancer, breast self-examination, clinical breast examination and contraceptive methods to the women may influence their practice in long run.
- Maternal Near Miss (MNM) study suggested the need of revision of the MNM guidelines and the important points for revision have been communicated to Government of India.
- A recombinant fragment of human surfactant protein D binds Spike protein and inhibits infectivity and replication of SARS-COV-2 in clinical samples.
- Elective module on Diagnosis and Management of PCOS developed for the Indian Medical Graduates including Medical Officers of the Primary Health care system.
- Development of Guidelines for the Diagnosis and Management of PCOS initiated for the Indian Healthcare system.
- Molecular diagnosis of clinically suspected cases of disorder of sex development was

carried out. This would greatly help the clinician in management of the disorder.

- Guidance for management of pregnant women in COVID-19 pandemic was developed for health care providers, which was included in the Advisory of ICMR.
- A registry was launched by ICMR-NIRRH in joint collaboration with Maharashtra medical education and drugs department (MEDD) and BYL Nair Charitable hospital, MCGM, Mumbai. The systematic collection of maternal and neonatal data is useful for policy makers to address the burden of COVID-19.

COVID-19 PANDEMIC

- Provided COVID-19 testing to the extent of ~80,000 tests as of now in our role as a high throughput testing centre with the COBAS 6800 testing platform.
- Participated in national exercise for validation of Rapid Antibody Tests and national validation exercise of RT-LAMP assay developed by NIV (Mumbai unit) as Centre of Excellence (CoE) for validation and quality assurance for reagents related to COVID-19 testing.
- Till date, total of 191 VTM/ VLTm/ MTM kits and 10 RT-PCR kits have been validated (commercial & batch testing).
- As a regional Depot since March 25, 2020 and Central Depot since June 1, 2020 a total of 35 testing labs, validation centres and other depots were supplied with reagents across Western India. The combined value of all 63,40,836 COVID-19 tests (VTM, RT-PCR & RNA Extraction) stored and distributed was ~ Rs. 150Cr.
- Established a biorepository of samples from COVID-19 infected individuals to serve as a national resource for COVID-19 related research studies.

ICMR- NATIONAL INSTITUTE OF NUTRITION, HYDERABAD (ICMR-NIN)

Nutrient Requirements for Indians – Recommended Dietary Allowances (RDAs) and Estimated Average Requirements (EARs)

In view of the changing food habits, physical activity patterns, nutrition transition and health status of various groups, ICMR-NIN, this year released the latest Nutrient Requirements for Indians and Recommended Dietary Allowances. For the first time, the report includes the Estimated Average Requirements (EAR) and Tolerable Upper Limits (TUL) of nutrients alongside RDAs. While RDAs are daily dietary nutrient intake levels which would be sufficient to meet the nutrient requirements of nearly all healthy individuals, EARs are the average daily nutrient intake levels of population. These recommendations are the basis for defining the nutrient levels in policies and programs. The EARs and TUL are not only useful in evaluating the nutritional status of populations or groups but also in defining the regulation on food fortification and nutrient supplementation etc. Hon'ble Union Minister for Health and Family Welfare Dr Harsh Vardhan released this document in ICMR in Sept 2020.



Fig. 2: Hon'ble Union Minister for Health and Family Welfare Dr Harsh Vardhan released the latest Nutrient Requirements for Indians and Recommended Dietary Allowances in ICMR in Sept 2020.

WHAT INDIA EATS – REPORT

The report, for the first time, analyses the data from earlier diet surveys and gives an overview of the dietary patterns across the country projected based on food groups. This report gives details of

“Regional Dietary Pattern of Indian Population.” Dietary data analysis of adults in urban and rural India showed that an average adult from urban India consumed 1943 Kcal/day, 289 g carbohydrates, 51.6 g fat and 55.4 g protein. In rural region, an average adult consumed 2081 kcal/day, 368 g of carbohydrates, 36 g of fat and 69 g of protein. As per food groups, the total energy (E) intake from cereals contributed to 998 Kcal/day, while visible fats and pulses & legumes contributed to 265 Kcal/day and 119 Kcal/day respectively in urban areas. In contrast, the total energy intake from cereals was much higher (1358) Kcal/day, and considerably lower from fats (145 Kcal/day), pulses and legumes (144 Kcal/day) in rural areas. Milk and milk products contributed almost similar in urban (99 Kcal/day) and rural areas (87Kcal/day). As per the recommendations, not more than 45% of energy should be contributed by cereals and millets, whereas the actual contribution was 51% in urban region and 65.2% in rural region; while pulses, legumes, meat, poultry and fish contributed to mere 11% of the total energy per day in urban areas and rural areas, as against the recommended minimum intake level of 17% of total energy from these foods. This report was also released by Dr Harsh Vardahan, Hon’ble Union Minister for Health and Family Welfare in Sept 2020.

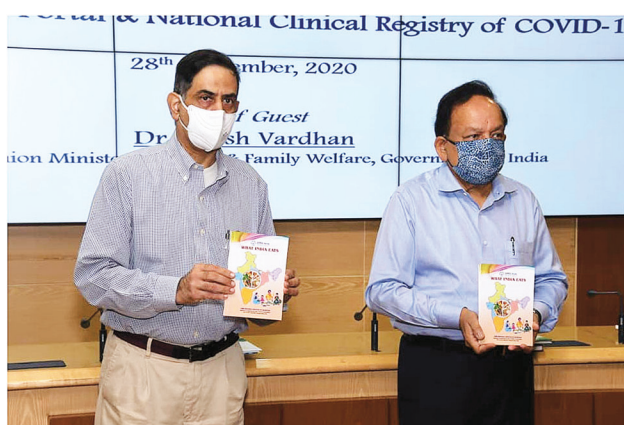


Fig. 3: “Regional Dietary Pattern of Indian Population” was released by Dr Harsh Vardahan, Hon’ble Union Minister for Health and Family Welfare in Sept 2020.

Nutritional status of below 12 years Children of Muzaffarpur district, Bihar: A Rapid Nutrition Assessment

Periodic outbreaks of Acute Encephalitis Syndrome (AES) resulting in high incidence of morbidity and mortality among children residing in rural areas of Muzaffarpur district, Bihar prompted a study to assess the nutritional status of the children residing in litchi growing and AES affected and non-affected areas. It was found that the intakes of all the nutrients except protein and thiamine were below the recommended levels. The overall prevalence of underweight, stunting and wasting among children (< 5 years) was 29%, 44% and 10%, respectively (Figure 1). The prevalence of anaemia was about 70% in younger children, while it was lower among older children (47%). However, the prevalence of B12 deficiency was 43-67% among younger and older children (Fig 4).

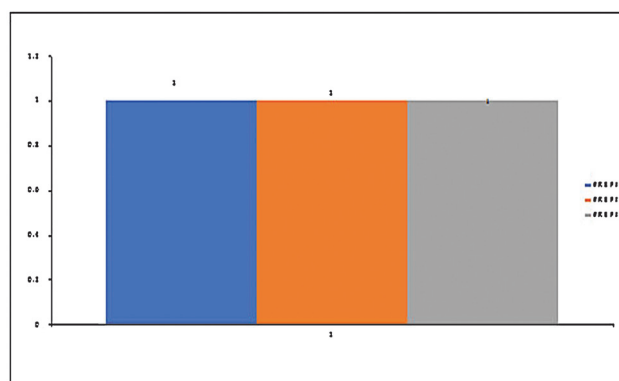


Fig. 4: Prevalence (%) of vitamin B12 deficiency among Children in Muzaffarpur.

Prevalence and predictors of vitamin B12 deficiency: genetic associations for low vitamin B12 levels - multi-centre a pan India study

The objective of the study was to evaluate the contribution of vitamin B12 deficiency to the burden of anaemia independently and/or in conjunction with iron and folate deficiency and also to identify the genetic factors associated with vitamin B12 levels in Indian population. This study was carried out in 8 states covering a total of 4613 individuals. The overall prevalence of anaemia was 35%, while B12 deficiency was 21%. The prevalence of anaemia was highest in Assam (70%) and lowest in Meghalaya (12%), while prevalence of B12 deficiency was lowest in Assam

(3%) and highest in the state of Gujarat (36.7%) (Fig 5).

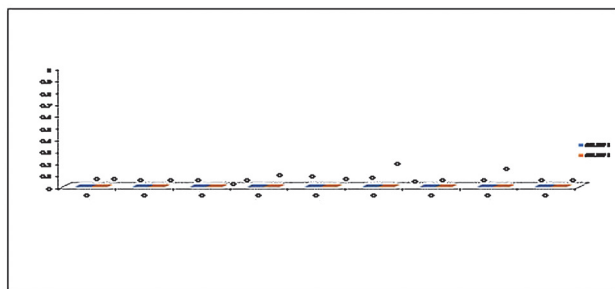


Fig. 5: Prevalence (%) of vitamin B12 deficiency and anemia among adult population in India.

Investigation of Eluru Mysterious disease break out

An Epidemiological Investigation of an Acute Neurological Outbreak in Eluru, Andhra Pradesh was conducted. In this comprehensive analysis, 10 heavy metals, 37 pesticides from blood, urine, water, foods including vegetables, rice, pulses, and 37 herbicides, mycotoxins and bacteriological from food samples were analysed. From these tests and investigations, we confirmed that the outbreak was due to pesticide organophosphate (Triazophos) contamination of water.

Impact evaluation of “screen and treat” approach for anaemia reduction: a cluster randomized trial in rural Telangana

Developed and field tested a customised software to coordinate study activities. Telephonic interviews were conducted in 300 frontline workers to understand the feasibility of resuming study activities as well as delivery of health and nutrition services post COVID-19 lockdown. Developed behaviour change communication materials to address the barriers for program uptake. Initiated a sub-study to assess ASHA workers’ perception of using electronic decision support system to distribute IFA supplementation. Field-tested the implementation of awareness campaign based on the health belief model.

Adaptations to health and nutrition service delivery in COVID-19 in India

The study helped in enhancing understanding of the extent of health and nutrition service deliveries disrupted during COVID-19 lockdown and the facilitators and barriers for resuming the services.

Convening the maternal nutrition technical e-dialogues (monthly webinars)

Funded by UNICEF, this is an initiative to conduct a year long series of webinars, three webinars have been conducted during Jan, Feb and March 2021. This series of monthly webinars has been initiated to strengthen the maternal nutrition status by bringing clinicians, public health practitioners and nutrition researchers on a common platform to discuss the ways to improve maternal nutrition.

Developing Micro-greens (MG) Start-ups for Promoting Livelihood and Nutritional Security in Urban Areas

MGs are nutrient rich foods with a variety of digestible vitamins, minerals and phytonutrients. They enclose living enzymes and nutrients along with good flavor, color and texture. Recommendation about more nutritious MGs for propagation and agriculture exploitation as well as economic gain while meeting the nutritional requirements of the population are being explored in association with ICMR-MANAGE.

Vitamin A deficiency (VAD) among under-five year children in India

As per the Comprehensive National Nutrition Survey (CNNS 206-18) data the national prevalence of biochemical VAD in 1-4 y children was 15.7%; and only 3 states had significant prevalence of >20%. Based on the dietary intakes from NNMB and NSSO data, the cumulative intake of vitamin A along with the universal VAS might exceed the upper limit considering the overlap with the ongoing fortification (Fig-3). This raises the need for considering a targeted state-based VAS program in place of the nation-wide universal VAS program (policy document submitted).

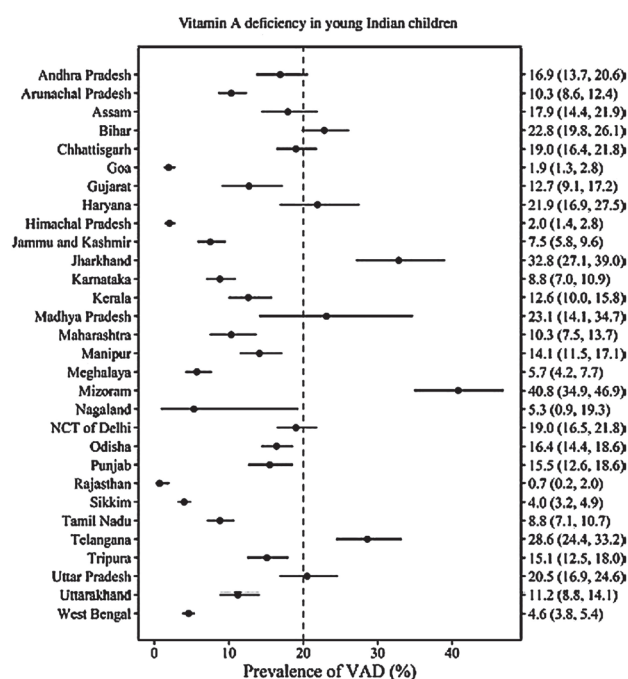


Fig. 6: Prevalence of vitamin A deficiency among children (1-5y) across geographical states of India.

Amelioration of insulin resistance by TLR-2 ligands from *Mycobacterium tuberculosis*

Several lines of evidences suggest a role of proinflammatory signals emanating from Toll-like Receptors (TLRs) play a role in the development of insulin resistance and diabetes. However, it has been found that the dichotomous signaling responses to the downstream of TLR2 activation is dictated by the nature of interaction of TLR ligands to its leucine rich regions (LRR motifs) located on the TLR2 ectodomain resulting in either pro- or anti-inflammatory responses. Using homology modeling we identified some proteins which can interact with the human TLR2 ectodomain. One of the proteins, PPE18, belonging to the PE/PPE family was found to induce IL10 production and could significantly ameliorate palmitate-induced insulin resistance in 3T3-L1 cells.

Characterization of reproductive function and epigenetic changes during omega-3 (n-3) fatty acid deficiency in pregnant mice

Maternal intakes of n-3 PUFAs are far from optimal during pregnancy and lactation in India. Moreover,

the requirement of n-3 increases due to an excess intake of n-6 PUFA. The current study found that maternal n-3 PUFA deficiency alters uterine artery remodeling and placental epigenome in the mice.

Impact on the maternal exposure of Bisphenols: implication to developmental programming of metabolic and reproductive functions in offspring

An *in vivo* study that assessed the impacts of maternal exposure of Bisphenol A (BPA) and its safer substitute showed that Plastic-derived compounds profoundly alter body fat accumulation and male fertility parameters in the adult offspring.

Dermal penetration of pesticide residues in farm women workers: Assessment of cost-effective protective gear as a preventive measure (DST SEED)

A cost effective Personal protective equipment (PPE) was designed and developed under the project and were provided to the farming community. Pesticide residues were significantly lower in washing of hands/wipes/patch samples. Residual metabolites in blood/urine samples were also lower among those who used the cost effective PPEs. Inflammation markers, such as serum CRP, IL-6, TNFa, IL-1b and Cortisol were low and Vitamin A, E and total protein levels were better among those who used the NIN PPE, compared to those who were not using PPEs. The absorption through skin, thereby in to the blood seems to have been less among those who are /were using cost effective PPES, hence the levels of residual metabolites viz., DMP and DETP in urine/blood samples was found to be less as compared to those who have used commercially available PPEs and those who have not used any PPEs.

Prevalence of fluorosis in the community of selected districts of India (Prakasam district from Andhra Pradesh) and development of an appropriate intervention model for prevention and control of fluorosis

Dental fluorosis screening was done in 60,000 population from 30 villages of Prakasam District as part of the ICMR Taskforce. The results revealed that the percentage of dental fluorosis in 5-18 years age group was 5.11% in category I (8 villages; <1.00 ppm fluoride in drinking water), 13.07% in category II (7 villages; 1.5-3.0 ppm fluoride) and 16.19% in category III (9 villages; >3.00 ppm fluoride). The urinary fluoride was significantly higher in category III as compared to category I and category II. The T3 levels significantly increased and TSH levels were significantly lower in category III as compared to category I and category II. There was a significant increase in SGOT in the category II & III compared to category I. The fluoride levels in the food samples were higher in category II & III than in category I.

Development of New Bio-Marker for Quantification of Acetylcholinesterase (Ache) Enzyme Activity, Organophosphate, Carbamates, and Nerve Agent in Biological and Ambient Matrices

A series of experiments were performed varying the concentration of blood and substrate with optimal sensitivity using 50- μ mole substrate and 50- μ L blood. The reaction was complete within 30 minutes. Further trials to reduce volume of blood to 25- μ L and reaction time to 15 minutes have also shown positive results, validation for the same is in progress. This method was validated on blood drawn from OP poisoning patients admitted in Osmania hospital, Hyderabad, Telangana and method was found sensitive, accurate and less time consuming for determination of AChE.

Oral toxicity study of a new *Salmonella* killing bio-control agent NINMB 13076 bacteriophage

Oral toxicity study of the phage NINP13076 provided data on safety of using *Salmonella* killing lytic bacteriophages. The study revealed that the lytic bacteriophages are specific to *Salmonella* and

will not harm the probiotic microbiota and are likely to be safe for use in food preservation.

Development of e-learning modules on nutrition and health under Poshan Abhiyaan initiative of Govt. of India

The Institute in association with the Ministry of Women and Child Development (MWCD), Government of India had developed 12 e-learning modules. These are uploaded on ICMR-NIN website (<https://www.nin.res.in/paelm.html>) providing cross-links MWCD and SWAYAM portals. These are useful for general public and also frontline functionaries like Anganwadi Workers. As in March, 2021, more than 8,00,420 hits have been recorded on the ICMR-NIN website and around 73,315 candidates (27,059 females and 46,162 males) have registered.

Targeted nutrition communication for promoting consumption of micronutrient rich foods among rural households by developing dietary diversity score

Developed a contextually relevant methodology to assess dimensions of the rural food environment using a novel 5A's approach i.e., availability, affordability, accessibility, acceptability and accommodation. A Diet Diversity Score was developed and validated. This can provide a quick assessment of micronutrient intake status of the households. Of the 13 food groups if a household scores 10 their diets could be considered diverse enough to meet the basic micronutrient requirements. For promoting knowledge and practice of consuming micronutrient rich foods, innovative multi-component nutrition communication materials in the form of videos, annual calendar, pamphlets, and booklets were designed and disseminated in the study villages.

Promoting Nutrition and Health of Corporate Employees with Workplace Intervention- A Study Using Communication for Behavioral Impact (COMBI) Approach

This ongoing study aims to develop a multi-component Workplace Health Programme (WHP). The formative research has identified the opportunities and barriers of introducing a WHP at worksites of varied operational sizes. A checklist has been developed to capture the food and physical activity environment of the workplace. The health and nutritional status (Biochemical assessment, diet recall, anthropometry, KAP questionnaire) of corporate employees have been assessed. A theoretical framework of a multi-component, flexible workplace intervention programme model has been developed based on COMBI approach.

PUBLIC HEALTH

- In view of the changing food habits, physical activity patterns, nutrition transition and health status of various groups, ICMR-NIN, this year released the latest Nutrient Requirements for Indians and Recommended Dietary Allowances. For the first time, the report includes the Estimated Average Requirements (EAR) and Tolerable Upper Limits (TUL) of nutrients alongside RDAs.
- Nutritional status of below 12 years Children during an outbreak of Acute Encephalitis Syndrome (AES) hit Muzaffarpur district, Bihar was assessed through a rapid survey.
- An Epidemiological Investigation of an Acute Neurological Outbreak in Eluru, Andhra Pradesh was conducted. In this comprehensive analysis, 10 heavy metals, 37 pesticides from blood, urine, water, foods including vegetables, rice, pulses, and 37 herbicides, mycotoxins and bacteriological from food samples were analysed. From these tests and investigations, we confirmed that the outbreak was due to pesticide organophosphate (Triazophos) contamination of water.
- NIN-ICMR is one of the partners of the ICAR-Consortium Research Platform on Crop Bio fortification involving numerous crops and nutrients. Several crops and nutrients have been evaluated. Zinc content and bioavailability was high from 'DHAN' rice. Two bio fortified maize lines that provide more than 60% RDA have been identified.
- Studies on trans fatty acids (TFA) in commonly consumed processed foods have revealed that snack items like *kachori*, *samosa*, *chikodi*, potato chips and bakery items contain high level of Elaidic acid, but the levels of TFA within the same foods vary drastically. The use of partially hydrogenated vegetable oil (*vanaspati*) in the preparation of the foods is the main source of TFA in the diet, although FSSAI imposed upper limit of TFA in PHVO.
- Bio monitoring of blood trans-fatty acid (TFA) levels in India has been initiated. Preliminary analysis has indicated that plasma TFA levels are lower in India compared to the USA, but levels of the individual TFA varies within states. TFA levels are higher among subjects older than 30 years as compared to those lower than 30 years of age.
- Studies on the Particularly Vulnerable Tribal Groups (PVTGs) Chenchu and Kolam tribes and their food habits has shown that the resource base of indigenous foods used by the tribe is slowly dwindling and there is a need to conserve and mainstream the important nutritious indigenous foods through policy environment.
- Studies on micro greens show that they have better levels of essential nutrients as compared to their counterparts. Scientific evidence of its nutritional and health benefits can bring about their incorporation into mainstream food system.
- A pilot study on Chronic Kidney Disease (CKD) in tribal population revealed high levels of heavy metal content and pesticides in the food chain to be the cause of CKD in Telangana state.
- Contributed to the policy document that is considering a targeted state-based VAS program, in place of the nation-wide universal VAS program that is currently the norm.

- The national prevalence of low serum zinc concentrations (SZC) among preschool (17%) or school age children (16%) was lower than 20%, which is considered the cut-off indicating a problem of public health significance, with variations by state and socio-economic status. In adolescents however, the prevalence of low SZC was 31%, which warrants further investigation into the cause and remedies.
- An animal study on the impact of vitamin D insufficiency on muscle metabolism showed impaired functional parameters in muscle such as contraction, energy metabolism and mitochondrial biogenesis; thereby indicating that subclinical deficiency as seen in humans may impair muscle function.
- Use of the cost effective Personal protective equipment (PPE) that was designed and provided to the farming community showed significantly lower pesticide residues in washing of hands/wipes/patch samples. Residual metabolites in blood/urine samples were also lower among those who used the cost effective PPEs. Inflammation markers, such as serum CRP, IL-6, TNFa, IL-1b and Cortisol were low and Vitamin A, E and total protein levels were better among those who used the NIN PPE, compared to those who were not using PPEs.
- An oral toxicity study of a new *Salmonella* killing bio-control agent NINMB 13076 bacteriophage clearly showed the lytic bacteriophages are specific to *Salmonella* and will not harm the probiotic microbiota and are likely to be safe for use in food preservation.
- When the role of viruses, expression of MPPED2 and p16 in the pathogenesis of cervical carcinogenesis was examined by immunohistochemical expression for p16 & MPPED2 on 150 malignant and 50 normal cervical tissues, it was observed that in cervical carcinoma, the expression of p16INK4A and MPPED2 proteins is directly associated with the union of high-risk HPV into the host cells. For the first time, it was reported that there is a significant correlation between the p16INK4A and MPPED2 proteins in cervical carcinoma.
- Findings of studies by molecular biology group indicate that some TLR2-ligands identified by homology modeling can ameliorate palmitate-induced insulin resistance and can be used as a lead molecule for translational research and development of therapeutics for treatment for diabetes.
- Animal studies indicate that dietary intake of n-3 PUFA may improve placental functionalities during the development of the fetus. However, further study is required to confirm these findings in humans.
- Findings of adaptations to health and nutrition service delivery during the COVID-19 pandemic in India have been shared to the concerned authorities of the State of Telangana.
- Completed development of E-module to facilitate the training for trainers who are involved in implementation of Anemia *Mukt Bharat* programme.
- Developed a contextually relevant methodology to assess dimensions of the rural food environment using a novel 5A's approach i.e., availability, affordability, accessibility, acceptability and accommodation. A Diet Diversity Score was developed and validated. This can provide a quick assessment of micronutrient intake status of the households.

ICMR-NATIONAL ANIMAL RESOURCE FACILITY FOR BIOMEDICAL RESEARCH, HYDERABAD (ICMR-NARFBR)

This institute is currently under establishment to build the state of art facilities with GLP standards and international accreditation for biomedical research. The facilities will be created to develop and provide access to a range of laboratory animals and related technological resources to enable rapid advancement of biomedical research in the country, mainly to facilitate research in medical colleges,

research and academic institutions, universities, and biotech, biopharma companies. The mandate is to develop products at a less expensive means and make it available for common man.

The institute will be a platform to acquire specialized skills in designing of animal experiments to scientists and technologists. Besides, it will also provide a strong support for biomedical research using extensive and well-designed physical facilities to provide national information services that promote conservation and well-informed animal research efforts. In a nutshell, it will serve as a nodal point for networking similar facilities for coordinating activities as a “Catalyst for discovery” for all scientific investigations throughout the country.

Once established, this institute will play a very important and crucial role in the coming years with its international standard infrastructural facilities; with its specific objectives to provide the required quality (SPF) biological resources to the needy national and international institutions and by offering the best services for conducting preclinical safety studies for the development of drugs, vaccines, recombinant products, GM foods and medical devices. The institute with its exclusive large animal BSL3 facility in the campus will always have an edge over others to help progress of biotech, bio-pharma and biomedical research in the country.

It will establish all protocols and standards for testing safety and efficacy of all those products and become an authorizing and certifying body on behalf of Government of India.

EXTRAMURAL RESEARCH

BASIC REPRODUCTIVE BIOLOGY AND FERTILITY REGULATION

Phase-III Clinical Trial with an Intravasal Injectable Male Contraceptive –RISUG®

Under this program, the following studies were undertaken:

To have a perception of the RISUG injected subjects (both husband and wife) regarding their psycho-social and sexual behaviour

The CDSCO directed ICMR to collect information from the RISUG (Reversible Inhibition of Sperm Under Guidance) injected subjects regarding their psycho-social and sexual behaviour after the injection. Therefore, to collect this information, a detailed proforma as well as an instruction manual was developed to obtain data regarding perception of the RISUG injected subjects on their psycho-social and sexual behaviour after RISUG injection. A pilot study was undertaken at LNJP Hospital at eight RISUG injected subjects. The data obtained from the pilot study was discussed with the Experts Committee of the project and after their approval, the proforma and the instruction manual was circulated to all the participating centres of this clinical trial. The centres have started collecting the data through the prescribed proforma.

ICMR has received data of forty-nine subjects from four centres. Because of the COVID-19 Pandemic, the centre could not collect the complete data during the year. ICMR is continuously pursuing the participating centre to collect the data on psycho-social and sexual behaviour aspects from the remaining RISUG injected subjects through the prescribed proforma. The total data which will be obtained from all the participating centres will be analyzed and conclusion will be drawn.

Clinical Reversibility Studies of Injectable Intravasal Contraceptive for the Male

The FNAC study clearly indicated that RISUG does not completely block the vas-deference hence there is a possibility of the reversibility of the procedure. As per the direction of the CDSCO, a detailed protocol has been developed for undertaking clinical reversibility study of injectable intravasal male contraceptive – RISUG at the following two centres:

- (i) Dept. of Urology, Dayanand Medical College and Hospital, Tagore Nagar, Civil Lines,

Block-B, Udham Singh Nagar, Civil Lines, Ludhiana, Punjab 141001.

- (ii) Dept. of Surgery, Maulana Azad Medical College, New Delhi – 110002.

The protocol was discussed with the ICMR Experts Committee and after the approval of the committee, the final protocol was submitted to the CDSCO for approval. The CDSCO has granted permission to undertake the clinical reversibility study with RISUG at the above-mentioned two participating centres.

Phase-I-II Clinical Trials on the Revived Recombinant Vaccine against Human Chorionic Gonadotropin (hCG)

The Phase-I-II clinical trial with recombinant beta hCG vaccine is ongoing at AIIMS, New Delhi and SGRH, New Delhi to determine the safety and immunogenicity of recombinant hCG-LTB vaccine in the women who are healthy and sexually active. The study is also to prove recombinant hCG-LTB vaccine ability to prevent pregnancy in sexually active women without inducing any impairment of ovulation, derangement of menstrual regularity and bleeding profiles.

Till now around 103 (AIIMS-38, SGRH-65) women of reproductive age who fulfilled the inclusion criteria were contacted and counselled at both the participating centres i.e. All India Institute of Medical Sciences (AIIMS), New Delhi and Sir Ganga Ram Hospital (SGRH), New Delhi. Out of that, 80 subjects could not compete the exclusion criteria's and therefore excluded from the study. Remaining 23 subjects were screened for pre-immunization investigations. Out of 11 subjects screened at AIIMS, 4 subjects were excluded because of the following reasons: 2 because of low progesterone level; 1 was out of station for longer duration and 1 discontinued because of their own personal reasons. But at AIIMS centre, one woman screened twice hence total 06 subjects were enrolled at AIIMS. Similarly, at SGRH out of 12 subjects, 8 subjects were excluded because of the following

reasons: 2 because of low progesterone level; 1 woman was detected hypothyroidism; 1 refused for IUCD insertion; 1 removed IUCD after first stage of screening; 1 woman was having skin allergy and 2 subjects were ANA positive. Therefore, in remaining 10 subjects i.e. 6 at AIIMS and 4 at SGRH vaccination with 1.5mg of DNA and 100µg of protein was given as per the provision of the protocol. All clinical and laboratory examination were carried out at different stages of follow up as per the provision of the study protocol.

During the year, out of 6 subjects at AIIMS, in 2 subjects nodule formations at the site of vaccination were reported whereas out of 4 subjects at SGRH, in 3 subjects the nodule formations at the site of vaccination were reported. In spite of the COVID-19 pandemic, all the subjects who were having nodule formation were followed for their clinical and laboratory examination at their respective participating sites. New subjects could not be enrolled as the matter has been reported to the Data Safety Management Board (DSMB). The follow up of other subjects including the subjects who are having the nodules is going on.

National Registry of ART Clinics and Banks in India

National Registry of ART Clinics and Banks in India is under the process of establishment, as per the provisions of ART (Regulation) Bill. Under National Registry, around 1905 ART Clinics and Banks have been identified. Out of that 542 ART clinics have been enrolled as they were in compliance with the provision of National Guidelines for Accreditation, supervision and regulation of ART Clinics in India. Applications of 783 ART clinics are under evaluation process. 358 clinics have been contacted regularly through email and telephone but they have not yet submitted their application for enrollment to ICMR.

The National ART Registry received 7 applications for export and import of human embryos/ gametes through Directorate General of Foreign Trade, Dept.

Table. 1. The status of ART Clinics and Banks.

ART Clinics				ART Banks	ART Clinics & Banks identified by ICMR, yet no response received from them (F)	Grand Total G=(D+E+F)
Enrolled (A)	Under Process (B)	Enrolment Cancelled (C)	Total	Under Process (E)		
542	783	2	1327	220	358	1905

of Revenue, Ministry of Finance, Govt. of India. On being satisfied with the provisions of the ICMR Guidelines for export of human embryos/ gametes, 2 NOCs have been issued to export embryos from India to abroad. Remaining 5 applications were for import of embryos/ gametes. Since, the DGFT have banned the import of embryos/ gametes therefore these applications have been forwarded to DGFT for consideration. The DGFT requested ICMR to develop guidelines for import of human embryos/ gametes. ICMR developed these guidelines and sent to DGFT through Dept. of Health Research for consideration.

Assisted Reproductive Technology (Regulation) Bill was subjected to consultation with all the Ministries and Depts. of Govt. of India and based on the comments received, the bill was revised and submitted to Cabinet for approval. The cabinet has approved the ART (Regulation) Bill for placing in the Parliament for consideration. The surrogacy regulation bill, which was approved by the Lok Sabha, was discussed in the Rajya Sabha. The Rajya Sabha has forwarded the Surrogacy Regulation Bill to the Parliamentary Standing Committee for their comments and suggestions.

Effects of Non-ionizing Electro Magnetic Field (EMF) on Human Health

This is an ongoing prospective multi-disciplinary cohort study with the primary objective of finding effects, if any, of radio frequency radiations (RFR) emitted from cell phone on human health with special reference to ENT, Neurological, Cardiological, Reproduction, Oncological, Bio-chemical and Hematological disorders. The

associated objectives of the study, which is second part of the study, are also to find out the physical characters of the RFR emitted both from cell phone and cell phone towers and to find out health related problems and complaints reported by the peoples residing near cell phone towers at various distances.

After completing the exclusion and inclusion criteria, a cohort of 4185 healthy male and female volunteers ranging 18 to 45 years of age have been created under six study groups. The distribution of these subjects is given below:

STUDY GROUPS

I	Heavy exposure male group (using cell phone more than 4 hrs/day)	-	809
II	Moderate exposure male group (using cell phone 2 to 4 hrs/day)	-	1480
III	Control male group (using cell phone up to 30 min./day)	-	741
IV	Heavy exposed female group (using cell phone more than 4 hrs/day)	-	200
V	Moderate female group (using cell phone 2 to 4 hrs/day)	-	414
VI	Control female group (using cell phone up to 30 min./day)	-	540
	Total	-	4185

These subjects have been followed every year for their clinical and laboratory parameters under various disciplines i.e. (i) ENT, (ii) Neurology, (iii) Cardiology, (iv) Reproduction, (v) Oncology, (vi) Biochemistry, (vii) Hematology etc. at AIIMS, New Delhi.

Though the detailed analysis of the subjects is underway but to assess the trend in various clinical and laboratory parameters, an interim analysis has been done and the salient observations made during these consecutive follow-ups up-to seven years are given below:

- The increasing trend in air conduction, bone conduction and speech recognition threshold indicate that the sensitivity of hearing is decreasing gradually during the consecutive follow up visits which indicate the possibility of gradual sensory neural hearing loss in exposed groups. The Data Safety Management Board (DSMB) and Experts Committee formed the opinion that overall cell phone use has the effect of progressively increasing adverse effect on auditory system which needs to be followed for longer duration.
- The decline in levels of testosterone have been noticed in exposed groups therefore majority of androgen dependent parameters like sexual desire & sexual activity, sperm count, sperm motility, percentage of live sperm, percentage of morphological normal sperm etc. are decreasing in male subjects of exposed groups during the consecutive follow up visits. The Data Safety Management Board (DSMB) and Experts Committee formed the opinion that use of cell phone has progressively increasing adverse effect on sperm morphology and seminal plasma. This trend needs to be followed to draw the conclusion whether these changes are resulting in infertility.
- Increase incidence of irregular menstrual cycle and decrease in sexual desire and frequency in female subjects of exposed groups were noticed during the consecutive follow up visits.
- Memory, fluency, visuospatial-abilities and overall Addrenbrooke's Cognitive Examinations-Revised Score (ACE-R) were reduced significantly in highly exposed and moderately exposed male and female groups during consecutive follow-up visits.
- Epworth Sleepiness Scale Score & Diagnostic and Statistical Manual of Mental Disorders, IV Edition (DSM-IV) criteria score were increasing significantly in both moderate and highly exposed male and female groups during consecutive follow-up visits.
- Percentage of the people reporting numbness, extreme tiredness and itching increased in highly and moderately exposed male and female groups during the consecutive follow up visits.
- The percentage of women reported lump or thickening around the breast increased in highly and moderately exposed female group during the consecutive follow up visits. But malignancy could not be established by Mammography.
- Though no significant difference was found in terms of clinical parameters on cardiological observations but significant changes in frequency of snoring and increased levels of Cholesterol, LDL and Triglyceride and decreased levels of HDL in exposed groups needs to be followed for longer duration to draw a meaningful conclusion.
- It was observed and recommended by the DSMB and Experts Committee that the clinical and laboratory parameters of cardiovascular, neurological and oncological disciplines showed decreasing or increasing changes but they are within the normal range. The members of the board viewed that the present observations are not sufficient to draw any conclusion at this stage. Therefore, to draw any meaningful conclusion from these observations it is necessary that this study should be continued for longer duration.
- The percentage of apoptosis in lymphocyte and levels of malondialdehyde were increasing in male and female subjects of exposed groups.
- The levels of superoxide dismutase (SOD) were decreasing both in male and female subjects of exposed groups.

- The decreasing trend in total leukocytes and monocytes counts and increasing trend in lymphocytes counts were noticed both in male and female subjects of exposed groups.

The above observations indicate that biological changes are well evident in both male and female subjects of exposed groups in comparison to control group. But to find out whether these biological changes will result into health hazard / disorder, the subjects of the cohort need to be followed for long duration. Statistically significant and clinically relevant conclusion can only be drawn and with long term follow-up of the enrolled subjects for their clinical and laboratory investigations.

Health survey of the people residing near cell phone tower

To study the most probable health problems, if any, associated with exposure of Radio Frequency Radiation (RFR) emitted from cell phone towers on human health, a health survey in Delhi on the population residing at various distances from the cell phone tower is being coordinated. This is a part of the above-mentioned main study.

In this study, till now around 4436 subjects have been contacted randomly, who were residing at the various distances near 265 cell phone towers. Only 1268 subjects could provide the information as per the prescribed questionnaire out of 4436 subjects after repeated contacts and pursuance. But because of exclusion criteria's, 878 subjects could only be included in the analysis. The data of 878 subjects who have completed the exclusion criteria successfully is under detailed analysis. However, the results of the interim data analysis are given below:

- Out of 878 subjects, 69% are male and 31% are female ranging from 18 to 50 years of age.
- Both male and female subjects surveyed were divided into two groups i.e. 18-30 year old and 31-45 year old.
- Out of 32 health symptoms, in male subjects, 16 symptoms were significantly higher in the

subjects residing near cell phone tower i.e. 10 to 100m in comparison to the subjects residing at 300m or beyond 300m.

- Similarly, out of 32 health symptoms recorded in female subjects, 14 symptoms were significantly higher in female subjects residing near cell phone tower i.e. 10 to 100m in comparison to the female subjects residing at 300m or beyond 300m.

Table. 2. The adversely reported symptoms which are significant (*) in male and female subjects residing at various distance from cell phone tower.

Male	Female
Headache*	Mental stress*
Mental stress*	Depression*
Depression*	Migraine Disability assessment*
Migraine Disability assessment*	Sleepiness*
Sleepiness*	Fever*
Weight Lose*	Long Term Constipation*
Visual Loss*	Change in the size of stool*
Fever*	Hyper Pigmentation*
Fatigue*	Erythema*
Presence of long-lasting sore in the mouth*	Purities*
Presence of white patches inside the mouth*	
Presence of white spots on the tongue*	
Heart Diseases*	
Long Term Constipation*	
Change in the size of stool*	
Hyper Pigmentation*	

To have a correlation between the adversely reported symptoms by the people residing near cell phone tower at various distances and power density of the respective cell phone tower, the power density was measured of 420 cell phone towers at various times.

Table. 3. The details of the measurements.

Descriptions	Quantity	No. of Antenna/ Tower	Time during Survey conducted
Number of Tower Survey	420	-	-
Number of Tower survey Day time	51	-	11 AM- 1 PM
Number of Tower survey during Day & Night time	369	-	11 AM – 1 PM & 19 PM – 21 PM
Higher power density during day time	1 7 5 / 4 2 0 (41.66%)	3-24	-
Higher power density during night time	1 2 2 / 3 6 9 (33.05%)	6-18	-

The data analysis to find out the correlation between the adverse symptoms reported and the power density of the respective cell phone tower is going on.

To Restraint or Regulate the Reproductive Health Issues of Human from Jammu and Kashmir Region

This study is going under the centre of advanced research and this will help us to evaluate the incidence and prevalence of diseases related to human reproductive system in the state of Jammu and Kashmir. Moreover, the study will also reveal clinical reasons of falling reproductive health through genetic analysis. Further, this important study will help to create awareness regarding preventable measures regarding reproductive health.

Till now, 2979 samples from the cases of primary infertility, Secondary infertility, PCOS, Ovarian Cancer, Idiopathic males and controls have been recruited. From the collected data it was found that the 14.32% of primary infertile males were diagnosed with erectile dysfunction, whereas 11% has recurrent abortions. In primary infertile females about 32% of females have irregular periods, 11.6% of females were diagnosed with PCOS, 2% of females were diagnosed with endometriosis, 3% of females were diagnosed with fallopian

tube blockage and about 33.3% of females were infected with varicella infection. Further, genetic analysis was done, which include, Karyotype, PCR Based screening of critical genes, Whole-exome sequencing, micro-RNA Analysis, and microarray analysis for gene expression on selected cases. The Genotyping of Ovarian cancer samples for newly identified genetic variant rs2853677 of TERT GENE was also performed, where. Strong association between TERT polymorphism rs2853677 with Ovarian Cancer was observed. Five manuscripts have been published from this study till now. Further several workshops and seminars have been organized for capacity building to create awareness regarding preventable measures regarding reproductive health.

To evaluate the feasibility of multigene panel for diagnosis and management of Autism Spectrum Disorder in early neonatal period

The objectives of this study is to analyze DNA samples from Autistic and controls children using a multigene panel and identify gene-disease relationship and variants specific to Indian population using Chromosomal Microarray and Next Generation Sequencing Technology. The centre is evaluating the predictive value of the screening tool using latest data analysis tools and statistics to identify genes and variants specific to Indian population.

Till now 70 samples and 10 controls from various centres including AIIMS, New Delhi have been collected and analyzed. COVID-19 pandemic has led to a shortage of samples because no OPD's were opened for any of the sample collection sites. It is expected the same to resume now and be able to complete the set of samples required for the study.

NATIONAL CENTRE FOR TECHNOLOGY IN FAMILY WELFARE (NCTFW), IIT, KHARAGPUR

NCTFW was established by the Ministry of Health and Family Welfare (MOHFW), Government of India as a continuing program with expertise and specialties to expeditiously respond to technological

problems which are in the National Family Welfare program. Since its establishment, the NCTFW is being funded by the Ministry of Health and Family Welfare (MOHFW), Govt. of India directly but on the direction of the MOHFW, now ICMR is funding the NCTFW since Sept., 2019 as one of the Centre of Advanced Research (CAR) of ICMR.

Under this centre, the following studies have been undertaken.

Upgrading the RISUG manufacturing facility for large scale manufacturing of RISUG pre-filled syringes (to be used for clinical reversibility study and Phase-IIIb clinical trial)

The RISUG manufacturing facility established at IIT Kharagpur needs to be upgraded for supply of RISUG prefilled syringes to be used for clinical reversibility study, Phase-IIIb clinical trial and also for post marketing surveillance. This is as per the requirement and direction of the DCGI.

Existing RISUG manufacturing facility has been upgraded as per the requirement and direction of the drug regulatory authority the officials from central DCGI and Govt. of West Bengal Drug regulatory authorities had visited twice the RISUG Manufacturing facility at IIT Kharagpur. The site visit teams had suggested some modifications in the RISUG manufacturing facility and the NCTFW is under taking these modifications.

RISUG® Male injectable contraceptive: pH and free DMSO method of analysis standard protocol

RISUG® (Reversible Inhibition of Sperm under Guidance) is a hydrogel and is useful as a vas deferens injected reversible male contraceptive which has successfully completed phase III clinical trials in India. RISUG® has the characteristics of both, an implant and a medical device. The physical and chemical forms of RISUG® differ from the conventional drugs present in the medical pharmacopoeia. This warrants different testing procedures. The term “pH” usually refers to an

aqueous system. For an aprotic solvent like DMSO, pH is not defined. Hence pH of RISUG® having ~60% DMSO is not strictly defined. It is, therefore, important to attempt quantification. The centre has performed free DMSO assessment. In RISUG, all the DMSO is in bound form, mediated by chemical and physical bonds. The main chemical bonds are: covalent, ionic, hydrogen and charge transfer bonds. The chemical bonds are with the maleic group of styrene maleic anhydride (SMA); styrene maleic acid as well as with the styrene component of SMA. FT-IR and NMR spectra generated did not show the presence of native DMSO. Furthermore, DMSO was found to be physically trapped in the long chain of SMA-DMSO complex. This was validated by Raman spectroscopy, where the vibrational Raman spectra did not show native DMSO peaks. Also, the Operational and Technical methods related to renovating RISUG® R&D Unit [e.g. Facility planning and Designing as per GMP requirements, Operational feasibility of timely renovation of sterile air handling unit, Material Requirement Planning, Electricity distribution planning, Scientific experiment planning and GMP facility, Layout design etc.] have been planned. Currently, the centre is working extensively towards addressing these requirements for standardized production of RISUG®. Also, the list of documents provided as per schedule M Drug and Cosmetics Act 1940 [Rules 71,74,76 and 78] are under preparation - this is a critical requirement for any drug manufacturing unit.

Polyvinyl Alcohol and Styrene-Maleic Anhydride blend polymeric gels as intra-vaginal female contraceptive

The use of polymeric hydrogel RISUG® for the purpose of fabricating a complete biodegradable non-hormonal female contraceptive implant was evaluated. Different formulations of RISUG® hydrogel were developed by grafting with suitable bio-polymers like polyvinyl alcohol in order to fabricate non-hormonal female contraceptive implants.

Table. 4. Compositions of PVOH/ RISUG® hydrogel polymeric films.

Sample description	PVOH concentration	RISUG® concentration
R0	10%	0
R0.5	10%	2.5%
R1	10%	5.0%
R1.5	10%	7.5%
R2	10%	10%

Physiochemical characterization for all the polymeric formulations were evaluated to identify the chemical integrity and mode of interaction between the polymeric mixtures with the Active Pharmacological Ingredient (API) RISUG®. Selective antimicrobial property and antiviral property of RISUG® polymer was also evaluated. Cytocompatibility for all the polymeric formulations were evaluated using respective cell lines. In vivo biocompatibility of the polymeric formulations was evaluated by histological and immunohistochemical evaluation of respective rat tissue sections. Hematology, blood biochemistry and organ toxicity for the polymeric formulations was also performed to reveal the biocompatibility of all the polymeric formulations. A complete preclinical study for all the contraceptive formulations were successfully evaluated and published in peer reviewed journals. The results indicate that RISUG® is extremely promising to be formulated as various forms of non-hormonal female contraceptive implant at respective concentrations.

Clinical trial for the non-hormonal female contraceptive implant has to be performed in order to develop the implant as a commercially viable product in future. The effects of this complete biodegradable non-hormonal female contraceptive device for patients with endometriosis and Pelvic Inflammatory Disease (PID) remain to be evaluated.

Transcervical delivery of contraception in female

This particular study was aimed towards testing a new transcervical sterilant that becomes effective

immediately with a high effectiveness rate, and added advantage of being potentially reversible.

Sterilant: The sterilant that was investigated was a polymer compound (named FerroCept) which inactivates both ovum and sperm. The compound has a spikulated structure (spikes or points on the surface at a micro scale) and has magnetic and electrical-conducting properties to facilitate placement and removal. It has shown potential for reversible female contraception without totally obstructing the tubal lumen, thereby maintaining near-normal physiological conditions, a benefit for potential reversibility. The sterilant was delivered to the fallopian tubes trans cervically and the positioning of the drug imaged by ultrasound and X-ray imaging.

Developing methodology for cannulating a closed cervix with a large bore cannula

Various methods were tried and tested for insertion in the closed cervix. Finally, micro endoscopes of 1.9mm diameter specially made by C-Link Imaging, Los Angeles USA were procured and the centre was able to put that in through larger cannula pipes to observe the inside of the reproductive tract and identify the correct position for insertion of the drug. The injection procedure was perfected by initially trying out on female goat cadavers.

Device development and Implantation

A special injector designed specifically for FerroCept delivery was inserted through the split plastic tube. The probe consists of a stainless-steel hollow tube through which the drug is injected. A balloon collar was fitted on the tube which can be inflated to prevent backflow of the drug. After injection on one uterine body, the hollow plastic probe along with the special injector is pulled back to the internal OS and inserted in the other side guided by palpation. This procedure was carried out in cadaver with FerroCept. Also, therapeutic diathermy (150-200mA) was applied for 5 minutes on the lower abdomen to stabilize the drug in the fallopian tubes. After the procedure,

the reproductive tract was extracted and the drug distribution checked. It was observed that the drug reached both the fallopian tubes and this procedure was finalized and accepted. With the method described above, the external and internal cervical os was easily traversed by the metallic probe and guided to the right uterine body by palpation.

The main achievement of the study is that it is possible to deliver the drug, Ferrocept into the fallopian tube of the animal with even so called “closed” cervix. The initial results reveal that Ferrocept has adequate contraceptive efficacy. SMA, the main component of the drug has potential HIV inhibitory property. Therefore, it may be expected that Ferrocept, along its proven contraceptive efficacy, will integrate improved reproductive health with HIV prevention.

Understanding the mechanism of recurrent spontaneous miscarriage of unknown etiology

Metabolic profiling of uterine fluid from women with Idiopathic Recurrent Spontaneous Miscarriage (IRSM) could provide a meaningful insight into the microenvironment of the implanting embryo. The serum metabolites, L-lysine, L-arginine, L-glutamine, L-histidine, L-threonine, L-phenylalanine, and L-tyrosine were found to be significantly up-regulated in IRSM as compared to controls and indicate their possible involvement in the molecular mechanism of exaggerated inflammatory response and vascular dysfunction associated with poor endometrial receptivity. Also, metabolic profiling of uterine fluid from these women indicated altered glucose and lipid metabolism, disrupted energy metabolism cycles and excessive protein degradation. FT-IR and Raman imaging of endometrium of women with IRSM obtained during implantation window is currently underway to generate biochemical signatures specific to the disease for better understanding of the disease pathophysiology, since as the term “idiopathic” suggests, the disease remains largely unknown.

Development of dendritic cell vaccine for the treatment of recurrent/metastatic reproductive cancers

Dendritic Cells (DCs) have unique characteristics and are considered the most effective antigen-presenting cell (APC) responsible for primarily sensitizing naïve T cells to specific antigens. Our group has used GMP grade recombinant SPAG9 protein for DC based vaccine immunotherapy in cervical cancer patients for better cancer treatment.

Therefore, the Centre is undertaking research to evaluate the identified biomarkers (SPAG9, AKAP4, HSP70-2) for early detection and diagnosis in cervical and ovarian cancer patients in southern and northern regions of India; follow up of the treat cervical and ovarian cancer patients for persistence/ progression and recurrence, employing identified biomarkers; preclinical evaluation of therapeutic and prophylactic SPAG9 cancer vaccine in animal model system; evaluation of cell-based vaccine therapy-Dendritic cell-based immunotherapy for epithelial ovarian cancer patients who have failed two systemic therapies; in-depth research on immune responses in ovarian cancer patients immunized with dendritic cell-based immunotherapy from southern and northern regions of India.

THE WORK UNDER THE CAR

Ovarian cancer: Blood samples were collected from 79 patients of epithelial ovarian cancer and 227 patients of cervical cancer patients (before or after neoadjuvant chemotherapy) for early detection and diagnosis of biomarker study.

The percentage of ovarian tumor was determined by a trained cytologist. Cells were frozen with 10% DMSO containing freezing mixture and stored in liquid Nitrogen. The protocols for the generation of DCV and the immune assays to be used in the project have been standardized. Histotypes are yet to be determined for 6 patients in ovarian cancer and 1 patient in cervical cancer.

For the follow up study: Blood samples are collected as scheduled.

Table. 5. The number of follow up samples collected so far.

	Presentation	1 st follow-up	2 nd follow-up	3 rd follow-up	4 th follow-up
Cervical cancer	65	65	35	11	4
Ovarian cancer	23	23	9	5	1

Cervical cancer cases

A total of 41 cervical cancer patient's blood samples were collected. The age ranged from 31-68 (median-52) years. Two patients had adenocarcinoma, 26 patients were of squamous cell carcinoma, 4 patients had keratinizing squamous cervical cell carcinoma, 2 patients had non-keratinizing squamous cervical cell carcinoma, and 5 patients had poorly differentiated cervical cancer.

Ovarian cancer cases

Blood samples from 46 ovarian cancer patients were collected after informed consent to the patients. The age ranged from 31-75 (median 46) years. The patients were diagnosed with adenocarcinoma (37), Serous adenocarcinoma (2), Serous papillary adenocarcinomas (2), mucinous carcinoma (1) and poorly differentiated carcinoma (4).

Early detection and diagnosis in cervical and ovarian cancer patients

SPAG9 gene and protein expression was carried out in 41 cervical and 46 ovarian and cervical cancers. SPAG9 gene and protein expression was detected in 90% of cervical cancer and ovarian cancer patients.

Preclinical evaluation of therapeutic and prophylactic SPAG9 cancer vaccine in animal model system

B-16/F10 melanoma cancer cells were injected subcutaneously for immunized animals to study the tumor progression, growth and / or arrest. At the end of the study, animals were sacrificed; and various molecules involved in apoptosis, cell cycle and EMT will be studied by IHC and Western Blotting. Sera were collected after every immunization to check SPAG9 humoral response.

WOMEN REPRODUCTIVE HEALTH

Capacity building through HRRCs for screening of common cancers (oral, breast and cervical)

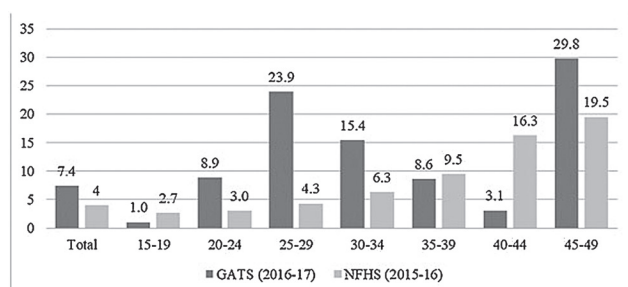
This study is being undertaken at 3 ICMR HRRC centres to create awareness regarding oral, breast and cervical cancer among women attending out-patient and in-patient services in tertiary care hospital and to provide facility for opportunistic screening of oral, breast and cervical cancer to women attending out-patient services in the department of Obstetrics & Gynaecology. The study also aims to provide pre-service and in-service training to doctors and nurses for screening of oral, breast and cervical cancer in tertiary care hospitals. The study operationalizes the Government of India guidelines for screening and management of common cancers. The study has completed three years and screened around 3000 women. Training modules were made for the screening of CA cervix, breast and oral cancer in the project. Video presentations were made & displayed at various sites in the OPD for the purpose of creating awareness among females regarding cervical, breast and oral cancer. Self breast examination was taught to all the females included in the screening programme.

Smokeless Tobacco and Reproductive Health

Assessment of harmful effects from smokeless tobacco (SLT) and areca nut use remains to be neglected among females, especially pregnant women, despite causing much preventable morbidity in mothers and the neonates. Hence, a study aiming to understand SLT and areca nut use and consequence in women of reproductive age as a means to develop training and behaviour change intervention models for cessation is ongoing. The study is examining the association between

socioeconomic factors of SLT use among women of reproductive age and adverse pregnancy outcomes using Demographic and Health Surveys in selected south Asian countries (Afghanistan, India, Nepal, Maldives and Pakistan). The study further aims to develop and test Behavioural Change Intervention (BCI) tool(s) for SLT and areca nut cessation among women belonging to reproductive age group.

Table 6: Percentage of Pregnant Women, reporting any kind of SLT use, India.



ICMR Registry of PPIUCD and Centchroman Contraceptive Users

The Government of India has introduced some new contraceptive methods in its programme including (Post partum IUCD) PPIUCD and Centchroman. There is limited data on the user characteristics and continuation rates or adverse effects associated with the use of these contraceptives. This ongoing study at 6 sites is planned to understand the satisfaction and continuation rates among women using Centchroman and postpartum IUCD and to document the side effects/adverse effects of Centchroman and PPIUCD. Findings at one year are tabulated. A total of 10073 women were recruited and 33,083 women were counselled for PPIUCD and centchroman contraceptive. Women are being still followed up; and PPIUCD expulsion and removal have been observed in 804 and 1477 respectively. Data generated from this project till date was presented at various conferences and 14 publications in National and International journal have been made from this project.

INFERTILITY AND PREGNANCY LOSS: ASSESSMENT AND INTERVENTIONS

Immuno-modulatory effect of Intralipid in women with recurrent implantation failure

with elevated uterine Natural Killer cells (RCT)

Objectives of this study are to evaluate the role of NK cells in implantation failure and to study the immunomodulatory effect of intralipids in women with elevated NK cells undergoing fresh IVF/ICSI on implantation rate and clinical pregnancy rate. The observation of increased Natural killer cells (NK cells) in the endometrium of women with reproductive failure has suggested they may play a role in this pathogenesis.

Molecular Analysis of promising immune-regulatory pathway involved in Recurrent Pregnancy Loss (RPL)

This study aims to investigate the role of HLA-G and FOXP3 polymorphisms in the regulatory sequences (3'UTR and promoter) in women with recurrent pregnancy loss in comparison with parous women and estimates the circulating sHLA-G and FOXP3 levels among RPL and parous women and anti- (IL-4, TGF- β) inflammatory cytokines among RPL and parous women. Immunoregulatory molecule, HLA-G is expressed in non-villous cytotrophoblast cells at maternal-fetal interface at initial stages of pregnancy, promotes tolerance by inducing immunosuppressive Treg (CD4+ CD25+ FOXP3+) cells. Reduced levels of HLA-G and FOXP3, a master regulatory transcription factor of Treg cells may impact the anti-inflammatory milieu during pregnancy. The genetic alteration in these genes may disturb the pregnancy outcome. The ongoing study will assess any relation of the pathway with RPL.

Psychosocial Dynamics of Pregnancy Loss: Development of a Multidimensional Scale & Development and Efficacy (a Randomized Control Trial) of a Group Psychological Intervention Module

Pregnancy loss is a painful and traumatic event that can occur at any time during the pregnancy. The ongoing study aims to provide efficacious psychological treatments for females who have

experienced pregnancy loss. These treatments will be in the form of manual or e-modules formats which are presently non-existent in India. Once it is done through present RCT study, these females either at the hospital or at their home can use both manual and e-modules.

Burden of Still births & early neonatal deaths and their risk factors in selected districts of Haryana: A multicentric task force study

This study was done with the objectives - to study the risk factors of still birth including demographic and clinical factors during antenatal and intra-natal period in a tertiary care setting; to find out the incidence of still birth in a tertiary care setting; to establish linkages with the district health system for timely referral and the new knowledge generated will be used to help formulate policies for improving obstetric care thereby decreasing the still birth rate in tertiary care setting. The focus was on the modifiable risk factors of stillbirth like optimising any medical disorder prior to planning pregnancy, early and adequate antenatal care so that stillbirths can be minimized. Also it has been found that the intrapartum causes account for a significant proportion (20%) of the cases. Improving management during labour can take care of the big number of stillbirths.

Determinants of still birth among deliveries in tertiary care centre

Stillbirth is an important, yet most poorly understood adverse outcome of pregnancy. In the past few years a lot of attention has been given to maternal, neonatal, and child health; but stillbirths still remain invisible. Stillbirths are neither mentioned in the Millennium Development Goals, nor in the Global Burden of Disease metrics. At national level too, in policies, programmes, and investment agendas stillbirths are not emphasised upon. Data on and solutions for stillbirths need to be organised and communicated so that strategies can be formulated for prevention of stillbirths

in middle or low income countries in limited resource settings. The current study is done with the objectives - to study the risk factors of still birth including demographic and clinical factors during antenatal and intra-natal period in a tertiary care setting; to find out the incidence of still birth in a tertiary care setting; and to help formulate policies for improving obstetric care thereby decreasing the still birth rate in tertiary care setting.

ICMR CENTRE FOR ADVANCED RESEARCH IN MECHANISMS LEADING TO PRE ECLAMPSIA

The Centre is undertaking studies to examine the possible factors involved in the pathology of preeclampsia at early and later stages of gestation and establish the role of long chain poly unsaturated fatty acids (LCPUFA) and micronutrients in mechanisms associated with pre eclampsia,. The study would be useful in development/ validation of biomarkers for early prediction of pre eclampsia; providing information on mechanistic aspects of pre eclampsia; and understanding the neurodevelopmental outcome of children born to women with Pre eclampsia.

A total of 1076 pregnant women have been recruited early in pregnancy and followed at 4 time points until delivery. Information on subjects clinical history, medication, SLI, physical activity, 24 hour dietary recall, food frequency questionnaire, ultrasonography and color Doppler measures were recorded at each time point. Biochemical analysis of various parameters like fatty acids, micronutrients, oxidative stress markers and angiogenic markers, growth factors is ongoing. Children are being followed up for anthropometry at various time points and developmental assessment at 2 years of age. Preliminary analysis suggests that

- Women who develop PE have a higher age, BMI and blood pressure right from early pregnancy until delivery as compared to non-PE women.

- Percent women in the PE group conceiving through IVF and IUI was higher as compared to the non-PE group and delivered by caesarean section.
- Majority of the women in the PE group were nulliparous. TSH levels were observed to be higher in women with PE in early pregnancy.
- Fetal measurements by USG such as BPD, HC, AC and fetal weight at 32-35 weeks were lower in women with PE as compared to non-PE group.
- Doppler measure such as mean uterine artery PI was higher in PE as compared to non-PE group.
- Women with PE had placentae with lower thickness and had a higher percent of bilobed and irregular shaped placentae.
- Babies born to mothers with PE had a lower birth weight, length and head circumference. The percent of SGA babies was higher in the PE group as compared to non-PE group.

Gene specific methylation analysis of selected candidate genes *PIGF*, *FLT-1*, *HIF1A*, *HIF3A* and *PEMT* shows significant hypomethylation at various CpG sites in the *PIGF* promoter region and *FLT-1* gene and significant hypermethylation on two CpG sites in the *HIF3A* gene and one CpG site in *HIF1A*. This disturbed methylation patterns of genes may influence the process of placental angiogenesis in women with preeclampsia.

INNOVATION IN MATERNAL HEALTH

Development Of Fetal Growth Nomograms Standards Specific To The Indian Antenatal Population

Assessment of the fetal growth is an essential part of prenatal care; the aim being to detect suboptimal growth as restriction of the fetal growth has immense implications for the neonatal wellbeing. There are no established ultrasound derived fetal growth nomograms specific to our Indian population. This study aims to establish a reference

for fetal growth pattern in our population based on serial ultrasound scans right from early pregnancy so as to provide an effective reference tool to be uniformly applied in our health systems and ultrasound software to detect suboptimal fetal growth.

Development of Novel Female Condom

The currently marketed female condoms have been found to lack an ease of application, less sexual pleasure and expensive. The existing female condoms are bulky and hence women are hesitant to use them due to their size. The willingness to pay a higher price up to the levels of the manufacturing cost of the existing ones in the market is found to be unacceptable among the female populations. Accordingly, there is a need for an effective female condom that overcomes the shortcomings associated with the current female condoms. This revealed a strong need to look for other lesser priced and better acceptable product variants of female condoms. The objective of the proposal is to develop novel female condom, with aesthetic appearance, improved ease of application, increase sexual pleasure and affordability. The female condom (FC) is the only safe and effective female-initiated method that provides simultaneous protection against unintended pregnancy as well as sexually transmitted infections (STIs), including HIV/AIDS. But unlike the male condom, it also covers parts of the external female genitalia. With the recognition that gender-based inequalities are major forces driving the HIV and AIDS pandemic, the development of a barrier method over which women have some control became imperative. Thus this device empowers a woman to protect herself from unintended pregnancies and STDs without depending on the male partner.

LABOUR ROOM INTERVENTIONS

The effectiveness of Peanut Ball device during labor on maternal & neonatal outcomes and stress level in low-risk primigravida women - A Randomized controlled trial

The objectives of this study are to determine the effectiveness of the use of a peanut ball device during labour in terms of maternal outcomes such as the pattern of uterine contractions, duration of active stage of labour, duration of the 2nd stage of labour, nature of delivery, need for pain medications, perception of pain and occurrence of Post-Partum Haemorrhage. The study also assesses the effectiveness of the use of a peanut ball device during labour in terms of neonatal outcomes such as fetal heart rate patterns, neonatal Intensive Care Unit (NICU) admissions, APGAR score, stress levels (cortisol levels), satisfaction rates and birth injuries. The study is about to complete one year.

Prevalence, Procreation, Persecution and Prevention regarding Caesarean-Section Deliveries/Births: A Systematic Review and Meta-Analysis

It is assumed that around 15% of the pregnancies tend to land into any complication and need surgical intervention. However, in the age of worldwide inequities, the CS procedure is both underused and overused. This study is being carried out with an objective to assess the prevalence of CS deliveries across different regions of the world, stratified by type of health facility, rural-urban settings, age groups, socioeconomic status and education level of the delivering women, major indications, risks associated with unnecessary CS and prevention thereof.

Quality of intra-partum and immediate post-partum care of mothers and newborns: An implementation research to improve performance of LaQshya program

LaQshya initiative has been launched to fast track quality of care, with a 360-degree approach towards (a) structural and (b) process improvement around labor room and maternity OT in Government facilities. Considering the rapid nature of the interventions for LaQshya, learnings from different contexts shall augment the progress of Quality Improvement for intra and immediate post-partum

care of mothers and their young ones. In this proposed study, district health system shall entirely lead and implement the LaQshya interventions as desired under the program guideline; the research team shall closely observe, document bottlenecks, and co-create strategies to overcome these in partnership with health system and primary implementers. The overall implementation strategy will be to catalyze the working of the health system leveraging currently available human as well other resources and accelerate the process of improvement.

