



Annual Report

2018-19



Indian Council of Medical Research
New Delhi

Annual Report 2018-19



icmr
INDIAN COUNCIL OF
MEDICAL RESEARCH
Serving the nation since 1911

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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 2018-19. ICMR scientists worked as a team to achieve the goals in sync with government policies and programmes in the field of biomedical research. There were several significant achievements of the year. A booklet ‘Report on Global Smokeless Tobacco Control Policies and their Implementation’ was released in April 2018. This report is the first ever compilation of the global progress made in implementing smokeless tobacco control policies in respect of the WHO Framework Convention on Tobacco Control. The report includes contributions and inputs from more than 60 national and international experts working in the field of tobacco control. National Tobacco Testing Laboratory was formally inaugurated at NICPR on 31st May 2018. This is a state-of-the-art laboratory intended to provide scientific inputs for implementation of directives of WHO Framework Convention on Tobacco Control (FCTC) in the South-East Asia Region; contribute to technology validation and assist Government of India in development and monitoring of strategies for harm reduction of tobacco products.



ICMR-NICPR has been identified as one of the nodal centers for training of master trainers to implement population based screening program for prevalent cancers by Govt of India.

NIOH initiated Associate Fellow of Industrial Health (AFIH) course along with its regional centres. Associate Fellow of Industrial Health (AFIH) is a three months full time Post Graduate Certificate course in Industrial Health approved by Directorate General Factory Advice Service & Labour Institutes (DGFASLI), Ministry of Labour & Employment, Govt. of India.

NCDIR developed National Stroke Care Registry Programme with the objective to generate reliable data on pattern of stroke, care and treatment from major hospitals that treat stroke patients in India. Also, the centre released “Common EC forms for ethics committee review” on 7th December 2018.

ICMR-NIN has developed a communication kit called “My Plate for the day to prevent hidden hunger” which has a simple visual representation of various food groups to be consumed in a day by an individual intending to reach a 2000 kcal diet. This is clubbed with an easy-to-understand table depicting amounts of raw foods (from various groups) to be chosen to get 2000 kcal energy and 60 g protein. The kit was released by the Hon’ble Vice President of India on 14th Dec 2018 as part of NIN Centenary Year celebrations.

ICMR has supported both field and laboratory investigation for management of outbreak due to pandemic H1N1, ChikV, Dengue, JE, Chandipura, Measles, Rubella, Chicken Pox and Hepatitis A, E by immediate diagnosis and recommendation for control, within minimum turnaround time. The reports were provided to respective authority within 6-24 hours in emergency/outbreak situations.

During 2018-19 around 30 outbreaks were investigated.

ICMR- RMRC Bhubhneshwar is involved in health impact assessment of Pradhan Mantri Ujjwala Yojna (PMUY). The centre has been designated as apex laboratory for JE diagnosis by the state government and has been supporting the various programmes of NVBDCP, IDSP and implementation of RNTCP.

ICMR-NIRT Successfully launched and completed first round of online TB course for Doctors. Centre's study on pharmacokinetics of second-line anti-tuberculosis drugs in children with multidrug-resistant tuberculosis generated pharmacokinetic data for the first time in MDR-TB children in India. Majority of the children had therapeutic drug levels indicating the adequacy of drug dosages.

ICMR-NIV carried out Laboratory diagnostic confirmation of NiV outbreak, in Kozhikode, Kerala State. The centre Isolated and sequenced Nipah virus. Nipah POC qRT-PCR validation was developed by MolBio Commercial company [Truenat test chips].

ICMR-NIV also provided Laboratory support in the investigation of Canine Distemper virus outbreak in Lions in Gir forest, Gujarat in September, 2018. 1094 samples from 313 lions were tested & 68 lions were found positive for Canine distemper virus (CDV).

ICMR-RMRC Jodhpur conducted study to assess probable estimate of magnitude of the problem of sickle cell disorders in the state of Rajasthan. Total 36709 individuals have been screened so far, out of which 4949 (13.48 %) individuals were found to be positive cases. During the year 2018-19, a total of 17529 women from Jalore, Pali and Jodhpur districts, have been imparted training for breast self examination. A total 229 suspect cases of Breast Cancer have been identified and cases have been recommended to consult PHC Medical Officer.

ICMR-NIE initiated a two year NCD epidemiology fellowship program with five fellows. The Southern hub of India Epidemic Intelligence Service Programme (EIS) program was established at NIE during 2018. Five officers are undergoing the program in the first cohort.

Under Human Resource Development (HRD), ICMR selected 144 candidates for Junior Research Fellowship (JRF) through national level exam conducted in July 2018, 882 medical undergraduates were selected for short term studentship (STS), Post-doctoral Research Fellowship (PDF) was granted to 49 candidates and financial assistance was given to a total of eight clinical scientists through newly launched Nurturing Clinical Scientists Scheme. MD/Ph.D Programme is continuing in three universities and thirteen students were selected. A total of 312 non-ICMR scientists were given financial assistance to attend conferences abroad. ICMR institutes continued to provide training to various State level health officials.

During this period, 6 patents (3 Indian and 3 international patents) have been granted to ICMR. A total of 19 patents (13 Indian and 6 international patents) were maintained and 9 International patent applications were maintained.

To celebrate 150th birth anniversary of Mahatma Gandhi a commemorative issue (Collector's edition) entitled, "Gandhi and Health @150: Footprints of ICMR's century-long journey" was brought out. This book was released by His Holiness, The Dalai Lama on 20th March, 2019 at Dharamshala.

To enhance the visibility of ICMR, a new logo was designed as well as to address the need for uniformity of ICMR brand across its institutes and project ICMR brand as the apex health research organization,

a comprehensive branding exercise was undertaken. As a celebration of ICMR's century-long journey and in recognition of the work done by its researchers, a coffee table book titled "Touching Lives" was released by Hon'ble Shri J.P. Nadda, Union Health Minister.

ICMR 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.

ICMR, through online system, received 2636 extramural adhoc proposals, and 1697 extramural SRF & RA fellowship proposals, out of which 429 extramural adhoc proposals and 813 SRF & RA fellowship proposals were technically approved after elaborative evaluation. Eight specified 'Call for proposal' programmes pertaining to certain priority areas, were also launched during the year, which resulted in receipt of 1998 proposals online. ICMR Scientists published over 829 research papers in national and international journals.



(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.

In the year 2018-19, ICMR-NIOH identified serum club cell protein (CC16) along with silica dust exposure history which may be useful as a suitable biomarker for early detection of silicosis, which perhaps is the first of its kind in South-East Asia.

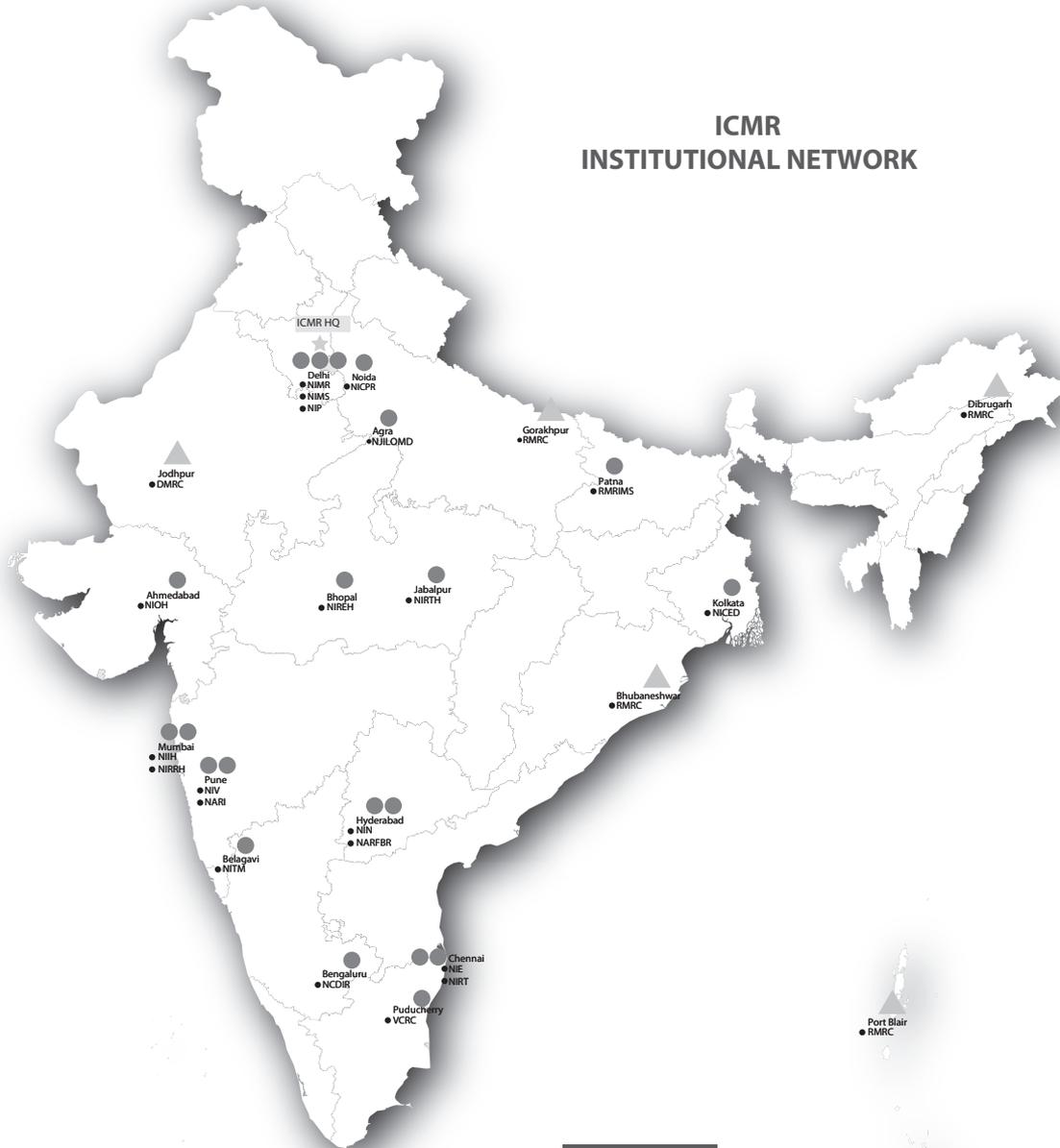
ICMR-NIOH researched for best possible chemical spot assay for detection of lead. The results are suggestive for its possible beneficial use in occupational lead exposure condition for early and onsite detection of lead in sweat. The centre also initiated Associate Fellow of Industrial Health (AFIH) course at NIOH along with its regional centres. Poison Information Centre at NIOH (NIOH-PIC) is one of the five WHO recognized poison centers in India. Centre also collects epidemiological data with special emphasis on poisoning cases in relation to occupational health and the data is provided to WHO. In the year 2018, a total of 479 poisoning cases were referred to PIC-NIOH.

ICMR-NICPR initiated population based screening program for prevalent cancers by Govt of India. The institute has been identified as one of the nodal centers for training of master trainers to implement this program.

Till date, there has been no non-invasive drug delivery system reported for the treatment of Diabetic Retinopathy. ICMR-NIN developed a core-shell nanoparticle-based delivery system loaded with triamcinolone acetonide. ICMR-NIN developed a multi-grain product by combining millets, grains and soy. This formulation was tested for acceptability in the form of Roti and was found to be high in fiber and protein. Roti prepared from this atta preparation was used as a meal to replace lunch with multigrain roti for a period of three months among 50 diabetic subjects. The multigrain product consumption significantly reduced the mean glycosylated hemoglobin from 8.0 to 7.4 and mean diastolic blood pressure reduced from 86 to 81 and the consumption also improved the insulin sensitivity when compared with control group.

At ICMR-RMRC Bhubneshwar, the Health Technology Assessment of a neonatal hearing impairment device, SOHUM is being carried out prior to its introduction into RBSK. During the year 2018-19; a total of 25258 women from Jalore, Pali and Jodhpur districts have been covered by RMRC Jodhpur, and information about awareness about signs and symptoms and risk factors of breast cancer were collected. A total of 17529 women have also been imparted training for breast self examination.

ICMR INSTITUTIONAL NETWORK



ABBREVIATIONS

- INSTITUTES**
- NILOMD - National JALMA Institute for Leprosy & Other Mycobacterial Diseases, Agra
 - NIOH - National Institute of Occupational Health, Ahmedabad
 - NTM - National Institute of Traditional Medicine, Belagavi
 - NCDIR - National Centre for Disease Informatics and Research, Bengaluru
 - NIREH - National Institute for Research in Environmental Health, Bhopal
 - NIRT - National Institute for Research in Tuberculosis, Chennai
 - NIE - National Institute of Epidemiology, Chennai
 - NIMR - National Institute of Malaria Research, Delhi
 - NIMS - National Institute of Medical Statistics, Delhi
 - NIP - National Institute of Pathology, Delhi
 - NIN - National Institute of Nutrition, Hyderabad
 - NARFBR - National Animal Resource Facility for Biomedical Research, Hyderabad
 - NIRTH - National Institute of Research in Tribal Health, Jabalpur
 - NICED - National Institute of Cholera and Enteric Diseases, Kolkata
 - NIH - National Institute of Immunohematology, Mumbai
 - NIRRH - National Institute for Research in Reproductive Health, Mumbai
 - NICPR - National Institute of Cancer Prevention and Research, Noida
 - RMRIMS - Rajendra Memorial Research Institute of Medical Sciences, Patna
 - VCRC - Vector Control Research Centre, Puducherry
 - NARI - National AIDS Research Institute, Pune
 - NIV - National Institute of Virology, Pune
- REGIONAL MEDICAL RESEARCH CENTERS**
- RMRC, Bhubaneswar - Regional Medical Research Centre, Bhubaneswar
 - RMRC, Dibrugarh - Regional Medical Research Centre, Dibrugarh
 - RMRC, Gorakhpur - Regional Medical Research Centre, Gorakhpur
 - RMRC, Port Blair - Regional Medical Research Centre, Port Blair
 - DMRC, Jodhpur - Desert Medicine Research Centre, Jodhpur

LEGEND

- ★ ICMR HEADQUARTERS
- INSTITUTES
- ▲ REGIONAL CENTRES

ICMR-NIRT Centre's study revealed that evening DOTS serve as an alternative choice for easy drug dispensing. Centre developed a documentary animated film on TB awareness for school students. Centre developed a documentary animated film on TB awareness for school students under the study titled "Utilization of school students as ambassadors in TB sensitization in an urban slum, Chennai city."

ICMR-NIV carried out Laboratory diagnostic confirmation of NiV outbreak. The centre Isolated and sequenced Nipah virus; Phylogenetic analysis revealed clustering with Bangladesh strain; 2004. The source of Nipah Infection was traced from Pteropus Bats to Human. Nipah POC qRT-PCR validation was developed by MolBio Commercial company [Truenat test chips]. ICMR-NIV also provided Laboratory support in the investigation of Canine Distemper virus outbreak in Lions in Gir forest, Gujarat in September, 2018. Full genome (~ 15.6 kb) was retrieved from 11 samples, Phylogenetic analysis revealed Indian strain clustered with East African strains.

For the first time in the country, ICMR-RMRC Port Blair carried out a comprehensive health and nutritional survey among the isolated tribe, Jarawas. The survey showed that the tribe is suffering from high prevalence of anaemia and that hypertension and dyslipidaemias are starting to become prevalent among the adults.

A new scheme of ICMR "Nurturing Clinical Scientists Scheme" is being instituted to foster high quality research opportunities. Fresh MBBS/BDS candidates within two years of completing their degree are eligible to apply (Interns/MD/MS/MDS are NOT eligible) in the cutting edge areas of Fundamental Basic/Clinical Research in communicable and non communicable diseases, and reproductive health including nutrition *etc.* at MCI/DCI recognized medical/dental colleges/ICMR network of Institutes/Centers, among others. Special focus will be on fundamental research in priority areas identified by ICMR from time to time, keeping in mind the National Health Policy 2017.

A special issue on 'Challenges in Control of Smokeless Tobacco Use' was brought out by IJMR cell in July 2018. In this special issue one View point, six review articles, three systematic reviews and four original articles were published. Another special issue on 'Nutrition Research: Commemorative issue on 100 years of National Institute of Nutrition, Hyderabad' was brought out in November 2018 with 18 review articles.

During the period, eight specified 'Call for proposal' programmes pertaining to certain priority areas were launched online. These included a). Call for Submission of Concept Proposals for Task force in Nanomedicine b). Task Force on Rare Diseases c). Call for Proposals for participation in studies on Health Care Access among Tribal Population d). Call for Proposals on Systematic Reviews in areas of National Health Priorities e). Call for Submission of Concept Proposals on "Dengue Viral Disease f). Call for Submission of Concept Proposals on "HIV/AIDS g). Call for concept proposals for identifying Young and Middle level Faculty to participate in Research Methodology Workshop h). Call for Proposals on Tribal Health Research.

The ISRM division developed the improvised, completely GIGW compliant ICMR website which increased the outreach to approx 35-40,000 visitors per day. The division worked tirelessly to enhance the outreach of five Social Media Handles of ICMR-- Facebook, Twitter, YouTube, Instagram and LinkedIn. On an average, 30-35 infographics and 4-5 banners per month were designed, throughout the year, which increased the visibility of the organization manifold. These infographics and banners were based on specific days of medical significance e.g. World TB Day; specific events like Antimicrobial

resistance week; specific causes like cancer awareness, Healthy nutrition campaigns, events/activities of ICMR & its institutes.

ICMR participated in Pride of India Expo during 106th Indian Science Congress, a 5 day exhibition during 3rd to 7th Jan, 2019 at Lovely Punjab University, Phagwara. The Science Congress was inaugurated by the Hon'ble Prime Minister of India Shri Narendra Modi on 3rd Jan., 2019. The Pride of India Expo was inaugurated by Dr Harsh Vardhan, Hon'ble Union Minister of Science & Technology and Earth Sciences on 3rd Jan, 2019, who visited the ICMR pavilion and interacted with the ICMR scientists.

ICMR Coordinated with DBT in organizing the Health Conclave with the theme Life Style Diseases: Risk Factors and Preventive Strategies as part of India International Science Festival (IISF) at Indira Gandhi Pratishthan, Gomti Nagar, Lucknow on 7th October, 2018. Prof Balram Bhargava, Secretary to the Government of India, Department of Health Research and Director-General of Indian Council of Medical Research, New Delhi presided over this event and gave key note address on "Value Conscious Innovations".

Dr Chanchal Goyal
Scientist E,
ISRM Division

CONTENTS

Editor's Desk	v
Communicable Diseases	1
Reproductive Health	39
Nutrition	62
Environmental and Occupational Health	66
Non-communicable Diseases	78
Basic Medical Sciences	87
Regional Medical Research Centres	104
Supporting Facilities	124
ICMR Institutes/Centres	152

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 2018-19 are detailed in this chapter.

INTRAMURAL RESEARCH

ICMR-NATIONAL INSTITUTE FOR RESEARCH IN TUBERCULOSIS, CHENNAI

Department of Clinical Research

- STREAM Study – Multi-country trial to evaluate shortened drug regimens in Multi Drug Resistant Tuberculosis.
- TBM Kids Trial – Multi-country trial to determine optimal regimen for tuberculous meningitis in children.
- METRIF Trial - A phase IIB Open Label Randomized trial to evaluate the anti-bacterial activity, pharmacokinetics, safety and tolerability of Metformin when given along with rifampicin, isoniazid, pyrazinamide and ethambutol in adults with newly diagnosed

sputum positive pulmonary tuberculosis: an 8-week study.

- HICON-R Trial - Multi-centric Phase II clinical trial to evaluate the safety, tolerability, pharmacokinetics and anti-bacterial activity of High dose rifampicin versus Conventional dose of Rifampicin in drug sensitive adult patients of pulmonary tuberculosis (HICON-R).
- A study on the role of mobile phone intervention in improving the adherence to chemoprophylaxis for paediatric contacts of sputum positive adult TB patients.

Department of Socio-Behavioral Research

- Targeted Intervention to Expand and Strengthen TB Control in Tribal Populations under the RNTCP, India (TIE-TB Project).
- Patients' perception on Quality of Care in TB Care Settings in Chennai.
- Utilization of school students as Ambassadors in TB sensitization in Chennai.

Health Economics studies

- Establishing Regional Resource Centre for Health Technology Assessment in India (HTA-In).
- Health Technology Assessment for screening of Type 2 Diabetes & Hypertension in India
- STREAM-II: The Evaluation of a Standardized Treatment Regimen of Anti-Tuberculosis Drugs for Patients with MDR-TB – Health Economics Component – India.

- Social network analysis as a tool to improve active case finding at community level in Chennai, South India.

Department of Epidemiology

- Monitoring and evaluation of the TB free Chennai initiative.
- Study of TB prevalence in Tiruvallur District.

Department of Bacteriology

- Validation of indigenous diagnostic kits (Truant) for Tuberculosis.
- Whole Genome Sequencing of drug resistant strains of *M. tuberculosis*.
- Testing of newer molecules and compounds for anti-tubercular activity.
- Building laboratory, Surveillance and Workforce capacity to detect, respond to and prevent drug resistant tuberculosis in India.
- Cambridge-Chennai Centre Partnership on Antimicrobial Resistance in Tuberculosis: Focus on Novel Diagnostics and Therapeutics: Host Directed Therapy through autophagy stimulation.
- Prevalence of TB infection and disease among the pediatric household contacts of MDR TB patients.

RNTCP ACTIVITIES IN NATIONAL REFERENCE LABORATORY

NIRT is one of the 6 National Reference Laboratories for TB in India - closely monitors five states (Andhra Pradesh, Gujarat, Kerala, Tamil Nadu, Telangana State) and five Union territories (Andaman & Nicobar, Puducherry, Lakshadweep, Daman & Diu and Dadra & Nagar Haveli) for RNTCP activities in India.

Department of Biochemistry & Clinical Pharmacology

- Pharmacokinetic study of second-line anti-TB drugs in children and adults with MDR-TB
- Therapeutic Drug Monitoring in drug sensitive, non-responding pulmonary TB patients

Department of Biostatistics

- Identifying Tuberculosis case clusters in Tamilnadu using model based approach and GIS

Department of Immunology

- Population based study of gene repertoire associated with drug tolerance and their in vivo expression.
- Genomic surveillance of *Mycobacterium tuberculosis* isolated from cattle and their handlers in Southern India.
- Molecular analysis of monocyte subsets from humans infected with *M. tuberculosis*.

Department of HIV studies

- Identification of innate immune factors and local immune responses responsible for protection against HIV infection in the mucosal microenvironment of HIV exposed seronegative women.
- Differences in neutrophil responses during the course of anti-TB treatment
- Biomarkers for Tuberculosis Diagnosis and Treatment Response
- Cohorts for HIV Resistance and progression in Indian children and Adults

International Centre for Excellence in Research

- Study of immunology of TB with malnutrition
- Study of TB co-morbidity with diabetes mellitus.
- Characterization of immune responses in TB lymphadenitis.
- Characterization of immune responses of TB in Pregnancy.

Public Health Relevance

- Completed enrolment to an international multicentric cohort of minimal Pediatric TB using four month regimen. Trial has major implications for the management of minimal TB in children.

- Centre's study revealed that evening DOTS serve as an alternative choice for easy drug dispensing.
- Successfully launched and completed first round of online TB course for Doctors.
- Whole genome sequencing of the Indian clinical isolates of mycobacteria improved ability to detect multidrug-resistant mutations, not otherwise detected by LPA and MGIT.
- Centre's finding that the majority of *M. tuberculosis* lineages (Lineage 1, 3 and 4), responsible for disease worldwide exhibit macrophage-induced tolerance to rifampin suggests that strategies to inhibit efflux-mediated tolerance may be effective in shortening treatment regimens for the majority of patients.
- Centre's studies confirmed the presence of *Mycobacterium tuberculosis* in cattle and this raises important public health concerns in India.
- Centre's study on pharmacokinetics of second-line anti-tuberculosis drugs in children with multidrug-resistant tuberculosis generated pharmacokinetic data for the first time in MDR-TB children in India. Majority of the children had therapeutic drug levels indicating the adequacy of drug dosages.
- Centre developed a documentary animated film on TB awareness for school students under the study titled "Utilization of school students as ambassadors in TB sensitization in an urban slum, Chennai city."
- Centre established a Regional Resource Centre for Health Technology Assessment in India (HTA-In).

ICMR-NATIONAL INSTITUTE OF CHOLERA AND ENTERIC DISEASES, KOLKATA

COMMUNITY BASED STUDIES

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

SaniPath-Typhoid project is investigating the environmental transmission dynamics of *Salmonella Typhi*, the causative agent of enteric fever, and quantifying the behavioral risk patterns using innovative laboratory and social science approaches. The results of the study will help in developing and validating an environmental surveillance plan for detection of pathogens causing enteric fever. This could assist in assessing the focal disease load and implementing targeted vaccination campaigns.

Immunogenicity and Safety of Rotavac® and Rotasiil® Administered in an Interchangeable Dosing Schedule among Healthy Indian Infants: A Multicentric, Phase IV, Open-Labelled, Randomized, Controlled Trial.

Two rotavirus vaccines (Rotavac and Rotasiil) are available through the public health systems in India. This study, initiated at the request of the MOHFW, aims to examine the immunogenicity and safety of delivering mixed regimens, comprising of both vaccines, compared to single vaccine doses (either Rotavac or Rotasiil). The study will help in informing the scaling up of both the rotavirus vaccines through the national immunization program in India.



Fig. 1. Rotavirus Vaccine Interchangeability Trial enrolls its first participant.

National Surveillance System for Enteric Fever in India.

Building on ICMR-NICED's experience and expertise on conducting disease surveillance, a community-based site was established to study the

burden of enteric fever in eastern India through this project. This multi-centric study will yield community-based disease burden estimates in India, which shall advise the process of implementation of typhoid vaccines.

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

This collaborative, multi-partner effort aims to assess the impact of the implementation of the Typhoid Conjugate Vaccines by the Navi Mumbai Municipal Corporation. Impact of vaccination on disease burden (through facility-based surveillance), program evaluation of vaccine introduction, AEFI reporting patterns, and economic evaluation of vaccine introduction are being studied.

LABORATORY-BASED STUDIES

Emergence of Azithromycin Resistance Mediated by Phosphotransferases Encoding Gene *mphAin* Diarrhoeogenic *Vibrio fluvialis*.

Circulation of azithromycin resistance *V. fluvialis* isolates with high azithromycin MICs is worrisome, since it may limit the treatment options of diarrheal infections.

Studies on Haitian Variant *Vibrio cholerae* strains manifest Higher Virulence in animal models.

Haitian Variant *Vibrio cholerae* strains manifest higher virulence in animal models and show a more severe clinical outcome, suggesting that this could be due to the greater virulence of these strains compared to the canonical El Tor strains circulating earlier. Results also indicated the need for identifying and tracking the mode of spread of these new hyper-virulent *V. cholerae* O1 strains in the population to prevent the severity and intensity of the outbreaks in populations living in high risk areas.

Characterization of *Vibrio cholerae* regulatory protein CytR in chitin utilization and pathogenesis.

A present study demonstrated that CytR, a regulator in *V. cholerae* played a role in bacterial

motility and mucin penetration. Results showed that Δ CytR mutant failed to adhere with intestinal cells, leading to reduced fluid accumulation and decreased colonization during infection.

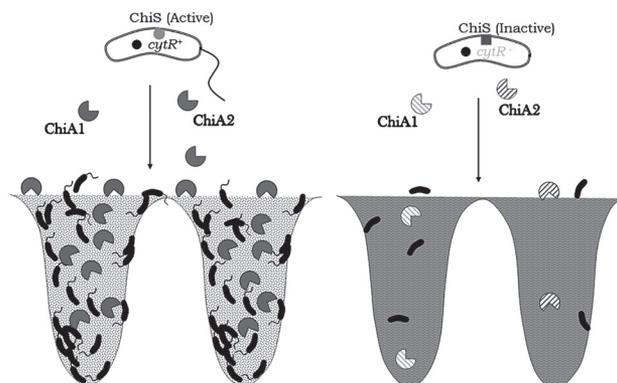


Fig. 2. CytR in *V. cholerae* regulates bacterial motility and mucin penetration, and is a candidate for targeted drug development to reduce pathogenesis.

The role of short chain fatty acid in cholesterol homeostasis: implication in gut immunology.

It was found that short chain fatty acid regulates cholesterol synthesis by downregulating miR122 inhibiting pathogen invasion.

Burden of antibiotic resistance in neonates from developing societies (BARNARDS).

This project provides the means to understand the impact of multidrug resistant Gram negative bacilli on morbidity and mortality among neonates with sepsis. The project has assessed the transmission of resistant enteric organisms from mother to child, an important aspect of neonatal sepsis. Robust understanding on the prevalence of multidrug-resistant gram negative bacteria associated with neonatal sepsis, presentation of resistance mechanisms and targeted sequence analysis will provide comprehensive understanding of the risk factors associated with maternal flora and subsequent transmission among neonates to cause sepsis.

High Resolution Structural studies of Newly Isolated Shigella Phages by Cryo-electron Microscopy and Image Processing.

High Resolution Structural studies of Newly Isolated Shigella Phages by Cryo-electron

Microscopy and Image Processing study revealed the morphology of a newly isolated Shigella phage.

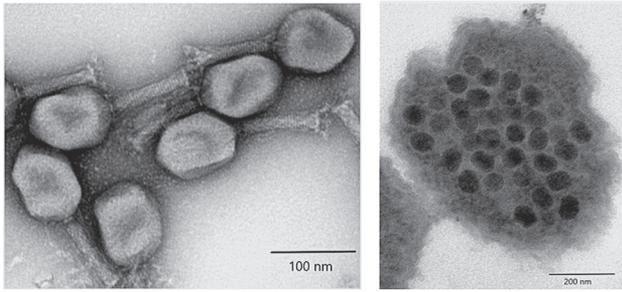


Fig. 3: (Left) Negatively stained shigella phage particles. (Right) Intracellular progeny phage particles inside Shigella flexneri cell thin section Studies with translation potential.

Development of a next generation Outer Membrane Vesicles (OMVs) based immunogen against multi drug resistant non-typhoidal Salmonella mediated gastroenteritis.

This project has been built on previous outcomes and patent related to the development of a novel OMV-based vaccine against enteric fever. The current study aims to investigate a candidate vaccine, and its immunomodulatory activity against multi drug resistant non-typhoidal Salmonella.

Screening of small molecules with antiviral activity as adjunct therapy for viral diarrhoea.

RA-839, a small molecule with potent and highly selective agonistic activity towards cellular redox stress-sensitive Nuclear factor erythroid-derived-2-like 2 (Nrf2)/Antioxidant Response Element (ARE) pathway was identified as a potent and selective inhibitor of rotavirus propagation in vitro.

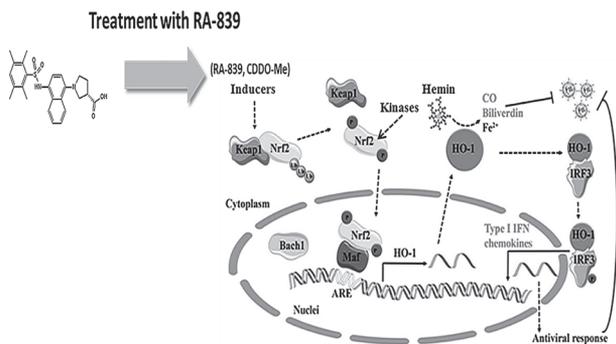


Fig. 4: RA-839, a highly selective agonist of cellular redox stress-responsive transcriptional regulator Nrf2, shows potent antiviral efficacy at sub-cytotoxic concentration.

Development of highly efficacious vaccines against enteric fever using designed peptides as adjuvants.

A synthetic cationic peptide (VG16KRKP) was evaluated for its adjuvant properties to a novel subunit vaccine developed and the augmentation of humoral and cell-mediated immune responses was studied.

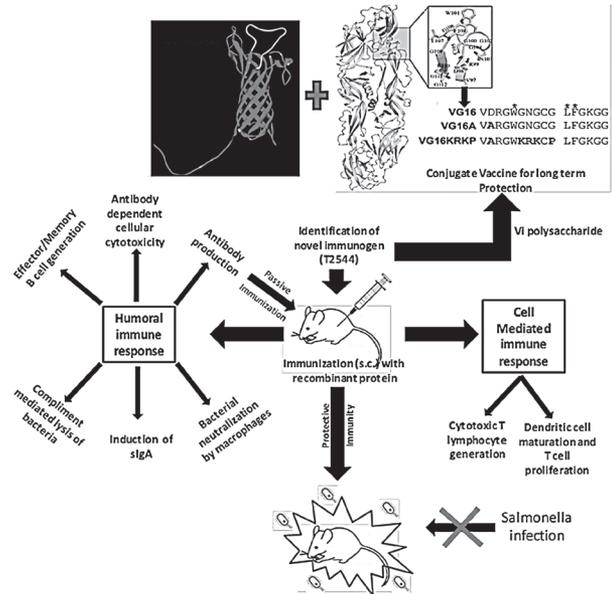


Fig. 5: Novel vaccine formulation containing T2544 and synthetic peptide against Salmonella Typhi.

Therapeutic intervention of Shigella flexneri host pathogen interaction by a small molecule herbal compound.

Therapeutic intervention of Shigella flexneri host pathogen interaction was observed in a small molecule herbal compound known as Caps. The molecule induced autophagic activity at low doses, inhibiting intracellular S flexneri proliferation.

Studies on the immunomodulatory properties of SsIE, a potent vaccine candidate against neonatal septicemic E. Coli.

SsIE, a secreted and cell-associated lipoprotein of neonatal septicemic E. coli promotes macrophage activation and M1 polarization, crucial in framing host's innate immune response and also elicits Th1-specific adaptive immune response.

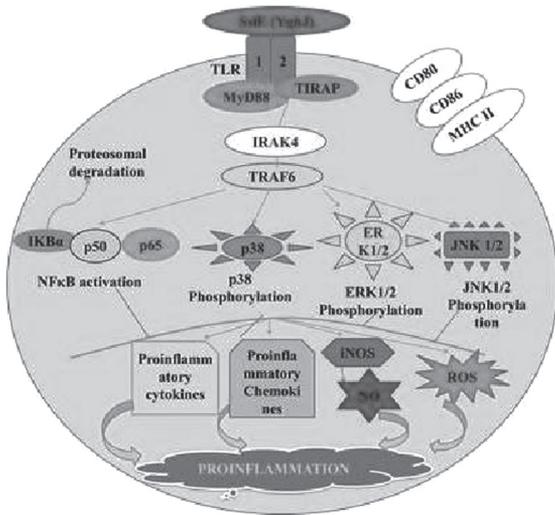


Fig. 6: SsIE, a molecule with translational potential, induced proinflammation and macrophage activation and emerged as a vaccine candidate against septicemic *E. coli*

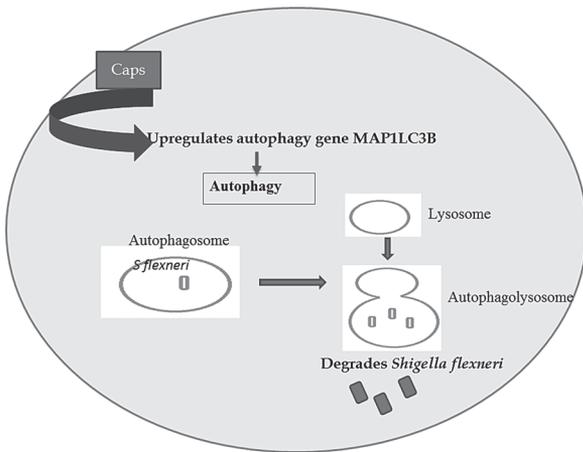


Fig. 7: Caps, a herbal compound induces MAP1LC3B gene which regulates autophagy.

HIV RESEARCH

Multiple research studies and programmatic activities on HIV are being carried out at ICMR-NICED. Key efforts include:

- (i) HIV Sentinel Surveillance (HSS), (ii) Finding drivers of HIV epidemic in select N-Eastern states, (iii) ART Impact evaluation for East and N-E states under National AIDS Control Program, (iv) External Quality Assessment of HIV testing as National Reference Laboratory, (v) Quality evaluation of HIV, HBV & HCV diagnostic kits, (vi) Molecular assay for HIV among babies (up to 18 months age) born to HIV infected mothers, (vii) HIV viral load estimation for PLHIV under ART, (viii) Assessment

of HIV drug resistance mutations (Transmitted & Acquired), (ix) Integrated Counseling and testing for HIV.

Major findings include:

- Level and trend of HIV epidemic and correlates among different risk population and concurrent presence of overlapping HIV epidemic drivers, primarily hetero-sexual (casual sex among young population), beside IDU driven epidemic as found earlier in N-E state helped in focused intervention planning.
- Absence of transmitted HIV drug resistance mutation indicates success-potential of current ART regimen under National AIDS Control program.

STUDIES ON VIRAL DISEASES

Surveillance and molecular characterization of enteric viruses among children (<5y) reporting with acute gastroenteritis.

Revealed one or more viral pathogen as identified in ~45% of the children hospitalized for treatment of acute gastroenteritis with moderate to severe dehydration.

Circulating Dengue Serotypes in 2018 in West Bengal.

During 2018, most of the districts of West Bengal including Kolkata suffered from dengue.

Studies on genomic variation of hepatitis C virus in high risk group population in Eastern part of India; Molecular diversity of Hepatitis C virus in a tertiary care hospital of Manipur, India.

Most of the hemodialysis patients were infected with HCV genotype 1c (~72%), whereas thalassemia patients were infected with HCV genotype 3a (~78%). Thalassemia patients with lower age group have greater chances to clear the virus.

INFLUENZA STUDY

Tested 391 samples to understand current circulating strain among the elderly and found 9.46% positive for influenza viruses.

Virus Research and Diagnostic Laboratory

Surveillance for a number of viral infections of public health importance were undertaken through the Viral Research and Diagnostics Laboratory (VRDL). Summary of activities are tabulated below:

Investigations Performed	Total No. of Samples Tested in 2018-19	Positive Samples	Isolation Rate
Rotavirus Ag ELISA	410	145	35%
Scrub typhus IgM ELISA	527	156	30%
Hepatitis E IgM ELISA	348	88	25%
Respiratory panel PCR (other than Influenza)	451	104	23%
Dengue IgM ELISA	926	213	23%
Hepatitis A IgM ELISA	376	85	23%
Dengue NS1 ELISA	1005	206	20%
Influenza panel PCR	2669	545	20%
Chikungunya IgM ELISA	357	38	11%
Hepatitis B Surface Ag ELISA	164	15	9%
Chikungunya PCR	1173	68	6%
Hepatitis C Ab ELISA	149	8	5%
Zika PCR	1090	0	0%

- Ongoing research involves monitoring of Dengue serotypes, Chikungunya, Influenza virus and drug resistance pattern (neuraminidase inhibitor) among the circulating strains.
- As a regional centre, regular training of healthcare professionals is conducted in the form of hands-on-workshops covering epidemiology, specimen handling and transport, serological and molecular diagnosis of emerging viral diseases, cell culture techniques, laboratory safety and quality assurance.

STUDIES ON PARASITIC DISEASES

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

Primary survey and pre deworming prevalence mapping has been completed in the states of Uttar

Pradesh, Telangana, Chhattisgarh, Tamil Nadu, West Bengal, Sikkim, Tripura, Assam, Meghalaya, Manipur, Mizoram, Arunachal Pradesh and the data has been shared with Ministry of Health and Family Welfare.

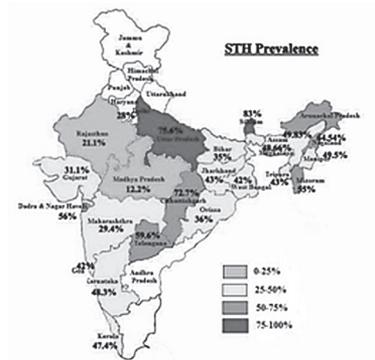


Fig. 8: Prevalence mapping of STH in India showing pre deworming prevalence in children

CAPACITY BUILDING

- The institute invests heavily in building the healthcare capacity of the nation. During 2018-2019, 72 PhD students (13 completed); 11 post-doctoral trainees; 59 Master’s students got trained at the institution.
- Five foreign fellows worked in the institute during 2018-2019. Eighty Homeopathy students were trained in the basics of research and laboratory practices. Over 150 healthcare professionals were trained under various HIV training programs.

Divisions of Epidemiology and Biostatistics, Training and Extension, and Virology (through NACO/HIV, VRDL) conduct regular training programs targeting MD students, medical college faculty, program managers, and public health personnel. Seventy-seven participants, from VRDLs, VDLs, and medical colleges were trained in 2 hands-on training workshops organized by the VRDL.

ICMR-NATIONAL INSTITUTE OF MALARIA RESEARCH, NEW DELHI

EPIDEMIOLOGY AND CLINICAL RESEARCH:

Monitoring efficacy of antimalarials

NIMR is monitoring the therapeutic efficacy of antimalarials used in the national programme. The results of these studies have helped to provide inputs for policy changes from time to time. NIMR is carrying out studies in Northeastern states of India namely Dhalai, Tripura; Lawngtlai, Mizoram; Udalgiri Assam and West Garohills, Meghalaya. Till date, forty patients were enrolled at Udalgiri, Assam. Patients were followed up for 28 days and treatment failure was not observed in any of the case.

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. The slide bank consists of over 6000 slides of different species and densities of malaria parasites and negative slides. All the samples collected so far were diagnosed by polymerase chain reaction as well as microscopy. The blood smears are stored and maintained by ICMR-NIMR, New Delhi.

Quality Assurance of Malaria Rapid Diagnostic Tests

The project was initiated to assess the quality of RDTs procured and supplied by NVBDCP. NVBDCP is the nodal centre and ICMR-NIMR is National Referral Laboratory for this project. Quality assurance (QA) panels were prepared from time to time. Over 90 QC panels have been prepared till date. As a part of the Pre-dispatch QA, RDTs were assessed to ensure their quality with known negative and positive samples before they were supplied to various states. During 2015-2019, 155 batches of RDTs received from NVBDCP through pre-dispatch programme have been tested by NIMR and except 5 batches, all were found to be acceptable. The long-term testing of these RDTs which was performed 6 months prior to expiry showed that among 85 lots tested so far, five lots results were deferred.

Sl. No.	Year	Pre-Dispatch			Long term		
		Lot Tested	Lot Passed	Lot Failed	Lot Tested	Lot Passed	Lot Failed
1	2015	49	49	0	0	0	0
2	2016	27	27	0	21	21	0
3	2017	11	11	0	51	48	3
4	2018	53	48	5	9	7	2
5	2019 Till March	15	15	0	4	4	1
	Total	155	150	5	85	80	5

Post-dispatch QA is carried out to assess the quality of RDTs at periodical intervals with low parasite density positive panels. Nineteen RDTs are drawn at random from each district from different levels (PHCs, Sub-centre, ASHAs) and tested with QC panels. This process is repeated quarterly. During 2015-19, over 4095 RDTs from 13 states were tested. The overall concordance recorded was 99.08%.

Screening of erythrocytic stage secretory proteins for detection of malaria parasite

To investigate the utility of glutamate dehydrogenase as molecular target for malaria diagnostics, this exploratory study is under progress. For three Glutamate dehydrogenase (GDH) gene from *P. falciparum* genome B-cell epitopes were identified using bioinformatic analysis. The predicted epitopes specific to each gene are (a) NADP-specific GDH (Chromosome 14; NCBI Gene ID-811745; Protein ID-XP_001348337.1, MGGGKGGSDFDPKGKSDN; PCTDVPAGDIGVGGR), (b) GDH putative (Chromosome 14; NCBI Gene ID-811868; XP-001348460.1, PMGGGKGGSDFDPKGKSEN), (c) GDH putative (Chromosome 8; NCBI Gene ID-2655330; XP_001349494.1, NEQYSSDKYFPTFEET; PFQQGKLRKNGGVPHD). The predicted epitopes were synthesized commercially. Simultaneously, centre has established gene cloning, protein expression and purification platform in the laboratory, to clone, express and purify *P.*

falciparum glutamate dehydrogenase as positive control. Centre purified the recombinant protein upto 90% successfully. On the other side, animal experiments in animal research facility of NIMR to raise polyclonal antibodies are ongoing and subsequently ELISA will be performed to check the antibody titer against the positive control and predicted epitopes.

Fever Clinic

At fever clinic, 123 malaria cases were diagnosed from January 2018 to December 2018. 72 % were males while 28 % were females and Peak of the malaria cases was observed in the month of August and September. All the confirmed malaria cases were given treatment as per the national treatment guidelines.

NIMR is one of the sentinel surveillance sites for diagnosis of dengue and chikungunya. A total of 808 dengue cases and 68 chikungunya cases were diagnosed in 2018. Gender wise distribution of dengue cases was 62 % males and 38 % females. Maximum number of cases reported in the month of October. Dengue serotyping was performed in 11 samples and DEN- 3 was found in all the samples.

Malaria elimination model – Punjab

Malaria disease burden in the Punjab state has been worked out based on one year's surveillance data and cases reported at government/private health facilities. The incidence of malaria in this study has been worked out as strata specific for high, medium and low endemic areas in the state. Based on the actual number of malaria cases reported from high, moderate and low transmission study area, the number of malaria cases from three strata of the state have been estimated to be 3979, 1039 and 106, respectively. Thus, the estimated number of malaria cases from the state should be around 5124 (range 4360-5888) per annum, which are about 7-8 times more than the reported cases by the state government. However, even after the estimated number of cases, the state still qualifies for malaria elimination as per criteria of malaria elimination.

The molecular study revealed the existence of sub-microscopic malaria cases in the low transmission areas of Punjab. Compared to light microscopy (LM) and rapid diagnostic test (RDT), PCR has detected 1.3% additional positive cases. Such undetected parasite positive cases may pose bigger problem any time due to continued transmission. Therefore, application of more sensitive diagnostic tools such as PCR and LAMP in combination with conventional methods may be much more useful particularly in low transmission settings to achieve malaria elimination.

Preliminary investigation of Chikungunya vectors during Chikungunya outbreak in Ranchi, India

Breeding of *Aedes* species was carried out in Hindpiri, Karbala Nagar and Harmu area of Ranchi city. A total of 928 households were inspected. Of these, 72.7% households were infested with breeding of *Aedes* species. Three species of *Aedes*, namely *Aedes aegypti*, *Aedes albopictus*, and *Aedes vittatus* were identified in Chikungunya affected areas. *Aedes aegypti* was most prevalent in the Chikungunya affected areas and species composition was >70.5%. The results have shown that the average stegomyia indices were house index (HI) 72.7, container index (CI) 55.2 and breteau index (BI) 395.4. The highest House/ *Aedes* Index (HI/AI), Container Index (CI) and Breteau Index (BI) were observed in Hindpiri (87.1), Harmu (57.2 and 426.5), respectively.

Insecticide susceptibility result revealed that *Aedes aegypti* was resistant to DDT as only 7.5% mortality was observed. Exposure of *Aedes aegypti* to malathion and deltamethrin induced 100% mortality indicating that species were susceptible to malathion and deltamethrin. It can be concluded preliminarily that *Aedes aegypti* and *Aedes albopictus* were well established within the urban agglomeration of Ranchi city with the survey area showing high adult and larval indices which may be the probable reason for the sudden spurt of chikungunya infection in these areas.

Epidemiology of *Plasmodium knowlesi* transmitted malaria in India

A total of 186 blood slides were collected from the patients suffering from *Plasmodium falciparum* and *Plasmodium vivax* malaria from dense forest area. Simultaneously filter paper blood samples were collected for PCR analysis. Out of 186 blood slides, 4 slides revealed some unusual parasitic morphology such as amoeboid structure, thick chromatin and extended cytoplasm which are generally not observed in human *plasmodium species*. PCR analysis of all the samples is in progress.

VECTOR CONTROL

Maintenance of stock of larvivorous fish *Gambusia* and *Guppy* in Guwahati metropolis and suburban settlements for biological control of mosquito breeding.

Stocks of both *Guppy* and *Gambusia* are being maintained in Guwahati metropolis. These larvivorous fishes are supplied to various districts of Assam and other establishments including cantonment areas on their request. Other north-eastern states were also provided fish on their request. So far, in 2018 as many as 60000 *Gambusia* fish have been supplied to Assam, Arunachal and various military establishments in Guwahati city. Other States have also requested for supply of larvivorous fishes but due to non availability of operational costs it could not be supplied.

PARASITE BIOLOGY AND DRUG DISCOVERY

Crucial residues in cysteine proteases of parasite mediate hemoglobin hydrolysis

Falcipain-2 (FP2) and falcipain-3 (FP3) constitute the major hemoglobinases of *Plasmodium falciparum*. Centre has identified an individual residue within the Hb binding domain of both falcipains (Glu¹⁸⁵ of FP2; Asp¹⁹⁴ of FP3), essential for Hb degradation. Mutation of these residues didn't alter activity against smaller substrates but ablated their ability to degrade Hb. Residue swap

experiments of these residues within falcipains restored hemoglobinase activity, suggesting functional conservation at this position. This study indicates that targeting exosite-based interactions could offer a new field to explore in malaria therapeutics, as exosites when compared to active site encounter little-to-no drug pressure, therefore could be less susceptible to emergence of drug resistance.

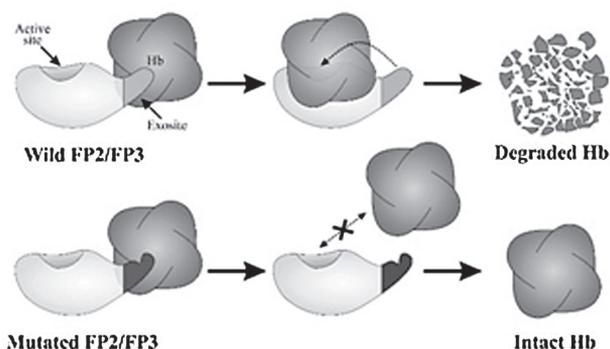


Fig. 9: Schematic representation of cysteine protease interaction with haemoglobin and its breakdown based on biochemical study.

The Representation showed that C-terminal part of enzyme interacts with haemoglobin and some residues at c-terminal play critical role in interaction.

Uncovering key interacting partners of kelch13: the primary driver of artemisinin resistance.

Centre has recombinantly expressed Bric-a-Brac/ Poxvirus & Zinc-finger (BTB/POZ) and propeller domain of *PfK13* protein and antibodies were generated against recombinant *PfK13* protein. Co-immunoprecipitation (CoIP) assays and mass spectrometry have identified following interacting proteins with *PfK13*- Thioredoxin-like mero protein (PF3D7_1104400), Pyridoxal kinase (PF3D7_0616000) and Trafficking protein particle complex subunit 3-putative (PF3D7_0418500). These interacting proteins with *PfK13* are important components of the biological redox system, invasion and transport strengthens the idea that *PfK13* plays a crucial role in maintaining the oxidative stress, invasion and vesicular transport pathway within *P. falciparum*.

The Ramachandran plot shows the stereochemical quality of the models. ProSA- Z-score plot shows that the model structure lies within the range of native protein score of similar size.

Characterization of an unusual protease: metacaspase-3

Unlike other clan CD peptidases, PfMCA3 has an atypical active site serine (Ser1865) residue in place of canonical cysteine and phylogenetically forms a distinct branch across the species. To investigate whether this domain retains catalytic activity, centre expressed, purified and refolded the Peptidase_C14 domain of PfMCA3. PfMCA3 was found to express in all asexual stages with maximal expression observed during the ring stage. Enzymatic assays showed PfMCA3 to exhibit trypsin-like serine protease activity with Ser1865 acting as a nucleophile to cleave trypsin substrates. Its activity was further inhibited by trypsin-like serine protease inhibitor. PfMCA3 was found to be inactive against caspase substrate and insensitive to caspase inhibitors. Overall, this study characterizes a novel metacaspase of *P. falciparum*, different from human caspases and not responsible for the caspase-like activity, therefore, could be considered as a potential chemotherapeutic target.

Allosteric site inhibitor disrupting activation of cysteine proteases of plasmodium falciparum

Centre designed and synthesized six azapeptide compounds, among which, NA-01 & NA-03 arrested parasite growth by specifically blocking the auto-processing of falcipains. Inhibitors showed high affinity for enzymes in the presence of the prodomain without affecting the secondary structure. Binding of NA-03 at the interface induced rigidity in the prodomain preventing structural reorganization. Study further reported a histidine-dependent activation of falcipain. Collectively, for the first time centre provided a framework for blocking the allosteric site of crucial haemoglobinases of the human malaria parasite. Targeting the allosteric site could provide high selectivity and less vulnerable to drug resistance.

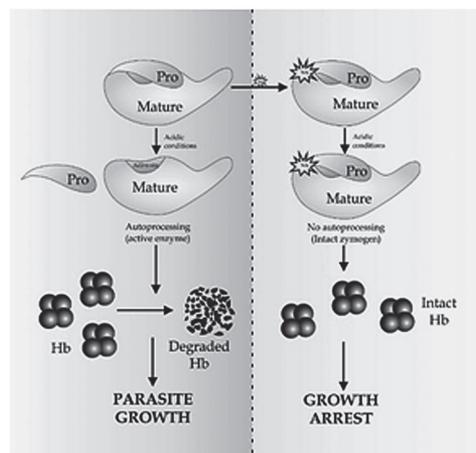


Fig. 10: Schematic representation of the allosteric site inhibition in falcipain.

In natural condition, a prodomain dissociates from the complex and active enzyme cleave hemoglobin. While in the presence of allosteric inhibitor which bind at the interface of the complex and block the processing of active enzyme, therefore no cleave of haemoglobin and consequently arrest the parasite growth.

Absence of artemisinin resistant genotype in Plasmodium falciparum isolates from Central and Northeast India

A total of 236 dried blood spots collected from two sites each at Central (n=62) and Northeast India (n=174) in 2017-18 were investigated for the prevalence of mutations in kelch-13 gene. The objective was to investigate WHO validated mutations in kelch-13 propeller domain, which were reported to be involved in artemisinin resistance. In total, n=162 isolates were successfully PCR-sequenced for whole kelch-13 gene. The results showed absence of any mutation in kelch-13 propeller domain. However, only 2 non-synonymous mutations named K189T (Central India; n=08, Northeast India; n=02) and T192A (Northeast India; n=01) were observed and n=39 (Central India; n=09, Northeast India; n=30) isolates showed variations in the number of ATA repeats, which adds repeats of Asparagine (N) at 137th-142nd amino acid position in kelch-13 gene. Majority of isolates (Central India; n=33, Northeast India; n=79) showed wild-type kelch-13 gene.

Characterizing the drug resistance polymorphisms and in vitro sensitivity in *Plasmodium vivax* isolates.

The prevalence of mutant alleles in *pvm*dr-1, *dhfr* and *dhps* genes along with in vitro CQ sensitivity in *P. vivax* isolates was studied. Genotyping of the drug resistance genes viz *dhfr*, *dhps* and *pvm*dr-1 was carried out in 32 *P. vivax* samples and the in vitro susceptibility was determined for CQ sensitivity by the SMI technique. The PCR sequencing for *pvm*dr-1 genes in 32 samples showed five non-synonymous mutations at codons and the prevalence of *pvm*dr-1 mutations was of eight types of haplotypes were observed on sequencing. The *dhfr* and *dhps* genes on sequence analysis revealed the presence of wild type genes in the isolates. The median range for IC₅₀ was 68.9nM. There was no difference in the IC₅₀ and IC₉₀ values between the groups. To associate the point mutations in the drug resistance genes with CQR requires further research in more number of samples and molecular surveillance regularly in *P. vivax*.

VECTOR-PARASITE INTERACTION BIOLOGY

Interorgan Immune communication keep mosquitoes healthy

Under pathophysiological alteration in response to microbial exposure in the mosquito *Anopheles stephensi*, first study examined the AMPs expression in three important mosquito tissues such as MG, FB, and HCs. Later study also traced the molecular link of the signaling transmitters, i.e., REL and the synthesizer of NO, i.e., NOS, controlling AMPs expression. Study found that each tissue has unique ability to respond local/systemic challenges; however, HCs are more specialized than the gut and FB to recognize and discriminate-specific antigens. This study also demonstrates that both REL and NO participate in the overall management of the interorgan immune communication, but each tissue specifically maintains the interorgan flow of signals (Fig. 11). A deep understanding of the factors controlling interorgan immune communication could enable us

to translate this knowledge to design a strategy to block pathogen development and its transmission by vector's genetic modification strategies.

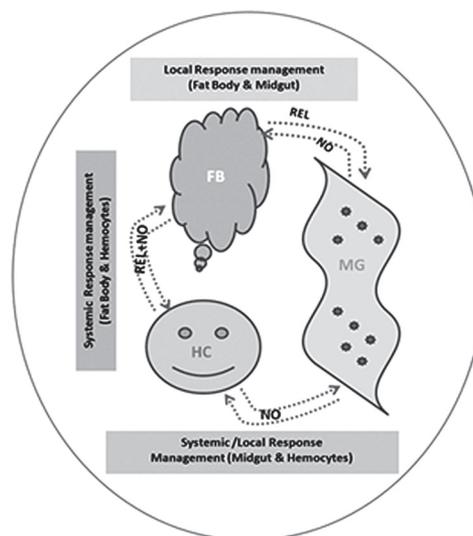


Fig. 11: Proposed working model for functional validation and establishment of immune co-ordination and participation of relish (REL)/nitric oxide (NO) synthase regulating AMPs response.

To establish possible flow of signal relationship, centre interpreted the cross tissue experimental data as below:

(i) Endogenous bacterial feeding: demonstrating NO dominantly regulate flow signal from midgut (MG)-to-FB and/or MG-to-hemocyte (HC); (ii) Exogenous bacterial injection: demonstrating REL dominantly regulate flow signal from FB-to-MG; while NO regulate HC-to-MG. A synergistic relationship of REL/NO between FB and HC was established by combining individual and mixed Gram negative & Gram Positive bacterial challenge experiments. For details refers full text publication link <https://www.frontiersin.org/articles/10.3389/fimmu.2018.00148/full>

ICMR-VECTOR CONTROL RESEARCH CENTRE, PUDUCHERRY

STUDIES ON ELIMINATION OF LYMPHATIC FILARIASIS (LF)

An alternate triple drug regimen (Ivermectin, Diethylcarbamazine and Albendazole) for the Mass Drug Administration (MDA)

ICMR-VCRC continues to undertake operational research that contributes to LF elimination at global and national level. One of the major studies was a community based block randomized trial (a part of multi-centric study) carried out in Yadgiri district, Karnataka with an objective of finding an alternate and more effective drug regimen for Mass Drug Administration (MDA) to accelerate Elimination of Lymphatic Filariasis. Treatment of over 4500 participants with a new drug regimen of single dose of 3-drugs (Ivermectin, diethylcarbamazine and albendazole) showed that this regimen has no safety concern, and was acceptable to the community, more efficacious and effective compared to the currently used 2-drug regimen (diethylcarbamazine and albendazole). The outcome of the study was a major evidence-base for the WHO to recommend this regimen for MDA for LF-elimination in specific situations. The Technical Advisory Committee (TAC), Ministry of Health, Govt. of India has approved this regimen for LF-elimination in India. Further, the NVBDCP has identified five districts for implementing the three drug regimen on a pilot scale.