A randomized controlled trial of abused pregnant women to improve health status

An important factor contributing to the under utilization of skilled birth care in facility set up arises due to disrespect and abuse (D & A) experienced by the women during ante-natal care (ANC), intra and post-natal care. Satisfaction and trust in health care facilities and providers is eroded. This can cause delayed or non-utilization which in turn, effects women's health and birth outcomes. This study is being done with the Objectives - to assess the effect of disrespect and abuse of women in maternity care on psychological wellbeing; to study the impact of D & A during maternity care on psychological wellbeing (in stress, depression, anxiety and PTSD indicators); and to develop the appropriate intervention package for improving the psychological wellbeing of the women. This study is being done as descriptive Cross-sectional study using mixed method approach in Block PHCs/ additional PHC of 5 states. At its core, D&A is a human rights issue. Disrespectful and abusive care is a violation of women's rights to life, health, bodily integrity, self-determination, privacy, family life and spiritual freedom, and freedom from discrimination. A culture of mistreatment endangers both mother and baby, physically and psychologically, directly or indirectly. Despite worldwide declines in both maternal mortality and infant mortality over the past 10-20 years, the rates of improvement have been much slower for the low resource countries. Hence it is critical to

generate data relating to disrespectful and abusive care practices and its influence on psychological well being and satisfaction during maternity care, particularly in India. This is a first of its kind study of the Disrespect and Abuse (D & A), where PHC and Sub-centre level data will be collected.

Respectful Maternity Care Initiative – ICMR Task Force Study in collaboration with White Ribbon Alliance India (WRAI)

Facility-based care for childbirth is one of the key strategies to reduce maternal and perinatal morbidity and mortality. Various policies have been put in place by different governments and health systems such as use of incentives, education and community mobilization to increase facility births. However, many women decide not to seek facility-based care for childbirth, despite recognizing the associated health benefits. This decision is often based on their previous experiences of poor quality care, including poor treatment, abuse, discrimination and neglect while in facilities. It is therefore critical for the maternal health community to ask how it can prevent such mistreatment, and better meet women's socio-cultural, emotional and psychological needs as part of broader efforts to provide better quality care. The objectives of the study are - to review available standards for Respectful Maternity Care (RMC) and adapt them in the Indian context; to engage maternity care stakeholders to create awareness, recognize and report on deficits in RMC; to document typology of RMC deficits in labour rooms; and to identify challenges, barriers and facilitators in implementing RMC standards in facilities. This study will address the mistreatment of women when, where and how it occurs; so that effective, sustainable, measures/ interventions can be implemented in the health system to prevent disrespect and abuse and improve women's birthing experience.

ICMR research initiative on Gestational Diabetes Mellitus (GDM)

There is no adequately powered study, which provides evidence that the currently commonly

used criteria for GDM (DIPSI and IADPSG) help identify women and inform their management, to improve either perinatal or long-term outcomes in Indian women. The lack of consensus results in confusion and inconsistent screening and diagnosis. A prospective multi-centre observational cohort study would be shortly initiated to evaluate maternal and fetal outcomes in women diagnosed with GDM or normoglycaemia using IADPSG criteria, among women diagnosed with normoglycaemia by DIPSI criteria. The study findings may enable government and concerned authorities to revise policies for GDM diagnosis in health programs. There is limited literature available on the barriers, challenges and facilitators for implementing the GDM guidelines in different healthcare settings across India. To assess the implementation of the GOI guidelines for the diagnosis and management of GDM at different levels of health care delivery at both rural and urban settings across India and determine the challenges at individual, provider, community and health systems for implementation of the guidelines, a multisite mixed method prospective cross-sectional study in collaboration with the state and district health system would be carried out across six regions of the country. Based on the results of this situational analysis, a multipronged intervention package model for implementation at district level would be developed.

ICMR research initiative on Maternal Near Miss

On the continuum between normal health and death extremes, pregnancy is thought of as uncomplicated, complicated, severely complicated (potentially life-threatening) or life-threatening. A "Near Miss" represents one of the two possible outcomes of a life-threatening complication: the mother either survive and become a "Near Miss", or she dies and become a maternal death. The potentially life-threatening complications may precede the development of a life threatening complications as well long-term sequelae, even if they did not suffer the life-threatening event during pregnancy and childbirth. This concept was

included in the revised framework of maternal near miss measurement by the WHO maternal morbidity working group. Identifying and register these women; and the factors associated with them will help plan strategies to prevent or reduce the burden of the disease and delay their complications. This strategy is in tune with SDG goal 3 of ensuring health and well-being for all as a healthy mother can ensure a healthy child and contribute better to the family's well-being.

Assessing increasing burden of PCOS among women

Polycystic ovary syndrome (PCOS) is rising in epidemic proportions parallel to the epidemic of diabetes mellitus and has its impact on health of girls, young women especially in their reproductive phase of life that has potential of transferring the condition to future generations. There is a close link to other lifestyle diseases like Diabetes mellitus, obesity, heart disease etc. To address the issue in the country Indian Council of Medical Research (ICMR), has taken an initiative to conduct first nationwide prevalence assessment of PCOS through the multicentric ICMR-PCOS task force study. The study includes estimation of national prevalence, phenotypic variation, quantitate the burden its co-morbidities, compare the variation of efficacy of standard therapeutic modalities for metabolic dysfunction in PCOS women (2 sites – AIIMS & SKIMS) and to assess knowledge and management practices among service providers in public health sector on PCOS in its Phase-I. The ongoing phase-I is surveying women subjects (~1000 rural, N=500 and urban, N=5000 per site) aged 18-40 yrs. from 6 geographical zones of the country i.e. North, South, East, West, North-East and Central India. The coordinating centre, SKIMS, Srinagar has set up “PCOS Station”, it is a one-stop facility for PCOS comprehensive care and for capturing clinical data that remains functional on every Thursday. Beside the coordinating Centre has successfully created a central laboratory facility using high end system of (ECLIA) technique with good sensitivity and specificity. Despite, the exceptional situation

related to the COVID-19 pandemic that has imposed unprecedented constraints. The project has almost completed the enrolment process and over 75 percent of subjects are done with detailed investigations (Clinical, biochemical, hormonal and 30-35 percent of subjects are with ultrasound pending).

CHILD HEALTH

Advanced Research on Paediatric Kidney Diseases

The Centre for Advanced Research in Pediatric Kidney Diseases at the All India Institute of Medical Sciences (New Delhi) was sanctioned in 2017 and is an open-ended research program that has enabled establishment of a facility for epidemiological, clinical and translational research, relevant to the national needs. Proposals in the program have provided leads into the pathogenesis of kidney diseases and efficacy of various therapies. The program enabled formulation and revision of guidelines for common clinical diseases, and brought together physicians and scientists working on children with kidney diseases from across the country on a common platform. Specific output from the program is highlighted below: i) **Development of evidence-based guidelines** for managing common kidney diseases, such as hemolytic uremic syndrome, urinary tract infections and nephrotic syndrome ii) **Training of residents and Pediatricians** in Pediatric Nephrology through specialized annual training courses iii) **Generation of evidence** on issues related to epidemiology, pathogenesis and/or therapy of kidney diseases of childhood, with focus on nephrotic syndrome, hemolytic uremic syndrome (HUS), and vesicoureteric reflux, as follows: a. Establishment of a biorepository and longitudinal disease registry for patients with HUS, which will serve as a useful resource for studies into disease pathogenesis and clinical outcomes in relation to therapies of disease characteristics. b. Whole exome sequencing in almost 25% of 100 patients with non-diarrhoeal and non-autoimmune

HUS shows significant variants in genes regulating the complement pathway c. Whole exome sequencing for significant variants in 50 patients with the severe phenotype of vesicoureteral reflux. d. Establishment of a facility to estimate leukocyte levels of cystine, a useful tool for diagnosis and monitoring of therapy in patients with cystinosis, an inherited cause of chronic kidney disease in children.

Advanced Research on Respiratory Diseases in Children

Centre for Advanced Research in Respiratory Diseases in Children was sanctioned in August 2018 for 5 years to AIIMS, New Delhi. It includes 5 sub projects. Despite COVID-19 pandemic, the progress towards achieving the stated objectives is ongoing. Cystic fibrosis registry has been started successfully under the project and till now from 4 centres, 200 children have been enrolled. It is planned to expand and include all children under follow-up at the project sites and subsequently to other centres in India. A simplified diagnostic algorithm based on history, simple lab tests and aquagenic wrinkling has been developed. Mutation studies are ongoing. Initial results suggest that the mutations among Indian children suffering from cystic fibrosis are different and there is regional variation also. Consensus based management protocol suitable for India has been developed. A point of care diagnostic test (High speed video microscopy) for primary ciliary dyskinesia has been developed and is undergoing testing. Mutation studies for primary ciliary dyskinesia are ongoing. Initial observations suggest profile of mutations in India are different. Details of clinical manifestations, imaging findings and other investigations of patients suffering from interstitial lung disease are being recorded and being processed to develop diagnostic algorithm. Mutation studies on interstitial lung disease are ongoing. Data collection is ongoing for morbidities in immune deficiency disorders. There have been three publications so far from the project and three presentations have been made in conferences,

out of which, two have one first and second prize respectively.

Establishment of Health and Demographic Surveillance System in Dibrugarh District, Assam

Health is a fundamental human right. Attending the highest possible level of health is the most important social goal worldwide. Health and Demographic Surveillance Systems are used to provide a framework for prospective collection of demographic and public health data within a community. Assam HDSS has been set up to establish population-based health and demographic surveillance system for epidemiological and programmatic evidence/intervention in Dibrugarh district of Assam. The project has successfully established a health and demographic surveillance system in Dibrugarh district of Assam. A total of 1,06,769 (Village: 46,762 Tea Garden: 60,007) participants from sixty villages and twenty tea gardens were included in the baseline survey consisting of 52,934(49.6%) male and 53,835(50.4%) female subjects. Till 31st October, 2021, a total of 75,686 individuals (Village: 40,726 Tea Garden: 34,960) from 16,292 households were followed up. Of these, 38,177(50.4%) are male and 37,509(49.6%) are female subjects. All information was recorded using unique mobile application software developed for this purpose. Further, this mobile application was upgraded for Pan India use i.e. it can be utilized for data collection in HDSS sites of other parts of the country.

It was found that average family size (4.9 vs. 4.4), number of females per thousand male populations (1017 in tea garden vs. 954 in rural populations) were significantly higher in tea garden community than that of rural population. Considering 2011 census data, the study did not show any major change in family size for rural population. The prevalence of self-reported diabetes, stroke and heart diseases were found to be more in villages as compared to the tea gardens. On the other hand, the prevalence of tuberculosis is significantly higher in tea gardens than villages.

Dibrugarh-HDSS also aimed to determine epidemiological risk factors for maternal mortality and identify high risk population. During the reporting period from 01.01.2021 to 31.10.2021, Dibrugarh-HDSS recorded 3 (three) maternal deaths from tea garden community. Verbal autopsy was performed for all the cases. We have also followed up the birth events in the study area including still-birth. Dibrugarh-HDSS recorded a total of 1211 births [619(51.1%) in villages and 592 (48.2%) in tea gardens] in the population under surveillance from 01.01.2021 till 31.10.2021. There were 1211 live births, 21 still births, 14 induced abortions and 7 miscarriages. During the reporting period (01-01-2021 to 31-10-2021) a total of 654 deaths were recorded. Of these 20 were recorded as infant death in the surveillance area.

The mean birth weight was significantly higher in villages (2844.8gm) as compared to tea gardens (2693.5). The prevalence of LBW in tea garden community was found to be significantly higher than villages (28.4% vs. 15.6%).

Dibrugarh-HDSS has also been able to develop longitudinal database and created several cohorts e.g. pregnant cohort, LBW cohort, new-born cohort, stroke cohort, hypertension cohort, etc. Dibrugarh-HDSS has worked towards capacity building across different institutions and 2 PhD scholars are pursuing their PhD in the Dibrugarh-HDSS platform. Linkages have been established with ABITA (Assam Branch Indian Tea Association), National Health Mission, Assam Medical College, Tea Garden authorities of all the tea gardens in surveillance area and Dibrugarh University. Further, networking has been established with 227 core stakeholders. A total of thirty-two community awareness meetings were organized by Dibrugarh-HDSS which were attended by 1137 people from villages and tea gardens. These meetings served the purpose of awareness generation and capacity building of different cadres of health and community workers.

Impact of the COVID-19 Pandemic on Health of Pregnant Women and their Neonates

Pregnant women and neonates have been identified as high risk population during the COVID-19 pandemic. However, there is a lack of data on the effect of the disease in this population. A registry on pregnant women and their neonates affected with COVID-19 was initiated in 2020. The registry is receiving data from 21 centres all over the country and has recorded data on approx. 5000 pregnant or post partum women along with about 3000 neonates. The registry is web portal based, which has been designed by ICMR. The registry is collecting data on epidemiology, demographic details, clinical features, severity, treatment and outcomes among pregnant women and neonates. The registry has been able to collect data on all the three waves of COVID and the data is presently being analysed.

ICMR initiative for rare diseases afflicted population in India

More than 70 million people in India suffer from the plethora of rare diseases, manifesting in childhood, which remains with them throughout their lives. ICMR National Registry for Rare and other Inherited disorders (NRROID) was initiated in November 2019 in collaboration with AIIMS, New Delhi and 7 other nodal centres, to collect useful data on demography, phenotype, natural history, evolution and outcomes of specific disease with/without treatment. Other objectives of the registry are to support research on genetic, molecular and physiological basis of rare disease, to establish a patient base for evaluating drugs, medical devices, and orphan products and to connect affected patients families, and clinicians. The disorders on which data is being collected have broadly classified under six categories viz. Lysosomal storage disease, inborn errors of metabolism, skeletal dysplasia, haematological disorders, primary immune deficiency, neuromuscular disorders. 19 centres from all over the country are contributing to the registry at present. Data on over 4000 cases of rare diseases has been collected till date under the registry.

Determining cause of death in under-5 children using Minimally Invasive Tissue Sampling (MITS)

A pilot study was conducted, with objective to build capacity of health care professionals for performing MITS along with creating logistics and infrastructure for determining causes of death in U5 children and stillbirths in a tertiary hospital setting in Delhi and to explore its feasibility and acceptability for providing a foundation to future pathology based mortality surveillance in India. For the purpose of the study, Child Health and Mortality Prevention surveillance (CHAMPS) protocol was adapted to suit local needs. Initially a formative research was conducted to assess the feasibility and acceptability and identifying challenges. Following the formative part, MITS was implemented. A total of 684 deaths were notified during the study period out of which 466 were approached for consent. 183 MITS were completed successfully with approx. 50% acceptance rate. It was concluded that it is feasible to perform MITS in a tertiary care hospital. There was good concordance between the clinical and the MITS findings. In 20% of the cases MITS modified the clinical diagnosis. Comparing the level of expertise at a tertiary care hospital and district and sub district level hospitals, it was postulated that MITS might be an even more helpful option for these settings.

Aetiology, risk factors and antibiotic sensitivity pattern in neonatal sepsis

Sepsis is a major cause of neonatal mortality. It is seen that the epidemiology of neonatal sepsis differs considerably in the developed and developing countries in terms of profile of etiological bacteria and their antibiotics susceptibility pattern. Even within the developing nations geographical variation in the above profiles is seen. The risk factors and the clinical presentations of neonatal sepsis are much varied and differ according to the age of onset, and also on the causative organism. The present study is therefore undertaken to find out the common bacterial pathogens and their

susceptibility pattern in neonates with sepsis in different tertiary care centres in Assam which can help to design any intervention or management strategy. A total of 998 suspected neonatal sepsis samples have been collected till now from the 4 study sites i.e. 251 (Tinsukia Civil hospital), 42 (Dhemaji Civil Hospital), 284 (SMCH) and 421 (FAAMCH). The culture positivity rate of sepsis amongst newborns are as follows- 49% (123/251), 21.4% (9/42), 29.6% (84/284) and 13.3% (56/421). Gram positive and gram negative organisms were found at a rate of 30.3% (76/123) and 18.7% (47/123) in Tinsukia respectively, a rate of 77.8% (7/9) and 22.2% (2/9) in Dhemaji, a rate of 25% (21/84) and 25% (21/84) in Silchar and a rate of 62.5% (35/56) and 37.5% (21/56) in Barpeta respectively. The most common bacteria isolated from LGB, Tinsukia was Coagulase negative staphylococcus (35.6%) followed by *Klebsiella pneumoniae* (22.2%). In Dhemaji, the most common bacteria found was *CoNS* (66.7%) followed by *E.coli* (11.2%). In Silchar, the commonest bacteria found was *Klebsiella pneumoniae* at a rate of 57.1% causing neonatal sepsis. *Staphylococcus aureus* was seen to cause neonatal sepsis at a higher rate of 44.6% followed by *Klebsiella pneumoniae* (33.9%) in Barpeta. Considering the maternal risk factors, mothers occupation ($p=.015$) is found to be significantly associated with the rate of neonatal sepsis in Tinsukia. Also, in Dhemaji mother's qualification ($p=.008$) and in Barpeta, vaginal discharge ($p=.027$) is found to be significantly associated with neonatal sepsis which are derived by multivariate logistic regression analysis. Amongst clinically suspected neonatal cases, it was found out that males had higher rate of sepsis than females in all the 4 sites. On the other hand, early-onset sepsis (EOS) was found at a higher rate in Tinsukia, Dhemaji and Barpeta. Antibigram profile of the isolated organisms have revealed that gram positive organisms have shown higher rate of resistance towards beta lactams, quinolones, sulphonamides, lincosamides, macrolides, oxazolidinones class of antibiotics while gram negative organisms showed higher rate of resistance towards beta lactams,

beta lactamase inhibitors, aminoglycosides, tetracycline, sulfonamides class of antibiotics. PCR was performed for the 88 gram negative isolates of which 25 of them showed the presence of *icd* and *adk* genes specific for *E.coli* while 10 showed the presence of *tonB* and *gapA* genes specific for *Klebsiella pneumoniae*. As per project's protocol, a 10% (07) of the isolates are sent to NICED, Kolkata for external quality assurance for first year and also the results for the second year external quality assurance is awaited. Molecular characterization for the remaining isolates is on progress as per the protocol provided by NICED, Kolkata.

ICMR Centre for Advanced Research in Evidence-Based Child Health (Phase – II)

The Centre completed 04 sessions of prioritization workshops with chief discussant from ICMR, NITI Aayog, WHO regional office of South-East Asia, University of Sussex UK, Govt. of UP, Former Secretary DHR, members from Health Parliament, faculty from AIIMS, and PGIMER for prioritizing topics for a systematic review on child health. Four systematic reviews on paracetamol exposure and asthma, Hypothyroidism in pregnancy and its impact on fetal and maternal outcomes in India, Effects of probiotics on the frequency of CD4+ T-cells in HIV infected children and adolescents, and Isoniazid versus alternative regimens for the treatment of latent Tuberculosis in children were completed. One Health Technology Assessment (HTA) on the diagnostics tools for diagnosis of Tuberculosis/MDR-TB under NTEP was completed. Three policy brief documents on “Hypothyroidism in pregnancy and its impact on fetal and maternal outcomes in India”, “Probiotics for a proactive GUT”, and “Isoniazid versus alternative regimens for the treatment of latent Tuberculosis in children” were drafted. The CAR established networking with HITAP Thailand, Cochrane India Network, AIIMS, NITI Aayog, PGI, NIRT Chennai, National Institute for Research in Tuberculosis, and other institutes from different countries. Conducted several capacity-building workshops on: “How to practice evidence-based child health”, “Health

economics”, “Development of research protocol”, “Health technology assessment”, “Evidence-based medicine made easy”, and “Systematic review & GRADE”. The CAR supported Indian scientist in literature/database searching, training through online course, webinar series, and supported to compile the reviews proposed by the participants. During the pandemic, the CAR also conducted webinar series on COVID-19 infection and children (each alternate week).

Capacity Building for North East Region in Evidence Based Medicine

Background: An online mentoring approach in combination with the onsite mentoring would be effective in using the resources to the fullest. The ECHO (Extension for Community Healthcare Outcomes) model could be adopted for the online approach, as it would be easy for the healthcare workers to attend the sessions and interact without being compelled to travel. **Method :** The online sessions on evidence-based medicine has been conducted for healthcare professionals (pediatricians and research scientists) in the northeastern region of the India. These sessions were conducted by collaborating with ECHO (Extension for Community Healthcare Outcomes) to connect with a number of medical colleges, Health facilities and ICMR MRHUs in the Northeastern region of the country. Practice-based learning modules and didactic presentations were conducted in this mentoring process. Sessions on evidence-based medicine were included, medical literature searching through medical databases, critical appraisal of randomized controlled trials and systematic reviews, framing of research question and development of protocols. After the enrolment of the participants for the online course, the completion and registration of a systematic review protocol was considered necessary in order to get the certificate for the course. **Result:** During this period (April 2019 to July 2020), considerable progress has been made in attaining the objectives of the project. The ECHO model utilizes video conferencing softwares to connect the mentors

from PGIMER to the participants in remote areas in the North East over the internet. The Scientists involved in conducting these sessions received a 2 day training in New Delhi on how to use the ECHO Model and trouble-shooting. The sessions were started online with real time transmission to the North East Region Participants from 3-4 pm Wednesdays fortnightly. The number of Participants enrolled for the online mentoring program is 49. Total 27 sessions were conducted during this period with 25-35 (Average) participants per session. One workshop was conducted onsite during this period in Guwahati, Assam, with title “National Workshop of Skill building in Systematic reviews in the North East Region” on 26th and 27th of September, 2019. **Conclusion:** Due to this project, more and more people are taking interest in evidence based medicine in the NER. The participants trained through these capacity-building courses also help in developing systematic review questions and thereby help in policy guidance at various levels. The case based discussion in these sessions also help the medical professionals in the remote regions in getting important inputs from experts in the host institute.

Centre of Advanced Research (CAR) in Pediatric Emergency Care at PGIMER Chandigarh

During the reporting period two projects were carried out under the ICMR Centre for Advanced Research” in Pediatric Emergency Care at Advanced Pediatrics Centre, Department of Pediatrics PGIMER Chandigarh.

To establish a computerized database of pediatric emergency cases

This project is ongoing from March 2018. In the current year (2020-21) the team further refined the module to incorporate CLINICAL DETAILS, TREATMENT and OUTCOME and integrate it with already existing module. A ‘discharge advice’ module was also created and integrated to complete follow up advice. It also has provision to collect

data on ICD diagnosis, different hospital outcomes and discharge notes.

Software piloting: (January - February 2021)

The complete software was checked and piloted in January – February 2021. The output in pdf format requires further fine tuning.

Ongoing data entry: (March 2019 – January 2020)

Final version of triage software is continued to be implemented since 2018. All consecutive children visiting emergency department have their triage details entered into the database and stored electronically. Currently, for every month, triage details of about 2500 children have been recorded in the database.

Developing an emergency treatment protocol for diagnosis and management of tropical infections in critically ill children to improve clinical outcomes

Objective: Systematic review of available pediatric literature on tropical diseases and formulation of graded, evidence-based guidelines for diagnosis and management of critically ill children presenting with tropical infections Literature review: All indexed publications from all standard databases (EMBASE, PUBMED, SCOPUS, etc.) were screened by a team of project medical officer, investigator and one external expert familiar with the retrieval of medical literature using standard screening words such as ‘tropical fever’, ‘tropical infections’, ‘tropical diseases’, ‘dengue’, ‘scrub typhus’, etc. The search focused on diagnosis and management of tropical diseases in Indian children. Team of experts selected relevant articles and the final set of research papers for review were prepared for the protocol development Protocol development: A writing group was formed with team of internal and external experts in the field. The PI and the writing group have gone through each of the articles and classified them according to hierarchy of evidence. Using an iterative consensus process, the group is in the process of developing an

evidence-based emergency diagnosis and treatment protocol for the clinical condition. The first draft with recommendations has been prepared and is undergoing evaluation with internal experts.

Impact evaluation of “screen and treat” approach for anemia reduction: a cluster randomized trial in rural Telangana

Objective: To assess the effectiveness of population level screening followed by targeted IFA supplementation according to the grade of anaemia for increasing the mean population level hemoglobin and reducing the prevalence of anaemia as compared to the existing anaemia control program. **Methodology:** This cluster randomized trial is being conducted in 14 villages of Telangana to enrol all the village residents (approximately 14000) in the study. Half of the villages are randomized into intervention arm and half to the control. Intervention includes screening for haemoglobin estimation using a portable autoanalyzer and providing treatment with iron folate tablets to those who are diagnosed to have mild or moderate anemia. Severe anemia cases are referred to health facilities for treatment. In the control villages, there is no intervention by the researchers and the usual anemia control program activities are ongoing. At 6 months, anemia prevalence is being estimated in all study participants from the intervention as well as control villages to assess the difference in anemia prevalence in the two arms. The custom software was field tested among 106 households and 42 frontline health workers from the study area prior to start of the community trial. The software captured the process flow accurately and generated decisions correctly. Additionally, the application for endline data collection and the dynamic dashboard for trial monitoring were developed during the reporting year.

The community trial was initiated in June 2021. Till Jan 2022, the internal pilot study was completed in 3+3 clusters. About 2091 blood samples were collected. The overall prevalence of anemia was around 25 %. The highest anemia prevalence was

among women (43%) and 6-59 months old children (38%). About 1466 participants are receiving IFA (therapeutic or prophylactic) depending upon their anemia status. Based on the internal pilot study in 3 clusters, the sample size for the cRCT was finalized to include 14 clusters. The study is ongoing to complete the sample size and the endline data collection is expected to complete by November 2022.

Effect of daily supplementation with multiple micronutrients and iron folic acid compared to iron folic acid alone in children aged 6 to 59 months on anaemia prevalence and haemoglobin concentration: A randomized controlled trial in urban Delhi

Sub Study 1: Effect of biweekly preventive supplementation with multiple micronutrients and iron folic acid compared to iron folic acid alone in children aged 6 to 59 months on haemoglobin concentration and anaemia prevalence: A randomized controlled trial in rural Haryana.

Background: Around 60% of children below 5 years have anaemia which has consequences on cognitive development, school performance, physical growth and work productivity later in life. India has a national program in place that provides iron folic acid syrup to children but still the proportion of anemia in children is decreasing very slowly. This study is being conducted to understand that if children are given iron and folic acid along with other micronutrients (vitamins and minerals), will this decrease the overall burden of anemia, as compared to giving only iron folic acid.

Methods: This is an individually randomized controlled open-label efficacy trial to be conducted in Primary Health Centres (PHCs) in Palwal, Haryana. A total of 1300 children aged 6-59 months will be enrolled and given 100 doses of bi-weekly supplementation with 20 mg iron, 100 mcg folic acid and erythropoiesis relevant micronutrients in the intervention group; and 20 mg iron along with 100 mcg folic acid in control group. Primary

outcomes will be mean hemoglobin and proportion of children with anemia. Iron parameters (serum ferritin, transferrin receptor, percent transferrin saturation and total iron binding capacity), micronutrient levels (Vitamin B12, zinc and folate) and inflammatory markers (hs-CRP and AGP) will also be assessed in a sub-sample. Cost-effective analysis of supplementing iron folic acid (IFA) with multiple micronutrients compared to IFA alone will also be done.

Results/ Progress: The study team was recruited and trained, and the study forms were developed, tested and finalized. The team initiated the enrolment of the children in the study on 12th February 2021 and on 29th September 2021, all the 1300 children were enrolled. The intervention delivery is ongoing. The outcome assessments have been started since 01/02/2022 and the outcome assessment is planned to be completed tentatively by October 2022. As on 25th February 2022, blood samples in 103 children have been collected for outcome assessment. The team has also started data collection for cost-effectiveness in 1st week of January 2022. This data is planned to be conducted in a sub-sample of children (330 children).

Sub Study 2: Effect of daily therapeutic supplementation with multiple micronutrients and iron folic acid compared to iron folic acid alone in mild to moderate anemic children aged 6 to 59 months on anaemia cure and haemoglobin concentration: A randomized controlled trial in rural Haryana.

Background: Around 60% of children below 5 years have anaemia which has consequences on cognitive development, school performance, physical growth and work productivity later in life. This study is being conducted to understand that if children with mild to moderate anemia are given iron and folic acid along with other micronutrients (vitamins and minerals), will this increase hemoglobin concentration and anemia cure rate, as compared to giving only iron folic acid.

Methods: This is an individually randomized controlled open-label efficacy trial to be conducted in Primary Health Centres (PHCs) in Palwal, Haryana. A total of 1300 children aged 6-59 months with mild to moderate anaemia ($Hb \geq 7$ g/dl and <11 g/dl) will be enrolled and given 90 doses of daily supplementation with 3 mg/kg/day of iron, 100 mcg of folic acid and erythropoiesis relevant micronutrients in the intervention group; and 3 mg/kg/day of iron along with 100 mcg of folic acid in control group. Micronutrient levels, serum hepcidin and high sensitivity C-reactive protein (hs-CRP) will be assessed in a sub-sample at baseline. Primary outcomes will be mean haemoglobin and proportion of children cured of anemia. Iron parameters (serum ferritin, transferrin receptor, percent transferrin saturation and total iron binding capacity), micronutrient levels (vitamin B12, zinc and folate) and inflammatory markers (hs-CRP) will also be assessed in a sub-sample. Cost-effective analysis of supplementing iron folic acid (IFA) with multiple micronutrients compared to IFA alone will also be done.

Results/ Progress: The study team was recruited and trained and the study forms were developed, tested and finalized. The team initiated the enrolment of the children in the study on 8th March 2021. As on 25th February 2022, a total of 1268 children (1268/1300; 97.5%) were enrolled. The enrollments are expected to be completed by Mid-March 2022. The primary outcome assessments have been completed in 645 children. The outcome assessments are planned to be completed by June 2022. The team has also started data collection for cost-effectiveness in 1st week of January 2022. This data is planned to be conducted in a sub-sample of children (330 children).

INDIA PEDIATRIC HIV COHORT

Background: The ICMR task force study was conducted in two phases i.e., 2011-14 and 2014-18. At the end of this study, a cohort of 2022 HIV exposed children (230 HIV infected and 1694 HIV uninfected and 98 HIV untested children)

were identified belonging to 977 families across the district. From 2018 onwards, this cohort was unfollowed till date. Now, this phase III (2020-22) ICMR task force study is taken up to revive the already identified cohort and to reach for new pediatric cases, to test its earlier-HIV-untested children. The primary objectives are contact and revive the cohort of children of the ICMR pediatric task force study (Phase 1 and/or 2) in Belgaum district, follow up the cohort for morbidity and mortality four times in a year and to link them to appropriate health care facilities in the district, determine the factors influencing ART coverage among HIV infected children in Belgaum district of Karnataka state.

Methodology: The study is being implemented in Belgaum a Category “A” district as defined by NACO in 2008. Administratively, Belgaum is divided in to 10 sub-district or taluka levels. These 10 sub districts will be divided into two sites (five talukas in each site). Informed consent will be obtained from the parents/guardians of the eligible children who are enlisted in the phase1 and/or 2 of ICMR task force study. These children will be approached at their residence/other place of convenience as preferred by the family (in view of HIV-related confidentiality issues). Planners would be prepared based on the date of recruitment into the phase 3 study and the age of the child, to conduct scheduled data collection. Haemoglobin estimation will be done in first visit and exit visit. HIV testing will be done once a year for HIV negative children. The data collection will be done using study software on a hand held device/tablets.

Progress: Ethical clearance was obtained from both the sites institutional ethical committees. The following tools required for the data collection was developed: 1. Line list of children of phase 1 and/or 2 study. 2. Child form (C form) 3. Informed consent form/Accent form 4. Acute and chronic morbidity form 5. Health care facility mapping form. The list of 461 children (HIV infected and HIV affected) to be revived is segregated from Phase 2 data. Study Software is developed by a technical team, which

is dynamic real time platform for the data entry into the software. This real-time dash board has the individual complete data and also the summary statistics, is password protected and it is protected against misuse, as it stores confidential data of HIV positive children, The software was tested and retested for functionality. Permission for from KSAPS, Bangalore is awaited to begin the field work.

Phase III, Multicentre, Randomized, Double-blind, Placebo-controlled Study to Evaluate Efficacy of Probiotic Supplementation for Prevention of Neonatal Sepsis in 0-2 Months old Low Birth Weight Infants in India

Neonatal infections (pneumonia, septicaemia, meningitis) are responsible for more than a quarter of the 1 million neonatal deaths every year in India. Low Birth Weight (LBW) is an important indirect cause of death in neonates, accounting for 40% to 80% of neonatal deaths. These neonates have poor cognitive function and compromised immune functions. In LBW infants, infections are known to spread rapidly leading to severe disease and death. Prevention of infection in low birth weight babies would directly decrease the neonatal morbidity and mortality. Currently there are no preventive interventions available for neonatal sepsis other than general measures of hand-washing, exclusive breastfeeding etc. Management of neonatal sepsis with antibiotics faces the problem of drug resistance, attributed to availability over the counter, indiscriminate use and incomplete courses in India. Immune-modulation/immune-potential with the use of probiotics may prove to be an option. The proposal for this study has been granted award of funding under MRC/NIHR/DFID/Wellcome Trust, Joint Global Health Trials. preparatory phase are being completed. A tripartite agreement between the sponsor and the pharmaceutical companies for supplies of investigational products (IPs) has been signed and a clinical trial agreement between the sponsor and the participating sites is being signed. Staff recruitment at Collaborating sites is under process. The study protocol has been reviewed by

the Research Ethics Committee of the LSTM, UK as suggested by MRC. The Trial has been registered at CTRI. The CT-NOC from CDSCO has been obtained. During the reporting period activities of the implementation phase of the trial have been initiated. An investigator's meeting, site feasibility and site initiation visits were completed at the six subject recruitment sites. A Hands-on workshop for the lab technicians was conducted centrally at AIIMS, New Delhi. First Trial steering Committee and the Data Monitoring Committee meetings were held.

THE ICMR - COCHRANE AFFILIATE CENTRE

The Cochrane Collaboration (www.cochrane.org) is a global independent network of researchers, professionals, patients, carers, and people formed to organise medical research findings to facilitate evidence-based choices about health interventions. It includes 53 review groups that are based at research institutions worldwide. In 2020 a Cochrane India Network was established with nine Affiliate centres across India. ICMR, New Delhi was invited to become part of the Cochrane India network. The functions of the Cochrane India Network Affiliate, Indian Council of Medical Research, at ICMR Hqrs would help fulfill the deliverables mentioned in the Evidence to policy translation activities listed in the Pillar-4 of the ICMR Strategic Plan and agenda 2030 document. The function of the Cochrane Affiliates would include: 1. to promote Cochrane and its work in India, 2. to support and develop the community of Cochrane members in India and 3. to disseminate Cochrane systematic reviews locally based on stakeholder network, the media and other communication channels.

NUTRITION

Improving health and nutritional status of vulnerable segment of population by implementing multi-component health and nutrition education intervention as a sustainable model of intervention

The study was initiated in 41 districts of 20 States (including all 8 north-east states). The study has been completed at all sites except two sites. Preliminary analysis of Haryana State indicated improvement in timely initiation of breastfeeding (less than an hour) by 33%. Similarly, pre-lacteal feeding among infants declined by 11%. Among infants, exclusive breastfeeding for 6 months increased by 30% while initiation of complementary feeding at 6 months by increased by 25%. Among pre-school children, exclusive breastfeeding for 6 months increased by 12%. Improvement was also observed in the percentage of children who received de-worming tablets in last 6 months by 21%.

Prevalence of fluorosis in the community of selected districts of India and development of an appropriate intervention model for prevention and control of fluorosis

This study is currently ongoing at 7 locations in the country (covering one district each in Orissa, Madhya Pradesh, Telangana, Chandigarh, Bihar, Rajasthan and Assam). Preliminary analysis indicated prevalence of dental fluorosis as 37%.

Assessment of Iodine status among pregnant women in selected districts of India

This study is being carried out at 10 locations in the country. Preliminary analysis indicated insufficient iodine intake among pregnant women as the median urinary iodine concentration (137.5 µg/l) was less than the recommended median urinary iodine concentration for pregnant women by WHO i.e <150 µg/l. Similarly, the pooled median urinary iodine is higher among non pregnant women (144.0 µg/l) as compared to pregnant women (137.5 µg/l).

Prevalence of vitamin A deficiency disorders among children aged 6-60 months in selected districts of India

It has been initiated recently at 7 locations of the country (Assam, Odisha, Telangana, Bihar, Madhya Pradesh, Rajasthan and Uttar Pradesh). Preliminary analysis indicated prevalence of Bitot's spots

among children aged 6-60 months as 0.6% and prevalence of night blindness among children aged 24-60 months as 0.2%.

Division of Nutrition supported 51 adhoc projects from different parts of the country in varied fields like community based surveys to laboratory experiments. Some of these studies are evaluation of prevalence, risk factors, consequences of thiamine deficiency among apparently healthy community dwelling Kashmiri population; effect of Vitamin C and Thiamine in patients with sepsis; role of calorie restriction along with a modulator on circadian rhythm regulation and their combined effect on glioma suppression; etc. Approx. 90 fellowship research studies were supported.

CENTRE FOR PROMOTION OF NUTRITION RESEARCH AND TRAINING (CNRT) WITH SPECIAL FOCUS ON NORTH-EAST, TRIBAL AND INACCESSIBLE POPULATION

CNRT has a NABL accredited Clinical Biochemistry laboratory where biological samples collected from the field for various biochemical parameters like lipid profile; Vitamin A, Vitamin E, Thyroid profile etc are being analyzed. The Centre/laboratory is supporting the ongoing task force studies as well as researchers/ scholars from different Medical Colleges/ Universities for their thesis/ dissertation work.

ENVIRONMENTAL & OCCUPATIONAL HEALTH

Research in priority areas of occupational and environmental health relevant to national needs for various working groups is actively undertaken by the ICMR-National Institute of Occupational Health, Ahmedabad, the ICMR-National Institute for Research in Environmental Health, Bhopal and ICMR-Bhopal Memorial Hospital & Research Centre, Bhopal. Major highlights of various programmes undertaken by the ICMR in the areas of occupational and environmental health during the year 2020-2021 are given below.

INTRAMURAL RESEARCH

ICMR-NATIONAL INSTITUTE OF OCCUPATIONAL HEALTH, AHMEDABAD (ICMR-NIOH)

A study to evaluate the serum fibroblast growth factor 21 in allostasis and allostatic load among industrial workers

To assess the effect of Allostatic load (AL) on levels of serum FGF21 among industrial workers with contemplation of lifestyle confounding factors. The study was executed with cross sectional study design in the industrial set-up. A total of 169 male industrial workers were enrolled and investigated the AL and levels of serum FGF21. AL was measured using primary, secondary mediators and anthropometric markers. Serum levels of FGF21 were determined using the ELISA method. About 45.6% of workers had allostasis (normal) and 54.4% of workers

had an AL. Higher levels of serum FGF21 were noted in workers with AL ($P=0.006$) and increased AL component score ($P<0.001$). The association between serum FGF21 and AL was assessed using logistic regression models with un-adjustment and adjustment of confounding factors. Serum FGF21 levels was significantly associated with AL (OR [95% CI], 1.004 [1.001-1.007]; $P=0.008$). The study identified that 54.4% of workers had allostatic load (stress) and the FGF21 was significantly elevated in AL condition and it could be used as potential biomarker for early detection of stress at work place. These findings presented for the first time in the relevance of FGF21 in workers under the condition of AL

Respiratory morbidities in school children of critically polluted Industrial Area of Gujarat

Children living in the Critical Polluted Area (CPA) are at high risk for respiratory disease with respect to deleterious exposure of various air pollutants. Current available literature of Indian studies have limitations with their design (cross sectional nature) and majority of them have neither addressed the potential confounders nor measured ambient air pollutants exposure among the children. Present longitudinal observational study was aimed to explore whether children who were raised in CPA area are at higher risk of respiratory illnesses and have reduced lung function compared to those children raised in places with relatively better air quality. Present study enrolled and followed up 733 students (CPA area, $n=546$ & control area, $n=187$)

for a year. Both indoor and outdoor air quality parameters of the study area was significantly poor as compared to control area. Average URTI and LRTI episodes of entire year for study area students were significantly higher (URT episodes- 5.25 v/s 3.58, LRTI episodes- 0.65 v/s 0.35) compared to control area students. Abnormal PFT were observed among 19.2% of study and 8.8% of control students. Air conduction parameters (both, small & large airways) were significantly lower among study students in comparison to control students.

Assessment of Environmental Pollution Exposure & Cardio-Respiratory Morbidities Among AMTS bus drivers

A total number of 238 bus drivers from Ahmedabad city were screened for cardio-respiratory health during their duty hours and compared with controls (admin staff of AMTS, n=73). Additionally, pollutants exposure at 20 different AMTS bus routes during duty hours was also measured. Personal air sampling during duty hours (TWA, 8 hrs) revealed that PM_{2.5} and PM₁₀ exposure were 970.9 (258-1340) µg/m³ and 1111.7 (298-1480) µg/m³, respectively, and found higher than CPCB ambient air quality standard guideline. Respiratory problems (e.g. cough and dyspnoea) were found significantly higher among AMTS drivers as compared to control group. Pulmonary Function Test (PFT) was found abnormal (25% high) among bus drivers as compared to controls (8.5% high). More than 65% of bus drivers were observed at High BMI ranges. Mean PFT parameters FEV₁/FVC and FEF_{25%-75%} (which represents flow of air in large and small airways, respectively) were significantly lower among drivers compared to control subjects ($p < 0.001$). Around 14% bus drivers were hypertensive and were unaware, while 9% drivers were having unregulated BP beside-being on medication. As per WHO/ISH 10-Year CVD risk score, substantial higher risk (>10%) for ischemic heart disease were observed among drivers (27%) compared to controls (17%). The study revealed that bus drivers were found not only

at high reparable dusts (PM_{2.5} & PM₁₀) exposure but also at higher cardio-respiratory risk and related health problems.

Multicentre Task Force Entitled “Study to Assess the Exposure and Health Effect of Pesticides

A national study on potential toxicity and health hazards associated with endosulfan exposure was carried out to generate data which initiated scientific database at national level. The study analyzed samples from Maharashtra (n=836) and Telangana (n=704) centres. Pesticide residues were found in 3.67% blood samples whereas 6% serum samples contained pesticide residues. The concentration ranges of Dichlorvos, Profenophos, Quinalphos and Buprofezin were 124 - 154 µg L⁻¹ and 27 - 60 µg L⁻¹, 129 µg L⁻¹ and 10 µg L⁻¹ respectively in blood samples. The concentration ranges of Dichlorvos, Profenophos, Cartap Hydrochloride, Acephate and Quinalphos were 23 - 248 µg L⁻¹, 43 - 51 µg L⁻¹ and 66 - 346 µg L⁻¹, 32 - 39 µg L⁻¹ and 25 µg L⁻¹ respectively in serum samples. The concentration ranges of Dichlorvos, Acephate, Phorate, Monocrotophos, Quinalphos and L-Cyhalothrin were 11 µg L⁻¹, 28 - 952 µg L⁻¹ and 36 µg L⁻¹, 12 - 63 µg L⁻¹, 29 µg L⁻¹ and 12 µg L⁻¹ in urine samples.

Monitoring of Pesticide Residues at National Level

This is a pan India project wherein many laboratories are participating viz., those under the aegis of Ministry of Agriculture, Indian Council of Agriculture Research, Indian Council of Medical Research, Council of Scientific and Industrial Research, Ministry of Chemical and Fertilizer and Ministry of Commerce and State Agricultural Universities. A total of 749 samples (farmgate (n=629) and market samples (n=120)) in addition to fruits (n=96), milk (n=30) and water (n=20) were analyzed using UPLC-QTOF-MS and GC-MS for pesticide residues. Maximum pesticide residues were found in Bitter gourd, Brinjal, cabbage, capsicum, cauliflower, cucumber, green

chili, tomato, okra, bottle guard, cluster beans, apple, banana and mango, pomegranate and orange. Overall, 0.20% of the samples reported concentration above Maximum Residue Limits (MRL). Majority of food samples were safe for human consumption.

A carbon nanotube based miniaturized sensor for differential diagnosis of ACO from asthma and COPD

In this study in collaboration with IIT Kharagpur, the team tried to develop a Carbon Nanotube (CNT) based nanosensor for differentiating between asthma and COPD. The study identified few markers based on preliminary findings that are presently being translated on the CNT based nanosensor for robust detection of the disease. Integration of the fabricated device with the presently existing diagnostic method i.e. spirometry, is expected to help the clinicians in differential diagnosis of obstructive respiratory diseases and would help in a better disease management.

Protective effects of biochanin A and coenzyme Q10 combination against chromium induced toxicity in experimental model

The objective of this project was to assess the selected natural compounds could counteract the toxicity induced by these heavy metals, and also to decipher the molecular mechanism involved in functioning of these natural compounds on the genetic level.

Metamobilome based environmental antimicrobial resistance assessment in pharmaceutical industries cluster of Ahmedabad area

Initiated new intramural project which later received extramural financial support for cataloguing the metamobilome based environmental antimicrobial resistance (AMR) patterns in pharmaceutical industries clusters of Gujarat. The approach intending to apply the whole genome sequencing technique for identification for identification of known and potential new plasmids which

potentially can promote newer AMRs via horizontal gene transfer.



Fig. 1: Collection of soil and sludge samples for antimicrobial residues analysis and plasmids isolations for deep genome sequencing.

Explorative study to assess the health status of Lead smelting plant workers

Lead (Pb) smelting workers are predominantly exposed to high lead levels and prevalent with high blood-Pb concentrations. This occupational group is at possibly high risk to develop lead toxicity because of low awareness of health hazard and poor hygiene practice in occupational exposure. The present study aimed to evaluate blood Pb and cadmium (Cd) levels and associated health status among occupationally exposed individuals. Total 157 participants (>18 years of age) were recruited in the study, who were employed in a Pb smelting plant and were handling raw material, furnace, electrochemical refining, maintenance and others like by products and utility services, as per the national ethical guidelines for biomedical and health research involving human suggested by ICMR. The Blood-Pb and Cd concentrations were determined as per standard NIOSH method using microwave assisted acid digestion and ICPMS technic. Haemoglobin levels were determined using hemoque tool. Blood pressure was measured using digital sphygmomanometer adhering to American Heart Society guidelines. Statistical analysis was performed using Statistical Package for Social Science version 17.0. The study population was observed average B-Pb level of $36.75 \pm 1.05 \mu\text{g/dL}$ (mean $\pm$ SE) and B-Cd levels of $0.15 \pm 0.01 \mu\text{g/dL}$ (mean $\pm$ SE). Approx 44.6% workers were found higher B-Pb levels than upper acceptable limit of $40 \mu\text{g/dL}$ (Medical Surveillance Guidelines – OSHA,

USA), whereas 4.5% population were found high B-Cd levels than upper acceptable limit of 0.5 µg/dL (OSHA). Elevated B-Pb and B-Cd levels were found significant association with employment elements and socio economic status of the individuals. Higher proportion of pre-hypertensive and hypertensive individuals were found among both groups with B-Pb levels below and above 40 µg/dL. Prevalence of musculoskeletal symptoms was higher among individuals with elevated B-Pb levels. Lead exposed individuals with BLL ≤ 40 µg/dL are at equal risk of health hazards as those with BLL > 40 µg/dL. Lead (Pb) smelting workers with predominantly high blood-Pb concentrations were shown higher prevalence of Hypertension and musculoskeletal consequences.

Assessment of health status of vendors exposed to bioaerosols in vegetable market

Vegetable market workers are at risk of being exposed to environmental bioaerosols and organic dust produced from the vegetable and market waste which poses harmful effects on their respiratory health. The study was aimed to understand the distribution pattern of microbes, endotoxin, (1-3)-b-D Glucan and dust in the ambient environment and also its adverse effect on the respiratory health of the workers. A cross-sectional case control study. Material and Methods: Air samples were analyzed for determination of the microbial load such as bacteria, fungi, organic dust, endotoxin and (1-3)-b-D Glucan from different sites of wholesale vegetable markets of Ahmedabad as well as compared with those in residential outdoor air. The highest bacterial and fungal load were observed during monsoon season followed by winter season. Enterococcus, Acinetobacter, Shigella, Citrobacter, Staphylococcus and Bacillus species were dominant bacterial isolates and Aspergillus, Fusarium, Penicillium, Curvularia, Mucor species were dominant fungi reported from different sites of vegetable markets. The organic dust concentration calculated were ranged from 1.18 to 5.21 mg/m³. Endotoxin and (1-3)-β-D Glucan were estimated from the dust samples which were higher in market

sites as compared to residential areas. Prevalence of respiratory symptoms viz. cough, phlegm, dyspnea, allergy in workers were higher as compared with residential control subjects and the difference was statistically significant, (P<0.05). Findings from the study indicated that the prevalence of respiratory health symptoms were higher among worker than residential control. Measures should be taken to prevent and reduce environmental bioaerosol exposure in vegetable markets.

Serum proteomic profiling differences study among silicosis, moderate silica dust exposed workers & healthy control subjects

The aim of the study is to compare the proteomic profile of x-ray confirmed silicosis patients (workers) and moderate silica dust exposed workers with that of the healthy age- and sex-matched non-exposed control subjects. Thus, the project hypothesizes that critical factor for lung injury during silicosis/silica dust exposure may associate with alteration of serum proteome as compared to the healthy nonexposed controls, which can be identified by mass spectra MS-based protein profiling and relative quantification. On completion of the study, it is expected that a bioinformatics-based model will be developed targeting serum biomarker that may provide a new insight of diagnostic biomarker(s) for silicosis, or similar kind of silica dust exposed workers including silico-TB in the country.

Assessment of lead toxicity in urban industrial residents of Gujarat

Heavy metal lead is one of the most significant environmental health threats to general population especially, vulnerable groups like, children and pregnant women. USEPA data revealed poor air quality in many cities with high levels of nitrogen dioxide, sulphur dioxide, particulate matter, ozone, carbon monoxide and lead; however, lack of awareness in developing and underdeveloped countries make the situation more worsen. Lead has no biological function and has no safer levels as its presence causes multiple irreversible damages in different body parts such as, brain,

liver, kidney, bones and hemopoietic system etc. The recent CDC reference value for blood lead is 3.5µg/dL, above which is considered a cause for concern and treatment, though most of the studies including India, have considered blood lead level of >100µg/L for statistical evaluation. Further, no base line lead toxicity data is available for general population in India, neither we are aware of blood lead status over the years. Therefore, in the above perspective, the hypothesizes that base line blood lead level of general population and its trend over the years on fixed cohort will be achieved by year-wise.

PUBLIC HEALTH

- It is observed that 54.4% of workers had allostatic load (stress) and the FGF21 was significantly elevated in such condition and it could be used as potential biomarker for early detection of stress at work place. These findings presented for the first time in the relevance of FGF21 in workers under the condition of allostatic load.
- The respiratory morbidities in school children of critically polluted industrial area of Gujarat showed Abnormal PFT were observed among 19.2% of study and 8.8% of control students. Air conduction parameters (both, small & large airways) were significantly lower among study students in comparison to control students.
- The Ahmedabad Municipal Transportation Service drivers study revealed that bus drivers were found not only at high respirable dusts (PM_{2.5} & PM₁₀) exposure but also at higher cardio-respiratory risk and related health problems.
- The findings from musculoskeletal disorders among urban metropolitan hairdressers has reported the estimates on work related musculoskeletal disorders (WMSDs) in India. Findings may prove as a compelling evidence for well-informed decision making in future on workers' compensation related to MSDs that historically been found responsible for at least one third of the labour time losses. Among other benefits, findings may contribute in devising effective regulations under health and safety provisions which would be highly valued for informal sector workers especially females who also represent this workforce in large numbers.
- The serum proteomic profiling among silicosis among exposed workers observed that critical factor for lung injury during silicosis/silica dust exposure may associate with alteration of serum proteome as compared to the healthy nonexposed controls, which can be identified by mass spectra MS-based protein profiling and relative quantification.
- The evaluation of effectiveness of BCG vaccine study included 183 elderly participants in the age group of 60 to 80 years who were given BCG vaccination and followed up six months post vaccination. The control group consisted of 118 subjects. The enrolment was done during the period 28th August to 27th October, 2020. The data was regularly submitted to the project coordinating institute, ICMR-NIRT for further analysis and report writing.
- A sudden outbreak was reported in Eluru with neurological symptoms like seizures, loss of confusion, etc among individuals from Eluru town since 4th December 2020 onwards. Whilst initially the symptoms were observed only in children, these were soon reported in adults too. With an aim to identify the contaminant and its source, ICMR-NIOH analyzed pesticide residues (n=60) using GC-MS/MS and UHPLC TOF-MS. Blood, water and food samples (n=165) were analyzed and sample results communicated to ICMR-NIN, Hyderabad.
- Monitoring of pesticide residues in food products helps to assess the potential health risk and regulate MRLs for safe human consumption.
- Assessment of pesticide related morbidity profile in the selected populations, burden

of pesticide and their metabolites in general population and possible health effects.

- It was observed that Infection Control Practices (ICPs) are not prioritised in Veterinary medicine professionals.
- It was also observed that cattle play an important role in transmission of leptospirosis in human in South Gujarat.
- Lead (Pb) smelting workers with predominantly high blood-Pb concentrations are prone to develop Hypertension and musculoskeletal consequences.
- It is hypothesized that individuals with higher levels of phthalates and PAHs will exhibit adverse health outcomes. Since studies along these air pollutants have been scanty a joint study with Emory University, USA would be proposed to study will the relation of exposures to phthalates, PAHs, as assessed via bio-monitoring.
- The bioaerosols study among vendors in vegetables market showed that the prevalence of respiratory health symptoms were higher among worker than residential control. Measures should be taken to prevent and reduce environmental bioaerosol exposure in vegetable markets.
- Mental health of health care worker engaged in COVID-19 was evaluated and the remedial suggestions were shared to reduce their burden. Strategies for preventing mental health burden of health care workers in similar future situations were shared.
- National workshops were conducted for sensitizing about 45 health care (medical) professionals on occupational health and safety.

PATENT

- **Patent # PCT/IN2021/050793:** A diagnostic device and method for differentiating Asthma-COPD Overlap Syndrome (ACO) from Asthma and COPD.

ICMR-NATIONAL INSTITUTE FOR RESEARCH IN ENVIRONMENTAL HEALTH, BHOPAL (ICMR-NIREH)

Density mapping and characterization of non communicable disease related built environment attributes in urban slums of Bhopal

Global burden of four main types of non-communicable diseases i.e. cardiovascular diseases, cancers, chronic respiratory diseases and diabetes (41 million deaths or 71% of all deaths globally) is well documented. Tobacco use, physical inactivity, harmful use of alcohol and unhealthy diets are the most important risk factors for NCDs and therefore prevention and control of these risk factors is important component of developmental resolutions including Sustainable Developmental Goals (SDGs). SDG target 3.4 is set to reduce by premature mortality from NCDs by one third through prevention and treatment and promote mental health and well-being by 2030 (relative to its 2015 levels). Built environments play important role in the epidemiology of NCDs by influencing NCD related human behaviour like walking, leisure, and transport-related to physical activity, which, consequently, affect the burden of NCDs.

The present study was designed for density mapping and characterization of NCD related built environment attributes (NCD attributes) in urban slums of Bhopal. The centre used, NCDs Environment Assessment Tool (NEAT) and Geographic Information System (GIS) to characterize distribution of NCD attributes and find out its possible association of prevalence of NCD in the neighbourhoods. Study focussed on 32 slum clusters of Bhopal covering a population of 6134 during September 2019 to January 2020. The study collected data from total 1146 NCD attributes located in the study area having defined selection criteria. Operationally, the attributes were classified into seven types (establishments, parks, enclosed physical activity areas, street vendors, weekly

market, place of worship and health care providers / centre) to facilitate data collection regarding specific services provided. Establishments were the most frequently encountered (685, 60%) of NCD attributes, followed by street vendors (172, 15%). Total 436 (63.6%) establishments had a permanent structure and 443 (64.7%) establishments were in unorganized sector. Owing to the overlap in the services available at establishments and the environment at establishments, team presented according to the products and / or services they availed e.g. grocery shops, tobacco outlets and restaurants. Street vendors selling at fixed point also supplemented services offered by establishments (grocery, tobacco and restaurants).

At grocery shops most frequently available products were chips, chocolates and candies (72-77%). Almost every second grocery selling establishments sold some form of packaged or ready to eat food. Street vendors also played important role in availing ready to eat food items. Fresh fruits (3.3%) and vegetables ((11.4%) were available at relatively lower proportion of grocery shops. Street vendors played a more important source of fresh fruits and vegetables for the community. The vendors selling while moving revealed little higher percentage of vegetable availability (66.1%). In the present study, centre identified total 72 tobacco shops. Tobacco shops, which mainly avail tobacco and related products, are popular establishments in Indian settings. In addition to tobacco shops, 214 grocery shops, 5 restaurants and 18 street vendors (i.e. tobacco selling establishments or TSE with other services or products) also availed tobacco (Density 36.88 / km²). Accordingly, collective number and density of tobacco outlets was 336 (29.32%) and 50.37 / km² respectively. The median density of tobacco outlets was higher in the service areas 71.0 / km² (IQR = 45.9 – 131.0) as compared to their density of buffer areas (50.83/km²) suggesting that they cluster near slum habitations. The environment at tobacco shops and TSE with other services or products was substantially different.

Sixty one percent establishments offering services as restaurants were fast food centres. Only 14.1%

restaurants availed salads in the menu. The number and density of establishments likely to promote healthy behaviour like parks, enclosed physical activity area were very low (8.25 and 2.85 per km²). Eight (25%) clusters didn't have a single park or physical activity area in their 400m service area. Only 18 (32.7%) parks were in regular use by residents for physical activity. This finding is of particular importance in a community where 76.1% population reported leisure time sedentariness.

The proportion of establishments having any kind of promotion / advertisements of products that can influence NCD related lifestyle of customer (tobacco, junk food or even healthy eating habits) ranged from 1.8 to 3.9%. However, it was observed at many establishments that products like packed high calorie food items (chocolates, biscuits, chips, namkeen) and tobacco products were displayed at cash counter. Such displays are likely to promote the products indirectly.

Classification and regression tree (CART) analysis revealed a non-zero (4.8572) intercept and positive correlation between tobacco habit and tobacco outlet density. Lower prevalence of hypertension was ecologically associated with tobacco outlet density of < 58 per km² service area. These findings indicate that the proportion and density of healthy NCD attributes was lower as compared to the unhealthy attributes. The density of tobacco outlets was associated with tobacco habit and prevalence of hypertension.

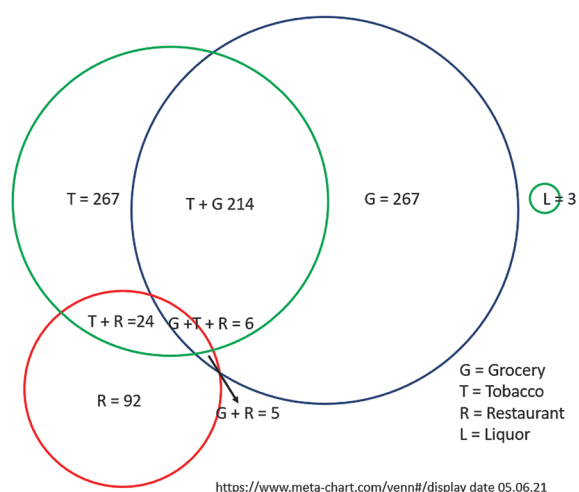


Fig. 2: Venn Diagram of Products / services available for sale at the establishments.

Aberrant circulating epigenomic signatures: development and validation of minimal-invasive biomarkers for trans-generational monitoring of air pollution associated cancers

Air pollution arising from a composite mixture of pollutants is now considered as a serious health concern. The global impact of pollutant exposure can be understood by the fact that in 2017, it was the 5th major risk factor for mortality worldwide and was associated with approximately 4.9 million deaths and 147 million years of healthy life lost as reported by SOGA, 2019. Molecular mechanisms underlying particulate matter (PM) induced human pathologies is not only governed by oxidative and/or inflammatory route but also by their intricate and cross-linking signaling pathways leading to epigenetic modifications. This study aimed to characterize the aberrantly circulating epigenomic signature profiles in defined population sets exposed to varying quantum of air-pollutants using a pan-India approach. The investigations were being carried out in different cities of low-risk and high-risk air pollution zones based upon ambient air quality. Circulating levels of methylated DNA, post-translational histone H3 and H4 modifications, expression profiles of nuclear transcription factors and epigenetic modifiers were examined. Relative expression analysis of a panel of 88 genes revealed alterations in the thirteen gene transcripts regulating various biological processes. Functional characterization of the isolated epigenomic signatures and differential expression of a panel of ccf-miRs were also assessed and reported previously. The levels of fpg and lncRNAs among the individuals exposed to a varied quantum of PM was also assessed.

The expression levels of fpg and lncRNA were assessed by quantitative real time PCR approach. The assessed lncRNAs include SNHG, DLX6, PICART, SOX2OT, UCA1, GAS5, CHAF, HPRT, PVT, H19, HOTAIR, FAS-ASI, MHRT, MALAT, ANRIL, MIAT and CARL, while GUSB glucuronidase beta was utilized as internal control.

dCt values were obtained by subtracting Ct value of internal control to the Ct value of the test gene. ddCT values were obtained dCt (high-risk)- dCt (Low-risk) followed by implicated in the formula $2^{-(ddCt)}$ to calculate the fold change.

The higher activity of fpg observed among high-risk group suggested the occurrence of oxidative DNA damage among these individuals. While the quantitative analysis of fold change in the expression of 17 lncRNAs reported marked alterations in the expression profiles of the lncRNAs from high-risk and low-risk population. The expression of SNHG, SOX2OT, CHAF, HPRT, PVT and MALAT were down-regulated while the expression of DLX6, PICART, UCA1, GAS5, H19, HOTAIR, FAS-ASI, MHRT, ANRIL, MIAT and CARL were found to be up-regulated.

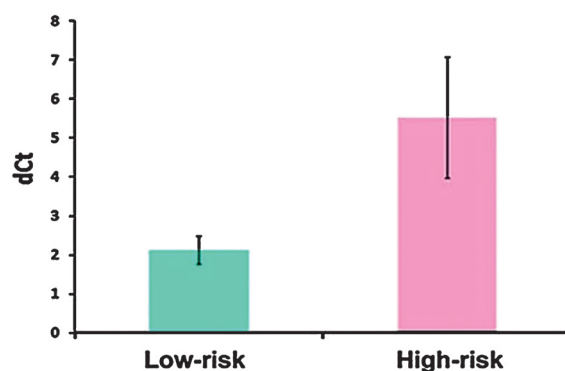


Fig. 3: Graph showing the dC_t values for fpg calculated as the difference of internal control from their respective test values.

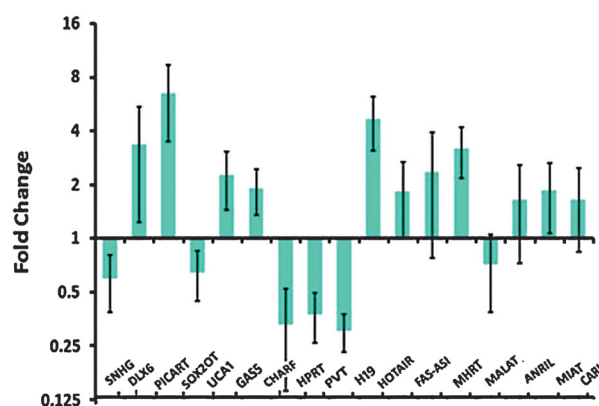


Fig. 4: The graphical representation of the expression profile of lncRNAs in the high-risk and low-risk groups. The fold change was calculated as $2^{-\Delta\Delta C_T}$ by identifying (dC_t) as the difference of internal control from their respective test values

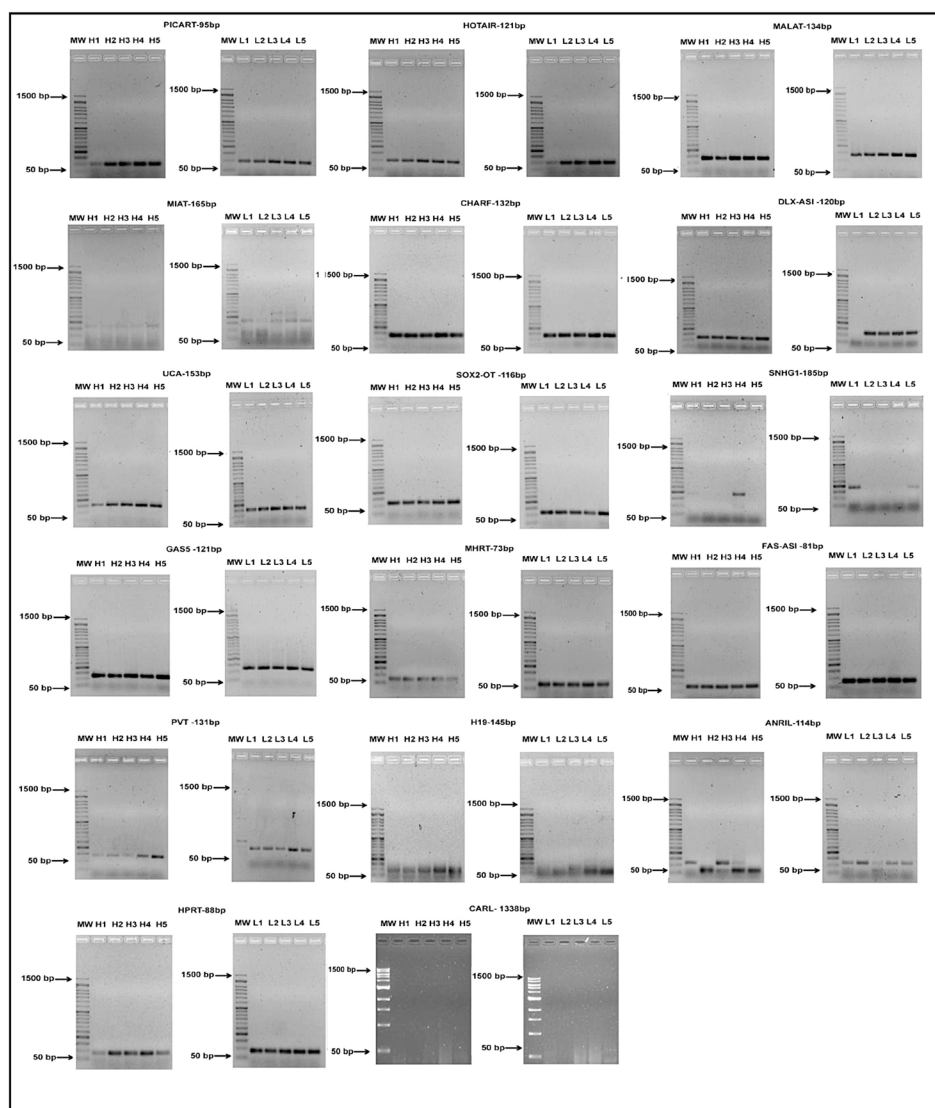


Fig. 5: Representative gel images showing the results obtained for the 17 lncRNAs. MW: High molecular weight marker, H1-H5: High-risk sample 1 – 5, L1-L5: Low-risk sample 1-5.