MATHEMATICAL MODELING

- **Prospects of elimination with 3-drug regimen over 2-drug regimen:** The LYMFASIM simulation model was applied in settings with 3-5% MF-prevalence post 10 MDA of DA with 50% MDA coverage to compare the impact of the 3-drug regimen (Ivermectin, DEC & Albendazole) on LF elimination with the currently used 2-drug regimen. The model predictions showed that the 3-drug regimen with >65% coverage can achieve elimination in 2-3 rounds. The outcome facilitated the WHO to make a recommendation on the number of MDA rounds for different situations using the 3-drug regimen for LF-elimination.
- **Optimizing evaluation unit (EU) size for transmission assessment survey (TAS):** Currently, TAS is the WHO recommended protocol for making programmatic decision on stopping MDA in an evaluation unit (if district population \leq 2 million). Modelling studies

at VCRC, simulating TAS results at district level showed that despite passing TAS after 7 MDAs, the district could have sub-districts with risk of continuing transmission (hotspots) in 19-39% villages/wards. Therefore, the feasibility of downsizing EU for TAS needs to be explored from district to a sub-district.

Vector surveillance for monitoring and evaluation

A two-stage cluster-design based vector surveillance strategy (sampling design, gravid-trap, molecular xenomonitoring-MX) was developed for monitoring filarial infection and stopping MDA, and validated at an evaluation unit earlier. The results provided evidence for MX as an alternative or supplementary strategy for stopping MDA. This protocol was further validated in three different settings [Transmission assessment survey (TAS) passed once, twice, and failed]. MX results are in agreement with TAS. MX is recommended by the WHO for its adoption as a standardized protocol for global and national LF elimination programme (WHO/HTM/NTD/PCT/ 2013.10; NVBDCP Guidelines, 2016 (Draft)) for stopping MDA or post-MDA surveillance. MX is also considered by the WHO as a surveillance tool for post-validation phase.

Enhanced community compliance

The determinants of compliance were identified using intervention mapping model in three districts (Muzaffarpur in Bihar, Nalgonda in Telengana and Surat in Gujarat) under MDA. Changed objectives were derived with practical solutions and intervention plan for specific situation was designed jointly with programme.

Studies on *Aedes* surveillance and dengue, chikungunya and ZIKA prevention

DENGUE PREVENTION (IVM) IN PUDUCHERRY

Puducherry district, Union Territory of Puducherry (population of 9.5 lakhs) has been reporting dengue outbreaks in recent years. In 2017, a total of 4568

cases (incidence 4.8 per 1000) and 7 deaths and in 2018, a total of 420 dengue cases (incidence 0.42 per 1000) and 2 deaths were reported. Using the data on dengue cases reported by state NVBDCP, spatial distribution maps highlighting 'hotspots' are prepared. The ICMR-VCRC has established vector surveillance in Puducherry district, covering 31 sites, randomly selected from all the 31 Primary Health Centres (PHCs). In each site, minimum 40 households are being surveyed. The data on vector breeding indices in these sites and spatial hotspot maps of dengue cases are shared regularly online with state NVBDCP, the Dengue Management Group created by the Honourable Lt. Governor of Puducherry involving all relevant Departments and stakeholders and for the public.

The vector surveillance data along with community grievance registration system of the State Govt. serve as the guiding tool for planning and implementing dengue specific control activities including the visit of high power team and dengue control squads to problem areas.

Vector surveillance for ZIKA in selected high risk areas in India

ZIKA–vector surveillance is being carried out in collaboration with seven ICMR Institutes (NIMR, NIRTH, and RMRCs at Bhubaneswar, Port Blair, Dibrugarh and Belagavi). *Aedes* specimens collected from 46 districts distributed in 13 States were screened for ZIKA infection by RT-PCR. Altogether, 55089 specimens of *Aedes* mosquitoes (*Ae. aegypti* – 31636; *Ae. albopictus* – 22289 and *Ae. vittatus* – 1164) were screened for ZIKV infection in 4679 PCR pools and none was found infected with ZIKV. However, 3 PCR pools were found positive for DENV infection.

ICMR-NATIONAL INSTITUTE OF VIROLOGY, PUNE

Influenza Diagnostic Services/Outbreak Investigation

The group is providing diagnostic support to patients suspected for Influenza infection, samples referred by different clinics/hospitals across Maharashtra.

2716 clinical samples were tested using real time RT-PCR and 691 (25.44%) were found positive for influenza viruses. 605 (22.28%) were Influenza A/H1N1pdm09, 63 (2.32%) A/H3N2 and 23 (0.85%) were Influenza B virus positive respectively. Peak influenza activity was observed during September-October. Further, 935 A(H1N1) pdm09 positive clinical samples were assessed for H275Y mutation responsible for Oseltamivir drug susceptibility by real time RT-PCR. All were found sensitive except 6 samples [Pune (n=1), Chennai (n=1), Jaipur (n=4)] with reduced susceptibility. Circulating A/H1N1pdm09 virus from 2018-19 are similar to vaccine component A/Brisbane/02/2018. Phylogenetic analysis of A/H3N2 virus HA gene grouped in Clade 3C.2a1b with similarity to A/Singapore/INFIMH-16-0019/2016 which was the 2018-19 northern hemisphere vaccine component. Both Victoria and Yamagata lineages of influenza B were co-circulating and are similar to B/Colorado/06/2017 and B/Phuket/3073/2013 vaccine components.

Creating laboratory network for enhancing diagnostic capabilities for surveillance, outbreaks and epidemic investigations of high-risk group of viral pathogens causing respiratory infections

A network of laboratories has been established in the country to carry out surveillance for respiratory viral pathogens, Influenza and RSV, hMPV, PIV, adenoviruses and rhinoviruses. Of 6250 patients that were enrolled, 1617 throat/nasal swabs samples from Acute Respiratory Infections (ARI) and 4633 from SARI patients were tested for different respiratory viruses by duplex real time PCR. 19% and 39% positivity was detected in ARI and SARI cases respectively. In ARI, 10% samples were found positive for Influenza virus, hRSV (2%), hPIV (2%), adenovirus (2%), rhinovirus (1%), hMPV (1%). In SARI, Influenza virus was detected in 13% samples, RSV (9%), Rhinovirus (5%), PIV (4%), hMPV (3%), Adenovirus (3%) and co-infection in 2% samples.

Tracking community mortality due to respiratory syncytial virus in Melghat, a tribal

area in Maharashtra

A total 1107 samples were tested for RSV virus by real time RT-PCR to identify RSV associated mortality in infants/children below 2 years of age. RSV-B was detected in 363 (32.8%) samples and peak activity was observed during the month of August and September. Seven deaths were associated with RSV B detection.

Etiology of childhood pneumonia in India (ICMR Multicentre study)

A total of 371 and 198 throat /nasal swabs from KEM Pune and PGI Chandigarh respectively were received for respiratory virus detection. RSV B was detected in 120 (21%) samples and influenza was detected in 22 samples. The other viruses detected were hRV (25) hPIV (16) hMPV and Adeno (11).

Strengthening/promoting evidence-based advocacy for influenza prevention and control in India

Community-based surveillance is being conducted among an open cohort of 1114 elderly to find the burden of illness for influenza and RSV among elderly in India. Trained project nurses conducted household surveillance five days a week to screen and enroll individuals for the presence of acute respiratory infection [ARI]. After 34 weeks of follow-up, total 31246 [88.1%] visits have been conducted. The incidence rate in ARI was 41.4 per 1000 elderly per week. Total 301 samples were collected and influenza positivity was 27 [9%] and influenza-associated ARI incidence rate was 3.6 per 1000 elderly per week. The RSV positivity was 9 [0.3%].

Hospital based surveillance of rotaviruses and strains in children with acute gastroenteritis

The study involves hospital-based surveillance of acute gastroenteritis cases among children <5 years age for determination of the disease burden, seasonal distribution and circulation pattern of prevalent G-P genotypes of rotavirus A (RVA). Fecal specimens collected from 116 children, hospitalized with acute gastroenteritis at Pune, Maharashtra (Western India) that were screened for

RVA showed 31.9 % positivity (n=37). Among RVA positive cases, 40.5% presented with severe disease and 54.5% as moderate disease. G3P[8], G1P[8], G9P[4], G1P[6] G2P[4] with predominance of G3P[8] RVA strains (67.6%) was observed. Mixed infection of rotavirus genotype G1G9P[4] was detected in a single specimen.

Acute gastroenteritis outbreak in Rahude and Kalwan in Nashik district of Maharashtra

An outbreak of acute gastroenteritis was reported on 8th and 12th July, 2018 at Rahude and Kalwan village of Nashik district, Maharashtra. Investigation was conducted for viral etiology. Fecal specimens (n=16) collected from the outbreak area (Rahude, n=13; Kalwan, n= 3) for Rotaviruses (RVA, RVB and RVC), Norovirus, Enteric adenovirus, Astrovirus and Enterovirus. All specimens showed absence of viral etiology with an exception of a single specimen tested positive for enterovirus.

Detection and characterization of Enteroviruses associated with Hand, Foot and Mouth disease (HFMD)

HFMD cases were reported from Pune and Kolhapur. Seventy five of 92 (81.52%) clinical samples (n=68) tested positive for enterovirus by RT-PCR using 5'NCR specific primers. Positive specimens were further subjected to typing using VP1 gene. Sequencing and phylogenetic analysis revealed the presence of CVA16 [42,(59.15%)], CVA-6 [28,(39.43%)] and Echo-1 [1,(1.40%)].

Identification and Molecular Characterization of Rota and Noroviruses in Neonates admitted at Neonatal Intensive Care Unit (NICU)

Stool specimens (n=701) collected from the neonates (n=621) admitted mainly for prematurity, low birth weight and associated respiratory distress syndrome were tested for rotavirus and genotyped using VP7 and VP4 genes. Rotavirus was detected in 24.3% of neonates and majority of them (98.68%) were asymptomatic. Predominance of unusual G12P[11] strains (97.1%) was observed. Phylogenetic analysis of the partial VP7 coding

gene revealed that all G12 strains clustered in lineage III and shared 96.94%-100% (nucleotide) and 96.26% -100% (amino acid) identities among themselves, and 95.69%-98.98% (nucleotide) and 94.77%-98.98% (amino acid) with other lineage III G12 strains respectively.

Investigations of human clinical specimens collected during encephalitis outbreaks and diagnostic services to suspected Japanese encephalitis and Chandipura encephalitis patients from India

During 2018-19, 552 cases referred from all over India to encephalitis group were screened for viral etiology. JEV positivity was detected in 25/552 (4.5%) of the cases. Majority (17/25) of the JE positives were children. Sporadic cases of Chandipura and Herpes simplex encephalitis were observed in state of Gujarat and Maharashtra respectively. Under sero-surveillance, anti-JEV NABs were detected in 6/51 (12%) contacts from Maharashtra and 23/46 (50%) contacts from Maharashtra (7/23) (15%) and 16/23 (35%) from Gujarat. Presence of anti-JEV NABs was also observed in pig sera from Madhya Pradesh (MP) (5/14) indicating circulation of JEV in MP State. In support of vector surveillance, sandfly pools were referred from Gujarat and 12 pools of Culex mosquitoes from MP to investigate role in JE / WNV transmission in the region. None of the vectors were positive for the viruses tested. A genetically divergent CHPV strain (2015) was isolated from a fatal human case (Gujarat, 2015) and its full genome sequence (11120 nucleotides) revealed 11% divergence with the Indian isolates obtained till date and 24% divergence with strains isolated from Nigeria and Senegal.

Development of IgG detection ELISA to diagnose post exposure to Chandipura virus (CHPV)

An indirect IgG detection ELISA was developed where purified Indian strain 034267 was used as coating antigen and anti-human IgG HRP (gamma chain specific) was used as secondary antibody. A

panel of 215 retrospective, anonymized, archived serum samples were used for assay evaluation, which included samples from post CHPV outbreak fever survey from Panchmahal, Gujarat (2009), sera received from CHPV non-endemic region (2012-2017) and archived serum samples referred from AES cases from a CHPV endemic area Dahod, Gujarat (2018). Test cut off was average OD of negative (0.111) + 3 SD (0.202). *In vitro* neutralization test by CPE method using an Indian strain 034267 was the 'gold standard' for assay evaluation. A neutralizing antibody titer ≥ 10 was considered as presence of neutralizing antibodies. In evaluation, the new ELISA had specificity 99.15%, sensitivity 100%, PPV 98.97% and NPV 100% and concordance 99.5%.

Detection of CHIKV antigen from infected mosquito in C MAb based antigen capture ELISA (Ag Cap ELISA)

A tool to detect CHIKV antigen from mosquitoes (*Aedes aegypti*) which would indicate approaching CHIKV activity has been developed. Anti-Capsid protein MABs to CHIKV were generated and used for the development of an Ag Capture ELISA which detected CHIKV from laboratory infected mosquitoes. Female *Aedes* mosquitoes fed on CHIKV infected infant CD1 mice were harvested on 0 to 10th PID (n = 10) were triturated and tested in parallel in an Ag Cap ELISA and qPCR. A pool of 10 uninfected mosquitoes served as negative control. Three experiments were performed, cut off for positivity was mean OD of negatives + 3SD (0.095-0.109). The virus was detected in infected mosquitoes from day 0-10 PI in Ag Cap ELISA (Range of ODs 0.119-0.399) and the results co-related well with qPCR which was reflected in CT values less than 35, a cut off of qPCR. To mimic field conditions combinations of infected and uninfected mosquitoes was tested; in both the assays CHIKV was detected from single infected mosquito in a pool of 10.

Development of an attenuated Japanese encephalitis Genotype I virus vaccine candidate through reverse genetics approach and studies on its protective efficacy

Development of reverse genetics system for genotype I JEV 0945054 was reported earlier. The expressed recombinant virus was studied for growth kinetics in BHK-21 cells, virulence in experimental animals and immunofluorescence assay in comparison to the parental virus. This study reports the analysis of comparative biological properties of parental and recombinant virus in mouse model. The infectious clone was studied for its virulence, infectivity in mice, antigenic characteristics and growth pattern in *in vitro* system in comparison to parental strain. The results indicated that the both parental and the recombinant virus are similar in biological and antigenic characteristics. The developed infectious clone will be explored in determining virulence determinants, attenuation and knocking out of *Flavi* cross reactive domains to explore it in development of specific sero-diagnostic assays.

Japanese Encephalitis Epidemiology in Central Part of India - Enhanced Sentinel Surveillance for Etiological Contribution and Burden following Vaccination in Maharashtra and Telangana

The activities, initiated on 30th June 2017, were undertaken at three site laboratories (Nagpur, Wardha and Warangal). Acute neurological illness among children and adults was tracked for estimation of incidence of AES and contribution of JE, other viral and bacterial agents. On an average, 55-60 neurological illness patients were hospitalized at three sites per month among children and adults. The proportion of AES among acute neurological illness patients was 16.5% (89/540) among children and 24.7% (124/502) among adults. The clinical specimens (n=394) were collected during 9 months' period for the etiological testing. JE was confirmed in 38 (42.7%) of 89 AES cases among children and 30 (24.2%) of 124 cases among adults during the period. Additional viral agents included CHPV (0), HSV (0), Dengue (4) and Chikungunya (8). The non-viral causes included Malaria (1), Leptospirosis (1), Typhoid (3) and Scrub typhus (3).

Seroprevalence of Dengue and Chikungunya Virus Infections in Western India - A Retrospective and Prospective Cross-sectional Study

The retrospective testing of sera collected during serosurvey in Pune city and Goa State was undertaken for estimating change of seroprevalence of Dengue and Chikungunya virus infections. Dengue seroprevalence in Goa was 36.1% in 2009. The Dengue seroprevalence among <18 years' age group in Goa was 26% in 2010 as against 17% in 2009 ($p<0.05$). In Pune city, Dengue seroprevalence was 59.5% in 2009. It was significantly higher than in Goa in 2009 ($p<0.05$). Dengue seroprevalence was higher (60-80%) in older adults as compared to children. Higher seroprevalence of Dengue was observed in Maharashtra than Goa in 2009. Chikungunya seroprevalence was similar (8%) in Goa and Maharashtra. However, the Chikungunya seroprevalence of 8% in Goa in 2009 increased to 13% in 2010. The prospective serosurvey undertaken in 2019 would help understand increase in seroprevalence in a decade.

Molecular characterization of dengue viruses circulating in India

Investigation of circulating serotypes of DENV revealed that DENV-3 and DENV-1 were the dominant serotypes detected in Pune, Nashik and Kolhapur districts while DENV-4 was the dominant serotype detected in Nagpur and Wardha districts of Maharashtra. DENV-1 was observed in high numbers in the samples received from Kerala, Himachal Pradesh and Gujarat while DENV-2 was observed in high numbers in samples from Telangana and Andhra Pradesh. DENV-3 was observed in high numbers in the samples received from Rajasthan and New Delhi while DENV-4 was observed in high numbers in samples from Andaman and Nicobar islands. Envelope gene sequencing and phylogenetic analysis involving representative samples revealed circulation of genotype I and genotype V of DENV-1, multiple lineages of GIV genotype for DENV-2, GIII genotype for DENV-3 and GI for DENV-4.

Development of One step real time RT-PCR for genotyping of Dengue virus serotypes

A one-step real-time RT-PCR to discriminate between the major circulating genotypes of DENV-1 was developed and validated using 40 samples, for which the envelope (E) gene sequence and genotyping data was available. Additional 296 samples from selected Southern and Western states of India were genotyped using the real-time RT-PCR assay. Among the samples used for validation, the genotyping results were concordant with sequencing results for 39 samples (97.5%). Additional testing revealed that the DENV-1 Asian genotype (GI) was the predominant genotype in Tamil Nadu and Kerala, the southern states. The DENV-1 AM/AF (GV) genotype was the predominant genotype in Maharashtra, a western state of India.

Molecular characterization and phylogeography analysis of Chikungunya virus circulating in India

E2-E1 gene sequencing of the Indian isolates from 2015-17 representing four affected areas in Karnataka (Bengaluru), Maharashtra (Nasik, Pune) and New Delhi was done and phylogeography analysis was carried out. All the study isolates of 2015-2017 except one isolate from Bangalore clustered in a single clade along with sequences from 2009 onwards from the States of Tamil Nadu, West Bengal, Kerala and Andhra Pradesh in the Indian Ocean Lineage (IOL). The geographical ancestral state of this cluster was identified to be India with state probability value 1, suggesting the indigenous evolution of the CHIKV strain of recent outbreaks in India. The spread from India to the countries China, Hong Kong, Japan, Pakistan, Bangladesh, France, Italy and American Samoa was also noted in recent years. The study reveals that IOL strains have established persistent transmission in India and the issue of India as a reservoir for the global IOL introductions need to be addressed.

Structure-based design and evaluation of the antiviral activity of selected lead compounds against Chikungunya

Two compounds including a xanthonoid (OCL-105) and a flavonoid (OCL-108) were found to be effective against CHIKV in the primary antiviral screening assay and considered for in-depth antiviral activity studies. *In vitro* studies revealed that OCL-105 displayed a dose-dependent inhibition against CHIKV replication with minimal toxicity. OCL-105 inhibited CHIKV efficiently at 8 μ M only when added before infection or together with the virus. There was also a significant reduction in viral RNA copy number, based on real-time RT-PCR analysis and CHIKV antigen under pre and cotreatment conditions. In case of OCL-108, primary *in vitro* studies using the foci forming unit (FFU) assay indicated that the compound is effective at 10 μ M only during post treatment. Bioinformatics docking studies revealed that OCL-105 can interact with multiple CHIKV target proteins, the E2-E1 heterodimeric glycoprotein and the ADP-ribose binding cavity of the nsP3 macrodomain. OCL-108, binds with considerable binding affinity in the nsP1 methyltransferase and nsP2 helicase protein-protein interaction interface.

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

Solid lipid nanoparticles (SLNs) were synthesized by a modified solvent emulsification method in order to study their potential to form complex with siRNA and to evaluate their efficiency in inhibiting CHIKV growth *in vitro*. Stearylamine (SA) was also used as cationic lipid and charge inducing agent in the SLN formulation. The antiviral activity of SA in *in vitro* system was further investigated. The SLN was characterized for particle size, surface charge, and serum stability. The siRNA loaded SLN (siRSLN) and SA was tested for cytotoxicity and antiviral activity was determined by FFU assay and quantitative RT-PCR. The optimized siRSLN indicated a size of 130 nm and 2 mg SA sufficiently induced 39.2 mV surface charges for enhanced *in vitro* transfection. Gel electrophoresis indicated no unbound siRNA from the complex indicating better complexation and stability up to 24 days. Treatment of SA at concentration of 25 and 50 μ M showed significant reduction at 16h and 24h post treatment.

The findings highlight the antiviral potential of SA against CHIKV infection.

Enhancing biorisk mitigation awareness in public health community and creating laboratory networks for enhanced diagnostic capabilities to deal with surveillance and outbreaks of Viral Hemorrhagic Fever and Respiratory Illness diseases

Under this project on-site and off-site training programs for management, scientific, technical and laboratory engineering personnel were organized by ICMR-NIV, Pune. More than 79 participants were trained during the year 2017-18. This has increased awareness on Biorisk management and engineering controls required for safely operating biomedical laboratories and infection control practices in the public health settings. This has also created laboratory networks for enhanced diagnostic capabilities for surveillance, outbreaks and epidemics investigations for VHF causing pathogens. Through this network first Zika outbreak from Rajasthan, India was reported by SMS Medical College, Rajasthan.

Nationwide serosurvey of Crimean Congo Hemorrhagic Fever Virus (CCHFV) in domestic animals and Epidemiology, risk factors and seroprevalence of CCHF infection among humans in rural population in Gujarat (NIV-ICAR- Gujarat)

Indigenous Anti CCHF sheep, cattle/goat, human IgG ELISA and Anti CCHF Human IgM detection tests were developed and transferred to commercial partner. Apart from these three ELISA technologies were released for commercial production by ICMR to Zydus Cadila.

Using these indigenous kits the presence of CCHF in naïve areas of Gujarat like Panchmahal and Devbhoomi dwarka was reported; suggesting under diagnosis of CCHF in Gujarat. The study also shows close contacts and neighbors have a seven fold threat of contracting the disease than general population.

Seropositivity amongst livestock and humans were reported to animal husbandry network units and Primary Health centres respectively as a part of awareness. Centre was able to track two Indian traveller cases from Oman (2016) and Dubai (2018) because of the awareness and available diagnostic tools.

Sero-prevalence of NiV specific antibodies among close contacts Kerala, 2018

The study findings indicate that subclinical infections occurred among close contacts of patients during the Nipah Virus (NiV) outbreak in Kerala, India, but were infrequent. In addition, study found that risk for subclinical infections was higher among persons with a history of exposure to body fluids of NiV patients than for those with only physical contact. The NiV strain responsible for the Kerala outbreak was closer to the Bangladesh strain and was more pathogenic. Although previous studies did not show any subclinical infections during NiV outbreaks with the Bangladesh strain, this study suggested that NiV strain of Kerala outbreak generated asymptomatic infections. This study also found that IgM could be detected ≤ 2 months after NiV infection and the immunoglobulin class switch to IgG could occur beyond 2 months.

Identification and characterization of novel viral isolates using Next-generation sequencing platform

The study using NGS platform, encompasses isolation and characterization of known and novel viruses. This platform has not only helped in the identification of novel viruses such as Kundal and Wad Medani but also to identify the currently circulating strains of known pathogenic viruses such as Zika, Nipah, and Canine distemper virus. Diagnostic assays (molecular and serological) that can lead to the identification of the novel viruses from the clinical samples are in development stages.

Study of KFD viremia and antibody kinetics in patients and disease progression in monkey model

An algorithm was proposed using this study for conducting KFDV diagnostic tests as per post onset day. KFDV can be detected on human clinical specimen using Real-time reverse transcriptase PCR (RT-PCR) from 1-3 POD, anti-KFDV IgM ELISA from 24-145 POD and IgG ELISA from 6th POD to at least 3 years of post-infection. Study has tested follow-up samples of these patients till three years and anti-KFDV IgG antibodies were detectable till the last collection. In monkey model, detection of viremia started from 1 PID to 11 PID in monkeys with high dose. In monkeys with low dose of virus, viremia started from 3-10 PID, indicating a three-day shift when compared to high dose. IgM and IgG antibodies were detected from 6-42 PID and 14 PID onwards in high dose and 9-34 PID and 18 PID onwards in low dose.

Investigation of Nipah virus outbreak in Kozhikode district, Kerala state during May-June 2018

An outbreak of NiV was reported from Perambra village, Kozhikode district of Kerala state during May-June 2018 which cost 17 lives. ICMR-NIV has investigated the outbreak to determine the association of *Pteropus* bats (fruit bats) in virus transmission. NIV team trapped 65 bats (52 *Pteropus* and 13 *Rousettus*) from the outbreak area and real time RT-PCR screening revealed the presence of NiV RNA in 19% of the samples (throat, 15% and rectal swab, 8%). The relatively high proportion of *Pteropus* bats that tested positive for NiV in throat and rectal samples in the outbreak area suggests a possible link to the initiation of the outbreak.

Countrywide survey of Nipah virus in *Pteropus* bats

In the wake of the Nipah virus outbreak in Kerala state during May-June 2018, the Secretary, DHR & Director General, ICMR instructed the Director, NIV to conduct a survey of Nipah virus in *Pteropus* bats across the country. ICMR-NIV team has commenced *Pteropus* bat trapping activities since January 2019 after completing the formalities (forest permissions etc.) and trapped 361 bats from

four states (Odisha, Gujarat, Telengana, Punjab) and one Union territory (Chandigarh). None of the samples tested positive for Nipah virus by real time RT-PCR suggestive of no activity of the virus in these states. Further studies to trap bats from other states and Union territories are in progress.

Studies on the bionomics of Phlebotomine sand flies in Nagpur division of Maharashtra and Andhra Pradesh and to determine their role in transmission of Chandipura virus

A year round study was conducted in Vidarbha region of Maharashtra to determine the breeding patterns, species composition and seasonal prevalence of sand flies. Field surveys were carried out in 23 villages in Nagpur, Bhandara and Gondiya districts of Maharashtra during 2017-18. The collections mainly comprised of *Sergentomyia* species, predominantly *Ser. babu* which constituted 74% of the total collection. *Ser. punjabensis* and *Ser. bailyi* contributed to 19.7 and 5.1% while the population of *Phlebotomus papatasi* and *Ph. argentipes* was negligible (~1%). *Sergentomyia* spp. was collected from almost all the habitats including living rooms, class rooms and anganwadis that are in close contact with humans especially children. All the sand flies were processed for virus isolation in cell culture but efforts were futile. Extremely low number of *Ph. papatasi* and *Ph. argentipes* were noted in the study area. Climate change and insecticide application might have contributed for their elimination/decrease in population. Conversely, *Sergentomyia* spp., was found predominantly resting indoors in close contact with humans. This is suggestive of a shift in their breeding habitat and warrants further investigation to understand their role in the maintenance and transmission of viruses and other pathogens.

Avian Influenza animal-human interface studies

Studies on the susceptibility of avian influenza (AI) viruses isolated from India to neuraminidase (NA) inhibitor antiviral drugs oseltamivir and zanamivir revealed the natural occurrence of a novel I117T mutation in highly-pathogenic AI H5N1 virus showing cross resistance to the drugs. Similar

studies on low-pathogenic AI H9N2 viruses under the selection pressure of NAIs, showed the presence of NA substitutions R292K and E119D with oseltamivir and zanamivir, respectively. The studies highlight continued antiviral surveillance among human and avian HPAI and LPAI viruses.

Influence of differential charge in residues of non-structural 1 (NS1) protein of LPAI (H11N1 & H9N2) and HPAI H5N1 viruses dictate attenuation of the host interferon response, a possible strategy of HPAI virus to evade the host innate-immune assault.

First report of low-pathogenic AI H4N6 virus from environmental specimen in Pune district, Maharashtra belonging to the Eurasian lineage, resembling to H4N6 viruses from Mongolia and Netherlands, showing 98% identity of the M protein with the H11N1 virus isolated from the droppings of a Eurasian spoonbill in the state of Maharashtra during AI surveillance (2007), indicating intermingling of genes among the migratory birds at stopover sites.

DIAGNOSTIC VIROLOGY GROUP

Resource Centre for Virus Research and Diagnostic Laboratories

The year witnessed an expansion in the number of functional Virus Research and Diagnostic Laboratories. The RCVRDL continued to provide scientific, technical and logistic support to the laboratories in the network. Five training programs were conducted for VRDLs during the period, and three on-site, hands-on training programs on real-time RT-PCR detection of Zika virus were provided, to laboratories in Gujarat, Rajasthan and Maharashtra. A total of 131 scientific and technical staff received training. One laboratory was also trained on molecular detection of Influenza virus. The launch of a nation-wide systematic surveillance of influenza virus circulation and evaluation of antiviral susceptibility of influenza A(H1N1)pdm09 strains, in December 2018, was a major milestone. The Quality Control/Quality Assurance programs for serological tests continued uninterrupted

during the period, and summary reports have been issued to the participating laboratories. As part of the External Quality Assurance program, coded sample panels for dengue, chikungunya and JE IgM ELISA tests were sent to 21 laboratories each in phase 1 and phase 2. An External Quality Assurance panel was distributed to 35 VRDLs, and 31 of them participated in the program. The overall concordance rate of the results with those from RCVRDL was 93.8%.

Surveillance of Zika virus infections in India

The project was initiated to bolster the national preparedness against Zika virus disease, following the massive Zika outbreaks that occurred in Brazil and other countries since 2015. The RCVRDL has been serving as the apex laboratory for coordinating Zika surveillance activities in the country. Continuing the surveillance, the RCVRDL and 35 Zika-trained laboratories screened a total of 35389 samples (including 26078 samples of sera, 8758 samples of urine and 553 samples of plasma/CSF/other specimens) from 1st April, 2018 till 31st March, 2019. During the proactive surveillance, a case of Zika infection was confirmed by RCVRDL in an 85-year old female resident of Jaipur in Rajasthan, on 21st September, 2018. Upon directives from the ICMR and the Ministry of Health & Family Welfare, Zika surveillance was stepped up in Jaipur, and a total of 4722 samples of patients with Dengue-Like Illness (DLI) (residing within a 3-km radius of the house of the index case) were screened by in-house and CDC Trioplex real-time RTPCR for Zika detection. A total of 153 cases of Zika infection were identified among patients, their contacts and pregnant women were identified, and another 6 cases were also identified during routine surveillance. The Government of India declared this as the first Zika outbreak in India. Majority of the patients had a mild illness, and no cases of microcephaly or Guillain-Barre syndrome were detected among the infected, till date. However, two Zika-infected pregnant women had miscarriages, and two delivered healthy infants. Co-infection with dengue was detected in one patient. In a major development, the first

Zika virus isolate in the country was obtained from the samples collected during the Jaipur outbreak. Detailed characterization of the isolate is currently in progress. Analysis of partial genomic sequences of the Zika strains from Jaipur revealed their clustering with strains from French Polynesia, Brazil and Italy. Results also indicated that the Jaipur strain probably evolved from a distinct Asian lineage ancestor of Zika virus. Data also indicated a probability of rapid diversification of the strains from the older Asian strains.

Congenital Rubella Syndrome Surveillance in India

The Congenital Rubella Syndrome Surveillance project was initiated in 2016 with the primary objective to generate estimates of disease burden and monitor progress made by rubella control program. Besides this the project also aims to estimate rubella sero-prevalence among pregnant women. The CRS surveillance system is generating quality epidemiologic data about CRS in India. Genotyping of the samples from patients revealed that the circulating genotype of rubella virus was of type 2B. The results of serosurvey indicated high levels of rubella sero-positivity in pregnant women and in the absence of routine childhood immunization indicates continued transmission of rubella virus in cities where sentinel sites are located.

Characterization of diversity of measles viruses in India - genomic sequencing and comparative genomics studies

For the first time, complete genome sequencing of twenty Measles Virus (MeV) isolates were carried out. All the Indian D4 isolates (n=8) are observed to deviate from the standard MeV genome length due to insertions or deletions in the intergenic regions between the matrix and the fusion genes. Identical insertions or deletions at equivalent positions have been previously reported in D4 isolates from Italy and USA. Phylogeny with global isolates revealed genotype-based spatio-temporal clustering, which suggests presence of two lineages of D4 and multiple lineages of D8 isolates to be circulating

in India. Estimated genome-wide and gene-wise nucleotide substitution rates of Indian MeV are comparable with those of global isolates. Selection pressure analysis indicated modest role of positive selection in MeV evolution corroborating with their serologically monotypic nature. Selection was found to be operational across all MeV genes except L-gene in global isolates. No positively selected sites were observed in Indian isolates implying absence of new emerging lineages. Mutations observed in H-protein are not expected to alter antigenicity and structural stability, indicating effectiveness of vaccines in current use. Full genome analysis of additional 25 MeV isolates, which were sequenced, is in progress.

Genome sequencing and antigenic characterization of wild type rubella viruses isolated from India

For the first time, full genome sequencing of five RuV isolates obtained during the years 1992, 2007, 2008 and 2009 from the States of Karnataka, Kerala and Maharashtra was carried out. Antigenic studies by neutralization tests showed 86.76% agreement between two FRNTs (RuV wild type and vaccine strains) when 68 serum samples were challenged. The FRNT titres to vaccine strain was significantly higher than the wild type strain in both males (1.246 vs 0.765, $P < 0.001$, Paired t-test) and females (1.873 vs 1.011, $P < 0.001$, Paired t-test). However, antigenically both RuV wild types and vaccine strains showed similarity.

Revealing True Diversity of Measles viruses Circulating in India, 2012-17

The genotyping of circulating measles virus (MeV) is essential to measure the impact of immunization. MeV genotyping is primarily based on the Nucleoprotein (N) or hemagglutinin (H) genes. Study of the genetic diversity of 67 Indian MeV isolates (2012-17) using matrix-fusion (M/F) non-coding region revealed, 7.7%, 3.9% and 1.9% mean divergence amongst M/F, Nucleoprotein (N) and Hemagglutinin (H) genes, respectively. For the first time, indels were documented in Indian MeV D4 genotypes that may serve as marker for tracking

transmission pathways. Thus, sequencing of M/F non-coding region could be useful for determining the diversity of MeV in a large country like India.

Fever with skin rash cases in the Maharashtra State - India, 2014-17

From 36 districts of the MS, 2795 fever with rash cases (1428 males and 1367 females) were referred. The majority of the cases (93.3%, n=2609) were under 15 years of age. About 17.7% (494) cases had a history of measles immunization. Virus isolation was attempted from 107 throat swabs and 84 urine samples obtained from 191 cases using Vero hSLAM cells. The results confirmed measles in 1756 and rubella in 282 fever with rash cases by serological and molecular tools. 170 of 382 and 35 of 149 specimens were positive for measles and rubella RT-PCRs, respectively. Sequencing of the representative PCR products showed the circulation of measles virus genotypes D4 (n=26) and D8 (n=107), and rubella virus genotype 2B (n=1). Twenty-three measles viruses were isolated and genotyped, of which, 6 were D4 and 17 were D8 genotypes. Amongst the measles-immunized individuals, 51.2% (253/494) had laboratory-confirmed measles. Overall, 72.9% fever with skin rash cases (n=2038) from the MS was confirmed for measles/rubella. The contribution of measles was higher than rubella in the fever with rash cases. As expected, more fever with rash cases were documented in children compared with adults and highlighted the need to increase measles-rubella immunization coverage.

Antibody and memory B cell responses in Hepatitis E recovered individuals; 1-30 years post Hepatitis E virus infection

Generation and persistence of anti-hepatitis E virus (HEV) antibodies are considered as correlates of protection against HEV infection. However, issues like longevity of immunological memory following recovery from hepatitis E still remains a puzzle. This study assessed the levels and persistence of anti-HEV antibodies in hepatitis E recovered individuals 1-30 years post HEV infection. The

frequencies and functionality of recombinant HEV capsid protein (rORF2p)-stimulated memory B and T cells were also investigated 1-16 years post infection. Anti-HEV antibodies persisted in 91% and HEV-specific memory B cell responses were detected in 95% of hepatitis E recovered individuals. CD4⁺ and CD8⁺ T cells displayed an effector memory cell phenotype in hepatitis E recovered individuals. In conclusion, long-lived anti-HEV antibodies and HEV-specific memory B cells are maintained for several years in hepatitis E recovered individuals. Involvement of CD4⁺ and CD8⁺ effector memory T cells is an important observation since it is inextricably linked to long-lasting protective immunity. In addition to anti-HEV antibodies, possible role of memory B cell response against HEV re-infection could also be considered.

Hepatitis E virus seroprevalence among blood donors in Pune, India

Blood transfusion is a recently reported route of HEV transmission. It is a bigger concern in regions where large scale HEV genotype 1 infections occur causing more severe disease. This present study aimed to assess the prevalence and rate of HEV infection in the blood donors of Pune, India. A total of 2447 healthy blood donors were screened for anti-HEV IgG and IgM antibodies. Anti-HEV IgM antibody positives were further subjected to ALT measurement, HEV RNA detection, viral load quantification and phylogenetic analysis. Anti-HEV seroprevalence rate was 17.70%, while IgM prevalence rate was 0.20%. Two of 5 IgM-positives tested positive for HEV RNA. The viral load ranged from 3.5×10^4 - 4.6×10^5 copies/ml and belonged to HEV genotype 1. HEV prevalence rate of 17.70% in the blood donors of Pune, India, a developing country, goes at par with the developed countries. Current data of 0.20% [5 of 2447] blood donors positive for anti-HEV IgM and 2 of them being HEV RNA positive suggest a need for consideration of cost-effective evaluation towards pooled HEV RNA testing in blood banks.

Cellular antiviral responses against hepatitis B virus

It is known that the host immune responses are the main determinants of hepatocellular injury during hepatitis B virus (HBV) infection. Mutations in pre-core (PC) and basal core promoter (BCP) regions of HBV genome have been implicated in various liver associated clinical complications with high mortality rates. We analyzed host cell responses generated upon infection with wild type (WT) and BCP/ PC mutant (MT) viruses using replication competent clones. Our hypothesis was, HBx and HBe proteins counteract each other to establish balance between pro- and anti-apoptotic pathways in WT virus infection, while, absence of HBe in MT virus leads to cell death. For that, we cloned these two genes and carried out co-transfection experiments. HBx and HBe, both proteins reduced MT virus induced cell death significantly. However, HBe was more effective in down regulating cellular antiviral and apoptosis pathways as compared to HBx protein. Cells infected with MT virus used miRNA mediated signaling and communicated death signal to other cells. These results suggest that absence of HBeAg leads to serious liver injury in individuals infected with BCP/PC HBV mutant virus.

Investigating the role of papain like cysteine protease in hepatitis E virus replication

Papain-like cysteine protease (PCP) of Hepatitis E virus (HEV) has the ability to hydrolyze SUMO, NEDD and ISG15 and ubiquitin moieties from host proteins. To identify cellular proteins that are targeted by HEV PCP for de-ubiquitination/ de-ISGylation/ de-SUMOylation/ de-NEDDylation, we infected human hepatoma cells (S10-3) with HEV and did pull-down of proteins with these modifications and carried out LC-MS analysis. PCP de-ubiquitination targets were mostly proteins involved in transcription, mRNA processing and stabilization of cell structure. De-ISGylation and de-NEDDylation targets were protein components of cellular processes that regulated viral genome replication and viral life cycle. De-SUMOylation targets were mainly proteins involved in mRNA

metabolic processes. These results suggested that HEV PCP significantly modulates RNA processing, translation, cellular trafficking, and extracellular signaling pathways during its replication in host cells.

BACTERIOLOGY GROUP

Diagnostic Support for confirmation of Cholera outbreak in tribal area of Maharashtra

An outbreak of acute watery diarrhea was reported in Rahude, a tribal village located in a notified area of Surgana taluka, Nashik district, Maharashtra in July 2018. 195 case-patients were identified among 850 residents. The referred faecal samples were negative for Rotavirus (Group A, B, C), Norovirus, Enteric adenovirus, Astrovirus and Enterovirus. *Vibrio cholerae* O1 Ogawa Biotype El Tor was isolated from five of 14 referred faecal samples. Molecular and phylogenetic analysis of the five isolates of *V.cholerae* showed that the strains were of subtype O1 Haitian-type strain of ctxB7 genotype. Analysis of the tcpA gene of the isolates showed that the strains were closely related to the polymyxin B sensitive strain which has recently been detected in India. A post outbreak survey confirmed that the cholera outbreak occurred in this tribal village due to a combination of risk factors including lack of safe water, poor sanitation and improper waste management compounded by seasonal rainfall and flooding.

CORE FACILITY ACTIVITIES

BIOINFORMATICS

Phylogeography of Kyasanur Forest Disease virus (KFDV) in India

Phylogeography analysis was undertaken based on 48 whole genomes (46 newly sequenced) from different geographic locations, covering Karnataka, Goa, Tamil Nadu, and Maharashtra spanning the period 1957–2017. The emergence time for KFDV was estimated to be ~1953 from Karnataka. Dispersal from Karnataka to Goa and Maharashtra was indicated. Maharashtra represented a new source for transmission of KFDV since ~2013 as recent multiple virus transmissions from

Maharashtra to Goa were noted. The Bayesian skyline plot revealed an increasing trend from 2015 which is reflective of the proliferation of the virus to the neighboring states of Karnataka and also the recent exchange of viruses between neighbouring states. The findings indicate the need to curtail the spread of KFDV by surveillance measures and improved vaccination strategies.

Implementation of an algorithm for a provisional intra-genotypic lineage classification system for human Rotavirus C strains

For each gene of human Rotavirus C, an intra-genotypic classification scheme into lineages was proposed by estimating the most appropriate cut-off for percent nucleotide identity (PNI) by using the algorithm of Rotavirus Classification Working Group recommendation. The PNIs for all possible pairs of sequences were calculated in MEGA6. For ML tree of each gene, different choices of possible lineages were considered by observing the bootstrap supports and the geographical region of circulation. For each such choice, frequency graphs were constructed showing the frequencies of “within lineage” and “between lineage” PNIs. The most suitable cutoff value for PNI, to classify the gene into certain number of lineages, was estimated as the percentage at which the ratio of the frequencies of “between lineage” identity and the “within lineage” identity dropped below 1. The proposed cut-off values of the nucleotide divergence for classification ranged from 1% to 5% with majority between 3-4%.

Bioinformatics characterization of Chandipura virus proteins

Chandipura virus (CHPV) causes encephalitis in pediatric population and since 2003 several outbreaks were documented from different states of India (Andhra Pradesh, Maharashtra, Gujarat). In the present project we are analysing all the CHPV proteins using bioinformatics tools in order to understand the properties, variability amongst the strains. Results indicated that the G-protein is highly conserved in terms of antigenicity. We have also identified a conserved B-cell epitope on

the G protein which overlaps with a MHC Class II epitope responsive to all alleles prevalent in the affected population groups in India.

MATHEMATICAL BIOLOGY - DISEASE MODELING

Meteorological parameters modulate Chikungunya and Dengue occurrences in India (2010- 2016)

In the present project, we study the effect of meteorological factors (like Maximum and minimum temperatures, rainfall, etc.) on the all India occurrences (confirmed cases) of dengue and chikungunya. While disease data were obtained from NVBDCP and IDSP, meteorological data were obtained from IMD and analyzed mathematically. Rainfall has been found to modulate occurrences of chikungunya across all states of India. For the most affected states Maharashtra and Karnataka, lower rainfall years resulted in a greater number of cases compared to the heavy rainfall years. Spatio-temporal analyses revealed the distributions of rural outbreaks of Dengue and Chikungunya across India. Rainfall was found to be the principal factor that modulated dengue and chikungunya occurrences.

To study the Abundance and Diversity of Mosquito population in Pune during winter and pre-monsoon season (2018)

To understand the diversity of mosquito demographics, we conducted a survey of mosquito population in Pune Urban Zone (PUZ) covering winter and pre-monsoon seasons 2018. Findings revealed the existence of 14 mosquito species in PUZ covering five genera: *Culex*, *Anopheles*, *Aedes*, *Armigeres* and *Monsoonia*. Seasonal variation of mosquito abundance was observed along with seasonal variability in demographic diversity (determined in terms of Simpson's Index of Diversity and the Shannon-Wiener's diversity index). The *Culex* mosquitoes were most abundant during the study period. Regression modeling revealed that maximum temperature, humidity and

rainfall modulated mosquito abundance during the winter and pre-monsoon season in 2018.

Electron Microscopy: Ultrastructural cytopathology of vascular endothelial cells infected with Dengue virus

High resolution transmission cryo-electron microscopy imaging with 3D electron tomography studies on dengue 2 virus infected primary human endothelial cells showed evidence of significant cytoplasmic vesiculation and reticular transformations. Consistent and in continuation with our previous studies mitochondrial changes were also evident with clustering. The 3D reconstruction imaging revealed several fundamental and novel changes. This included presence of aggravated trans-endothelial channel formation, caveolar prominence suggestive of vesiculo-vacuolar organelle formation (VVO) and changes in Wiebel-Palade bodies. Correlative functional studies showed enhanced platelet binding with the endothelial cells suggestive of overall activation. These findings couples with the earlier studies showing changes in overall lipid composition of dengue virus infected endothelial cells provides fundamental insights into metabolic pathology of endothelial cells in dengue disease. Further studies are ongoing to characterize these changes further at a cellular and molecular level with an objective of potential therapeutic interventions.

BSL3 LABORATORY

Among various studies that were undertaken, polio sero-surveillance studies as a part of the surveillance for the Global Polio Eradication Program and primate experiments with the Kyasanur Forest disease virus were conducted.

FIELD UNITS

NIV-KERALA UNIT

- **Diagnostics support to Kerala state government**

Overall, a total of 2575 samples from 1913 patients were processed for 7134 various tests. During the

Nipah virus outbreak at Kozhikode, Kerala, PCR based detection of Nipah virus was established at NIV Kerala unit. During post flood outbreak of leptospirosis in Kerala, PCR and serology based diagnostics set up was established at NIV Kerala unit. Hospital based surveillance for Zika virus was also carried out in Kerala.

- **Case based Surveillance of Measles and Rubella infection in Kerala state (WHO programme)**

A total of 646 samples were received and processed for Measles and Rubella IgM and PCR. Out of 519 samples tested, 267 samples were positive for Measles IgM. Out of 254 samples tested, 05 samples were positive for Rubella IgM. Of 91 samples, 48 were positive for Measles PCR. All the PCR positive samples were sequenced and found to be of the D8 genotype.

- **Potential species distribution and detection of Kyasanur Forest Disease (KFD) virus in tick population in forest area of Kerala**

Four genus and nine species of ticks were observed from forest vegetation; of these predominant species were *H. spinigera* (51.92%), *H. turturis* (33.59%) and *H. bispinosa* (11.7%). 2. The temperature range from 26-30°C and relative humidity from 65-75% was more favorable to support high questing nymph tick density 3. Host seeking larvae and nymph are highly active from October to February (range from 300 – 4500/month) however in the present study less number of larval and nymph ticks (range from 100-2000/month) were observed during this period due to the flood.

- **Impact of climate change on mosquito abundance in coastal brackish water and wetlands of Alappuzha district Kerala**

Two genus and eight species of larval mosquitoes were observed. In the sea shore (Brackish water), *Culex sitiens* was the predominant species with acidic pH – 3.6 to 6.9 and high salinity 8 – 35 parts per thousand (ppt) during summer season and in monsoon season *Cx. tritaeniorhynchus* was predominant species with pH 7.4 – 8.2 and low

salinity 0 – 8ppt. In paddy fields (fresh water), *Cx. tritaeniorhynchus* and *Cx. gelidus* was the predominant species in both summer and monsoon season with alkaline pH average 8.2 and salinity 0 to 5ppt. *Cx. tritaeniorhynchus* adapted to survive in brackish water up to 7.5 ppt salinity, in both laboratory and field.

- **Community engagement in control of some vector borne diseases: a community based Intervention in Alappuzha Municipality**

The research had two phases (Formative Phase and Intervention Phase) and implemented to understand the perception of the community and the factors influencing the engagement with the social environment, how the health system's mechanisms respond towards issues of vector borne diseases along with the objective to develop a feasible community intervention model. The intervention could make a strong feeling that the community engagement can reduce and combat the burden of diseases with appropriate bottom-up plans. The changes due to the collective community based engagement have been noticed by the Alappuzha Municipality and they officially expressed the willingness to implement this model program in all the 52 Municipal wards of Alappuzha.

NIV BENGALURU UNIT

- **Surveillance of Acute Flaccid Paralysis cases from Karnataka, Kerala states and southern parts of Bihar -Virus Isolation / Intra Typic Differentiation / Environmental Surveillance**

Bangalore unit received and investigated 6212 samples from Karnataka, Kerala & Bihar. Virus isolates were positive for L20B cell lines in 1.85% (115) of samples and 21.8% (1359) of samples were positive only in RD cell lines. Of 115 isolates 08 samples were NPEV by PCR. Real time RT-PCR for ITD confirmed SL1 in 34 samples, SL3 in 47 samples and both SL1+SL3 in 26 samples. During Jan to March 2019, 18 sewage samples were received from four sites of Bangalore city.

4 samples were L20B positive and three samples were Polio Vaccine strains and one sample was NPEV by PCR.

- **Surveillance of Measles cases from Karnataka and Kerala State, as a part of WHO-SEAR Measles Laboratory Network in the WHO's Global Measles Elimination Programme**

Bangalore unit received total of 811 samples (Serum-673, Throat swab/Urine-138) from Karnataka and Kerala. Measles IgM antibodies were positive for 14% (94/672) of samples. Measles PCR was positive for 2.3%(16/672) and Rubella PCR was positive for 5.7%(8/139) of samples. Ten Measles isolates were isolated. D8 genotype was reported.

- **Congenital Rubella Syndrome (CRS) Surveillance**

The unit investigated 45 cases fulfilling all clinical criteria for congenital Rubella syndrome. Laboratory report on serology revealed that 9 cases were positive for IgM antibodies and 4 cases were positive for IgG antibodies. 37 throat swabs were received and tested for PCR and found two cases positive.

- **Evaluation of Point of Care test device under field conditions for measles diagnosis and genotype determination**

97 outbreaks (757 cases) were investigated from 14 districts of Uttar Pradesh during August 2017 to 2018. Measles IgM POCT using CAP has similar performance to Siemens/ serum. Oral Fluid (OF) samples were 10% less sensitive. PCR on used POCT is positive in >90% used IgM positive OF/ POCT and 50% CAP/POCTs in early samples.

- **Laboratory diagnosis of human samples for KFD virus infection**

1628 suspected cases were received from Shivamogga VDL, of them 1103 cases were tested for RT-PCR and found 106 positives and 1116 cases were tested for KFD IgM antibodies by ELISA test and found 42 cases positive.

NIV, MUMBAI UNIT

- **National Polio Surveillance Project (NPSP), India:** The objective of the program is to carry out stringent surveillance with continuous monitoring of polio viruses until global eradication of poliovirus is achieved. During April 2018 to February 2019 all the isolates were found to be Sabin-like poliovirus type 1 and type 3 and non-polio enteroviruses. In India there has been a switch from trivalent OPV (tOPV) to bivalent OPV (bOPV) since April 2016 under poliovirus 2 (PV2) containment. Therefore, detection of PV2 is considered as an alarming situation. NIVMU was involved in investigations of such episodes in India.

- **Measles and Rubella Surveillance**

The objective of this surveillance program is the elimination of measles and control of rubella. During the period April 2018 to Feb 2019, a total of 253/448 (56.47%) were positive for presence for antibodies against Measles and 33/448 (7.36%) were positive for Rubella. The measles viruses belonged to D8 genotype whereas rubella viruses belonged to 2B genotype.

- **Strengthening laboratory quality management systems including EQA of DHR/ICMR VRDL laboratories for laboratory confirmation of outbreaks including measles and rubella**

To develop WHO proficient laboratories for measles and rubella surveillance in India, training was given to the measles and rubella WHO network and ICMR-VRDL laboratories on serology and molecular diagnostics of measles and rubella. On-site reviews of these laboratories were conducted to assess their competency and quality. Laboratories in India were also to explore their feasibility as medical college-level VRDLs and also their feasibility for inclusion in measles and rubella network.

- **Comparative evaluation of immunogenicity of bivalent oral poliovirus vaccine (bOPV) and monovalent oral poliovirus vaccine type**

1 (mOPV1) when administered in the EPI schedule with a dose of Inactivated Polio vaccine (IPV) at week 14 and assessment of immunogenicity of IPV only schedule in the EPI - A multicentric open label randomized controlled trial

The goal of this study is to compare immunogenicity against poliovirus type 1 by bOPV and mOPV1 when given as a part of routine immunization schedule at birth, 6, 10 and 14 weeks along with one dose of IPV at week 14. The testing of all sera (n=2254) received under this study against poliovirus type 1, type 2 and type 3 was completed. Results of these specimens have been submitted to NPSP, WHO for analysis.

- **Comparative evaluation of immunogenicity of various schedules, dosages and delivery options to provide fractional Inactivated Poliovirus Vaccine (IPV) in routine immunization in the post tOPV-bOPV period - A multi-centric open-label randomized controlled trial (India IPV fractional dose study)**

The objectives of the study are to compare the immunogenicity against types 1 and 3 polioviruses in all the three vaccination schedules. A total of 2302 sera were tested against poliovirus type 1, type 2 and type 3 serotypes using microneutralization assay as per WHO guidelines. Results of these specimens have been submitted to NPSP, WHO for analysis.

- **Enteroviral investigation of Hand, Foot and Mouth Disease (HFMD) cases in Mumbai, May- September, 2018**

CVA-6 and CVA-16 caused HFMD outbreak in Mumbai with one case of recurrent HFMD caused by CVA-6 and CVA-16 in an interval of 21 days. No case was detected due to EVA-71 infection.

- **Studies on poliovirus infections in children with immune-deficiency**

Susceptibility of children with Primary Immunodeficiency (PID) to Sabin vaccine virus and mutated virus excreted by these children are

major risks to Global Polio Eradication Initiative. The objective of the project is to screen the immunodeficient patients for polio and non-polio enterovirus infections, to characterize the isolates and to identify the long-term excretors. 224 fecal Samples of 89 PID patients (10 SCIDs, 7 CVIDs, 14 XLAs and 58 other PIDs) with humoral, combined and other PIDs were assessed and followed up for enterovirus excretion of which 11 (12.35%) were positive for Non-Polio enteroviruses and 4 (4.49%) were positive for polioviruses. The study highlights the need of screening all the patients with combined immunodeficiency for poliovirus excretion and intermittent follow-up of their immune parameters if found positive, in order to manage the risk of iVDPV excretion in the polio eradication endgame strategy.

- **Cytokine responses to EV71 genotypes in cultured human cells**

EV71 commonly causes HFMD in children, but can result in neurological complication such as AFP, aseptic meningitis, encephalitis in severe cases. The pattern of cytokine/ chemokine release by human monocyte/macrophage cell line (THP-1) infected with EV71 genotypes (D, G and C isolated at NIVMU) were analyzed in-vitro in order to gain information on clinical severity and pathogenesis of these Indian strains. THP-1 cells were further differentiated into macrophages and infected with the three EV71 genotypes. The Immunofluorescence Assay (IFA), Single step growth curve and Flow cytometry revealed that all three genotypes infect human macrophages. The culture supernatants of the infected macrophages tested by Cytometric Bead Array showed that the indigenous EV71 genotypes (D and G) induced release of pro-inflammatory cytokines.

- **Investigation of host genetic susceptibility markers to Enterovirus A71 infection in Indian population**

EV-A71 has caused large-scale epidemics of HFMD in Malaysia, Taiwan, Singapore, China and other Asian countries since 1997. Pathogenesis studies have identified SNPs in about 12 genes that likely

influence susceptibility, severity and treatment prognosis. Centre developed multiplexed SNP assay exploring 15 genetic markers in 12 genes involved in the outcome of EV-A71 infection. Prevalence of genetic susceptible markers may assist evaluation of risk of EV-A71. Prior knowledge of prevalence of the genetic susceptibility markers in Indian populations may be useful for planning control measures in case of outbreaks of EV A71. No such information is presently available. The assay has been submitted for IPR via ICMR HQ.

- **CD155/PVR Knockout Cell Strains from Human Rhabdomyosarcoma Cell Line (RD) for use in Polio and Non-Poliovirus Diagnostics and Research**

As per GAPIII, potentially poliovirus containing material/ clinical specimens should not be inoculated in poliovirus permissive cell lines in laboratories. Study has successfully knocked out CD155/ PVR from RD cells using CRISPR/ Cas9 technology. The CD155/PVR knockout cells RD can be used safely in all non-polio laboratories wanting to grow non-polio enteroviruses from clinical samples for diagnostic purposes and research without the fear of poliovirus growth as inadvertent contamination. The CD155/PVR knockout RD cells will find wide applications in laboratories worldwide. It is envisaged that the WHO Global Polio Laboratory Network will also support use of CD155 knockout RD cells for Enterovirus work in the 146 network laboratories. Newly developed CD155/PVR knockout RD cell line has been submitted for IPR via ICMR HQ.

PUBLIC HEALTH RELEVANCE

Nipah virus (NiV) outbreak

- Laboratory diagnostic confirmation of NiV outbreak, Kozhikode, Kerala State
- Isolated and sequenced Nipah virus; Phylogenetic analysis revealed clustering with Bangladesh strain; 2004
- Traced the source of Nipah Infection from Pteropus Bats to Human.
- Similarity between NiV sequence from Pteropus giganteus (fruit bat) and human sample from Kerala: 99.7-100%

- Seroprevalence of NiV specific antibodies among close contacts Kerala showed low sub-clinical rate of NiV infection.
- Nipah POC qRT-PCR validation developed by MolBio Commercial company [Truenat test chips]

ZIKA VIRUS DISEASE

- Zika virus outbreak was first time documented in Rajasthan, India
- Genetic analysis of the samples showed evidence of recent evolution of Zika and indicated circulation of two Zika virus strains in India
- The mutation linked to fatal microencephaly (S139N) and higher transmissibility (A188V) was not observed for Rajasthan, ZIKV [2018] sequence.