Environmental health study of gaseous air pollutants and heavy metals in Ggroundwater in Nagda Region

The industries situated in Birlagram Industrial Area are the source of pollutants like CS_2 , H_2S , HCl , Cl_2 , SO_2 and SO_3 . Considering the wide range of adverse health effects on exposure to these gases and contaminated groundwater especially on neurological, respiratory and cardiovascular system, a study was carried out to assess the concentration of effect of gaseous air pollutants and groundwater contaminants on the population residing in the close vicinity of the industries especially in the downwind and downstream areas of Birlagram Industrial Area, Nagda.

This study was designed as cross sectional study comprising of environmental and health monitoring components. To have representation of downwind and downstream population, firstly the map of area 10kms in the vicinity of the industry is divided into four quadrants. From each quadrants participants were taken from varying distances viz 0-2 km, 2-5 considering the dispersion of gaseous pollutants. As North-East is the downwind and downstream direction where exposure is likely to be higher, 1500 participants will be selected from villages in this quadrant (500 participants each from 0-2km, 2-5km and 5-10km) while 500 participants each will be chosen from villages in remaining three quadrants i.e., NW, SE and SW.

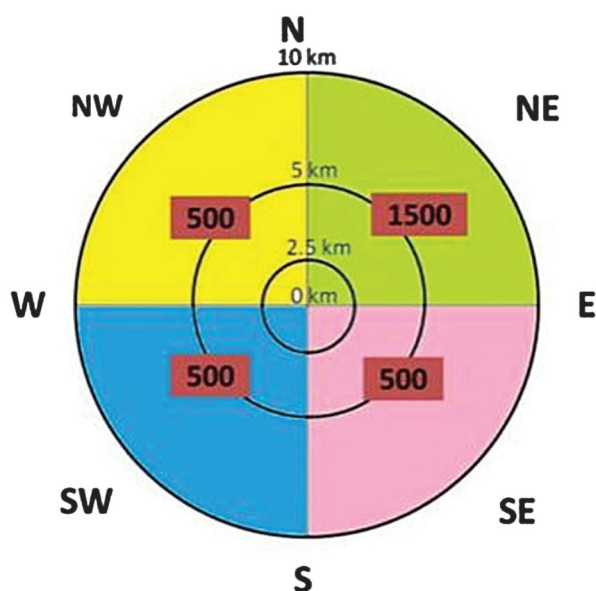


Fig. 6: Quadrant wise selection of study participants.

Also to correlate the heavy metals in ground water a subsample of the selected individuals (approx. 300) from downstream villages will be subjected to blood metal analysis for Pb, Hg and Al.

The monitoring of the pollutant gases viz., CS₂, H₂S, HCl, Cl₂, SO₂ and SO₃ will be monitored at the workplace as well as in the ambient air. The diurnal and seasonal concentration of said gases will be monitored in the study area considering various influencing factors such as probably exposed population, wind speed and direction, topography, etc. The gaseous monitoring will be carried using standard sensor based monitors as per the existing standards /guidelines/ procedures of CPCB.

Representative groundwater samples (250 mL) will be collected from the selected downstream villages for analysis for the presence and concentration of heavy metals such as lead, mercury and aluminium and anions such as chloride and sulphate. 30-40 samples from each selected village will be taken for such analysis. Collection will be done as per standard protocol in the pre-cleaned high density polypropylene (HDPE) bottles and its transport to laboratory for further processing and analysis. Analysis of heavy metals viz Pb, Hg and Al in the collected groundwater samples will be carried out

using inductively coupled plasma optical emission spectroscopy (iCAP 7400 Duo ICP-OES,) using the EPA method 200.7 (revision 4.4). Detection of chloride and sulphates will be carried out using titration methods.

The health assessment of the subjects will include Questionnaire-based collection of data on demography, exposure and lifestyle followed by clinical history and examination. The investigations such as Complete Blood Count, Random Blood Glucose & Lipid profile (Total cholesterol, HDL, LDL, Triglyceride), Urine Iodine Azide test and Blood levels of Lead (Pb), Mercury (Hg) and Aluminum (Al). In the phase wise implementation of the project first two phases of 500 participants each is completed and data entry and sample analysis is in progress.

Effects of improved information and volunteer support on segregation of solid waste at the household level in urban settings in Madhya Pradesh, India (I-MISS)

The purpose of this project is to develop a better understanding of household waste management for improved well-being and ultimately societal and environment sustainability. The team will conduct focus group discussions and interviews to understand local stakeholders' perceptions and beliefs of different kinds of waste segregation management at household level. Further through a cluster randomized trial, centre aims to understand if intervention involving trained volunteer to deliver improved information on household waste segregation (I-MISS) for 12 months along with routine activities carried out by municipal corporation can be used to increase waste segregation at household level in comparison to only routine activities on household waste segregation carried out by municipal corporation. The project focuses on urban settings of Ujjain city in Central state of Madhya Pradesh, India. The study objectives are connected and relevant to the government of India initiative of clean Indian mission and smart cities that aim to develop

citizen friendly and sustainable cities across India, which includes effective waste segregation and management systems in urban communities as a focus. The project is built on the interdisciplinary strengths of the teams in the Sweden and India, leveraging each team's complementary intellectual contribution whilst providing opportunities for learning and capacity building across the teams.

A Systematic Review and Meta-Analysis of interventions targeting household waste segregation is registered. Initial screening of more than six thousand articles were done. The team seeks to extract information on the type of interventions published in literature targeting household waste segregation.

To understand local communities' perceptions and beliefs about waste segregation/management, as well as challenges and opportunities at the household and community level, more than nine focus group discussions was conducted in different locality of study. The members included male and female residing in slum and non-slum area of the project site. FGD topic guide was developed. The FGDs were transcribed and translated. The analysis of data is underway (Table 1).

S. N.	Date of FGD	Location	Type	M/F	No of Participants
1	12/03/2021	Ward 1	Slum	M	8
2	13/03/2021	Ward 1	Slum	F	7
3	13/03/2021	Ward 1	Non Slum	F	6
4	17/03/2021	Ward 21	Non Slum	M	7
5	24/03/2021	Ward 18	Slum	F	7
6	25/03/2021	Ward 04	Non Slum	F	6
7	25/03/2021	Ward 18	Slum	M	8
8	27/03/2021	Ward 04	Non Slum	M	7
9	31/03/2021	Ward 09	Non Slum	F	9



Fig. 7: Focus Group Discussion with community members on household waste segregation.

Investigation on drinking water as a potential source of Endocrine disrupting chemicals (EDCs) to humans: An exploratory study in Jabalpur MP

In India Plastic bottles, containers and water storage tanks are commonly available and frequently used for the storage of drinking water and food across the country. The plastic tanks and bottles available in the market today are mainly manufactured from Polyethylene, Polypropylene, Bisphenol, High Density Polyethylene, Polyethylene Terephthalate and cross-linked Polyethylene, or Thermoplastic Polymer, which are categorized under endocrine disrupting chemicals (EDCs) that are well-known health risks for end users. These chemicals get released or leached in water when stored for a long time and when these reservoirs are washed with detergents. Leaching also occur when these are exposed to high temperature as well as from natural breakdown. When these plastic tanks are exposed to strong heat, especially in the long summer months when the mercury rises above 40°C, the leaching of chemicals is accelerated and toxins mix with water.

However, to team's current knowledge, no specific attempt was made to quantify EDCs in stored overhead water tanks and packaged drinking bottles in India. For instance, Bisphenol A severely affects the endocrine system and is also known to cause cancer, diabetes, asthma, cardiac problems and reproductive system irregularities in women.

However, in India research on EDCs exposure and its health risk implication to humans is lacking and has not been addressed by the scientific and medical communities so far. Currently, the recognition and understanding of EDCs is relatively new and is yet to be investigated thoroughly. The aim of this study was to investigate the presence of endocrine disrupting compounds; Phthalates, BPA and Dioxin, compound in bottled water, stored overhead plastic water tank and waste water treatment plants (WWTP) and to estimate their impact on estrogen receptors which leads to potential risk to human health.

The study site is Jabalpur which meets its domestic and commercial water requirements from surface and sub- surface water sources. The surface water sources comprise Khandari Reservoir, Gaur River, Pariyat Dam, Phagua Nallah and Narmada River. The Surface water from these sources is treated at water treatment plant located at Ranjhi, Bhongadwar, Lalpur (Phase I & II) and Ramnagra. The Treated water is being supplied to the Jabalpur City.

Water samples will be collected in duplicate in 1 litre glass bottles, prepared by rinsing the bottles with methanol. The lids of the bottles will be lined with tin foil to prevent the samples from coming into contact with plastic lids, which can be a possible source of EDC contamination. The pH of the water samples will be adjusted to 3. The water will be stored at 4°C in the dark till extraction, in order to minimize sample degradation. To account for seasonal variations in levels of EDCs samples will be collected from the identified sites in summer

and winter. EDCs that will be analyzed in water Phthalates (DEP, DEHP, and DBP), BPA and Dioxin.

A pre-tested structured questionnaire will be administered in each selected household. Questionnaire will be used for collecting information about on general health and personal habits. Whole blood and urine sample will be collected from inhabitants from selected houses using overhead plastic water tanks at home, after obtaining informed consent, for measurement of EDCs: Phthalates (DEP, DEHP, and DBP), Bisphenol A (BPA), Dioxins. 5 ml of venous blood samples will be collected from each volunteer. The blood sample will be centrifuged to obtain serum. Spot sample of urine (approx. 20ml) will be collected using sterilized polyethylene bottles. All biological samples will be stored at -20°C till analysis. Prior to analysis, frozen samples will be allowed to thaw at room temperature.

Samples will be analyzed by gas chromatography coupled to a quadrupole mass spectrometer (GC–MS). Target compounds will be quantified using internal standard quantification selecting the base peak of each compound with the software. SPE-GC/MS method is described in a previous study which provided mass spectral characterization, quality control and quality assurance parameters.

Calibration standards are prepared at 25ppb, 50ppb and 100ppb concentrations for each Dimethyl phthalate, Diethyl phthalate, Benzyl butyl phthalate, Di-n-butyl phthalate, Bis (2-ethylhexyl) phthalate, Di-n-Octyl-phthalate through dilution of the stock standard solutions with methanol.

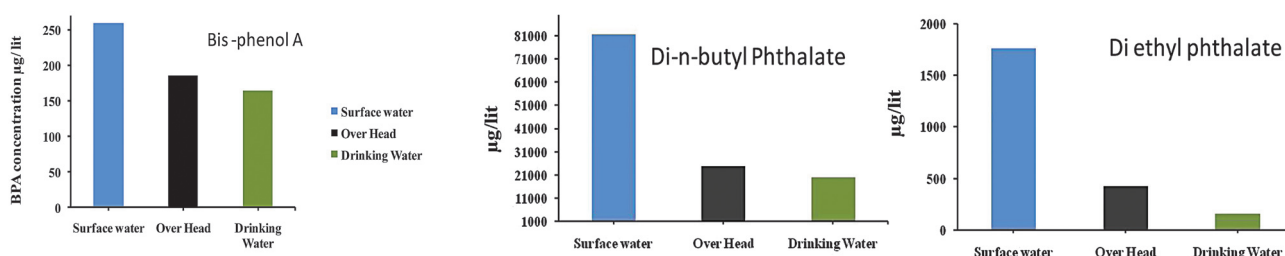


Fig. 8: Average concentrations of the BPA DnBP and DEP in the Surface water, direct over head tank and drinking tap water in Jabalpur.

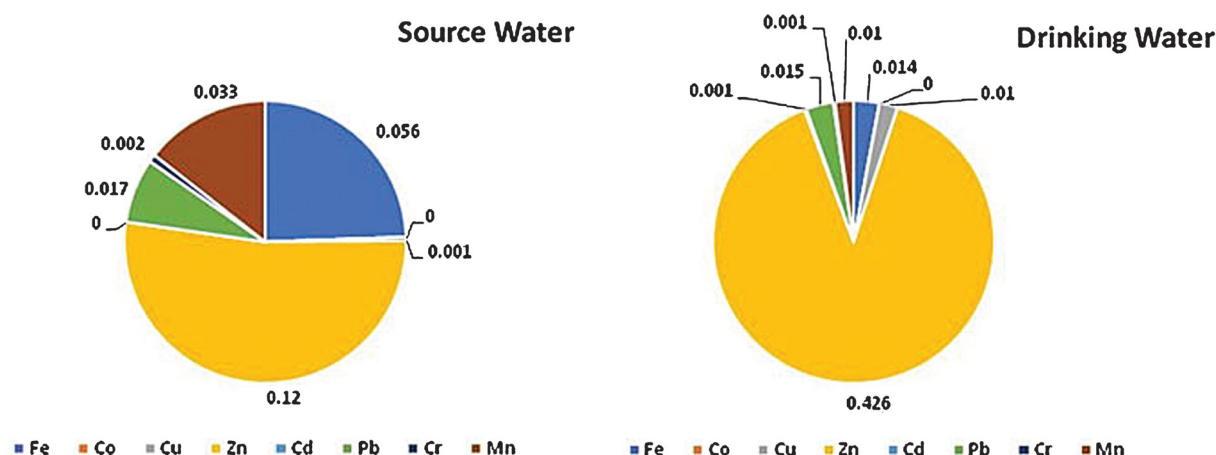


Fig. 9: The concentration (ppm) of different heavy metals in the source water and drinking water samples collected during winter season.

A genomic and metagenomic insight into the anthropophilic behaviour in *Aedes aegypti*, a highly efficient arboviral disease vector

Vector-borne disease is a global health problem and vector control is the only effective way to curb the menace of this problem till date. However, control of any vector-borne disease depends on the in-depth knowledge of the biology and behaviour of the vector mosquitoes which is a highly complex and heterogeneous in nature. Mosquito bloodsucking behaviour is one of the intrinsic characteristics which have a profound role in disease transmission. However, very less effort has been put in understanding the genomic basis of mosquito host preferences and anthropophilic nature of vector mosquitoes.

Objectives

- To assess the SNPs associated with human and non-human blood meal preferences in relation to the differentially expressed genes in chemosensory organs of *Aedes aegypti*.
- To assess the influence of gut microbes in mosquito blood meal preferences in *Aedes aegypti*.
- To develop SNP based genetic markers that could be used for rapid quantification of the degree of anthropophily in *Aedes aegypti* vector mosquitoes.

Mosquito Collection: Adult *Aedes aegypti* mosquitoes will be collected from houses and cattle sheds residing within the same premises to control the bias created by incomplete penetrance. Mosquitoes will be collected by aspirator based method from inside human houses and from cattle sheds. In the laboratory, collected mosquitoes will be sorted, identified and all blood-fed mosquitoes will be stored in RNA Later until further processing.

Mosquito processing and Molecular assays: All full blood fed *Ae. aegypti* mosquitoes will be bisected into two parts, abdomen and head & thorax. Total RNA will be extracted from head+thorax region and total genomic DNA will be extracted from abdomen region using standard methods. The specific host species that each mosquito had fed upon will be determined by a multiplex PCR assay on DNA extracted from abdomens. RNA isolated from the individual head-thorax region will be screened for the presence of DENV, chikungunya and Zika virus by using reverse transcriptase PCR assays. Those *Ae. aegypti* mosquitoes which are found to be fed on human blood and on other non-human blood without having any of the above arboviral infection will be used for further analysis. Approximately 50 human blood meal positive *Ae. aegypti* mosquitoes without viral infection and 50 non-human blood meal positive *Ae. aegypti* mosquitoes without viral infection will be selected. DNA isolated from abdomen will be used for whole genome sequencing.

and gut microbiome sequencing using standard method and platform. RNA extracted from head & thoracic parts will be used to assess the level of gene expression associated with mosquito host preferences. cDNA library will be prepared from the RNA and each cDNA library will be sequenced using standard method and platform.

Data analysis: RNA assembly and expression profiling of genes associated with blood meal preferences will be determined by using methods described by Lombardo et al., 2017. After assessing the quality of the reads, the reads will be aligned with the whole genome sequence of *Ae. aegypti* as reference sequences. Different tools such as BWA-

mem, Genome Analysis Tool Kit (GATK), VCF tools will be used to align and SNP identification. To identify SNPs associated with the specific blood meal source, study will use a principal component analysis (PCA) based method GCTA and a linkage disequilibrium network analysis (LDna) based method on all wholegenome sequenced individuals. This will partition individuals into different clusters. Genomic differentiation among these clusters will be further used to map against the reference sequence to find its location on the genome. The study will try to develop molecular diagnostic markers for different blood meal preferences by using SNP information and differential gene expression information (Table 2).

Table. 2. 16s metagenomic sequencing characteristics and numbers of bacterial species, genus and family identified in each sample.

Sample ID	Total number of reads	Number of Mapped reads	Number of bacterial family identified	Number of bacterial genus identified	Number of bacterial species identified
Sample 02	1555874	723077	192	317	608
Sample 22	2347626	1378565	155	22	375
Sample 28	2611692	1533754	144	218	360
Sample 51	2536179	1491420	152	228	364
Sample 87	2079136	1150327	168	223	365
Sample 126	2436686	1371876	160	216	355
Sample 159	1969385	1004371	184	286	517
Sample 160	2185609	1490229	109	166	278

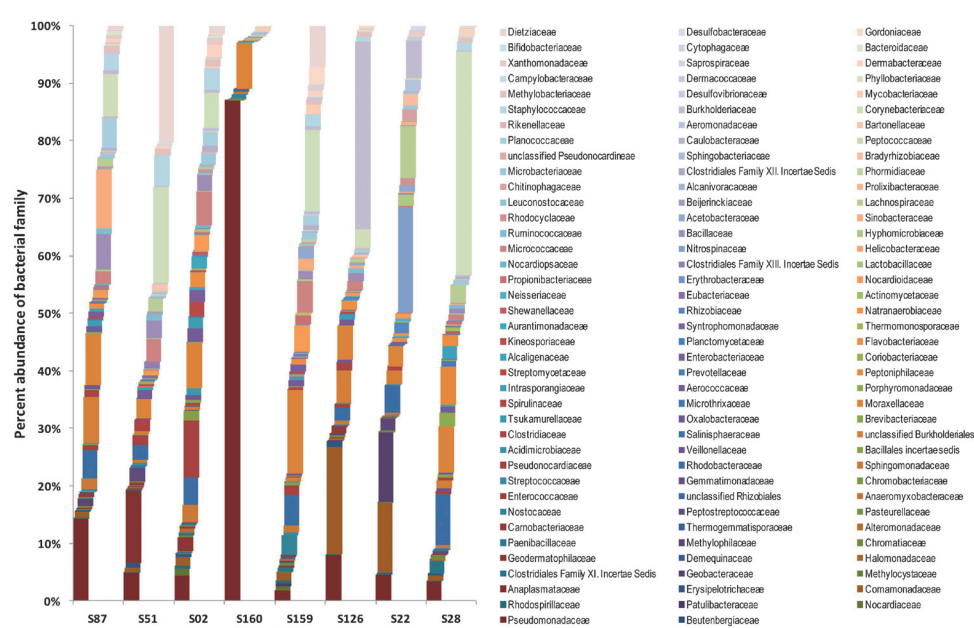


Fig. 10: Relative abundance of bacterial family identified through 16s metagenomics in different *Ae. aegypti* mosquitoes.

A pilot study on health effects of simultaneous exposure to multiple heavy metals in two different settings of Bhopal; Phase- I: Assessment of heavy metals in the ground water from a solid waste disposal site and an industrial area in Bhopal

This pilot study was aimed to capture information on levels of heavy metal contamination (As, Cd, Pb and Hg) of groundwater in three different localities representing a municipal waste landfill site (Bhanpur), an industrial area (Mandideep), and a control locality (Adampur Chawni), and assess, if any, the observable metal exposure associated health issues among residents in these localities.

Groundwater samples for analysis of As, Cd, Pb and Hg were collected for three seasons (pre-monsoon, monsoon and post-monsoon) from localities within 1 km radius of the landfill site and the industrial area. For baseline information on level of these metals in groundwater, samples for all three seasons were also collected from Bhopal city's countryside. Analysis of Pb, Cd, As and Hg in the collected drinking water samples was performed on iCAP 7400 Duo ICP-OES (ThermoFisher Scientific Pvt Ltd) using the EPA method 200.7 (revision 4.4). The questionnaire-based survey to ascertain health problems that may arise from drinking water contaminated with Pb, Cd, As and Hg also conducted among 285 individuals from the three localities. The analysis of metals levels in the collected ground water samples and comparison of morbidly pattern was performed on SPSS version 25.

The median concentration of four heavy metals in the collected groundwater samples showed that the recorded seasonally or yearly median concentrations of all the metals were well within the permissible limits as per Indian Standards. Further, we computed seasonal and locality-wise variations in the levels of metals using nonparametric Kruskal-Wallis test (skewed data). Although the median levels of metals in any of the study locality were considerably low, we observed a significant locality-

wise difference in the concentrations of As ($p = 0.000$), Cd ($p = 0.006$), and Hg ($p = 0.000$) during post-monsoon; As ($p = 0.000$), and Hg ($p = 0.049$) during pre-monsoon, and Pb ($p = 0.011$) and Cd ($p = 0.000$) during monsoon seasons. On the yearly basis, a significant difference in concentration of all four metals was observed at the three different localities. The levels of Cd and As were recorded comparatively low in Adampur than Bhanpur or Mandideep, irrespective of the seasons. The levels of Pb and Hg were comparatively high in Bhanpur and Adampur, respectively. Based on these results, it can be stated that even though the recorded levels of toxic As, Cd, Hg and Pb are within permissible limits, some of these metals were relatively more abundant in Bhanpur and Mandideep compared to the control site.

The questionnaire-based survey to ascertain health problems that may arise from drinking water contaminated with Pb, Cd, As and Hg among 285 individuals from the three localities showed that only a few health problems, such as black pigmentation on nails and skins, numbness and tingling in extremities, chronic fatigue, and anemia were significantly different among the three study sites. Both in absence of significant difference for majority of health issues and below permissible levels of heavy metals in the study localities, the team presumed that the 3-4 health issues found significantly different among study sites may have non-specific underlying causes.

Overall, the results show below permissible levels of toxic As, Cd, Hg and Pb in the groundwater in the Mandideep, Bhanpur or Adampur towns of Bhopal Madhya Pradesh, India, and also found no evidence of direct health issues arising from metal exposure.

WORKSHOP CONDUCTED

“Five days hands on workshop on Basic Molecular Biology Techniques and cytogenetics” sponsored by DST-SERB, Govt. of India at ICMR-NIREH, Bhopal from 15th March – 19th March’ 2021.



Fig. 11 & 12: Hands on workshop on Basic Molecular Biology Techniques and cytogenetics.

ICMR-BHOPAL MEMORIAL HOSPITAL & RESEARCH CENTRE, BHOPAL (ICMR-BMHRC)

The Bhopal Memorial Hospital and Research Centre (BMHRC) and its Outreach Health Centres were started with a mission to provide free health care to those affected by the Bhopal Gas tragedy, and to provide affordable healthcare to the public at large. The hospital was started in 2000, while services at the outreach centres were initiated in 1998. Healthcare services have been continuously provided since then to the victims of the gas disaster, their dependents, and to the public at large. Beneficiaries of the Ayushman Bharat Pradhan Mantri Jan Arogya Yojana (AB-PMJAY) have also received free in-patient services. This scheme provides free access to health insurance coverage for low income earners in the country.

CLINICAL WORK

- Clinical work at BMHRC involves treatment of patients in the out-patient department (OPD), investigations (Pathology, Radiology and Microbiology), procedures and surgeries, in-patient department (IPD) care and rehabilitation. 17 specialties are present at the main hospital.
- OPDs are run at the eight Health Centres 6 days a week, Radiological and Pathological investigation are done here too.

- The clinical work at BMHRC and its 8 Health Centres continued during the whole year (2020-2021) in spite of the ongoing COVID-19 pandemic. However, because of inability of patients to come during the lockdown and stoppage of public transport services, the overall admission /attendance were affected.

PATIENT DATA

- The OPD footfall in the hospital and health centres in the year 2020-21 was approximately 32,000 per month.
- Inpatients in the year 2020-2021 were approximately 400 per month.
- Nearly 4.5 lakh patients and their children are registered at BMHRC and its 8 health centres for health care. Free health care services are provided to all registered gas victims and their children/dependents. The doctors, nurses, paramedical staff and all employees of BMHRC (hospital and health centres) have worked continuously during this period in spite of the pandemic to provide timely and excellent health services to the patients.
- Total number of patient visits in BMHRC in the period April 2020 to March 2021 was 3,78,562.
- Total number of diagnostic investigations done in this period are 3,95,810 (radiology, microbiology, pathology and biochemistry). In addition, there were approximately two lakh COVID-19 tests (RT-PCR, Rapid Antigen

tests and Cartridge-based Nucleic Acid Amplification Tests) carried out during this period at BMHRC, Bhopal.

- 872 COVID-19 suspects /cases were admitted and provided treatment in the COVID-19 isolation facility.

TEACHING/TRAINING ACTIVITIES

- DNB Ophthalmology has been initiated at BMHRC, Bhopal and one student has joined this course in September, 2020.
- Permission received to start MD Anaesthesia course. Intake of students for the course will be through NEET-PG, which has been postponed due to the COVID-19 pandemic.
- Teaching activities have continued online in both Bhopal Nursing College and Paramedical Institute of BMHRC. Regular online tests and examinations have also been conducted during this period.

The Bhopal College of Nursing conducts the following courses

- Post Basic BSc Nursing
- B.Sc. Nursing
- M.Sc. Nursing

Admissions were taken into Post Basic B.Sc Nursing and M.Sc. Nursing in 2020-21. Total number of admissions in the year was 37.

The Paramedical Institute at BMHRC conducts the following Diploma Courses

- Diploma in Anesthesia Technician
- Diploma in Blood Transfusion Medicine
- Diploma in Dialysis Technician
- Diploma in Cath Lab Technician
- Diploma in Medical Lab Technician
- Diploma in Optometry & Refraction Technician
- Diploma in Perfusion Technician
- Diploma in X-Ray & Radiographer Technician

55 new admissions were taken in the year 2020 into the various courses. Currently there are 120 students pursuing their paramedical courses in the institute.

TRAINING / INTERNSHIP

Clinical Training / Internship

- Clinical training was imparted from local medical colleges in the last year (2020-2021) to one student in Medicine, one student in Anesthesia and two students in Cardiovascular surgery.
- Five students of Psychology did internship in the department of Psychiatry during this period.
- Training was also imparted in Dietetics to one student for six months.
- Eleven students did internship with training in Physiotherapy under the department of neurosurgery.

Training conducted by NRL, BMHRC, Bhopal

- Virtual Sensitization program was conducted by NRL. BMHRC along with NTI Bangalore on “CBNAAT EQA Phase IV Implementation in Goa” on 17th August 2020.
- Virtual Sensitization program was conducted by NRL. BMHRC along with NTI Bangalore on “CBNAAT EQA Phase IV Implementation in Chhattisgarh from 18th to 20th August 2020.
- Virtual training for IRL Bhopal and IRL Indore was conducted on “TB diagnosis and detection of Rifampicin resistance by TrueNat” on 11th January 2020.
- A virtual training for IRL Chhattisgarh was conducted on “TB diagnosis and detection of Rifampicin resistance by TrueNat” on 15th January 2021.
- Virtual training for IRL, Goa was conducted on “TB diagnosis and detection of Rifampicin resistance by TrueNat” on 27th January 2021.

- A virtual training for IRL Itki, Ranchi, was conducted on “TB diagnosis and detection of Rifampicin resistance by TrueNat” on 29th January 2021.
- Onsite training on SL-LCDST at IRL Goa was conducted on 16th March 2021.

Trainings attended by NRL, BMHRC Staff

- Virtual training on LCDST for Newer Drugs conducted by NIRT Chennai 07th January 2021.
- Training for master Trainers on “TB diagnosis and detection of Rifampicin resistance by TrueNat” conducted by CTD on 8th January 2021.
- Virtual training on LIMS- Logistics module conducted by CTD with FIND on 20th January 2021.

NACO (Integrated Counselling and Testing Centre)

- Training and support visits: 35.

Blood Safety Training for the Blood Bank Medical Officers and Lab Technicians was

conducted by the Department of Transfusion Medicine

- Medical Officers (Non BCSU): 24.
- Medical Officers (BCSU): 07.
- Lab Technicians (BCSU and Non BCSU): 70.

Training in Research

- Short-term training in Research was imparted to two students, three students attended summer internship/training in Research.
- Eight students went through project training in the year 2020 - 2021.

Hospital-associated Infection Control activity

The Hospital-associated Infection Control committee was formed during this COVID-19 pandemic period and trained the entire BMHRC employees (both permanent and temporary) on infection control measures. All trainings were done following COVID-19 guidelines and an undertaking was signed by all employees to follow COVID-19 norms.



Fig. 13 &14: Infection Control activity.

- Bhopal Nursing College conducted an e-poster competition on the 21st of June on the theme “Yoga at home and Yoga with family” and “Yoga converting COVID-19 crisis into an opportunity”.
- Vigilance Awareness Week was observed from 27th October to 2nd November, 2020.

The vigilance pledge was taken taking social distancing measures online by the Director and all BMHRC employees. Also, Poster and Slogan competitions were held during this period.



Fig. 15: e-poster competition on the 21st of June on the theme “Yoga at home and Yoga with family” and “Yoga converting COVID crisis into an opportunity”.



Fig. 16: Vigilance Awareness Week.



Fig. 17&18: Guest lecture on the “Insights of Gender Inequality”.

A guest lecture on the “Insights of Gender Inequality” was delivered by Ms. Deepika Suri, IG (Crime against women), followed by a lecture for “bringing remote issue of gender sensitivity in broad daylight” by Prof. Prabha Desikan, Director, BMHRC, Bhopal, during the training program for BMHRC faculty on the 12th December, 2020.

Voluntary Blood Donation Camp during Pandemic by the department of Transfusion Medicine

In spite of the COVID-19 pandemic, blood and its components have been provided to all needy patients. Twenty-four hours blood donation camps as per new guidelines of NBTC were done in the year 2020-2021.



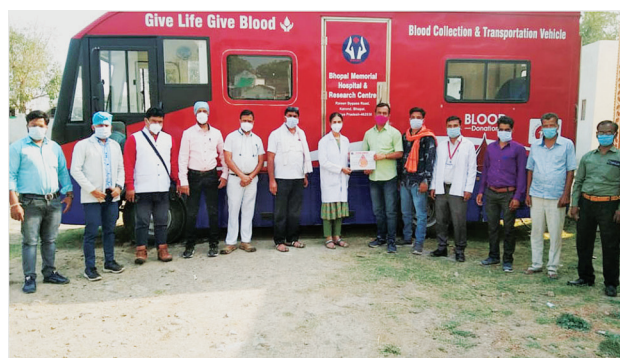


Fig. 19 & 20: Blood Donation Camp during Pandemic.



Fig. 21 & 22: Blood Safety Training Programs.

Swachhta Workshops organized at Health Centres

- Swachhta awareness programs were also conducted in the nearby localities with frequent visits and demonstration of various hygienic practices.
- Cleaning and beautification of surrounding areas, tree plantation, disposal of unserviceable items and broken furniture was done by staff.



Fig. 23, 24, 25 & 26: Swachhta workshops.

RESEARCH WORK

- Evaluation of the operational feasibility and performance of 'TB Detect' and TB Concentration & Transportand 'TB DNA Extraction' kits in field settings under the National Tuberculosis Elimination Program.
- Molecular characterization of *carbapenemase* resistant Gram-negative bacilli at a tertiary care hospital in Central India.
- *Amaranthus tricolor* formulation is a nutraceutical and can serve as an immunomodulator against COVID-19 infection-an in vitro mechanistic study.
- Identification and evaluation of a biomarker panel for early detection of pancreatic ductal adenocarcinoma and to assess whether a common etiopathology increases the risk in diabetes mellitus patients.
- Can the combination of Temozolomide and Curcumin inhibit autophagy in Glioblastoma? A pilot study.
- Experience with PPE kit: An observational study.
- Assessment of Phyto – macromolecules for potentiating the action of antibiotics to combat Sepsis and upsurge Wound healing.
- Effect of Aerosol box on the anxiety of anesthesiologist for intubation during COVID-19 Pandemic.
- Analysis of occurrence of cystoids macular edema in diabetic patients undergoing phacoemulsification surgery.
- Perception of academic stress on exposure of online learning during COVID-19 among nursing students.
- To study the prevalence of diabetic retinopathy in diabetes mellitus patients and its correlation with various associated risk factors: Descriptive Cross- Sectional Study.
- Evaluation of a new biomarker panel to identify high risk group for type 2 DM and its related complications: a clinical approach to validate the glycemic memory theory.
- Can the combination of Temozolomide and Curcumin inhibit autophagy in Glioblastoma? A pilot study.
- Assessment of partakers in tumor micro-environment for prognosis of glioma using liquid biopsy: a unique clinical approach.
- Deciphering the epigenetic signature of glioma: prognostic relevance in tumor recurrence.
- Quality assurance of biodosimetry, capacity building and establishment of baseline for cytogenetic parameters.

The department of Research organized a mini-symposium on the “Molecular Epidemiology of COVID-19” on 14th March, 2021 and a guest lecture on the “Management of COVID-19 using indigenous natural products” on the 19th March, 2021.

NON COMMUNICABLE DISEASES

In the area of non-communicable diseases, ICMR's National Institute of Cytology and Preventive Oncology, Noida continues to carry out research studies for prevention and early detection of cancer. The National Centre for Disease Informatics and Research, Bangalore focuses on the National Cancer Registry Programme and related activities like software module for cancer registration, patterns of cancer patient care and survival studies. National Institute for Implementation Research on Non Communicable Diseases (NIIRNCD) has been working in the following major research areas during the reported period viz. Early detection of breast cancer, Sickle cell anemia and other studies mainly on IDD, tuberculosis, H1N1, silicosis, snake bite, etc.

Major highlights of various programmes undertaken by ICMR in the area of non-communicable diseases during the year 2020- 21 are given below.

INTRAMURAL RESEARCH

ICMR-NATIONAL INSTITUTE OF CANCER PREVENTION AND RESEARCH, NOIDA (ICMR-NICPR)

National survey for state-wise prevalence of microbiologically confirmed pulmonary tuberculosis in India (ICMR & WHO Collaborative project)

ICMR-NICPR is carrying out the survey in Delhi and western Uttar Pradesh. A total of 15 clusters

have been completed so far enrolling a population of 15794, and 1678 sputum samples were tested. Of these, 42 were positive by CBNAAT.

Setting up of Population Based Cancer Registry at National Institute of Cancer Prevention & Research covering Gautam Budh Nagar

The PBCR has been set up to cover the rural and urban population of District Gautam Budh Nagar (G.B. Nagar), Uttar Pradesh. The total cases of cancer patients registered during the reporting period (April 2020 – March 2021) for the year 2018 was 2071 and for year 2019 was 284. Total mortality in cancer cases for the year 2018 was 180. Various new hospitals of Delhi – NCR were visited for the collection of cancer cases. A total of 16 new hospitals have been added during the reporting period. Mortality data was collected from various hospitals, CMO office and Nagar Palika.

Development of DNA vaccine Constructs against India-specific HPV-16 Variant: Enhancement of Immunogenicity of L1 construct and characterization of T-cell Epitope based E6/E7 construct

This project was aimed for enhancing the immunogenicity of DNA based vaccine constructs (HPV 16 L1) by using genetic and non-genetic adjuvants and also characterization of T-cell Epitope of E6/E7. HPV-16 L1 variant construct together with non-genetic adjuvant (MF59 & GM-CSF) for antibody titer by ELISA was tested in mice model. On comparison between the group

injected with pV16V construct along with GM-CSF, an elevated level of antibody titer ~ 4 folds ($p < 0.002$) were found than pV16V MF59. Also, for E6 & E7 gene constructs, dose dependent responses of cytotoxic T lymphocyte, and tumor protection effect was found in animal model. In future, we hope to improve the methodology in administrating the DNA vaccine constructs into cells, for example gene gun device and focusing on increasing the cytotoxic T lymphocyte response.

Comparative study of Genetic, Clinical and Epidemiological factors of Breast Cancer in Indian population

This study aimed to identify the mutational landscape of breast cancer in Indian population along with its putative pathway(s) through whole exome sequencing and transcriptome analysis. Whole exome sequencing and analysis revealed that variants per sample ranged from 558 to 1144 and a total of 38,143 variants were localized in 9564 genes (Fig.1). Data indicated some novel genetic alterations in different sub types of breast cancer patients. A significant association of genetic alterations and clinic-epidemiological variables was also observed. Currently, the whole exome and transcriptome data is being validated which may give some novel insights for the breast cancer treatment and management in Indian population.

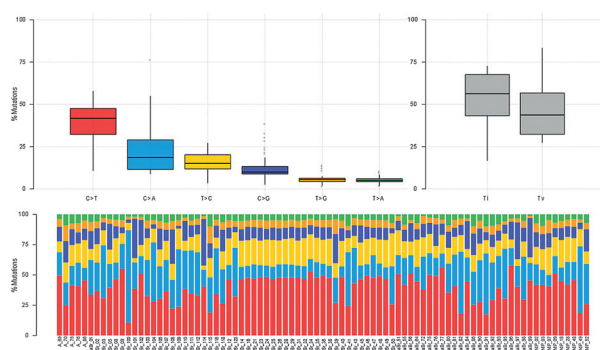


Fig. 1: (A-C). Representative image of the mutation type and its percentage. A) Box plot showing mutation type B) Box plot showing Ti/Tv ratio C) Bar graph showing the mutation percentage patient wise. (Ti-Transition, Tv-Transversion).

Screening and early detection of cervical, breast and oral cancer in Cachar, Assam: A pilot project

This project was undertaken to initiate a systematic population-based cancer screening in Cachar district and link the cancer screening services for appropriate evaluation and treatment facilities at tertiary level. In this project, 19535 males and 26623 females were screened for oral, breast and cervical cancer. The total number of precancers/abnormalities diagnosed were 1242 (oral- 863, cervix-135, breast-244) and the number of cancer cases diagnosed were 22 (oral- 12, cervix-2, breast-8). All the precancers (oral- 863, cervix-135, breast-244) and 17 cancers (oral- 10, cervix-1, breast-6) were treated.

Screening and early detection of cervical, breast and oral cancer in Dibrugarh, Assam: a demonstration project in TATA Tea gardens

This project was undertaken to assess the training needs of medical officers working in the tea garden health facilities for screening of cervical, breast and oral cancer and assess the effectiveness of training package in improving knowledge and building skills of medical officers of tea garden health facilities in detection, work up of screen positive cases for treatment and referral. In this project, 2534 households were covered and 631 beneficiaries were screened. The total number of precancers/abnormalities diagnosed were 38 (oral- 22, cervix-6, breast-10).

Oral Cancer Screening: development of research partnership and feasibility study

In this project, team proposed a new international, leading interdisciplinary group to: (a) develop and evaluate a novel screening strategy in resource-limited settings; (b) build national/regional capacity to conduct high quality research; (c) use this capacity to support wider prevention efforts within the region; and (d) provide robust evidence to up-scale for long-term sustainability. A total of 1200 individuals were screened by the Community health workers/ASHAs, of which 1018 participants were enrolled & screened at NICPR-Health Promotion Clinic (HPC). A total number of 246 oral

abnormalities were detected and 27 oral cancers were diagnosed.

Next generation EGFR inhibitor identification using ligand based QSAR technique

A machine learning-based desktop application for screening inhibitors against double mutated EGFR, a therapeutic drug target of clinical relevance in Lung cancer was developed (Fig. 2).

Fig. 2: A machine learning-based desktop ap.

Role of methylated CpG binding proteins and its involvement in the regulation of BRCA1, BRCA2 and p16 gene promoter in breast cancer cell lines

The efficacy of Resveratrol as an anticancer drug in breast cancer and potential inhibitory effects on breast cancer progression, cell invasion and migration was demonstrated in an in-vitro study.

To identify the mechanism involved in developing resistance against Abemaciclib and Palbociclib in ER+ve, PR+ve and HER-2 –ve breast cancer

The differential expression of genes associated with apoptosis, cell survival, transporters, and cell-cycle confirmed the chances of acquired-drug resistance for Abemaciclib and Palbociclib in breast cancer. These proteins have been reported to play key roles in therapy resistance, or as potential drug targets for breast cancer.

National Tobacco Testing Laboratory (NTTL) at NICPR

The NTTL is providing analytical facilities for tobacco and tobacco products. In the year 2020-2021, smokeless tobacco (SLT) samples were received from Food Safety Officers, Govt. of Karnataka and Govt. of Bihar, Department of Commercial Taxes, Govt. of Karnataka, Dr Nuan Ping, Chair, WHO TobLabNet for method validation and also Reference samples from MoHFW for analyzing tobacco constituents. The Lab analyzed 179 SLT samples for about 1000 Tests for the various parameters such as Nicotine, Moisture, Total sugars, Ammonia, Volatile Bases, Chloride, Humectants and pH.

Addressing Smokeless Tobacco Use & Building Research Capacity in South Asia (ASTRA)– A randomised-controlled, feasibility trial for smokeless tobacco cessation

This study is being conducted in collaboration with the University of York, United Kingdom to identify the feasibility and effectiveness of behavioural support therapy in enabling quitting smokeless tobacco (SLT) among adults. Recruitment of participants has been completed and follow-ups are under process. A factsheet has been prepared on Smokeless Tobacco Cessation in India (Fig. 3).

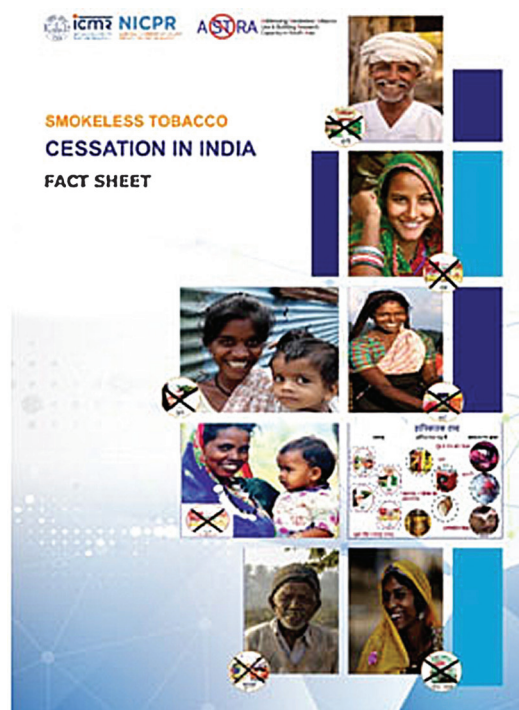


Fig. 3: Factsheet on Smokeless Tobacco cessation in India (ASTRA Project).

Strengthening Bio-chemicals research policy capacity building and cessation support to advance smokeless tobacco control in India

This study has been initiated for characterization of the common microorganisms present in processed tobacco products and to understand the molecular mechanism involved in the development of lesions of oral cavity among SLT users. During the reporting period, local SLT samples were procured and the biochemical and genetic characterization of microbial contaminants in these SLT products is under process.

ICMR Task Force Study on Smokeless Tobacco and Reproductive & Maternal Health (ICMR SLT-RMH Study)

This study has been designed to understand the socioeconomic and cultural norms towards SLT and areca nut use among women of the reproductive age group and to develop and test a behavioral intervention package to change the attitude and practices using Information Education Communication (IEC) strategies. A total of 36 women aged 18-49 years have been enrolled for in-depth interviews along with 14 healthcare workers and community stakeholders as Key Informants Interview in GautamBuddh Nagar. The initial findings have shown that addiction, substance use in the household, lack of awareness about the adverse health effects and unavailability of tobacco cessation services as the key determinants of SLT use. Also, surrogate advertisements, easy availability and affordability of the SLT products contributed to the sustained use of SLT during pregnancy and lactational period. Among the frontline health workers, 18.9% reported using areca nut, while 13.2% reported using both areca nut and gutkha. Thus, SLT consumption among healthcare workers, community acceptance and lack of cessation services concomitantly contributes to SLT use among women in the reproductive age group.

WHO FCTC Global Knowledge Hub on Smokeless Tobacco

- a) **Online Consultation on Effective implementation of measures for control of smokeless tobacco use in India** was held with 11 high burden states of India which includes Bihar, Kerala, Madhya Pradesh, Uttar Pradesh, Uttarakhand, Manipur, New Delhi, Goa, Tripura, Jammu & Kashmir and Telangana during March to August. Technical Support and assistance were provided to state of Kerala and Madhya Pradesh, to enforce Food Safety and Standards regulations on pan masala and other forms of smokeless tobacco products.
- b) **Virtual Consultation Program on effective implementation of measures to eliminate SLT** - A virtual program for Food Safety Commissioners and Food Safety Officers from states of Uttar Pradesh, Uttarakhand, Manipur, New Delhi, Goa, Tripura, Jammu & Kashmir and Telangana was conducted on “effective implementation of measures to eliminate SLT” from August 18-27, 2020.
- c) **Online webinar on “Protecting Youth from industry manipulation & preventing them from tobacco & nicotine use”** was organized on “World No Tobacco Day” on 31st May 2020. Experts highlighted the harmful effects of tobacco and nicotine use on human health. Discussion on Strategies/policies to protect youth from the manipulations of tobacco industries were highlighted. Experts explained the tricks used by tobacco industries for luring youth and vulnerable groups.
- d) **An Online course on Smokeless tobacco cessation** was held in collaboration with the Department of Health Sciences, University of York, United Kingdom, during July 10, 2020 to August 10, 2020. A total of 168 participants (health care professional, policy makers and students) from 10 different countries attended the course.
- e) On the occasion of World No Tobacco Day, 2020 (May 31, 2020), a ‘One stop

repository for Smokeless Tobacco control' (Fig.4) was launched ([URL:http://smokelesstobaccocontrolindia.com/](http://smokelesstobaccocontrolindia.com/)).



Fig. 4: State-of-the-art website as 'One stop repository for Smokeless Tobacco control' launched by WHO FCTC Global Knowledge Hub on Smokeless Tobacco.

- f) Statement Issued to partner Countries- for strengthening Tobacco Control and Prohibiting Spitting in Public Places** - The Statement emphasizes on the need to win this war against the global tobacco epidemic by bringing tobacco control measures into sharp focus along with COVID-19 containment measures. The statement was supported by the WHO FCTC Secretariat.

ICMR Task Force study on mental health and social stigma among healthcare personnel involved in the management of COVID-19 patients in India

This qualitative study carried out among 90 healthcare workers, including staff nurses, doctors, lab technicians and supporting staff (ambulance services etc.) who were involved in the management of COVID-19 patients. Majority of healthcare workers were in the age group 18-24 and 25-31

years. About 46% of the healthcare workers felt responsible for some of the problems which their colleagues or patients were facing. Nearly, 40% of the healthcare workers reported that they did not enjoy normal day to day activities in their life, and 20.7% reported loss of sleep due to work related issues. Detailed analysis is being done.

Establishment of Model Rural Health Research Unit (MRHRU) at CHC Khotpura, Panipat, Haryana

This is a DHR-funded Scheme intended to create infrastructure at the periphery for transfer of technology to the rural level for improving the quality of health services to rural population; ensure an interface between the new technology developers (Researchers in the Medical Institutions; State or Centre), health systems operators (Centre or state health services) and the beneficiaries (communities in rural areas); and ensure the much-needed geographical spread of health research infrastructure in the Country. ICMR-NICPR has been designated as the Mentoring Institute for the MRHRU at CHC Khotpura, Panipat, Haryana. A Scientific Research Advisory Committee for MRHRU at Panipat, Haryana was constituted, and three research projects submitted by the Dept of Microbiology at Kalpana Chawla Govt Medical College, Karnal (linked medical college) were discussed.

PUBLIC HEALTH

High Throughput Viral Diagnostic Laboratory (HTVDL) for COVID-19 testing

It was established at ICMR-NICPR (Fig. 5). The Laboratory was inaugurated on 27th July 2020 by the Honorable Prime Minister (Fig. 6) and is the largest facility in the country for RT-PCR testing. More than 10 lakh RT-PCR samples for COVID-19 have been tested so far including Honorable Members of Parliament, their families, and staff during the monsoon session (Fig. 7). This facility caters to western Uttar Pradesh and Delhi.



Fig. 5: High Throughput COVID-19 testing facility at ICMR-NICPR.



Fig. 6: Online inauguration of the COVID-19 testing laboratory by the Honourable Prime Minister (left) and parallel unveiling of the plaque at the Laboratory by Director, ICMR-NICPR.

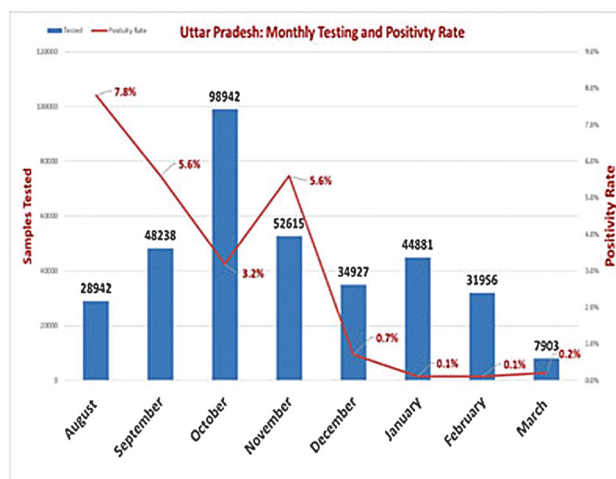
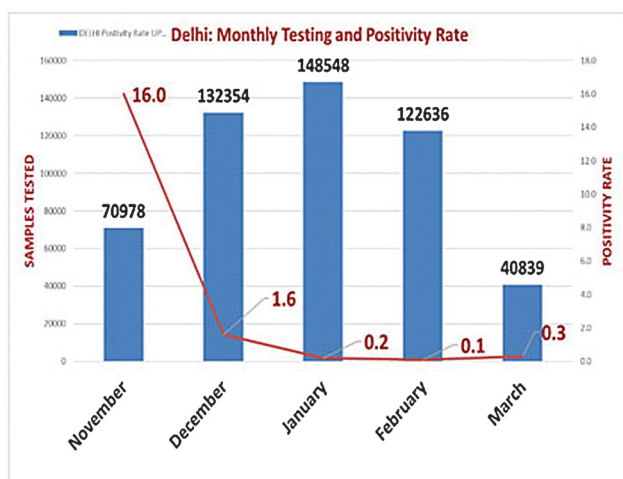


Fig. 7: Graphical representation of the monthly testing and positivity rates of samples from Delhi (left) and Uttar Pradesh (right).

Population-based sero-epidemiological studies measure the extent of SARS-COV-2 infection

ICMR-NICPR was one of the nodal centres covering three districts (Amroha, Saharanpur and GB Nagar) and 30 clusters (Fig. 8). In first round of survey during 11-17 May 2020, the COVID-19

sero positivity ranged from 0.50% to 0.75%. The second round of sero survey was conducted during 17-22 August 2020, with additional objective to estimate the age and sex-specific sero-prevalence. The sero positivity in this round ranged from 4.5% to 12.5%. Third round of sero survey was conducted during 21-28 December 2020 to estimate the sero-

prevalence for SARS-COV-2 infection in the general population and health workers at the national level and determine the trend over time among general population. The samples collected from general population were 1200 and from health workers were 300. Sero positivity in selected districts ranged from 13.1% to 27.4% among general population and 13.0% to 28.0% among health workers.



Fig. 8: National population based sero-surveillance for SARS-COV-2, sample collection from community (left) and team ICMR-NICPR for the sero survey (right).

Ban on spitting Smokeless Tobacco products and Spitting in public places during COVID-19 pandemic

A comprehensive ban on SLT and public spitting in India to contain COVID-19 Pandemic and strengthen tobacco control was drafted by the WHO FCTC Global Knowledge Hub on Smokeless Tobacco at NICPR.

- In response to the above initiative, an appeal to the General Public from the ICMR was issued

advocating “Not to consume and spit SLT in Public” on April 4, 2020. (URL: <https://www.icmr.nic.in/content/covid-19>).

- In continuation to this, the Tobacco Control Division of Ministry of Health & Family Welfare, Govt. of India, also released the same appeal through an order no. Z.21020/19/2020-TC, for the general public on April 10, 2020 (Fig. 9). Following this appeal, 20 States and 1 Union Territory have released the notifications to ban SLT use and spitting during COVID-19.

No. Z.21020/19/2020-TC
Government of India
Ministry of Health & Family Welfare
(Tobacco Control Division)

Nirman Bhawan, New Delhi
Dated the 10th April, 2020

To,

The Chief Secretaries of all States/UTs

Subject: COVID 19 and spitting of Smokeless Tobacco in Public - regarding.

Sir/Madam,

I am directed to refer to the subject mentioned above and to say that Indian Council of Medical Research (ICMR), Department of Health Research, Govt. of India has issued an appeal to the General Public namely “Not to consume and spit Smokeless Tobacco in Public”.

2. As per the appeal “Chewing Smokeless Tobacco products, Paan masala and areca nut (supari) increases the production of saliva followed by a very strong urge to spit. Spitting in public places could enhance the spread of the COVID19 virus”. In view of the increasing danger of COVID-19 pandemic, ICMR has appealed the general public to refrain from consuming the smokeless tobacco products and spitting in public places during the COVID epidemic.

3. The State/UT Governments have necessary authority under the Epidemic Diseases Act, 1897, the Disaster Management Act, 2005 and also under various provisions of Indian Penal Code 1860 and Code of Criminal Procedure (CrPc) to deal with Covid-19.

4. In this background, it is requested that necessary preventive measures may be taken under the appropriate law to prohibit the use and spitting of chewing smokeless tobacco products in public.

5. This issues with the approval of the competent authority.

Yours faithfully,

(Pradip Kumar Pal)
Under Secretary to the Government of India

Fig. 9: Appeal issued by the Tobacco Control Division of Ministry of Health & Family Welfare, Govt. of India regarding not to consume and spit smokeless tobacco in public places to help in COVID-19 containment efforts.

COMMUNITY OUTREACH PROGRAMS

These were organized with college students and the bridge population including bus drivers at UPSTRC, Noida on the National Cancer Awareness Day, 7th November 2020.

Capacity building programs

- DHR-funded Hands-on workshop on Research Methodologies in Molecular Biology** (January 28-31, 2020). Twenty participants (20) from various disciplines (MBBS/MD/MS; MDS/BDS; AYUSH; PhD) participated in the workshop.

- b) **Training of master trainers (TOTs)** - Medical Officers and Nurses from the state of Madhya Pradesh (Feb and Mar 2021).
- c) **Capacity building of various cadres of Health Care Providers in cancer screening** through NICPR-ECHO program - Medical Officers-4 batches (256), Dentists-4 batches (354), Gynecologists-1 batch (54), Nurses-2 batches (212).
- d) **Hands-on workshop on cervical cancer screening for pathologists** (March 4-6, 2020). The workshop was attended by 35 participants from across the country.
- e) **Cloud-based Hands-on Workshop on “Computational Structure based Screening and Explicit Molecular Dynamics”** (March 23 – 24, 2021) was attended by 59 participants.

ICMR-NATIONAL CENTRE FOR DISEASE INFORMATICS AND RESEARCH, BENGALURU (ICMR-NCDIR)

National Noncommunicable Disease Monitoring Survey 2017-18

The Report of “National Noncommunicable Disease Monitoring Survey 2017-18” was released on 25th January 2021 to mark the Foundation Day of ICMR-NCDIR, Bengaluru.

Ref: <https://www.ncdirindia.org/nnms/>



Fig. 10: National NCD Monitoring Survey 2017-18 Report.

- It is the largest NCD survey in the country to measure progress of the country towards achieving the national NCD targets funded by the Ministry of Health and Family Welfare, Government of India.
- The Survey covered a national representative sample of 12,000 households equally distributed among urban and rural areas.
- The key survey findings are that-
 - ♦ two in every five adults had three or more risk factors for NCDs and a quarter of adolescents were not doing sufficient physical activity.
 - ♦ Only every two in five and one in five adults (30-69 years) got their blood pressure and glucose levels measured in last 1 year preceding the survey.
 - ♦ Primary and secondary public health care facilities were not fully prepared to address NCDs.
 - ♦ The survey recommends developing prioritized NCD research agenda and setting up of NCD Surveillance units to manage the rising burden of NCDs in India.

Launch of Foundation Day and 10th Anniversary of ICMR – NCDIR on 25th January 2021

Hon'ble Union Minister of Health and Family Welfare, Govt. of India, Dr Harsh Vardhan launched the Decadal year celebrations of ICMR-NCDIR on 25th January 2021 and released the Report of “National Noncommunicable Disease Monitoring Survey 2017-18” and the e book on “Framework for Telemedicine use in Management of Cancer, Diabetes, Cardiovascular Diseases, and Stroke”.



Fig. 11: Foundation Day and 10th Anniversary of NCDIR invitation.

Release of Report of National Cancer Registry Programme 2020

ICMR – NCDIR is celebrating the 40 years of setting up of the ICMR National Cancer Registry Programme (NCRP) which was sanctioned on 11th December 1981 in a project mode with few registries, which over 40 years has grown leaps and bounds. NCRP has been the flagship program of ICMR and NCDIR, and provided robust cancer statistics to guide its prevention and control efforts. The quality of data, coverage and its use has increased several folds over the past decades.

The Report of National Cancer Registry Programme, 2020 was released on 18th August 2020.

Ref: https://ncdirindia.org/All_Reports/Report_2020/default.aspx

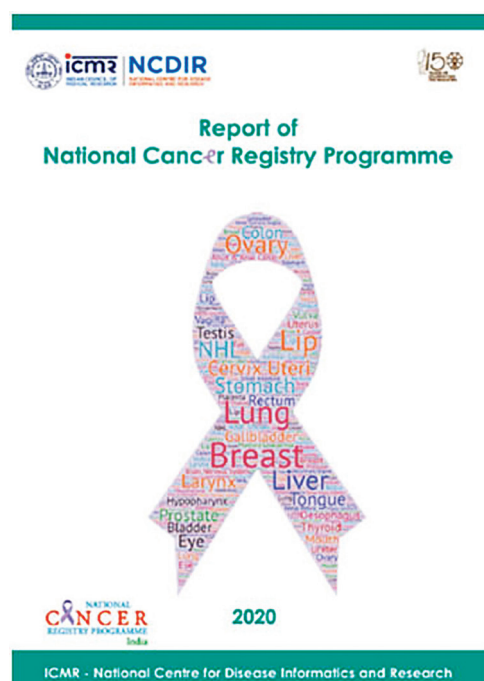


Fig. 12: The Report of National Cancer Registry Programme, 2020.

Key elements of the Report

- Covers a composite five-year data (2012-2016) from 28 PBCRs and 58 HBCRs.
- The data is represented zone wise for six zones: North, South, East, West, Central and North East.
- Cancer of lung, mouth, stomach and oesophagus were the most common cancers among males.
- Cancer of breast and cervix uteri were the most common cancers among females.
- Tobacco related cancers are estimated to constitute 27% of all cancers in India.
- There is a rise in the trend of incidence of cancer breast while cancer cervix uteri is on the decline
- Cancer burden is estimated to increase to 1.57 million by 2025 in India from 1.39 million in 2020.

Profile of Cancer and Related Health Indicators in the North East Region of India – 2021

The report has been released on World Cancer Day i.e., on 4th February 2021.

Key elements of the Report

- Gives an overall description of cancer statistics through a pooled analysis of all eight North East States' data as well as individual state analysis.
- Cancer continues to be a public health problem in the Northeast.
- Highest cancer incidence: Males –Aizawl district, Mizoram (269.4 cases per 100,000) and Females- Papumpare district, Arunachal Pradesh (219.8 per 100,000).
- Less than one-third of breast, cervix, head and neck, stomach and lung cancer are in localized stage at the time of diagnosis.
- The proportion of cancer patients seeking treatment outside NER is highest for Sikkim (95.3%) followed by Nagaland (58.1%)
- Projected no of cases - 57,131 cancer cases in the region in 2025.
- Report will find wide use among stakeholders, from policymakers to laypersons, in understanding cancer profile in the northeast region and framing control measures.

Ref: https://ncdirindia.org/All_Reports/NorthEast2021/Default.aspx

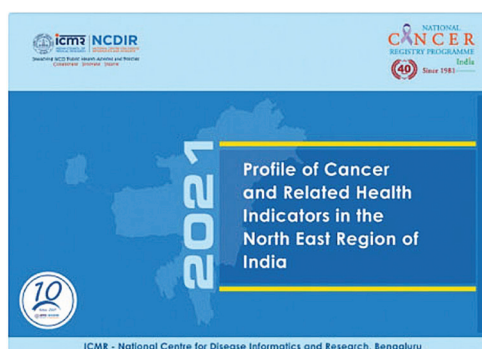


Fig. 13: Report of North East Region of India, 2021.

Signing of Memorandum of Agreement between ICMR-NCDIR and the National Health Authority for technical collaboration in the areas of NCDs especially – cancer and stroke

National Health Authority (NHA) and NCDIR have signed a MOA in July 2020 for collaboration

- To strengthen data analytics in areas of cancer and stroke.
- To develop policy briefs / position papers / workshop papers / reports / research papers.
- To jointly engage with key stakeholders for improving quality of patient care for NCDs.

Framework for Telemedicine use in Management of Cancer, Diabetes, Cardiovascular Diseases, and Stroke in India

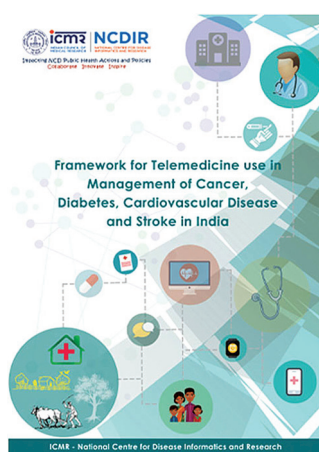


Fig. 14: Telemedicine Guidelines.

An e book on “Framework for Telemedicine use in Management of Cancer, Diabetes, Cardiovascular Diseases, and Stroke” was released on 25th January

2021 to mark the Foundation Day of ICMR-NCDIR, Bengaluru. The framework provides steps for use of telemedicine (TM) for Cancers, Diabetes, Heart Diseases and Stroke. Principles of approaching these common NCDs is addressed. They have been drafted by subject experts drawn from all over the country.

The report can be downloaded from https://ncdirindia.org/All_Reports/Telemedicine/Default.aspx.

Guidance for appropriate recording of COVID-19 related deaths in India

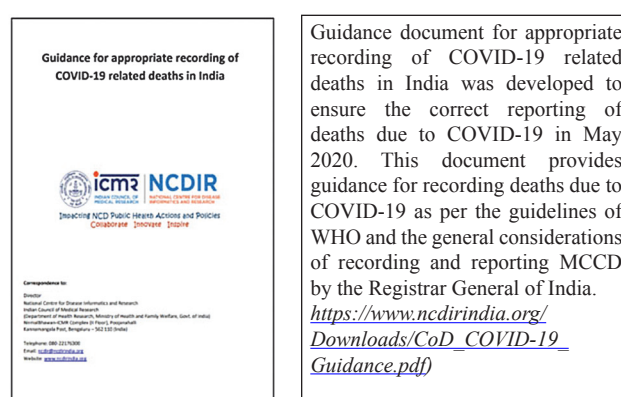


Fig. 15: Guidance Document – COVID-19 death.

National Guidelines for Ethics Committees Reviewing Biomedical & Health Research during COVID-19 Pandemic, April 2020

National Guidelines for Ethics Committees Reviewing Biomedical & Health Research during COVID-19 Pandemic was released in April 2020.

Ref: http://ethics.ncdirindia.org/asset/pdf/EC_Guidance_COVID19.pdf

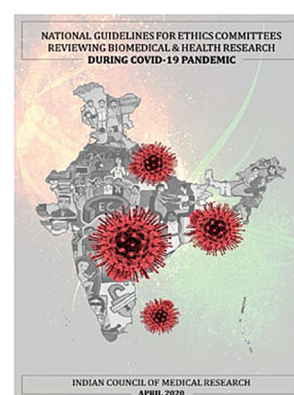


Fig. 16: National Guidelines for Ethics Committees during COVID-19.

India was the first country in the world to develop National Guidelines for Ethics Committees reviewing research during COVID-19 pandemic along with SOP's for emergency review.

Prepared to facilitate easy understanding for the Ethics Committees (ECs) to conduct review in expedited manner in the current prevailing pandemic situation. It is expected that this guideline will be useful not only for ethics committees but for all stakeholders in research and public.

SOP Template for Emergency EC meeting during COVID-19 Pandemic, April 2020

Ref: https://ethics.ncdirindia.org//asset/pdf/SOP_Template_EC_COVID19.pdf

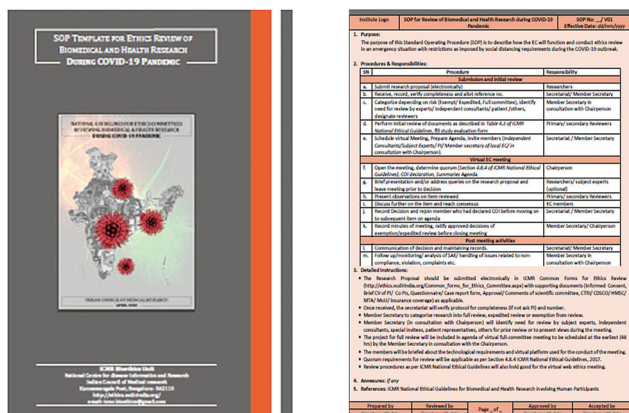


Fig. 17: SOP Template for Emergency EC meeting during COVID-19 Pandemic, April 2020.

The Standard Operating Procedure (SOP) template was developed to guide the Ethics Committee for the conduct of ethics review in an emergency situation with restrictions as imposed during the COVID-19 outbreak. The SOP template highlights the step by step procedure for submission and initial review of the protocol, virtual EC Meetings and post meeting activities. A table has been used for illustration which succinctly describes the roles and responsibilities of the EC Members and researchers. The template intends to serve as a handy reference for all ECs across the country to ensure facile and sturdy ethics review of not only COVID-19 related research but also other new and ongoing non-COVID-19 health research.

Training on “An update on ICMR National Ethical Guidelines with special Reference to Epidemiological Research” on 3rd November 2020

ICMR Bioethics Unit organised the online training for ethics committee members from various Central / Regional / State medical institutions and medical colleges, non-governmental or private centres who were involved in the review of research related to establishing data collection for Registry purpose mainly focused on cancer, CVD, Diabetes and Stroke. The participants were briefed about the recent ICMR National guidance on EC review during COVID-19 pandemic. About 179 participants from 159 institutes participated in the training.

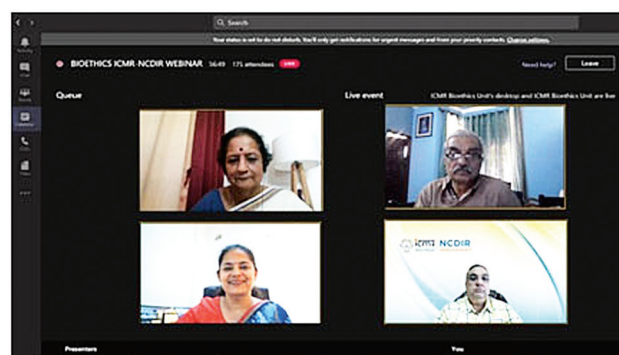


Fig. 18: Training on “An update on ICMR National Ethical Guidelines with special Reference to Epidemiological Research”.

ICMR BIOETHICS UNIT

This unit was designated as a WHO collaborating centre for strengthening Ethics in Biomedical and Health Research. It is the first centre for strengthening research ethics amongst 11 countries of the South East Asia Region of WHO.

ICMR Training on Roles & Responsibilities of Ethics Committee members held on 16th March 2021

An online training program was organized on 16th March 2021 by ICMR Bioethics Unit, NCDIR, Bengaluru which is also a WHO Collaborating Centre for Strengthening Ethics in Biomedical and Health Research to train the Ethics Committees members in their roles & responsibilities.

Participants were from across the country as well as from several neighbouring countries. An eminent panel of experts representing a multidisciplinary ethics committee shared their perspectives. The training was live streamed on You Tube. More than 700 participants benefitted from this training.



Fig. 19: ICMR Training on Roles & Responsibilities of Ethics Committee members held on 16th March 2021..

Coordination with NECRBHR, DHR for Registration of Ethics Committee and related activities

ICMR Bioethics Unit was involved in drafting the requirements for setting up of an Office for Ethics Committee Registration (OECR) at DHR. Detailed checklist of documents required for registration of ethics committees (ECs) along with the undertaking were also drafted and harmonised with Central Drugs Standard Control Organization (CDSCO) requirement for registration & re-registration of ECs was submitted to DHR. Further, ICMR Bioethics Unit also assisted in designing the

content for the online web portal that facilitates the registrations of ethics committees reviewing the biomedical and health research. To facilitate the registration of ECs, DHR has developed a separate online portal “National Ethics Committee Registry for Biomedical and Health Research (NECRBHR)” that is available at <https://naitik.gov.in/DHR/Homepage>.

Reconstitution of Central Ethics Committee on Human Research (CECHR)

In order to undertake high priority quality ethics review of COVID-19 related biomedical and health research, the CECHR committee was reconstituted on 6th May 2020 by Director General, ICMR to review both COVID-19 related and non-COVID-19 research led by ICMR. In the COVID-19 pandemic situation to expedite the review process, the committee met virtually through web conference or tele / video conferences. The committee has met regularly and reviewed more than 23 large research studies of ICMR Headquarters (in a short time frame of 24-72 hours). It is proposed that the CECHR would take up a greater role and be involved in also closely guiding the development of all ethics policy documents, advisories and guideline being coordinated by ICMR Bioethics Unit.

Webinars on Disease Awareness and Other Topics

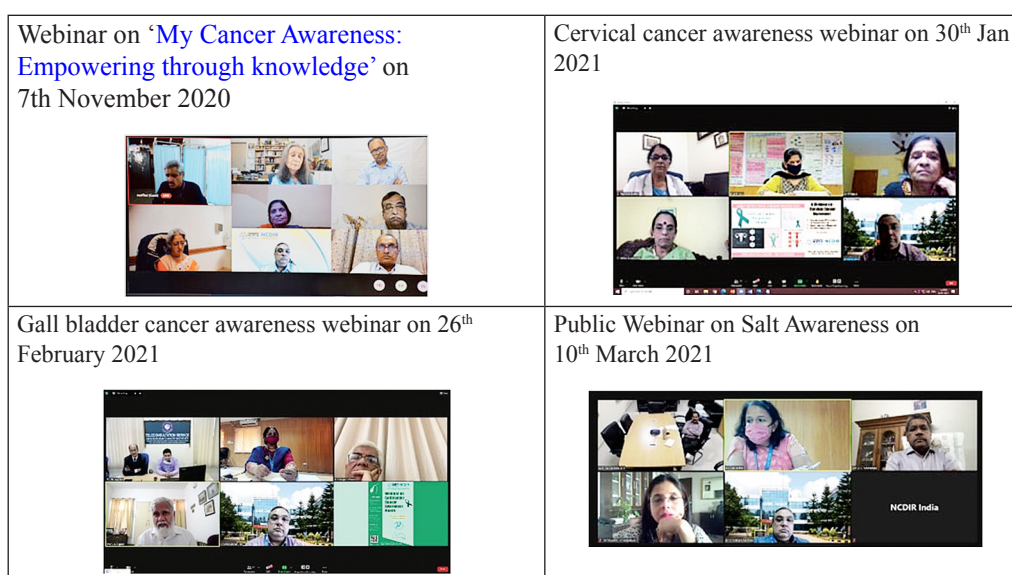


Fig. 20: Photos of various webinars.

ICMR-NCDIR NETWORK

This expanded with addition of centres in the following projects.

- (a) Hospital Based Cancer Registries - 16 centres have been registered.
- (b) Hospital Based Stroke Registries - 10 centres have been added.
- (c) Diabetes National Model Study - 4 Model Rural Health Research Unit (MRHRU) have been registered.
- (d) Hospital Based Cardiovascular Disease Registry and Patterns of care for Heart failure in North-East Region of India – 3 centres have been registered.
- (e) Implementation of NCDIR electronic Mortality software (NCDIR e-Mor) in hospitals of the National Cancer Registry Programme (NCRP) network in North East India– 1 centre has been registered.
- (f) Implementation of NCDIR electronic Mortality software (NCDIR e-Mor) in hospitals of the National Cancer Registry Programme (NCRP) network – 7 centres have been registered.

ICMR-NATIONAL INSTITUTE FOR IMPLEMENTATION RESEARCH ON NON-COMMUNICABLE DISEASES, JODHPUR (ICMR-NIIRNCD)

COVID-19 CONTAINMENT

Setting up of COVID-19 RT-PCR Testing Facility

- A proposal for performing COVID-19 RT-PCR testing at our Institute's virology laboratory was sent on 14th Apr'2020 along with the details of infrastructure and trained personnel.
- Approval for testing was granted on 17th Apr'2020. The testing was initiated from next day with 62 samples.

- *Round the clock* testing facility started functioning from April 18 2020.
- Trained 50+ staff in COVID-19 testing methods.
- Tested over 2.3 lakh samples so far.
- Turn around time from reception to reporting : - <24 hours.
- Samples were provided by state health authorities from Jodhpur, Jalore, Kota, Bundi, Baran, Jaipur, Sawai Madhopur, Karauli, and Bharatpur districts.

Setting up of COVID-19 Testing Kits Validation Centre

- Designated as COVID-19 kit validation centre on 4th June 2020.
- Validation of 119 kits (80 RT-PCR & 39 RNA Extraction Kits) completed till date.
- Average turn around time of around 48 hours is one of the fastest among all the validation centres in our country.

Setting up of Regional Depot for COVID-19

- ICMR has designated four institutes as a central depot and 16 institutes as Regional Depots to coordinate and distribute test kits throughout the nation. Among these 16 regional depots, our institute has been designated as a regional depot for 25 government labs spread over 19 districts of Rajasthan performing real-time RT-PCR tests to diagnose COVID-19.
- Our Regional Depot started functioning from April 19 2020.
- A total of around 22 lakhs reactions (13 lakhs RT-PCR kits / 7 lakhs RNA Extraction kits & 2.5 lakhs VTMs) were distributed through our Depot to government labs in Rajasthan under proper packaging and transportation conditions (maintenance of cold chain).

Establishment of a network of ICMR-COVID-19 biorepositories in India

The objective of the project was to establish organized and dedicated bio-repositories of well

characterized clinical samples of COVID-19 patients for future research. NIIRNCD, Jodhpur is one of the bio-repository centre and samples of the patients admitted to local medical colleges were collected. Serum, plasma and swab samples of 79 participants were collected in a systematic manner and stored in the bio-repository.

BCG Vaccine Trial against COVID-19: A Multicentric Trial to Evaluate the Effectiveness of BCG vaccine in Reducing Morbidity in Elderly individuals in COVID-19 Hotspots in India

SARS-COV2 viral infection is spreading rapidly throughout the world. Based on the capacity of BCG to reduce the incidence of respiratory tract infections in children and adults, to exert antiviral effects in experimental models; and to reduce viremia in an experimental human model of viral infection, the hypothesis is that BCG vaccination will partially protect against mortality in high-risk, elderly individuals. Study is being conducted in India over 11 different sites and our Institute is one among them. Out of 691 screened subjects, 301 have been vaccinated and 161 were kept in control group. The total sample size of this study is 1,555. Currently, Six Month Follow-up (i.e. Last follow-up) of the recruited subjects is ongoing.

SARS-COV2 - ICMR-SERO SURVEY: PHASE 1 TO PHASE 3

National Sero-surveillance to monitor the trend of SARS-COV-2 infection transmission in India: Community-based surveillance. Jodhpur and Jaipur, as a part of National Sero-surveillance Survey for COVID-19 (60 districts nationally). A total of 3 sero surveys have been conducted in year 2020; May (2020), August (2020) & (Dec-Jan 2021). Phase-I, Phase-II, Phase-III: were carried out in Dausa, Jalore and Raj Samand districts of Rajasthan. There were a total of 400 subjects sampled from each districts with 10 clusters (Rural & Urban) both in all the phases.

COVAXIN SAFETY MONITORING

Around 2000 subjects were monitored for COVAXIN, ICMR-Bharat biotech Indigenous

vaccine for nCoronavirus prevention; out of total of 1251 monitored; only 71 (12.5%) subjects had minor adverse drug reaction. There was no hospitalization or death reported from the group studied; suggesting excellent safety of COVAXIN from the group data studied.

Strengthening state non communicable Disease programme for early detection of Breast cancer involving strategic education and awareness among women: A Joint Programme of State Government of Rajasthan and ICMR-National Institute for Implementation Research on Non Communicable Diseases, Jodhpur

The aim of the study was to strengthen state breast cancer screening programme and develop a referral system for diagnosis and treatment of suspected cases at state medical colleges/ District Hospitals. During the year 2020-21, information about awareness about signs and symptoms and risk factors of breast cancer were collected from 13,012 women (30-65 years) from Jalore, Pali and Jodhpur districts. A total of 18,110 women have also been imparted training for breast self-examination. A total of 31 suspect cases of breast cancer were identified by different modes. Out of them, 17 had undergone Clinical Breast Examination at PHCs and 06 at Private hospitals. A Telephone cell has been created in our Institute for follow-up regarding BSE and referral cases. 56,267 calls were made for 1st follow, out of which 13 suspect cases were identified and 553 calls for 2nd follow up were made.

Assessment of Neonatal Screening Approaches for Sickle Cell Disease and the Effect of Early Intervention in Management of the Disease in Tribal Population

The objective of the multi centric project was to undertake a newborn screening program for Sickle cell anemia (disease) in tribal populations of TSP areas of state for (a) early detection (b) to understand the magnitude of the problem and (c) to understand

the barriers for undertaking such programme. The screening of neonates was carried out at Kotda and Jhadol blocks of Udaipur District of Rajasthan. During the year 20-21, centre has screened 323 newborns for haemoglobinopathies and 56 out of them, are sickle cell disorder with a prevalence of 17.33%. Among the sickle cell disorder newborns, 3 were homozygous (disease) and 53 were heterozygous (trait). In 2019-20, 829 newborns were tested for various haemoglobinopathies. In total, 1152 newborns were screened for the haemoglobinopathies. All the homozygous were followed up and febrile illness, moderate acute malnutrition (MAM) and ARI were reported in newborns.

National Tuberculosis Prevalence Survey: Joint study of Indian Council of Medical Research, Central TB Division, Ministry of Health and Family Welfare Division & World Health Organization

Tuberculosis continues to remain one of the most serious health and developmental problems in India. With a quarter of the world's tuberculosis (TB) patients living in India, an estimated 2.3 million new cases and 300,000 deaths each year, the disease is a massive public health challenge for the country. First Nationwide Survey which was done during 1955-1958 and a number of surveys in geographically defined areas conducted earlier confirmed that the disease was highly prevalent throughout the country. Monitoring the progress of TB control programs by estimating disease burden in the community has been a challenge. Nationwide survey for TB was never repeated after 1956 and hence it is important to know the disease burden at national level for implementing National Strategic Plan to End Tuberculosis in India by 2025. This National TB Prevalence survey is being conducted with primary objectives of estimating point prevalence of microbiologically confirmed pulmonary TB among persons aged ≥ 15 years in India at National level and also individually for 20 states / state groups.

- NIIRNCD, Jodhpur is the nodal centre for this survey in the state of Rajasthan.
- 36 randomly selected clusters with a study population of 28,800 in Rajasthan are currently being surveyed by the NIIRNCD team in association with the Rajasthan State TB Cell and District health authorities.
- Till the end of Mar 2020, 15 clusters covered and 16th cluster is under progress.
- 11842 participants were registered 42 cases of active tuberculosis were detected during this survey period.

Systematic pulmonary tuberculosis case finding among malnourished children admitted in Nutritional Rehabilitation centres – Rajasthan

Indian Council of Medical Research – India TB Research Consortium (ICMR – ITRC) funded a multisite interventional research study to be carried out at 6 sites of north India, Rajasthan was one among these. Study aimed to assess the implementation status of government guidelines for screening of malnourished children admitted in nutritional rehabilitation centres for tuberculosis. Second objective of the study was to estimate the prevalence of pulmonary TB among admitted malnourished children. Eight NRCs from 8 districts from North-western Rajasthan were selected in this study. Study found out poor implementation of NRC guidelines. Retrospective data of previous 3 months since the beginning of study found that out of total 189 admitted children, only 16 were assed for TB by CBNAAT test of gastric aspirate/lavage sample for TB diagnosis. There was not any case diagnosed with TB. Study recruited 552 prospective cases, which were subjected to meticulous history taking, clinical examination, chest X-ray, Mantoux test and gastric aspirate/lavage sampling for TB testing by molecular based diagnostic test viz. Cartridge Based Nucleic Acid Amplification Test (CBNAAT) and TruNat™ – a indigenously developed and ICMR endorsed gene-based TB detection technology. Out of these

522 children, total 39 children were found to be positive for TB on CBNAAT and/or TruNat™. On extrapolation these figures, a prevalence rate of 7065 cases/100,000 children was obtained, which is many times higher than the reported/estimated prevalence of TB among general population of country. The findings were disseminated among the stakeholders involved.

Early diagnosis & development of a referral system for silicosis among sandstone miners

The project has almost met sample size despite challenges of COVID-19 (n=450). Developed a referral model based upon symptoms. The project started by screening the mines and quarry workers using demographic data, pulse oxymetry and anthropometric measurements were taken. Those with SpO2 levels below 95% with or without symptoms were referred to Community Health Centre Fidusar for further management. There was a high correlation between lower pulse oxymeters scores and X-ray chest (postero-anterior view). Pilot data demonstrated predictors of respiratory symptoms among mine workers e.g. duration of work in mines & quarries, age, smoking status, gender etc. Respiratory symptoms were found among the residents who lived close to mine areas as well. The project has proposed that pulse oxymetry can be used as a cheap & inexpensive tool for screening of mine & quarry workers. This is because the current data suggests that those with age > 30 years & working in mines & quarries for 10 years or more have values of oxygen saturation (SpO2) below 95%. This could be due to development of inflammation and fibrosis that has not reached to clinical threshold.

Longitudinal Silicosis Study Balesar (LSSB) among silica exposed sand stone mine workers in Balesar, Jodhpur

Under this project it is aimed that all the permanent residents of this block and working as sandstone mine workers will be enrolled and longitudinal follow up will be carried out and screening

through spirometry, PA chest X-Ray as per ILO specifications and sputum examination (for TB symptomatic) will be carried out for each subject. The mapping of all 228 villages spread across 23 Panchayats has been completed. Under this project a laboratory for enrollment of subjects into the study has been established in collaboration with CHC Balesar. The pneumoconiosis board has been formed at the block level. 349 confirmed and certified silicosis subjects have been enrolled in the study so far since, January, 2021. Further the study is under progress.

Assessment of iodine status among pregnant & lactating women and 6-11 years children in selected districts of Rajasthan

This project has been initiated in January, 2021 with aim to carry out cross sectional study to assess the urinary iodine level among pregnant & lactating women and 6-11 years children in Rajasthan & to estimate the iodine content in edible salt samples collected from household of study along with Nutritional counseling for population for IDD program of Govt. of India. A total of 297 households have been covered from 28 villages of Barmer block of Barmer district out of which 164 were school children (6-12 years), 69 pregnant women of third trimester, 82 lactating & 88 NPNL women. Urine and salt samples collected were 403 for estimation of UIE and Salt Iodine. Analysis of salt Iodine in 259 sample revealed that 58.7 percent household use adequately Iodized salt i.e. 15 PPM & above whereas 41.3 percent use inadequately iodized salt in rural areas of Barmer district. Nutrition Counseling were provided to all the 297 HHs subjects regarding the IDD program of Govt. of India. Project is in progress.

Assessment of Iodine adequacy in Urban Slum Population of Jodhpur city (Funded by ICMR in collaboration with CNRT)

This project is initiated with aim to assessment of urinary iodine status among 6-11 years children, pregnant and lactating women; determination

of iodine level in edible salt samples collected from households and Nutritional counseling for population for IDD program of Govt. of India. The data has been collected 22 wards have been completed covering 510 households (394 school children (6-12 years of age), 85 pregnant women of 3rd trimester and 86 lactating women) were examined for their Socio-demographic profile, Anthropometry & dietary intake along with a casual urine samples for estimation of Urinary Iodine Excretion (UIE) levels and salt Sample to estimate Iodine content of salt sample. Nutrition Counseling were provided to all the 510 HHs subjects in the form of lectures regarding Intake of Iodized salt and their storage etc. and Knowledge of Iodine deficiency disorders and their prevention at community Level and at HHs level. Educational printed material, in local language/Hindi, in the form of pamphlets and pictorials were distributed. Analysis of salt iodine revealed that only 37.8 percent women at HHS level use adequately Iodized salt i.e. 15 PPM & above. It need attention that 62.2 percent women use inadequately iodized salt in urban slum areas of Jodhpur which need attention.

Social Determinants of Low Birth Weight: A Hospital Based Study

It is an intramural programme of ICMR-NIIRNCD aim to determine the prevalence of low birth weight; to know the socio-economic factors associated with low birth weight and to implement and test a social and health interventions/awareness to reduce the prevalence of low birth weight in the study population. The study was proposed to be initiated in March, 2020, but due to the unprecedented COVID-19 pandemic across the world including in India, it could not be initiated. Project activities have been started in March, 2021 as the number of active cases and new cases in the country have been declining steadily over the last 4 months. Assessment of a total of 21 subjects has been completed and out of which two subjects are found to have low birth weight.

Community based Nutrition Intervention models using local food preparations of Pearl Millet & food habits to address the problem of anemia & malnutrition in Rajasthan

This is an intramural project initiated in February, 2021 with aim to address the problem of anemia & malnutrition in Rajasthan (*Leads of Translation Project on Pearl Millet*); to do the improvement in the food practices of the rural population w.r.t. to local pearl millet preparations and to study the barriers, if any, related to it; promotion of inclusion of Pearl millet in Public Distribution System and Promotion of Inclusion of Pearl millet products in the Mid Day Meal Program for the school children a state level program involving Ministry of Women & Child Development and Human Resource Development. Meeting has been made with Director, Public Health, Directorate of Medical & Health Services, Jaipur, and Director, ICDS Department, Jaipur for their contribution in the implementation of this project at the directorate level and in the field at all levels i.e. from Director, Deputy Director, CDPOs, ACDPOS, LS/supervisors, ASHA / AWs or equivalent workers for implementation at community level along with different trainings and meetings. This project is in progress.

Nationwide Study to estimate the incidence, mortality, morbidity and economic burden due to snakebites in India. (DHR-ICMR Taskforce project)

This is a multicentric study at 21 locations in India. NIIRNCD is one of the site where the study has been initiated with aim to estimate the incidence, mortality, morbidity and economic burden due to snakebites in India. Project re-started in January 2021 due to COVID-19 restrictions. So far, recruitment of the project staff has been done and training of the project staff related to snakebite identification and management of snakebite has been done from 25th-26th February 2021. Telephonic communication with community leaders (Sarpanch) has been done

& total of 311 calls have been done in Udaipur district reporting around 3 cases of snakebites. For Bikaner district 176 calls have been made with 2 cases being reported and in Jaiselmer, the 35 snakebites have been reported and followed till today. This project is in progress.

Model Rural Health Research Unit, Bhanpur Kala, Jaipur (Rajasthan)

Model Rural Health Research Unit (MRHRU) of Rajasthan is established at the CHC complex of Bhanpur Kala, Jaipur. The objectives of the setting up of MRHRU in different states of India by the Department of Health Research is to create infrastructure at the periphery for transfer of technology to the rural areas for improving the quality of health services of rural population; to ensure an interface between the new technology developers (Researchers in the Medical Institutions; State or Centre), health systems operators (Centre or state health services) and the beneficiaries (communities in rural areas) and to ensure the much needed geographical spread of health research infrastructure in the rural areas.

- **Point of Care:** Point of care technology Cardiotocograph has been executed and found to be effective and life saving for rural population. 149 participants got the benefits of point of care technology Cardiotocography in MRHRU and its interpretation from experts of SMS Medical College, Jaipur through WhatsApp. Point care technology was used for the detection and treatment of H1N1 in 35 patients and 38 cases examined for the Tb through TrueNat.
- **Mapping of Sickle Cell Anemia, β -thalassemia:** A total of 769 individuals were screened for beta- thalassemia and sickle cell disorder and out of them 68 were found to be β -thalassemia positive and prevalence was found 8.84%. No sickle cell disorder case has been reported from the study area.

EXTRAMURAL RESEARCH

DIABETES

Investigations of Association of Mutations in MODY and NDM by Translational Genomic Research

The project is aimed at screening of genetic abnormalities involved in the etiology of neonatal diabetes, monogenic syndromes and hyper-insulinemia. Monogenic diabetes patients including Neonatal Diabetes Mellitus (NDM), Congenital Hyperinsulinism (CHI) and Maturity Onset Diabetes in the Young (MODY) are shifted from insulin therapy to oral hypoglycemic agents.

Registry of People with Diabetes in India with Young Age at Onset

By end of phase II, around 20,000 young diabetes patients in the registry were enrolled.. Contrary to expectations, around 25% subjects in ≤ 25 years were reported to Type2 Diabetes. YDR is uniquely positioned to establish cohort of type 1 diabetes and type1 diabetes. Data entry software was developed in-house.

ICMR-India National Diabetes Study, (ICMR-INDIAB)

It is the only nationwide survey of diabetes & pre-diabetes completed in all states of country including risk factors-hypertension/ diabetes/ lipids/obesity/ diet. The weighted prevalence of diabetes is 5.9% whereas weighted prevalence of pre-diabetes is 13%.

Impact of Yoga on Chronic Care

Beneficial effects of yoga were reported on cognitive parameters & inflammatory markers but failed to delay initiation of insulin therapy in patients with type 2 diabetes.

Cancer Management Guidelines

The Indian Council of Medical Research constituted a Task Force on Guidelines for Management of Cancers. A total of 20 documents have been published so far (Buccal Mucosa, Gastric, Colorectal, Gall Bladder, Tongue, Non Hodgkin's Lymphoma –HG, Soft Tissue Sarcoma, Multiple Myeloma, Breast, Esophagus, Paediatric and Soft Tissue Tumors and Lymphomas; Uterine, Ovary, Cervix, Larynx and Hypopharynx Cancers, Pancreas, Hepatocellular Carcinoma, Neuroendocrine Tumours, Uterine Cancer, Ovarian cancer, Acute Myeloid leukemia, Myelodysplastic Syndrome, etc). It is available at ICMR website (www.icmr.nic.in) and summary is also published in journals. Work on formulating 17 consensus documents is ongoing.

Screening and Early Detection of Cervical, Breast and Oral cancer in Cachar, Assam: a pilot project

The proposal was aimed at capacity building. A mobile application had been developed, which can be used for data collection online as well as offline. Cachar staff and Medical Social Workers were trained using ECHO (Extension of Community Health Outcomes). ASHAs empowered for establishing chain for diagnosis and referral mechanism (Cachar).

Strengthening State Non-Communicable Disease Programme for early detection of Breast Cancer involving strategic education and awareness among the women: a joint programme of State Government and ICMR-Desert Medicine Research Centre, Jodhpur

The study is aimed to strengthen state breast cancer screening programme and develop a referral system for diagnosis and treatment of suspected cases at state medical colleges/ district hospitals. The project facilitated strengthening state NCD programme for diagnosis and treatment of suspected cases at medical colleges/institutes (NIIRNCD, Jodhpur).

Indian Childhood Collaborative Leukemia (ICiCle) Group Multicentric Study for Children with Acute Lymphoblastic Leukaemia (ALL)

The ICiCle study is focused on using risk stratification to accurately identify patients who require the least therapy and delivering a curative approach for this population. The study has demonstrated better outcome using less intense therapy in children at low risk of relapse.

India Cancer Research Consortium (ICRC)

India Cancer Research Consortium (ICRC) was established (in July 2019) under aegis of ICMR-DHR with aim to bring all the stakeholders working in cancer research under one umbrella. Seven Thematic Working Groups identified are: (i) Prevention and Epidemiology; (ii) Diagnostics; (iii) Therapeutics; (iv) Palliative Care; (v) Innovation and (vi) Clinical Trial.

CARDIOVASCULAR DISEASES

Risk Factor Control Initiative-India Hypertension Control Initiative (IHCI)

The primary goal of IHCI is to reduce cardiovascular disease, particularly by improving the control of high blood pressure. The implementation partners include Ministry of Health and Family Welfare, WHO, ICMR, Academic institutions and state governments. It now aims to strengthen the hypertension management in 100 districts where National Program for Prevention and Control of Cancer, Diabetes, CVD and Stroke (NPCDCS).

Crucial Components of Effective Hypertension Care



Fig. 21: Crucial Components of Effective Hypertension Care.

Activities related to decentralization of hypertension management is done by involving AYUSH practitioners & Nurses for screening, referring to higher facilities and regular monitoring and maintaining treatment of blood pressure. Auxiliary Nurse Midwives/ ASHA are trained to educate the patient and drug refills at the sub-centre level/ Health and Wellness Centres for patients diagnosed and initiated on hypertension treatment. Monitoring systems with standard indicators and documentation mechanisms that ensure collection of data for the key monitoring indicators, mainly control rates are being used. A digital information system, Simple App, an android based phone app was developed and field-tested with the help of health care providers and patients in Punjab to assist in storage and retrieval of patient information. Simple allows medical staff to use their time more effectively and efficiently when treating patients with hypertension.

Overall, 81 districts across 18 States have enrolled more than 1.4 million patients in 8,300+ health facilities. The drugs availability at the district level has improved in the initial 26 districts due to better planning, streamlining of procurement process and field level monitoring.

HEART ATTACK INITIATIVE

Delhi Emergency Life Heart-Attack Initiative: MISSION DELHI

The project uses Nurses on motor cycle as 'First Responders'. This team makes assessment for Acute Coronary Syndrome (ACS) and monitor vital signs. Thrombolytic therapy is initiated on advice of Consultant and patient is shifted to AIIMS. In Phase I, infrastructure setup was done and SOPs were created. Phase II is implementation and Analysis Phase. Refresher training by Northern Ireland Ambulance Services (UKSAS) was provided to Nurses in ACLS (Advanced Cardiac Life Support).



Fig. 22: Mission Delhi.

ICMR STEMI ACT

ST elevated myocardial infarction (STEMI) is the commonest form of acute coronary syndrome (ACS) in low income countries and is a major cause of morbidity and mortality. Timely initiation of thrombolysis based reperfusion has been demonstrated to be effective in lowering mortality. The project has been initiated in 7 districts of 6 States.

HEART FAILURE PROGRAM

National Heart Failure Registry

National Heart Failure Registry (NHFR) is a registry of acute decompensated heart failure patients admitted in 53 participating hospitals from 24 states and 2 union territories. The nine Nodal centres and the five participating centres under each one of them have recruited 10700 patients and are following up the patients. Follow up is ongoing.

NEUROSCIENCES

Stroke Initiative

Establishment of Clinical Stroke Care Pathway using Mobile Stroke Unit in Assam

The project at Tezpur was initiated on 1.02.2019 and Mobile Stroke Unit (MSU) was fabricated and received on 11.01.2020. The project at Dibrugarh

was initiated on 7.03.2019 and the MSU received on 9.07.2021 and made live on 11.01.2021. There was delay in procurement of MSU, making MSU live in field and other project activities due to COVID-19.

Thrombolysis was not being done at TMC and AMC before these projects were initiated. The model used at Tezpur and Dibrugarh is a physician based stroke care model. Stroke units were established in TMC, BCH, Tezpur and AMC, Dibrugarh. All 3 hospitals received trainings for stroke care. These Units have recently started thrombolysing (giving a clot buster therapy) ischemic stroke patients.



Fig. 23: Mobile Stroke Ambulance.

Establishment of Population Based Stroke Registry and Clinical Stroke Care Pathway using Mobile Stroke Unit in Dibrugarh, Assam

The population based stroke registry is developing an integrated network system for registering stroke cases in two blocks of Dibrugarh district (Barbaruah and Lahowal) by utilizing the support of ASHA workers, ANMs, MOs of health facilities, general practitioners and specialist of Assam Medical College and private hospitals/nursing homes in the area. Networking with 15 hospitals including Government hospitals, private hospitals, scan centres, tea garden hospitals and municipality offices has been done. During the reporting period, a total of 2152 cases have been registered. Out of the total stroke cases, major stroke type was hemorrhagic [1283 (59.6%)] followed by ischaemic [664(30.9%)].

STROKE REGISTRIES AND SURVEILLANCE SYSTEMS

Study of Feasibility in Establishing a Stroke Surveillance and Management System through Community involvement and Technology Use in Rural Tirunelveli (MRHRU Field Practice Area)

The primary objective of this study is to assess the feasibility of establishing a stroke surveillance and management system in rural Tirunelveli under the MRHRU field Practice area. Women Self Help Groups (WSHGs) were identified as key informants. Incidence of stroke is 50/10,00,000. Ischaemic stroke is most common (83.9%). The Mobile App - Tamil Nadu Accident Emergency Initiative - Stroke Mobilization Assessment and Rapid Treatment” (TAEI SMART) has been developed and a Stroke care pathway is being developed. The key informants include different group of people as Multipurpose health care worker, Accredited Social Health Activist (ASHA), Anganwadi workers (ANW), members of local Self-help groups (SHG) and some volunteers. The study has collected 215/250 key informants for both blocks as proposed.

Development and validation of a comprehensive clinical and neuropsychological test battery for use in the Indian context for patients with Vascular Cognitive Impairment

A multidisciplinary research group, for the first time in India, developed a comprehensive neuropsychological and behavioral test battery, the ICMR Neuro Cognitive Tool box (ICMR-NTB), in five different Indian languages that can be used to assess cognitive impairment due to stroke and other dementias in different populations within India. The ICMR NTB meets diverse needs: a short version for the busy OPD to a comprehensive version for more in-depth testing or research purposes. It is planned to provide this free of cost for use by the clinician and dementia researchers.

Indian Stroke Clinical Trial Network (INSTRuCT)

The Indian Stroke Clinical Trial Network (INSTRuCT) was setup by ICMR. A total of 25 stroke centres across the country have been included in INSTRuCT. India is the only developing country with a Government sponsored Stroke network.

Following trials are being conducted under INSTRuCT network.

NATIONAL TRIALS

Secondary Prevention By Structured Semi-Interactive Stroke Prevention Package in INDIA (SPRINT INDIA) Trial

SPRINT is a multicentre, randomized, parallel-design, adaptive and blinded end-point clinical trial of sub-acute stroke patients. Twenty six centres were participating initially. Four new centres were added so as to meet the target number of stroke patients. Study material/Intervention was developed in the form of Stroke Prevention Workbook in 11 languages namely, English, Hindi, Punjabi, Malayalam, Tamil, Telugu, Kannada, Bengali, Assamese, Gujarati and Marathi.

AyuRvedic TrEatment in the Rehabilitation of Ischemic STrOke patients in India: A Randomized controlled trial (RESTORE)

Ayurveda, the traditional Indian system of medicine, has certain beneficial effects in the rehabilitation of stroke patients but its efficacy has not been proven by high quality clinical trials. The study hypothesizes that Ayurveda is superior to physiotherapy in improving the sensorimotor recovery of ischemic stroke patients.

INDIANSTROKE RESEARCH NETWORK

Fever, hyperglycemia, swallowing and hypertension management in acute stroke: A cluster randomized controlled trial

A total of 3012 patients were screened across 6 different medical colleges and 6 district hospitals

connected to these medical colleges. The study found that medical colleges are treating relatively high volume of stroke patients and have huge monitoring and management gaps to allow quality improvement. District hospitals uniformly tend to transfer problem prone patients to medical colleges. Six workshops were done as planned intervention to improve quality of management. FeSSH, Significant knowledge improvement in temperature management, glucose monitoring and swallowing management was noted after training. Feasibility of blood collection from periphery was demonstrated.

Indian Multiple sclerosis and Allied Demyelinating Disorders registry and Research Network

This is a first dedicated Indian network database of MS and allied demyelinating disorders. This will help collect data at presentation and on follow up of all patients with MS and allied CNS demyelinating disorders so as to optimally describe the demographics of the disease, risk factors, pattern of presentation and disability, medication response, imaging patterns, pregnancy outcomes and long term course of the disease etc. The study also plans to setup a repository of biological samples and radio-images from these patients.

CENTRE FOR ADVANCE RESEARCH AND EXCELLENCE

Kidney Disease: Biomarkers & newer Therapeutics

This centre is aimed for development of newer non-invasive biomarkers for early prediction of kidney disease. In order to assess therapeutic potential of exosomes in diabetic kidney disease; fifteen genes mostly related to inflammatory pathways were downregulated in the kidneys of exosome treated diabetic rats relative to vehicle treated DM rats.

Paediatric Uropathies & CKD

A significant association has been found with the A allele of the AGTR2 gene at rs3736556 with

development of PUJO and VUR. Also, these subjects were more likely to develop renal scarring if they were found to harbor the D allele (ACE I/D polymorphism) as well.

Estimating biomarkers in DBS for cardiovascular risk assessment in geriatric population

The dried blood spots DBS assay was found to be linear, sensitive, accurate and precise with acceptable recovery and matrix effects for HbA1c, Creatinine, HDL-C, ferritin and hs-CRP. It was concluded that the HbA1c, Creatinine, HDL-C, ferritin and hsCRP can be reliably measured from DBS samples and are readily transferable to a liquid phase for analysis, thus offering a convenient alternative for monitoring of CVD risk factors.

Overuse injuries among school-going children in Manipur

Overall prevalence of overuse injuries in Manipur was found to be 14.39% among school children. Commonest overuse injuries were backpain (27.22%), neck pain and arm pain (22.58%), chondromalacia patellae (13.2%) and shin splint (10.81%). Common contributing factors to overuse injuries were long term use of poor ergonomic furniture (34.94%), mobile phone addiction (27.60%), overtraining (15.05%), bad road condition, hilly terrain, poor condition of the training field (16.02%) and poor quality of footwear (6.37%). The study highlighted the important fact that overuse injuries in school going children are preventable.

NEUROMUSCULAR DISORDERS

Mitochondrial Respiratory Chain Disorders (MRCD) – Proteomic analysis of Complex I and IV deficiencies

The study revealed isolated and multiple complex deficiencies with a diagnostic yield of 40% which was better than conventional histochemical methods (10% in this study). Spectrophotometric assays of the respiratory chain complexes are thus

established as a cost effective routine diagnostic test for the first time in the country, as a self-sustaining model.

Human Skeletal Muscle Disease Bio-Bank

The Bio Bank was established in 20-03-2017 at NIMHANS, Bengaluru. During the year under report, a total of 242 fresh muscle, 113 blood, 100 serum and 4 skin punch biopsies of patients diagnosed as skeletal muscle disorders were collected. The major categories that have been banked till now include muscular dystrophies, neurogenic atrophy, inflammatory myopathies, congenital myopathies and metabolic myopathies. Fibroblast cultures have also been initiated across the neuromuscular disorders. To summarize from 2017 till date a total of 5365 (internal) and 5102 (referral) muscle biopsies and their related materials – serum, DNA have been banked till now. Long term objective is to provide a rich source of biological material from a wide spectrum of muscular disorders & add iPSC bank and facilitate future experimental and functional studies.

Snakebite

Venomous snakebite is a significant cause of morbidity and mortality in India. The National Health Profile 2019 data on snakebites reported 164,031 snakebite cases and 885 deaths in 2018. The project on “Nationwide Study to estimate incidence, mortality, morbidity and economic burden due to snakebite in India,” has covered 13 states, 34 districts, 336 blocks across the country. The project on ICMR National Snakebite Project (INSP) on capacity building of health system on prevention and management of snakebite envenomation including its complications. The study has been initially piloted covering 2 states (Odisha from East and Maharashtra from West) covering one district each.

Assessment of Impacts of PMUY

Four short term studies (as Pilot study) has been initiated in the 3 different centres (KEM, Pune, RMRC, Bhubaneswar and PGIMER, Chandigarh)

to assess the barriers to and facilitators of uptake and sustained use of LPG, challenges faced by LPG distributors in providing LPG connections through PMUY and also health outcomes of adoption and sustained use of LPG and also toward exclusive use by ensuring increased use through a second LPG gas cylinder and reducing availability of the traditional Chula.

Sharing the collective information of the patients from Kerala with the Government of Kerala for Dialysis outcomes, Hypertension and Diabetes

Lack of a renal registry means that there are few reliable statistics on Renal replacement therapy (RRT) in India. The objectives are to follow kidney failure patients starting dialysis in Kerala state for a duration of five years to assess health outcomes in patients starting dialysis therapy and capture their state of health at the time of commencing dialysis and subsequent follow-up visits. Online template has been developed to systematically collect patient wise information on a continuous basis, patients reporting for dialysis and their outcome through information collected at each follow up visit. The template can be accessed at <https://dialysis.icmr.org.in>. Patient registration form has been divided into three types of broad forms namely enrolment form, baseline form and follow up form.

INTESTINAL DISEASES

The centre is focusing on Intestinal diseases with major emphasis on Inflammatory Bowel disease (Ulcerative colitis, Crohn's Disease), Celiac disease and Abdominal Tuberculosis. **IBD NutriCare App**, a mobile app has been developed which will help patients in recording their real time diet data on a regular basis, track their nutrient intake, monitor their disease activity, and keep a tab on their medicine intake and lifestyle.

Prevalence of Non-Alcoholic Fatty Liver Disease (NAFLD) and its association with cardio- metabolic disease risk factors in North India

It was aimed to assess the prevalence of non-alcoholic fatty liver disease (NAFLD) residing in Urban and Rural areas of North India. Higher NAFLD prevalence of NAFLD was reported in Urban site (65.7%) as compared to rural (61.1%). Urban female (67.4%) reported higher prevalence than male (64. 2%). Prevalence of NAFLD increases with increase in BMI.

ORAL HEALTH

Cleft Lip and Palate Anomaly in India: Clinical Profile Risk Factors And Current Status Of Treatment: A Hospital Based Study

The nationwide multicentric project was initiated to identify the pattern, ascertain risk factors, establish the spectrum of problems of cleft patients, protocols of treatment given to these children and their actual treatment needs. There was a wide variation in age of primary lip repair (3-72 months) and palatal repair (6-72 months). Among 5-14 years of age, 34% of patients had a post-surgical oronasal fistula. The majority of cases (87%) did not have any history of dental or orthodontic treatment. The otological afflictions in cleft subjects were high; 18.6% of patients presented with affected hearing, and 21.6% had tympanic membrane afflictions. Nearly 23rd children (66.7%) had misarticulated speech, 44% had velopharyngeal dysfunction, and 51.6% had partially intelligible to unintelligible speech pattern. Out of 15 families with three generations of CLP that underwent whole-exome sequencing, three families showed pathogenic variants in the three families, and the other three families showed a genetic variant of uncertain significance.

ICMR-NATIONAL CENTRE FOR ASSISTIVE HEALTH CARE (ICMR-NCAHT)

It is aimed to address the various challenges such as innovation, design, redesigning existing devices, materials and technology available for assistive technology. The ICMR-NCAHT will provide support across the following verticals to meet its objectives: to conduct a comprehensive and ongoing

analysis of the Landscape of disability vis-à-vis assistive technologies, covering the related issues from multiple aspects such as burden of disease preventable by ATs, penetration of ATs, barriers to access, unmet needs and value chain gaps; to create a repository of knowledge with regard to ATs, to assist various stakeholders including doctors, patients, NGOs, welfare organizations, innovators and Governments in making prudent decisions pertaining to ATs and rehabilitation; to undertake and foster the innovation, framework for validation of new and existing technologies, implementation and scaling of novel ATs; to liaise with NHA to ensure expeditious addition of ATs to the list of reimbursable interventions; to bring all stakeholders under one banner with the common cause of disability rehabilitation chiefly through ATs; to enhance national capacity in training of personnel for innovations for novel ATs, disability research and public policy briefs; to conduct public policy landscaping and make relevant policy recommendations to improve access to and utilization of rehabilitative ATs; and to liaise with Industry and Bureau of Indian standards to facilitate creation of relevant standards in a manner that facilitates local manufacturing, ensures patient safety and a level playing field for all players.

CARE on Neuro-Assistive Technologies for Stroke Recovery

Centre for Advanced Research and Excellence (CARE) on Neuro-Assistive Technologies for Stroke Recovery has been initiated at AIIMS-Delhi in collaboration with IIT-Delhi. Primary objectives of the Centre are to optimize the robotic hand exoskeleton for upper limb rehabilitation in stroke patients; to design a piezoelectric hand glove (robotic glove) with machine interface for hand biomechanics and function; to explore the potential of virtual reality (VR) and /or its integration to robotic exoskeleton for neuro-rehabilitation; and to study the efficacy of these on upper limb hand function in stroke on clinical scales and functional MR imaging. Secondary objectives are to develop the module for cloud based tele-rehabilitation monitoring for robotic exoskeleton, which include to improvise the device to include proximal joints exercise in the device, to take patient feedback and optimize the robotic device accordingly; to use the device in different operational mode and evaluate if any enhancement is required in the capability of device; to provide real time feedback of robotic hand glove for neuro-quantitative assessments like muscle and joint torque, angular displacements, and hand position; and to explore the role of non-invasive brain stimulation (TMS & tDCS) and robotic glove for upper limb function in stroke.

BASIC MEDICAL SCIENCES

The Basic Medical Science division coordinated intramural research in the field of basic medical sciences at the National Institute of Pathology (NIP), New Delhi, National Institute of Immunohaematology (NIIH), Mumbai and National Institute of Traditional Medicine (NITM) at Belagavi. The extramural research was undertaken in several areas viz. Genomics, Stem cell research, Nanomedicine, Haematology, Biochemistry, Pharmacology, Physiology, Human genetics, Allergy, Immunology, Translational Neuroscience, Drug development initiative and Toxicology. The division also coordinated NAC-SCRT secretariat and Standing committee on national list of essential medicines (NLEM). Interagency partnership programs were pursued in traditional and folklore medicine with Department of AYUSH. The Division assists Drug Controller General of India for evaluation of Investigational New Drugs (chemical, biological & Stem Cell / Cell based Therapy) dossiers for approval of clinical trials/ marketing of new drugs in the country.

INTRAMURAL RESEARCH

ICMR-NATIONAL INSTITUTE OF IMMUNOHAEMATOLOGY, MUMBAI (ICMR-NIIH)

HEMATOGENETICS

Interim Satellite Centre on Sickle Cell Disease at Chandrapur, Maharashtra

The centre was established in Chandrapur with a high prevalence of hemoglobinopathies to cater to patients of central India. Comprehensive diagnostic facilities, including HPLC and molecular diagnosis, were established at the centre and it is currently running programs like population screening, antenatal screening, newborn screening, and antenatal diagnosis. A cohort of >700 patients with SCD, including sickle- beta-thalassemia, has been established and evaluated regularly in sickle cell clinic established in the civil hospital. Apart from these, some important research projects were carried out, including understanding the role of the ubiquitin-proteasome system, microparticles, ion channelopathies and microRNA regulation on the pathophysiology of SCD. A comprehensive longitudinal cohort study for organ damage among Sickle Cell Disease patients has also been recently initiated.

Assessment of neonatal screening approaches for sickle cell disease and the effect of early intervention in the management of the disease in tribal populations

The study's main aim was to establish newborn screening for sickle cell disease in tribal populations of 6 different states (Maharashwtra, Gujrat, Rajasthan, MP, Tamilnadu, Orissa), followed by regular follow up and comprehensive care of the babies identified with SCD. To date, 13080 newborns were screened and generated a cohort of 111 patients with SCD.

Training of in-service clinicians from Government Hospitals and outreach programme for Aspirational Districts

Under the 'Clinical Genetics' fellowship, six months of training is provided to the in-service clinicians in the diagnosis and management of various inherited diseases with a particular focus on haematological and immunological diseases. The eventual aim is to establish these facilities at different government hospitals and establish a smooth referral pattern for these disorders.

In the outreach program, antenatal screening of the pregnant women and newborn screening program was established in the 'Aspirational District' of Nandurbar. Till now, a total of 1810 antenatal women were screened. Of these, 432 (23.86%) women were screened at the first trimester. Of the eight couples at risk, two couples underwent prenatal diagnosis. The team has also screened 2947 newborns for SCD, and 32 newborns were identified as SCD.

Assessing the role of microRNAs in clinical severity of Thalassemia Patients and hydroxyurea mediated HbF induction

The main aim of the study was to evaluate the role of miRNA expression on hydroxyurea-mediated foetal haemoglobin. It was observed that the pattern of miRNA expression was significantly different after induction of HbF by Hydroxyurea treatment. The role of miRNAs was studied through *in vitro* cell culture transfection method. Centre documented that miRNA regulate γ -globin expression by targeting globin gene modifiers such as BCL11A, MYB, KLF and GATA 1. Thus, the study helped to understand the mechanism of γ -globin activation through miRNA mediated regulation. The study provided a promising approach to develop miRNA as a novel therapeutic target for hemoglobinopathies patients.

Red cell membrane molecular pathology in hereditary spherocytosis (HS) in India

Hereditary Spherocytosis (HS) is the most common inherited anaemia varying from mild to severe

haemolytic anaemia characterised by the presence of spherocytosis. During three years, 864 cases were investigated with particular reference to red cell membrane protein defects. A total of 130 HS cases were diagnosed based on clinical and family history, peripheral blood smear examination, EMA dye-binding test. Centre developed a new Mean Fluorescence Intensity (MFI) range for diagnosis of HS on an Imaging flow cytometer (IFC) (Amnis ImageStream[®] Mark II, Seattle, WA). Seventeen cases of HS with dRTA having a *SLC4A1* (A858D) missense mutation were diagnosed. Transfusion dependent patients were characterised by a targeted Next-generation sequencing (NGS) Panel and further confirmed by the Sanger sequencing. Total 68 mutations were identified, including 22 novel *ANK1* mutations, one reported and one novel *SPTA1* mutations, 18 novel and five reported *SPTB* mutations, 4 reported *SLC4A1* mutations causing HS. Four novel and 4 reported in the *SPTA1* mutations causing HE/ HPP. Four novels and 5 reported *PIEZO1* mutations causing HX were identified. This study data enabled to understand the mutation spectrum of all the gene variants providing a molecular basis for HS in the Indian population.

PAEDIATRIC IMMUNOLOGY AND LEUKOCYTE BIOLOGY

Centre of excellence for the diagnosis, management, and research of primary immune-deficiency disorders

This project aims at establishing the state of the art facilities for diagnosis of PIDs at NIIH, including simple and cost-effective diagnostic tools, designing algorithms for the diagnosis of different PIDs suitable for the Indian population, increasing our knowledge of complicated diseases and creating trained human resources in the area of PID. The project was initiated in 2017. Total 5600 patients from >100 centres across India have benefited from the state of the art diagnostic facilities established at ICMR-NIIH. A cohort of 936 patients with PID has been established. Many vital observations

from these large cohorts have helped to propose an appropriate diagnostic approach for patients with PID.

Centre has also established facilities for genetic counselling and prenatal diagnosis for the affected families. To date, team has offered prenatal diagnosis to 61 families affected with severe PIDs (HLH, CGD, SCID, XLA and MHC-II deficiency).

Multicentric study to understand the pathophysiology of inherited disorders among patients presenting with BCGosis and BCG adenitis

Serious side effects of BCG vaccination may be a manifestation of Primary Immunodeficiency Diseases (PIDs). This study aimed at looking at the prevalence of PIDs amongst patients with BCG complications and establish guidelines for the evaluation and management of these patients. Prospectively, 38 patients with BCG complications were enrolled in the study from 2019. Impaired immunity was detected in 16/38 (42%) of the patients, including SCID (4 cases), CGD (2 cases) and MSMD (10 cases). This study highlights the need of investigating children with BCG complications for underlying IEI.

TRANSFUSION MEDICINE

Centre of excellence for advanced research in immunohaematology and transfusion medicine and create a national rare donor registry

COE aimed to study different immunohaematological aspects of blood banking in India with a vision to develop the molecular immunohaematology reference laboratory.

Centre has initialised screening of regular blood donors for all blood groups antigens and preparing a database for transfusion management of blood recipients. This will be utilised to establish 'National Rare Donor Registry of India'.

Genotyping methods were standardised and used for accurate RhD typing, screening for minor blood group antigens in multi-transfused patients and human neutrophil antigen typing. Centre has also established a noninvasive foetal RhD typing method by real-time PCR from cell-free DNA isolated from maternal plasma, which is being validated for noninvasive fetal RHD genotyping. An in-house NGS panel developed is being developed to resolve complex cases in blood group serology by predicting the antibody specificity.

THROMBOSIS AND HAEMOSTASIS

Comprehensive genomic and functional evaluation of factors influencing CAD and Myocardial Infarction in young patients

There have been many studies on conventional risk factors in CAD and MI, but there is still no identification of definitive predictive markers for MI <40 years of age. Next-generation Sequencing (NGS) of the genes involved, followed by functional studies of the most probable variants, could give us definitive predictive markers for MI below 40 years of age. To initiate, clinical exome sequencing on 30 patient samples showed 25 pathologically significant variants in 23 patients. The preliminary data has yielded novel variants in infrequently reported genes in young patients with MI. Further functional studies on more samples may help understand specific markers or mechanisms that may be either independently or synergistically associated with AMI/ CAD.

Platelet phenotyping (surface receptors, granules, secretion and signal transduction) and genotyping of unclassified heritable thrombocytopenia and platelet function disorders

Inherited platelet function disorders (IPFDs) make up a significant proportion of bleeding diatheses, but remain poorly understood and are often difficult to diagnose. The development of a laboratory diagnostic strategy and identifying the underlying

molecular pathologies for rare inherited platelet disorders is essential.

In this study, study team could identify the rare mutations in the *RASGRP2* gene affecting the platelet function in our group of patients and highlight the relatively high occurrence of defects that are otherwise considered rare in the published literature.

CYTOGENETICS

Understanding the role of epigenetic factors in Fanconi anaemia phenotype and cancer predisposition

A molecular study of 20 confirmed Fanconi anaemia (FA) subjects revealed mutations in six complementation groups, important in genetic counselling and disease management. Global methylation analysis of FA subjects revealed methylation of DNA repair genes, tumour suppressor genes, oncogenes, transcriptional factors, immunity-related genes, which may be associated with phenotypic variability, bone marrow failure and cancer development. The first time we have proposed Nitrosative stress in FA subjects as 3-nitrotyrosine [*3-NT*] levels were significantly ($p < 0.05$) elevated, causing genomic instability. Genotyping of the *NOS2* gene c.1823C>T (p. Ser608Leu) (rs2297518), showed statistically significant ($P < 0.05$) association with FA.

The study's interesting observation is that the severe shortening of telomere length in FA subjects FANCL complementation group. The telomere length can be considered a biological marker to understand the disease's prognosis as FA subjects primarily treated with androgens.

Study of the molecular pathology of idiopathic aplastic anaemia

Though several factors associated with aplastic anaemia, the molecular mechanism is not entirely not understood. Our study identified ten variants in *RTEL1*, *TINF2*, *MYSM1*, *MDM4*, *VWF*, *HFE*, *RAD50*, and *SLC29A3* genes. The genes are

majorly involved in Telomere regulation, DNA repair and cell cycle regulation. However, large sample size and functional studies essential to understand the role of variants in AA.

EXPERIMENTAL AND CLINICAL IMMUNOLOGY

Study on blistering autoimmune diseases (ABD) in understanding etiopathogenesis among patients from western India

This study aims at understanding the spectrum of autoantibodies and their correlation with disease activity and the clinical course of the disease. This year one hundred fifty newly diagnosed pemphigus patients were analysed for age, gender, clinical features, the results of histopathology, enzyme-linked immunosorbent assay (ELISA). Anti-Dsg1 and anti-Dsg3 were studied in them. Ten patients have been followed up every six months interval for their IgG1 and IgG4 autoantibodies to anti-Dsg3. Eighty patients of Pemphigoid were also investigated for BP180 and BP230 autoantibodies and their association with disease severity.

TRANSFUSION TRANSMITTED DISEASES

Characterisation of circulatory tumour cells (CTCs) for hepatocellular carcinoma (HCC) using mainstream detection

The project focussed on the identification and characterisation of CTCs using Imaging Flow Cytometry. 35 cases of HCC and 30 cases of Liver Cirrhosis were recruited for this study. Preliminary comparison of AFP marker positive cells in two groups showed statistical significance. Further characterisation and analysis of CTCs may provide information for early detection of HCC.

Study of genetic factors and immune parameters focusing on the transmission of HBV in household contacts of classical HBV cases

The project will help in understanding the transmission pattern of HBV among household

contacts of HBV cases. Next-Generation Sequencing Analysis of a family with varied manifestations of HBV (Chronic HBV and Occult HBV infection) showed reads aligning to the HBV genome. The study of viral mutations and host factors may help understand the varied manifestations of the virus within a family.

COVID-19

An in-house lateral flow immunoassay (LFIA) based point of care (POC) test using gold nanoparticle labelled antigens/antibodies for detection of COVID-19 IgG/IgM antibodies

An in-house lateral flow immunoassay (LFIA) based point of care (POC) test using gold nanoparticle labelled antigens/antibodies for detection of COVID-19 IgG/IgM antibodies”, an LFIA for COVID-19 IgG and IgM antibodies has been developed. The validation by Rajiv Gandhi Centre for Biotechnology (RGCBC)-DBT showed the sensitivity of 96% and 90.67% and specificity of 95.2 and 98.8 % for IgG, IgM respectively. The technology has been transferred to Transasia Pvt. Ltd. and Sidak Life Science for commercialisation.

A Phase II, Open-Label, Randomized Controlled Trial to Assess the Safety and Efficacy of Convalescent Plasma to Limit COVID-19 Associated Complications in Moderate Disease

This study, also known as PLACID Trial, was initiated with the primary objective to assess the safety and efficacy of the convalescent plasma therapy in moderate disease. ICMR-NIIH, in collaboration with KEM hospital, Mumbai, was one of the sites for the Trial. ICMR-NIIH took responsibility for laboratory investigations for donors and recipients, study coordination at the site, and archiving site data.

National sero-surveillance to monitor the trend of SARS-COV-2 infection transmission

in India: Community-based surveillance in hotspot cities

ICMR-NIIH was involved as a nodal centre in Mumbai for ICMR. Under this project, a total of 500 samples were collected from 5 different containment zones in Mumbai by two survey teams from ICMR-NIIH as a baseline survey conducted in May.

COVID-19 serosurvey for healthcare workers in collaboration with Kalyan Dombivli Municipal Corporation and IMA Dombivli

This project was undertaken to study the transmission of SARS COV2 infection among frontline health care workers. Under this project, 500 samples were collected from healthcare workers involved in the care of COVID-19 patients in the Dombivli area of Mumbai. The study was carried out between Jul 21 to Aug 3. Overall, 11 % (55/500) participants were detected with IgG antibodies to SARS-COV2. A higher incidence of infection of 17.2% was found among those involved in non-COVID-19 areas compared to 9.6% among those dedicated to providing care to COVID-19 patients. Multivariate analysis for factors which might affect the development of antibodies, namely providing direct care to COVID-19 patients (Adjusted OR 16.4, 95% CI 3.3 – 126.9, p 0.002) for long hours and irregular use of PPE (Adjusted OR 3.78, 95% CI 1.1 – 11.9, p 0.02) were associated with an increased incidence of seropositivity. Prophylaxis with Hydroxychloroquine (HCQ) may have a role in reducing the vulnerability to infection as depicted by univariate and multivariate analysis (Adjusted OR 0.55, 95% CI 0.3-0.9, p 0.047).

As a part of ICMR Immunoprofiling (IP) consortium for COVID-19 project entitled “Integration of Extended Immune Monitoring (ExImm) and clinical parameters for early prediction of disease trajectory/progression, treatment planning and prophylaxis to improve COVID-19 prognosis”

This study will provide crucial “disease-specific information” to manage COVID-19 by early

segregation of high-mortality risk patients and provide solutions for prophylaxis to prevent further spread of the disease. Patient enrolment was initiated under the project in January 2021.

Exploring lymphocyte subsets and cytokine profile in Paediatric Inflammatory Multisystem Syndrome temporally related to SARS-COV-2 infection (PIMS-TS)

This study was initiated in September 2020 as an intramural project in collaboration with ICMR-NIRRH Mumbai and B.J Wadia Hospital for Children, Mumbai. Fifteen patients with PIMS have been enrolled under the project, and the analysis is being carried out.

Role of Vitamin D and angiotensin-converting enzyme 2 in endothelial dysfunction among COVID-19 patients from Mumbai, Maharashtra

This study was initiated in September 2020 to examine the effect of serum levels of ACE and Vitamin D 25(OH) D3 levels among COVID-19 patients. So far, 120 clinically and RT-PCR positive cases of COVID-19 have been enrolled, and 20 patients have been followed up at four weeks interval after the first admission. Clinical severity and laboratory parameters at the time of evaluation have been compared in them. Molecular analysis for ACE (I/D) polymorphism and VDR gene polymorphisms and are in progress.

Studies on ABO histo-blood group genes as potential genetic susceptibility factors to SARS-COV-2 infections: an exploratory study

Blood group antigens are glycoproteins/proteins in nature and act as receptors or co-receptors for various microorganisms, parasites, and viruses. Individuals who secrete ABO antigens in saliva are termed secretors and those who do not are termed as non-secretors. This study is being undertaken to expand the current knowledge on the association of the ABO histo-blood group system to COVID-19 pathophysiology, which may help to find out the potential biological marker(s) known to predict the

host genetic susceptibility towards SARS-COV-2 infections.

PUBLIC HEALTH

- Satellite centre for Hemoglobinopathies at Chandrapur is providing comprehensive diagnostic facilities for hemoglobinopathies, including HPLC and molecular diagnosis, and is currently running programs like population screening, antenatal screening, newborn screening, and antenatal diagnosis. The centre has established a cohort of >700 patients with sickle cell disease (SCD) and currently conducting multiple research projects focused on various aspects of SCD.

- Centre for Research, Management and Control of Hemoglobinopathies at Chandrapur.

This centre was sanctioned considering the high prevalence of hemoglobinopathies in central Maharashtra. It was inaugurated in Feb 2018 by the Hon'ble Prime Minister. This centre will provide diagnostic services including genetic diagnosis and prenatal diagnosis, support State and District administrations for control and management of haemoglobinopathies, carry out basic and translational research in the area of haemoglobinopathies and strengthen the capabilities of Government Medical Colleges in the region through collaborative research and contribute to human resource development. Construction of the centre was initiated in Nov 2019. It is expected to be completed in June 2021.

- Initiated multicentric newborn screening program for SCD. The study involves newborn screening for SCD in tribal populations of 6 different states for early detection and providing comprehensive care to the affected babies.
- Initiated antenatal screening for hemoglobinopathies and newborn screening for six inherited diseases in 'Aspirational District' Nandurbar under the DBT UMMID initiative.

- Established For the first time in India facilities for noninvasive fetal RhD typing for management Rh-HDN.
- Established the state of the art facilities for resolving complex cases of blood group serology and providing compatible rare blood to a patient.
- The state of the art diagnostic facilities for IEI established under ‘Centre of Excellence for diagnosis, management, and research of Primary Immune-deficiency disorders’ are being utilised by more than 100 centres across India and outside India like Bangladesh, Nepal, Sri Lanka and UAE.
- COE provides tests for functional validations of variants identified on NGS analysis, which is critical for the management of the patient and genetic counselling of the families. Accurate diagnosis of some of these PIDs has resulted in targeted therapies, resulting in significant improvement in the morbidity and mortality seen in these patients. Some of these assays also help monitor the patients after initiation of specific therapies and post transplantation recovery.
- Initiated fellowship in ‘Clinical genetics’ for in-service clinicians aimed at focused training in the diagnosis of various inherited haematological and immunological disorders under the DBT UMMID initiative. Every year two permanent faculty members from government institutes receive training in the area of genetics of immunological and immunological diseases for six months. The eventual aim is to establish these facilities at different government hospitals and establish a smooth referral pattern for these disorders.
- A multicentric study on Systemic Lupus Erythematosus (SLE) from the North-Eastern Region of India: Early diagnosis to research potential for understanding disease pathogenesis has been approved under the ICMR-NE Taskforce project.
- Patent entitled “A rapid, simple and cost-effective lateral flow immunoassay for the diagnosis of severe Haemophilia A and von Willebrand disease” has been filed, and the technology has been transferred for commercialisation.
- An in-house lateral flow immunoassay (LFIA) based point of care (POC) test using gold nanoparticle labelled antigens/ antibodies to detect COVID-19 IgG/ IgM antibodies was developed by ICMR-NIIH and has been transferred to Transasia Pvt Ltd for commercialisation.
- A simple gold nanoparticle-based lateral flow immunoassay based test has been developed for the point of care diagnosis of Glanzman’s thrombasthenia (GT) that can offer the diagnosis of a severe GT within 15 minutes of the sample application. It has been sent for patent application.
- Standardisation of In-house antigen ELISA for ADAMTS13.
- Established method for non-radioactive assessment of VWF multimers.
- Prepared ‘Training Manual for Hemoglobinopathies and Hemophilia’ with Blood cell- Ministry of Health and Family Welfare, Government of India.
- Prepared two modules for Indian medical graduates and medical officers working in the periphery on “Approach to Hemoglobinopathies” and “Transfusion reactions and approach to thrombocytopenia.” Under ICMR Taskforce study on Rational Use of Medicines.
- ICMR-NIIH is identified as a nodal centre for Hemoglobinopathies, PID and Bleeding disorders under this ICMR initiative. The forms for data collection for these disorders were finalised. The online portal is now available, and data entry has been initiated under the project.
- Specialised diagnostic services are provided by different departments, including transfusion medicine, hematogenesis, hemostasis and thrombosis, paediatric immunology and leukocyte biology, cytogenetics, and clinical

and experimental immunology. More than 20,000 patients from India and abroad have availed these diagnostic facilities.