Canine Distemper virus disease in Lions

- Laboratory support in the investigation of Canine Distemper virus outbreak in Lions in Gir forest, Gujarat (September, 2018).
- 1094 samples from 313 lions tested & 68 lions were found positive for Canine distemper virus (CDV). Full genome (~ 15.6 kb) retrieved from 11 samples
- Phylogenetic analysis: Indian strain clustered with East African strains
- Investigation of outbreaks of Severe respiratory disease
- High mortality in Pune & in a tribal area (Melghat) caused by RSV
- Contributions to National Programs of Measles elimination & Rubella control and AFP Surveillance
- Strengthening of DHR/ICMR VRDLs for laboratory confirmation of outbreaks including measles & rubella
- AFP Surveillance: Maharashtra, Madhya Pradesh, Goa
- Environmental surveillance: Mumbai (6 sites), Hyderabad (4 sites), Patna (3 sites)
- Translational research
- Total number of diagnostic kits supplied: 10,636

- Total number of kits launched: 3. NIV JE IgM Capture ELISA kit evaluated by Dr. Jane Basile, CDC, USA and found satisfactory in terms of manufacturing

Human Resource Development

- RC-VRDL conducted 08 trainings and trained 131 scientific and technical staff from different VRDLs on different aspects of bio-safety, outbreak investigation, biomedical waste management, ELISA, PCR and real time PCR.
- Training for foreign nationals [Sri Lanka, Indonesia, Bhutan, Nepal, Myanmar] were arranged to enhance capacity for Biosafety and laboratory capacity enhancement
- On-site Hands-on Training Program on detection of Zika Virus by Real-time RTPCR at Gujarat, Rajasthan and Maharashtra
- WHO orientation workshop on Biosafety and Biosecurity in the context of Emerging Infections was conducted during this year for VRDLs (Fig. 12).



Fig. 12: Workshop on Biosafety and Biosecurity.

- Six students guided by NIV scientists awarded Ph.D. Degree by Savitribai Phule Pune University (SPPU)
- Twenty-one students passed out of the M.Sc. Virology post-graduation course of NIV [affiliated to SPPU, Pune].

Diagnosis of Clinical samples

- NIV tested clinical samples referred by hospitals across the country for viral infections viz: dengue, chikungunya, influenza and other respiratory viruses, Japanese encephalitis,

Chandipura virus, Herpes virus, hepatitis viruses, measles, Polio, rubella and highly pathogenic viruses, i.e., KFD, CCHF, Hantan, Nipah.

ICMR-NATIONAL AIDS RESEARCH INSTITUTE, PUNE

Community / Clinic / Programme settings

- A study was initiated to determine the safety and tolerability of dolutegravir co-administered with other anti-retrovirals to people living with HIV (PLH) in post market scenario. Frequency of any adverse event and/or serious adverse event attributable to Dolutegravir in participants initiated on Dolutegravir based regimen is being recorded.
- Investigation on anti-bacterial activity of metformin, by measuring the time to sputum culture conversion in liquid media, when given daily for 8-weeks along with standard first-line anti-tuberculosis treatment (ATT) in newly diagnosed sputum positive Pulmonary TB (PTB) cases was initiated. Recruitment of participants in the study is being carried out satisfactorily.
- Trend of HIV prevalence among women attending antenatal care clinics, in Maharashtra, India was studied. HIV sero-reactive status of 15-18 year old primigravidae (0.3%) could serve as a proxy indicator of HIV incidence in heterosexual general population of the state.
- A Phase-III double blind randomized control trial of vaccines VPM1002 and Immuvac was initiated with incidence of TB over 3-year period among healthy household contacts of newly diagnosed sputum positive PTB patients as primary end point. Safety and efficacy of these vaccines will be assessed against placebo in this multi-centric clinical trial.

Laboratory investigations

- 'Alleviating Anaemia through Food Fortification at Scale' is an impact evaluation study of an intervention aimed at reducing

anaemia and other micronutrient deficiencies by providing multi-nutrient fortified rice through the Public Distribution System (PDS) of the State Government of Tamil Nadu. ICMR-NARI with is partnering with this project and providing laboratory services for testing biomarkers in dried blood spots.

- HIV drug resistance survey to assess acquired drug resistance among patients before initiating and after administration of antiretroviral therapy at 12 months and 48 months in India was initiated. The objective of this study is to assess national scenario of drug resistance in population receiving first line regimens under National AIDS Control Program (NACP).
- An exploratory study was conducted on cumulative drug resistance pattern in bacterial species in faecal samples. This small scale investigation highlighted the possibility of development of a methodology independent of culture techniques that could provide indications towards pre-existing anti-biotic resistance in bacterial population in faecal samples.
- Evaluation of 'Xpert HIV-1 Qual testing kits' for diagnosis of HIV-1 infection in infants born to mothers living with HIV was conducted. The evaluated Xpert HIV-1 Qual test was found comparable with the currently available Abbott Real Time HIV-1 Qualitative test. The test has the potential of being used as a Point of Care (POC) test for rapid and accurate diagnosis of HIV infection in infants.
- A study was completed on 'HIV-1 pol gene diversity and molecular dating of HIV-1 C from Sri Lanka'. The investigation examined diversity of HIV-1 pol gene and time to most recent common ancestor (tMRCA) for HIV-1 C in Sri Lanka. Bayesian skyline plot analysis was employed to estimate the population dynamics.

Public health Relevance

- Spiked detection of HIV in Unnao district of Uttar Pradesh (UP) during November 2017

was investigated by the scientists of ICMR-NARI during October-December, 2018. Draft report generated on this investigation with recommendations helped UP-State AIDS Control Society to plan future interventions.

- Support was extended to activities pertaining to management of Nipah virus outbreak in Kerala. Standard operating procedures for storage, reconstitution and administration of monoclonal antibody m102.4 received from Australia in June 2018 for its potential use on compassionate ground were prepared by the scientists of ICMR-NARI.
- National AIDS Control Organization supported – Pune Municipal Corporation (PMC) - ART Centre was operated by the scientists of ICMR-NARI. A total of 3557 patients were under active care and 3554 were alive and on ART during April 2018 - March 2019.
- ICMR-NARI as a Regional Institute, has been supervising implementation of India's HIV Sentinel Surveillance (HSS) in 5 states and 2 Union territories since 2006. The 16th HSS round was initiated, in 247 Antenatal Clinic-attende (ANC) sites from 1st January 2019 where ICMR-NARI is responsible for a few western States.
- External Quality Assurance (EQA) Programme for HIV serology, CD4 count estimation, Confirmation of HIV-2 diagnosis and Evaluation of Genius[™] HIV1/2 Confirmatory Assay were carried out by ICMR-NARI as crucial support to national program. Consortium activities of 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 conducted. Moreover, immunology, virology, serology and microbiology laboratories at the institute received recognition as WHO pre-qualification laboratories for diagnostics.

ICMR – RAJENDRA MEMORIAL RESEARCH INSTITUTE OF MEDICAL SCIENCES, PATNA

Over the periods, the institute has been involved in providing support in Kala-azar elimination at the national level through various intramural and extramural researches on epidemiological, diagnostic, treatment, vector control, operational and applied basic research. Our major research collaborators include: WHO, MSF, DNDi, BMGF, Kalacore consortium, DST-India, Sun Pharmaceutical Industry Ltd., Calila Health Care Ltd., etc. Apart from Kala-azar, research activities are also started on other Tropical disease viz: TB, HIV and Viral diseases. A field-based study conducted in highly endemic area revealed 2.1% asymptomatic cases (120 of 5794 screened population). Out of 120, 99 asymptomatic cases were followed quarterly and 40% (39 of 99) of these converted in VL cases with average duration of 78 days. ADA and IL10 was found as possible biomarker for asymptomatic to disease conversion.

In terms of treatment seeking behaviour, average duration of attending PHC by Kala-azar cases (16.75 ± 3.64 days of fever) confirms compliance of NVBDCP guidelines for Kala-azar elimination program at periphery level. Further, trend analysis of secondary data under a retrospective study revealed that projected incidence of Kala-azar cases will be under controlled situation in the year 2018-2020 subject to continuation of the existing intervention tools. However, three districts of Bihar namely Saran, Saharsa and Gopalganj may need special attention. Remote sensing and GIS based geospatial risk modeling has been successfully developed that can be used for mapping of high-risk zone for kala-azar.

Post-treatment follow up of Kala-azar cases treated with three different regimens i.e. single dose Ambisome (SDA), Ambisome plus Miltefosine (AMB+MF) and Miltefosine plus Paromomycin (MF+PM) revealed more PKDL development in

patients treated with MF+PM (7.4%) than SDA or AMB+MF (2.9%). A field based study conducted in Kala-zar endemic areas revealed that long time (6-8 hours) sun-exposed population are at high risk for PKDL development.

Single dose AmBisome (10 mg/kg b.w.) treatment in children Kala-azar cases (5-15 years) was found safe and highly effective with 98% final cure rate. Combination therapy of AmBisome (5 mg per kg b.w. for 6 days) plus miltefosine for 14 days was found better than monotherapy of AmBisome (5 mg per kg b.w. for 8 days) in treatment of HIV-VL co-infected cases. In a vis-a-vis comparison, miltefosine was found to be more effective than AmBisome in treatment of PKDL.

In respect of vector control, after reporting first time DDT-resistance in sandflies, the DDT susceptible and resistant colony have been established in the RMRIMS insectariums. A study on mechanism of DDT resistance in vector revealed that GST protein plays a role in DDT resistance in vector. *P. argentipes* was found susceptible to the insecticides; Alphacypermethrin, Deltamethrin and Primiphos methyl, that can be used as alternative if resistance develops with any one of the insecticides. Further in order to improve vector control strategies, the combination of IRS+ITN was found more effective as compared to IRS or ITN alone. However, community acceptance was found higher for ITN (87%) than IRS. Clerodolone, isolated from 9th Fraction of Methanol phase of hexane extract of leaves, was identified as an active compound having insecticidal effect to *P. argentipes*. A study on sandfly bionimics revealed that indoor soil rich in aluminium, calcium, magnesium, sodium and potassium and outdoor ambient with plants like banana, bamboo, sugarcane, etc. are suitable breeding sites for *P. argentipes*.

The previously developed “Vaishali model” for Kala-azar elimination has now been considered for elimination of Kala-azar in other districts of Bihar. As per directives of Directorate of NVBDCP, the Vaishali model is being replicated by RMRIMS in

the two most kala-azar endemic districts (Saran and Siwan) of Bihar.

BASIC AND APPLIED RESEARCH

Studies on parasite survival revealed that stress induced phosphorylation of *L. donovani* eIF2 α (*LdeIF2 α*) has crucial role in parasite differentiation (promastigote to amastigote) and survival during host invasion. Inhibitor of Serine Peptidases 2 of *L. donovani* (LdISP2) significantly inhibits trypsin and chymotrypsin activity inside the sand fly mid gut and promotes parasite survival. LdISP2 promotes parasite survival in human host by inhibiting MASP2 mediated lectin pathway activation and up-regulation of C5aR signaling. Further, it was observed that *Leishmania* infection upregulates zinc transportaiton inside host macrophase and regulates anti-leishmanial immune response while zinc chelation favours parasite clearance.

On immunological aspect, it was observed that after *L. donovani* infection, miR-150 expression was significantly increased in CD4⁺ T cells. miR-150 regulates the MAPK pathway and help in production of pro-inflammatory cytokines. Arsenic exposed *Leishmania* parasites consume more glucose, release more lactate and found more virulent than unexposed in infection establishment by down regulating protective cytokine. Hypertriglyceridemia significantly reduces IFN- γ level and induces IL10 level in VL infection. Further, neutrophil trafficking in macular PKDL patients was found to be abrupted, which might be a reason for difficult treatment of macular lesions.

It was observed that anti-saliva antibodies (SP15 family proteins) of *P. argentipes* counteract with vector saliva during infection and neutralize the disease manifestation. It can be explored as vector-based vaccine candidate for VL. Further, the ODC DNA construct showed high Immuno prophylactic activity against VL.

The studies on disease progression revealed that activation of Calcium channel blocker (CaMKII) activates MAPKinase signaling cascade in leishmania infection. Iron concentration plays a significant role in promastigote to amastigote

transformation mediated by ROS and Fe-S cluster assembly proteins as a sensor.

Proteomic profiling of secreted proteins of *L. donovani* by LCMS/MS revealed 32 proteins significantly up-regulated and 16 proteins down-regulated in Amphotericin-B resistant strains as compared to sensitive strains. Out of 32 upregulated proteins, 2 were new secreted proteins (one from nucleotide metabolism and another from amino acid metabolism), that can be explored as new drug target.

Enoyl-acyl carrier protein-reductase of *Leishmania donovani* (*LdENR*), showing 99% similarity with putative *LdENR* gene, was confirmed as a suitable drug target using triclosan ($MIC_{50} = 30\mu M$ for *L. donovani* promastigote as well as amastigote). After evaluation of different doses, β -D Glucan (50mg/Kg body weight) was found most effective in Hamster VL model for adjunct therapy without any drug-drug interaction with SAG and Amphotericin B. The earlier evaluated plant extract formulation for its use in blood/ blood products free culture for *L. donovani* was also found effective in culture of *E. histolytica*, cell lines and PBMCs.

The division of Bioinformatics is actively involved in *in-silico* identification of effective vaccine candidates, designing anti-leishmanial drugs as well as development of Leishmaniasis Database & search tools. During the reporting period, a comprehensive database on Leishmania inhibitors, LeishInDB (<https://leishindb.biomedinformri.com>), has been released. LeishInDB, is a web-accessible resource of small molecule inhibitors having a varying degree of activity towards *Leishmania* sp. The database includes searchable information of >7000 small molecules collected from >600 literature and contains complete information of tested small molecule inhibitor against *Leishmania* and its activity values. The researchers may utilize the available information for repurposing the inhibitors as well as for the investigation of new therapeutics. Thirty six (36) novel compounds have been identified through *in-silico* computation analysis followed by MD simulation, of which 2 molecules were confirmed as potent inhibitor of *L. donovani*.

It is noteworthy to mention that the Institutional Ethics Committee of RMRIMS, Patna has been accredited by NABH w.e.f. 21st Dec. 2018. Moreover, aimed to improved implementation of kala-azar elimination programme at grass-root level, Induction training to Kala-azar Technical Supervisors and VBD consultants was organized. Reorientation training of Medical Officers and Lab. Technicians was conducted on PKDL diagnosis & treatment. Lab. Technicians of Bihar were also trained on “Diagnosis of Vector borne diseases”.

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

VECTOR AND VECTOR BORNE DISEASES

Status of artemisinin resistance in malaria parasite *Plasmodium falciparum* in Nigeria, Africa.

Since the amino acid (AA) mutations at the *P. falciparum Kelch13 (Pfk13)* gene provides resistance to ART and Nigeria is a highly malaria endemic country, we were interested in molecular epidemiological surveillance in this gene from two southwestern states of Nigeria. None of the different validated and candidate AA mutations of *Pfk13* gene conferring resistance to ART could be detected in *P. falciparum* sampled. Therefore, based on the monomorphism at the *Pfk13* gene and non-association of mutations of this gene with mutations in three other drug-resistant genes in malaria parasite *P. falciparum*, it can be proposed that malaria public health is not under immediate threat in southwestern Nigeria concerning ART resistance.

Molecular epidemiology of drug-resistance in Nigeria, Africa

Among many hurdles, evolution and spread of drug-resistant *Plasmodium falciparum* parasites constitute major challenges to malaria control and elimination. In the present study, centre has followed molecular methods to detect both the known and emerging mutations in three genes (*Pfprt*, *Pfdhfr* and *Pfdhps*) of *P. falciparum* conferring resistance to chloroquine and sulfadoxine-pyrimethamine

from two different states (Edo and Lagos) in southwestern Nigeria (Fig. 13). High diversities in haplotypes and nucleotides in genes responsible for chloroquine (*Pfprt*) and sulfadoxine (*Pfdhps*) resistance are recorded (Fig. 13). Furthermore, many unique haplotypes of *Pfdhps* and *Pfprt* were found to be segregated in these two populations. Moreover, detection of strong linkage among mutations of *Pfprt* and *Pfdhfr* and feeble evidence for balancing selection in *Pfdhps* are indicative of evolutionary potential of mutation in genes responsible for drug resistance in Nigerian populations of *P. falciparum*.

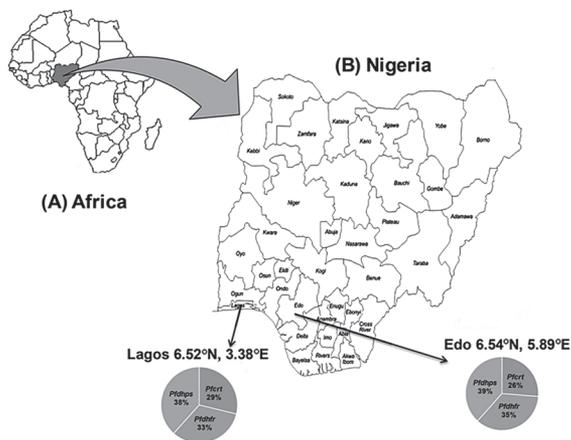


Fig. 13: Map of Africa and Nigeria showing collection sites and frequency distribution of different haplotypes of three drug-resistant genes in the malaria parasite, *Plasmodium falciparum*.

Molecular diagnosis of malaria parasites

The prevalence of malaria in disturbed and conflict affected areas of Jagdalpur, Chhattisgarh, and Balaghat, Madhya Pradesh was recorded by microscopy and PCR. Microscopic examination of slides showed presence of only *P. falciparum* and *P. vivax*; whereas PCR analysis of more than 900 samples showed 18% had mixed infection (double and even triple) with four parasite species of Plasmodium (*P. falciparum*, *P. vivax*, *P. malariae* and *P. ovale*).

Study on *HRP2* and *HRP3* gene in *Plasmodium falciparum* parasites from Odisha state, India: A prospective evaluation

Evaluation of presence or absence of *pfhrp2* and/ or *pfhrp3* gene of *P. falciparum* parasite samples from a malaria-endemic site of Kalahandi district,

Odisha, India was done to guide Malaria control programme for procurement and implementation of appropriate malaria rapid diagnostic tests (RDTs). The sensitivity of various RDTs used for malaria diagnosis varies in the field. Albeit at low frequency (2.2%), the *Pfhrp-2/3* gene deletion was noted *P. falciparum*, in the high malarial endemic area of Odisha. Further, as an offshoot of the project a total of 514 microscopy and PCR positive samples for *P. falciparum* were selected for the study of genetic diversity of *pfgdh*, *pfldh* and *Pfaldolase*. Sequencing analysis of *pfgdh* gene showed that gene is highly conserved and only three synonymous SNPs were observed with no amino acid change among the isolates. Very little sequence diversity was observed in *Pfgdh* in comparison to the low level of diversity in *ldh* and *aldolase* gene.

Efficacy and safety of artemether-lumefantrine (AL) combination therapy for the treatment of uncomplicated *Plasmodium falciparum* malaria in 4 Tribal dominating states in India: Madhya Pradesh, Maharashtra, Chhattisgarh and Odisha

The samples were collected from four tribal dominated districts of Madhya Pradesh, Maharashtra, Chhattisgarh and Odisha. Therapeutic efficacy was determined in 356 (94.7%) patients who completed their 28 days follow-up. Adequate clinical and parasitological response (ACPR) was observed in 98.9% cases with four cases (1.1%) of late parasitological failure (LPF). Neither early treatment failure (ETF) nor late clinical failure (LCF) was observed in this study. Also, in most of the patients (65%) parasitaemia was cleared within ≥ 24 hrs. Out of four cases of late parasitological failure, two cases were of recrudescence and rest two were of re-infection as determined by PCR and sequencing. Molecular study revealed that no functional mutation against *PfK13* was present in the study areas.

Pilot and Validation Study of a New Malaria and Sickle Cell Disease Diagnostic Device

A total of 300 patients were enrolled in the study and were analyzed by microscopy, RDT, PCR and

Gazelle™ (a malaria diagnostic device). The sensitivity of Gazelle™ was found to be 98%, 78%, 82% whereas the specificity was found to be 97%, 99% and 99% in comparison to microscopy, RDT and PCR respectively. The accuracy of Gazelle™ was 94.7% in comparison to microscopy whereas it was 94.3% for RDTs and 95.4% for PCR. Further, Gazelle™ shows better sensitivity, specificity and accuracy in diagnosis of malaria naïve cases. Gazelle™ may be a potential diagnostic solution for settings where there is a need for speed, accuracy and ease of use.

Mandla-Malaria Elimination Demonstration Project (MEDP)

MEDP is a first of its kind public private partnership between the ICMR, Government of Madhya Pradesh and the Foundation for Disease Elimination and Control of India (FDEC, India). This project is being carried out in tribal district Mandla. Using T4 (track, test, treat and track) stagey. Total of 1, 61,235 fever cases have been tracked and tested and a total of 399 cases of malaria were diagnosed. Out of 399 malaria positive cases, 65.6 % cases were caused by *P. falciparum*, 31% by *P. vivax*, and 3.2% due to mixed infections. The highest number of cases were reported from Mawai block whereas as lowest were reported from Narayanganj blocks the district. The entomological studies revealed significantly higher vector density in villages having annual parasite index <1. Significant higher vector density was in the month of July and lowest was in May. Proportion of vector was significantly higher in foothill terrain. The bioassays show 82 to 100% corrected percent mortality of *An. culicifacies* on one day post spraying and 41 to 62% on day 30 after spraying. No *An. culicifacies* and *An. fluviatilis* detected positive for sporozoite. *An. culicifacies* sibling species C was most prevalent (52%) followed by E (32%) and B (16%). *An. fluviatilis* sibling species T was most prevalent (73%) followed by U (27%). The evaluation of ASHA, highlighted the need of refresher training on malaria to grass root level staff. In comparison with the previous year data almost 90% reduction was found in the study area (Fig. 14).

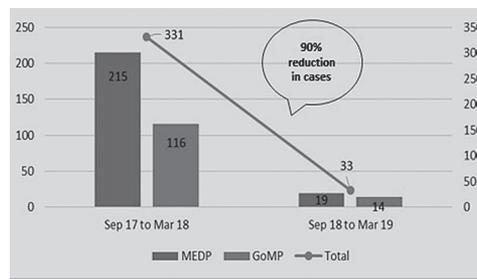


Fig. 14: Showing about 90% reductions in indigenous Malaria cases in comparison to 2017-18 cases. Number of malaria cases (n=331) in year 2017-18 are given on Y axis; cases (n=33) in 2018-19 are on secondary axis.

Study of asymptomatic malarial infection in low and high malaria transmission areas in Madhya Pradesh

Initial sampling and microscopic analysis of slides of 422 samples collected from Balaghat district showed 5.7% malaria positivity with dominant of *P. falciparum* (100%). However, the molecular analysis of 320 samples shows the presence of four species of malaria parasite and mixed infection in Balaghat. Out of 320 samples analysed by PCR, 25 % samples were found positive for *P. falciparum*, 5.9 % for *P. vivax*, 1.9 % for *P. malarie* and 1.5% for *P. ovale*.

Monitoring of insecticide resistance in malaria vectors in Madhya Pradesh state

Groups of districts based on spray history in the last 5–10 yr as Group A (IRS with pyrethroids), Group B (IRS with DDT), and Group C (without IRS) revealed decreased mortality of *An. culicifacies* (91.7%) to alphacypermethrin in Group A. *An. culicifacies* from all the areas showed resistance to DDT and malathion, however, in areas (group B and C) the species registered higher mortality to pyrethroids in the range of 96.7 to 100%. Malathion was not sprayed regularly in these areas and the observed level of resistance to malathion could be due to selection by its use in agriculture/forestry. This study will provide an updated map for insecticide resistance in malaria vectors against commonly used insecticides based on the study.

EXTRAMURAL RESEARCH

- ICMR with its 10 institutes worked together under the umbrella of Tribal Health Research

Units (THRUs) to improve the health of tribal people through improved diagnosis and develop strategies for management of various infectious diseases as well as non-communicable diseases. Phase I of the multicentric Task Force study on tribal TB entitled, “Estimate the burden on TB among the tribal population and develop the innovative health system model to strengthen TB control in the tribal areas” was completed in seven states in May 2018 and phase-II in nine states is ongoing. The prevalence of TB from phase-I study showed highest prevalence in Odisha (486 per 100,000) and Madhya Pradesh (484 per 100,000) among the tribal 328 cases per 100,000 population.

- As per the directive of the National Schedule Tribe Commission of Govt. of India, a project to assess the health of tribal people living in the Tamnar Block, Chhattisgarh to study the morbidity profile of the people living in fourteen villages around the “Gare Palma” project area and compare the disease morbidity pattern, nutritional status with the villages far away (19 control villages) has been initiated. The project has been initiated in view of rising complaints of health problems like cancers, chest diseases, dermatological problems etc. in people residing in the said fourteen villages.
- Three task force projects were initiated in North-East. The projects aim at estimating burden of acute viral hepatitis and chronic liver diseases in northeast India. Laboratory strengthening for diagnosis of viral hepatitis is also being undertaken. Efforts have been initiated to estimate the burden of human pulmonary Paragonimiasis in crab eating communities and smear negative suspected TB cases from some states of India.
- Several initiatives have been taken under the India TB research consortium, with an aim to provide evidence based solutions to TB elimination program in India. Several new regimens for treating drug sensitive as well as resistant TB are underway viz-a-viz adjunct therapy with metformin; improving treatment effectiveness by giving DOTS + Inhalational INH and Rifabutin, repurposing econazole etc. In addition, a prevention of disease trial with two vaccines VPM1002 and Immuvac have been initiated to assess the feasibility of preventing TB in HHC of Newly Diagnosed Sputum Positive PTB Patients. National TB Prevalence survey has been initiated. Multicentric study on reducing activation of TB by improvement of nutritional status has also been initiated.
- Surveillance for monitoring trends of antimicrobial resistance is being continued in tertiary care hospitals under the ICMR-AMR network. Five workshops on antimicrobial stewardship program (AMSP) were conducted across the country to train more than 300 staff from 50 hospitals across the country. Studies on AMSP initiated to assess antimicrobial consumption, adding drugs to formulary restriction and the culture rates in the institutions who participated in trainings. In view of ICMR’s initiative on AMR, GARDP signed an MoU with ICMR in 2018 to support clinical research related to antibiotics, drug discovery and related challenges and conservation strategies for antibiotics. New treatment options for neonatal sepsis are priority for this collaboration. An observational study to map neonatal sepsis in three hospital clusters in three cities (Mumbai, Chennai, Delhi) and clinical trials for using fosfomycin compare efficacy to existing combinations being used has been initiated.
- A study has been initiated at 21 sites in India to assess the impact of Pneumococcal conjugate vaccine recently introduced in a few states by Govt. of India. The study will assess the replacement of pneumococcal serotypes pre and post introduction of PCV in India.
- The Post Elimination Agenda for Kala-Azar in India (SPEAK India) Consortium was set up in the year 2018. ICMR collaborated with London School of Hygiene and Tropical

Medicine (LHSTM), BMGF and MOHFW to develop SPEAK-India. Under this consortium four projects have been funded by BMGF on Surveillance, Transmission, Health Systems and Modelling.

- Validation of Immunogenicity of HIV-I Indian Subtype C Vaccine constructs in rhesus macaques and preclinical safety evaluation of vaccine constructs in Mice/Rats and Rabbits”- The vaccine was found to be moderately immunogenic and further immunogenicity studies will be carried out by third party. Development of ELISA based hybridization in aqueous solution assay for simultaneous detection of gene amplification products of HIV-1 & 2 RNA/HCV RNA/HBV DNA in plasma samples- Validation of diagnostic kit for detection of HIV is in process.
- Serosurveys for estimating population immunity for measles and rubella have been initiated at nine sites in the country. These serosurveys will help understand the population immunity gaps and additional efforts required to accomplish the goal of measles and rubella elimination program.
- Following the declaration of Zika virus disease as a public health emergency of International concern by WHO in 2016, ICMR had set up human surveillance for Zika virus (ZIKV) disease at 35 sites in the country. In addition, mosquito surveillance was set up at 8 sites in the country. Till August 2018, 76000 human and 50,000 mosquito samples were screened for ZIKV. In September 2018, ICMR surveillance picked up outbreaks of ZIKV in Jaipur, Rajasthan

and Bhopal, Madhya Pradesh. A total of 159 positive cases including 62 pregnant women were detected in Jaipur, whereas 130 cases, including 40 pregnant women were detected in Bhopal. Three mosquito pools were found positive from Jaipur. ICMR led surveillance was instrumental in timely detection and containment of outbreaks at both Jaipur and Rajasthan. ZIKV was isolated from the samples obtained from Jaipur and complete genome sequencing was done. The strain is related to Brazil ZIKV, however known mutations for microcephaly were absent. ICMR continues to maintain high quality surveillance for ZIKV in various parts of the country.

PUBLIC HEALTH RELEVANCE

- Establishment of MERA-India (Malaria Elimination Research Alliance –India): MERA-India has been launched on 24th April 2019, at ICMR in collaboration with WHO, NVBDCP and MOHFW. The targeted, multi-institutional, operational and translational studies will be undertaken involving ICMR and non-ICMR partners to identify and address the existing gaps and roadblocks to eliminate malaria by 2030.
- Establishment of Satellite Center for One Health, Nagpur: MoU between ICMR and Maharashtra Animal and Fisheries Sciences University (MAFSU) has been signed for developing this Satellite center in MAFSU campus. Preliminary scientific discussion with MAFSU is underway and scientific agenda is being drawn for carrying out joint research.

REPRODUCTIVE HEALTH

ICMR is undertaking research in the field of reproductive health through its research institution National Institute of Research in Reproductive Health, Mumbai as well as extramural research projects. These studies are aimed to protect and enhance the reproductive 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

FEMALE INFERTILITY AND ASSOCIATED REPRODUCTIVE DISORDERS

Implementation of Multidisciplinary Model of care for Women with Poly Cystic Ovary Syndrome (PCOS).