- The Institute offers prenatal diagnosis for various inherited disorders to couples referred from different parts of the country, and more than 300 affected families take advantage of these services every year.

PATENT

- A rapid, simple and cost effective lateral flow immunoassay for the diagnosis of severe Haemophilia A and von Willebrand disease

The commercial party has been finalised and kits will be prepared.

- ICMR COVID-19 Rapid Antibody detection kit

Under the extramural project entitled “An in-house lateral flow immunoassay (LFIA) based point of care (POC) test using gold nanoparticle labelled antigens/antibodies for detection of COVID-19 IgG/IgM antibodies.” 300 kits were sent for validation. Sensitivity was 96% and 90.67% and specificity was 95.2 and 98.8 % for IgG and IgM, respectively.

The working cost is around 100 to 120 Rs.

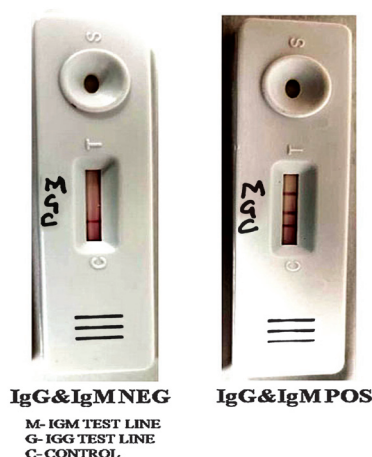


Fig. 1: ICMR COVID-19 Rapid Antibody detection kit.

After the technology transfer meeting held on 18th Dec 2020, 7 companies were selected. MOU and other documents have been signed with 2 companies – Transasia Pvt. Ltd. and Sidak Life Science and technology has been transferred to these 2 companies.

ICMR-NATIONAL INSTITUTE OF PATHOLOGY, NEW DELHI (ICMR-NIP)

In vitro evaluation of effect of PKCε silencing on tumour invasiveness in urothelial cancer

The effect of silencing of PKCε & PKCζ in Urothelial cancer cell lines (T24, 5376, HT-1376 & TCCSUP) was studied. The successful silencing of PKCε and PKCζ were demonstrated by decreased expression of PKCε & ζ RNA and protein expression by RT-PCR and Western blot in silenced bladder cancer cell lines. PKC ε & ζ knockdown was followed by cDNA Microarray of control and silenced cell lines. A set of differentially expressed genes were obtained. In each set of cell lines approx 50,000 gene were found to be upregulated and 40,000 to be downregulated. Comparative analysis was conducted for each set of cell lines which included pathway enrichment and visualization via GSEA and Cytoscape. The enriched set was compared for identifying the effect of PKC silencing on the invasion and development of bladder cancer. This will provided an insight in developing/encouraging PKC inhibitors specific targeted therapies.

In vitro and *in vivo* anticancer efficacy of combination therapy with alpha linolenic acid, lignans and BCG against urinary bladder cancer

Intravesical BCG therapy after transurethral resection is standard treatment for nonmuscle invasive bladder cancer. A major challenge with the BCG therapy is its severe side effects, such as BCG sepsis, immunosuppression, hematuria, active urinary tract infection, and mild cystitis. To overcome these adverse effects combination therapy, a treatment modality that combines two or more therapeutic agents, can play important role. The antitumor potential of alpha linolenic acid (ALA), secoisolariciresinol diglucoside (SDG) and BCG alone and in combinations on three human bladder cancer cell lines: one nonmuscle invasive cell line (5637) and two muscle invasive cell lines

(T24 and HT1376); and one urothelial bladder cell line was investigated to identify potential new therapeutics.

The IC₅₀ of the drugs based on MTT assay and Combination Index (CI) of drugs using Chou and Talalay method was calculated. The drug combinations ALA+ BCG and SDG+ BCG; ALA+ SDG+ BCG showed the CI<1 i.e. synergism or additive effect. Cell viability assay using the drug combinations were also performed. Results obtained from different combinations show the inhibition in bladder cancer cell lines. 5637 and T24 cell lines are most susceptible towards combination treatment with SDG and BCG suggesting the efficacy of the combination treatment in both muscle-invasive and non-invasive tumours. *In vivo* studies are in progress.

Investigating the role of negative regulators of Wnt signaling pathway in prostate cancer and exploitation of their therapeutic potential

Gene expression analysis of *RNF43*, *ZNRF3*, *NKD2* and *APCDD1* genes revealed that *ZNRF3*/*RNF43*, *NKD2* and *APCDD1* expression was decreased in prostate adenocarcinoma, with highest decline in the mRNA expression of *NKD2* gene. On correlating the gene expression status with age, PSA level and Gleason score, no significant association was noted.

To study the antitumour potential of Pashanbheda, Punarnava, Gokshura, and Badra on the human urothelial cell carcinoma (UCC) cell lines

The project is designed to study the molecular mechanism behind the action of aqueous and hydroalcoholic extracts of *Pashanbheda* (*Berberia lingulata*), *Punarnava* (*Boerhavia diffusa*), *Gokshura* (*Tribulus terrestris*), *Badra* (*Aerva lanata*) for their antitumour potential on human urothelial bladder cancer cell lines and the action of extract with commercially available drugs for bladder cancer.

In present study, cell viability assay was used for preliminary evaluation of chemotherapeutic potential of selected plants on Bladder cancer. Cell viability was evaluated through trypan blue assay and further validated by DAPI staining. The cytotoxic effect of selected plant aqueous extract on T-24 cells was differed from each other. Among different aqueous extract, Pashanbheda aqueous extract exhibited the highest chemotherapeutic effect on T-24 Urothelial carcinoma followed by Gokshura, Punarnava and Badra (effect: Pashanbheda>Gokshura>Punarnava>Badra). The effect of Pashanbheda was also displayed through morphological changes/damage to T-24 cells under inverted microscope, while least anticancer potential was observed with Badra aqueous extract. No anticancer cytotoxicity was observed below 250 µg/ml of either Punarnava, Gokshura or Badra. The LC₅₀ value of Pashanbheda was 384 µg/ml at 96 h post-treatment period. Present results obtained with Pashanbheda indicating the presence of bioactive phytochemicals, although synergism with other major / minor constituents has to be taken into account, therefore now the centre is using bioactivity guided-based fractionation (based on polarity) to identify the potential anticancer compounds present in this unexplored plant Pashanbheda.

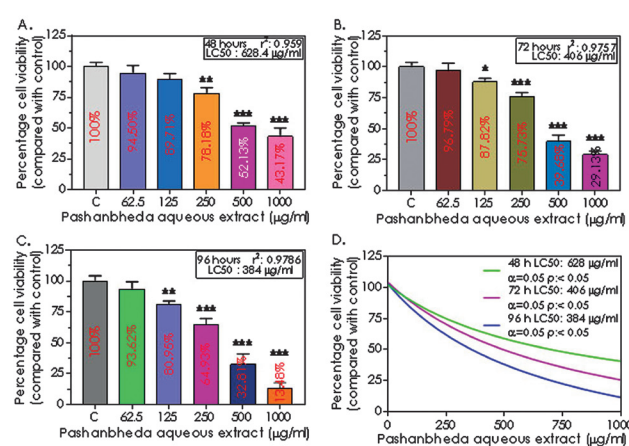


Fig. 2: Aqueous extract of Pashanbheda reduces T-24 cell viability at 48, 72 and 96 h post-treatment period. Cells were treated with either PBS (pH 7.4) as control or extract and result is expressed as mean $\pm$ SD of n=8. * vs. control, * p <0.05, ** p <0.01 & *** p <0.0001.

Integrated *In silico* and *In vitro* Study of Novel Aromatase Inhibitors for Breast Cancer Treatment

The main goal of this project is computational aided drug design and search then will continue to work out with in-vitro studies to implement as many specific objectives as are feasible given time restrictions.

The crystal structures of human aromatase cytochrome P450 complex known inhibitor was retrieved from the Protein Data Bank (PDB ID 3EQM) (<http://www.rcsb.org/>). Protein preparation was done using the protein preparation wizard in Schrodinger Maestro v9.8 shown in figure 1(A). A number of steps are involved in protein preparation. These steps performed by the essential tasks for fixing the structure and deleted unnecessary chains and waters and fixed or removed the het groups. Optimized protein structures were minimized using the optimized potential for liquid simulations (OPLS-2005) force field, by converging heavy atoms to RMSD of 0.3 Å. The ligands were prepared by using ligprep Schrödinger suite. This process consists of a series of steps that perform conversions, apply corrections to the structures, generate variations on the structures, eliminate unwanted structures, and optimize the structures. The public resource such as ChEMBL Database was used. This manually curated database offers the potential tools to interrogate targets. The building of ligands library is very crucial in terms of drug designing. Schrodinger suite allows to carried out molecular docking and virtual screening to screen in-house database for a wide community of structural biology and medicinal chemistry. After receptor and ligand preparation, docking runs were performed against the in-house database. The ChEMBL database was docked against the crystal structure of aromatase defined as a target. Build up a compounds library will have to filter out the library depending on molecular descriptors and many conditions to find one best effective compound. The virtual screening workflow protocol was done and examined the top compounds for its binding free energies.

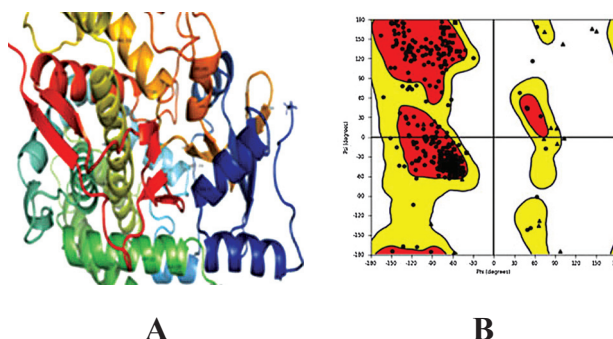


Fig. 3: Protein structure and Ramachandran Plot: (A) Prepared protein structure (PDB ID: 3EQM); (B) Ramachandran plot output without ligand of 3EQM structure based on with energy minimization, modified from Schrodinger Protein preparation wizard. The areas marked in red are most favored region, additionally allowed (yellow), generously (fawn) and disallowed (white) regions for amino acid.

Comparative analysis of Genetic, clinical and epidemiological factors of breast cancer in Indian population

Transcriptome profiling of breast tumor tissue (N=28) was performed on Ion proton. Total 2060 DEGs are observed between tumour and adjacent normal. 946 genes observed to upregulated while 1120 genes are downregulated. List of top 25 pathways enriched by 2060 deregulated genes was presented. PCLO gene was upregulated while OBSCN, RP1L1, and SVEP1 were downregulated. PCLO and OBSCN are part of interactome involving TP53, TTN and PIK3CA, hence it might be of interest for further evaluation. Validation will be performed on final analysis of transcriptome data.

Role of long non-coding RNA MEG3 in breast carcinogenesis

The aim of the project is to understand the mechanisms through which MEG3 is functioning in breast cancer cells and contributing to breast carcinogenesis. Earlier we found MEG3 to be downregulated in breast cancer cell lines by qPCR. We restored the expression of MEG3 in breast cancer cell lines by making stable cell line of T47D with MEG3 lncRNA. We identified some of the differentially expressed genes by 2-D electrophoresis followed by MS-MS analysis yielded several proteins that are differentially

expressed after MEG3 induced expression. We found some of the cell cycle proteins to be regulated by MEG3 by western blot analysis in the previous year. In the year under report we have analysed MEG3 targets using *in silico* tools to understand the pathways through which this lncRNA likely targeting various molecules. We found genes such as RPGR, RP11, SNX8, EMC, ABI2, GOLGA6L22, GOLGA6L2, GOLGA6L6, FAM98B and MLYCD to be top 10 targets (Table 1), having binding energy <-30 K. Cal/mol. Suggesting them to be some of the likely targets, some of which we will be validating experimentally. Pathway analysis of the predicted targets yielded from the following pathways Transcriptional misregulation in cancer, Calcium signaling pathway, MAPK signaling pathway, signaling pathways regulating pluripotency of stem cells, HIF-1 signaling pathway etc. Further analysis was done to predict the miRNAs that are likely targets to this gene. The team found several miRNAs that are likely targets for this lncRNA, that majority of these miRNAs belong to miR families, such as miR-551, miR-130, miR-132, miR-7, miR-133, and miR-9 families, suggesting miRNAs of these families may likely be targets and regulated by the MEG3 lincRNA which need to be established experimentally.

Table. 1. Showing gene targets for MEG3 predicted by rtools

	Sum of Energy	Min of Energy	Transcript ID	Transcript Name
1	-12,612.40	-80.57	ENST00000378505	RPGR-009
2	-8,075.27	-50.89	ENST00000627551	RP11-573D15.8-018
3	-7,776.33	-49.96	ENST00000622895	GOLGA6L22-002
4	-7,324.27	-77.30	ENST00000334976	EMC10-001
5	-7,031.41	-70.94	ENST00000222990	SNX8-001
6	-6,202.98	-55.23	ENST00000619213	GOLGA6L6-001
7	-6,040.38	-46.86	ENST00000567107	GOLGA6L2-002
8	-5,954.19	-52.60	ENST00000295851	ABI2-001
9	-5,893.03	-34.76	ENST00000369373	NBPF20-001
10	-5,717.20	-93.75	ENST00000623111	MIR6820-001

Targeted sequencing of breast cancer specific genes in early onset breast carcinoma

The project is aimed to identify sequence variations and chromosomal rearrangements of deregulated genes in early onset breast cancers. In the present study whole exome sequencing in

34 breast tumours (genomic DNA isolated from tumours) and 8 healthy control samples (genomic DNA isolated from PBMCs) for variants, among patients analysed 13 are early onset tumours (≤ 40 years) and 21 are late onset tumours (≥ 55 years). Using Partek flow software, we have analysed the data using hg19 as reference. Then we obtained list variants present in patients and control samples, the variants present in breast tumours different groups were obtained by subtracting the variants found in any of the controls. In the current year under report we have analysed the exome data using MAF tools to identify clinically significant genetic alterations that are found in early onset and late onset breast tumours. We identified genes such as top significant genes that are altered between early and late onset tumours using oncoplot. Genes such as *TTN*, *MUC3A*, *OBSCN*, *AHNAK*, *FAM171B*, *HRNR*, *MAGEC1*, *RPL14*, *CACNA1A*, and *CPEB* were some of the top genes found to be differentially altered between early and late tumours. Currently team is in the process of validation of some of the identified variants.

Study on Gene Expression and Hypermethylation Profiles in Early Onset Breast Cancer

The present study is aimed to investigate genetic and epigenetic factors associated with early onset breast cancer in Indian women with objective to elucidate molecular pathogenesis by highlighting the changes in gene expression and methylation profile.

Gene expression profiling of breast tumours by microarray earlier in our laboratory, to identify the breast cancer genes that are differentially expressed, one of the class of genes we identified to be differentially expressed were genes involved in ECM and anion transport, overexpression of the genes such as COL1A1, COL5A1, COL10A1, COL11A1, COL12A1, CTHRC1, CELSR3, and SLC16A3 and downregulated expression of the genes such as COL14A1, FXD1 in breast cancer patients. In the year under report we analysed the

expression of the above genes by qPCR in breast cancer patients gain insight into the clinical relevance of their deregulated expression in breast tumours. QPCR analysis has shown up-regulated expression of several of the ECM and anion transporter genes viz. COL1A1, COL5A1, COL10A1, COL11A1, COL12A1, CTHRC1, CELSR3, and SLC16A3, and down-regulated expression of COL14A1 and FXYD1. Overexpression of *SLC16A3* was associated with lymph node positivity ($p=0.004$), overexpression of *CELSR3* was associated with older age of the patients (>55 years of age) ($p=0.049$), overexpression *COL12A1* was associated with hormone receptor positivity ($p=0.05$) compared to the other subsets. On the other hand, *COL14A1*, and *FXYD1* down-regulation was found to be associated with basal subtype ($p=0.045$, $p=0.024$), down-regulated expression *FXYD1* was also found to be associated with the advanced stage of the tumours ($p=0.009$). Further, using *in silico* tools we have predicted miRNAs which might have a regulatory role on these genes, we have obtained the list of miRNA that are already reported to be differentially expressed in breast tumours, and identified the ECM and anion transport genes that are likely under the regulation of these miRNA. We carried out target prediction using 341 experimentally validated miRNA in breast cancer. The miRNAs which might potentially be targeting collagen and anion transport genes that were selected for the present study were predicted. We found a 98 miRNAs to have one or more genes using miRWalk software, MiRNAs, hsa-miR-1301-3p, hsa-miR-409-3p, hsa-miR-485-3p, hsa-miR-485-5p, hsa-miR-502-5p, hsa-miR-520d-3p, hsa-miR-601 were found to have a maximum of 7 genes (*COL11A1*, *SLC16A3*, *COL1A1*, *COL5A1*, *COL12A1*, *CELSR3*, and *COL10A1*) as targets suggesting a high probability of their involvement in the regulation of the predicted target genes. Then we tried to identify the miRNAs families which are co-expressed and may be involved in the co-regulation of collagen genes in a synchronized manner. MiR-154 family, miR-515 family, mir-10 family members were among the miRs to have highest number of target genes. The role of such predicted miRNAs, need

to be validated experimentally to establish the mechanistic regulation of respective genes.

Clinical decision support system to identify histogenesis in cases of carcinoma with unknown primary (CUP)

Total 469 samples of primary carcinoma were scanned, uploaded to developed database. Scripts for digital image processing and image stratification between tumour and normal have been developed. The graphical user interface has been developed. An annotated image database of high quality images will be a national resource of educational material and also a source for other morphometric and pattern recognition projects. The pattern recognition based classifier is developed for prostate cancer and is now being applied to other organ cancers.

Proteomic Analysis of Plasma Extracellular Vesicles to Identify Circulatory Biomarkers for Gallbladder Carcinoma

Earlier, we performed quantitative proteomic analysis of plasma-derived EV proteins that showed a total of 95 proteins with altered levels in GBC in comparison to controls. Clinical verification of three proteins MME (early stage), NT5E and ANPEP (both early and advanced stages) was earlier performed in blood plasma in 68 individual clinical samples (33 controls and 35 GBC cases).

The centre performed the verification in additional 38 samples. The sample size is now 100 (45 controls and 55 GBC cases) which includes the samples used for discovery study (proteomics) and an independent cohort. The data is now re-analyzed accordingly. Fig. 1 shows the ROC curve analysis for determining sensitivity and specificity of NT5E, ANPEP and MME.

IHC analysis is now performed in additional 50 samples and now the data is presented with 70 samples. The study found a significant difference (p value <0.05) in expression level of NT5E and MME in GBC cases in comparison to controls.

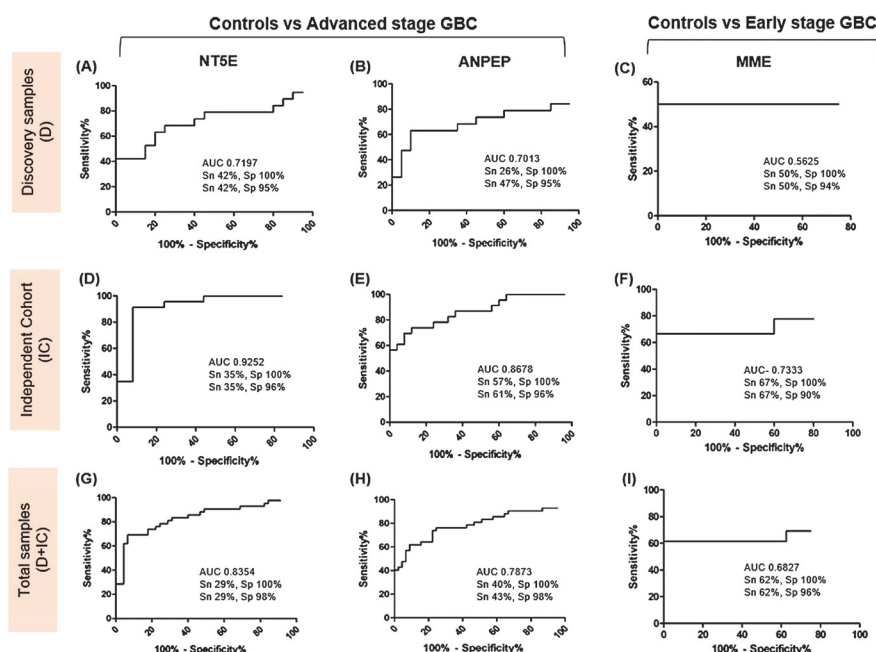


Fig. 4: ROC curve representing sensitivity and specificity for NT5E, ANPEP and MME. ROC curve showing AUC, sensitivity and specificity for NT5E, ANPEP and MME in plasma samples from discovery cohort (A, D, G), an independent cohort (B, E, H) and combined cohort (discovery + Independent cohort) (C, F, I). AUC for independent cohort was increased for all the three proteins in comparison to the discovery cohort.

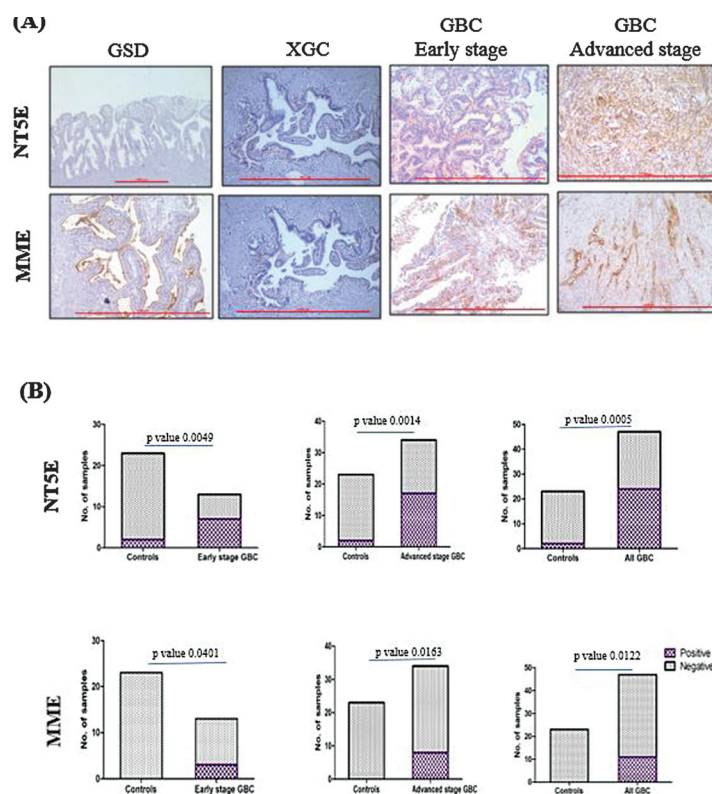


Fig. 5: IHC analysis to study the expression of NT5E and MME in controls and GBC cases. (A) Representative IHC images showing the expression of NT5E and MME in controls and GBC cases. IHC was performed on formalin-fixed paraffin-embedded (FFPE) tissue microarray (TMA) and individual tissue sections. An in-house TMA block was constructed using the FFPE blocks and included 6 controls (6 GSD cases) and 14 GBC cases (2 early stage and 12 advanced stage). Each TMA block consisted of tissue cores of 2 mm diameter and 4 μ m sections were cut from the TMA block for carrying out IHC. Individual tissue sections (FFPE) of 33 GBC (11 early stage and 22 advanced stage) and 17 controls (10 GSD and 7 XGC cases) were also for IHC analysis. IHC results showed positive expression for NT5E in 53.84% of early and 50% of advanced stage GBC cases while MME showed positive expression in 23.07% of early and 23.52% of advanced stage GBC cases. (B) The statistical analysis showed a significant difference between cases and controls for NT5E and MME for both early stage and advanced stage GBC.

Deregulated Proteome Analysis of Lymph Node Metastatic Gallbladder Carcinoma to Identify Novel Therapeutic Targets

Lymph node (LN) metastasis is the earliest sign of metastatic spread and is one of the strongest and established predictors of poor outcome in gallbladder carcinoma (GBC) patients. The patients with LN metastasis (node positive) have a significantly worse survival (median survival of 7.3 months) than patients with node-negative disease (median survival of 22.7 months) inspite of standard treatment which includes extended surgery followed by chemotherapy, radiotherapy and targeted therapy. Therefore, effective targeted therapy for LN metastatic GBC is an urgent need for the improved survival of these patients.

Here, the team performed iTRAQ-based quantitative proteomic analysis using tissue lysate from LN positive and LN negative patients and identified 116 differentially expressed proteins (69 upregulated and 47 downregulated proteins) in LN positive cases. Some of the functionally relevant proteins with high fold change includes carbamoyl-phosphate synthase [ammonia], mitochondrial isoform a precursor (CPS1), betaine--homocysteine S-methyltransferase 1 (BHMT).

Evaluation of immune status and parasite load in patients of post kala-azar dermal leishmaniasis (PKDL) in response to treatment with miltefosine and amphotericin B

PKDL patients (n=40), were administered with three different drug regimens: Miltefosine (MIL) monotherapy [Group-I], MIL and Liposomal Amphotericin-B (LAmB) combination therapy [Group-II] and LAmB monotherapy [Group-III]. Various parameters inclusive of parasite load by qPCR in slit aspirates,– Pro/Anti-inflammatory cytokines (IL-4, IL-6, IL-10, IL-12p70, IL-17A, IFN- γ , TNF- α , IL-1 β , IP-10, MCP-1, IL-13 and IL-2), Nitric Oxide (NO) and Total Thiol (TT) levels in the plasma of PKDL patients at different time points of treatment Pre-Treatment (PTx), Mid-Treatment

(MTx) and Post-Treatment (PoTx) in patients treated with different drug regimen (Miltefosine (MIL) monotherapy (N=14) / Liposomal Amphotericin-B (LAmB) monotherapy (N=5) and LAmB+MIL combination therapy (N=15) were investigated. The parasite load differed significantly at PTx- versus POTX stages ($P < .001$), and PTx vs MTx stages ($P < 0.01$). Levels of IL-2, IL-4, IL-13 and IL-1 β were undetectable in plasma of healthy individuals and PKDL PTx cases. Significantly elevated levels of IP-10, TNF- α , IFN- γ , IL-10, IL-17A and IL-12p70, in PTx- PKDL samples were observed that declined post-treatment when compared to their levels in control healthy samples. However, levels of MCP-1 and IL-6 increased significantly at POTx stage. Plasma NO concentration in PKDL cases was significantly high ($p < 0.0001$) compared to controls and decreased with treatment and differed significantly amongst different treatment stages - PTx vs MTx, PTx vs PoTx, and MTx vs PoTx ($p < 0.0001$). Plasma total thiol (TT) levels of pre-treatment PKDL healthy controls were significantly low and restored to normal in PoTx PKDL cases.

Whole genome sequence analysis of drug sensitive and resistant Leishmania isolates originated from patients of kala-azar and post kala-azar dermal leishmaniasis

Bioinformatics analysis of genomic data obtained from *in vitro* adapted artemisinin resistant (K133AS-R) and paromomycin drug resistant *L. donovani* parasite (K133PMM) compared to wild type (K133WT) revealed 240 single nucleotide polymorphism (SNPs), 237 insertion/deletion (InDels), 616 copy number variations (CNVs) (including 377 deletions and 239 duplications) and trisomy of chromosome 12 specifically in K133AS-R. While 259 SNPs, 187 InDels and 546 CNVs (359 deletions and 187 duplications) along with a unique chromosomal ploidy of chromosome no 6, 9, 12 (trisomy) and 5 (tetrasomy) in case of K133PMM. Chromosome number 31, reported to be supernumerary chromosomes in different species of *Leishmania*, is enriched in genes involved in iron metabolism and membrane transporters essential

for parasite survival. Ploidy change of chromosome number 5 and 12 observed in our study, contain genes involved in protein degradation and parasite mobility respectively. Decrease in chromosomal ploidy of resistant parasite compared to sensitive one was also observed in chromosome 15, 20 and 23. Recent studies link aneuploidy to adaptation,

suggesting that aneuploidy may provide a transient route for rapid adaptive evolution in microbial populations and assists parasite to survive under stress condition. Variation in gene dosage due to loss or gain of chromosomes results in higher phenotypic diversity or pathogenic potential in aneuploid microbial populations.

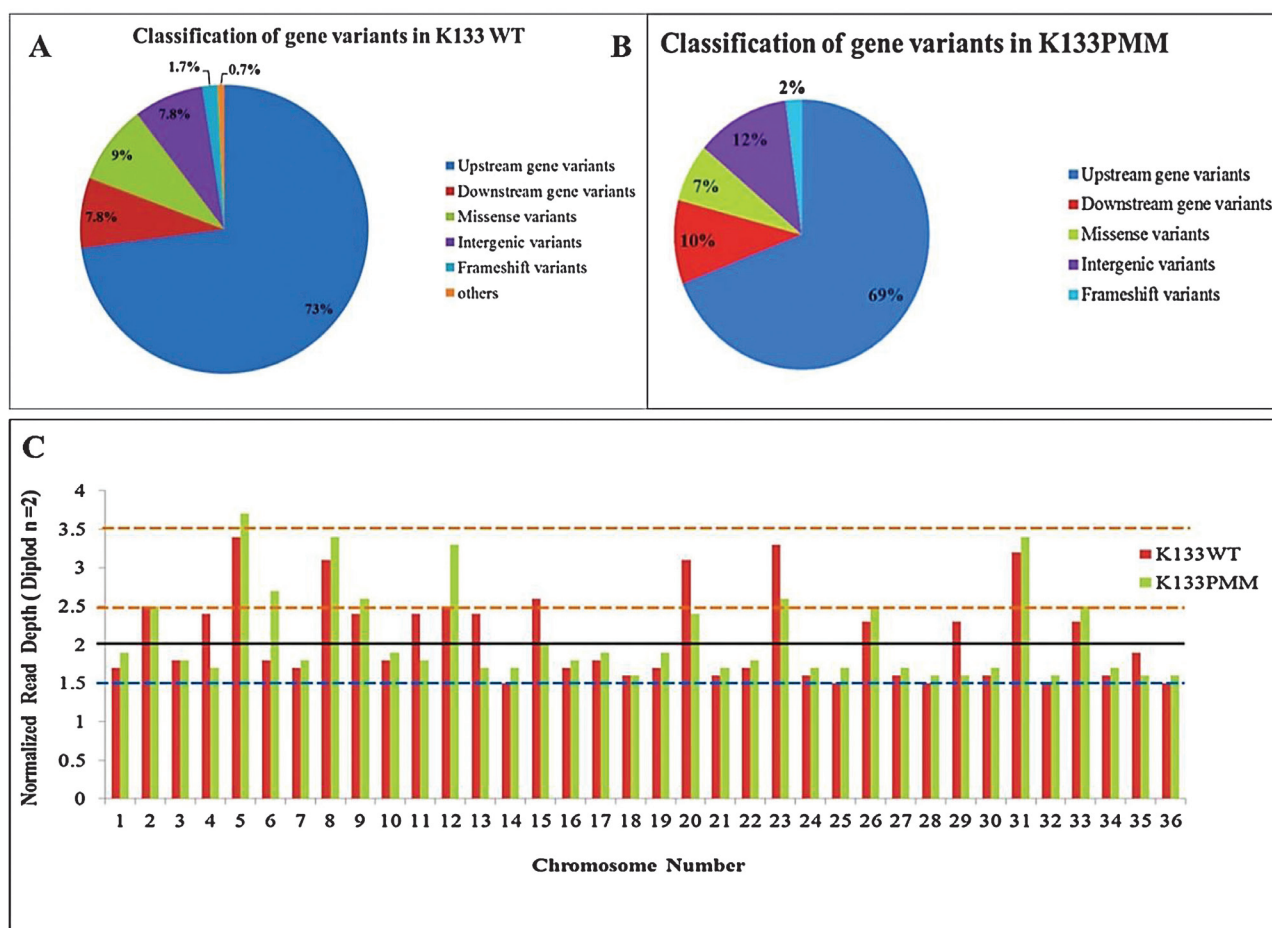


Fig. 6: Comparative genomic data analysis of K133PMM with K133WT. (A) Venn diagram showing percentage and types of SNPs present in K133WT and K133PMM (B) Chromosomy estimation of *L. donovani* parental (K133WT) and paromomycin resistant K133PMM cell line.

Comparative study of host cell modulation by miltefosine (MIL) resistant and sensitive *Leishmania donovani* parasites

This study aimed to investigate the differential capability of miltefosine resistant and sensitive *L. donovani* parasite in modulating the host cell in terms of gene expression and immune response. RNA sequencing data showed differential modulation in host gene expression upon infection

with LdMIL-R and LdMIL-S parasite. A total of 1131 genes were found to be differentially expressed in LdMIL-S infected macrophages when compared with LdMIL-R infected macrophage. GO enrichment analysis showed that genes involved in immune system process, immune response, cytokine signalling, cellular response to cytokine stimulus were primarily up regulated in macrophages infected with LdMIL-S parasite. Real time PCR data showed expression of TNFAIP6

(4.05 fold, $p < 0.05$) and LAMP3 (8.45 fold, $p < 0.05$) was significantly up regulated in LdMIL-R infected macrophages when compared with LdMIL-S infected macrophages. The expression of TNF, CCR7, CXCL2, IL12B, CXCL8 and SOCS3 were several fold higher in LdMIL-S infected host macrophages when compared with LdMIL-R infected macrophages.

Development of novel quantitative isothermal fluorescence based rapid detection method for diagnosis of malaria

Efficient and accurate diagnosis of malaria is important for global malaria control as it helps in reducing complications and mortality. The study aimed to develop a field applicable an isothermal fluorescence based rapid assay for simultaneous detection of *P. falciparum* and *P. vivax* along with the estimation of the parasite count. SYBER green I based lamp assay was developed with a detection limit of 0.71 parasite/ul for *P. vivax* and 2 parasites/ul for *P. falciparum*. The lamp assay was adapted to Genei III fluorimeter based isothermal RealAmp assay with distinct melting peaks for *P. vivax* and *P. falciparum* ($82 \pm 0.8^\circ\text{C}$ and $86 \pm 0.7^\circ\text{C}$ respectively). A multiplex RealAmp assay developed for simultaneous detection of *P. falciparum* and *P. vivax* showed comparable results between Ct value of qPCR and tp (time of positivity) with RealAmp assay. A strong correlation was also found in parasite load obtained from RealAmp assay and qPCR. The novel and rapid molecular assay developed in the study will facilitate speciation of parasite and determination of parasitemia in malaria patients. In addition, the assay can be used in the endemic field area with battery operated equipment and minimal pre and no post processing steps and will be a step towards promoting use of molecular diagnosis of malaria at field level.

Genomic analysis of virulence and antimicrobial resistance determinants of hypervirulent *Klebsiella pneumoniae*

The hypervirulent *K. pneumoniae* (hvKp) isolates have higher virulence and cause tissue invasive

infections than classical *K. pneumoniae* (cKp). The convergence of virulent and resistant strains that cause severe and untreatable invasive infectious disease is worrisome. In the present study, clinical samples collected from patients' reporting at Safdarjung hospital were screened for hyper-virulence by a) String test, b) Siderophore production assay and c) molecular detection of virulence genes. *K. pneumoniae* strains were assessed for their susceptibility to different clinically used antimicrobial agents using VITEK-2 compact-automated system. A total of 116 *K. pneumoniae* isolates were collected from patients reporting at Safdarjung Hospital. A phenotypic and molecular characterization for hyper-virulence was performed for 75 isolates whereby, 5.3% isolates demonstrated viscous string formation and 76% isolates were positive for siderophore production assay. Virulence genes *rmpA*, *fimH1*, *iucA*, *ybtS* and *entB* were positive among 40%, 84%, 58.67%, 44% and 98.67% of isolates. With the set criteria, a total of 33.3% isolates were categorized as hvKp. A low antibiotic susceptibility profile (only 8% sensitive, 88% as XDR and 4% as PDR isolates) was observed in the putative hvKp isolates. In view to have a comparative genomic analysis between hvKP and cKp isolates, a whole genome sequence analysis pipeline was developed. Findings from this study reflects emerging threat of multi-drug resistant hvKp isolates in the hospital settings that warrants an immediate attention towards the increasing spread of hvKp strains.

A pilot study to determine causes of death in under-five children in a tertiary hospital in India using MITS technique

SOPs and forms for various stages of case assessment, sample collection and specimen testing were created and/or optimized according to the local scenarios and complications. Total 183 MITS (including 50 stillborn cases) were performed and found ~ 50% success rate in receiving consent. Histopathology was performed on Lungs, Liver, Kidney, Spleen and Brain to find cause of death.. Cause of Death (CoD) was decided by an expert

panel after presentation of each cases clinical history, course in hospital, treatment given, lab reports, radiology findings, MITS pathology, microbiology tests for blood culture, lung tissue culture, CSF culture, GeneXpert, malaria, HIV, TAQ array tests on 4 samples in each case to look for organisms, etc. TaqMan® Array Cards (TACs) technology were used to detect the multiple pathogens from blood, CSF, nasopharyngeal swab and stool samples from all MITS cases After the final analysis, causes of death could not be assigned in 33 cases. These cases are now being re-evaluated and re-tested.

Efficacy of myeloid growth factor nanoparticles for methotrexate induced neutropenia

The aim of the study was to develop cost effective therapeutic application by the targeted delivery approach of G-CSF by PLGA nanoparticles to minimize the adverse effect on peripheral tissue exposed to high concentration of CGSF. Further the cost and therapeutic quantity of G-CSF (300ug)

may be reduced to one-third which augments cost effective application of colony stimulation factors.

Firstly, the targeted delivery of PLGA and SLN nanoformulations were studied. The targeted delivery of filgrastim to bone marrow is required to decrease the incidence of neutropenia/febrile neutropenia. Mannose-anchored PLGA nanoparticles of G-CSF were prepared by chemical synthesis process The targeted delivery of filgrastim in nanoparticulate system was achieved by molecular dynamics (MD) simulation studies. Two matrices comprising PLGA and SLN (tripalmitin, core component of SLN system) were modelled separately with proposed drug filgrastim. The mass density maps of each nanoparticle system i.e. PLGA and Tripalmitin showed an increase in density towards the end of the simulation. The contact numbers attained equilibria with the average number of approx 1500 contacts in case of Tripalmitin-Filgrastim system. While PLGA-Filgrastim system shows lesser contacts as compared to Tripalmitin with average contacts of approx. 1000.

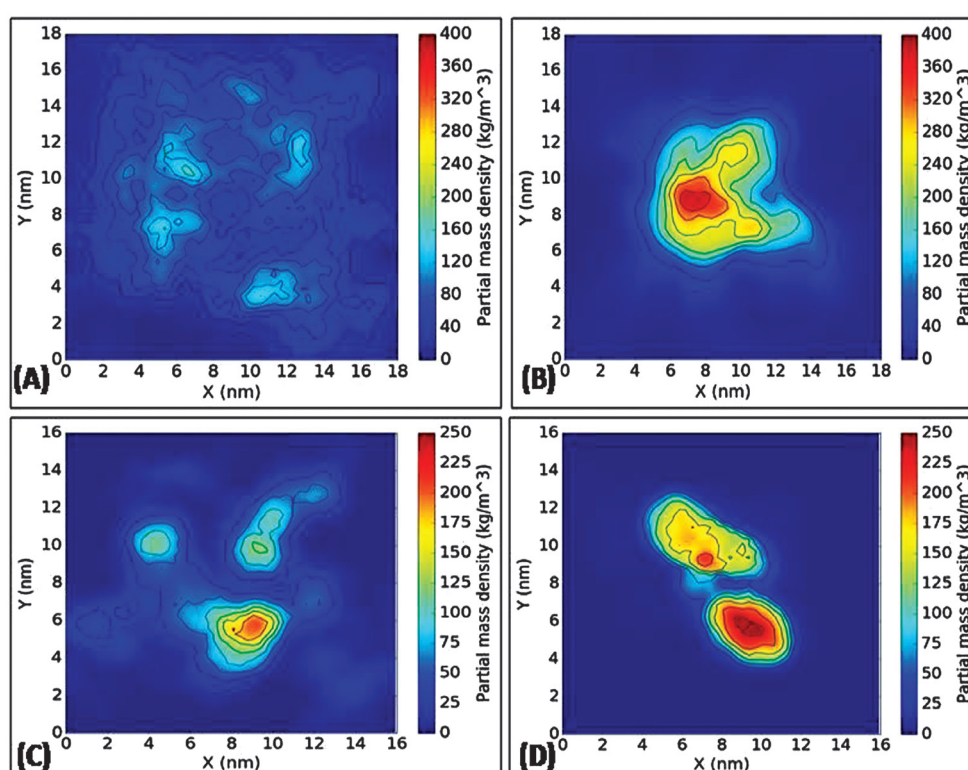


Fig. 7: Density map of the PLGA system and Tripalmitin system respectively at the beginning of the simulation and at the end of the simulation length. (A) Mass density of PLGA of the starting structure. (B) Mass density of PLGA oligomers at 500ns. (C) Mass density of Tripalmitin of the starting structure. (D) Mass density of Tripalmitin chains at 500ns.

Findings of study revealed that both nanoparticle systems assumed to be good model for drug-carrier systems. Though SLN systems were thought to be more appropriate than PLGA, still the in vivo findings could ascertain this hypothesis in futuristic work.

Identification of metabolic markers in Rheumatic Heart Disease (RHD) with Atrial Fibrillation using untargated LC/MS based Metabolic Approach

The aim of the study is to understand the difference in pathways leading to stroke in patients of RHD with Atrial Fibrillation (AF) and Normal Sinus Rhythm (NSR). A total of 50 RHD patients and 49 age sex matched healthy controls were enrolled. Untargated LC-MS analysis was performed among the groups. 351 metabolites were identified in blood plasma through UHPLC-MS/MS analysis. 25 metabolites were significantly differentially expressed in the blood plasma samples of *RHD* patients as compared to healthy controls. Among these 25 metabolites 17 metabolites were up regulated and remaining 8 metabolites were down regulated. Hierarchical cluster analysis was performed to provide intuitive visualizations of the differences in metabolites among patients and healthy controls, the result was displayed as heatmap. Statistically significant metabolites were subjected to KEGG pathway analysis. Purine metabolism pathway was significantly altered ($p=0.01$) with more than 2 hits.

Integrative analysis of psoriasis transcriptome for identification of potential therapeutic targets

The aim of the study is to identify the differentially regulated genes in psoriatic patients as well as its clinical subtypes, which can be targeted for the therapeutic purposes.

Microarray data information was retrieved from freely available data sources (NCBI-GEO). The raw data files were discretely imported into R, version 3.6.1. Background correction and

normalization were performed based on the robust multiarray average method embedded in the Affy package in Bioconductor version 3.8 (<https://bioconductor.org/>). Bioconductor package GEO query and limma were used to identify differentially expressed genes (DEGs) between the study groups. The probable role of the DEGs in biological process, molecular function and cellular component were determined using clusterProfiler. The role of different DEGs in diverse metabolic pathways was identified using Kyoto Encyclopedia for Genes and Genomes (KEGG). The DEGs were annotated based on gene-disease association data from knowledge bases through DisGeNET and target validation. The gene-disease network was visualized by assimilating the data into Cytoscape v3.7.1. CytoHubba was employed to identify hub genes. Topology of 12 built-in parameters i.e. MCC, DMNC, MNC, Degree, EPC, Bottleneck, Eccentricity, Closeness, Radiality, Betweenness, Stress, and Clustering Coefficient were used to calculate hub scores for the PPI network. The top 10 genes in each 12 built in parameters were sorted and genes identified in at least six parameters are contemplated as high-confidence hub targets with possible biological significance. The gene ontology analysis of top three modules was performed by STRING Enrichment plugin.

Under this study, analysis of 22 psoriasis associated high throughput microarray profiles based on subtypes and disease state, revealed 4177 differentially expressed genes (DEGs) to be associated with Psoriasis and its various subtypes. Among 4177 psoriasis associated DEGs, 2416 DEGs were already present in the database and our study has identified 1761 (42%) new DEGs in psoriasis transcriptome. Top clusters obtained after MCODE analysis of identified DEGs were highly enriched in pathways involving cell cycle, chemokine signalling pathway, cytokine-cytokine receptor interaction, IL-17 signalling pathway and TNF signalling pathway indicating involvement of immune related pathways.

The gene-disease network for 20 highest ranking genes associated to psoriasis in each group were also

found to be associated with another dermal diseases including rosacea, acne, eczema, cutaneous lupus erythematosus and other inflammatory conditions.

Developing predictive model for the early detection of Intrauterine Growth Restriction (IUGR) in new-borns from polycyclic aromatic hydrocarbons concentration (PAHs) in maternal blood

Under this study, 177 study subjects (80 cases and 97 controls) were recruited and a total of 531 biological samples including placenta, maternal and cord blood were collected. Socio-demographic characteristics of the cases and controls were compared. Extraction of polycyclic aromatic hydrocarbon (PAH) from placenta, maternal and cord blood in HPLC grade solvent (n-Hexane 8: 2 Acetone) was carried out by liquid liquid extraction method. The study samples are being analyzed for PAH concentration by reversed phase HPLC using a Shimadzu HPLC System Model LC-20AD, equipped with a variable wavelength UV-Visible detector (SPD-20A) and a Luna C18 (250 x 4.6 mm, 5 µm) analytical column from Phenomenex (USA). Shimadzu SPD-M20A Diode Array Detector was employed for the measurement of the UV-Visible spectra at 190-800 nm. HPLC conditions were optimized for achieving best chromatographic separation of mixed PAHs in tissue and blood. For this purpose, different proportions and different flow rates of mobile phase (Acetonitrile: Water) were evaluated with individual standards as well as a standard mix {1 ml each of 16 standard (conc. of 10ug/ml of ACN)}.

Education, dietary habits, birth weight, placental weight and its ratio & ponderal index were found to be the statistically significant between AGA and IUGR babies. Consumption of non-vegetarian diet, particularly grilled food, exposed the mothers to PAHs probably resulting in higher rates of IUGR cases. The higher levels of PAHs are observed in IUGR cases and might be attributed to traffic / air pollution, food habits.

Old Drugs New Tricks: Drug Repurposing for Psoriasis Treatment Using In-silico Approach

The available biologics for psoriasis treatment include anti-inflammatory, steroids, immunosuppressive drugs etc. These are reported to be associated with significantly increased risk of serious infections and have also been reported to show the major contradictions in patients with tuberculosis and cardiovascular disorders. Therefore, the aim of the study is to repurpose the approved or in clinical phase drugs of the associated autoimmune disorders and comorbid condition using network pharmacology-based methods, molecular docking and machine learning approach by utilizing the information available on public domain.

Preliminary work included compilation of psoriasis associated 21 autoimmune diseases, 5 cardiovascular risk disease, 1 gastrointestinal disease, 1 hepatic disease, 1 chronic kidney disease, 1 infectious disease, 1 lung disease, 1 inflammatory disease and 1 mood disorder. FDA approved drugs pertaining to the diseases above were retrieved from DrugBank, PubChem and PharmGKB databases with information including SMILE structure, targets, target actions and target organism. Based upon the retrieved information, 516 drugs and 2193 targets were manually curated for all psoriasis associated diseases under the study. For retrieved drugs, Drug promiscuity was calculated. 92% (476) of 516 drugs had lower promiscuity with <10 targets, followed by 5.6% (29 drugs) with <20 targets, 1.1% (6 drugs) with <30 targets, 0.58% (3 drugs) with <40 targets, 0.38% (2 drugs) with <50 and 1 drug i.e., Fostamatinib (DB12010) was found to be most promiscuous with 300 targets. Gene ontology based enriched drug-target interaction network retrieved 5063 edges. An additional set of 3082 edges were added to the network based on molecular function Gene Ontology (GO) based mapping of the targets. On combining the Drug-Bank DTIs and GO mapping DTIs 7063 edges with 2193 unique targets with respect to 516 drugs were further used to determine the NBI score.

For the entire network comprising of 516 drugs and 2193 targets, NBI association scores were computed. In order to create a prioritization list, we applied a metric where a target was only prioritized for a drug if its association score was more than 20% of the maximum score in the sorted list with unconnected targets. This led to identification of 358 potential DTIs which are prioritized based on their NBI association scores.

After screening, 358 potential DTIs are identified for repurposed drugs. Top 5 DTIs included, Rotigotine (DB05271), Esmolol (DB00187), Etoricoxib (DB01628), Triamcinolone (DB00620) and Flupentixol (DB00875).

Mental health and social stigma among healthcare personnel involved in the management of COVID-19 patients in India

The study group consisted of doctors, nurses, ambulance emergency response teams, lab personnel, X-ray technicians and others who were directly involved in patient care in COVID-19 designated hospitals, from facilities involved in triaging services and referrals to the COVID-19 designated hospitals or labs processing the COVID-19 samples. In addition to healthcare workers the study included the accredited social health activist (ASHA) and community health workers involved in case identification, contact tracing, prevention and control measures for COVID-19. The health care workers were further stratified as those employed in private and public facilities. Of the various activities, those involved in isolation of COVID-19 cases (57.9%), caring the patients with symptoms (58%), those in the intensive care units (58.3%), those involved in contact tracing (60.1%) and screening (59.9%) and in transporting COVID-19 patients were at significantly higher risk of psychological distress. Of the total 48 HCWs who reported transporting the COVID-19 patients (5%) as their main occupation, there were 79 others who were involved in quarantine, contact tracing, isolation or symptoms identification. 46 HCWs who reported being involved in all activities related to the management of COVID-19 patients 56.5% had significantly high levels of GHQ. However, those

involved in sample testing alone did not show a higher GHQ level. Community care workers alone had lower GHQ levels but if these HCWs were also involved in other occupations like contact tracing, isolation, end of life support or bereavement then they reported higher GHQ levels.

ICMR-NATIONAL INSTITUTE OF TRADITIONAL MEDICINE, BELAGAVI (ICMR-NITM)

Workshops on Augmenting Local Resources for Primary Healthcare and Better Livelihood in Tribals

80 home herbal gardens have been established among Siddi and Gowli tribal households in 3 tribal settlements from Uttara Kannada District, Karnataka.

Assessment of burden of anemia among pregnant women in Lambani tribe from Gadag District, Karnataka

63 Lambani pregnant women from 11 tribal settlements were investigated, of which 76% are mild to moderately anaemic. Among the anaemics, 19% have depleted iron stores and one woman is with severe risk of iron overload. All of them have normal serum folate levels from 0.005 to 0.015 µg/ml. while, one have Beta- Thalassemia Minor in Hb electrophoresis.

Validation of diabetic wound healing activity of essential oil from *Mammea suriga* flower buds

A total of 22 chemical compounds were identified in mass spectra from the essential oil of flower buds of *M. suriga*, in which copaene and squalene were the major oils. The oil exhibited significant antimicrobial activity against *Proteus vulgaris* (22.66±0.33 mm), *Salmonella typhimurium* (20.67±0.33 mm) and *Staphylococcus aureus* (20.00±0.57 mm), compared to standard streptomycin. In DPPH radical scavenging activity, the IC₅₀ values of essential oil and standard quercetin were 16.40±0.18 µg/g and 12.40±0.18 µg/g, respectively, while nitric oxide scavenging

activity showed the higher IC₅₀ than that of the standard ascorbic acid.

A validation study demonstrated that the standardized chloroform extract (CE) of *Stephania hernandifolia*, an ethnomedicinal herb possesses antiviral activity against HSV-1F and clinical isolate HSV-1VU-09 at EC₅₀ of 4.32 and 4.50 µg/ml, with Selectivity Index of 11. Further, CE at non-toxic dose interact at early life cycle of the virion and prevent the viral attachment, by direct inactivation or modifying the virion or host cell surface to prevent the virus entry into the host cell. Another study on differential activation of TLR2 by TLR2 dimer-specific ligands on anti-HSV-1 innate immune response showed that TLR2/2 ligand- induced IFN-β in neurons, while IFN-α in astrocytes and these IFNs subsequently induce the expression of IFN stimulatory genes like viperin, Ch25H, OAS2, latent RNase (RNase L), protein kinase R (PKR), and interferon-induced proteins with tetratricopeptide repeats (IFIT) 1. These genes with antiviral functions help to block viral attachment, protein synthesis, and egress.

A collaborative study on novel cyclic peptide-1 (ASP-1) isolated from *Bacillus subtilis* with potent anti- MRSA activity, revealed that at an MIC of 8.0-64 µg/ml ASP-1 cause drastic changes in the cellular architecture of *S. aureus* ATCC 29213 and a MRSA isolate by damaging cell wall, membrane lysis and leakage of cytoplasmic contents, compared to oxacillin-treated MRSA. Another study with silver nanoparticles (Ag-NP-AE) synthesized with the aqueous extract of *Albizia lebbek* bark, demonstrated significant activity against 14 multidrug-resistant (MDR) clinical isolates with zone diameter of 10.4–19.5 mm and MIC of 0.5–0.84 µM (0.085-0.143 µg) compared to its extract (10.2–15 mm; MIC 128– 1024 µg/ml). The nanoparticle scavenge free-radical at 15–20 µM and is nontoxic up to 50 µM; while 100% killing was observed at 0.50 µM within 2–4h of exposure. Further, we have demonstrated that 6-Gingerol (6-G), of ginger, can restrict bacterial growth inside the lungs, spleen and liver of M.tb infected mice with increased expression of pro-inflammatory cytokines and enhanced Th1/Th17 responses. Thus it has excellent potential as an adjunct drug, with

isoniazid. Interestingly, 6-G displayed stark anti-tubercular activity against dormant/starved bacilli and drug-resistant variants.

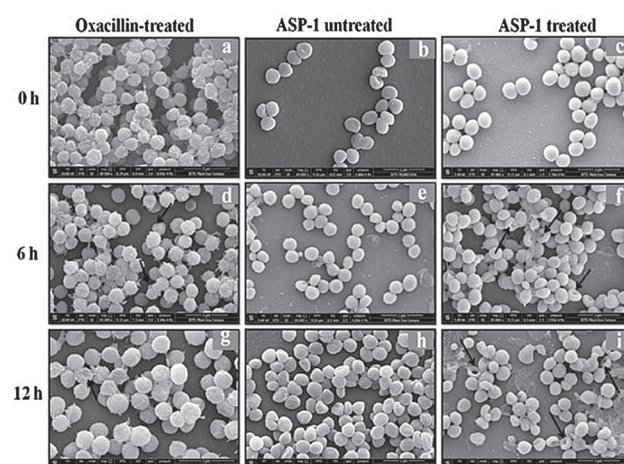


Fig. 8: SEM images of oxacillin-treated, ASP-1 untreated and treated MRSA-4 bacteria. The SEM images of oxacillin (MIC 32 µg/ml)-treated cells at 0, 6, 12 h (a, d, g); Few cells appear healthy by septum formation, other turned biconcave and deformed, and a single cell near the centre have circular depression at 12 h (d, g); SEM images of untreated MRSA-4 cells showing normal morphology and several cells at dividing stage (b, e, h); Micrographs of ASP-1 treated cells (c, f, i); cells of normal morphology at 0 h (c); biconcave elliptical cells with central collapses, deep craters and deformations (f-i); and ASP-1 (16 µg/ml) treated cells at 12 h, showing centrally collapsed biconcave cells with spewed-off contents after lysis (i). Black solid arrows indicated major structural changes.

A series of study highlights the promise of selected novel and potential anti-viral phytopharmaceutical that bind to Furin and TMPRSS2 receptor of host cells, a few of them showed antiviral response in preclinical and clinical study with good therapeutic safety-index. This strategy may limit life-threatening COVID-19 infection and its mortality through nano-suspension based intra-nasal or oral nebulizer spray, in mild to moderate infection. Next, the team evaluated glucoraphanin, vitexin, niacinin as a potential inhibitor of spike protein and (3CLpro) of COV-2 through docking, target analysis, toxicity, ADME prediction and Molecular-Dynamic simulation and found that these molecules have good solubility, pharmacodynamics and target accuracy. Interestingly niacinin, vitexin, glucoraphanin obey Lipinski's rule along with their stable binding towards target protein of the virion, which makes them suitable for further biochemical and cell-based assays followed by clinical investigations for their potential use in COVID-19. Silymarin, from *Silybum marianum*

with versatile immuno-pharmacological effects, have therapeutic potential against COVID-19 due to its cytokine regulating action, binding on TMPRSS2, down-regulation of pro-inflammatory cytokines, antioxidative, anti-platelet and antiviral properties, along with ability to induce endogenous antiviral cytokine ISG15.

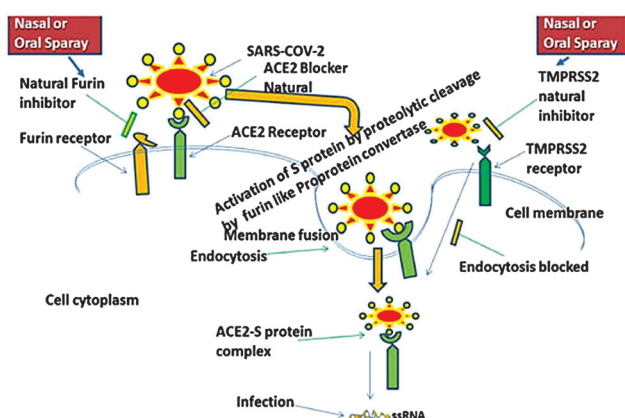


Fig. 9: Infection pathway of cellular infectivity of SARS-CoV-2 via Host cell protease surface receptor and subsequent drug targeting through phytocompounds mediated nasal or oral nebuliser for blocking of host-virus interaction during early endocytosis.

Developing herbal solutions for COVID-19, based on TM leads: We are in the process of developing a formulation from Grandmother's recipe that can block the dual hotspots of SARS-CoV-2 with human host.

The centre has coded Complete Genome Sequences of NITMA1086 and NITMA1139, Two SARS-CoV-2 Isolates from Belagavi District, Karnataka Harboring the D614G Mutation.

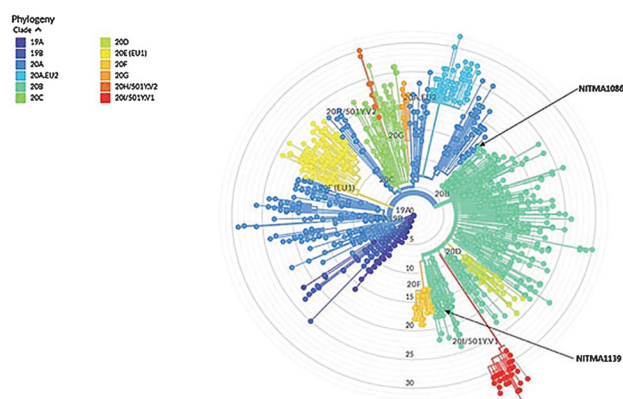


Fig. 10: Complete Genome Sequences of NITMA1086 and NITMA1139, Two SARS-CoV-2 Isolates from Belagavi District, Karnataka Harboring the D614G Mutation.

Identified Potential Herbal Drug Candidates from Traditional Practices against Hepatitis B virus: HBV-RT structure was Modeled and validated the functional state of HBV-RT and identified phytocompounds: C287, C288, 289, C297 from the plant NITM-17 and C242 from NITM-15 as the potent drug molecules against HBV-RT.

PUBLIC HEALTH

In a rapid response to COVID-19 pandemic, ICMR-NITM established COVID-19 RT-PCR testing laboratory facility in April 2020 and till date the diagnostic service is being provided to 1.7 lakhs people in Belagavi and neighbouring district, in collaboration with Dept. of Health and Family Welfare, Govt of Karnataka.

80 home herbal gardens were established among Siddi and Gowli tribal households in 3 tribal settlements, with training on their utility in primary healthcare. This will help to address the primary healthcare issues in the tribal community.

Reported the mutational spectrum of circulating SARS-CoV2 strains in Belagavi.

PATENT

Software Bot for automated entry of COVID-19 testing results into ICMR portal.

EXTRAMURAL RESEARCH

IMMUNOLOGY

Morpho-functional dynamics of brain macrophages from early embryo to late adult rodent model: A developmental approach to age related innate immunoreactivity in brain at Netaji Subhash Open University, West Bengal

Present study on microglia from pre-birth to maturation in normal physiological condition in rodent brain which aid us to understand the base line microglial features during life-stages may act as the reference frame to investigate microglial

behavior at various forms of neuropathogenesis. The study resulted in three publications for knowledge dissemination.

A study on the role of microparticles in the pathogenesis of Rheumatoid Arthritis and Juvenile Idiopathic Arthritis carried at JIPMER, Puducherry

The present study also supported the autoantigen exposure by MPs, the effect of synovial fluid-derived MPs and MPs pulsed APCs in stimulating cells of the adaptive immune system in RA especially on autoreactive T and B cells are warranted. The study resulted in two publications.

A study on Recombinant Antigens as a Tool for Analyzing Antibody Response Among Dengue Patients to Understand Pathology and Pathogenesis done at BIT Campus Tiruchirappalli

An antibody against C, E, M, NS2a, NS3 and NS5 were present in the serum and anti-E antibodies and anti-M antibodies was found in high titers. Also, nine recombinant plasmids have been synthesized that can express recombinant dengue viral proteins with biological activity.

PHARMACOLOGY

A study on Role of neprilysin in the development of cardiovascular and renal complications associated with type 1 diabetes was done at BITS-Pilani

The study comprehensively demonstrated the protective effects of NEPi and ACE2 activator combination against DCM. The NEPi/ARB and NEPi/ACE2 activator combination therapies offer new treatments options to prevent the development of DCM, DN and other diabetic vascular complications.

Anti-leishmanial activity of a novel carbazole alkaloid mahanine

Its mechanism of action and drug delivery through liposomal formulation done at IICB-Kolkata.

PHYSIOLOGY

A study on evaluation of autonomic functions in patients of spinocerebellar ataxia types 1, 2 and 3 and comparison with morphological changes in brain was carried out at AIIMS, Delhi

The findings highlighted an interesting pattern of differential brain areas involved in the three SCA subtypes. The correlation analysis reveals an intriguing pattern of association of brain areas involved in central autonomic function modulation and different autonomic parameters in SCA patients. Based on the findings of clinical score, autonomic score and MRI, the results indicate a generalized severity pattern of SCA as follows SCA2> SCA1> SCA3.

STEM CELL RESEARCH

Generation of corneal endothelial cells from induced pluripotent stem cells at Vision Research Foundation, Chennai

Two strategies were employed for deriving corneal endothelial cells from neural crest lineage cells. In the first strategy; iPSCs post 24 days into neural crest lineage differentiation were cultured in the presence of corneal endothelial differentiation medium. In the second strategy, the neural crest lineage cells were sorted using magnetic activated cell sorting (MACS) before differentiation to corneal endothelial cells. While strategy 1 predominantly gave rise to neuronal and glial cells, the strategy 2 revealed increased proportion of neural crest stem cells which differentiated in corneal endothelial cells as revealed by the expression of ZO1, Na⁺ K⁺ ATPase and AP2.

STEM CELL RESEARCH AND THERAPY

A study on Epigenetic Mechanism in Embryonic Stem Cells Pluripotency and Differentiation was carried at University of Hyderabad

The results highlight the importance studying chromatin condensation dynamics as an important epigenetic mechanism manifested by various epigenetic features of chromatin which has wider applications in fundamental understanding of biology of ESC differentiation and its applications thereof in understanding human diseases.

A study was done on Gradient of chemical cues and differentially pre-induced mesenchymal stem cells in an injectable hydrogel for osteochondral tissue regeneration at IIT-Kanpur

They developed an in-house bioreactor to culture the fabricated hydrogels and test their efficacy to regenerate the osteochondral interface *in vitro*. The bioreactor has the potential to provide different cues to the cells in the chondral and sub-chondral region enabling the native tissue-like environment.

TRADITIONAL MEDICINE

A study on Prebiotic potential and other beneficial effect of ocimum, ginger and pipernigrum on immune-inflammatory diseases conditions done at ICMR-NIN, Hyderabad

Enhanced intestinal integrity and immune regulation resulted in reduced OVA specific-IgE levels, as well as inflammatory markers and amelioration of allergic inflammatory condition. Furthermore, regulation of blood glucose, serum insulin and blood lipids in diabetes model by the extracts of *O. sanctum*, *Z. officinale* and *P. nigrum* suggests immense potential of these herbs with further studies.