PCOS is becoming an area of national as well as global concern. Women with PCOS are at increased risk of developing infertility, obesity, type 2 diabetes mellitus, hypertension, dyslipidemia, atherosclerosis and endometrial cancer. In our cohort, metabolic syndrome by NCEP ATP III criteria was found among 28% (n=220) women with PCOS. Therapy should focus on reproductive, metabolic, cosmetic and psychological aspects of PCOS and social support. An integrated multidisciplinary model of care for women with PCOS to address most concerns of women with PCOS has been initiated at the institute with a team

of IVF specialist, endocrinologist, dermatologist, dietician and yoga expert. This is a unique model for research and services in PCOS and is first of its kind in the government research Institute in India.

Estimating Prevalence, Phenotypes, Comorbidities and Risk Factors of PCOS- A Multicentric Study.

All the preparatory activities for this task force study in terms of finalizing study tools, recruiting staff, training, mobilizing community both in urban and rural areas, getting ethical approvals, and finalizing investigation procedures were done during the year. Study participants were approached at households as per the sampled electoral voter list and consent was obtained. During the reporting period, eligible women were enrolled at urban and rural areas. The study was registered with the CTRI and protocol was submitted for publication by the study coordinator.

Exploring Genetic Markers for PCOS by Re-sequencing of GWAS Loci in Indian Women.

Given that ethnicity influences the phenotypic diversity in PCOS, current study seeks to examine the associations of variants in genes previously identified in earlier genome-wide association studies viz. *LHCGR*, *THADA* and *DENND1A* with PCOS risk in a well phenotyped population of control and PCOS women. Data analyzed so far revealed no significant difference in the frequency distribution of the polymorphisms, rs13429458 of *THADA* and rs13405728 of *LHCGR*, between controls and women with PCOS, while the genotype distribution of rs2479106 polymorphism tended to

be different between controls and PCOS women. The study will enhance understanding of genetic patterns of PCOS specific to the Indian population.

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

Redox homeostasis in follicular microenvironment is very important for oocyte development which may be disrupted in Follicular Fluid (FF) of women with PCOS. Glutathione plays a central role in maintaining redox homeostasis. Glutathione (GSH) and GSH/GSSG ratio was significantly lower in PCOS than in control women indicating increased oxidative stress. Advanced oxidized protein products, a marker for protein oxidation, was found to be significantly higher in FF from PCOS women than in controls. Transcript levels of GLUT4, the principle glucose transporter in granulosa cells (GC's) were reported to be lower in PCOS women than in controls. This suggests that redox balance and glucose metabolism dynamics in oocyte microenvironment may be compromised. It is planned to investigate other antioxidant molecules and transcript levels of key metabolic enzyme in GCs.

Studies to Evaluate the Effect of Metformin on Endometrial Functions.

Metformin is the most cost-effective, oral, FDA approved anti-diabetic therapy. Unlike other anti-diabetic drugs, metformin does not induce hypoglycemia and is well tolerated drug with minimal side effects. Due to its diverse systemic effects involving glucose metabolism, metformin is used for the treatment of infertility in Polycystic Ovarian Syndrome (PCOS). Metformin is known to improve ovulatory rates, menstrual cyclicity and pregnancy outcomes in PCOS women. However, there is lack of data evaluating the effects of metformin on endometrium and endometrial receptivity. Therefore, the present study was undertaken to evaluate if metformin has direct effects on endometrium. It was previously reported that a low concentration of metformin induces proliferation in endometrial Ishikawa and HEC-1A

cells as opposed to inhibition in low concentration. In the reporting year, centre evaluated the effect of low concentration of metformin on activation of AMPK (AMP activated protein kinase) in Ishikawa cells. It was observed that metformin causes up regulation of pAMPK within 1h and 2h of treatment in Ishikawa cells. It remains to be elucidated whether metformin induced AMPK activation is responsible for its proliferative effect in Ishikawa cells.

Pathways to Oncogenesis in the Pathophysiology of Endometriosis.

Endometriosis is a polygenic and multifactorial gynecological condition known to affect every 1 in 10 women in their reproductive age globally. Although considered benign, the disease shares several features such as proliferation, angiogenesis, invasion, etc. with cancer. The present study was undertaken to investigate whether the eutopic endometrium of women with endometriosis shows activation of oncogenesis-associated pathways. Towards this, RNA Seq analysis (outsourced to Genotypic Technology, Bangalore) of mid-proliferative phase eutopic endometrium of women with and without endometriosis was previously carried out. In the reporting year, mid-secretory phase endometrial samples from women with and without endometriosis were analyzed for their global mRNA and miRNA profiling. Gene annotation enrichment analysis of differentially abundant mRNAs revealed 'Pathways in Cancer' such as PI3K-AKT pathway, Ras signaling pathway, Proteoglycans in Cancer as the top-most dysregulated pathways in women with endometriosis. Results so far revealed dysregulation in the expression of genes involved in oncogenesis in the eutopic endometrium of women with endometriosis and this was evident in mid-proliferative as well as mid-secretory phases of the menstrual cycle.

The Factors of Relevance in Endometrial Adhesiveness to Embryonic Cells.

The initial interaction between endometrial Cell Adhesion Molecules (CAMs) and their cognate

ligands on the blastocyst plays a key role in defining the outcome of pregnancy. This entails not only optimal levels but also appropriate localization of specific CAMs on the plasma membrane of endometrial as well as embryonic cells. However, this warrants extensive investigations on identification of proteins localized in the plasma membrane of endometrial epithelial cells. During the reporting year, the cell surface of Ishikawa cells was developed. Gene ontology analysis revealed the association of 1964 proteins with the plasma membrane. Extensive data mining revealed experimental evidences of 936 of 1964 proteins expressed in human and rodent endometrium.

Role of Homeobox Gene HOXA10 in Pathogenesis of Endometriosis.

The aim of this study is to understand the roles of HOXA10 gene in the pathogenesis of endometriosis. Centre has developed mice that are transgenic for HOXA10 shRNA which have lower than normal levels of HOXA10. Analysis of the expression of the endometria of these transgenic mice revealed endometrial hyperplasia and endometritis. At the cellular level, these animals demonstrate hyperproliferative activity and inflammation. Studies are ongoing to determine how loss of HOXA10 contributes towards inflammation and fibrosis the hallmarks of human endometriosis.

Understanding the Molecular Basis of Embryo Implantation.

Implantation of the embryo to the endometrium is a rate limiting step of successful pregnancy. Defects in the process of embryo implantation lead to infertility and failure of embryos to implant is a major cause of poor success rates of assisted reproduction. In this project, it is aimed to investigate the mechanisms by which embryo breach the endometrial epithelium and leads to decidualization of stromal cells. Using mouse as study model, it has been observed that in response to embryonic signals, the endometrial epithelium produces OVGPI which is required for efficient attachment of trophoblast cells.

Understanding the Molecular Mechanisms of Gonadal Development in the Mouse.

This study aims to understand how the developing gonads differentiate in to testis or ovaries. The earlier studies have shown that the homeobox gene Lhx2 is expressed in a sexually dimorphic manner with higher expression in developing ovaries as compared to testis. Centre analyzed the phenotypes of mice lacking Lhx2 and observed that there is defective entry of germ cells in meiosis in the XX gonads. This effect seems to be due to failure of the retinoic signaling pathway. The team is dissecting the further steps that are awry in Lhx2 deficient gonads with a goal to determine the genetic control of meiosis.

Search for a Molecular Marker Capable of Predicting Ovarian Response to FSH Treatment in Indian Women.

In human assisted reproduction, the ovarian response to exogenous recombinant Follicle Stimulating Hormone (FSH) therapy is variable and difficult to predict. The purpose of this study was to investigate effects of genetic variants in anti-mullerian hormone (AMH) and AMH type II receptor genes on ovarian response. In this prospective observational study, the study genotyped the AMH C-649T, G146T, G252A, G303A variants in 135 women undergoing their first cycle of controlled ovarian stimulation for IVF. The total amount of exogenous FSH required by subjects with wild type genotype of AMH C-649T, G146T, G252A, G303A was significantly lower than subjects with polymorphic genotype. These results indicate that CC genotype at position C-649T, GG at position G146T, AA at position G252A and AA at position G303A of AMH gene might be associated with poor response. The recruitment of remaining participants to study FSHR, AMH and AMHR2 gene polymorphisms is in process.

Identification of hFSHR Antagonist and Agonist Modulators.

A small molecule (1,3-diphenyl-1H-pyrazole-5-carboxylate) and 2 peptides have been identified

by a combination of dry and wet lab methods to behave as hFSHR antagonists. The contraceptive potential of one of the peptides is being explored using rat models.

MALE INFERTILITY AND ASSOCIATED REPRODUCTIVE DISORDERS

Defining the Role of Glucose Regulated Protein 78 (GRP78) in Sperm.

GRP78, a resident endoplasmic reticulum (ER) chaperone is expressed on the cell surface in exceptional conditions as seen in cancer cells and macrophages. It was previously reported that GRP78 tyrosine phosphorylation significantly increases during epididymal maturation and in human sperm, GRP78 phosphorylation is significantly reduced in asthenozoosperm. The data suggests that $\alpha 2M$ interacts with sperm surface GRP78 during epididymal transit, increases GRP78 phosphorylation thereby activating cofilin pathway which prevents flagellar F-actin depolymerization. As F-actin is required for maintaining sperm motility, this finding has significant implication as previous reports show reduced GRP78 phosphorylation and altered actin based motility pathway in asthenozoosperm.

Development and Validation of a PCR based Technology for Detection of Yq Microdeletions in Diagnosis of Male Infertility.

Y chromosome microdeletions are a major genetic cause of male infertility. In this translational research project, we aim to develop diagnostic test for detection of Yq microdeletions. A multiplex PCR was developed by the laboratory that makes use of 16 STS markers that can detect Yq microdeletions. This assay has been optimized in the lab and the sensitivity, specificity and performance parameters are being evaluated. Second party validation is ongoing. Future studies will involve developing these PCR in an easy to use kit format.

RTI/ STIS/HIV/ MICROBICIDES

Identification and Validation of Potential Drug Targets for *Candida* spp. using in silico and Wet Lab Methods.

Proteomes of *Candida albicans*, *Candida tropicalis* and *Candida glabrata* have been analyzed to identify potential targets and drugs. 15 targets were identified for *Candida* spp based on the *in silico* analysis. 10 drugs were found to be potential inhibitors for 8 of 15 identified targets based on sequence and structural similarity of the known drug targets. 2 of the 10 drugs were tested for anti-*Candida* activity and both were found to have inhibitory activity by broth microdilution assay.

Quantitative Structure Activity Relationship (QSAR) studies on AMPs and developing a steady state model that simulates AMPs binding to membrane.

In this study, QSAR models were built in an attempt to understand relevant chemical properties for biological activity of Anti Microbial Peptides (AMPs) from the cathelicidin family, and to evaluate the effectiveness of QSAR to predict the activity of rationally designed peptides. A steady state model has been built to predict the mode of action of the mechanism of AMP binding. The model has been found to predict accurately aggregation, number of sites, co-operativity and strength of binding for experiments found in literature.

Development of a Multistrain Probiotic Lactobacillus Formulation Effective Against Reproductive Tract Infections.

The study evaluated the stability of seven freeze dried probiotic vaginal lactobacillus strains (selected from 324 urogenital isolates) using skimmed milk as a cryoprotectant across various temperatures (room temperature, 4°C and -20°C) for a period of three consecutive months. Most isolates were viable and maintained inhibitory potential on urogenital pathogens after storage at 4°C and -20°C for 3 months.

Refining and Validation of Resazurin-based 96-well plate method for Assessment of Antimicrobials against Laboratory Pathogens.

The resistance detected by the REMDDA (Resazurin based Microtitre Disc Diffusion Assay) test was

comparable with conventional Disc Diffusion Assay (DDA) for nineteen antimicrobial agents (a total of 7537 antimicrobial discs for 1115 pathogens) suggesting REMDDA as an efficient alternative in low resource settings. The disagreement between the two methods was observed for quinolones antibiotics used for evaluating susceptibility of *Proteus*, *S. aureus* and *Pseudomonas*.

Haplotype Reconstruction Assisted Analysis of Drug Resistance in HIV-1C Sequences.

Drug Resistance Mutations (DRMs) are caused by suboptimal adherence to HIV ART and constant viral evolution driven by poor proofreading activity of reverse transcriptase. Pol sequencing of PBMC derived proviral DNA from 32 HIV-1 clade C infected individuals from Mumbai, India, along with quasispecies reconstruction, concomitant with a novel control DCPM, afforded detection of DRMs, mutation interaction as well as hypermutated sequences at frequencies as low as 10% (spearman $r=0.91$, $p<0.0001$). The protocol has diagnostic utility in resistance monitoring within a resource limited setting with proviral DNA obtained through dried blood spots.

Immune Signatures for HIV-1 AND HIV-2 induced CD4+T Cell Dysregulation in an Indian Cohort.

Identifying unique immune signatures associated with slower AIDS progression in HIV-2 infected individuals may provide therapeutically useful insight into the management of HIV infection. In untreated HIV-2 infected individuals, T cell activation was lower compared to ART naïve HIV-1 infected individuals and higher than the seronegative individuals ($n=111$). Dysregulation of IL-2 and IL-7 homeostasis persists in CD4+T cell subsets irrespective of presence or absence of viremia or antiretroviral therapy in HIV infection. Results implicate novel immunomodulatory therapeutic strategies for both HIV-1 and HIV-2 infection.

Investigation of Integrin alpha4beta7 Expressing Immune Cells in Sexually Transmitted Infections

/ Reproductive Tract Infections (STIs/RTIs) and HIV.

Retinoic Acid Receptor (RAR) levels can contribute towards alteration in Retinoic Acid (RA) dependent gene expression of integrin alpha4beta7 during HIV infection. Analysis of RAR mRNA expression in PBMCs revealed a significant alteration in ART naïve HIV positive women compared to HIV negative controls. A positive correlation of mRNA expression of RARs with that of integrin beta7 observed in HIV negative women was lacking in case of HIV positive women. Further studies will examine the relation between expression of integrin alpha4beta7 and RARs in the course of RTIs and STIs.

Variants of Human Leukocyte Antigen and their Possible Association with HIV Transmission.

Human Leukocyte Antigen (HLA) molecules play a key role in regulating the immune response towards infectious agents like Human Immunodeficiency Virus type-1 (HIV-1). HLAs influence transmission as well as the progression of HIV-1 towards Acquired Immune Deficiency Syndrome (AIDS). Roles of HLA-A and HLA-B have been documented extensively; however, HLA-C has been poorly studied. The present study evaluated the role of HLA-C in discordant couples and mother-to-child cohorts. The frequency of HLA-C*07 was higher both in HIV-1-infected spouses and infants as compared to exposed uninfected spouses and infants, although, this was not significant. HLA-C*15 was significantly higher in HIV-1-exposed uninfected babies as compared to infected babies. HLA-C*07 may be a susceptible allele in HIV-1 transmission, whereas HLA-C*15 may be a protective allele in mother-to-child cohorts, independent of feeding options and treatment. These findings could be important in targeting immune responses via population-specific vaccine strategies against HIV-1.

MENOPAUSE AND OSTEOPOROSIS

Identification of Estrogen-Regulated Proteins in the Secretome of Osteoblast and Osteoclast Cell Differentiation.

This study explores role of Estrogen (E) in maintenance of bone mass and revealed that estrogen promotes bone formation by enhancing the survival of bone forming cells, osteoblasts via autophagy. It inhibits differentiation of osteoclasts as well as their survival through up regulation of LYN, a tyrosine kinase, required for mediating action of estrogen on osteoclast. The study proposes LYN as a promising therapeutics target for the management of osteoporosis in future.

A Study of Lifestyle and Genetic Factors in a Tribal Population of NE India and their association with Bone Health and CVD Status.

This study investigated association between the cardiac risk factors viz. lipids and Homocysteine (Hcy) with Bone Mineral Density (BMD), the measurable determinant of fracture risk in women. The association is found to be not only confined to elderly women as reported but in cohort of young women. The study will enforce initiation of appropriate interventions for preventing manifestation of diseases associated either with dyslipidaemia or low BMD.

Reversal of Lactation Associated Bone Loss in Women belonging to Low Socio Economic Strata: A Pilot Study.

The research study on Reversal of Lactation associated bone loss is first of its kind among low-income population. The study focused on evaluation of the Traditional Diet Foods (TDF), the micro and macronutrient estimations, bone mineral density and laboratory investigations related to the bone health. Lactating women were at risk for low bone mass and osteoporosis at the spine. TDF consumed by lactating women (1.5 to 3 months post-delivery) helped them to reach closer to RDA levels for energy, calcium and proteins. For iron and fats they were 1.2 to 2 times higher. A significant decline in dietary calcium, dietary iron and a reversal of calcium and phosphorus ratios was observed on discontinuation of TDF. The non-lactating women diets were closer to 50 % of RDA for carbohydrate, calcium, iron, while it was over 80% of RDA for energy, proteins, magnesium and

fiber reflecting deficient nutrient intake. Traditional dietary foods are an excellent option for lactating women and they should continue these foods until the complete breastfeeding period of 6 months post-partum. Intensive IEC should be advocated to promote continued intake of TDFs by lactating women.

Bone Exercise for Life: An Intervention Model on Bone Health and Quality of Life among Menopausal Women.

This study on awareness of osteoporosis in 440 peri menopausal low income women regarding awareness of osteoporosis revealed that over one half of the women population had heard of osteoporosis /osteoarthritis word, however only 30.9% could differentiate it from osteoarthritis. Incorrect /poor knowledge regarding osteoporosis and risk factors existed among approx. 40.7 % of the women. Awareness of importance of calcium rich foods, sunlight exposure and exercise for bone health and its practice was significantly incongruent to life style practices. Barriers spelt were, lack of family support/ time, no facilities for exercise or yoga, financial reasons etc. Screening for osteoporosis, targeted IEC material will help improve their approach towards healthy life style. Over 2/3rd population was aware of fall prevention and fractures, but was not aware (approx. 80%) of diagnostic aids for osteoporosis. They expressed need to have community-based clinics, free diagnosis and treatment by government facilities. The community awareness so generated by this study may inculcate community acceptance of preventive and therapeutic measures for osteoporosis, thus eventually women would help themselves improve their quality of life.

Osteoporosis Screening and Intervention Programme Using AYUSH Approach: A Community based Programme in Maharashtra State.

Public Health Initiative program was undertaken to address and sensitize menopausal osteoporosis among community, health-care professionals,

policy makers, and the public by screening for the burden of disease using camp approach. With the conduct of 13 camps and clientele registered at the Bone Health Clinic, 1467 women were screened for Osteoporosis out of which 39.5% were diagnosed with osteoporosis and were given Ayurvedic medicines (Tab Ghanavati /laksha Guggul) for Osteoporosis. Over half of the population was above 50 years of age, reflecting that the aged women took benefits from the community-based camps. More than 2/3rd of the women screened had low haemoglobin levels (< 10 gm). Among the non-communicable diseases, osteoporosis (39.5%) was commonly seen followed by hypertension (38.2%) and diabetes (17.9%) with only 14% normal individuals. Vata, Pitta, Vata Pradhan or Pitta Pradhan Prakruti had strong association with low bone mass [$p=0.000$] (age and sex matched Z scores) while it showed no significance with the osteoporosis. Risk factors for osteoporosis were significantly associated with osteoporosis except tobacco use, sedentary lifestyle. The community based camp approach is one of the best modality to screen women, especially aged to increase access to diagnosis and treatment. The increasing prevalence of osteoporosis among these women, lack of awareness, necessitate that intervention programs to be included in the regular health care.

MATERNAL AND CHILD HEALTH

A Systematic Review on Interventions to Improve the Quality of Care in Pregnancy and Childbirth in Rural India.

Findings of a Systematic Review on Interventions to improve the quality of care in pregnancy and childbirth in Rural India revealed that trained community health workers have potential to improve quality of care by creating awareness on pregnancy related issues. This contributed to increase in institutional deliveries along with other interventions such as upgrading PHC to provide 24x7 intrapartum care with additional trained ANM, introduction of mobile clinic to provide comprehensive pregnancy care, integration between various related programs and implementing Janani

Shishu Suraksha Karyakram (JSSK) scheme resulting in significant reduction in maternal and child health mortality.

Improving Reproductive Health Seeking Behavior and Service Utilization by Tribal Women through Involvement of Self Help Group (SHG) Women in Maharashtra.

An intervention study involving SHGs for improving reproductive health seeking behavior and service utilization by tribal women in tribal blocks of Nashik district demonstrated that SHGs could identify about 300 women reporting with reproductive health complaints and 63 of them availed services at the public health facilities. This model could be upscale for mobilizing women to take cognizance of their problems and reach health facilities through facilitation by SHGs.

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

A study undertaken to operationalize the Maternal Near Miss (MNM) Review guidelines developed by the Government of India at selected tertiary hospitals in Maharashtra could help identify 58 MNM cases in 3 months where majority (24) had Pregnancy Induced Hypertension, Haemorrhage (10), ectopic pregnancy & septic abortion (3 each) and others (18 including sickle cell disease, cardiac dysfunction etc.)

Evaluation of Factors Affecting Innate Immunity in Women with Pre-Eclampsia (PE).

A study to evaluate factors affecting innate immunity in women with Pre-Eclampsia (PE) in a prospective study cohort of healthy pregnant women found significantly decreased serum levels of SP-A, SP-D, P4/E2 ratio at 10 -20 weeks of gestation in women who subsequently developed severe Early Onset Pre-Eclampsia (EOPE) between 24 -34 weeks of gestation. The study suggests that serum levels of SP-A, SP-D, P4/E2 ratio are novel risk factors and may be useful for early prediction of severe EOPE in Indian women.

Possible Involvement of Paternal Epigenetic Factors in Recurrent Spontaneous Abortions.

Studies were carried out to elucidate the methylation status of the DMRs of imprinted genes in the spermatozoa of male partners of women experiencing Recurrent Spontaneous Abortions (RSA). The results suggest that aberrant paternal imprinting could be a risk for RSA and analysing sperm epigenome would be important to elucidate paternal causes of RSA as well as other pregnancy disorders.

Detection of Infections Associated Preterm Births.

Intrauterine bacterial infection is a common cause of preterm births and vaginal colonization of these bacteria predisposes the mother to deliver preterm. This project aims to develop a multiplex PCR assay to detect common vaginal infections observed in women with preterm births. Based on published data from India, the team has shortlisted eight bacteria species that are commonly found in vagina of women who deliver preterm. Studies are ongoing to develop multiplex PCRs and detect the bacteria in vaginal swabs.

Developing an Immunochromatography Based Strip Test for Analyzing PlGF Concentration for Prediction of Risk for Developing Preeclampsia.

Using commercial antibodies, an in-house ELISA was standardized which could detect recombinant PlGF in picogram range. Urine samples from healthy pregnant women and women with preeclampsia would be tested using this ELISA.

Developing a Gene Based Knowledge based on Endometriosis.

Endometriosis is a disorder with complex genetic aetiology. A number of genes have been reported to be associated with this disease. A comprehensive resource with information on genes, reported mutations, gene ontology and pathways will prove useful to researchers working towards understanding the genetic aetiology of the disease. The Endometriosis knowledge base

holds information on 831 manually curated genes associated with endometriosis, their reported polymorphisms/ mutations, details of the studies conducted, gene ontology and pathways.

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

Screening of 167 neonates for early detection of congenital cytomegalovirus (CMV) in a tertiary care hospital setting using a non-invasive, multiple sample, CMV DNA PCR test found 12 neonates to be positive of which 3 were confirmed by sequencing. The utility of this protocol in guiding treatment and management of paediatric CMV infection which is-a leading cause of birth defects as well as childhood mortality and morbidity could be explored for implementation in future newborn screening programs.

To Assess Magnitude and Factors Associated with Vitamin D Deficiency in Children between 1 to 5 years.

A community based cross sectional study among 426 apparently normal children revealed high prevalence (77.2%) of Vitamin D Deficiency (VDD) with significant association with poor sun exposure. 50.7% children with VDD {25(OH)D levels <20ng/ml} had low Vitamin D Binding Protein (VDBP) levels. Normal Parathyroid Hormone (PTH) levels were observed in majority of children (81%). These findings highlight the need of redefining cutoffs of 25(OH) D among under five children in India.

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 conducted in Dahanu and Palghar in Palghar district of Maharashtra in ten villages (five in each block). The study involved baseline survey, intervention phase and post intervention survey. The study participants included pregnant women, adolescent girls and under-five children. However, post intervention survey was not conducted among

the pregnant women. Improvement in nutritional status among under five was noted in post intervention survey as compared to baseline survey. The pre and post intervention findings indicated that there was an improvement in nutritional status of the under fives. For normal children, it increased from 73% to 90%, for Moderate Acute Malnutrition (MAM) it reduced from 21.6% to 10% and for Severe Acute Malnutrition it reduced from 5.4% to none in post intervention survey as compared to pre intervention survey.

Impact of Measles Rubella (MR) Vaccination Campaign on Population Immunity in India [IMRVI study].

As part of a larger study, Measles Rubella Pre Campaign (community-based) survey was conducted among children 09 months to < 15 years from July –Sep 2018 in 30 clusters of Palghar district. 577 serum samples were tested for IgG antibodies to measles and rubella viruses using EIA. Only 68% of the children were immune to Measles and 46% against rubella. Post MR Campaign survey will be conducted from April –June 2019.

GENETIC RESEARCH CENTER

Identification of Genetic Aberrations in Ion Channel Genes in Epileptic Syndromes and Channelopathies.

Epilepsy is a common, heterogeneous and complex neurological disorder. However, several epilepsy syndromes are caused by mutations in genes encoding ion channel proteins. Among 15 patients with wide spectrum of epileptic phenotypes, 6 of them had mutations in *SCNA1* gene including two novel mutations. Novel mutations in *DCX* gene have also been identified in a familial case of Isolated Lissencephaly Sequence (ILS). In a family with Hereditary Neuralgic Amyotrophy (HNA), a pathogenic mutation in *SEPT9* gene has been identified.

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.

About one-third of the global burden of mental illnesses is found in India and China, greater than all developed countries put together. Among mental illness, Schizophrenia is a devastating mental disorder characterized by reality distortion. A total of 50 patients including 4 familial cases of adolescent onset Schizophrenia cases were recruited in the study. Whole exome analysis of one affected family and one individual case revealed common variants in Calcium Channel Gene *CACNG1* gene, identified in all the affected individuals. iPSCs were developed using PBMCs isolated from whole blood of the affected family members by transducing with the sandai virus containing Yamanaka Factors. The iPSCs colonies obtained were characterized for pluripotency markers, OCT4 and SOX2.

Identifying Cytogenetic Abnormalities in Cases of Disorders of Sex Development.

Sex development is genetically and hormonally controlled process. Mutation of SRY is the cause of complete pure gonadal dysgenesis in 10-15% of patients. Remaining individuals may bear mutation in the SRY regulatory elements/genes involved in the testes determining pathway. Analysis of 50 patients with disorder of sex development identified two novel and 3 known pathogenic mutations in *SRD5A2* gene. The commonest variant p.L89V has been identified in 35 patients in *SRD5A2* gene. In another patient with complete androgen insensitive syndrome, one novel splice site mutation has been identified in *AR* gene.

STEM CELL BIOLOGY

Pluripotent Stem Cells in Adult Tissues.

Various adult tissues including bone marrow, testis, ovary, uterus, pancreas exhibited two populations of stem cells including small sized, pluripotent very small embryonic-like stem cells (VSELs) that undergo asymmetrical cell divisions to give rise to slightly bigger 'progenitors' (HSCs, SSCs) which in turn undergo rapid, symmetrical cell divisions

and clonal expansion. VSELs are relatively quiescent, and have the ability to differentiate into 3 germ layers *in vitro* suggesting a regenerative potential whereas lineage restricted 'progenitors' only differentiate into tissue specific cell types. A simple and robust protocol has been developed to enrich VSELs from various adult tissues without using techniques like FACS or MACs. Stem/progenitor cells in bone marrow decrease in number and differentiation ability with age. VSELs in both young and aged mice increase in number in response to chemotherapy (5-fluorouracil, 150 mg/Kg) to restore homeostasis and later revert to basal numbers by tenth day in young but not in aged mice.

NATIONAL CENTRE FOR PRECLINICAL REPRODUCTIVE AND GENETIC TOXICOLOGY

MicroRNA Regulation in Prostate and Ovary upon Exposure to Endocrine Disruptors.

Endocrine disruptors like Bisphenol- A mimic endocrine hormones and cause various developmental and reproductive disorders in animals and humans. MiRNAs are short, non-coding RNAs that function in regulating the expression of genes via mechanisms like mRNA degradation, translation inhibition, promoter binding, protein binding or by direct interaction with non-coding RNA. Alteration of miRNA expression leads to changes in their target gene expression which results in the development of cancer. Differentially regulated expression of miRNA Let7 family and their target gene HMGA1, HMGB1 and AR were analysed. Expression of miRNA Let7 target gene HMGA1 was decreased whereas HMGB1 and AR showed a significant increase in the prostate tissue of perinatally Bisphenol- A (BPA) exposed F1 generation rats. Findings suggest that BPA can induce cancer in the prostate tissue of perinatally exposed F1 generation male rats.

Deciphering the Molecular Mechanism of Triclosan on Hypothalamus Pituitary Gonadal Axis.

Male progeny sired by pregnant dams administered with different doses of Triclosan, a broad spectrum antimicrobial agent, showed decreased testosterone and sperm count, with no effect on sperm motility. Significant perturbations in the testicular histology and expression of steroid hormone receptors (ER α , ER β and AR) were also observed. The F1 female rats showed decreased litter size, reduced mean fetal weight and crown-rump length of F2 fetuses with an increased pre- and post-implantation loss.

Deciphering the Effects and Mechanism of Action of Butyl Paraben on Fertility.

Perinatal Exposure to n-butylparaben, resulted in delayed age of vaginal opening, perturbed estrus cycle and folliculogenesis with impaired levels of steroid hormones in the F1 female rats. The F1 male rats showed delayed age of testis descent, preputial separation with decreased sperm count, motility and daily sperm production in the exposed groups. The exposed F1 male and female rats were sub-fertile with increased pre- and post-implantation loss at PND 75.

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

Cypermethrin (CYP) is a potent endocrine disruptor and reproductive toxicant. Previously, centre reported perinatal exposure (GD 6 to PND 22) of pregnant rats to CYP (0, 10, 25 mg/kg BW/day) impairs testicular steroidogenesis, fertility and lead to increased PIL/POL in F1 progeny. During the reporting year, F1 progeny sperm global and Igf2-H19 DMR methylation status was studied. A significant global hypermethylation and IGF2-H19 DMR hypomethylation was observed. These observations indicate that these epigenetic modifications possibly contributed to increase PIL/POL in F1 male sired unexposed female rats.

REPRODUCTIVE CANCERS

PSP94 as an Adjunct Marker for Serum PSA for differentiating between Benign Prostatic Hyperplasia (BPH) and Prostate Cancer (PCa).

This study is being carried out to ascertain whether serum PSP94/PSA ratio could help in reducing the number of biopsies in patients having lower urinary tract symptoms along with prostate pathophysiology and PSA values between 4- 20 ng/ml. Total 721 study participants have been enrolled so far from 3 municipal hospitals in Mumbai. Out of these, 484 (67%) gave their blood samples for serum PSA. Amongst these, 150 (31%) participants were found to have PSA values between 4- 20 ng/ml and the study is ongoing.

Deciphering the Role of PSP94 and CRISP3 in Ion-Channel Modulation.

Membrane proteins from a CRISP3 expressing prostate cancer cell line were isolated and subjected to immunoprecipitation using anti-CRISP3 antibody. CRISP-3 interacting proteins are being identified by LC-MS.

Development of a Bilex ELISA for Detection of PSP94 and PSA in Human Sera.

This study is being carried out to develop a sensitive and specific bilex ELISA for simultaneous measurement of PSP94 and PSA in human serum. Both PSA and PSP94 proteins have been purified from human seminal plasma in large amounts. Polyclonal antibodies to both proteins have been developed in two animal species and have been characterized. Standardization of the ELISA is in progress.

Identification and characterization of membrane-bound estrogen binding proteins in prostate cancer cell lines.

Mechanisms by which estrogen promote prostate tumorigenesis are not completely understood. The aim of study has been to investigate whether estradiol binding proteins exist on the plasma membrane and whether they are functional. Towards this, we previously demonstrated the presence of conventional estrogen receptors on the plasma membrane of non-tumorigenic and tumorigenic prostate cancer cells. The centre also demonstrated that this plasma membrane-localized estrogen-

binding proteins, transcribed by the same genes encoding conventional nuclear estrogen receptors, enter into the exocytic pathway. However, unlike conventional estrogen receptors, these proteins do not mediate proliferation in prostate cancer cells. Investigations carried out during the reporting year demonstrated that unlike cell-impermeable estradiol, cell-permeable estradiol does not lead to increased migration and invasion in prostate cancer (DU145) cells. During the reporting year, centre also made attempts to investigate whether the plasma membrane of mouse prostate epithelial and stromal cells bind to cell-impermeable estradiol. Flow cytometric analysis revealed binding of cell-impermeable estradiol to mouse primary prostate cells. Future studies will be undertaken to determine whether the functions of cell surface estrogen receptors, as revealed using in vitro assays, are operative in- vivo in a mouse model.

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

The aim of the study was to know the awareness about breast cancer and breast self-examination. A community level survey was conducted among 480 women of age 18 to 55 years residing at low socio economic community. Only half (49%) of women had ever heard of breast cancer. Majority of these women had heard about breast cancer through television (45%) or from a doctor (21%). A lump in the breast (64%), lump in armpit (48%) and changes in breast size (48%) were reported as sign of breast cancer by women.

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

The centre screened Cell-free Supernatants (CS) of 324 vaginal Lactobacilli isolates for their anti-proliferative potential against cervical cancer cell lines (Caski, C33) by MTT assay. The centre's study showed that 32 vaginal lactobacilli isolates exerted cytotoxic effects on cervical tumour cells expressing

HPV 16 and 18 together, but only 2 isolates showed effect on cervical cancer cell lines negative for HPV. Further, 54 isolates were effective against vaginal cells and 19 isolates against endocervical cells. This indicates cytotoxic effect of Lactic Acid Bacteria (LAB) isolates is mediated through HPV sequences. The shortlisted isolates having effect on HPV 16 and 18 would be further characterised using Gram staining, colony morphology, H₂O₂ production, Lactic acid production and partial identification carried out using partial Sanger sequencing. Also, their combinatorial effect would be determined against cervical cancer cell lines. The isolates showing highest cytotoxicity in combinatorial assay would be further shortlisted for purification of bacteriocin and exopolysaccharides.

Evaluation of Biomarkers for Early Detection of Cervical Cancer in Indian Women.

HPV E6/E7 oncogene expression was assessed by real time PCR test for identifying cervical cancer risk in Pap negative cases and women with minor cytological abnormalities like ASCUS and LSIL (n=44). The test was also beneficial as a triage test after HPV DNA testing in differentiating the false positive cases, thus reducing the psychological burden associated with over-referral of these cases for colposcopy.

Expression of Natural Killer and Natural Killer T Cell Receptors and their Association with Ovarian Cancer.

Preliminary data from forty-two Serous epithelial ovarian cancer cases revealed dysregulation of activating receptors of Natural Killer (NK) cells. Expression of NKG2D and CD161 is affected significantly in ovarian cancer cases. Similarly, adhesion marker DNAM-1 is significantly downregulated in these patients. These cells probably cannot form synapse with the target leading to loss of lytic activity of NK cells.

Evaluating the Potential of Trop2 as Immunotherapeutic Target for Ovarian Cancer.

Site-directed mutagenesis approach identified the key amino acids regulating the proteolytic cleavage

and possible post-translational modification/s of human Trop2. A novel N-terminally cleaved form of Trop2 named Δ N-Trop2 (delta N trop2) was identified in certain cancer cell lines and the specific cleavage residue was identified. Future studies are aimed at investigating the effect of anti-Trop2 antibodies on cancer cell migration and invasion.

HEALTH TECHNOLOGY ASSESSMENT

HTA on Long Acting Reversible Contraceptives

to answer the policy question of whether another LARC (Nexplanon, a sub-dermal contraceptive implant) could be added to the contraceptive basket of the national family planning program. The study on HTA on Long Acting Reversible Contraceptives addressed a policy question of whether another LARC (Nexplanon, a sub-dermal contraceptive implant) could be added to the contraceptive basket of the national family planning program. The results of the decision analytical model showed that an additional cost of 17,716 INR will be incurred by the Indian government to gain one Quality Adjusted Life Year (QALY) if Nexplanon is added to the current basket of contraceptive choices in the public health system. This shows that the intervention is very cost-effective in reference to the threshold of GDP per capita.

EXTRAMURAL RESEARCH

BASIC REPRODUCTIVE BIOLOGY AND FERTILITY REGULATION

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

After the approval of the Data Safety Management Board (DSMB) cum Experts Committee, the final report of the clinical study was submitted to the Ministry of Health and Family Welfare, Govt. of India and the Drugs Controller General of India (DCGI) for their consideration. The DCGI has suggested to taking the following steps:

- (i) To obtain data on sexual and psychosocial behavior of the RISUG injected couple
- (ii) Develop a clinical reversibility protocol for undertaking the study

(iii) To find out the status of the spermatogenesis, it was recommended to have testicular biopsy/ FNAC of few RISUG injected subjects.

The questionnaire along with instruction manual for obtaining data on sexual and psycho-social behavior of RISUG injected couple have been prepared and is under pilot testing at one center. The protocol for under taking clinical reversibility study with RISUG is being prepared. The testicular biopsy/ FNAC study is under process.

Phase I-II Clinical Trial on Safety, Immunogenicity and Probing Efficacy of the Revived Recombinant Vaccine against human Chorionic Gonadotropin (hCG).

The first recombinant hCGβ-LTB contraceptive vaccine in the world for preventing pregnancy in women has been developed in India and has been proved safe and effective under pre-clinical toxicity studies. To determine the safety and immunogenicity of hCGβ-LTB Vaccine in sexually active healthy women and prove its ability to prevent pregnancy without impairment of ovulation and derangement of menstrual regularity and bleeding profiles, the clinical trial has been initiated.

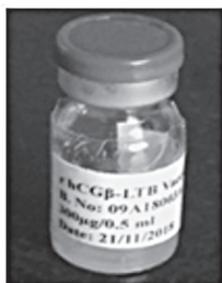


Fig. 1: A vial of hCGβ-LTB protein vaccine formulated for the clinical trial.

National Registry of ART Clinics and Banks in India.

As per the provision of ART (Regulation) Bill, a National Registry has to be created to ensure optimal functioning of all the ART clinics and banks in the Country as a Central Database and helping them to take care of Infertility problem through practice of ART. Under National Registry around 1814 ART Clinics and Banks have been identified. Out of 421 approved ART clinics, only 07 clinics are IUI clinic

and out of 489 under process ART clinics, 31 are IUI clinics. The status of these ART Clinics and Banks are given below as Table 1.

Table 1: The status of these ART Clinics and Banks

S. No.		ART Clinics	ART Banks	Total
1	Total no. identified	1607	207	1814*
2	Total no. enrolled	421	-	421
3	Total no. of confirmed Clinics and Banks under process	817	207	1024
4	Total no. of Clinics and Banks yet to respond	368		368

* One ART clinic enrollment cancelled

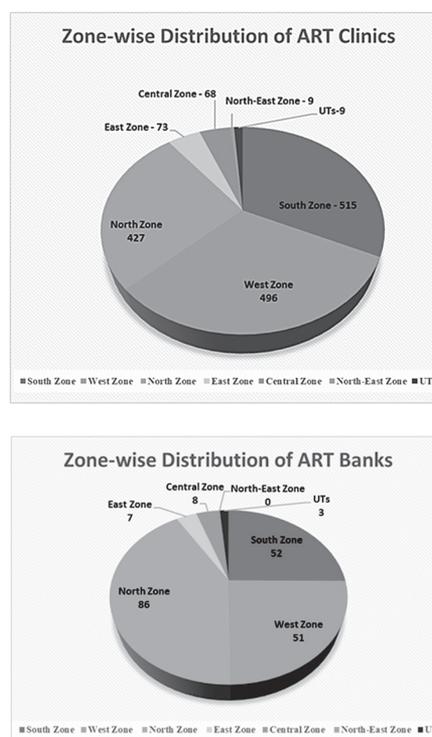


Fig. 2 & 3: Zone-wise distribution of ART Clinics and Banks in India.

To obtain online monthly data from all the enrolled ART clinics regarding all their activities related with treatment and management of infertility, their outcome and side effects if any, a detailed proforma has been designed which is under process of finalization. On the direction of Director General of Foreign Trades (DGFT), ICMR-National Registry has developed guidelines for (i) Export of Human Embryos and Gametes and (ii) Import of Frozen Human Embryos and/or Gametes which were sent to DGFT. DGFT has approved the guidelines for

Export of Human Embryos and Gametes and based on these guidelines, the ICMR-National registry has issued 11 NOC's for export of human embryos / gametes for the treatment of infertile couple themselves.

Identification of Disease specific proteins associated with endometriosis in Indian Women.

To describe the use of serum and peritoneal fluids from the women as a biological sample for the discovery of biomarkers associated with endometriosis as a first step towards the development of a noninvasive diagnostic test for this disease, this study was undertaken. Serum and peritoneal fluid were collected from 100 women aged 18 to 35 years undergoing laparoscopy, which was indicated for the evaluation of infertility, pelvic pain, or for tubal ligation. Endometriosis was diagnosed laparoscopically. Matrix Metalloproteinases (MMPs), Cytokines and Human Neutrophil Peptides 1, 2 and 3 (HNP1-3) were measured. The results of the study indicated that serum biomarkers for endometriosis could lead to earlier diagnosis and treatment. This could avoid the repetitive laparoscopic procedure which is invasive and many patients will not opt for that. The serum biomarkers can also be used to know the recurrence of endometriosis and pre-ART assessment. The above-mentioned serum markers can be used as panel of biomarkers for the diagnosis and prognosis of endometriosis which can avoid the 2nd and 3rd laparoscopic procedure in stage III and IV. Serum biomarkers will not only help shorten the time to diagnosis, but also pave the way to new therapies.

In vitro spermatogenesis as a method to bypass pre and post meiotic barriers to spermatogenic process and restoration of fertility.

Spermatogenic failure is responsible for a large proportion (~23%) of infertility cases in human. It has been recently demonstrated that male Germ-line Stem (GS) cells, the in vitro counterpart of Spermatogonial Stem Cells (SCC), can be successfully isolated from both neonatal and adult testes. These GS cells retain their spermatogenic

potential and, upon testicular transplantation, can repopulate the empty seminiferous tubules of infertile males to restore the fertility. Therefore, the present study was undertaken to develop an in vitro spermatogenesis system as a method to bypass the pre- and post-meiotic barriers to spermatogenesis and restoration of fertility in infertile males. The experiments were conducted on mice model in the first phase and the optimized results were then be extended to human in the second phase for their possible clinical application in future.

Isolation of spermatogenic and germ line stem cells, characterization of gem line stem cells and identification of Air-liquid interface culture conditions was done. Scaffolds for tissue engineered testicular construct were designed and fabricated to provide the micro-architecture of the testis for physical support as well as signaling molecules to replace the need of donor testis in organ culture system. Seeding of scaffold was done to produce tissue engineered testicular construct.

The in vitro spermatogenesis system will have marked pragmatic value in offering ex vivo systems for the artificial maturation of immature germ cells in male infertile cases. The system will also facilitate i) mechanistic studies on spermatogenesis, ii) preservation of male fertility in patients such as childhood cancer patients, patients undergoing gonadectomy and patients with Klinefelter's syndrome and cryptorchid testes and iii) identification of pharmacological agents of male contraception via the inhibition of signaling pathway involved in spermatogenesis. The system will also provide opportunities for the transgenic manipulation of male germ cells in animals.

Male infertility: demographics, etiology and outcomes of standard clinical practice.

There is no large-scale data on the clinical profile, etiology and treatment outcomes of male infertility in Indian men. In order to develop policies and guidelines for evaluation and management of male infertility the present study was undertaken to evaluate the demographic and clinical profile of infertile men, classify the etiology of male infertility

and assess outcomes of current management strategies.

The study was designed as a prospective observational cohort of infertile men, presenting to the Urology clinic of All India Institute of Medical Sciences, New Delhi 447 infertile men were enrolled in the study, of which 422 completed the evaluation. Almost all have undergone prior intervention (445) and the use of tobacco (423) and alcohol (426) is common. An etiological diagnosis can be achieved in nearly 95% men, azoospermia and oligoasthenoteratospermia contribute around 40% cases each, obstructive azoospermia in 20% and sexual dysfunction is an uncommon cause of infertility. The majority of patients (72.5%) are advised ART but few (18%) actually received the treatment with high success rate (38%). Surgery is recommended in fewer patients (7.3%) but a higher percentage (58%) received the recommended treatment with acceptable success rate (33.3%). More than one in three couples who received the intended treatment is able to achieve pregnancy. Overall, only 24.4% patients received the advised treatment with a 36.8% pregnancy rate. The incidence of genetic abnormalities was 4.2% (18/422). Delay in presentation could be due to lack of awareness, limited availability of facilities, social taboos and scarcity of government healthcare centres.

This data is essential to formulate policies and guidelines on the optimum evaluation and treatment of such men. It is also essential to identify gaps in current knowledge, determine areas of future research and define the indications for ART in male infertility.

Analysis of sperm DNA damage in fathers of children with non-familial childhood cancer.

Childhood cancer is a major global health issue. Each year, one lakh children die from cancer before 15 years of age and more than 90% of them are in resource limited developing countries. DNA integrity of germ cells is necessary for accurate transmission of genetic information and birth of

healthy offspring. It is known that men with high levels of sperm DNA damage experience pre and post implantation losses, have greater incidences of children with congenital malformation and childhood cancers. This is due to high levels of sperm DNA damage. Sperm exist in a state of oxygen paradox and are most susceptible to oxidative stress induced mitochondrial and nuclear DNA damage. Thus, it was planned to analyze all cases with non-familial Retinoblastoma and leukemia (parents'somatic cell negative for mutations in BCR-ABL fusion oncogene and Rb gene) for seminal oxidative stress and DNA damage. This may actually prevent cancer in other offspring. Thus, this project is planned to study the father of children with non-familial cancer for the role of oxidative stress parameters as ROS, sperm DNA damage and telomere length and telomerase concentration. In this retrospective study, it is planned to analyze couples whose offspring are undergoing treatment for childhood cancer. In these cases, the cytogenetic and molecular analysis was done from peripheral blood of both the partners to exclude the familial cases. The complete gene and promoter regions of Rb1 gene (tumour suppressor gene implicated in retinoblastoma) and BCR/ABL oncogene gene (implicated in leukemia) were screened in blood DNA in both the male and the female's partners. All cases and controls showed 46, XY chromosomal complement in cytogenetic analysis by G banding. There were significantly high ROS, DFI and 8-OHdG in smokers and alcoholics compared to non-smokers and non-alcoholics. ROS and 8-OHdG were also significantly higher in alcoholic + tobacco users compared to non usergroups. The sperm telomere length was significantly shorter and telomere activity was significantly higher in cases compared to controls. Out of 105 cases, 85% had lower and 15% had higher telomere length than the cut off value of 0.75 obtained by ROC analysis. Among 110 controls, 80% had higher and 20% had lower telomere length than the cut off. The sperm telomere length was significantly shorter in smokers, alcoholics and pesticide-exposed cases compared to the non-smokers, non-alcoholics and cases not

exposed to pesticides respectively. The relative telomere activity per cell in cases was significantly higher ($p < 0.0001$) compared to controls. Out of 50 cases, 62% had higher and 32% had lower telomere activity per cell than the cut off of 29 established by ROC analysis. There was significant reduction in oxidative stress markers after Yoga based lifestyle intervention.

The results of this study would help in elucidating the relationship of cancer in the offspring with the DNA damage in the sperm of the father and would also offer significant hope in the treatment of childhood cancer.

MATERNAL HEALTH

ICMR– Centre for Advanced Research (CAR) on Investigating Mechanisms leading to Preeclampsia.

Preeclampsia continues to adversely affect 5-8% pregnancies. In the CAR, the human studies are ongoing to examine the association of maternal Long Chain Polyunsaturated Fatty Acids (LCPUFA) and micronutrients with clinical outcome in preeclampsia and to understand the underlying key biochemical and molecular mechanisms. Preliminary analysis suggests that women who develop preeclampsia have a higher age, BMI and BP in early pregnancy as compared to normotensive women. Findings indicate differential methylation of PIGF and HIF3A genes between the normotensive and preeclampsia groups indicating disturbed methylation patterns of genes which may influence the process of placental angiogenesis in women with preeclampsia. Animal study indicates the beneficial effects of omega-3 fatty acid and vitamin E supplementation in case of Late Onset Preeclampsia, reduced the percentage of fetal resorptions and normalized the angiogenic factors. These findings may have implications for reducing IUGR and spontaneous abortions in women with preeclampsia.

Long term morbidity in Maternal Near Miss.

For every woman who dies from pregnancy or childbirth-related causes, it is estimated that twenty

more suffer from severe pregnancy-related illness or complications. Data till date indicates that the incidence of MNM was 6.9 per 1000 live birth and the most common life-threatening complication leading to it was hypertensive disorders in pregnancy. At 12 months, nearly 50% of MNM have complications such as persistent hypertension, stroke, chronic kidney disease and mental health problems and add to the burden of NCD in the community. MNM Clinics have been set up in the participating sites where comprehensive check-up of MNM women and their new-borns can be done at one place and will pave way for improving clinic-based care for MNM. In another study the Government of India guidelines on MNM are being operationalized in selected tertiary care hospitals to train staff from department of Obstetrics & Gynaecology, Medicine, Surgery and Anaesthesia and form MNM review committees.

Systematic Approach for Assessment of Maternal Deaths in Rajasthan.

A feasibility study is ongoing in Jodhpur & Udaipur districts representing the better and poor performing districts to assess the magnitude and trend of maternal deaths; its underlying factors; identify the barriers and challenges in reporting maternal deaths and to shape the pathways for improved reporting and prevention of preventable maternal deaths.

Burden of still births & early neonatal deaths & their risk factors in selected districts of Haryana.

The study is ongoing in 10 district hospitals of Haryana to study the contributory modifiable factors of stillbirths; identify the delays using verbal autopsy; classify stillbirths and early neonatal deaths according to CODAC and ICD PM classification and test the feasibility of study tool to identify the burden of stillbirth & early neonatal deaths. Capacity building of providers in the study districts to use the results to stratify and plan preventive strategies is also being done.

Feasibility of using two simple tools to improve the documentation process in labour room in the peripheral health facilities of Odisha.

Prasavsheets[©] and a simplified still birth case record developed by ICMR were introduced in five facilities of Kalahandi district to assess the feasibility and effectiveness of the tools in improving labour room documentation. The results were compared with control facilities in Kandhamal district. The still birth case sheet was found to be quite useful and effective to identify the risk factors associated with still birth; adherence to partograph plotting and its completeness improved by 53.7% in the intervention sites; effectiveness with respect to early detection of any complication and prompt management was found to be better 8% in intervention facilities; the discharge sheet was very simple and providers felt that it took less time for completion. The Prasavsheets[©] was found useful in the designing of a uniform case sheet for public health facilities and adapted by Ministry.

Impact of Behavioral Intervention Package on the health status of married abused pregnant women attending antenatal clinic of hospital in Delhi.

A randomized controlled trial is being carried out to assess the incidence of Domestic Violence (DV) and to evaluate the effectiveness of behavioral intervention package in coping with DV and its adverse outcomes.

MATERNITY CARE INITIATIVE.

A 20 site multicentric study is being carried out in collaboration with Centre for Catalyzing Change/ White Ribbon Alliance India. This is a mixed method study with an observational component of labor and delivery processes and interview of healthcare providers (n=60) to understand their perspective of respectful maternity care (RMC). The gaps in RMC were identified in the seven domains; and the variations recorded during day time and night time shifts; and with respect to the cadre of health providers who would require sensitization and training for RMC. The study is ongoing.

PREVENTION OF UNINTENDED PREGNANCIES/HIV/STIS

Evaluation of progesterone vaginal ring as a new contraceptive option for women in India.

An open label, non-randomized, comparative and non-inferiority trial was carried out jointly by ICMR and Population Council through 20 tertiary hospitals to evaluate the Progesterone Vaginal Ring (PVR) as a new contraceptive, designed for self-use by breastfeeding women to extend the period of lactational amenorrhea and promote birth spacing.

Women were enrolled at 4-6 weeks postpartum and given the option of choosing PVR or IUD for contraception. The results indicate that PVR is non-inferior to the IUD in its efficacy to prevent pregnancy indicated by a pregnancy rate of 0.7 vs. 0.4 per 100 users respectively at 12 months of use. The continuation rates in the PVR group compared to the IUD group were similar at one month use and gradually decreased over time. At 12 months, the continuation rate was 56.9 for PVR and 78.5 per 100 users for IUD. Acceptability among users of PVR and IUD indicates more than three-fourth of women in the PVR group and 69% in the IUD group who completed 12 months plan to use the device in the future.

Feasibility of Oral TDF-containing PrEP, administered, once daily orally to Men having Sex with Men (MSM) and Transgender Women(TGW) in India.

A prospective two-site cohort demonstration project using observational study design has been initiated to study the feasibility of daily usage of Tenofovir (TDF) containing oral pre exposure prophylaxis (PrEP) in Men having Sex with Men (MSM) and Transgender Women(TGW) for prevention of HIV in India. The study would assess whether oral PrEP can be added to a package of HIV prevention interventions in community settings and through clinical facilities for MSM and TGW in India, and will assess retention, acceptability, adherence, potential unintended consequences, such as changes in use of condoms, risk perception and behavior and other HIV preventive interventions.

Effect of timing of insertion of puerperal intrauterine contraceptive device CuT380A on expulsion rates.

It is an observational comparative prospective study. Results indicated that PPIUCD is safe, there was no incidence of perforation or infection or irregular bleeding in women who accepted PPIUCD, up to 3 months follow up. The overall expulsion rate was 4.4% which was slightly higher (non-significant) in the immediate (within 10 minutes of delivery) group when compared to the early (between 10 minutes to 48 hours of delivery) insertion group. Ultrasound before discharge helped in detecting wrongly placed IUCDs. Sensitizing the antenatal women with educational videos and reinforcement in labor is an important step in acceptance of PPIUCD. The training for residents can be easily achieved.

NCDS IN WOMEN

Prevalence, regional phenotypic variation, comorbidities, risk factors of Poly Cystic Ovary Syndrome (PCOS).

It is being evaluated through a 10 site multi-centre study across India. A subset of drug naïve participants will be randomized to receive metformin or oral contraceptive pills for the treatment of PCOS for six months and the therapeutic response to these drugs will be studied.

Screening and early detection of cervical, breast and oral cancer.

A demonstration project in seven TATA Tea gardens is being carried out in Dibrugarh, Assam to train the health care providers in screening of common cancers and to operationalize government guidelines for cancer screening. A Software has been developed to collect household data and identify members with high NCD risk score and prioritize them for screening. Doctors, nurses and community health workers were trained to carry out screening and data collection as per protocol. The results of the study will inform the about the

opportunities and challenges in operationalization of the government of India guidelines in the field situation.

CHILD HEALTH

Cluster Randomized Trial of a mHealth Intervention “ImTeCHO” to Improve Delivery of Proven Maternal, Neonatal and Child Care Interventions through Community Based Accredited Social Health Activists (ASHAs) by Enhancing Their Motivation and Strengthening Supervision in Tribal Areas of Gujarat, India.

A two-arm, stratified, cluster randomized trial with an innovative intervention based on mobile-phone technology (mHealth) was conducted to improve performances of ASHAs through better supervision and support in predominantly tribal and rural communication of Gujarat, India. The units of randomization were Primary Health Centres (PHC). The intervention was a mobile-phone application used in the public health system and evaluated in three ways: (1) Mobile-phone as a job –aid to ASHAs (2) Mobile-phone as a job – aid to Auxiliary Nurse Midwives (ANMs) to facilitate referrals & home –based-care (3) Web-interface as job –aid for medical-officers and PHC staff. Participants of the study were pregnant women, mothers, infants, ASHAs and PHC staff. Outcomes were measured by conducting household surveys at baseline, and post-interventions compared with usual practice in the control area. The primary outcome of coverage of at least two home visit within first week of birth and a modified composite coverage index was 10.2% (adjusted effect size 10.2, [95% CI 6.4, 14.0] and 4.9% (adjusted effect size 4.9, [95% CI: 0.2, 9.5]) higher respectively in intervention arm compared to the control arm. There were significant improvements in coverage and quality of home visits by ASHAs during antenatal period, home based newborn care, early initiation of breast feeding and exclusive breast feeding. Use of ImTeCHO mobile and web-based application as job aid by government ASHAs and PHC staff can improve coverage and quality of MNCH services

in hard to reach areas. The intervention has been adopted by Govt. of Gujarat for up scaling in all districts of the state.

Cohort study of Children (0-14 years) exposed to maternal HIV (Phase II) of the Estimating Disease Burden of Pediatric HIV in a “A” category district in India.

The objectives of the phase 2 cohort study was to estimate the incidence of HIV; to describe and compare the patterns and determinants of various morbidities; to assess nutritional status and the mortality among this children. The study universe included 291 health care facilities (149 Govt and 146 Pvt), 985 households. The preliminary results show reduction in the vertical transmission from 7.8 to 6.3 per 100 positive pregnancies. Almost 50 % of all children whether HIV positive or negative, tend to be undernourished (as per anthropometry). ‘z’ scores for weight for height and weight for age were significantly lower for HIV-infected children compared to HIV un-infected. HIV infected children tend to have 2.5 times higher morbidities than HIV un-infected: the significantly higher morbidities included ARI, skin diseases/conditions, mouth ulcers/oral candidiasis and TB.

Descriptive Epidemiology of Unintentional Childhood Injuries in India.

This study is ongoing at 11 sites of 8 states in India to estimate the prevalence and the determinants of unintentional injuries among children 6 month to 18 years.

A pilot study to determine causes of deaths in underfive children in tertiary hospital setting using Minimally Invasive Tissue Sampling Technique (MITS).

A pilot project has been initiated to build capacity and test feasibility and acceptability of MITS in a tertiary hospital setting and to standardise the methodology including grief counseling. Project is ongoing at Safdarjung Hospital New Delhi, ICMR National Institute of Pathology, New Delhi and formative research by INCLEN Trust New Delhi.

Analysis of data on formative research is ongoing. Following training, MITS has been initiated. Funding support has been received from Bill and Melinda gates Foundation.

Multicentric Project entitled “The study of hemoglobinopathies and G6PD deficiency among the tribals of Dharampuri, Vellore and Nilgiri hills, Tamilnadu.