PUBLIC HEALTH

The Standing National Committee on Medicine (SNCM)

It was constituted by Ministry of Health and Family Welfare with a mandate to revise National List of Essential Medicine (NLEM) 2015. During the process of NLEM revision, SNCM Secretariat

has convened number of Core committee meetings, Stakeholders National Consultation Meetings, Sub-committee meetings, Expert group meetings, Special purpose meetings and Internal meetings to deliberate and revise the NLEM, 2015. All the sections of NLEM are deliberated in expert groups. In addition to the list of medicines, the committee also mandated to prepare the list of following essential healthcare products.

- Essential list of Medical Devices.
- Essential list of Medical Disposables and Consumables.
- Essential list of Hygiene and Other Healthcare products.

In view of the publication of WHO Essential Medicines List (EML), 2019, NLEM, 2015 was compared with WHO EML, 2019. All the medicines in NLEM, 2015 and WHO EML, 2019 lists were deliberated in detail among the various subject expert groups and inclusion/deletion /modification of the medicines in NLEM are recommended.

Till Date – SNCM Secretariat has convened 4 Core committee meetings, 3 Stakeholders national consultation meetings, 10 sub-committee meetings, 18 expert group meetings, 6 special purpose meetings and 15 internal meetings to deliberate and revise the NLEM, 2015.

Good Clinical Laboratory Practice (GCLP) Guidelines 2021

These were released with the aim to ensure the reliability and integrity of data generated by analytical laboratories while processing and reporting of specimens/samples, GCLP Principles are followed internationally. Good Clinical Laboratory Practice (GCLP) guidelines ensures to bridge the gap between the principles of Good Laboratory Practices (GLP) which were established for data generation for regulatory submissions and Good Clinical Practices (GCP) for ensuring the rights, safety and well-being of patients.

ICMR decided to revise its ICMR-GCLP 2008 guidelines so that they are in line with the newer developments in science, technology and medicine.

With the advancement in technology (e.g.- Stem cell products, Biologicals) and unfolding of various new factual evidences various new rules and regulations have come into effect such as-

- New Drugs and Clinical Trials Rules, 2018

- DAIDS Guidelines for Good Clinical Laboratory Practice Standards, 2013
- WHO GCLP Guidelines, 2009.

The final guidelines were published in January, 2021.

REGIONAL MEDICAL RESEARCH CENTRES

To deal with health problems of the regional and marginalised population, ICMR has established a total of four Regional Medical Research Centres, which are located at Port Blair (Andaman Nicobar), Bhubaneswar (Odisha), Dibrugarh (Assam) and Gorakhpur (UP). The mandate of these institutes is to focus on the regional health problems and find suitable solutions with the help from the respective state governments. The significant outcome of the research activities carried out by these centres during 2020-21 is mentioned below.

INTRAMURAL RESEARCH

ICMR-REGIONAL MEDICAL RESEARCH CENTRE, BHUBANESWAR (ICMR-RMRCBB)

ESTABLISHMENT OF NETWORK OF LABORATORIES FOR MANAGING EPIDEMICS AND NATURAL CALAMITIES (COVID-19 RELATED ACTIVITIES)

Supporting COVID-19 pandemic investigation in the state

During March, 2020, samples suspected for COVID-19 were received from different government and private hospitals for laboratory testing and the first positive case of SARS-COV-2 was recorded on 15th of March, 2020. Around

230, 722 samples were received and tested for COVID-19 and 23256 samples were reported as positive. Samples were referred from COVID-19 hospitals of different districts and some major health facilities like Capital hospital, AIIMS, SUM, KIMS, Apollo, Kalinga Hospital in Bhubaneswar and SCBMCH, Cuttack, MKCG MCH, Berhampur and VSS MCH, Burla from different districts in the state.

Setting up of high throughput BSL II plus facility for COVID-19 testing

The high throughput Cobas laboratory was developed with BSL2 plus facility and started functioning within a record time of 3 days. After approval of DG, ICMR, the laboratory set up was developed with funding support from State Government. The materials for laboratory set and 19 personnel were airlifted by Indian Airforce transport flight AN 32 from Chennai on 6th April, 2020 to set up BSL2 Plus laboratory for testing with Roche Cobas 6800 machine. Since then the laboratory has completed about 2 lakh testing. The laboratory is testing about 1000-1200 samples per day.

A total of 12305 samples were received in 2 phases from 5 districts i.e. Deogarh, Pakur, Godda, Dhanbad, Giridih and East Singhbhum on 20th June, 2020 & 11th April, 2021 from IDSP Jharkhand. All the samples were tested in COBAS Laboratory and reported to IDSP, Jharkhand within 48 hrs of receipt of samples. The online data entry

was also completed on real time basis in ICMR Portal.

The laboratory has tested all high priority and VVIP samples before and after various Legislative Assembly Sessions of Odisha State Assembly in 2020-21, Honourable President visit to Odisha in March, 2021 and Honourable Prime Minister Visit in May, 2021, Indian Hockey team members and support staff during their felicitation by HCM after their 2020 Olympic success.

The Antibody testing laboratory for SARS-COV-2 Antibody estimation (quantitative and qualitative) was established in June 2021, with two machines i.e., Roche Cobas e411 and Abbott architect 1000SR.

More than 50, 000 samples have been tested in the laboratory between July 2020 to March 2021. The samples collected from various rounds of serosurveys were tested from various districts of the states of Odisha (Ganjam, Gajapati, Bhubaneswar, Malkangiri, Rourkela, Berhampur, Cuttack, Odisha Anesthesia Society, Bhubaneswar Police Commissionerate, High Risk Population, Utkal Chemist & Druggist Association), 10 districts each of Jharkhand & Chhattisgarh.

The laboratory also estimated the IgG titre for the recovered cases for development of Convalescent Plasma bank for Convalescent Plasma Therapy at various Medical Colleges like SCB Medical College, MKCG, Berhampur and VSS, Burla.

Training and HRD development

A sensitization cum preparedness meeting was organised on 3rd February, 2020 on Novel Coronavirus outbreak at RMRC, Bhubaneswar which was attended by Laboratory supervisors, Medical superintendents and Technicians from various government and private health care facilities from various parts of the state. During this period RMRC, Bhubaneswar has supported the state health department by providing laboratory training on biosafety, sample collection, RT-PCR

testing and online data entry in ICMR portal. Since, March, 2020 training has been imparted to 92 laboratory personnel from 4 govt. medical colleges, 3 private medical college and hospitals, 10 district public health laboratories, 15 different private and government institutions. The laboratory also played an important role in guiding and supervising for setting up of laboratories required for testing of COVID-19 at district level and medical colleges in the state.

Conducting QA/QC programme

Being the regional VRDL in the state, the quality assurance and quality control programme for COVID-19 samples started in the month of March, 2020. The laboratory is a part of EQAS for COVID-19 and shown 100% concordance with NIV, Pune as well as with WHO. Initially there were 10 Govt. and Private hospitals/medical colleges in the state under supervision of ICMR-DHR and now it has been increased to 24 QC labs (12 govt. and 12 private labs) under Regional-VRDL. So, far around 400 samples have been checked by the VRDL and report has been communicated to DHR.

Designated as depot for reagents & kits

ICMR-RMRC, Bhubaneswar was designated as the depot for RT-PCR kits, RNA extraction and viral transport medium for the states of Odisha and Chhattisgarh since 22nd April, 2020. RMRC is maintaining and sending RT-PCR kits, RNA extraction and viral transport medium as per the requirements raised by the individual testing centres in Odisha and Chhattisgarh. The team are constantly coordinating with the various testing facilities in Odisha and Chhattisgarh.

Centre for Kit validation

VRDL of RMRC Bhubaneswar is identified as one of the validation centre for COVID-19 RT-PCR testing kits, RNA extraction kits, Antigen kits and VTM by DHR-ICMR since May, 2020. So, far 40 RT-PCR kits, 41 RNA extraction kits and 2 Viral Transport Medium kits and 12 lots of antigen

kits have been validated and reported to DHR/Companies.

Novel Technologies & studies

- 1st report from India on use and feasibility of saliva as alternative specimen of NPS for diagnosis of SARS-COV-2.
- 1st time reported the diagnostic accuracy of three antibody testing platforms ARCHITECT i2000SR (Abbott Laboratories, USA), Cobas e411 (Roche Diagnostics GmbH, Germany) and iFlash 1800 (Shenzhen Yhlo Biotech Co. Ltd., China).
- 1st time reported the feasibility of pooled testing for SARS-COV-2 infection in an automated high 2 throughput platform of Roche Cobas 6800.
- 1st time documented that the lower persistence of anti-nucleocapsid SARS-COV-2 antibody may not be the exact phenomenon as those cases were still seropositive against spike protein and help in neutralizing the virus.
- Ct value associated with the antibody response among the SARS-COV-2 infected individual.
- The centre 1st time documented that a single dose of BBV-152 and AZD1222 induced a high concentration of neutralizing IgG antibody in HCWs having a recovery history from COVID-19.
- 1st documentation from India to establish co-infection of SARS-COV-2 with other respiratory viruses and will provide a helpful reference for diagnosis of patients presenting with similar respiratory symptoms. The results will help in revising the existing diagnostic algorithm for respiratory illness. In the current pandemic situation, timely differential diagnosis and knowledge of co-infection will help the clinicians for better therapeutic intervention and improving the outcome of the disease.
- The centre led a study supported by the Odisha Mining Corporation to analyse the

epidemiology of COVID-19 pandemic in the state. This included collaboration with all relevant institutes in the state such as ILS, IIT, AIIMS, and state health department, wherein the clinico epidemiological characteristics were assessed in the early cases and clusters reported. Additionally, disease models were developed for informing preparedness of the state health system during the first wave. Microbiological and immunological studies were carried out as well.

Serial community serological surveys during SARS-COV-2 pandemic

Odisha: The centre carried out the surveys and collected samples and data from over 4000 participants in total from the 3 cities of Bhubaneswar (BBS), Berhampur (BAM) and Rourkela (RKL). Among them 2/3rd were male and the rest 1/3rd female. The average age of the participants was about 45 years. The seroprevalence or the proportion of people with antibodies across the three cities was 20.78%. In the month of August, this was highest in BAM at 31.14% followed by 24.59% in RKL and 5.24% in BBS. However, with time the seroprevalence of Bhubaneswar increased to about 50% in October. While females reported a higher seroprevalence (22.8%) as compared to males (18.8%), there was no difference in seroprevalence across age groups- implying that people from all ages were getting infected equally.

Among the study population, 6.12% had developed symptoms suggestive of COVID-19 in the past 30 days and about 10% had already been tested for COVID-19. A majority of the seropositive participants were asymptomatic (93.87%). Among those who reported symptoms, the most common symptom was fever followed by cough and generalized body and muscle pains.

The repeated cross-sectional studies were conducted in three rounds in Bhubaneswar in which 3693 participants were enrolled in the study. The seroprevalence for the city in the first round was 1.55%, second round was 5.27%, and in the third round was 49.04%.

In the first-round, the seroprevalence was found highest (1.68%) in the elderly population (age more than 60 years), whereas the seroprevalence for the second and third phase was highest (7.72% and 54.02%) in the age group 30-39 years. Overall, females reported a similar prevalence of 21.90% compared to males 20.42%. Seroprevalence was significantly higher among individuals with larger household sizes across all 3 rounds. Irrespective of the age group, the seroprevalence showed an increasing trend over the 3 time periods, with the highest seropositivity rates among individuals sampled between 16-18th September 2020.

Jharkhand, Chhattisgarh: The ICMR-Regional Medical Research Centre, Bhubaneswar, conducted a sero-surveillance study of COVID-19 pandemics in the state of Jharkhand in May 2020 and in Chhattisgarh in September 2020. The survey was conducted with the help of the ICMR TB Prevalence Team and the state government of the respective states.

From both the states a total of 5000 serum samples were collected from 10 different districts (with high, medium and low RT-PCR positivity rate) along with the demographic information and COVID-19 pandemic related infections, symptoms and travel history of each participant. The required sample size was determined on the basis of probabilities proportional to size (PPS) sampling methods given by the World Health Organization (WHO) for large clusters. Ten districts were chosen from each state and 500 samples were obtained – 240 from the community and 260 from high-risk groups. In addition, two administrative blocks were sampled from each district and three cluster villages were randomly selected – 40 samples from community members were collected from each village using a systematic random sampling approach; the high-risk categories were sampled from the district using purposive sampling methods.

The blood samples were collected by qualified personnel and centrifuged at the collection point, and the serum was deposited at the district / state

vaccine storage point or at the blood bank. Serum samples were transported to the ICMR-Regional Medical Research Centre, Bhubaneswar, which maintained a proper cold chain for further analysis. The study settings for each state were given below.

The samples were subjected to in vitro qualitative detection of antibodies (including IgG) to SARS-COV-2 in human serum and plasma. The assay uses a recombinant protein representing the nucleocapsid (N) antigen for the determination of antibodies against SARS-COV-2. The test is intended as an aid in the determination of the immune reaction to SARS-COV-2.

The sero positivity for Jharkhand was 0.6% (30/4766) in May, 2020 and 44.74% (1774/3965) in Jan 2021 respectively. The sero positivity for Chhattisgarh was 5.56% (283/5083) in September, 2021.

Multicentre trial to assess the performance of centralized assay solutions for detection of MTB and resistance to Rifampin and Isoniazid

Gene Xpert assay which has become available in large scale for testing MTB in many districts does not provide information on INH-resistance. Hence, a molecular diagnostic test for rapid identification of MTB with higher accuracy is the need of the hour. A project has been conceptualized with this idea in partnership with FIND India to evaluate a comparative study to estimate the diagnostic accuracy in Cobas as comparator with current gold standard.

An Open-Label, Non-Randomized, Two-Stage, Dose-Finding Study of Verapamil Tablet Formulation in Adult Tuberculosis Patients in Continuation Phase of Anti-Tuberculosis Treatment

Verapamil study is a dose finding study of the drug Verapamil, the dose of 120mg of Tab Verapamil was already done by NITRD Delhi. For the next doses of 480mg and 720mg of Tab Verapamil the study was to be conducted jointly by NIRT

Chennai and RMRC At present, pk sampling of three participants in the confirmatory group have been completed and discharged with stable vitals.

A Phase III, Randomized, Double-blind, Three arm Placebo controlled Trial to Evaluate the Efficacy and Safety of two vaccines VPM1002 and Immuvac(Mw) in Preventing Tuberculosis (TB) in Healthy Household Contacts of Newly Diagnosed Sputum Positive Pulmonary TB Patients

The TB vaccine sites at RMRC, Bhubaneswar and AIIMS, Bhubaneswar were initiated in December 2019. Due to COVID-19, less numbers of index TB cases were getting diagnosed at Bhubaneswar microscopy centres. As per recommendation of monitoring committee a new site at SCB Medical College & Hospital, Cuttack was initiated in July 2020. The house hold members (> 6 years of age) of newly diagnosed pulmonary TB cases were approached and brought to the TB vaccine sites for screening. In order to achieve enrollment target within the desired time line, participants were included from 9 districts of Odisha like Khordha, Puri, Nayagarh, Cuttack, Jajpur, Kendrapara, Bhadrak, Dhenkanal and Jagatsinghpur. Study could include 1742 participants from the three sites and following them periodically. So far 5 unrelated SAE has been reported to DCGI and after vaccination, 7 PTB and 2 EPTB cases identified in the vaccinated participants.

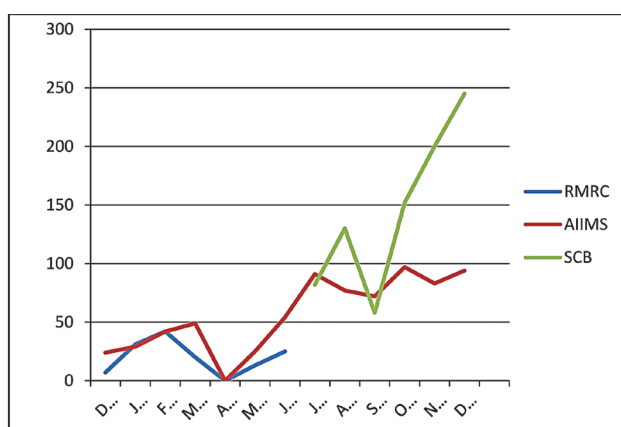


Fig. 1: Month wise enrollment of TB vaccine participants from December 2019 to December 2020.

Capacity Building for “A Phase III, Randomized, Double-blind, Three arm Placebo controlled Trial to Evaluate the Efficacy and Safety of two vaccines VPM1002 and Immuvac(Mw) in Preventing Tuberculosis (TB) in Healthy Household Contacts of Newly Diagnosed Sputum Positive Pulmonary TB Patients”

The capacity building project was initiated to make ready the sites, staff, training for the main trial. During this period, RCTCP staff was sensitized regarding the TB vaccine trial by the study team. Contacted index cases (newly diagnosed pulmonary TB cases) of 9 districts and arranged the transport of the eligible house hold members to TB vaccine sites following COVID-9 guidelines.

Table. 1. Number of index cases and their house hold members contacted for the TB vaccine trial.

	AIIMS, Bhubaneswar site	RMRC, Bhubaneswar site	SCB MCH, Cuttack site
No of Index cases contacted	194	49	294
No.of House Hold Contacts	1178	241	1390
Eligible House Hold Contacts	890	164	962
Enrolment for TB vaccine	737	138	867

National Reference Laboratory for TB

RMRC, Bhubaneswar is one of the six National Reference Laboratories (NRLs) of the country which supervises 10 states like Odisha, West Bengal and 8 North East states for quality TB diagnosis by RNTCP. NRL conducts annual On-site evaluation/ supervisory visits to laboratories for assessing quality of microscopy, Culture and DST, and for improvement of overall laboratory quality. NRLs also assist CTD, in developing laboratory guidelines, SOPs, conduct trainings to state level Intermediate reference laboratories and other technical issues. The functions of the NRLs include conduct of

Culture and DST trainings to the IRLs, develop SOPs for the technical procedures, equipment maintenance, infection control, and recording and reporting. In addition, NRLs are also responsible for the conduct of research for the programme and evaluation of newer tools for diagnosis of TB. NRL also provide technical support for establishment of new NTEP laboratories. NRL provides annual proficiency testing panel to the state laboratories for certification and check the quality TB diagnosis. It also provides TB diagnosis and follow up culture for MDR TB patients on DOTS Plus regimen to 10 districts of Odisha (Bhubaneswar, Puri, Nayagarh, Khordha, Rayagada, Kalahandi, Malkangiri, Koprapt, Nuapada & Nabarnagpur). NRL also act as a backup laboratory for the state culture and DST laboratories supervised by NRL.

TB Diagnostic services provided to the state

In 2020, a total 4778 numbers of samples has been received. Among that, 1504 samples were subjected to liquid culture, out of which 36.4% samples were MTB positive. A total of 2893 samples were subjected to FL LPA, the prevalence of isoniazid monoresistance, rifampicin monoresistance and MDR were 2.14, 0.38 and 1.2% respectively. A

total of 143 samples were tested by SLLPA, among which the prevalence of resistance to FLQ, SLID and XDR were 12.6, 2.8 and 0.7% respectively. During the period 1339 samples were run on CBNAAT machine for TB diagnosis and only 1% was detected as Rif resistant.

National Survey for the state-wise prevalence of microbiologically confirmed pulmonary Tuberculosis in India

The project was initiated at three states Odisha, Chhattisgarh and Jharkhand to estimate the state-wise prevalence of microbiologically confirmed pulmonary Tuberculosis cases. The participants were provided TB testing at the cluster site, near their village based on clinical examination, sputum examination, CBNAAT testing and Chest x-ray. The facilities were provided in a survey bus moved to cluster sites with the field team members. So far, centre has completed 10 out of 21, 13 out of 13, and 11 out of 18 clusters in Odisha, Chhattisgarh and Jharkhand respectively. The NTBPS team was also utilized for carrying out the COVID-19 sero-survey 3 times at 3 districts each having 30 cluster villages in respective states.



Fig. 2: Sample receipt, sanitation, and segregation.



Fig. 3: Testing and real time reporting in the ICMR portal.



Indian Air Force @IAF_MCC · Apr 7, 2020

#हरकामदेशकेनाम: यह कार्य ओडिशा में आईसीएमआर के परीक्षण प्रयोगशाला को सुविधाजनक बनाने और लोगों के मदद के लिए था। लोगों और चिकित्सा सामग्री को एक अल्प सूचना पर पहुंचाया गया था। एमसीयू तांबरम ने पूरे माल और यात्रियों की सुरक्षित रूप से स्क्रीनिंग की।



Fig. 4: Transport Aircraft AN-32 of Indian Airforce airlifted materials (3500Kg) and 19 engineers from Chennai for establishment of BSL II plus laboratory at ICMR-RMRC, Bhubaneswar.



Fig. 5: BSL II Plus facility established in record time of 3 days to initiate SARS-COV-2 testing at COBAS Laboratory.

ICMR-REGIONAL MEDICAL RESEARCH CENTRE, GORAKHPUR (ICMR-RMRCGKP)

Molecular diagnosis of SARS-COV-2 (nCOV-19) specimens obtained from Uttar Pradesh state health department

A total of 318,500 clinical specimens of suspected cases of COVID-19 were tested through Q-RT-PCR method from 23rd March 2020 to 28th February 2021 by ICMR-RMRC, Gorakhpur team. Major bust in testing was observed in month of November-20 and December-20 since beginning of the laboratory diagnosis of SARS-COV-2 virus at ICMR-RMRC, Gorakhpur. Overall positivity for nCOV-2 infection was 1.6% during the testing period. Maximum positivity was observed in the month of May-20 and lowest positivity was observed in the month of February-21. Maximum specimens were obtained from Maharaganj district followed by Kushinagar, Sant Kabir Nagar, Siddharthnagar and Basti districts of eastern Uttar Pradesh.

Molecular surveillance and assessment of genomic diversity of SARS COV-2 in Eastern Uttar Pradesh

ICMR-RMRC Gorakhpur is one of the national reference diagnostic laboratory of ICMR for testing and confirmation of COVID-19 suspected cases through RT-PCR in eastern Uttar Pradesh region. The samples have been received from various districts namely Gorakhpur, Maharajganj, Deoria, Kushinagar, Basti, Sant Kabir Nagar and Siddharthnagar, Azamgarh, Mau, Balia and Ayodhya. The majority of the cases (95%) were asymptomatic as compared to the mild and severe. The study will be helpful in knowing the pattern of diversity among the different strains of SARS-COV-2 and their clinical outcome (symptomatic, asymptomatic and severe). This study will fill the gaps regarding the genomic distribution of strains, mutational analysis and the clinical variations among the individuals.

Whole genome sequencing of approximately two hundred samples is being in process at NIV, Pune. Data analysis and phylogenetic characterization based on the initial data shows the sequences

retrieved belong to four different GISAID clades namely G, GH, GR and S.

Impact of COVID-19 on Maternal and Child health services in India

National Health Policy of India emphasises on universal health coverage with specific targets for reduction of both maternal and infant mortality in India by the year 2025. The impact of COVID-19 on the maternal and child health services is yet to be ascertained in India, however experience from even developed countries have shown disruption of essential health services especially health services for the pregnant mothers and new born. The study aims to assess the impact of the ongoing COVID-19 epidemic on the Maternal and Child health service in India. Although outreach services for MCH care has been restricted, Government of India has taken measures to ensure that beneficiaries visit peripheral facilities on particular dates as informed to them telephonically or through ASHAs. It would be important to assess the likely impact of these measures on the demand and uptake of MCH services amidst the fear and panic induced by COVID-19 and further guide policymakers to address the gaps.

The immediate impact assessment was done via two-pronged strategy.

- Rapid assessment survey with structured tools (questionnaires) through telephonic interviews/web-based surveys of both the Health care workers and MCH beneficiaries.
- Analysing the data available through Health Management Information System (HMIS) and SNCU online database.

A qualitative study on psycho-social issues and challenges of individuals diagnosed with COVID-19 in eastern Uttar Pradesh

This study was conducted to examine psycho-social issues and challenges of people diagnosed with COVID-19. A total number of 58 COVID-19 recovered in which 29 non-migrant and 29 migrant

COVID-19 recovered individuals have been enrolled from Gorakhpur, Basti, Sant Kabir Nagar, Siddharth Nagar and Maharajganj districts from northern Uttar Pradesh. A face-to-face and telephonic interview based on semi structured open-ended questions pertaining to seeking of experiences before and after discharge from hospital has been conducted over the COVID-19 recovered non-migrant and migrant individuals respectively. The content analysis of thematic responses of participants has been used to analyse the qualitative data. The data showed that most of individuals faced a lot of psycho-social issues during and after quarantine and isolation period. However, some of them not felt such kind of experience due to their relatives and family members also were there with them during quarantine and isolation period. Migrant workers were found with higher problems than the non-migrants. The experiences during different phases of being suspected, quarantine, confirmed with COVID-19 infection hospitalization, as well as at the time of journey have also been reported in this study.

Factors Related to COVID-19 Stigma: A Mixed Method Study

A list was prepared of all the people (age range 18-99 years) with the help of updated voter lists acquired from both districts—Gorakhpur (N=34, 86, 821, random number=31, 989) & Basti (N=18, 12, 434, random number=16, 627) for sample selection from community. The list of COVID-19 discharge cases also been acquired from both districts CMO offices for selection of COVID-19 recovered cases. Completed the selection of samples from community (n=109) using systematic random sampling from both districts in equal ratio of gender & rural-urban population. However, a simple random sampling technique has been used for selection of total 16 COVID-19 discharge cases from each district. Hence, the total number of samples for the study was selected as 250 samples from both the districts (Gorakhpur, n=125) & (Basti, n=125). The detail of number of selected samples in each category. Quantitative as well as

qualitative study has been conducted on above mentioned subjects. Collection and entry of data and analysis has been completed.

Diagnostic services for suspected Japanese encephalitis (JE) cases from eastern Uttar Pradesh

ICMR-RMRC Gorakhpur, undertake the routine investigation of clinically suspected Acute Encephalitis Syndrome (AES) cases admitted to the BRD Medical College (BRDMC), Gorakhpur and provides diagnostic services that guide the management of cases. All the AES cases hospitalized from 1st January 2020 to 31st December 2020 were investigated for detection of anti-*Japanese encephalitis (JE) virus* specific IgM (anti-JE IgM), anti-*Orientia tsutsugamushi* IgM (anti-OTs IgM), Dengue NS-1 antigen (DEN NS-1 Ag) and Anti-*Leptospira* IgM Antibody (Anti-*Leptospira* IgM) by ELISA assays, and for *Malaria diagnosis* rapid diagnostic tests (RDTs) was used as per the ICMR recommendations.

A total of 1019 clinical specimens (CSF and Serum) were collected from 565 AES cases. Seventy seven percent of the AES cases admitted to the BRD Medical College were found to be reactive to one or more aetiologies (Fig-1). Anti-JE IgM, anti-OTs IgM and DEN NS-1 Ag positivity were documented in 52 (10.3%), 329 (58.7%) and 13 (2.5%) AES cases respectively.

Development of diagnostic kit for rapid and early detection of *Orientia tsutsugamushi* based on isothermal recombinase polymerase amplification and lateral flow analysis

In this study, the type specific antigen 56kDa gene has been identified for the development of kit based on isothermal polymerase gene amplification and read out on lateral flow analysis. The 56-kDa full gene was cloned from Standard strains of OT including Gilliam, Karp, Kato and Kostival obtained from CDC. Further, the primers and probe for RPA were designed manually, according to the twistdx assay design manual. The three forward primers,

two reverse primers, and two probes were initially designed for optimization. The reverse primers used for RPA were labelled with biotin at 5' end. The probe was labelled with carboxyfluorescein (FAM) at 5' end and the 3' end was blocked with a phosphate group and an abasic site (THF) is introduced between the 30th and 31st base position. The abasic site in the sequence is recognized by the nfo endonuclease (IV) and cleaved leaving the 3' ends free for further extension. The nucleotide code degeneracy was added accordingly.

To optimize the RPA assay, various concentrations of forward/ reverse primer (200-420nM) and probe (60-120nM) were used to conduct the RPA-LF method. At the preliminary stage, we successfully optimized the diagnostic method for visual detection of *Orientia tsutsugamushi* prevalent strains, Gilliam and Karp, in India within an hour (including DNA extraction).

A study of psycho-neurotic disorders and socio-behavioral changes among AES/JE cases recovered in Gorakhpur

Various studies confirmed the occurrence of changes in brain due to AES/JE. And neuropsychiatric sequelae with cognitive and language impairment. And, psycho-neurotic disorders & behavioral asymmetries are associated with brain mechanism & its biological characteristics. Therefore, it is rational to investigate whether there is functional relation of AES/JE with psycho-neurotic disorders & behavioral changes. Available literature suggests that the study on relationship between AES/JE & psycho-neurotic disorder; & with socio-behavior aspects have not been carried out among AES/JE recovered cases in Gorakhpur. It's rational to believe that AES/JE recovered cases are more likely to develop more psycho-neurotic sequelae & socio-behavioral deviations due to changing in brain and neural mechanism.

All the prior formalities and procedures have been completed which is needed before the conduction of study. The procedure of sample selection has been framed. Data collection tools and questionnaires

along with consent letter and participants information sheet have been designed. The project has already been submitted to the IHEC.

Establishment of a Health and Demographic Surveillance System [HDSS], Gorakhpur, Uttar Pradesh

Baseline demographic data of HDSS area and Health Data from IDSP: It's essential to have prior information about the population which is going to be surveyed. In this regard, the centre had collected information from Census, local authorities like Gram Pradhans and village secretary. The centre has collected the basic socio-demographic data like population, geographical area, sex ratio, child sex ratio, total literacy rate, male literacy rate, female literacy rate, the percentage of SC/ST population and working population from census data and local authorities about 28 villages included in HDSS Gorakhpur site area. To know the disease profile of the HDSS site villages, team has collected health morbidity data from district hospital through IDSP network about the disease profile of OPD patients. This data will also help us in designing our morbidity schedule which will be covered in the next follow-up rounds of the survey.

Designing data collection tools and piloting: To form the basic household survey schedule, we first thoroughly study the existing survey schedules of In-Depth network, HDSS Vadu, NIE Chennai Ayapakkam Cohort and National Sample Survey Organisation (NSSO_ Round 71) and National Family Health Survey (NFHS) report. The questions were extracted from these questionnaires according to the objectives of our base line survey requirements. The questionnaire was prepared in two languages English and Hindi. After preparing the questionnaire we performed paper-based pilot survey on 23 households (123 individuals) in one of the 28 villages, to check the appropriateness of the questions to the target population and to modify the options provided in each question according to the target population. The data management system at NIE Chennai was reviewed. It was decided the IT team of NIE would support us in creating ODK

based data collection tools and managing the data on their server till GKP site get its IT section well established. After completing the pilot survey, the questionnaire was modified and discussed with other scientific and technical personnel of the institute and their suggestions were incorporated. After more modifications in our tool, we performed one more CAPI-based on ODK pilot survey on 85 households (378 individuals) in one of the 28 villages in August 2019.

Training of the Core Team and HDSS Staff: Core team attended training on HDSS system at NIE Chennai, RMRC Dibrugarh and HDSS Vadu. Two days training program was organised for HDSS Staff on Field activities staff, Social aspects of Community, Survey, and Handling on GPS, First Aid etc. on 26th and 27th September 2019 in ICMR RMRC GKP.

Mapping & Listing: Mapping and listing of every household in all 28 villages have been completed. A total of 27064 households have been listed. GPS mapping of 21 villages completed. At district level, from health department Chief Medical Officer (CMO) and Additional Director (AD) Health, Gorakhpur has been involved and from Gorakhpur Administrative Department District Magistrate (DM), Additional District Magistrate, Superintendent of Police (SP), Police Adhikshak (rural) Police Adhikshak (urban) and Thanadhyakshya are involved. At local Gram Pradhan of each village, Deputy Medical Officer and at local level Medical Officer-in-charge of the PHC, ANM and ASHA have been involved. Experts from other HDSS sites: Dr. Sanjay Juvekar (HDSS Vadu), Dr Manoj Murekhar & Dr Tarun Bhatnagar (NIE Chennai) has been involved.

Formation of Community Advisory Board: For the purpose of smooth and correct data collection and to enhance the community participation, Community Advisory Board was formed which consists of 148 members from the community (3 to 5 members from each village according to size of the village). Apart from them, CMO Gorakhpur, MOICs of block PHCs, Community Development

Block officials, Director ICMR RMRC Gorakhpur and PI of HDSS project are members. First meeting of CAB was held on 20th November 2019.

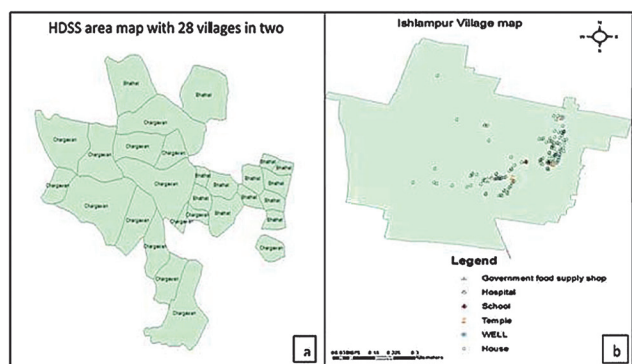


Fig. 6: GPS based map of the 28 villages and detailed map of a HDSS village.

National Survey for State Wise Prevalence of Microbiologically Confirmed Pulmonary Tuberculosis in India

A total of 34 clusters in 21 districts of eastern Uttar Pradesh is assigned to ICMR-RMRC team for the prevalence study of microbiologically confirmed cases of pulmonary tuberculosis. Fourteen clusters have been completed till 10 March 2021. More than fifteen thousand individuals were covered during the survey from completed clusters. More than ten thousand X-ray examinations were conducted by this team. Apart from this approximately twelve hundred CBNAAT diagnosis was also performed to confirm pulmonary tuberculosis and drug resistance in confirmed cases of pulmonary TB. A total of thirty three individuals were found positive, out of these twenty three were rifampicin susceptible, four were rifampicin resistant and six were rifampicin intermediate.



Fig. 7: Honourable Chief Minister Uttar Pradesh Shri Yogi Adityanath inspecting mobile laboratory unit of TB prevalence survey in presence of the Director Dr Rajni Kant, ICMR-RMRC, Gorakhpur.

Assessment of lymphatic filariasis transmission after post mass drug administration in Gorakhpur district

Filariasis is a neglected tropical disease caused by the infection of filarial worm *Wuchereria bancrofti* and *Brugia malayi* transmitted from human to human by mosquito biting. The government of India is signatory for the elimination of filariasis from India in 2020. All the districts have completed more than 5 rounds of Mass Drug Administration by the end of 2014, and are required to be evaluated to decide whether to stop or continue MDA program.

A post MDA filariasis parasite screening in mosquito vectors is necessary for the verification of interruption of transmission cycle of filariasis parasite in endemic area. A post MDA filariasis parasite screening in mosquito vectors is necessary for the verification of interruption of transmission cycle of filariasis parasite in endemic area. WHO recommends use of vector control measures where filariasis is co-endemic with malaria and dengue.

- Finalization of study villages from 19 administrative blocks of this district was completed.
- *Culex quinquefasciatus* mosquito collection was completed from three administrative blocks of Gorakhpur District.

Collection of Adult *Cx. quinquefasciatus* female mosquitoes from 24 (6 villages x 4 households) rural houses and 4 urban houses.

Genetics of susceptibility to encephalitis in Japanese encephalitis virus-infected children from Uttar Pradesh

TNFA rs1800629 G/A genotype [OR with 95% CI 1.91 (1.07-3.39)] and *IFNG* rs2430561 A/T genotype [OR with 95% CI 1.57 (1.11-2.21)] were associated with susceptibility to JE disease. CCR5 rs1799987 A allele was associated with JE in log-additive mode [(Odds ratio with 95% CI 1.38 (1.01-1.87)]. Analysis of genotype frequencies of *CD209* gene which codes for Dendritic Cell-Specific

Intercellular adhesion molecule-3-Grabbing Non-integrin (DC-SIGN), a receptor for flaviviruses including JE virus revealed that *CD209* -336 A/G genotype was significantly associated with JE disease in an over dominant mode (A/G vs. A/A+G/G) [Odds ratio with 95% CI 1.55 (1.08-2.23)]. The G/G genotype of *CD209* -336 polymorphism was with resistance to JE disease in recessive mode [Odds ratio with 95% CI 0.35 (0.13-0.95)].

Analysis of Q279R SNP in the *MMP9* gene which codes for matrix metalloproteinase revealed that the heterozygous genotype G/A was associated with JE disease [Odds ratio with 95% CI 1.50 (1.07-2.11)].

Setting up of AES Cell at Baba Raghav Das Medical College, Gorakhpur

During the study duration, 3679 AES cases were enrolled. 1619 patients tested positive for OT IgM (including samples from either CSF/ Serum) and 498 were positive for IgM JE. Results for scrub typhus PCR: 999/1736 (57.54%) where subtype seen were Gillium (90%) and Karp (10%). The rickettsia specific generic PCR amplified specific fragment in 26 specimens (whole blood) out of 229 total tested (11.3%). The sub sets of clinical samples were further tested for various suspected aetiologies according to the clinical features by various serological kits by using serum specimens for; Malaria 2/295 (0.67%), Typhoid 3/293 (1.02%), *Leptospira* 11/455 (2.41%), Measles 13/17 (76.4%), Mumps 12/17 (70.5%), HSV 1 & 2 (serum: 7/23 (30.4%), CSF : 3/7 (42.8%), *Rickettsia* 4/31 (12.9%) and Hepatitis E 1/40 (2.5%) infections.

Clinically patients who were scrub positive presented with longer duration fever (>7days) in (43%) and when compared with patients who were scrub negative-abdominal pain (18.65% vs 10.76%), hepatomegaly (28.48% vs 17.49%), splenomegaly (4.26% vs 1.17%), thrombocytopenia ($\leq 1,00,000/\text{cumm}$) and deranged liver enzymes (ALT ≥ 30 IU/dl, AST ≥ 30 IU/dl) was found to be more common among scrub positive patients. Non scrub patients had shorter duration fever (<3 days), and, altered sensorium (90.58% vs 85.37%) with a poorer GCS

and seizures (86.54% vs 80.54%) more commonly. Eschar was found in only 5 scrub positive patients and maculopapular rash was noted among 5.62% patients. Mortality among scrub positive was lower (11.92%) as compared to patients who were scrub negative (26.32%). Scrub typhus remained the major etiological agent (44%). JE is still an important etiology (13.76%). In a large group of patients (32.31%) with a significant mortality the etiology still remained unidentified.

Clinico-Epidemiological Dimensions of COVID-19 during Infection & Post-Discharge: A Case Series in and around Gorakhpur in Eastern Uttar Pradesh

The study was initiated from Basti district on May 15, 2020. Data collection was done by In-depth interviews using a semi-structured schedule and a GPS device. Centre also utilized data available from ICMR portal. A total of 8488 subjects were screened for COVID-19 during the study period from March 23 rd to May 15th 2020. A total of 204 lab-confirmed cases were detected in the 7 districts of eastern Uttar Pradesh. The median age of cases was 25 years (range: 2 months-71 years) and 180 (88.2%) of them were males. 197 (96.5%) of them were asymptomatic at the time of diagnosis. Of them, 147 (72.05%) in-migrated during mass migration from different places of the country (mostly Mumbai and other places in Maharashtra) after countrywide lockdown. None of them had recently travelled from any foreign country. Infection transmission in the region could be broadly classified in two phases. In first phase transmission was observed in three parallel situations.

First, a localised cluster containing 17 lab confirmed cases in Basti, showing familial transmission along with transmission from a funeral of first reported case of the region where source of infection in the index case could not be identified but the district administration and health system of Basti was able to control further transmission from this cluster. Second, was infection among people who attended

Tablighi Jamaat gathering. Total of 8 lab confirmed cases were directly linked to Tablighi Jamaat gathering. All of them were asymptomatic at the time of diagnosis and remained asymptomatic till recovery from infection. 6 of them were resident of Maharaj Ganj district, 2 belonged to Sant Kabeer Nagar district but no transmission was observed to any of their contact. Third, a local cluster of 24 infected individuals was observed in Maghar, Sant Kabeer Nagar where infection was brought in by a student who came from Deoband Saharanpur and stayed at home for 24 days before being isolated, coming in contact with 35 people (28 family members and 7 relatives). Later, 23 of them were tested positive for SARS COV-2 infection. Hence, first phase was successfully managed with contact tracing, containment, isolation and stopping further transmission.

The second phase starts with mass in-migration of labourers from different parts of the country. The initial success in control of transmission in the region was overshadowed with the mass in-migration of labourers. As of May 15th 2020, more than two third of total reported cases were migrant labourers.

Prevalence and abundance of ectoparasitic vectors of rickettsial pathogens and their animal hosts in areas reporting acute encephalitis syndrome (AES) in Gorakhpur district, Uttar Pradesh

This survey was performed from four villages of Gorakhpur district. A total of 3412 traps were set for the collection of rodents from studied villages. Four hundred four rodents were collected through these traps and trapping rate was 11.8 percent from these villages. These rodents were screened for the ectoparasitic infestation and two hundred thirteen (52.7%) rodents infested with ectoparasites. Major proportion of infestation of *Rhipicephalus Sanguinensis* (90.4%) ticks was obtained during the screening followed by *Xenopsylla cheopis* (2.17%) fleas and *Polyplax spinulosa* (0.14%) lice. Domestic animals were also screened for ectoparasites from

these studied villages. Maximum proportion of *Boophilus microplus* (58.3%) ticks was observed from domestic animals during the investigation followed by *Haemaphysus tuberculatus* (6.8%) lice and *Ctenocephalides felis* (4.4%).

National sero-surveillance for COVID-19

a) First sero-survey (May 2020)

For the first round of sero-survey, with the assumption of 1% sero-positivity, absolute precision of $\pm 0.95\%$, confidence interval of 80%, we need to enrol 361 (rounded to 400 individuals) from 10 clusters in a district. The wider precision has been taken to consider feasibility particularly in lockdown situation. Sample size for subsequent rounds will be adjusted (to account for better precision and acceptable confidence interval) after analysing the results from the first round of survey. The study findings were useful to guide in designing and implementing appropriate containment measures.

b) Second sero-survey (August 2020)

The seroprevalence obtained from the first survey for the selected districts (excluding containment zone) was 0.73% among the adult population. The doubling rate of cases in the country is approximately 4 weeks. Hence, the burden of infection is expected to become four times in August in comparison to the figure in May. Results of recent serosurveys in Delhi and Chennai indicate that the seroprevalence among 10-17-year-old children is similar to the adults. Considering a seroprevalence of 3%, relative precision of 14%, confidence interval of 95%, and design effect of 3.5 the sample size is calculated to be 22,041. Assuming a refusal rate of 20% we will need to enrol 28,000 individuals across the country. Centr will allocate a minimum of 400 individuals to each of the 70 districts that were included in the first survey. Within each of these 70 districts, 40 individuals will be included for the survey from each of the same 10 sampling units (villages in rural are assigned and wards in urban areas) that were selected in the first survey.

c) Third sero-survey (December 2020)

SARS-COV-2 poses a high occupational risk to healthcare workers who are at the forefront of management of COVID-19 cases in hospital settings. Knowledge of the burden of infection among healthcare workers is important to measure the risk of intrahospital and outside hospital transmission of SARS-COV-2, and evaluate the in-hospital infection control practices and adherence to non-pharmaceutical interventions as well. A sero-survey of SARS-COV2, conducted in August 2020 by Brihanmumbai Municipal Corporation, NITI-Aayog and Tata Institute of Fundamental Research, in Mumbai found that 27% health workers had developed antibodies. Another study in a private hospital in Mumbai reported that 91% of 23 healthcare workers with a previous history of RT-PCR-confirmed COVID-19 infection, 70% with previous COVID-19-like symptoms, and 4.3% of asymptomatic healthcare workers tested positive for IgG antibody using Abbott CLIA test. Considering the lack of information at a country level there is a need to generate evidence on the burden of SARS-COV-2 infection among healthcare workers, more so in light of the ongoing planning and prioritization for vaccination. It is proposed to conduct the third round of Serosurveillance to know the trend in spread and burden of SARS-COV-2 infection in the community and healthcare workers as per change in epidemiology and public health response to the epidemic in the country.

ICMR-RMRC, GORAKHPUR, KEYLONG FIELD STATION

The Field Station Keylong was established to address the prevailing health issues in tribal region where medical facilities are minimal. In 2020-2021, one project on reproductive health is on-going while that on community health need assessment was completed.

Study on Reproductive Tract Infection (RTI) among women in Lahaul & Spiti district

Reproductive tract infection among tribal women of Lahaul and Spiti is a major health concern. Due to heavy snowfall and temperature below -20°C , personal hygiene of the women is compromised. They are reluctant for bathing sometimes even during menstruation and thus favouring manifestation of myriad of pathogenic microorganisms in their body leading to RTIs. In this study, the patients were screened using symptomatic approach i.e. (those showing RTI symptoms) and bio-samples were taken from women who voluntarily agreed to provide the sample. Then the sterile swab was inserted through vaginal introitus about two inches deep and gently rotated for 10-30s so that the fluid gets absorbed onto swab as it gets moistened from vaginal walls. A total number of 690 high vaginal swabs containing vaginal sample were thus collected from tribal women and processed for per speculum examination for diagnosis of bacterial vaginosis (BV), trichomoniasis (TV) and candidiasis.



Fig. 8: Keylong : Study of RTI among local women.

ICMR-REGIONAL MEDICAL RESEARCH CENTRE, DIBRUGARH (ICMR-RMRCNE)

COVID-19

Population based serosurveillance for SARS-COV-2 infection in India

The first, second & third phases of national COVID-19 serosurvey completed successfully in three selected districts of Assam (*viz.*, Kamrup Metro, Udalguri, and Karbi Anglong). In Assam, over 2.6 to 20.9% of the adult population appeared to have been exposed to the SARS-COV-2 before the end of August 2020.

SARS-COV-2 serosurvey in Dibrugarh district, Assam

Seroprevalence of SARS-COV-2 infection investigated in 60 clusters of Dibrugarh. Relationship with demographic variables & comorbidities studied. Overall prevalence of SARS-COV-2 IgG antibody (which denotes past infection with the virus) was found to be 50.25 % in Dibrugarh district. The seroprevalence was higher in urban areas (59%) than in rural areas (41%). The seroprevalence was higher in subjects having comorbidities of hypertension (62%) and Diabetes mellitus (69%).

Evaluation of pooled sample testing for COVID-19 diagnosis

Pooled-sample testing for COVID-19 diagnosis by real-time PCR evaluated through a multi-site comparative evaluation of 5 & 10-sample pooling was done. It was found that pooling of 5 samples rather than 10 samples gave a consistent result across all the laboratories. Thus, pooling of 5 samples was recommended in low COVID-19 prevalence regions.

Evaluation of normal saline for sample collection for COVID-19 diagnosis

A comparative study conducted on efficacy of normal saline (as against commercially available

VTMs) for collection of samples for COVID-19 diagnosis by real-time PCR. It was found to have 100% concordance with VTM upto 10 days of collection of samples stored at Room Temperature.

ICMR-COVID-19 biorepository network in India

Establishment of a biorepository for COVID-19 positive cases has been initiated. Overall 114 COVID-19 positive cases have been included till date.

Follow-up of adverse effects following immunization (AEFI) with COVAXIN

The AEFI experienced by health care workers after receiving COVAXIN vaccination in Sonitpur district of Assam were followed up. A total of 1599 cases were followed over phone. Pain at injection site was the most common AEFI (12.6%) followed by headache (4.5%) & fever (3.2%) at 7-day post 1st dose of vaccine

Suspected SARS-COV-2 Reinfections in health care workers from Dibrugarh, Assam

Suspected SARS-COV-2 'reinfections' investigated. Not all resurgence of symptoms with positive test result were true reinfections, rather they may be labelled as retest positives. It is therefore very important to critically analyze the suspected cases of reinfection to be labelled as true reinfections.

COVID-19 associated stigma and related factors

COVID-19 being a new and contagious disease, facts and rumours often run along together. A mixed-methods study tried to understand COVID-19 associated stigma in the community. Data from Kamrup (metro) district showed high awareness about COVID-19 and a positive attitude towards infected persons from the neighbourhood. Fear of the disease during the initial days of the outbreak was more compared to the later phase of the outbreak.

Mental health & stigma in health workers involved in COVID-19 services

Investigated the mental health challenges faced by healthcare personnel during COVID-19. The occurrence of psychological distress, including depression, burnout, anxiety and other associated mental health outcomes among healthcare personnel (doctors, nurses, laboratory technicians, etc.) engaged in COVID-19 response was assessed to gain insights on the experiences with regard to stigma faced by the health care providers, challenges in work and family relationships and individual challenges (sleep, eating patterns etc.)

Impact of COVID-19 on maternal and child health (MCH) services

The MCH services through the public health system in the northeast were found to be affected by COVID-19 pandemic. Decline observed in JSSK beneficiaries, hospital deliveries, antenatal OPD turnouts, SNCU admissions and child immunization.

Expression profiling of hsCRP and ACE2 in COVID-19 patients

This recently initiated study would perform expression profiling of inflammatory genes *hsCRP* and *ACE2* among COVID-19 patients and assess relation with disease severity.

OTHER COMMUNICABLE DISEASES

Rickettsial diseases in the states of northeast India

The third phase of study on the epidemiology, disease burden and vectors of rickettsial diseases was conducted in Manipur, Tripura and Sikkim during the reporting period.

Climate change impact on seasonality and distribution of insect vector borne diseases

The peak transmission seasons of important insect vector borne diseases were described in Nagaland. High-risk geographical areas were mapped through

remote sensing and GIS. Six districts of Nagaland were highly affected by insect borne rickettsial diseases, viz. Phek (1.28%), Mon (31.28%), Tuensang (6.93%), Kiphire (3.7%), Kohima (3.96%) and Dimapur (2.77%). Scrub typhus (ST) cases were reported mostly among people residing in areas close to paddy fields (shifting and terrace cultivation sites) and forests.

Prevalence and drivers of zoonotic pathogens in livestock farms

Screening of seven bacterial zoonotic pathogens (*Brucella*, *Klebsiella*, *Campylobacter*, *Escherichiacoli*, *Leptospira*, *Staphylococcus* and *Salmonella*) along with their antibiotic resistance patterns were conducted among animal handlers from Assam and Meghalaya. *E. coli* was the most prevalent (32.2%) zoonotic pathogen among the handlers followed by *Klebsiella* spp. (6%) and *Staphylococcus* spp. (3.47%).

Clinical and epidemiological study of Lyme disease

In this recently initiated multicentre study spanning seven states of India, baseline data on Lyme disease would be generated. Feasibility of detecting the pathogen from clinical samples and ticks using TaqMan PCR assay would also be established.

Leptospirosis in Assam

Seroprevalence of Leptospirosis in distinct eco-geographical zones (viz. hills and plains) of Assam investigated. Hospitalized acute febrile illness patients screened for leptospirosis, too.

Quality assurance for Leptospirosis testing

An external quality assurance program for molecular diagnosis of Leptospirosis.

Quality assurance for scrub typhus testing

A quality assurance program for serological and molecular testing of scrub typhus in DHR virus diagnostic laboratories. Nationwide cut-off for anti-scrub IgM antibodies attempted.

Genetic and biochemical characterization of insecticide resistance in potential mosquito vectors of Japanese encephalitis in Assam

Insecticide resistance among principal JE mosquito vectors in Assam (*viz.* *Cx. Vishnui*, *Cx. Tritaeniorhynchus*, *Cx. Pseudovishnui*, *Cx. Quinquefasciatus*) were studied. Putative genetic polymorphisms in candidate genes (*viz.* *VSSC* gene, *CYP9M10* gene) influencing resistance patterns were investigated. Further, gene expression studies of cytochrome P450 genes have been performed.

Accelerated malaria control interventions in areas with Jhum cultivation

The operational feasibilities of low-cost, targeted and customized interventions malaria control among Jhum cultivators of hilly forested regions of 2 subcentres of Dhalai district in Tripura with major malaria burden (API: 50-200) evaluated.

Cytokines in relation to *Plasmodium vivax* malaria in Assam

Cytokine profiling was carried out in patients infected with *P. vivax* malaria (RDT, microscopy & PCR-confirmed). There were significant elevations in interleukin 6 (IL-6).

Etiologies in non-malarial fever cases

Investigation into the load and pattern of arthropod-borne viral and bacterial diseases along with their vectors, and their etiological contribution to non-malarial fever cases in Tripura.

Seroprevalence of *Toxoplasma gondii* and its risk factors in pregnancy

Studies on seroprevalence of *Toxoplasma gondii* in pregnant women from the tea-garden community of Assam detected 32.27% IgG positivity and 2.21% IgM positivity. The cases are being followed up to assess the pregnancy outcomes.

Mass Drug Administration (MDA) Coverage & Compliance Assessment Survey

To assist in lymphatic filariasis elimination programme, the MDA coverage and compliance

was surveyed in Dibrugarh district. An average difference of 18.5% found between MDA coverage and compliance. Need for additional mop-up rounds reiterated.

Surveillance of Food Borne Pathogens (FBP) from North-East India

Raw meat and fish samples from different local markets of Dibrugarh and Tinsukia districts were collected and tested for food-borne pathogens. Communication networks for food-borne disease information were set up involving State Health Authorities and Food Safety Officers.

Community-based study of *Cryptosporidium* spp

Diarrhoeal samples tested for *Cryptosporidium* spp. in four locations of Dibrugarh by microscopy, serology and molecular methods. Overall, 4.21% samples were positive for *Cryptosporidium* oocysts using modified ZN staining, 1.40% samples were positive by ELISA and 6.1% samples were positive in real time-PCR. Environmental water samples (both drinking and recreational) were tested as well.

A hospital-based study on neonatal sepsis in Assam

The bacterial aetiologies, antimicrobial sensitivity & risk factors of neonatal sepsis investigated in four different districts of Assam (*i.e.* Dibrugarh, Tinsukia, Dhemaji, and Silchar). Most common risk factors associated with sepsis were low birth weight and prematurity. Out of 205 culture positive cases, 55% were gram-positive and 45% were gram-negative organisms. The most common gram-negative bacteria isolated were *Klebsiella* spp. (85.7%) followed by *E. coli* (10.7%), *Acinetobacter* (3.6%). Antibiotic sensitivity pattern showed the highest resistance to ampicillin followed by gentamicin.

National survey for state-wise prevalence of pulmonary tuberculosis

So far, more than 11000 individuals have been covered. Based upon interview and X-ray reports, 1452 participants were eligible for CBNAAT

sputum test. All TB detected cases were reported to the respective district local RNTCP for treatment course and surveillance.

Molecular study on epidemiology & disease dynamics of *Mycobacterium tuberculosis*

Molecular investigations using NGS-sequencing of *M. tuberculosis* isolates from Tripura, Meghalaya and tea-gardens of Assam. Relationship of genetic, nutritional and behavioral characteristics of host with pathogen genetic profile explored.

Human pulmonary paragonimiasis in crab-eating communities & smear negative TB

The institute is leading this pan-India task-force study on pulmonary paragonimiasis that is often misdiagnosed as smear-negative pulmonary TB. Training of staff and supply of in-house developed ELISA kits to the study states completed. Experimental infection induced in Wistar rats. Paragonimiasis metacercariae were reported for the first time from Kerala.

Assessment of acute viral hepatitis and chronic liver diseases in northeast India

Hospital-based screening of hepatitis virus infections (A, B, C, D and E) along with genotype and subtype information in relation to liver diseases across 9 hospital sites from 8 states of northeast. Among the total 1548 screened cases, the various different clinical conditions include acute viral hepatitis (34.1%), acute liver failure (1.7%), chronic hepatitis (35.7%), liver cirrhosis (27.3%), and hepatocellular carcinoma (1.0%) respectively. Among the hospital sites, overall prevalence of various hepatitis viruses were: HAV 8.2%, HEV 6.3%, HBV 31.7%, HCV 15.3% and HDV 1.2%. Screening activities also carried out in pregnant women.

Sentinel surveillance for influenza including avian influenza in Dibrugarh

Overall, 1084 samples collected from Dibrugarh were tested for influenza virus during the reporting

period, out of which 9 were positive for influenza A (Influenza A subtype H3N2-4 and H1N1pdm09-5) and 15 were positive for influenza B (influenza B subtype-Victoria).

NON-COMMUNICABLE DISEASES

Self-monitoring and decision support for blood pressure control

A mobile-based application named “MyHeart” to facilitate self-monitoring and enabled with decision support facility developed for prevention and control of hypertension. Cluster-randomized trial conducted involving two districts covering 12 clusters (6 intervention and 6 control).

Population Based Stroke Registry in Dibrugarh, Assam

A rural population-based stroke registry covering two blocks of Dibrugarh district (Lahowal and Barbaruah) established. Feasibility of an acute stroke clinical care pathway also assessed using a mobile stroke unit (MSU) equipped with portable CT-scan. The registry has so far recorded 553 stroke cases (Male: 361, Female: 192) in the study area. In addition, it has also registered a total of 1599 (Male: 1044, Female: 555) acute stroke cases beyond the study area who came to the hospitals for treatment.

Health and demographic surveillance system in Dibrugarh, Assam (Dibrugarh-HDSS)

HDSS established for epidemiological and programmatic evidence/intervention in Dibrugarh district, encompassing 60 villages and 20 tea gardens. Baseline assessment covering 1, 06, 769 participants (Village: 46, 762 and Tea Garden: 60, 007) completed.

Screening, awareness & counselling for sickle haemoglobin in tea garden communities

Fieldwork activities were drastically affected by COVID-19 pandemic. Thus, educational videos / animations in local language were developed for awareness generation. These were disseminated

in the community via social media and digital platforms.

Haemostatic derangements in β -thalassemia syndromes

Biochemical and haematological characterization of the coagulation derangements involving clotting factors, platelets and endothelium conducted in various β -thalassemia syndromes.

Epigenetic modification and liver cancer risk in high incidence regions of northeast

Methylation profile of important tumor suppressor genes (*p16*, *APC*), DNA repair genes (*GSTP1*, *MGMT*) studied among liver cancer patients from Sikkim & Arunachal Pradesh.

IMMUNOLOGY

Human immune response to SA-14-14-2 vaccine

Integrative functional analysis of the immune responses against live attenuated JE vaccine was performed in humans (n = 94) on day-7, day-14 and day-28 post vaccination. a significant increase in the frequency of IgG-antibody secreting cells (ASCs) was observed at Day-7 after immunization in 38 individuals. However, no variation in frequency of total IgG-ASCs was observed on Day-7 after immunization in 36% subjects. Cytokine assays revealed higher expression of GRO-A, IL16, TNF-A and MIP-1B on day-7.

Helper T-cell repertoire in flavivirus infection and vaccination

Comprehensive assessment of the immunological aspects of the JE vaccine SA-14-14-2 was carried out with special reference to the role of follicular helper T-cells. Hospitalized JE virus-IgM positive 62 patients were enrolled as infected cohort. Healthy individuals with no existing JE virus-IgG/IgM antibodies were screened and 94 healthy consenting participants were vaccinated with JE vaccine SA-14-14-2 and enrolled in the study.

Merozoite surface protein and cytokines in malaria during pregnancy

Cytokine responses (from CD4 and CD8 cells) triggered by merozoite surface protein (MSP) and their role in the development of malaria during pregnancy investigated.

Mobile Application for Immunization Data in India – MAIDI

The Phase-I pilot study of the MAIDI m-Health application completed in four health sub-centres under Lahoal Block PHC of Dibrugarh. Acceptability and feasibility of the MAIDI application among beneficiaries as well as health care workers demonstrated.

BASIC RESEARCH

Anti-leishmanial properties of medicinal plants from North East India

Three promising compounds extracted from native plants of the northeast tested for anti-leishmanial activity in transgenic *L. donovani* amastigotes expressing intracellular luciferase (MHOM/IN/80/Dd8). Parasite killing was detected by luciferase assay.

Hybrid Para-Amino-Benzoic Acid-1, 3, 5-triazine derivatives for antimalarial activity

A library of 500 compounds was designed, out of which 5 potential compounds were synthesized. These were screened *in-vitro* for antimalarial properties in chloroquine sensitive *P. falciparum* strain (3D7) and chloroquine resistant *P. falciparum* strain (Dd2).

Point of care diagnostics and drug resistance monitoring technologies for malaria

A Proof-of-Concept developed for rapid, point-of-care, highly sensitive and highly specific visual detection (naked eye/ultraviolet illumination) of *P. knowlesi* DNA (A1H1 strain) in a single pot assay using isothermal-CRISPR.

Test kit to distinguish Japanese Encephalitis among closely related flavivirus infections

Peptide-based ELISA kit designed for facilitating the differential diagnosis of Japanese encephalitis (JE). Initial results demonstrate good ability to differentiate JE from Dengue.

Regional Viral Research and Diagnostic Laboratory (Regional-VRDL)

COVID-19 diagnostic services by real-time PCR provided for 223922 samples (from Assam, Nagaland & Arunachal Pradesh), of which 9771 were positive. Further, capacity building & training of health workers, and further quality control services carried out. Moreover, 8407 samples (nasopharyngeal swab/ throat Swab/ Blood/ CSF/ Stool) tested from different parts of northeast, out of which 711 samples were positive for various viral & non-viral pathogens.

DBT-Animal house facility for Biotechnology Research in North-eastern Region

Development of an advanced Animal House Facility that will be accessible to biomedical / biotechnology researchers from the entire North Eastern Region is currently under progress.

ICMR-REGIONAL MEDICAL RESEARCH CENTRE, PORT BLAIR (ICMR-RMRCPB)

RISK REDUCTION / ELIMINATION OF INFECTIOUS DISEASES

Double fortified salt (DEC + iodine) as a supplementary measure to the ongoing MDA for eliminating a persistent focus of diurnally sub-periodic *Wuchereria bancrofti* toward accomplishing elimination in the entire Nancowry group of islands

Four Isles in Nancowry group of islands were endemic for diurnally sub-periodic *Wuchereria bancrofti* (DspWb). Double fortified (DEC+iodine) was implemented in two of the four Islands to determine the impact of mass consumption of *Diethyl Carbinamine* (DEC) fortified salt on

LF infection. Supplementing MDA with mass consumption of DEC fortified salt (0.2% w/w) enhanced the reduction in microfilaremia (mf) and the infection levels were less than one. Thus the advantage of supplementing MDA with mass double fortified salt was demonstrated. The study further suggested the need to extend the distribution of double fortified (DEC+iodine) salt to the other two islands, where mf more than 1% were observed. DEC fortified salt strategy is ongoing in two islands (Kamorta and Chowra), endemic for DspWb infection towards the elimination of the DspWb from whole Nancowry group of islands, a lone focus India. The impact of mass consumption salt will be carried out at the end of December 2021, after one year post implementation.

Control of Tuberculosis among the Nicobarese of Car Nicobar: Consolidating the gains of a strengthened public health system and the recent socioeconomic progress

Out of six tribal groups of Andaman and Nicobar Islands, Nicobarese tribe a largest population constitute about 98% of the total tribal population and live in Car Nicobar Island. A population of about 17, 000 residing in about 3500 houses in 15 villages. Tuberculosis is one of the major public health problem among them. The study was initiated in March 2019 when a total of 45 patients were on the role of RNTCP, out of which 39 patients had pulmonary TB and remaining 6 had extra pulmonary TB. Six out of 39 had MDR TB and the remaining had infection with strains sensitive to all drugs. Towards the elimination the efforts implemented include 1) *Detection of TB among all chest symptomatic cases in the community*, 2) Continues counselling of alcoholic abusers and de-addiction program 3) Upgrading the component of contact screening into an active surveillance of contacts and monitoring of contacts with latent TB infection (LTBI) and create a sense of ownership among the people about the program. Interferon Gamma Release Assay (IGRA) to determine LTBI was conducted among 155 contacts and 81 were tested found positive for latent TB. The details were

shared with state and District officer for the specific therapy .

Establishment of a Network of Laboratories for Managing Epidemics and Natural Calamities: State Level Viral Research and Diagnostic Laboratory

In addition to providing viral diagnostic support to whole islands, the ICMR -RMRC contributed in diagnosis, contact screening and identification of hot spots during SARS-CoV2 /COVID-19 pandemic since from March 2020 as designated nodal COVID-19 laboratory using RT-PCR . The laboratory with BSL 3 facility is operational 24X7. Soon after, initiation of confirmatory diagnosis using RT-PCR, Andaman & Nicobar Islands, though there are resource constraint, reported the highest test per million in the Country . Anticipating a high workload and scarce availability of resources in the islands as well as the difficulties in procuring test materials and consumables, that have to be imported from Mainland- India, which is difficult in particular during the lockdown, a cost-effective pool testing technique was introduced for the first time at Andaman & Nicobar Islands in India . The technique facilitated the screening of a large number of samples in short duration with minimum resources and limited facilities, thus saving of considerable expenditure with minimum manpower and short processing time. A total 67000 samples were screened and identified 3400 positives up to March 2021 and support continued during second upsurge.

Study on the prevalence of oral premalignant and malignant lesions and the associated viral etiological agents among the tribal population of Car Nicobar Island

A total of 1239 individuals who gave informed consent were screened for any oral premalignant and malignant lesions. Among the individuals screened, the mean age of participants was 44 years and among them, 529 (43%) were males and 710 (57%) were females. The Nicobarese

largely belonged to Upper lower socio-economic class (60%) followed by lower middle (18%) and upper middle class (16%). The study showed that the usage of tobacco and alcohol were high among them. It was found that 10% (121) of the Nicobarese smoked cigarette and *beedi* and 86% (1062) of them used smokeless form of tobacco. The most common form of smokeless tobacco used were the combination of *Zarda* with betel nut and slaked lime (46%)/ *Zarda* with betel leaves, betel nut and slaked lime (26%) which were chewed by 67% of them every day. The use of *sukka*, a preparation with tobacco and lime which is placed in the buccal/labial vestibule is also predominant among Nicobarese, either used alone or in adjunct with other smokeless tobacco.

ESTABLISHMENT OF LEPTOSPIROSIS LABORATORY NETWORK ACROSS THE COUNTRY, QUALITY ASSURANCE AND EVALUATION DIAGNOSTICS

Providing quality assurance for both serological and molecular diagnosis in Leptospirosis for 30 DHR- virus diagnostic laboratories across the country

Leptospirosis is one of the most common emerging zoonoses worldwide with special reference to south east Asian countries where majority of countries including India are endemic. Global warming resulted extreme weather events such as cyclones and floods and thus exposure of large number of people to contaminated water bodies resulted occurrence of epidemics in several states associated with high morbidity and high case fatality. To maintain Quality, Assurance program was organised for Serological (ELISA IgM) and molecular diagnosis (RT- PCR) All 30 VRDLs reported the results with 100 % concordance for serological diagnosis whereas out of 23 laboratories, 18 laboratories reported the results with 100% concordance (Excellent), 3 laboratories with 95% concordance (Very good), one Laboratory with 90% concordance (Good) and remaining one Laboratory with 75% concordance (poor). Sentinel surveillance across the country

reported the disease at Punjab, Himachal Pradesh, West Bengal, Chhattisgarh, Andhra Pradesh, Telangana, Puducherry, Kerala, Jammu and Kashmir, West Bengal, Assam, Karnataka, Andaman and Nicobar Islands, Uttar Pradesh, Gujarat, Karnataka, Maharashtra, Tamil Nadu, Delhi and Haryana.

Truenat - micro real time-PCR for rapid diagnosis of leptospirosis at minimal resource settings

No confirmatory tests which is rapid and could be performed with minimum facilities available for leptospirosis. Molbio Diagnostics, Bangalore, developed a RT-PCR (Truenat™) that addresses some of the issues. It reduces the need for technical expertise and has the additional advantage of portability. The Truenat™ test revealed that the test gives almost similar test results of conventional RT-PCR with sensitivity of 97.4% and a specificity of 98.6%. It could be concluded that the test would be a useful tool for early diagnosis of leptospirosis with minimal facilities and the test results could be obtained within an hour and ensures that a specific therapy can be instituted during the early phase of the disease even at peripheral healthcare facilities as well during the outbreaks.

ONE HEALTH APPROACH - INTERSECTORAL COORDINATION - PREVENTION AND CONTROL OF ZOONOSIS

Strengthening of Intersectoral Coordination for Prevention and Control of Zoonotic Diseases – National hands on training workshop on leptospirosis

Ministry of Health and Family Welfare, Govt. of India launched a scheme “Strengthening of Intersectoral Coordination for Prevention and Control of Zoonotic Diseases with an objective to strengthen Intersectoral coordination between the different sectors. Development of Regional Coordinator (RC) is the key strategy of the program for strengthening

Intersectoral Coordination at the regional and state levels between different sectors for prevention and control of Zoonotic Diseases. RMRC Port Blair is identified as one of regional coordinator for strengthening Intersectoral Coordination between different sectors at four states / UTs, Andhra Pradesh, Tamil Nadu, Puducherry and Andaman & Nicobar Islands. Regional Medical Research Centre (RMRC) Port Blair organized Hands-on training workshop on diagnosis of Leptospirosis and tracking of animal vectors during 22nd - 25th March 2021. Participants from across the country attended the workshop. The states represented include Andaman & Nicobar Islands, Andhra Pradesh, Puducherry, Tamilnadu, Delhi, Himachal Pradesh, Goa, Punjab, Gujarat, Maharashtra, Kerala, West Bengal, Manipur, Assam and Uttar Pradesh.



Fig. 9: Secretary Health with participants. Hands-on training workshop on Laboratory diagnosis of Leptospirosis and tracking of animal vectors, 22nd - 25th March 2021.



Fig. 10: Panel discussions in Hands-on training workshop on Laboratory diagnosis of Leptospirosis and tracking of animal vectors, 22nd - 25th March 2021.

PUBLIC HEALTH

- SARS COV2 laboratory with BSL 3 facility is operational 24X7 and extended diagnostic support to whole islands. Soon after designation as nodal laboratory and initiation of confirmatory diagnosis using RT-PCR, , Andaman & Nicobar Islands, though there are recourse constraint, reported the highest test per million in the Country.
- Anticipating a high workload and scarce availability of resources in the islands as well as the difficulties in procuring diagnostic kits and consumables, that have to be imported from Mainland- India, which is difficult in particular during the lockdown, a cost-effective pool testing technique was introduced for the first time in India at Andaman & Nicobar Islands.
- Lieutenant Governors commendation certificate is awarded to RMRC in view of exceptional contributions provided to the whole Islands - diagnosis, contact screening and Identification of hot spots - SARS COV 2 / COVID-19.
- Demonstrated the advantage of novel strategy that supplementing MDA with mass double fortified salt (DEC+iodine) for eliminating diurnally sub-periodic *Wuchereria bancrofti* in two Islands. The study further extend the distribution of double fortified (DEC+iodine) salt to the other two islands, where mf more than 1% were observed towards the elimination of the DspWb from whole Nancowry group of islands, a lone focus India.
- The project on control of Tuberculosis among the Nicobarese Tribe of Car Nicobar: Consolidating the gains of a strengthened public health system and the recent socioeconomic progress is ongoing towards the elimination of TB among tribal population.
- Study on the prevalence of oral premalignant and malignant lesions and the associated viral etiological agents and identification risk factors among the tribal population of Car Nicobar Island is ongoing.
- Established leptospirosis diagnostic laboratories and conducted quality assurance for both serological and molecular diagnosis in Leptospirosis for 30 DHR- virus diagnostic laboratories across the country in view of emerging of leptospirosis in the country.
- Evaluated a Truenat - micro real time-PCR for rapid diagnosis of leptospirosis at minimal resource settings. The test results could be obtained within an hour and ensures that a specific therapy can be instituted during the early phase of the disease even at peripheral healthcare facilities as well during the outbreaks.
- National Hands-on training workshop on diagnosis of Leptospirosis and tracking of animal vectors organized during 22nd – 25th March 2021. Participants from across the country attended the workshop. The states represented include Andaman & Nicobar Islands, Andhra Pradesh, Puducherry, Tamilnadu, Delhi, Himachal Pradesh, Goa, Punjab, Gujarat, Maharastra, Kerala, West Bengal, Manipur, Assam and Uttar Pradesh .
- ICMR - RMRC Port Blair is identified as a regional coordinator for strengthening Intersectoral Coordination between different sectors at four stats / UTs, Andhra Pradesh, Tamil Nadu, Puducherry and Andaman & Nicobar Islands. Ministry of Health and Family Welfare, Govt. of India launched a scheme “Strengthening of Intersectoral Coordination for Prevention and Control of Zoonotic Diseases with an objective to strengthen Intersectoral coordination between the different sectors.
- Identified a total of 200 new leptospiral proteins differential expression level with respect to the induced physiological conditions as well as at sub-cellular level.
- Surveillance of High Risk Group Viral Pathogens Causing Influenza Like Illness in Car Nicobar indicated Influenza A and B responsible common pathogens.

SUPPORTING FACILITIES

During the period under report, Health systems research (HSR) and social and behavioural research (SBR) were intensified by starting new projects and with the completion of previous projects. Various new agreements and letters of intent were signed with different national and international organizations. Publication and information Division showcased the achievements of ICMR organization in various significant exhibitions throughout the country. The BMI Division strived to move the organization towards new goals of technology and digitization.

EXTRAMURAL RESEARCH

SOCIO-BEHAVIOURAL & HEALTH SYSTEMS RESEARCH (SBHSR) DIVISION

Healthcare access to the tribal population

The ongoing national task force projects addressed three important health issues of the tribal population. The first national task force project is to develop an effective care model for sickle cell disease (SCD) patients, which will be available at the primary health centre (PHC) level. This model aims to access the government health care system by the tribal population and for the capacity building in terms of knowledge and skill of the health care workers and infrastructure at different levels of the health system for screening and management of SCD. This study was implemented in the six tribal districts spread in six states. The screening system

has been developed under this project, which will be carried out in three levels. At the first level in the community, the accredited social health activists (ASHAs) and health workers have identified the patients based on the symptoms. A list of SCD related symptoms has been provided during the orientation of ASHA and health workers. These probable SCD patients are screened at the sub-health centre by the health worker. For this, sickle cell solubility test kit (Kruise Pathline Private Limited) is used. This is the first tier of screening for SCD. Those who are positive in the solubility test are screened at PHC through haemoglobin electrophoresis. Through this technique, the solubility positive people are diagnosed as SCD patients (Hb SS), carriers (Hb AS) and normal (Hb AA). Before initiating it, a rapid survey was conducted, and the total prevalence of SCD and carriers, respectively, was 1.52 (95% CI: 0.92-2.36) and 7.74 (95% CI: 6.32-9.36). The HbS gene had a frequency of 0.0539. A registry has been developed to record the details of patients and treatment.

The second component is treatment. All the doctors of these PHCs were given orientation in treatment by a clinical haematologist and treatment guidelines are provided. The PHCs are provided with the required medicines. Hydroxyurea is supplied. It is found during the formative phase that the communities' awareness of SCD is very poor. Only 32.1% (CI 31.2 to 33.1%) of participants had heard of SCD, 7.9% (CI: 7.3 to 8.4%) knew that SCD is hereditary, 19.4% (CI: 18.7 to 20.3%) knew that a blood test

could diagnose SCD and 23.9% (CI: 23.1 to 24.8%) knew that SCD is treatable. Only 13.1% (CI: 12.4 to 13.8%) knew that SCD could be prevented. Only 16% were aware of any SCD symptoms. Hence, several information, education and communication (IEC) and awareness programmes are going on in the community. Similar, orientation programmes have been developed for personnel of the health system. All these interventions are carried out through inclusive collaboration and community mobilization. Partnership building with multiple health and non-health partners and the community is one of the most important steps in implementing the intervention. Another vital component in enabling primary health care facilities to screen and manage SCD patients is capacity building and strengthening.

The second national task force project is to develop implementation strategies towards achieving universal health coverage by identifying and addressing the implementation barriers to improving access to health care services of assured quality without suffering financial hardship to the tribal community through the existing health care systems. This implementation research is going on in nine tribal districts. The formative phase of the research has been completed with the collection of both quantitative and qualitative data. Several access related issues from both the health system and the community are being studied. The focus is on the newly initiated Ayushman Bharat, and hence the issues related to access to newly established Health and Wellness Centres (HWCs) will be examined. These details will be used to develop an implementation research framework and plan to improve access and optimise the utilization of services of HWCs.

The third study is to develop implementation strategies for strengthening selected non-communicable diseases (NCDs) (hypertension and diabetes and chronic obstructive pulmonary disease (COPD)) related continuum of care under the National Programme for Prevention & Control of Cancer, Diabetes, Cardiovascular Diseases & Stroke

(NPCDCS) among scheduled tribe population. Also, implementation strategies for optimizing the NCDs-related services of HWCs are being developed and implemented. This implementation research is going on in six tribal districts. This implementation research with quasi-experimental design is being carried out in three phases - (i) formative research (pre-implementation phase), (ii) implementation research, and (iii) evaluation and dissemination for scaling-up of strategies. This study focuses on the activities of newly established HWCs and their activities related to the management of NCDs. The formative research is going on, and the findings of the formative research are helpful in developing the implementation research to avail the services of HWCs in promoting diagnosis and continuum of care of selected NCDs.

In addition to these three national task force projects, the Division has supported fourteen ad-hoc projects that addressed various tribal health and healthcare challenges. By organising ethnomedical practitioners in the Savara tribal group to engage with public health officials, an action research project in Andhra Pradesh is building models for effective preventive and curative care. It advocated a collaborative approach to healthcare for the tribal people, which is culture-sensitive and emotionally relatable to them because of the presence of their local healers in the care matrix. Mapping traditional medical practitioners (TMPs) in the study, PHCs reported that the patient load per month per TMP is 9.70. About 85% of the TMPs reported an experience of more than 20 years, and a little above 17% reported more than 35 years of experience. The most commonly treated illnesses by the TMPs are jaundice, gastric and stomach disorders, muscle and bone problems, and illnesses due to witchcraft/ancestral spirits/supernatural beings.

Another study looked at the health-seeking behaviours of tribal elders in Kerala and challenges related to healthcare service access and utilization. It highlighted barriers to tribal elders' access and utilisation of healthcare services, allowing policymakers to make strategy for optimal

healthcare system responsiveness. After adjusting for socio-demographic indicators and general household standard of living scores, the study evaluated the factors determining tribal older people's reliance on family members for healthcare service access. The functional ability of older persons as measured by instrumental activities of daily living (IADL) scale and activities of daily living (ADL) scale significantly and positively influenced their self-rated health. At the same time, perceived difficulties in accessing healthcare alongside multi-morbidity significantly reduced self-rated health. Another ethnographic study intended to examine the malaria prevention practices and treatment-seeking behaviour related to the tribal population of Chhattisgarh. Preventive, promotive and therapeutic care aspects will be designed in a participatory way with the local community and health care providers as part of the integrated intervention package.

The prevalence of urinary tract infections (UTI) among tribal women of Tamil Nadu was investigated. Preventive interventions, such as raising knowledge about UTI and using a foldscope to screen for bacterial infection, were introduced among tribal women. Foldscope was used to identify a few gram-negative microbes, pus cells, and RBCs within the first year. Foldscope would be utilized in the next step of the project to identify the organisms in the infected urine samples. The frequency of primary dysmenorrhea and the effect of a combined fitness training programme on accompanying menstrual symptoms among school-aged girls was reported from several tribal areas of Tamil Nadu. Out of 240 participants, 170 were found to have primary dysmenorrhea with pain, with 31% having mild discomfort, 28% moderate pain, 8% severe pain, and 4% having excruciating pain.

It has been observed that there is an improvement found in giving combined exercise training programmes among school-going tribal girls identified with primary dysmenorrhea. A study is being carried out to understand health-seeking

behaviour and to examine facilitators and barriers both from peoples' and providers' perspectives, which influence the delivery and utilization of maternal and child health services. Another study evaluated the effectiveness of health promotion intervention through community mobilization with women groups facilitated by ASHAs to improve maternal and child health status in the tribal population of Chittoor district. A model programme, Model for Oral Cancer Eradication, was conducted among the Narikurava tribal population in Puducherry to prevent, screen, and treat oral pre-cancer and cancer. During this investigation, precancerous and cancerous lesions were quantified, and screening and prevention strategies were developed. The majority of them consumed smokeless tobacco in varied forms. About 28% of the population had melanosis of the lips. None of the population exhibited facial asymmetry. 16.7% had palpable lymph nodes. But none were fixed. The palpable lymph nodes were attributed to other causes like periodontal and periapical abscesses, deep caries lesions, a grossly decayed tooth, pericoronitis, etc. Results indicated that about 41% of the participants knew about oral pre-cancer and cancer. 20% of the population knew that chewing tobacco causes oral cancer, and 22.8% thought that the growth of tissue in the mouth could be a sign of oral cancer. A study from Odisha is implementing as an accessible model for oral potentially malignant disorder screening in the tribal settings. A study is being conducted to strengthening the PHCs infrastructure for screening selective cancers has been initiated in a tribal district of Odisha. Monthly cancer screening clinics are being established in selected PHCs. It helps increase the stakeholders' knowledge, like female health workers and ASHAs, about the danger signs of different cancers. A study among North-East tribes of Assam and Mizoram documented various cardio-metabolic related risk factors, including hypertension, elevated fasting blood glucose, obesity, and metabolic syndrome with the help of artificial intelligence (AI) techniques, mainly machine learning tools such as classification,

clustering and prediction models, etc. It will further conduct health awareness campaigns on diabetes and cardio-metabolic disease among the tribal population of the North-East region.

In Uttarakhand, the ICAR's National Dairy Research Institute (Karnal) is implementing a dairy-based intervention among tribal communities. With a dairy-based intervention, this study aimed to alter the health-seeking behaviour of the people by enhancing their health and livelihood. An additional Delhi-based study examines the health status of migrating tribal populations in Delhi and the barriers to health care access. As part of a study conducted in Maharashtra, researchers applied the intersectionality theory to identify differences and similarities in indigenous communities. Inequalities in tribal health are examined from a political, social, economic, and cultural standpoint. Health services acceptance and uptake are also highlighted, and the hurdles and facilitators to their acceptance and uptake are identified. Another study from Maharashtra focused on improving access to cancer screening with the existing government health system and identified the challenges for the same. This study is implemented to screen common cancers and NCDs among women in a tribal block involving the state health system and the community. In the first year of the project, the qualitative research component of the study was completed. It was seen that there was limited knowledge regarding NCDs and common cancers among women. The women had heard about cancer and knew few causative factors and symptoms of oral and breast cancers because of advertisements on television and health education provided by health care workers. The women had limited knowledge about lifestyle factors like diet, salt, stress as causative factors for common NCDs like hypertension and diabetes. Traditional healers like Bhagats were sought for relief of symptoms. Economic burden, including health expenditure, proximity and trust, were the reasons for visiting the *bhagats* (faith healers) when they face discomfort or illness of any kind.

A study is intended to capture the broad transformations witnessed in tribal populations in terms of socio-economic change and issues in accessing health care facilities in the districts of Srinagar, Rajouri and Kargil. This study will also focus on the nature and extent of non-communicable diseases prevalent in the population. This study will specifically engage with barriers to using health care, the social and economic consequences of illness among the tribal population. A study to educate the tribes through health and nutrition education, group meetings, seminars with the help of tribal, health and women and child departments and NGOs, is initiated in tribal area of Telangana state. The study will help build a national collaborative effort for a multifaceted action plan to combat the growing burden of chronic kidney diseases (CKD) and their complications and focus on the causative factors of CKD burden in the tribal population. Generated data will help the state government of Telangana to develop a strategy for improved nutrition in tribes to reduce the CKD and NCDs burden.

Health systems research on road traffic injuries (RTIs)

Research is carried out to develop different decision support algorithms and identify suitable algorithms for handling post-crash care on road traffic injuries. This IT-enabled tool empowers the common man to just upload photos of the accident to the mobile application. The decision support system/algorithm of the tool will identify the location of the accident, evaluate the nature of the accident, the severity of the accident, the injured and initiate appropriate actions. This tool also identifies, selects the most appropriate hospitals, police stations, fire stations, etc. and alerts them immediately for effective handling of the injured. Another study is to design a novel On-Board Unit (OBU) for the driving environment. Using Dynamic Transportation System (DTS) as a part of vehicles can enhance driving by gathering and analyzing relevant data about the driving environment, giving the driver awareness while driving their car. The framework can distinguish different styles of driving behaviour

- drunk drive, distracted driver, fatigued driver, etc. OBU architecture has been built in with the idea of situation-awareness; it is divided into three stages representing the three fundamental subsystems of DTS – detecting, reasoning, and acting. The framework components interact to recognize abnormal behaviour shown by drivers, to alarm the driver and thus prevent accidents. It will send a notification to the nearest health centre after detecting the accidents based on the information given by vibration sensors.

A study is being conducted on two important National Highways (NH-91 and NH-93) of Aligarh district. It documented the RTIs surveillance in the urban and rural setup of Aligarh. The lacunae in data reporting and usage patterns of post-crash emergency care are addressed and resolved. For better usage of the “golden hour” after the crash, the study has captured the possible barriers and facilitators in providing early rescue. The intervention aims to improve the services at the crash site and a health facility and decrease the time in transportation of the patient from the crash site to the hospital. There is comprehensive study concerning the health systems responsiveness and the timely availability of medical care during the ‘Golden Hour’ of the road traffic injury. To fulfil this objective, the study included different levels of the hospitals and indoor patients who are victims of RTI. The social impact of RTI on the victim and their families, including their participation and utilization of health and social services, are also studied.

One study intends to examine to what extent road traffic injuries are rendered primary, secondary and tertiary care by the urban health services system. Mapping of the existing mechanisms and services within the health system is carried out. Further, based on close examination and analysis of these facilities, administrative and medical processes are being done to help delineate the inadequacies in the existing system. Opportunities for strengthening each level of care are also being explored to improve the response to RTIs, which in turn

can contribute to the strengthening of the urban health services system. Another study develops a unique online monitoring system with multiple components, aiming to optimise care of victims involved in road traffic accidents using integrated technology and medical delivery systems within the existing government and private health care delivery framework. This study exhibits several components, integrating modern technology with the medial delivery systems. These components are good anonymous citizen application, central command centre, central trauma registry and artificial intelligence.

Cultural epidemiological research has been undertaken in the Maharashtra districts of Satara and Palghar to provide evidence for enhancing the implementation of the National Collaborative Framework for Tuberculosis-Diabetes Comorbidity. It assessed the progress made by the Revised National Tuberculosis Control Programme (RNTCP) and the National Programme for the Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases, and Stroke (NPCDCS) in terms of joint TB-Diabetes collaborative activities as envisioned by the National Framework. The study would provide important insights into the ground-zero status of TB, diabetes comorbidity care, control and management issues from patients’ and providers’ points of view. Influence of demographic, clinical, genetic, and management patterns in maintaining long term abstinence among patients of alcohol use disorders who received treatment from de-addiction centres in Thrissur district, Kerala, was studied. This study evaluated the management pattern in different de-addiction centres and found the influence of treatment patterns on the outcome. It further evaluates the status of markers indicative of acute or chronic alcohol consumption (state markers) and markers of genetic disposition for alcohol dependence (trait markers) among the alcohol users.

Perspectives of people, physicians and pharmacists on sociocultural and environmental drivers of antibiotic resistance was studied in Karnataka.

This study is developing an innovative provider-based, individual-verified approach to estimate the burden of antimicrobial resistance in rural India. According to the pilot research to enhance the methodology, the first-year findings show that antibiotic awareness, attitude, and practices are good. Most respondents said it was inappropriate to use antibiotics prescribed by a friend or family member, and it was also inappropriate to repeat a previous prescription. In most cases, healthcare workers were the source of information concerning antibiotic resistance. Structure, staffing and factors affecting infection control were studied in Karnataka. It explored the existing structure and staffing pattern of the infection control department and to identify factors affecting infection control practices. Research from Chandigarh looks at the menstrual hygiene behaviours of adolescent females with intellectual disabilities. Early results suggested the average age of adolescents with intellectual disability at menarche is 13.2 years. Some caregivers informed that their daughters are experiencing irregular periods due to Polycystic Ovarian Disease (PCOD). Personal hygiene was the common, evident check for most of the caregivers of adolescents with intellectual disabilities. IIT-Kharagpur is conducting randomised controlled crossover research on mindfulness training to increase resilience among Indian college students. It developed and compared a mindfulness training intervention for improving attention and emotional regulation.

In the Alappuzha area, a qualitative study is conducted to determine the factors that influence acceptance and hesitation toward Japanese encephalitis vaccinations. This research covers the community's response, opinions, and perspectives, including their faith in vaccines, as well as the causes for vaccination acceptance and/or hesitation. The study also looks into how peer-to-peer communication affects vaccine reluctance. A prospective cohort study to understand the humanistic and economic burden of rheumatoid arthritis (RA) is studied in Puducherry. It assesses

the costs from the societal perspective using a bottom-up approach. The study shows the true burden of the diseases and the constant unease felt by the patients. Among the study population, 74.5% were housewives (home-makers). Most of the patients (64.5%) were not covered by any health insurance. Of those insured, 94.7% were covered by public/ government insurance schemes. Fourteen patients reported the loss of pay out of 65 who had paid work. Also, 47 patient attendees reported the loss of pay for accompanying RA patients to the hospital. The total cost estimated for RA was INR 27,723.12 per person per month. Of the total cost, 5.19% was health system cost, and 4.9% was an out-of-pocket expenditure. The indirect cost incurred by the patient due to loss of pay and replacement cost was INR 2,022 per patient per month, and it accounted for 18.16% of the total cost for RA. The intangible cost was high and contributed 71.75% of the total cost.

In Aizawl, Mizoram, research on living habits, daytime drowsiness, and chronotypes on sleep disruption and daily and seasonal sleep patterns is conducted among school children. This study looks at the elements that influence sleep length and quality. It also explains how living habits such as watching an electronic display at night, irregular dinner time, frequent caffeine consumption at night, sunlight exposure in the bedroom in the morning, and the room's brightness at night impact sleep and sleep-related variables. First-year results suggested that the morning type has the best sleep quality while the evening type has the worst. When we compared males and females, the effect of gender was not observed. In the different actigraphy parameters during weekdays and weekends, no significant difference was observed in all parameters.

Obstructive sleep apnea among commercial vehicle drivers and its correlates with road traffic accidents were studied in Delhi. This study determines the prevalence and risk factors for obstructive sleep apnea in commercial vehicle drivers. This study aims to develop strategies to increase awareness of the problem and develop an action plan for

managing obstructive sleep apnea. An educational intervention study to bring awareness of head injury while driving among patients with epilepsy is underway in Delhi. This study assessed the awareness in patients with epilepsy and their caregivers about driving prohibitions as per the motor vehicle act, 1938. Patients with epilepsy are to be educated through a multipronged educational intervention, and the intervention is to be evaluated. Cognitive and psychosocial intervention for persons with dementia in Rural India is underway in Chennai. This study identified resources for dementia care, including social support systems in the rural community. The feasibility of delivering a comprehensive intervention model including cognitive stimulation therapy is being studied.

The impact of migration on the psychosocial and economic well-being of elderly pandit migrants is being studied from selected north Indian cities. Health-risk behaviours among adolescents, particularly the role of difficulties in emotion regulation, parenting style and personality characteristics, are studied from IIT-Ropar. A case-control study design is being used in which initially assessment of adolescents for their indulgence into health risk behaviours would be done. Then the characteristic attributes of those high and low on specific behaviours would also be identified. Another study from Delhi assessed and identified factors affecting the availability, accessibility, acceptability and quality (AAAQ) of burns care in secondary and tertiary health care facilities. The co-designing approach to developing a care pathway with improved availability, accessibility, acceptability, and quality of burns care and rehabilitation is innovative. It would foster learnings for using a similar approach in other conditions requiring prolonged rehabilitation. Another study assessed the economic burden of childhood injuries in different sociocultural settings in Tamil Nadu and developed a cost-effective intervention model to prevent childhood injuries.

A community-based intervention study is initiated to determine the percentage of adult tobacco users

residing in the resettlement colony of Delhi who quit tobacco or attempt to quit tobacco use after behaviour modification therapy versus those given brief advice. These data on adult tobacco users will be assessed through questionnaires and analyses tests. Behaviour modification will be carried out using the Trans-theoretical Model of Behavior change. This study will help reduce the frequency of tobacco use, reduce the degree of nicotine dependence, and improve motivation to quit smoking as per the contemplation ladder.

A study is initiated to explore the experiences and needs of adolescent children living with a parent with mental illness with the ultimate aim of fostering the inclusion of their needs and concerns into mainstream mental health services. This study would help develop a theoretical understanding of children's experiences of parents with chronic illness and propose an intervention programme based on the needs of the children and test its feasibility. This study will also generate a checklist of the affected adolescent children and access to family functioning, coping and subjective well-being of adolescent children living with a parent with chronic illness. Another study attempts to illustrate the information about vulnerabilities faced by people with disabilities while accessing healthcare. A mixed-method approach will be used for collecting data. This study can be used as a base for formulating strategies to remove barriers and improve integration of persons with disabilities in society and understand healthcare provider's perspectives in the delivery of care for persons with disabilities.

A study is being undertaken to examine the association between substance abuse and suicidal behaviour among undergraduate students based on gender differences, behavioural changes, and patterns of substance abuse. It will be conducted in all provincial colleges of Assam. This study will help the parents and college authorities to understand the youths differently and make them aware of these evil social issues. This study will also assist them to be proactive to initiate appropriate

measures to prevent youth suicide and substance use. One study was initiated to help document the screen time in children in Lucknow, and it will help to find out the correlates and health outcomes of children aged 2 to 18 years of age. This study will also help to analyze screen time along with its correlates in children and would also help in setting guidelines at the national level. Multistage random sampling is used for enrolling students in the study. Counselling to the parents of the children will be provided in this study through a psychologist counsellor about the harms of using screen time and how to change their habit of using screen time.

A study is initiated to estimate the magnitude, burden and determinants of depression among young adults in selected higher educational institutions. This study will help strengthen individuals and communities by providing community-based gatekeeper training programs, inquiring about suicidal ideation, and improving access to services. This study will also help in forming mental health policy and the new mental health care bill. This study will also evaluate the feasibility of Let to Let out Depression Resource Centres among young adults. Another study to assess the self-reported multidimensional and structural relationship of health-related quality of life of TB patients, including multi-drug resistant and extensively drug-resistant TB patient's time points using the BSEM model. This study provides the impairment in HRQoL associated with TB at the initiation, at the end of the intensive phase, at the end of the continuation phase, and after three months of completing for anti-TB treatment. It also focuses on evaluating the impact of TB on quantitative measures of HRQoL of TB patients and demonstrates the association of HRQoL and adherence to TB treatment.

A study to explore the psychological impact of violence, psychosocial and rehabilitation needs, barriers and challenges in accessing services among women affected by gender-based violence (GBV) is going on. The study results will help frame a set of policy-level recommendations in providing

comprehensive psychosocial care and protection to women affected by GBV. The results will also facilitate policymakers, health administration, judiciary and various stakeholders to plan an effective strategy for improving the delivery of services to women affected by violence in the existing delivery system. A study to assess the perceptions of women regarding sexual harassment at the workplace in the health sector. This study will find the prevalence of sexual harassment using the Google forms with strict unanimity and decide how efficient the women are in their work. Thus, the study needs to address these grievances so that institutional efficiency also improves.

A study assesses the cognitive status in the community-dwelling older men and women and assesses the relationship between cognitive status and psychosocial factors among older people. This study tests the efficacy of a psychological intervention to improve the quality of life of older people. Psychological intervention may reduce the overuse of psychoactive medications and improve this vulnerable population's quality of life. A study to assess the lifestyle measures, education, and socio-economic status (SES) and how these traits are correlated with Coronary Heart Disease (CHD) risk factors in adolescent school children of Chittoor District, Andhra Pradesh. This study documents the information about SES, lifestyle, anthropometry, blood pressure, and biochemistry among adolescents. It assesses the CHD risk factors and examines the effect of social, economic, and behavioural factors on anthropometry and biochemistries for confounding factors. This study will also help frame policies for the welfare of adolescents and provide a platform to undertake subsequent genetic studies among adolescents.

A study reported the awareness, health-seeking behaviour and influencing factors, and social stigma related to two mycobacterium diseases (tuberculosis and leprosy) among the tribal population in relatively inaccessible areas of Pathanamthitta and Idukki districts of Kerala. The participants in the study had some knowledge

on TB and leprosy, which was significantly improved among participants. The area adopted for the study currently did not have any registered cases of tuberculosis or leprosy. According to the qualitative study, apathy, anxiety, lack of education, inaccessibility, fear of social status.

A study is conducted in Delhi to assess the spiritual problems and concerns faced by Indian palliative care patients and develop treatment guidelines. This study integrated the specificity of Indian society, culture, and spirituality. Another study analysed the constructed notions of employability of women TB patient workers across various work spheres and examined its implications for their employability. Financial support was one of the major unmet needs of working patients. The study also endorsed that occupational safety and health concerns are often less prioritized in informal work arrangements. Financial support was needed the most in the symptomatic period, during diagnosis and at the beginning of treatment due to TB's employment loss and earning loss.

A cross-sectional descriptive study was conducted to assess health literacy and its attributes among the adult population of Madhya Pradesh. The study concluded that a health information system should develop the contents based on the health literacy levels of end-users. A study was conducted to develop and validate a prototype of a web/mobile app-based positive psychological intervention for adolescents. With an increasing number of mental health cases in India, such e-intervention would be beneficial and cost-effective. The efficacy and effectiveness of IEC activities for health awareness and promotion among women were assessed in Rajasthan. Respondents acknowledged the sufficient supply of the materials, though mostly in the form of posters and pamphlets, which were reported to be futile. This study suggested the failure of reach of IEC media like radio, posters and hoardings that are heavily employed in promotional activities for health. Another study evaluated the IEC strategies employed and health education materials produced by different national programmes from providers' and users' perspectives. Though IEC strategies

and interventions have contributed to change in knowledge, behaviour and attitude of patients and the general population to some extent, it has been reported that there is still a wide gap and lack of awareness about their causes, available diagnosis and treatment options. A cross-sectional study assessed the impact of health education and awareness of the use of health care systems with the involvement of stakeholders in reducing neonatal mortality rate in the migrant population living in Hyderabad. The majority of the mothers were aware of the Janani Suraksha Yojana programme, and most of them utilized it. A community-based intervention from Delhi demonstrated the effectiveness of social and behaviour change communication (SBCC) strategy in preventing and controlling dengue in slums and slum-like pockets. Another study from Gujarat designed and tested a behaviour change strategy to improve uptake of services for severely malnourished children through the Integrated Child Development Services (ICDS) scheme.

A study from Chandigarh developed and implemented an innovative multi-level psychosocial intervention for sexually active men sex with men (MSM) to promote periodic HIV testing (as per the national guidelines). It has the potential to be scaled up in other parts of India and may contribute to a reduction in HIV transmission among MSM. Another study captured the morbidity load of a population, based on the type of illnesses prevalent at a given point of time, the treatment-seeking behaviour for those illnesses by levels of care and the cost involved in the treatment and the pattern of referral followed. It is to estimate the health care facility required to cater to the curative health care needs of the population across various levels. A study assessed the utilization and issues related to the effective delivery of the Government's health care services, schemes and programmes for marginalized groups in Maharashtra. This study found out key problems and issues related to health schemes that are meant for marginalized groups. A study from Tamil Nadu designed and evaluated the prototype health information system for rural women.

Impact analyses of the structural factors influencing effective service delivery and utilization of maternal and child health services were conducted in Kashmir. A comparative analysis of inequality in the primary health care system was conducted in Kerala and Assam. It identified the reasons for inequality and inequity in health care seeking. The impact of the involvement of self-help groups in improving reproductive health-seeking behaviour and service utilization by tribal women was assessed in the Nasik district of Maharashtra. This model is successful and can be scaled up in other tribal areas. Quasi-experimental research with pre and post without a control group was conducted to promote psychosocial competencies among rural Government school children in Karnataka. The outcome of the project would help in integrating psychosocial competency related activities in schools. A study assessed the internal consistency and content validity of comprehensive healthy eating and living index by adapting the healthy eating index and combining it with lifestyle indices for adolescents in the Indian context. Economic analysis of health-seeking behaviour of Hansen's disease (leprosy) was carried out in Tamil Nadu.

INNOVATION & TRANSLATION RESEARCH (ITR) & INTELLECTUAL PROPERTY RIGHTS (IPR), DIVISION

Development of a Non-Invasive Biodegradable Polymeric Micro projection Ocular Patch for Effective Corneal Delivery of Anti-Microbial Agents to Treat Fungal Infections of Eye

Designed and fabricated micro projection ocular patch, did in vitro characterization of drug loaded micro projection ocular patch and evaluated drug loaded micro projection ocular patch in vivo. Topical application of classical delivery systems like eye drops, ocular gels provide limited ocular drug bioavailability. The unique anatomical position, corneal-scleral barrier, nasolacrimal drainage, etc. may be attributed to the poor residence time resulting in poor drug permeation. Several attempts have been made in the past to address these challenges,

including nanoformulation-based delivery system (liposomes, micelles, nanoparticles), ocular inserts, ocular implants among others. These formulations provided marginal improvement in availability of drug at the desired site of action. Other procedures such as intrascleral, intravitreal injection were invasive in nature. A dissolvable polymer-based microneedle ocular patch (MOP) is developed using a micromolding technique.

The polyvinyl alcohol, polyvinyl pyrrolidone based MOP is designed in such a manner that drug limited to microneedle array only and concave base plate is drug-free. These microneedles are 500-550 μm in length and 250 μm in width at the base and tip diameter 20-30 μm . Further, the microneedle array has sufficient mechanical strength to sustain a target force required for insertion into the cornea. It can be used for the delivery of both hydrophilic and lipophilic drug molecules. All results of in-vitro, ex-vivo and in-vivo show its better performance over the existing marketed formulations. The effectiveness of MOP was established in in-vitro, ex-vivo, and in-vivo models. The MOP device can be further studied in clinical phases. It would be an essential drug delivery device possessing critical advantages, including improved ocular bioavailability, minimally invasive, reduced dosing frequency, and enhanced patient compliance, among others.

Biomaterial for designing of mandibular bony scaffold: Evaluation of Polymer-ceramic nano composite scaffold with BMP for critical size mandibular defects

Designed a 3D scaffold for mandibular reconstruction in critical size mandibular defects using a new material at IIT Kanpur. Synthesis, isolation & purification of BMP (Bone Morphogenic Protein) at IIT Kanpur, and compared the bone regenerative properties of this scaffold with or without BMP, with tricalcium phosphate and BMP in vivo (rabbit model) at KG Medical university, Lucknow.

A 3-D scaffold composed of Chitosan-gelatin nanohydroxyapatite reinforced with PCL nanohydroxyapatite nanofibres was developed and made osteo-inductive by incorporation of BMP-2 (bone morphogenic protein). Large maxillofacial bony defects resulting from tumor resections are serious reconstructive problems. Although autografts and allografts have been widely used, none of the available methods produce bone similar to the bone. Hence, tissue engineering strategies have been pursued, but with limited success due to shortcomings with 3-D scaffolding systems, cell infiltration and growth, or absence of appropriate growth and differentiation factors. Therefore, in this project a 3-D scaffold mimicking microenvironment of the bone, using a polymer-ceramic-nanofiber composite in the form of Chitosan-gelatin nanohydroxyapatite reinforced with PCL-nanohydroxy apatite nano fibres was developed.

The development of scaffold included synthesis and characterization of the individual constituents followed by in vitro and in vivo studies. The scaffold was made osteoinductive by incorporation of BMP-2 (bone morphogenic protein) and compared with Tricalcium phosphate scaffold with and without BMP in rabbit animal models. The novel biomaterial is a newly developed and tested bone substitute to be used as a graft material for maxillofacial bone defects. The physical properties of this biomaterial scaffold are quite superior to other comparable commercial bone substitutes like BTCP. In vitro studies demonstrated cell attachment and growth while in vivo studies exhibited better healing than comparable substitutes. Further studies directed towards incorporating stem cells originating from Dental pulp can be attempted to utilize the scaffold for bone tissue engineering. The scaffold along with DPSCs cultured in vitro can be grafted in critical defects created in rabbit bone for in vivo analysis.

Developing polymer based scaffold with electrical and topographical cue for neuraltissue engineering

Fabricated the chitosan based free standing neural scaffold – through normalcasted film and 3D electrospun film of polymer matrix composite. Engineered the composite for increasing its mechanical strength and electrical conductivity via alignment of CNTs inside polymer (chitosan) matrix, Evaluated bio compatibility, effect of electrical stimulation and topographical features on neuronal growth and Optimized the scaffold with additional functionalities to lead undifferentiated cells towards differentiation into neural cell lineage. Providing electrical cue through a soft polymeric neural scaffold for directional-neuronal growth is a challenge in itself, which has been addressed in this research. The shortcoming of existing polymeric neural scaffolds is mainly poor electrical conductivity or its absence altogether. Electrical conductivity is a critical cue for directional and accelerated growth of neurons. Carbon nano-tubes, with their excellent electrical conductivity, can be of help, if strategically aligned within the scaffold.

However, the reports available till date could only have CNTs aligned on the surface of hard substrate, which cannot be used as neural scaffold in-vivo. This research work was focused on engineering strategies for successful reinforcement of polymeric matrices with carbon nanostructures, namely, multi-walled carbon nanotubes (MWCNT) and graphene platelets (GNP). Through, rigorous comparative studies, the effects of alignment of these nanostructures within the polymeric matrices on physical and functional attributes of the scaffolds were evaluated. Successful alignment of MWCNT within the fibers of the scaffold improved conductivity as well as mechanical property. This scaffold was very efficient in healing injured sciatic nerve in rats. Besides, reinforcement of polymeric scaffold with GNP promoted radial stimulation, Electrical impulses stimulate directional growth of nerves. Existing nerve conduits without provision for electrical cues have limited efficiency of neural regeneration. This electro spun scaffold could completely regenerate injured rat nerve and restore motor function by guiding nerve sprouts towards

the freshly formed B ngner bands. Along with casted scaffolds reinforced with carbon nanotubes and graphene nano pellets individually developed, on which neuronal cells were differentiated. These scaffolds have significant potentials for neural tissue engineering applications, differentiating neural cells in neurological diseases.

Live Cell Electrospinning with Biomimetic Polymers for Bioengineered Bone Constructs

Performed osteogenic live cell electrospinning with bio-functionalizable polymers composed of aminoacids to evaluate cell viability and cell-migration across generated scaffolds and compare them against traditional electro spun nano fiber-cell seeding-incubation. Explored the osteogenic markers (osteocalcin, collagen I etc.) and related gene expressions (collagen I, II, osteocalcin, Alkaline phosphatase etc.) for understanding cellular functionality in cell impregnated scaffolds. The novel electrosun membranes were developed using live cell electrospinning technique using PCL as the structural framework and PVA as an aid to disperse the MC3T3 cells on the PCL frame and PGA as the bioactive polymer to improve bone tissue differentiation. The live cell electrospinning process preserved cell viability comparable to other live cell techniques reported in the literature. Importantly, the cells were shown to remain functional. Thus, the proposed method may have potential in solving the problem of homogenous cell distribution in bioengineered bone constructs.

Live cell electrospinning has gathered attention as a method for fabrication of tissue engineering scaffolds because of their ability to generate constructs with greater homogeneity in terms of cell distribution in the matrix. Several studies have documented live cell electrospinning technique preserves cell viability. However, ability of this technique to generate functional bone tissue engineering constructs has remained unexplored. In this work, a bone tissue engineering construct has been generated using poly (vinyl alcohol) as a vehicle to disperse MC3T3 cells onto a

polycaprolactone frame by electrospinning of the PVA-cell suspension with PCL solution in a coaxial set up. The constructs were characterized for physio-chemical properties and scanning electron microscopy was used to ensure that cell morphology remain unaltered due to the electrospinning process. Further, MTT assay was performed on day 1 and day 7 of culturing the construct and 81% viability immediately after electrospinning was found compared to positive control. Cell proliferation was also observed and confirmed by live/dead assay. In addition, alizarin red assay performed on the constructs after day 7 of culture exhibited that cells maintain functionality. Overall, it is concluded that engineered bone constructs can be fabricated by live cell electrospinning technique. Several parameters have been optimized and their effects on cell proliferation and differentiation observed.

The novel electrosun membranes were developed using live cell electrospinning technique using PCL as the structural framework and PVA as an aid to disperse the MC3T3 cells on the PCL frame and PGA as the bioactive polymer to improve bone tissue differentiation. The live cell electrospinning process preserved cell viability comparable to other live cell techniques reported in the literature. Importantly, the cells were shown to remain functional. Thus, the proposed method may have potential in solving the problem of homogenous cell distribution in bioengineered bone constructs. Manpower trained 3 but no paper or patent application was submitted by investigators.

Development of rapid point of care immunological and molecular diagnostics for lymphatic filariasis

It validated the utility (Sensitivity and specificity, both in lab and field conditions) of the developed filarial specific antibody detection ELISA and PoC diagnostics. Three diagnostic tests viz., a) Recombinant RMRCBLG1 antigen based Indirect ELISAs for detecting filarial specific IgG1 and IgG4 antibodies, and b) a lateral flow Point-of-Care diagnostic for detecting filarial specific developed

and the lab and limited scale field evaluation showed that are highly sensitive compared to microscopy and at least equal to that of the commercially available ICT test.

Lymphatic Filariasis (LF) is targeted for elimination by 2020, employing Mass Drug Administration (MDA) of Diethylcarbamazine/Ivermectin and Albendazole combination as strategy. Till date, several rounds of MDA have been carried out and the Transmission Assessment Surveys (TAS) is necessary for assessing the transmission, certification and surveillance post-elimination operations. There is a felt need for indigenous, less expensive and rapid diagnostics to cater to the needs of the national programme which requires millions of tests annually. Hence, an antigen biomarker (RMRC BLG1) from lymphatic filarial parasite, *Wuchereria bancrofti*, was identified, expression cloned and filarial specific IgG1 and IgG4 antibody ELISAs (IgG1 and IgG4) and a Lateral Flow Point-of-Care (PoC) tests were developed. The assays developed were validated both in the lab and field. There was no cross-reactivity when 4 malaria, 5 scrub typhus, 5 dengue samples and 4 helminth infections (Hookworm and ringworms) were tested. The sensitivity (%) and specificity (%) are 100, 98.8 and 100, 97.6, respectively. The positive predictive and negative predictive values of the two antibody assays are 98.04, 100 and 96.15, 100, respectively. Thus, these results showed that RMRC-BLG1 antigen based ELISAs have high specificity and sensitivity for detecting exposure to and active filarial infection.

Field validation of the two antibody assays was carried out in areas with (Vijayapur, Shirur, Badami and Guledgudd of Karnataka state and Goa) and without (Udupi Goa,) ongoing LF transmission and LF non-endemic areas (villages in Himachal and Uttaranchal states, and villages in Belagavi, Uttar Kannada and Chamarajanagar districts of Karnataka). Blood samples collected from endemic villages with ongoing LF transmission showed the presence of filarial specific antibodies. Interestingly, sera samples from Udupi, which

is declared as transmission free by the NVBDCP showed the presence of a significant prevalence of filarial antibodies (14.14%). The study also showed a high level of LF transmission in Jharkhand areas, as 68.42% endemic normal showed the presence of filarial specific antibodies. Sera samples collected from individuals residing areas in the Tarai region (Barkot) of Uttaranchal (considered as non-endemic for LF) showed antibody positivity. However, sera samples from LF non-endemic areas viz., Himachal Pradesh and from Siddi and Soliga tribal communities dwelling in deep forest areas of Karnataka state, did not exhibit the presence of filarial specific antibodies. These results indicate the high specificity of the RMRC-BLG1 antigen-based antibody ELISAs and their potential application in the diagnosis and monitoring of LF elimination programme. A prototype lateral-flow Point-of-Care (Lateral flow format) for detecting anti-filarial antibodies was developed in collaboration with Genomix Molecular Diagnostics Pvt Ltd., Hyderabad and in preliminary testing on 20 samples the test was positive for mf positives with the appearance of test line, and no test line in negative samples. The performance of the RMRCBLG1 IgG4 ELISA and RMRCBLG1 PoC test was assessed against standard tests viz., microscopy for microfilaria and commercially available Immunochromatography Card Test (ICT) for circulating filarial antigens using serum samples collected from Padeknur village, Vijayapur dist., Karnataka state. There was a good concordance between the performance of the two tests and ICT. Thus, the RMRCBLG1 IgG4 ELISA and RMRCBLG1 PoC test are highly sensitive compared to microscopy and at least equal to that of the commercially available ICT test

Multifunctional Porous Mineralized Bio ceramics/PSS Derivatives Nano composites Coatings on Electron Beam Treated Alloys Modulate the Directional Growth and Activity of Osteoblastic Cells for Orthopedic

The team synthesized the nano-composites scaffold (Phase I), synthesized minerals (Sr, Mg and Zn)

substituted hydroxyapatite (M-HAP) and M-HAP strengthen by Poly Sebacate Raffinose Citrate (PSRC) and Poly Sorbitol Sebacate Glutamate (PSSG) through novel microwave method. Investigators examined the influence of microwave irradiations on the microstructure, viscosity of slurry, porosity, and pore morphology of mineral substituted Hydroxyapatite/PSRC and PSSG nano-composites. Ascertained the compositional, structural purity, mechanical and thermal behavior of the synthesized bio-ceramics nanocomposite. Surface treatment and coating of porous nano-composites done in Phase II, with a view to promote the bio-resistivity of the implant metal (Ti alloys) sample, a suitable surface treatment procedure by electron beam treatment and achieved porous mineral substituted hydroxyapatite (M-HAP)/PSRC & PSSG nano-composites coating on the surface treated implant metal samples to improve the bio-resistivity, biocompatibility and mechanical properties of implant quality of Ti alloy. Resistivity of the nano-composites coatings with the aid of electrochemical and surface analytical techniques such as potentio dynamic polarization, electrochemical impedance spectroscopy, CV, XPS, FT-IR, XRD, SEM-EDAX and AFM, in-vitro testing of the implant coatings was done to study the biocompatibility of coatings in simulated body fluids, test the in-vitro behaviour of the coatings in cell culture medium, ALP activity level of the Osteogenic-related genes, Filopodia extension and morphology and In-vivo testing of the implant coatings. Further in-vivo experiments (Animal Model) in order to explain the applicability of the coatings yet to be done as a collaborative work in Sri Chitra Tirunal Institute of Biomedical Sciences and Technology, Trivandrum.

In bio-medical application, the clay/polymeric matrix processing many attentions from the researchers. This study introduces a new orthopedic titanium (Ti) implant with increasing bio-activity by treating the surface of Ti implant with bio-compatible composite coating. The hydroxyapatite (HAP)/Starch/Wollastonite (WST) clay composite was prepared by in-situ co-precipitation method

and the WST clay was prepared from bentonite clay. The osteoblasts activity of HAP was enhanced by adding minerals such as Mg^{2+} and Gd^{3+} into the HAP matrix to form MHAP ceramic. The final composite namely MHAP/Starch/WST was successfully coated on the orthopedic grade Ti plate by Electrophoretic Deposition (EPD) method. The functionality, phase analysis of the composite was evaluated by FT-IR and XRD analysis respectively. The mechanical properties of the composite were increased by presence of clay/polymeric blend in the composite. The Vickers microhardness of the MHAP/Starch/WST coated Ti was exhibited as 242 ± 1.92 Hv and the zeta potential value was showed as -16.76 mV for MHAP/Starch/WST composite. The morphology of the prepared composites and the apatite formation on the surface coated Ti was confirmed by SEM and HR-TEM analysis which indicates the bio-activity of the composite. This new bio-active implant will be useful for the bone regeneration application after more clinical studies.

Differential synchronous florescence-A new paradigm for probing oxidative stress and inflammation using serum samples

The team developed Device/Kit/Assay for detection and classification of diseased states according to vibrational spectroscopic signatures obtained from bodily fluids or their extracts. IoT based small devices for synchronous spectroscopy was designed for use in vibrational spectroscopic characterization. Two dimensional spectroscopic data showed presence of 2 or more characteristic contour peaks. Peak ratios were used to classify disease classes and machine learning methods could be applied to discriminate unknown samples into its respective class. Though patent is not filed the technique developed for using Raman harmonics of small volume of bodily fluid (or extract) diluted with aqueous media as disease state marker. Ratio of primary Raman peaks and Raman harmonics of small volume of bodily fluid (or extract), diluted with aqueous media, as disease state marker. Ratio of primary Raman and Rayleigh scattering as a signature of diseased state. Use of

2D synchronous spectral maps in aqueous sample discrimination. Magnification of signals by using bio material based films as amplifier. Use of nano-colloids to amplify signals. 1. Label free technique 2. Applicable wherever there is aqueous media based system. Thus, a versatile technique. 3. Can be done by layman. 4. Protein state determination is often an important step in disease diagnoses and follow up and can drive clinical decisions.

Hence, objectives achieved from this project by development of a one step optical technique for measurement of serum kynurenine/tryptophan (kyn/trp) ratio, Probing oxidative stress and inflammation using this technique. Assessment and diagnosis of different iron related disorders. Determination of drug (mainly iron chelating) efficacy and post operative health status. The variation of this ratio (trp/kyn) with iron overloading (development of fluorimetric serum ferritin sensor). PI found a tool to classify diseases which involve variations in ROS levels. As the technique can be scalable to deep learning and AI platforms, can develop inexpensive spectral tools using similar methodologies. The effects of chlorophyll A nanoparticles on the increment of NADPH/Trp ratio with respect to the Kyn/Trp ratio denotes that chlorophyll A nanoparticles might have a beneficial effect in shifting the redox balance more towards the reductive phase which is actually advantageous to the biological entity thus could have a checking or quenching effect on the oxidative stress mediated damages. So, it can be translated into the therapeutic domain with more research work on its mechanism of action. The varying Raman line increment in its intensities with serum samples of different disease classes which is characteristics of its class is indicative of the fact that this can lead us to a much simplified single step oxidative stress assessment. Possibility is there to develop a spectral metric for iron induced toxicity and undertake as ensign exercise on an epidemiological level. The team developed a PCA based algorithm to fish out the factors that causes the iron induced oxidative damage. The disease subclasses in which

the damage may vary in its extent can be classified using this powerful R based statistical tool.

Oxidative stress expresses an imbalance in a system constituting two species, reactive oxygen species (ROS) and antioxidants that detoxifies the ROS. Various disease conditions reflect differing extent of such imbalance. In Thalassemia (Th), the elevated level of ferritin indicating an increase in the biological free iron load eventually culminates into this imbalance. In inflammatory disorders like rheumatoid arthritis (RA), overload of iron is reported though not as much as that of Thalassemia, but good enough to cause oxidative Imbalance. Here team introduces a fusion of spectroscopically derived chemometric parameters like NAD/Tryptophan ratio, Kynurenine/Tryptophan ratio, Kynurenine/Tryptophan ratio and the altered spectral peaks of Raman line of water with statistical multivariate analysis by deploying Principal Component Analysis (PCA) on the stated evaluated parameters. In the process, the team developed a quantitative framework for classification of the said diseases. With the help of clustering tools in R, zoned out clear cut clusters representing each class of serum samples, the analysis of the so formed clusters depicted that the addition of chlorophyll to the serum samples have not only increased the clustering efficiency but also the robustness of the statistical data.

Thus, introducing chlorophyll based spectroscopic measurement which actually amplified the variation in the differential spectral pattern among the featured classes of diseases. This not only produced a classification with better resolution of the ROS dependent pathological conditions but also delivered a PCA based chemo metric hint at the effectiveness of chlorophyll as a potential oxidative stress quencher. Thus, casting a possible dual role of indicator dye and ROS quencher on chlorophyll. Moreover, the alteration in the spectral peak of Raman line among different classes of samples is suggesting towards the altered vibration energy level of water molecules present in the serums derived from blood samples of respective subjects.

Quantifying correlation between visual outcomes and biomechanical changes in cornea in Vivo after refractive surgery (Lasic and PRK)

The centre developed a simulation platform to predict post-operative corneal deformation after surgery and for diagnosis of disease. The scope of the technology was to calculate the preoperative biomechanical properties of the human cornea for diagnosis of diseases such as keratoconus and to predict biomechanical outcomes of surgeries performed on the cornea. The properties will be determined with air-puff non-invasive applanation of the cornea. This will assist in early detection of unwanted complications in the patient corneas. The technology be in the form of a software based simulation platform, which can be easily used by any eye surgeon. The software integrates tomography from conventional corneal imaging devices and finite element simulation routines to calculate biomechanical properties of the corneal tissue. High-performance computing and coupling with commercial air-puff applanation devices for pre-operative corneal biomechanical measurements and disease diagnosis. The project progressed well in first 2 years yet USP-Unique Selling Point envisaged in this project-A software platform that can be utilized by any surgeon, that platform is yet to come.

Smart phone enabled spirometer and respiratory sound-based point of care system

Spirometry is one of the most basic of Pulmonary Function Tests (PFT) and the measurements of this test, like Forced Vital Capacity (FVC), Forced Expiratory Volume in the first second (FEV1) and Peak Expiratory Flow (PEF), play an important role in the diagnosis of obstructive lung diseases like Chronic Obstructive Pulmonary Disease (COPD) and Asthma. The lack of Point-of-Care (POC), Primary care, and personalized applications prohibit individuals from monitoring their own lung conditions beyond the hospital visit. This work presents the design and development of a low-cost, portable, smartphone-enabled spirometer with an automatic disease classification system based on

the spirometric signal using a deep learning-based classification model.

The development of a spirometer for resource-limited settings should keep-in mind that the device should be portable, affordable, and user-friendly. Two approaches have been tried one is a differential pressure-based spirometer and another one is in-built mobile microphone-based spirometer. For differential pressure-based approach the main objective is to design and develop a portable Spirometer which can reliably extract pulmonary flow information, perform preliminary signal processing and store it in external memory and transmit it through wireless channels for further analysis to a smartphone with higher computing capability to display spirometric measurements and diagnose lung abnormality. The diagnosis of lung abnormality can be classified by a pre-trained deep learning model. The mobile microphone-based spirometer will record the spirometry sound data. It will then convert the times-series data to the frequency domain to gather further information and calculate flow-volume parameters of spirometry like FEV1, FVC, their ratio, and PEF. This is diagnostic tool in personal and point of care settings for patients with respiratory diseases. The developed deep learning-based pre-trained model can assist the patients by providing a preliminary diagnosis. As the spirometric results can be saved in the smartphone, it may be shared with the physician over the network.

The user-friendly interface and the decision-making ability make the applications distinctive. Patients in resource-limited settings may not have access to sophisticated health monitoring systems.

The main contributions of this work can be summarized as follows:

- A fleisch type custom airflow tube has been designed after studying the pressure distribution (Fig. 4(a)) and laminar flow simulation (Fig. 4(b)) in ANSYS.
- A portable printed circuit board (PCB) has been designed and developed to implement differential pressure based spirometer and the

data have been transferred to a smartphone via Bluetooth to display spirometric measurements

- Another spirometer has been designed that performs spirometry using the in-built mobile microphone and displays spirometric measurements; FEV1, FVC, FEV1/FVC%, and PEF (Fig. 2).
- A deep neural network-based classification approach using automatic feature extraction for spirometric data has been implemented.
- Real-time classification on smartphones using a pre-trained CNN model makes the device distinctive.

Manpower trained-1, the entire system consists of three major parts, A. a Breathing Circuit, B. a data processing unit on the microcontroller, and C. an Android application for display and classification.

To study the structure and blood flow of chorioretinal complex in human using optical coherence angiography

This study developed noninvasive three-dimensional depth resolved imaging of human retinal and choroidal blood circulation with a swept-source OCT/Angiography (SSOCT/A) system at 1060 nm centre wavelength. This is first time in India. The system has following features, high speed (105 A-lines/sec), high transverse (16 μm) and axial (6 μm) resolution, the system capable to generate 2D and 3D images of human eye and perform 3D scanning (10mm x 10mm x 5mm) less than 3 secs. Motion contrast OCT imaging was performed with the Amplitude Variation Field Subtraction (AVFS) and phase variance OCT (PV OCT) angiography method. We experimentally demonstrate the challenges and advantages of high speed OCT angiography (OCTA) in normal eyes and diseased eyes with Glaucoma, Diabetic Retinopathy (DR), Age-related Macular Degeneration (AMD), Choroidal Neovascularization (CNV), Geographic Atrophy (GA) Retinal detachment etc. The OCTA imaging was performed with a field of view of 16 deg (5mm x 5mm, within the Nyquist limit) and 30 deg (9mm x 9mm, exceeding the Nyquist limit). The data

were presented in en face projections generated from single volumes and in en face projection mosaics generated and compared with results obtained with a commercial OCTA instrument and with conventional ophthalmic diagnostic methods: fundus photography, fluorescein (FA), and indocyanine green angiography (ICGA). Investigators performed characterization and oxygen saturation studies of human retinal blood vessels with Principal Component Analysis (PCA) based Spectroscopic Optical Coherence Tomography-based Angiography. A single segmentation framework technique for segmenting the entire layers present in Chorio-Retinal complex of Human eye optical coherence tomography (OCT) images was explored. This automatic program is based on Graph theory method. This single program is capable of segmenting seven layers of Retina and Choroid scleral interface. Images using the high-speed system were more detailed and may rendered have better diagnostic utility because the imaged areas were sampled more densely.

Swept source optical coherence tomography (SSOCT) and angiography for 3D imaging of human eye was developed. This is first time in India. The system has following features, high speed (105 A-lines/sec), high transverse (16 μm) and axial (6 μm) resolution, the system capable to generate 2D and 3D images of human eye and perform 3D scanning (10mm x 10mm x 5mm) less Than 3 secs. This OCT angiography has been shown to provide detailed, depth-resolved images of vascular structures of the retina. Developed Prototype-Swept source optical coherence tomography (SSOCT) and angiography (SSOCTA) (first time in India) Glaucoma, Diabetic Retinopathy(DR),Age related Macular Degeneration(AMD),Choroidal Neovascularization(CNV),Geographic Atrophy (GA) Retinal detachment etc. High speed (105 A-lines/sec), high transverse (16 μm) and axial (6 μm) resolution, the system capable to generate 2D and 3D images of human eye and perform 3D scanning (10mm x 10mm x 5mm) less than 3 secs.

Validation of Osteocalcin kit A bone turnover marker for use in diagnosis and management of osteoporosis

Mumbai validated the developed ELISA prototype kit for human Osteocalcin on a large scale. Fabrication of the prototype kit for Osteocalcin, assembled the key immune-reagents generated in ready to use form and conducted stability studies of the kit (Shelf life) to carry out the validation studies of the kit at the identified centres with a defined protocol.

This study initiated Stabilization and Formulation of components of kit. Stability studies conducted at refrigerated and accelerated temperature to ensure that the prototypes have a longer shelf life. Individual components (antibody coated plates, lyophilized standards, primary polyclonal antibody affinity purified IgG and quality controls, secondary labeled HRP conjugate in liquid form and concentrated buffers immunoassay and wash solution were prepared and stored at 2-80C and 370C. The capture antibody coated plates were blocked with a stabilizing buffer and kept in a dry format at 2-80C. All the individual components were compared with freshly prepared reagents. They were checked at 3, 6, 9 and 12 months interval. The stability was assessed by comparing slope and intercepts of standard curves of preserved assays using freshly coated plate as reference.

A sandwich OC ELISA developed using immuno-reagents prepared indigenously and validated for analytical sensitivity, specificity, accuracy and compared with commercial kit. N- mid terminal, ELISA kit from IDS, USA. With increase in aged population and changes in lifestyle, osteoporosis and its related Fractures Osteoporosis has become an important Public Health care issue. Besides advocating consumption of proper food and better lifestyle, development of simple and affordable diagnostics tools is required for early identification of people at risk of developing osteoporosis. Salient Achievements- Reference norms on Indian population, Inhouse validation of the assay with samples, Results compared well with commercial ELISA kit, found Cost effective.

Development of structurally engineering artificial dura material (En-DURA)

Characterization of morphological, thermal, mechanical and dynamic mechanical properties of the bio-resorbable polymer-based patches to develop engineered fibrous assemblies for the fabrication of structural cores and to develop and characterize composite patches with structurally graded layers of polymer films and fibrous assemblies, investigated the in- vitro degradation and cytotoxicity aspects of composite patches. Successfully fabricated composite electrospun mats and solvent cast films based on home components and blends of aliphatic polyesters. Thermal and Mechanical properties of electrospun fibers, cast films and composite patches have been thoroughly investigated and were observed to remain in expected standards from a materials point of view. Tri-layer composite patches were fabricated using cast films and electrospun nanofibrous mats, using solvent adhesion and hot compression technique. The mechanical and visco-elastic properties of solvent cast films, fibers, and composite patches were thoroughly investigated. Short term in-vitro swelling and weight loss were observed for cast films, fibers, and composite patches.

Smartphone based optical microscope for clinical application

The team designed and developed and demonstrated the imaging quality of the designed smart phone optical microscope and validate the experimental results for its image quality with the standard optical microscope. With use of standard optical microscope from CarlZeiss's (model: Primo Star) which is often use for clinical diagnostic purpose, show the optical images of thin blood smear captured by smart phone microscope and by the optical microscope respectively. The intensity distribution vs pixel distance of the marked line in the identical position, a good degree of similarity of intensity distribution vs pixel distance in the image region. This suggests that the designed smartphone microscope can be reliably used for imaging of biological and other micro-particles.

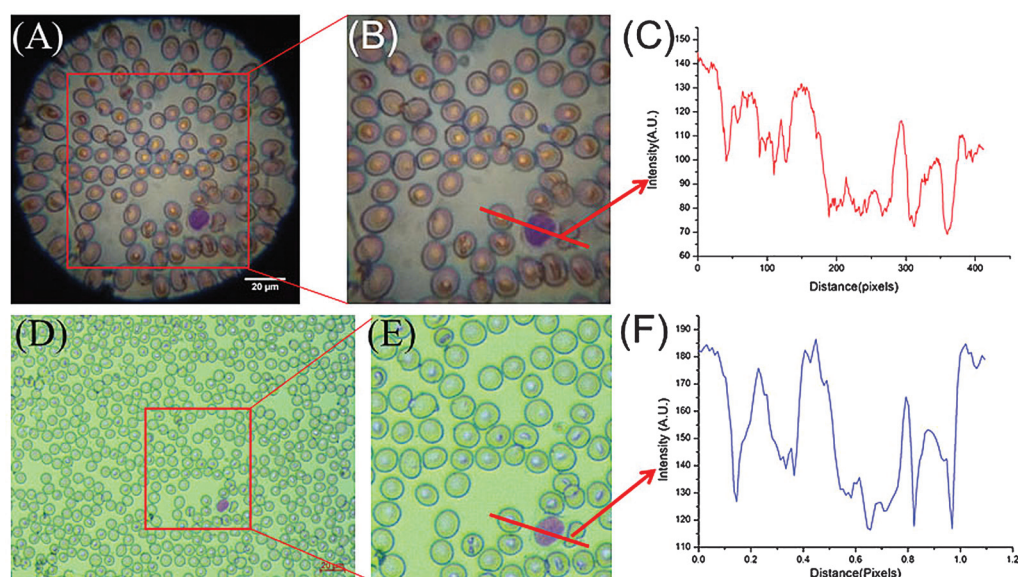


Fig. 1: smartphone microscope image of thin blood smear. (A) Smartphone microscope image, (B) corresponding image of a cropped region, (C) intensity profile of the marked region in (B), (D) a 40X/0.65 NA traditional microscope image of the blood sample, (E) zoomed version of the same region of interest (ROI) of the traditional microscope and (F) intensity profile of the marked region in (E). Scale bars are 20 μm .

The coupling of the compact optical set according to the camera of the smart phone converts it into a simple yet useful microscopic system with an overall optical magnification 520x. Owing to its simplicity in design, compact size and cost effectiveness, the team believes that the designed smart phone microscopic system is well-suited for educational purposes also and thus can be made accessible to those institutes where access to commercial grade optical microscope is not available. The low cost designed smart phone microscope can image an object well below 2 micron which is sufficient for many applications including pathological applications. Owing to its compact design, it is well-suited for in-field study such as mobile healthcare and education purposes. Furthermore, the cost involvement for development of the instrument is relatively very low, and a common citizen living in the interior place in our country will be able to afford it. Alongside to this, the position of the camera also changes with the variation of smart phone specifications. Thus, coupling of the same optical attachment would not be possible to different variant smart phone. This issue can be overcome by designing a universal attachment holder which will be done in the future

course of work. The team believes with the custom designed application the quality of the image scan enhanced significantly upon processing it in the cloud. The designed application requires only three simple steps (opening the app, uploading of the captured images from the gallery and processing) and one does not require any expertise to run the application. Alternatively, the application can also be used by an expert (pathologist or micro-biologist) who will validate the data once the captured image is sent to him or her.

Design and fabrication of a novel scoop stretcher for full body immobilization during causality transfer

The team designed a novel scoop stretcher that enables casualty transfer with full body immobilization. Investigator performed finite element analysis of the designed scooped stretcher and to analyze for stress distribution, translational displacement and deformation under static loading conditions. Fabricated the designed scoop stretcher and performed ergonomic assessment of the fabricated stretcher under replicas of casualties' physical environment.

Pre-hospital care of the individuals with spinal injuries requiring immediate hospitalization is a crucial task. Immobilization of body especially spine, is of prime concern during transfer of such patients for averting further consequences. The present work aims to redesign the existing scoop stretcher (SS) as segmented SS with multiple joints for possible full body immobilization during casualty transfer. An attempt has been made to provide head, vertebral column and pelvis immobilization ensuring patients' comfort while inducing segmented scooping of corresponding body parts. For design verification of various joints and segments of SS, a detailed FE static structural analysis has been performed ensuring its structural strength and possible weight reduction. A first prototype of the proposed design has been fabricated using CNC machining on individual segments of HDPE of dimension $0.42 \times 0.36 \times 0.07$ m. Proper experimental tests have been performed on fabricated prototype of SS and one of the commercially available SS to compare the mean range of motion (ROM) of various body parts for nine participants employing three scooping techniques (scissor, segmented scissor and side-by-side). Motion sensors of six-dimensional electromagnetic tracking system are utilized to capture the angular motion data of selected locations along the spinous process. The mean ROM (sagittal-lateral-axial) of the nasion, C3, T12 and L3 positions recorded are: (a) 0.860-0.540-0.820, (b) 0.410-0.530-0.670, (c) 0.200-0.360-0.440, and (d) 0.370-0.790-0.460 respectively during independent head scooping as scissor technique using the fabricated novel SS. Similarly, in trunk scoop, the ROM (sagittal-lateral-axial) values are (a) 3.770-2.040-2.940, (b) 1.740-1.440-2.990, (c) 1.900-1.070-2.560, and (d) 1.870-1.670-3.630 for the nasion, C3, T12 and L3 locations respectively. The lower body scoop presents ROM (sagittal-lateral-axial) values of (a) 0.430-0.430-0.350, (b) 0.290-0.410-0.270, (c) 0.390-0.360-0.340, and (d) 0.500-0.720-0.770 against the nasion, C3, T12 and L3 locations respectively. While using one of the existing SS, the mean ROM (sagittal-lateral-

axial flexions) recorded during full body scooping applied as scissor technique at the nasion, C3, T12 and L3 locations are (a) 4.570-2.870-4.390, (b) 6.60-6.520-5.540, (c) 2.410-5.30-3.80 and (d) 3.270-3.650-3.520 respectively. As evident, the mean ROM data observed for the proposed SS is much lower than the existing one.

The developed prototype comprises of multiple segments corresponding to human head, trunk and lower body regions. These segments are made up of HDPE plates connected through various joints (two turning (detachable), two turning (non-detachable), two push-button detachable and two sliding joints) reinforced through a stainless steel pipe framework. Each segment of the stretcher is again divided into left and right halves with a small clearance between them so as to avoid pinching of skin, clothes or hair between the two halves while scooping. The left and right halves of the scoop stretcher are joined with the help of two turning (detachable) joints at



Fig. 2: The developed prototype comprises of multiple segments corresponding to human head, trunk and lower body regions.

both the extreme ends of the stretcher. After attachment, this joint also enables turning movement which helps to apply scissor technique to scoop the body of the patient. The two halves of the head and neck part scoop the head and the neck portion of the casualty. The two halves of the trunk segment scoop the trunk portion. The trunk and the head part of the stretcher are connected with the help of two turning (non-detachable) joints which makes the two parts independent of each other's motion. This restricts unwanted motion in the vertebral portion, when head of the injured is being scooped and vice-versa. The thighs and lower pelvis parts are integral to each other and act as a single unit while scooping the pelvis portion of the patient. Here, scooping of the pelvis region is performed with the turning

(detachable) joint provided at the bottom-most end of the stretcher. After scooping, this segment of the stretcher is connected with the trunk one through two push-button detachable joints at the pelvis regions of the stretcher. The proposed design of the stretcher enables us to increase or decrease its length with the extension feature (two sliding joints with attached turning knobs) provided at the lower pelvis part. When not in use, the stretcher can also be detached in two parts and can be kept compact occupying less space.



Fig. 3: novel scoop stretcher for full body immobilization during causality transfer.

Operational evaluation of Health Account Scheme: Empowering people for health care through Multi-Sector Coordination

At three sites of rural-Hardoi, slum-Delhi, tribal-Arunachal Pradesh, team collected Health data from diaries to determine the acceptability of keeping a self-written health diary among members of low-income communities, with the aim of generating needed health data. ICMR identified three different types of impoverished community (tribal, inner-city slum and rural) in north India, and conducted a baseline survey to establish the sociodemographic properties of the members of 595 (tribal), 446 (slum) and 51 (rural) households. We designed health diaries with a single page to fill in per month, each with a carbon duplicate, and distributed diaries to willing participants. Health volunteers visited households each month to assist with diary completion and to collect duplicate pages for a period of one year. Comparison of the frequency of illnesses reported in health diaries with baseline survey data was done. A total of 4881 diary users (tribal: 2205; slum: 2185; rural: 491) participated in project. In terms of acceptability,

49.6% (1093/2205), 64.7% (1413/2185) and 79.0% (388/491) at the tribal, slum and rural sites, respectively, expressed satisfaction with the scheme and a willingness to continue. In the tribal and slum areas, we observed increased reporting of illnesses from health diaries when compared with baseline data. Influenza-like illnesses were reported with the highest frequency of 58.9% (2972/5044) at the tribal site. High levels of acceptability and participation among the communities observed from field studies. Timely preventive education and referrals to service providers after obtaining health data to allow improved planning was envisaged and achieved in this study.

However, four major gaps were observed in the existing health system during this Task force study, which is hampering door step delivery of quality health services. Hence Phase two study is planned and being field tested for improved manpower as grass root level by increasing skilled self employed health guides, lab on bike to fill the gap of testing labs, better communication and data sharing for timely analysis and use at local level by local service providers. Under these Task Force studies first time community became their health data providers. This ensured authenticity of data, contact for data updation helped in timely counselling and education.

INTELLECTUAL PROPERTY RIGHTS

Patents filed

A total of 15 patents applications were filed during Fiscal Year 2020-2021 with the Indian Patent Office. Out of these, twelve are from intramural institutes and three from extramural. One design application is filed. 5 PCT applications (One extramural and rest intramural) were filed during this period with 1 National phase applications in Singapore.

Patents Granted

During this period, 4 Indian patents and 2 foreign patents have been granted. A total of 36 patents were maintained.

Technology commercialization

Besides expanding patent portfolio, enormous efforts were being put towards commercialization of ICMR technologies initiating from website advertisement to showcasing at various exhibitions to finalize the collaborators till transferring the technologies. ICMR has been playing a pivotal role in testing, treatment, and aggressive research into drugs and vaccination to fight the Coronavirus pandemic. A total of 5 technologies related to COVID-19 viz. Kavach ELISA, Equine Anti Serum against SARS COV-2, COVID-19 rapid antibody detection kit, RT-LAMP assay for detection of SARS-COV-2 and Development of TaqMan SARS COV-2 multiplex RT PCR has been transferred to companies on non-exclusive basis. Three different technologies are under pipeline of technology transfer.

Collaboration

ICMR has also entered into an agreement with Federation of Indian Chambers of Commerce and Industry (FICCI) for both national and international commercialization of health technologies under HTAC program. HTAC program has three components viz. Commercialization component, training component and exposition components. Two components viz. training and exposition has been successfully achieved. Commercialization of three technologies is under process. The global COVID-19 pandemic has affected the ability of ICMR's scientists and senior administrators to attend a multi-day technology commercialization workshop, which was originally planned to be held in Austin, Texas. As an alternative, FICCI developed an online alternative course to sensitize 20 ICMR scientists in technology commercialization learning experience. Online lectures have been delivered on commercialization topics, along with Q&A sessions.

The Division is also actively involved in innovation and translation research activities which has wider societal impact. The following programs of ITR aims to promote technology advancement in the Country and thus promoting *Make in India*, *Skill India* and *Start-up-India* initiatives of the Government of India. These activities also encourage involvement

of private research facilities and healthcare start-ups in this process.

Medical Device & Diagnostic Mission Secretariat (MDMS)

The Indian Medical device market is currently valued at USD 5.2 billion and is experiencing a growth rate of 15% CAGR as against the growth rates observed by developed countries of the World including USA with growth rate of about 4% CAGR. India is dependent on imports for its medical device needs with 80% of medical devices being imported. In view of the huge import dependency and long technology development cycle of medical devices, there is an immediate need for providing holistic support across the medical device development and commercialization cycle including R&D, validation, scale-up, regulatory compliance, market access etc. ICMR has established "Medical Device and Diagnostics Mission Secretariat (MDMS)" under the Division of Innovation and Translational Research (ITR) at ICMR-Hqrs. The programme will promote innovative technology development, skill development and will foster indigenous manufacturing of medical devices to decrease import dependency of India. Two biodesign programs were initiated at IIT Kharagpur and IIT Hyderabad in July'2020. The project details are also available at <https://mdms.icmr.org.in/>

ICMR Centre for Innovation and Bio-Design (CIBioD)

At present, clinicians and domain experts are working in isolation with little success in producing medical devices and instruments for securing patents and having start-ups. The centre will create a platform for collaboration of clinicians and domain experts to share the idea and evolve the innovative and patent-oriented research. ICMR has initiated a task for project ICMR Centre for Innovation and Bio-Design (CIBioD) at PGIMER, Chandigarh. The CIBioD operates in collaboration with premier medical institute of the country PGIMER and the multiple reputed research institutes in technical domain like UIET (Panjab University), Central Scientific Institute Organisation (CSIO), Thapar Institute of Engineering and Technology (TIET),

Chandigarh. It incubates the projects, oriented towards the solution of medical bottle necks and the problems in the field of devices and instruments. The Centre promotes the problems faced by the clinicians from PGI and domain experts from various research institutes and the industry. The research is focused particularly in those fields in which Indian health industries are predominantly dependent on health imports. This will boost the health sector as well as medical devices and instrumentation industry. It will save the precious foreign exchange and will reduce the dependence of health sector on imports. This will also create a new job market besides boosting the pride of professionals, doctors and patients by using the indigenous devices and instruments. The project

details are also available at <https://www.cibiod.in/index.html>

Key achievement

CIBioD has submitted 06 patent applications to ICMR and has provided handholding support to 07 patent applications generated by its partners. During the 1st Year, CIBioD had conducted 04-Webinars Organized with 125+ participation in each and Organized Virtual/ Online International Summit with 2700+ participants. The centre has started a Promotion of Innovation & Entrepreneurship (PIE) programme and a Journal named 'E-Avishkar'. The technologies Jee 1- AAO, E-Stethoscope (Wireless Digital Stethoscope) etc. developed at CIBioD are at various stages of development (Fig 1 & 2).

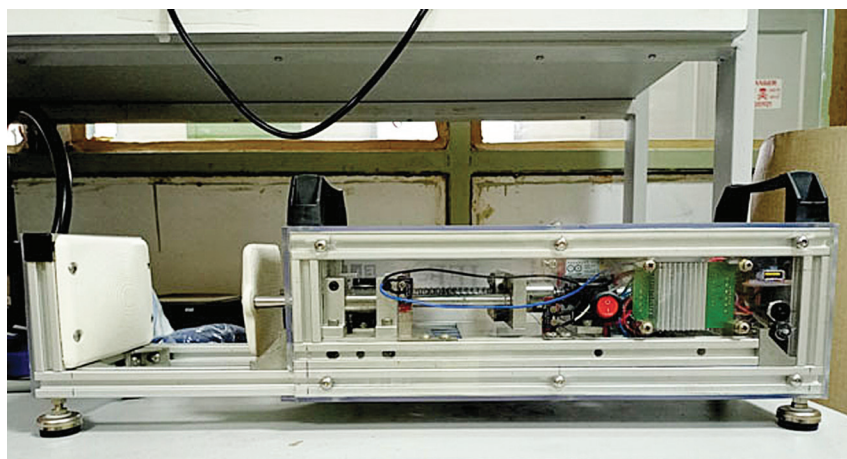


Fig. 4: A life saving machine with a new outlook and efficiency to serve more than one patient, optimisation is new mantra for new medical aids. Furthermore, with the advance technology portability and compactness are the additional advantages. Key features include Inspiration & Expiration Ratio (I/E) with range selection (1/ 1.5/ 2/ 2.5/ 3); Breath per minute: 10/ 12/ 14; Strokes :30mm/40mm/ 50mm.



Fig. 5: A low-cost mass-screening with a telemedicine - E-Stethoscope (Wireless Digital Stethoscope) developed by CIBioD. Portable and contactless device monitors PCG, ECG (One Channel), Body Temperature is suitable for every healthcare practitioner.

Large animal house testing facility at AMTZ, Vizag

Testing of innovative medical devices on large animals is a critical component for validating new medical devices before initiating human studies. India highly depends on such facilities in foreign countries for undertaking such studies. This adds to a lot of cost & discomfort and hugely increases the cost of product development. ICMR envisages to set-up large animal house testing facility at Andhra Pradesh Medtech Zone (AMTZ), Vizag to provide support for early stage trials, research & development, prototyping and technological assessment of functionally critical parts of medical devices (Fig 6). Once developed the facility will be open for use by both public and private players.



Fig. 6: Large animal testing labs established at AMTZ, Vizag.

Policy Document for Innovation and Entrepreneurship for Medical Professionals, Scientists and technologist at Medical / Dental/ Para Medical Institutes/ Colleges and allied Biomedical Research and Academic Institutions

Healthcare innovations and entrepreneurship are making forays in the Indian economy. ICMR as the apex medical research institution realized that there was need to strongly promote healthcare innovation and entrepreneurship at Medical / Dental/Para-Medical Institutes/ Colleges and allied Biomedical Research and Academic Institutions by creating a sustainable innovation ecosystem.

With immense knowledge and exposure to the unmet healthcare needs, Medical Professionals, Scientists and technologist should be at the forefront of medical innovation. This document is an attempt to enable institutions to actively support their personnel to contribute in innovation and entrepreneurship associated activities. It is envisaged that this initiative will promote Medical Device Innovations in the Country and thus promoting *Make-in-India*, *Skill India* and *Start-up-India* initiatives of the Government of India. ICMR in consultation with several stakeholders/ experts has formulated “Policy document for Innovation and Entrepreneurship for Medical Professionals, Scientists and technologist at Medical /Dental/ Para Medical Institutes/ Colleges and allied Biomedical Research and Academic Institutions”.

The salient features of the guidelines are:

- Establish a holistic innovation and entrepreneurship ecosystem in Institutes to facilitate the conversion of knowledge to innovation to entrepreneurship.
- Promote of innovation and entrepreneurship driven activities by the Faculty Member/ Researchers/ Trainees etc.

The implementation of these Guidelines will enable Institutes to acquire a portion of the recurring revenue stream from commercialization of an invention, which in turn can help make the intra-mural innovation process of the institute self-sustaining. However, the above would require putting in place effective techno-legal-administrative framework in place to complete the circuit from institutional ownership of IP to licensing it, realizing royalty on it and then re-investing the collected royalty into further innovations.

ICMR-Technology Transfer and Revenue sharing guidelines

ICMR develops biomedical technologies through in-house R&D at its network of Institutes across the country and through extramural research grants. The technologies, thus developed having

market and commercialization potential are transferred to industry for further development and commercialization for societal benefit. Thus, Transfer of ICMR Technology(ies) to Indian Industries contributes significantly to Self-Reliance in Technology, Industrial Growth and National Development. The Government of India emphasizing on the monetization aspects of public funding has set up monetization pipeline for imbibing the monetization of research leads to facilitate the research institution/departments/institutes for revenue generation and is urging the public funded Institutes to have suitable mechanisms in place for monetization of their research leads. As the government is moving ahead with the mantra of “monetise and modernize”, ICMR endeavours to promote technology transfer and commercialization of technologies developed through its funding support to create large scale societal impact. In this context, there is need to develop technology transfer guidelines with defined revenue sharing framework to ensure that revenue generated comes back to ICMR. In view of this, ICMR has formulated “*Technology Transfer and Revenue sharing guidelines*”.

The document includes guidelines of ICMR for technology-transfer with an objective to bring utmost transparency and provide equitable opportunity to all Industries/ stakeholders for licensing ICMR technologies/ Materials and join hands with ICMR for bringing them to the market for larger societal impact. These guidelines endeavours to disseminate ICMR technologies through a framework that ensures seamless transfer of technology to industry(ies) leading to indigenous product development and commercialization as per *Make-in-India* initiative of the Government. The guidelines also include a basic framework of the Royalty determination, its reporting and monitoring structure to ensure uniformity, transparency, and larger societal impact through commercialization. ICMR may take royalty based upon the support provided, brand name used, and/or use of ICMR Intellectual Property Rights (IPR). These guidelines will be referred to by the ICMR Institutes,

Industry, Academic institutes, and beneficiaries/prospective beneficiaries of ICMR while dealing with Technology-Transfer, collaborations, material transfer etc. of ICMR Technologies.

HUMAN RESOURCE PLANNING AND DEVELOPMENT (HRD), DIVISION

A. FELLOWSHIPS

JRF (Junior Research Fellowship) -ICMR JRF fellowship computer-based exam was conducted on December, 4th, 2020 in collaboration with the Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh and Tata Consultancy Services (TCS), at the 23 TCS exam Centres across India, due to the COVID-19 pandemic situation. In 2020, a total of 138 JRF (126 Life Sciences and 12 Social Sciences) were selected, out of which 40 JRFs have joined different Institutes/Organizations for pursuing Ph.D. to date and the total no. of ongoing ICMR-JRF from till batch 2019 is 508.

ICMR Centenary PDF (Post-Doctoral Fellowship) - A total of 72 PDF's proposals were received during 2020-21, 46 were shortlisted as per the eligibility criteria for personal discussion, out of which 19 PDFs were selected by the Selection Committee and were approved for funding. Sixteen (16) of them had joined for the year 2020-21.

MD-MS/Ph.D. Fellowship- Programme is being carried out at three Centres viz; King George's Medical University (KGMU), Lucknow, National Institute of Mental Health and Neuro Sciences (NIMHANS), Bengaluru and Sri Ramachandra Institute of Higher Education and Research (SRIHER), Chennai. During 2020 out of 15 allotted slots a total of 7 candidates were selected (KGMU- 2, NIMHANS- 1 and SRIHER- 4).

ICMR Chairs for Sr. retired medical/ biomedical teachers/scientists

- i. **Dr. C.G. Pandit National Chairs** - These prestigious Chairs of ICMR have a provision of remuneration of Rs 1.00 lakh per month

and contingency grant of Rs. 7.50 lakh/year per Chair. The duration of Dr. C.G. Pandit National Chair is for five years (three years extendable by another two years after assessment of the progress and plans). Retired medically qualified persons are eligible for one Chair and retired non-medical/ bio-medical/ professors/ bio-medical teachers are eligible for the other Chair. The persons should preferably be the Fellows of all the National Science Academies. At a given point of time, only two such Chairs will exist. For the year 2020, both the Biomedical and Clinical Chairs are ongoing.

- ii. **Dr. A. S. Paintal Distinguished Scientist Chairs of ICMR** - Distinguished Scientist Chairs are open to retired scientists/ medical teachers who may belong to Medical/Bio-medical/Life Sciences with the excellent track record in the field of medical application. All the perks/ remuneration of Distinguish Scientist Chairs of ICMR will be at par with the existing Chairs of ICMR *i.e.* Rs. 1.00 lakh per month as a remuneration and Rs. 7.50 lakhs per year as a contingency grant. The duration of Chair will be for five years (three years extendable by another two years after assessment of the progress and plans). Usually two Chairs will be established at one point of time; their number will not cross five at any given point of time. For the year 2020, all five Chairs are occupied.

STS (Short Term Studentship) - During the year 2020-21, a total of 10660 MBBS/BDS students registered from all over the country, out of which 6188 students finally submitted their proposals at the end of January 2020, which were reviewed by Scientists/Experts in the concerned subject areas of the 27 ICMR institutes. A total of 1252 students had qualified for carrying out the STS-2020 research project and the result was declared in March 2020, post which there was lockdown due to the COVID-19 pandemic situation and thus all Medical and Dental Colleges were closed and the qualified

students for STS-2020 were not able to carry out their research work in the year 2020, due to which the report submission deadlines were extended for the year 2021 as medical /dental colleges were not opened back then. Only in November 2021, a total of 942 students had submitted their final STS 2002 report and which has been successfully evaluated, and the result in to be declared soon. The stipend amount of Rs. 20,000/- for the two months research work, will be awarded to the final selected students and e-certificates will be also given.

Nurturing Clinical Scientists (NCS) Scheme- A total of 15 Clinical Scientists are ongoing to date and 2 candidates were selected for the year 2020, who will join in due time.

ICMR - Adjunct Faculty Scheme- The Scheme was implemented from April 2019 onwards after approval from the GC of ICMR. Three (03) Adjunct Faculty have joined in the year 2020.

B. FINANCIAL SUPPORT

MD/MS/DM/MCh/MDS thesis support - This scheme is primarily aimed at promoting good quality research in medical colleges through students pursuing post-graduation courses as well as to improving visibility and accessibility of their research work to a larger research audience, as it is mandatory to publish one paper in an indexed journal. For the June 2020 batch, 214 thesis proposals were received and 50 proposals were selected for financial assistance. Out of 474 thesis proposals received for the December 2020 batch, 51 proposals were awarded financial assistance for the year 2020-21.

International Travel Grant to non-ICMR scientists - A total of 266 applications were received in February 2020 for International travel grant support but due to COVID-19 lockdown, the scheme has been suspended until further orders by the Competent Authority of ICMR, due to the international travel ban imposed by the Govt. of India, and no applications were henceforth considered. A total of 22 applications of travel

before February 2020 were reimbursed in the year 2020-21.

DHR-ICMR Funded Workshops on Clinical Training/Translational Research - For the year 2020, a total of 35 workshop applications on Clinical Training/Translational Research were approved for funding support until January 2020, and the Scheme has been put on hold, until further notice due to COVID-19 lockdown.

C. MISCELLANEOUS PROGRAMS

ICMR Awards & Prizes - The ICMR Awards/Prizes 2019 were awarded in the year 2020-21. A total of 249 applications were received for the year 2020-21 and a total of 21 Scientists and young researchers were awarded in 14 different ICMR Awards/Prizes 2019 categories in the field of biomedical research.

INTERNATIONAL HEALTH (IHD), DIVISION

The International Health Division (IHD) in ICMR co-coordinates international collaboration in biomedical research between India and other countries as well as with national & international agencies such as Ministries of Health & Family Welfare and Science & Technology, Indian and foreign missions and WHO etc. There are few specific Agreements/MoUs/Special Arrangement signed by the Ministry of Health and Family Welfare with other countries and rest are those signed directly by ICMR/DHR with international organizations/ institutions such as INSERM in France, German Federal Ministry of Education and Research (BMBF) and Helmholtz Association (HGF) in Germany; National Institutes of Health (NIH) in USA; International AIDS Vaccine Initiative (IAVI), USA; Swedish Research Council for Health Working Life and Welfare (FORTE) in Sweden; National Health and Medical Research Council (NHMRC) in Australia; London School of Hygiene and Tropical Medicine (LSHTM) and Medical Research Council (MRC) in UK; Drugs for Neglected Diseases Initiative (DNDi) in Switzerland; Global Alliance for Chronic Disease (GACD); Research Council of Norway (RCN) in

Norway; Russian Foundation for Basic Research (RFBR) in Russia; National Institute of Infectious Disease (NIID) in Japan; The International Vaccine Initiative (IVI) in South Korea; African Union (AU) in Africa; Department of Medical Research (DMR) in Myanmar; Nepal Health Research Council (NHRC) in Nepal.

Purpose of International Cooperation

The purpose of these Memorandum of Understanding (MoU) and Joint Statements has been for exchange of scientific information; exchange of scientists/technicians; joint execution of scientific projects and organization of joint scientific, seminars, workshops and symposia in identified areas of cooperation.

Joint Working Group (JWG) and Joint Steering Committee (JSC) Meetings

The regular meetings of Joint Working Group (JWG) or Joint Steering Committee (JSC) with various countries/international institutes/ organizations are organized to review, develop and finalize joint collaborative programmes, decide future plans of action and identify priorities for bilateral cooperation.

- 9th meeting of the India-Belarus Joint S&T Commission meeting through VC organized by DST to highlight ICMR's international collaborative activities modes of cooperation held on 5th Aug, 2020.
- 10th India-Japan Joint Working Group, organized by DST, New Delhi & highlighted ICMR's collaboration with Japan held on 11th Nov, 2020.
- 11th India-Sweden virtual Joint Working Group (JWG) on Health, organized by MOHFW, New Delhi held on 8th Dec, 2020.
- Joint Working Group; business meeting of Indo-US VAP to discuss on COVID-19 vaccine efforts from the Indian and the US side and programmatic discussion & future direction for VAP, organized by DBT, New Delhi held on 15th Dec, 2020.

- 11th meeting of the India-Russia Joint Working Group on cooperation in Science and Technology, organized by DST, New Delhi held on 17th Dec, 2020.
- 13th virtual meeting on EU-India Steering Committee on Science & Technology Cooperation organized by DST & European Union held on 12th Feb, 2021.
- Virtual HIROs Teleconference, organized by MRC, UK held on 19th March, 2021.
- 1st working level meeting between officials from ICMR on NHRC (Nepal) to discuss way forward for ICMR-NHRC MoU signed in Nov, 2020/Jan, 2021 held on 25th March, 2021.
- 6th virtual meeting of the Permanent Working Group (PWG) on Science and Technology of the Shanghai Cooperation Organisation Member States held on 30th March, 2021.

In addition, the International Health Division has also represented ICMR in various bilateral/multilateral Joint Committee Meetings coordinated by MEA, MoH&FW and DST Govt. of India for cooperation with various countries.

Renewal/Signing of MoU

- An MoU between ICMR and Drugs for Neglected Diseases Initiative (DNDi), Switzerland signed in October, 2015 was renewed through exchange of letters/ Statement in September, 2020.
- An MoU between ICMR and Nepal Health Research Council (NHRC), Nepal was signed in November, 2020/January, 2021 from ICMR, New Delhi and NHRC, Nepal respectively. The MoU aims to enhance the bilateral cooperation between India and Nepal in the field of Health Research.

Health Ministry's Screening Committee (HMSC)

The research projects involving foreign assistance and or collaboration in biomedical/health research are submitted online by the Indian investigators

to ICMR for approval of Govt. of India through Health Ministry's Screening Committee (HMSC). The International Health Division of ICMR acts as the Secretariat for HMSC. The projects are peer reviewed by the concerned Scientific Divisions at ICMR and then placed before the HMSC for consideration and decision. During the year 2020-21, six meetings of Health Ministry's Screening Committee were held wherein 290 projects were considered and out of which 212 projects were approved for international collaboration/assistance with agencies from USA, Germany, France, Canada, Australia, Sweden, UK, WHO and several other Foundations and foreign universities.

Since the beginning of 2020, HMSC meetings are held at a regular interval of alternate months in a calendar year.

International Visitors/Dignitaries

The Division also organized/attended discussion during visits by various visitors to ICMR from the Embassy of South Korea and delegations from Myanmar & Brazil.

ICMR-DHR International Fellowship Programme

The ICMR International Fellowship Programme for Indian biomedical scientists aims to augment capacity strengthening of institutions involved in basic, applied, epidemiological and clinical sciences through exposure of Indian researchers to the latest international advancements in knowledge, to understand the disease and find strategies for their prevention and cure.

Announcement of applications for ICMR-DHR International Fellowships for senior and young Indian biomedical scientist for 2020-21 was put up on ICMR/DHR websites and also published in National Newspapers.

Selection Committee met on 11th May, 2020 (virtually) in addition to last meeting held in March, 2020 for selection of senior & young Indian scientists respectively but results have not been

announced due to restriction of international travel in view of the global pandemic situation.

The reports of senior and young ICMR-DHR International Fellows, who had undertaken the Fellowship during the year 2019-20, were placed on ICMR website.

India Africa Health Sciences Platform

Second call under ICMR/AU-STRC Health Practitioners/Research Capacity Building Scheme (Training Courses in India 2020) was launched with the last date of submission of applications on 29th February 2020. Call was for 8 training courses at 4 ICMR Institutes-NICPR, Noida; NIRT, Chennai; NIRRH, Mumbai and NIV Pune. Review of Applications has been done and the results could not be announced due to restriction on international travel in view of the global pandemic situation.

Guidelines and Call for Proposals (CFP) for joint health research projects under the ICMR/AU-STRC Research Grant Scheme have been finalized in consultation with AU-STRC. The CFP will be announced in 2021.

New initiatives

- **Newton Bhabha Fund Programme:** Indian Council of Medical Research partnered with British Council UK for the Researcher Links Workshops under the Newton Bhabha Fund Programme for a period of 3 years. Researcher links workshops are designed to provide financial support to bring together a UK/Indian bilateral cohort of early career researchers to take part in workshops to meet the overarching objectives.

For the year 2020-21, the second joint call of the programme was advertised in the areas of Cardiovascular pharmacotherapy in COVID-19 infections, Bio-banking, Public health preparedness and response to emerging diseases outbreak/pandemic, Capacity building of maternity care providers to improve perinatal outcome. Two applications in the area of COVID-19 and

Reproductive Health were selected for Researchers Link Workshop and result was announced.

- **ICMR/NIH/BMGF Clinical Research Fellowships:** The Indian Council of Medical Research (ICMR), the National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health (NIH) and the Bill & Melinda Gates Foundation (BMGF), signed a Declaration of Intent on 17th November, 2019 on clinical research fellowship programme. It is a programme for early and mid-career scientists within India and the USA to help in expanding the cohort of physician scientists focused on research that will advance discovery to improve clinical practice and benefit public health in both countries. The implementation plan and guidance document are under preparation in consultation with NIH & BMGF.



Fig. 7: Indian Council of World Affairs (ICWA) Webinar on “COVID-19 and Beyond; Priorities and Prospects for India-Africa Cooperation” held on 26th May, 2020.



Fig. 8: Volume V of document entitled “An Overview of International Collaborative health research projects approved by Health Ministry’s Screening Committee during August, 2017 to July, 2020” was released by the Secretary, DHR and DG, ICMR on 14th August, 2020.



Fig. 9: An MoU between ICMR and Nepal Health Research Council (NHRC), Nepal was signed in November 2020/January 2021 from ICMR, New Delhi and NHRC, Nepal respectively.



Fig. 10: Brazilian delegation led by H.E. Mr. Marcos Pontes, Minister of Science, Technology & Innovation, Govt. of Brazil visited ICMR Hqrs. New Delhi on 24th February, 2021.

RESEARCH MANAGEMENT, POLICY, PLANNING & COORDINATION (RMPPC), DIVISION

RMPPC is engaged in work related to health communications (including communications during COVID-19), preparation of various policy, planning documents, write-ups on achievements, impact analysis, etc. through coordination with various ICMR Institutes and stakeholder's consultations. The Division is also involved in Research synthesis through Evidence to Policy that helps people make well informed decisions about policies, programs and projects by putting the best available evidence from research at the heart of policy development and implementation as well as prepare Policy briefs on successful interventions.

COVID-19 Communications

Since ICMR was at helm of country's response to COVID-19, RMPPC division developed

and coordinated communications regarding COVID-19. It undertook multiple initiatives to develop a communication pipeline to media as well as general public.

- Development of network with media persons:** A close network with media persons (from electronic and print media) was put in place through an exclusive whatsapp group and a journalist database for national regional media. Regular interactions with media through telephonic medium (approx. 100 queries per day) were made. Daily media mapping was conducted.
- Press Conferences:** A number of press conferences were held at ICMR's Headquarters in the initial days. In addition to these, ICMR participated at MoHFW regular press conferences.
- Press Releases:** A number of press releases were developed time-to-time to inform and sensitize media about the latest developments in COVID-19 like collaborations of ICMR with BBIL for vaccine development; isolation of SARS-COV2 and its variants, achieving milestones in COVID-19 testing, development of new diagnostics like COVID KAVACH ELISA, Antigen testing, results of clinical trials like WHO Solidarity trial and PLACID trial.
- Opinion Editorials and Interviews:** The division coordinated a number of Opinion Editorials and interviews by DG, ICMR and other ICMR institution leaderships in prominent dailies like The Hindu, Hindu Business Line, The Indian Express etc.
- Media Guidelines:** To provide the authentic information and streamlining the process, media guideline for ICMR and its institutes was developed and circulated.
- Internal Communications:** To strengthen the internal communication, a team with representation from all institutes was developed

and regular interactions were done. Also, the rapid response team at ICMR was documented and placed at ICMR website for easy access by external organizations.

- *Radio Programme for Mass Awareness:* The division also planned and coordinated a 7-day programme on All India Radio on COVID-19 covering information about its all aspects, status and precautionary measures.
- *Crisis Communication Plan for Vaccine Trial:* Prepared Communication Plan for COVID-19 Vaccine Trial to be initiated at ICMR institutes
- *Film on Covaxin:* Developed the concept and coordinated the making of ICMR and WHO film on India's response to COVID-19.



Fig. 11: COVID-19 Updates.

Coordination of events at ICMR

The division lately has been the focal point for coordinating key events at ICMR like the inauguration of High-throughput COVID-19

testing facility at Noida, Kolkata & Mumbai by Hon'ble Prime Minister; inauguration of mobile COVID-19 testing lab by Hon'ble Home Minister; launching of Mobile Stroke Unit by Hon'ble Health & Family Welfare Minister; organization of vaccine symposium etc. The activities include coordination with ministries and stakeholder, development of press releases and social media content.

E- Samvad

A monthly newsletter (in Hindi and English) has been initiated by the division since June 2020 to showcase the activities and achievements of ICMR. A special edition on ICMR Women Corona warriors was also published in March 2021.

Development of Regional Communication Hubs

As a next step to upgrade the existing communication ecosystem, communications hubs in different regions of the country (South, West & East) have been formed. The institutes have been identified through their communications capacity, human resources availability and need for an active communications hub. The hubs constitute of a group of 2-3 members from the host institute including the Director of the institute, Nodal Communications Officer (NCOs) and Social Media Coordinators (SMC) identified in the first phase of the project. The following are the roles of the RCHs: Advisory for regional institutes on media communications and social media; Strengthen the media communications regionally for the ICMR; Identify training requirements and conduct them regionally; Conduct fortnightly meetings with regional NCOs to guide them on upcoming activities; Information and guide for collateral development for the centres.

Development and release of ICMR History Timeline

The history timeline of ICMR depicting 108 year journey of the Council since the day of its

inception in 1911, when it used to be known as Indian Research Fund Association (IRFA) was developed by the division. The timeline mentions important achievements - such as the discovery of the Bombay blood group; the birth of the Indian Journal of Medical Research; the delivery of India's first test-tube baby; and demonstrating for the first time in the world that home-based treatment of TB can be as successful as hospital-based treatment to role played by ICMR in tackling the diseases like Kyasanur Forest Disease (KFD), Nipah & Zika. It also captures policy and program interventions by ICMR and its institutes to control diseases like tuberculosis, malaria, polio and neglected tropical diseases (NTDs) that once affected the population at an epidemic level, and its pioneering work in the fields of maternal and child health, HIV, cancer and nutrition, among others. The timeline was unveiled by Hon'ble Union Minister for Health & Family Welfare.

India International Science Festival 2020

The division organized the Health Research Conclave on 23rd and 24th December 2020 during 6th India International Science Festival held on a virtual platform. The aim was to provide a platform where eminent health scientists and researchers can interact with each other as well as with media, policy makers and general public. The theme of the conclave was 'Health Research for Happy, Healthy and Self-reliant India' where eminent health experts spoke on emerging & remerging infections, integrated medicine, nutrition, universal health coverage & the eliminable diseases. More than 1000 delegates participated in the event. A speech competition was held for school students on theme "Healthy India, Fit India" and best three speeches were awarded. The event was a great success and attended by more than thousand participants across India and abroad.

The division also participated in Mega Expo held on 22nd -25th December 2020 during 6th India International Science Festival held on a virtual platform. More than 40 posters showcasing the

recent achievements and contribution of ICMR were displayed on the virtual platform and the stall was attended by visitors from India and abroad.



Fig. 12: Inauguration address by Hon'ble .HFM.



Fig. 13: Informative talks by eminent experts.

Azadi ka Amrit Mahotsav

A Nodal Communication Officers Meetings to plan the activities on the occasion of launch the India@75 initiative to commemorate the 75 years of India's Independence and for next 75 weeks was held on 11th March 2021. The team ideated and created a campaign with a hashtag #ICMR4NewIndia on the occasion of inauguration of "Bharat ka Amrit Mahotsav" 75 years of India's Independence. The campaign posts were shared by all ICMR institutional handles reached more than 3 million people on Twitter and led to 1.8K interactions. The tweet put out by ICMR HQ also received tremendous traction on social media. Developed the communication plan on Bharat ka Amrut Mahostav.

Evidence to Policy

A capacity building workshop was conducted at ICMR-NIRT, Chennai. 16 participants were trained in writing effective policy briefs. Several policy briefs on tribal health, tuberculosis etc. from ICMR were published on ICMR website after rigorous external review coordinated by division.

Refresher trainings in Health Communications

Several trainings were organized for newly appointed Nodal Communications Officers (NCOs) at ICMR institutes regarding press release preparation, Op-Ed writing trainings, Using social media for effective communications.

Briefing Document and Factsheet on Budget 2021 and Concept Note for Prime Minister's Atma Nirbhar Swasth Bharat Yojana (PM- ASBY) were created; planned for ICMR/DHR specific announcements. Two year Communication Plan was developed for PM-ASBY.

Webinar on Gandhi & Health

The division organised a webinar on Gandhi's perspective in times of health crisis by Dr Abhay Bang, Director SEARCH. An e- photo album & a compendium of ICMR activities commemorating 150th birth anniversary of Mahatma Gandhi was also released.

Inputs for PM/President/ Finance Minister's Speech, Parliamentary Questions and others

Division also coordinates activities of the Communication Group and public outreach related activities as well as helps in providing scientific inputs and assists in finalizing the Outcome Budget/Annual Plan/Annual Action Plan, etc. It also supervises and coordinates Parliament Questions/Parliamentary Assurances and other Parliamentary Matters including Parliamentary Standing Committee meetings and action taken reports. It also updates the work progress of Sectoral Group of Secretaries recommendations,

budget announcement, India@75 activities and Hon'ble Prime Ministers' announcements on 15th August 2020 from the ramparts of the Red Fort.

INDIAN JOURNAL OF MEDICAL RESEARCH (IJMR), UNIT

The Indian Journal of Medical Research (IJMR) is a monthly biomedical journal of national and international repute and is the flagship journal of the Indian Council of Medical Research (ICMR). During the financial year 2020-21, it has completed 107 successful years of uninterrupted publication, with 12 issues brought out in two volumes each year. The IJMR is available as full text, free on the internet with a searchable menu. With a wide circulation within and outside India, IJMR is included in all global indexing and abstracting services. The journal is also available full text free on the web at www.ijmr.org.in. The IJMR App has been made available for the Android version of the tablet as well as iPad since January 2017. Article submissions to the IJMR are now invited via a new platform <https://review.jow.medknow.com/ijmr>.

Besides publishing original research articles, the IJMR publishes Editorials, Commentaries and Review/Mini review articles on topics of contemporary biomedical interest contributed by eminent global experts. Other than these, Research Correspondences, View Points, Perspectives, Systematic reviews & Meta-analyses, Clinical Images, Student IJMR, Letters to the Editors and Book reviews are also published in addition to Policy Documents and Special/Status Reports occasionally. The impact factor for the year 2019 was 1.503 (Clarivate Analytics, 2020).

A total of 10 issues (including 5 special issues) were published in the 2020-21 financial year with the total number of submissions amounting close to 5000. Of these, 29 per cent articles were received from countries other than India. One thousand four hundred and seventy two reviewers were involved in the peer-review process, of whom 18 per cent were from foreign countries. Among those, 31.8

per cent were from USA, 8.3 per cent from UK, 4.5 per cent each from Italy and Turkey, 4.2 per cent from Australia and 3.8 per cent from Brazil.

Fig depicts the total number of articles published in the IJMR during 2020-21 under various categories; 38 per cent were original research articles, followed by 15 per cent review articles and 16 per cent research correspondences. Other than these, View Points, Perspectives, Special reports, Policy guidelines, Clinical Images, Editorials and Commentaries were also published.

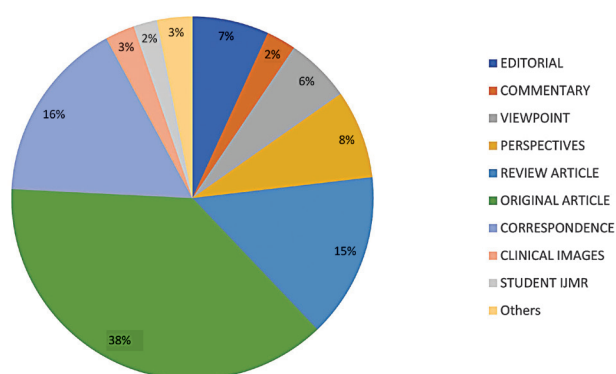


Fig. 14: Articles published in the IJMR under various categories during 2020-21.

A total of 190 articles were published in the said financial year, with 14.2 per cent articles from foreign countries such as the USA, UK, Turkey, Egypt, Germany, Brazil, Australia, Austria, France, Iran, Italy and Jamaica. Fig depicts the percentage of articles submitted, published and reviewers' contribution from India and foreign countries.



Fig. 15: Indian vs. foreign articles submitted, published & reviewers contributed in the IJMR during 2020-21.

In 2020-21, given the COVID-19 emergency scenario, efforts were doubled at IJMR to publish articles most relevant to COVID-19 in the fast track

mode to ensure dissemination of most opportune information to readers and policymakers. In this regard, such articles were made available online as Ahead of Print on www.ijmr.org.in on timely basis. Four special issues on COVID-19 were published in February & March 2020, May 2020, July & August 2020 and January & February 2021 while one special issue was published on 'One Health' in March 2021 (Fig.). The special issue on 'One Health' was released by Dr. Harsh Vardhan, Honorable Minister of Health and Family Welfare, Government of India. Drs Rajesh Bhatia & Priya Abraham were the guest editors of the special issues on India & COVID-19 (Parts I-IV) and Dr. Mohan D. Gupte was the guest editor for the One Health special issue, while Drs. Samiran Panda, Sukhadev D. Barbuddhe and Manju Rahi were the co-guest editors.



Fig. 16: Special issues on COVID-19 and 'One Health'.

MEDICINAL PLANTS (MPD), DIVISION

Development of a Phytopharmaceutical Formulation for Preventing or Delaying the Development of Type-2 Diabetes in Subjects with Pre-Diabetes

The first and second phases of the project on development of Phytopharmaceutical drug through chemistry, manufacturing and control (CMC); and pre-clinical pharmacological and safety studies have been completed. During the year, the third phase of the project on undertaking GLP regulatory toxicity studies on the developed product in the

laboratory animals has been completed. The fourth and final phase of work on clinical assessment of product efficacy and safety has been initiated. For this phase, an agency has been selected to conduct Phase I clinical trial through the process of Expression of Interest (EOI). The preparation and submission of IND document to DCGI is under process. Subsequent to successful completion of Phase I human trial, a multicentre, randomized, double-blind, controlled Phase II clinical trials will be undertaken on the developed product.

Development of a Formulation for Treatment of Sleep Disorders

The first, second and third phase of the project on product development through chemistry, manufacturing and control (CMC); pre-clinical pharmacological & safety studies; and GLP regulatory toxicity studies on the developed product have been completed. During the period, the fourth and final phase of project on clinical evaluation of efficacy and safety of the developed product has been initiated through a well designed, multicentre, randomized, double-blind, controlled clinical trial at 4 centres across the country. The clinical trial on the developed product has been initiated.

Joint Phytopharmaceutical Drugs Development Programme of CSIR, DBT and ICMR

This is a tripartite Inter-ministerial cooperation translational research programme of CSIR, DBT and ICMR on development of 'Phytopharmaceuticals'. Under this new initiative, out of the 9 therapeutic leads identified initially on joint development of Phytopharmaceutical drugs, 2 leads/projects, as mentioned subsequently, have been prioritized.

Cannabis based Phytopharmaceutical Drug (THC:CBD ratio, 1:1) in Management of Cancer Pain

Under this study, work has been completed with respect to identification, authentication and sourcing including cultivation of the plant (BRM)

and has developed revised method for separation of both CBD and THC enriched fractions using single plant material along with completion of standardization work using the chemical markers. The CMC-related quality control studies of raw material, enriched fraction and formulation development studies and some in-vivo efficacy validation studies has been completed.

The compiled IND related information on description of product, documentation of its traditional use, composition, safety, bioactivity, present usage, PK/PD, Monograph development, etc. have been generated.

Boswellia based Phytopharmaceutical Drug in Treatment of Osteoarthritis

Under this lead development, identification, authentication and sourcing of Botanical Raw Material (BRM) of Gum resin of *Boswellia serrata* and isolation and characterization of four markers (11-keto- β -Boswellic acid; 3-Acetyl-11-keto- β -Boswellic acid; 3-Acetyl- β -Boswellic acid and β -Boswellic acid) with their COA has been completed. The team prepared 6 batches of Boswellic Acid enriched fraction at lab scale with boswellic acids contents >40% and overall extractive value ~ 30 %. Also completed CMC-related quality control studies of BRM and enriched fraction as well as PK of enriched fraction/ marker.

Review Monographs on Indian Medicinal Plants

The programme aims at consolidation of Indian research contributions (published information) at the various National laboratories/institutions across the country in the area of medicinal plants and present the compiled information in series on Reviews of Indian Medicinal Plants which serve as comprehensive, informative and reliable information on new leads thus helping in systematic and planned evaluation of medicinal plants including drug design, basic and applied research. During the year, the monographs on 57 plant genera and 259 species covered under 23rd

volume have been published. The preparation of volume 24 is in progress.

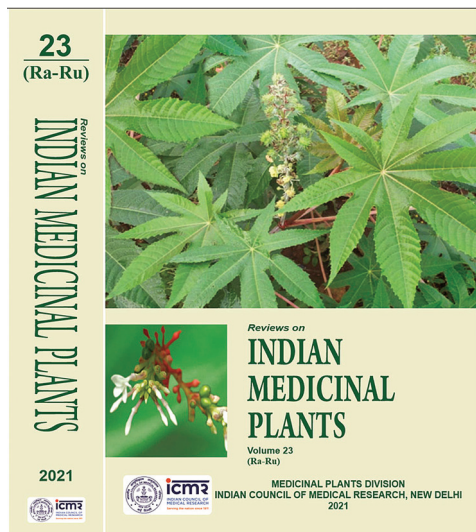


Fig. 17: Reviews of Indian Medicinal Plants Vol. 23.

Safety Review Monographs on Indian Medicinal Plants

The second volume of this publication covering 75 monographs have been completed and currently under review by the experts. This monograph documents comprehensive published information on medicinal plants mainly on their historical use, pharmacopoeial status, preclinical general toxicity/safety, mutagenicity/genotoxicity safety, reproductive safety, adverse effects observed in clinical trials, safety in pregnancy, safety in children, case reports and herb-drug interactions.

Development of Ethnomedicinal Data Base

Developing a new database which is going to comprise several thousand ethno-medicinal/folklore reports published on Indian Medicinal plants. This would help in developing new drugs, knowing their potential as nutraceutical, important phytoconstituents, lead molecules help in protection of IPR related issues etc.

PUBLICATION & INFORMATION (P&I), DIVISION

Dissemination of Biomedical Information

ICMR carried out few education and extension activities during the year in different parts of India

to disseminate the activities and achievements of Council at various platforms as well as to enhance the outreach of ICMR.

Ujwal Uttarakhand 2021

A 3 day exhibition held during 19-21st March, 2021 was attended by two Scientists from National Institute Malaria Research (ICMR-NIMR), New Delhi for exhibiting the publication, technologies apps. etc. The event was organized by Achievers Foundation, Rohini, New Delhi for participation in the above Mega Exhibition displaying of latest research activities and achievements for the betterment of the society.

Bengaluru Tech. Submit

A 3 day exhibition was held during 19-21st December, 2020 at Bengaluru. The Scientists from ICMR-RMRCT, Bhubaneswar had virtually participated in this exhibition and showcased various research activities and achievements of the institute.

Sarthak Education Vision

A 3 day exhibition was held during 15-17th March, 2021 at Bhopal. The Scientists from ICMR National Institute for Research in Environmental Health (NIREH), Bhopal (MP) exhibited the publication, technologies apps. etc.

BIOMEDICAL INFORMATICS (BMI), DIVISION

Data management and dissemination

In line with the objectives under the Pillar II of the ICMR Strategic Vision Document 2030, the division developed data collection and analysis portals for several programs of ICMR and other organizations. A few important programs for which the Division developed data collection and analysis portals include:

- **National COVID-19 testing data portal** (cvstatus.icmr.gov.in) and **COVID-19 Analytics Portal** (cvanalytics.icmr.org.in)

The division has designed and developed nationwide COVID-19 testing data portals. The portals facilitate the COVID-19 testing data entry across the country. Based on the stakeholder requirements, the COVID-19 testing data management system can be subdivided into two main modules i.e., cvstatus (for data collection) and cvanalytics (for data analysis). The data collection tool is mainly used by laboratories (labs) for entering the testing data. The data collection tool has the provision to submit data for samples tested using different techniques including RTPCR, TrueNAT, CBNAAT, and RAT. The data is collected based on a standardized Specimen Referral Form (SRF) developed by a group of experts. The data analytics tool is intended to use by officials at national, state and district levels for visualizing the data entered from the labs. The data analytics tool (cvanalytics) presents a detailed analysis of the collected data to the users (based on their role) for monitoring the ongoing scenario and formulating policies.

- **COVID-19 Testing Kit Validation (cvtestkit)**

ICMR is being also involved in validation of the new COVID-19 testing kits available in the market and to facilitate this validation process, cvtestkit portal was developed. The portal enables vendors to register their kits for the necessary validation and approvals. BMI Division enabled for electronic process of kit validation and testing.

- **COVID-19 Testing Lab Quality Control (covidqcqa):**

To monitor the quality of testing for COVID-19 test done by the approved laboratories, ICMR has followed inter-laboratory comparison i.e. random rechecking of the samples tested by these labs (ILQC). To ensure transparency and facilitate standardized data collection, covidqcqa portal was developed as is a web-based tool. The testing lab, regional QC lab and National QC lab entered their data on the web portal, which is collated by a team at ICMR headquarters.

- **COVID-19 Data APIs**

ICMR has provided APIs to several state authorities and labs for timely reporting of COVID-19 testing

data. During the second wave, the COVID-19 testing database grew rapidly in size, impeding the fetching of data. The COVID-19 Data APIs were developed to handle the challenge of the huge testing database and were provided to different organisations (NDMA, NHA, Aarogya Setu App etc.), states and city administration for real-time monitoring of the situation.

- **Antimicrobial Resistance Surveillance Network (AMRSN) available at <http://iamrsn.icmr.org.in>.**

It is a web based tool for collection, management and analysis of data generated by the ICMR AMRSN. The tool has recently been used for contributing AMR data to Global Antimicrobial Resistance Surveillance System (GLASS). The division signed a LoI with Department of Informatics, University of Oslo, Norway on developing an integrated system for surveillance of antimicrobial resistance.

- Leprosy Data Management System (Nikusht) available at <http://leprosy.gov.in>. It is a Web and Mobile based solution for systematic collection, management and real-time monitoring of Leprosy suspects and patients. The solution has been handed over to National Leprosy Eradication Program (NLEP).
- Jal Jeevan Mission is being implemented in partnership with States, to enable every household in villages to have functional household tap connection by 2024. The web-base and mobile app solution has been developed and made available to people/functionaries so as they are able to either test their water on their own using water testing kits or get it tested at the nearest lab. The portal is used to generate nationwide reports for decision support system at the appropriate levels. The system is helping in ensuring safe drinking water to every household, thus improving the quality of life of the people.
- Data collection portal for projects under the implementation research in mental health wherein the Division digitized 110 mental health related scales. The portal is being used

by 25 collaborating centres for submitting data on various aspects of mental health. The portal is available at <http://mentalhealth.icmr.org.in>

- Indicleft tool available at <http://indicleft.icmr.org.in>. It is a comprehensive web based tool developed for an ongoing study at AIIMS that collects data on various aspects of cleftlip and also provides information to the parents of cleftlip patients

In addition, the division is developing analytic dashboards and hosting services to various programs of ICMR and non-ICMR institutions such as Integrated Disease Surveillance Program (IDSP), Indian Rare Disease Registry available at <http://irdr.icmr.org.in/irdr/>). The division developed websites for Health Technology Assessment (<http://htain.icmr.org.in>) and Standard Treatment Workflows (<http://stw.icmr.org.in>).

ICMR-Aiims Computational Genomics Centre

Genomics tools and techniques are revolutionizing medical research through better diagnostics and prognostic markers and personalized risk models for non-communicable disease such as cancer. ICMR established a Computational Genomics Centre in collaboration with AIIMS. The Centre is fully operational and is assisting medical professionals from AIIMS and other medical research institutions in analyzing genomics data. The Centre has developed customized pipelines for making pangenomes, trios data analysis, association studies and rare variant identification.

The centre has also developed the customised pipeline for the analysis of the COVID-19 genome sequence for ICMR institutes. Information about the activities of the Centre is available at <http://genomics.icmr.org.in>.

Electronic Project Management System (ePMS)

Extramural research is promoted by ICMR through Open-ended research on the basis of applications for

grants-in-aid received from researchers/scientists in regular employment in the Universities, Medical Colleges, Postgraduate Institutions, recognized Research and Development Laboratories and NGOs from all over in India. In order to improve efficiency of processing of its Extramural Research Program and to save efforts of the Investigators, ICMR has shifted from manual receipt and processing of extramural projects to web-based interactive system since January 2012. ePMS is a cloud service for Project proposal submission, evaluation and monitoring system. The main vision of ePMS system is to provide Transparent & Centrally Controlled electronic Proposal Evaluation and Grant Disbursement to support R&D Institutions.

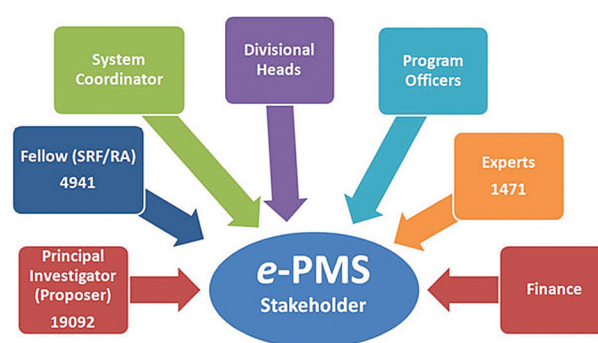


Fig. 18: Stakeholders of ePMS system.



Fig. 19: ePMS system as of today.

During the period total **773** technically approved Adhoc full proposals and **815** Technically Approved Fellowship (SRF/RA) full proposals processed by Technical Divisions and accordingly information updated on e-PMS portal.

Also, total **237** Technically Approved DHR-GIA full proposals were ported from DHR portal to e-PMS portal and processed by Technical Divisions and accordingly information updated on e-PMS portal.

During this period efforts were made for design and development of more user friendly e-PMS portal (<https://epms.icmr.org.in/>).



Fig. 20: Home page of new ePMS system.

Two ‘Call for proposals’ programmes were also launched during the year which resulted in receipt of **334** proposals online and after verifying/checking the duplication/incompleteness/Not in proper format/missing documents, all these proposals were forwarded to concerned division online for further processing. These included a). Call for proposal on Research areas in Leishmaniasis (ECD Division) (63 proposals), b). Call for proposal under North East Seed Grant scheme (RBMH&CH Division) (271 proposals).

ICMR Website

The division launched the improvised, completely GIGW compliant ICMR website on 15th August 2018, based on CMS frame, to enhance user friendliness, enriched content dissemination, latest technique based pages and user compatible design along with enhanced Security. The division is maintaining the ICMR website at <https://main.icmr.nic.in>. The site hosts various ICMR programs, activities, notifications, guidelines, reports, career opportunities in research as well as GOI initiatives followed by the organization.

Management of Direct Benefit Transfer (DBT) Schemes

There are currently 5 Direct Benefit Transfer schemes from ICMR. Division collects transaction data pertaining to direct benefit transfer schemes from e-PMS portal, technical divisions and Account section; then updates this information on the DBT portal every month.

ICMR INSTITUTES/CENTRES

ICMR INSTITUTIONAL NETWORK

1. **ICMR- National JALMA Institute for Leprosy & Other Mycobacterial Diseases (NJIL&OMD)**
Dr. M. Miyazaki Marg, PO Box 101,
Tajganj, **Agra** - 282001
Uttar Pradesh
<http://www.jalma-icmr.org.in>
2. **ICMR- National Institute of Occupational Health (NIOH)**
Meghani Nagar, **Ahmedabad** - 380 016
Gujarat
<http://www.nioh.org>
3. **ICMR- National Institute of Traditional Medicine (NITM)**
Belagavi, National Highway No.4,
Belagavi - 590010
Karnataka
<http://www.icmrnitm.res.in>
4. **ICMR- National Centre for Diseases Informatics and Research (NCDIR)**
Nirmal Bhawan - ICMR Complex (II Floor), Poojanahalli Road,
Off NH-7, Adjacent to Trumpet Flyover of BIAL Kannamangala Post,
Bengaluru - 562 110
Karnataka
<http://www.ncdirindia.org>
5. **ICMR- National Institute for Research in Environmental Health (NIREH)**
Kamla Nehru Hospital Building, Gandhi Medical College Campus,
Bhopal - 462 001
Madhya Pradesh
<https://nireh.icmr.org.in>
6. **ICMR- Bhopal Memorial Hospital & Research Center (BMHRC)**
Bhopal Memorial Hospital & Research Center Raisen Bypass Road,
Near Karond Chouraha, **Bhopal** - 462038
Madhya Pradesh
<http://bmhrc.ac.in>

7. **ICMR- Regional Medical Research Centre (RMRCBB)**
Chandrasekharpur, **Bhubaneswar** - 751023
Odisha
<http://www.rmrcbbsr.gov.in>
8. **ICMR- National Institute for Research in Tuberculosis (NIRT)**
No.1 Sathiyamoorthy Road Chetput, **Chennai** - 600031
Tamil Nadu
<http://www.nirt.res.in>
9. **ICMR- National Institute of Epidemiology (NIE)**
Second Main Road, Tamil Nadu Housing Board, Ayapakkam,
Near Ambattur, **Chennai** - 600 077
Tamil Nadu
<http://www.nie.gov.in>
10. **ICMR- Regional Medical Research Centre, NE Region (RMRCNE)**
Post Box No. 105, **Dibrugarh** - 786001
Assam
<http://rmrcne.org.in>
11. **ICMR- Regional Medical Research Centre, Gorakhpur (RMRCGKP)**
Baba Raghav Das (BRD) Medical College Campus,
Gorakhpur - 273013
Uttar Pradesh
<http://rmrcgkp.icmr.org.in>
12. **ICMR- National Animal Resource Facility for Biomedical Research (NARFBR)**
National Centre for Laboratory Animal Sciences, NIN Campus,
Jamai Osmania P.O. **Hyderabad** - 500 007
Andhra Pradesh
<http://www.narfbr.org>
13. **ICMR- National Institute of Nutrition (NIN)**
Jamai - Osmania (P.O.), Tarnaka,
Hyderabad - 500 007
Andhra Pradesh
<http://www.nin.res.in>
14. **ICMR- National Institute for Research in Tribal Health (NIRTH)**
Nagpur Road, Garha, **Jabalpur** - 482 003
Madhya Pradesh
<http://www.nirth.res.in>
15. **ICMR- National Institute for Implementation Research on Non-Communicable Diseases (NIIRNCD)**
New Pali Road, **Jodhpur** - 342 005
Rajasthan
<https://niirncd.icmr.org.in>
16. **ICMR- National Institute of Cholera and Enteric Diseases (NICED)**
P-33, C.I.T. Road, Scheme XM Belegghata
Kolkata - 700 010
West Bengal
<http://www.niced.org.in>

17. **ICMR- National Institute of Immunohaematology (NIIH)**
13th Floor, New Multi-storied Building, KEM Hospital Campus,
Mumbai - 400012
Maharashtra
<http://www.niih.org.in>
18. **ICMR- National Institute for Research in Reproductive Health (NIRRH)**
Jehangir Merwanji Street, Parel,
Mumbai - 400 012
Maharashtra
<http://www.nirrh.res.in>
19. **ICMR- National Institute of Pathology (NIP)**
Safdarjang Hospital Campus P.O. Box No. 4909, **New Delhi** - 110029
Delhi
<http://instpath.gov.in>
20. **ICMR- National Institute of Medical Statistics (NIMS)**
Post Box No. 4911, Ansari Nagar, **New Delhi** -110029
Delhi
<http://nims-icmr.nic.in>
21. **ICMR- National Institute of Malaria Research (NIMR)**
Sector-8, Dwarka, **New Delhi** - 110077
Delhi
<http://www.nimr.org.in>
22. **ICMR- National Institute of Cancer Prevention and Research (NICPR)**
I-7, Sector - 39, **Noida** - 201301
Uttar Pradesh
<http://www.nicpr.res.in>
23. **ICMR- Rajendra Memorial Research Institute of Medical Sciences (RMRIMS)**
Agam Kuan, **Patna** - 800007
Bihar
<http://www.rmrims.org.in>
24. **ICMR- Regional Medical Research Centre (RMRCPB)**
Post Bag No. 13, **Port Blair** - 744 101,
Andaman and Nicobar Islands
<http://www.rmrc.res.in>
25. **ICMR- Vector Control Research Centre (VCRC)**
Indira Nagar, **Puducherry** - 605006
Puducherry
<https://vcrc.icmr.org.in>
26. **ICMR- National AIDS Research Institute (NARI)**
G-73, MICD Complex, Bhosari, **Pune** - 411026
Maharashtra
<http://www.nari-icmr.res.in>
27. **ICMR- National Institute of Virology (NIV)**
20 A Dr Ambedkar Road, **Pune** - 411 001
Maharashtra
<http://www.niv.co.in>



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