Haemoglobinopathies are the commonest genetic defect worldwide and high incidence of various abnormal haemoglobins has been noted in India. This study proposes to screen population from the tribes of Dharmapuri, Nilgiri and Vellore District, of Tamil Nadu for Nutritional Anemia, Hemoglobinopathies and G6PD deficiency; determine the distribution of mutations causing hemoglobinopathies and G6PD deficiency and the effect of genetic ameliorating modifiers to assess the severity of the disease and develop and validate a Genetic Disease Risk Scores (GDRS) tool for identifying high risk cases for SCD. It is proposed to align project activities in line with recent guidelines from Ministry of Health & Family Welfare for screening of haemoglobinopathy. Project has just been initiated.

Establishment of Health and Demographic Surveillance System in Dibrugarh district, Assam (Dibrugarh –HDSS).

Upper Assam which includes Dibrugarh has the highest maternal mortality in the whole of India as well as high infant mortality. Several reports have shown that major portion of these deaths occur among the Tea Garden community due to low economic status, low awareness about health services and poor access and coverage by the routine health system. Health and Demographic Surveillance System named as the Dibrugarh HDSS is set up under ICMR Regional Medical Research Center Dibrugarh to collect population level epidemiological and programme relevant data. Preparatory Activities are ongoing. Census will begin soon.

Implementation Research Platform.

Realizing the need and relevance, a national platform for technical support for Implementation Research (IR) has been created to address maternal and child health issues including nutrition.

Seed Grant scheme.

In order to build capacity among faculties of medical colleges, universities and research institutes for carrying out research in health and biomedical sciences to address local health issues in the North East states, Seed Grant scheme is ongoing since 2011. During the year of reporting 17 new projects were approved and 18 projects were ongoing in various areas of health sciences. Thirty projects were completed and 8 papers have been published.

Cluster Randomized Trial of a mHealth Intervention “ImTeCHO” to Improve Delivery of Proven Maternal, Neonatal and Child Care Interventions through Community Based Accredited Social Health Activists (ASHAs) by Enhancing Their Motivation and Strengthening Supervision in Tribal Areas of Gujarat, India.

Evaluations have noted that coverage of selected MNCH services to be delivered by ASHAs is low. Proposed study aims to implement, and evaluate an innovative intervention based on mobile-phone technology (mHealth) to improve performances of ASHAs through better supervision and support in predominantly tribal and rural communication of Gujarat, India.

This was a two-arm, stratified, cluster randomized trial of 36 months in which units of randomization will be Primary Health Centres (PHC). The intervention is a newly-built mobile –phone application used in the public health system and evaluated in three ways: (1) Mobile-phone as a job –aid to ASHAs to increase coverage of MNCH services (2) Mobile-phone as a job – aid to ASHAs and to Auxiliary Nurse Midwives (ANMs) to increase coverage of care among complicated cases by facilitating referrals, if indicated and home –based-care (3) Web-interface as job –aid

for medical-officers and PHC staff to improve supervision and support to the ASHA program. Participants of the study were pregnant women, mothers, infants, ASHAs and PHC staff.

Primary outcome measures were a composite index made of critical, proven MNCH services and proportion of neonates who were visited by ASHAs at home within the first week of birth. Secondary outcomes included coverage of selected MNCH services and care sought by complicated cases. Outcomes were measured by conducting household surveys at baseline, and post-interventions which were compared with usual practice in control area where the current level of services provided by the government will continue. Primary analysis was done by “intention to treat”.

Eleven PHCs were randomly allocated to intervention (280 ASHAs, Population: 234134) and control (281 ASHAs, Population: 242809) arm each. 6493 mothers were surveyed after 12 months of implementing the intervention. The coverage of at least two home visits within first week of birth and modified composite coverage index was 10.2% (adjusted effect size 10.2, [95% CI 6.4, 14.0] and 4.9% (adjusted effect size 4.9, [95% CI: 0.2, 9.5]) higher respectively in intervention arm compared to the control arm. There were significant improvements in coverage and quality of home visits by ASHAs during antenatal period, home based new-born care, early initiation of breast feeding and exclusive breast feeding.

Use of ImTeCHO mobile and web-based application as job aid by government ASHAs and PHC staff can improve coverage and quality of MNCH services in hard to reach areas.

Cohort study of Children (0-14 years) exposed to maternal HIV (Phase II) of the Estimating Disease Burden of Pediatric HIV in “A” category district in India.

The objectives of Phase 2 cohort study were to estimate the incidence of HIV; to describe and compare the patterns and determinants of various morbidities; to assess nutritional status and the mortality among the children.

The study included 291 health care facilities (149 Govt and 146 Pvt), 985 households (231 with (a) positive children; 726 with (all) negative children and 28 with (all) untested children and 2022 children (230 HIV infected, 1694 HIV uninfected and 98 HIV untested children), across the district, as on closure of the phase two studies.

The Phase 2 study's preliminary results show reduction in the vertical transmission from 7.8 to 6.3 per 100 positive pregnancies. However, no factors could be indentified that were significant determinants of the risk of MTCT, as the sample size was smaller. Almost 50 % of all children born, whether HIV positive or negative, tend to be undernourished (as per anthropometry). Among the anthropometric measurements, z scores for weight for height and weight for height and weight for age were significantly lower for HIV-infected children compared to HIV un-infected. HIV infected children tend to have 2.5 times higher morbidities than HIV un-infected: the significantly higher morbidities included ARI, skin diseases /condition s, mouth ulcers/oral candidiasis and TB. Mortality among HIV- infected children were significantly higher than HIV uninfected in all ages groups: rates were 14.7 and 2.4 among 2-5 years of age, 17.8 and 1. Among 6-10 years children and 45.2 and 0 among 5-14 years of age groups, for HIV –infected and uninfected children respectively (per 1000 person months). Under –two mortality rate works out to be 86.6 per 1000 live births. The predominant causes of death were acute respiratory infection and diarrhoea among children less than one year of age and TB for children of older ages. Prematurity, low birth weight and malnutrition were most common underlying causes of death.

Descriptive Epidemiology of Unintentional Childhood Injuries in India.

Childhood injury is a major public health problem. According to WHO-Global burden of disease study, injury is one of the leading causes of death among children. Child survival interventions should include injury prevention. Attention and focused intervention for preventing childhood injury in

India is far from satisfactory. Effective public health approach for injury prevention depends upon the knowledge regarding the problem is and its risk factors. The task force study aims determining the prevalence and factors associated with unintentional childhood injuries across 11 sites of 8 state of India among children aged 6 month to 18 years.

This is a cross sectional survey with 2341 (both rural and urban households) sample size. During the preparatory phase, the questionnaire, operational manual and the training manual were developed. Sample size was calculated for each participating site for rural and urban areas. Villages/Wards were selected according to 2 stage cluster sampling with probability proportional to size (rural) and randomly (urban). Selected villages and wards are being mapped and houses are being numbered. Random selection of a household is done followed by consecutive 15 more houses to form 1 cluster and data is collected. 3 visits to locked or refused houses were being done before considering them as drop outs. The field investigators introduced themselves and conveyed the purpose of the survey, handed over information sheet on the project and obtained a written consent from the participant. Detailed general information of the members of the household and the injury details of children of age 6 months to 17 years, 11 months was being collected.

EMF HEALTH

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

The review of existing literature has not yet established conclusive evidence on the safety or risk of Radio Frequency Radiation (RFR) emitted from cell phone and cell phone towers but growing body of scientific evidences report that RFR emitted from cell phone and cell phone tower has bio effects which may lead to adverse health effects. In India, we have second largest number of cell phone users with highest tele density in the world, therefore ICMR is conducting a prospective multi-disciplinary cohort study with the primary objective

of finding effects, if any, of 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 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.

Cell Phone Study.

Under the prospective multi-disciplinary cohort study of cell phone 3637 male and female subjects (age 18 to 45 years) have been enrolled after fulfilling exclusion and inclusion criteria's under various study groups. These subjects have been followed for their clinical and laboratory examinations. The salient features of the study are given below.

The increasing trend in air conduction, bone conduction and speech recognition threshold, Epworth Sleepiness Scale Score & Diagnostic and Statistical Manual of Mental Disorders, IV Edition (DSM-IV) criteria score, 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. Even irregular menstrual cycle and decrease in sexual desire and frequency in female subjects in highly and moderately exposed female groups during the consecutive follow up visits was also observed.

The trend in decline of testosterone levels have been noticed in exposed groups resulting in decrease of androgen dependent parameters like sexual desire & sexual activity, sperm count, sperm motility, percentage of live sperm, percentage of morphological normal sperm etc.

The decrease trend in Memory, fluency, visuospatial-abilities and overall Addrenbrooke's Cognitive Examinations-Revised Score (ACE-R) were also observed in highly exposed and moderately exposed male and female groups during consecutive follow-up visits.

In 19 female subjects the lumps in breast were notice along with discharge from their nipples in female subjects of moderate and highly exposed group during consecutive follow-up visits.

The increasing trend in percentage of apoptosis in lymphocyte and levels of malondialdehyde were observed in male and female subjects of exposed groups. Similarly, the decreasing trend in levels of Super Oxide Dismutase (SOD) was observed both in male and female subjects of exposed groups.

White patches in the mouth of 17 male subjects and 2 female subjects were noticed in highly exposed and moderately exposed groups during consecutive follow-up visits.

Even long-lasting sores in the mouth of 59 male subjects and 19 female subjects were observed in highly exposed and moderately exposed groups during consecutive follow-up visits.

Cell Phone Tower Study.

Physical characteristics of RFR emitted from 307 cell phone towers, installed at five zones of Delhi (East, West, North, South & Central) was undertaken using NARDA instrument model No. NBM-520, during day and night, at various distances and frequencies. The higher Power Density (PD) was observed from 154 cell phone towers (50.2 %) during day and night at different distances and at different frequencies than the prescribed limit of power density. The measurement of PD was repeated at 100 cell phone towers and it was observed that at 34 cell phone towers (34.0 %) the PD was higher than the prescribed limit.

Health Survey Study.

Health survey based on the prescribed proforma was under taken of 1000 people (700 male, 300 female; age 18 – 45 years) residing at various distances from the cell phone tower in all the five zones of Delhi where the PD was above the prescribed limit. Univariant analysis was attempted which indicated that symptoms indicative of mental stress, depression, loss of balance, nausea, slurred speech, fever more than 10 days, headache, seizure,

etching, complain of constipation, blood clotting in veins both in male & female subjects increased in the people residing within 300m distance from the cell phone tower in comparison to the people residing beyond 300m distance. Even abnormal sleeplessness increased in both male & female subjects and decreased in sexual activity in female subjects residing within 300mts distance from the cell phone tower in comparison to the people residing beyond 300mts distance were observed.

INSTITUTIONAL STRENGTHENING

National Animal Resource Facility (NARF) for Biomedical Research.

To build state of the art infrastructural facility as a single stop solution and to make available all the resources for basic, applied and regulatory research to bio-tech, bio-pharma and bio-medical institutions in the country the Government of India accorded approval for its formation on 18th November 2015. The Department of Health Research (DHR) Ministry of Health & Family Welfare has conveyed the orders on 3rd December 2015 for creation of NARF institute. ICMR separately issued office memorandum and notification for establishing it as a permanent institute of ICMR and to merge the currently operating National Centre for Laboratory Animal Sciences with the new Institution on 1st Jan 2016.



Fig. 4: The Foundation Stone Laying Ceremony has been held on 07th May 2018 at ICMR-NARF Institute site at Genome Valley, in the presence of PEC Members and Dr. Balaram Bhargava, Secretary, DHR & DG, ICMR through Skype.



Fig. 5: Following the Foundation Ceremony, 11th PEC meeting has been held at ICMR NARF, NIN Campus for reviewing the progress on the construction of first phase buildings.



Fig. 6: 13th PEC meeting of the NARF Institute has been held on 13th Nov 2018 at NARF Class room, NIN Campus, Hyderabad.

NUTRITION

The ICMR continues to be instrumental in developing public health activities with many significant contributions in the country in the field of nutrition. It has been made possible by undertaking the laboratory and hospital based research with community based participation. The salient features of various research activities undertaken during 2018-2019 are given below.

INTRAMURAL RESEARCH

ICMR- NATIONAL INSTITUTE OF NUTRITION

- High prevalence of anaemia among vulnerable populations is associated with B12 and folic acid deficiency. A study conducted in eight states viz., Telangana, Madhya Pradesh, Odisha, Meghalaya, Tamil Nadu, Gujarat, Assam, West Bengal and Rajasthan showed varied levels of anaemia and the prevalence of vitamin B12 deficiency (<200 pg/mL) among different age groups was varied. It was highest in Gujarat (36.8%) and lowest in Meghalaya (17.3%)
- Awareness, knowledge and acceptance of Mid-Day Meal (MDM) were studied among the beneficiaries (over 3 lakh children) and other stakeholders in 21 states. The food is being cooked and served through school kitchens (83.4%) and central kitchens (16.6%). Most students (92%) attending schools were consuming MDM and acceptability was high (87%). Almost all parents (96%) felt that the MDM would benefit their children and increased school enrolment (84%) and attendance (85%). A considerable number of students were attending the schools without breakfast.
- Till date, there has been no non-invasive drug delivery system reported for the treatment of Diabetic Retinopathy. NIN developed a core-shell nanoparticle-based delivery system loaded with triamcinolone acetonide and evaluated its efficacy in a DR rat model. The drug loaded nanoparticles significantly improved structural and functional aspects of retina. This demonstrates the potential of a nanoparticulate delivery system for use as a topical formulation for treating DR.
- A study on Wilms' Tumor 1 (WT1) uncovered a pathogenic role of WT1 in Pulmonary Fibrosis (PF) by promoting fibroblast activation in the peripheral areas of the lung which can be a target for therapeutic intervention.
- A study that investigated the role of Ubiquitin-Proteasome System (UPS) and ER stress in the brain of diabetic rats suggested that altered UPS could be one of the underlying mechanisms of neuronal apoptosis in diabetes and chemical chaperones such as 4-PBA and could be potential candidates for preventing these alterations under hyperglycemic conditions.
- Iron bioavailability studies on indigenously developed triple fortified rice (Iron, Folic

acid, Vitamin B₁₂) during rinsing and different cooking methods showed retention of iron during rinsing with excess water was >95%, while folic acid and vitamin B₁₂ levels were reduced by ~25%. Water tight cooking (in electric cooker or on flame) of rice had no additional effect on the nutrient levels as compared to rinsed rice, implying their stability during cooking. However, cooking with excess water followed by decanting led to 50% loss of iron and ≥75% loss of folic acid and vitamin B₁₂.

- Among 400 milk products analyzed for the presence of S.aureus contamination was found to be highest in Khoa (66%) compared to other milk products. Of these, non-coagulase positive Staphylococcal isolates were more. The data will help set standards for microbiological quality of milk products.
- Based on histopathological evaluation, it was seen that ocimum and ginger administration to experimental animals showed high prebiotic potential and ameliorated inflammation
- Histopathological evaluation in SD rats of the traditional formulation cynodondactylon (Swarasa of Durva or DS) in menopausal syndrome through a reverse pharmacology approach, showed that the group administered DS in the highest dose showed most beneficial effect with respect to changes in uterine morphology.
- A study aimed to develop nutrient rich, low GI multiple whole grain product was conducted and a multi-grain product was developed by combining millets, grains and soy. This formulation was tested for acceptability in the form of Roti and was found to be high in fiber and protein.
- Roti prepared from this atta preparation was used as a meal to replace lunch with multigrain roti for a period of three months among 50 diabetic subjects. The multigrain product consumption significantly reduced the mean glycosylated hemoglobin from 8.0 to 7.4 and mean diastolic blood pressure reduced from 86 to 81 and the consumption also improved the insulin sensitivity when compared with control group.
- Studies on fresh/package tender coconut water collected from three Southern States of India has provided the information on extent of chemical contamination to FSSAI in order to facilitate them to look into the requirement for fixing the limits in order to evolve cut-off limits of our own in the Indian context.
- A cross-sectional study conducted among primary home food preparers (N=400) in rural and urban (@200 each) areas of Telangana helped develop and validate a Household Food Safety Index (HFSI). An 87-item comprehensive index questionnaire covering variables like knowledge, practices and enabling-environment was developed and associated with presence of high risk food borne pathogens in samples. Of them, 11 index variables were found to be significantly associated with food contamination. These 11 key variables were used to develop a household Food Safety Index (HFSI) that can rapidly ascertain food safety status at household level.
- These 11 parameters were collapsed into five context-specific 5 key messages. A communication campaign was carried out among households (N= 120) using the 5-keys to food safety and after the campaign, significant improvement was observed in HFSI scores.
- A study assessed quality and effectiveness of popular calorie counting apps. Top 20 apps were selected from Google Playstore and their quality was assessed using a 55-point scoring scale on attributes like standards used, content accuracy, user interface and sources of database. The mean (+SD) quality score was 36.95(±5.65). The calorie and activity recommendations were compared with standards and over 65% apps over/underestimated calorie intake

- Developed a ready-reckoner chart to inform the newly married couples and their family members on pre-conception nutrition and first 1000 days of life covering nutrition and health related aspects. This education material takes life-course approach of highlighting what needs to be done during critical periods and sensitive periods for cumulative effects on child health (future generations).
- ICMR-NIN has developed a communication kit called “My Plate for the day to prevent hidden hunger” which has a simple visual representation of various food groups to be consumed in a day by an individual intending to reach a 2000 kcal diet. This is clubbed with an easy-to-understand table depicting amounts of raw foods (from various groups) to be chosen to get 2000 kcal energy and 60 g protein. The kit was released by the Hon’ble Vice President of India on 14th Dec 2018 as part of ICMR-NIN Centenary Year celebrations.

EXTRAMURAL RESEARCH

A multi-centre task force study has been initiated w.e.f July, 2018 at 16 locations (Delhi; Bangalore; Bhopal, Kanpur, Srinagar, Nagpur, Ludhiana, Jaipur, Trivandrum, Rishikesh, Ahmedabad, Bhubaneswar, Jorhat, Dibrugarh, Agartala, Shillong) in the country with an aim to assess the **consumption pattern of food and food products/ items high in fat, salt and sugar, from organized and unorganized sectors**. Under the study, consumption pattern on both preceding day and preceding week is being collected using pre-tested questionnaire. Besides, commonly consumed food samples are also being collected from each site for analysis of fat, salt and sugar content. Blood samples are being collected from a sub-sample. A total of approx. 80,000 households (approx. 4 Lakhs population) will be covered under the study. So far, approx. 25,000 households have been surveyed.

Other ongoing Task Force studies are:

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” which is currently ongoing in 41 districts of 20 States (including all 8 north-east states).

Assessment of Iodine status among pregnant women in selected districts of India being carried out at 10 locations in the country

Prevalence of fluorosis in the community of selected districts of India and development of an appropriate intervention model for prevention and control of fluorosis currently ongoing at 7 locations in the country (covering one district each in Orissa, Madhya Pradesh, Telangana, Chandigarh, Bihar, Rajasthan and Assam)

Task Force entitled “**Prevalence of vitamin A deficiency disorders among children aged 1-5 years in selected districts of India**” has been initiated recently at 7 locations of the country (Assam, Odisha, Telangana, Bihar, Madhya Pradesh, Rajasthan and Uttar Pradesh)

Study entitled “**Development of District Level Model to address undernutrition and Hidden Hunger: An Intersectoral Approach**” has been completed. The data entry and analysis is being undertaken.

ADHOC STUDIES

The Division of Nutrition has been supporting Individual Scientists across the country through adhoc projects. Currently 17 adhoc projects are ongoing. A total of 27 new proposals have been recommended for funding in the year 2019-20.

FELLOWSHIP: Forty five fellowship research studies are being currently supported by the Division and 41 new fellowship proposals have been recommended for funding in the year 2019-20.

CENTRE OF EXCELLENCE: Centre of Excellence for Fluorosis Research and Mitigation of the Diseases in Rajasthan under Prof. (Dr.) A.K. Susheela, Executive Director, Fluorosis

Foundation of India, New Delhi completed its tenure. The centre worked to set up Infrastructure for diagnosis of Fluorosis in Teaching Hospitals; updated knowledge of Doctors through Continuing Medical Education (CMEs) in Teaching Hospitals; provided hand-on training to Dieticians for Diet Editing and Diet counseling etc.

CENTRE FOR PROMOTION OF NUTRITION RESEARCH AND TRAINING WITH SPECIAL FOCUS ON NORTH-EAST, TRIBAL AND INACCESSIBLE POPULATION: During the year 2018-19; a total of approx. 35,000 serum/ plasma/ urine/ salt samples were analyzed for

over 1.5 Lakhs determinants. The laboratory supported biochemical analysis under various Task Force studies undertaken by the Division besides samples collected under collaboration with different Medical Colleges/ Universities. Three Ph.D students submitted their thesis utilizing the facilities of the centre, out of which two have been awarded the Degree.

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 and the ICMR-National Institute for Research in Environmental Health, Bhopal. Major highlights of various programmes undertaken by the ICMR in the areas of occupational and environmental health during the year 2018- 2019 are given below.

INTRAMURAL RESEARCH

ICMR-NATIONAL INSTITUTE OF OCCUPATIONAL HEALTH, AHMEDABAD

Evaluation of CC16 as reliable biomarker for early detection of silicosis in occupational set up.

Club cell protein as a biomarker for early detection of silicosis, where age, sex and socio-economic status matched groups were chosen as healthy subjects (no exposure and no respiratory morbidity), moderately silica dust exposed workers from ceramic industry (4.2 ± 3.90 yr exposure) and X-ray confirmed silicosis workers from agate industry (23.1 ± 9.88 yr exposure) were chosen as cases. club cell protein (CC16) values in different biological fluids was measured.

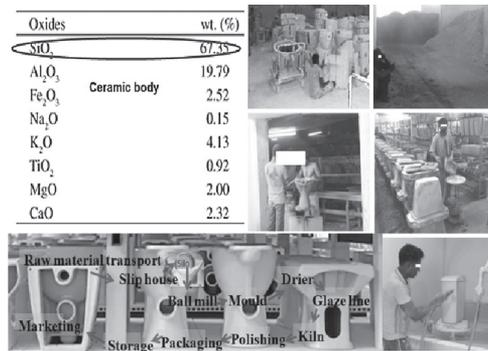


Fig. 1: Workers in agate industry, Gujarat.

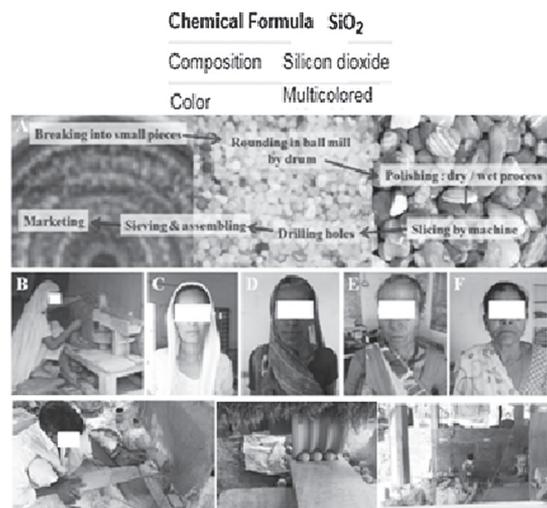


Fig. 2: Workers in agate industry, Gujarat.

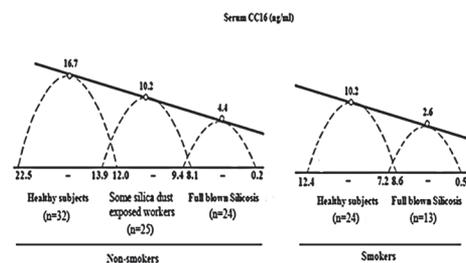


Fig. 3: Serum CC16 values with ranges in different study groups.

Because of high sensitivity and specificity (383%), centre calculated the best possible cut off values separately for non-smokers and smokers and found serum CC16 value is suitable biomarker for early detection of silicosis as compared to that of the urine and saliva values, where tobacco smoking has an additional effect irrespective of age and sex of the study participants. This is a very significant observation as till date no such data was published in Indian context, even we do not have any reference value in this regard. Overall, we revealed gradual downfall of serum CC16 due to early silicosis if the person is continuously exposed to silica dust, which perhaps is the first of its kind in South-East Asia. Previously confirmed silicosis cases were never subjected and their serum CC16 levels were never evaluated. Based on our data, we emphasized that silica dust exposed workers need to be periodically screened (annually) to assess their progressive lung damage: more the exposure, lesser is CC16 value; and more the lowered value; higher is the progression of disease. Also, recommended that reduce serum CC16 value with silica exposure history and breathlessness need urgent diagnosis for silicosis/silica dust-related respiratory morbidity in the country.

Development of novel, non-invasive, low-cost and, rapid detection system for lead in biological samples.

A transdermal patch based system has been developed where the sweat get absorbed in the patch and it was onsite detected, using color development reaction. Retention of colour suggest the presence of lead after one step development reaction. Study Checked the specificity of key chemical reaction (chemical spot test) utilized in the design of the device with 17 other metals. The results are suggestive for the 100% specificity with lead (Pb²⁺).

A paper based diagnostic method for differentiating asthma COPD overlap syndrome (ACOS) from asthma and COPD.

The study team identified few markers of ACOS (Interleukin 4; IL-4 and MCP-1) which are

presently being translated into a paper based semi-quantitation assay for robust detection of the disease. The objective is to develop a paper based semi-quantitation diagnostic method that can be used in capturing IL-4 and MCP-1 antigens, since IL-4 and MCP-1 molecules are significantly dysregulated in ACOS as compared with asthma and COPD. The paper based diagnostic tool has been selected keeping in mind technical feasibility, cost-effectiveness, simplicity of use and short time involvement to obtain results. This device could be technologically the “quick answer” to increase access to serum antigen testing for accurate diagnosis of ACOS.

Evaluation of Lead exposure among e-waste handlers.

The e-waste handlers from Ahmedabad and Bhavangar districts are evaluated for their environmental and blood lead concentrations along with haematological parameters. The average environmental Lead concentration was found $0.48 \pm 0.1 \text{ mg/m}^3$ which was more than 3 times higher of the permissible exposure limit of 0.150 mg/m^3 as per Indian factories act 1948. Till date 43 blood samples have been collected from e-waste handlers. The result of their mean blood lead level was found $5.3 \pm 3.4 \text{ } \mu\text{g/dL}$ which is also higher than the reference blood lead level of $5.0 \text{ } \mu\text{g/dL}$ as per recommended by CDC-NIOSH, USA in 2015. Their mean haemoglobin level was found $13.0 \pm 1.8 \text{ g/dL}$. Moreover, 46.5% subjects were found of elevated blood Lead level ($> 5 \text{ } \mu\text{g/dL}$, NIOSH-2015) range from $5.1 - 18.4 (8.0 \pm 3.0) \text{ } \mu\text{g/dL}$; whereas 34.1% subjects were found anaemic (Hb level $< 12.6 \text{ g/dL}$) with haemoglobin levels range from $5.6 - 12.5 (11.2 \pm 1.8) \text{ g/dL}$.

Scaling up of the implementation of essential interventions for occupational health in BOHS through Primary Health Care system.

The objective of this activity was to work out how Basic Occupational Health Services (BOHS) can be provided through primary health care system in India. A total of 60 PHCs from 14 districts of Gujarat were surveyed during this ongoing project.

Information were collected from 124 medical officers, 476 health professionals, including staff nurses and pharmacists and health workers working in the PHCs and their sub-centres.

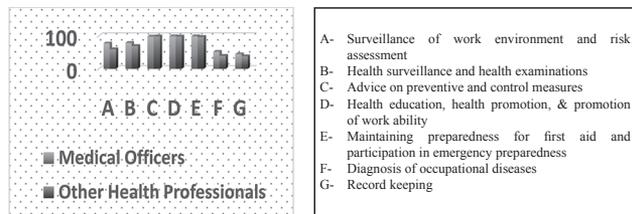


Fig. 4: Percentage of health professionals with overall weighted positive response to individual sections of BOHS.

The ongoing study at 60 PHCs revealed that all the respondents were in favour of catering the occupational health needs of the workers at the grass root level. However, the findings are a trend of limited knowledge and expertise among the health professionals at PHCs to serve the occupational health issues. It is noteworthy to mention that strengthening of physical resources to cater the occupational health needs to be reviewed. In tandem, suitable training modules on issues of occupational health delivery by the health professionals in PHCs needs to be designed and imparted. Based on the results obtained, special consideration needs to be given on developing modules for common occupational diseases, ergonomics, different modes of prevention in occupational diseases like hazard control, personal protective devices, health education etc. The modules prepared may be imparted to these health professionals in a comprehensive way of orientation (OTP) and re-orientation (RoTP) training programme modules to allow effective penetration of the occupational health knowledge among these professionals.

Occupational health risk among veterinarians and associated workers.

In this study, veterinarians total interviewed (n=565) from Gujarat and Maharashtra State were mainly male (90.4%) and only very few females (9.6%) had chosen field veterinarian as a profession. Very few veterinarians (5.3%) had Ph.D. qualification, where

42.5% and 52.2% were graduate and postgraduate in veterinary science respectively. Sixty percent of the respondents experienced automobile injury (more than 1, 3 and 5 times) which resulted into absenteeism from job. Among them, 56.2% of the respondents' absenteeism ranged from 1-30 days during last two yrs. 55% and 70% of the respondents reported animal related injury during the last two years and total carrier respectively. Twenty-five percentage and 52% of the total respondents agreed that they have got needle prick injury while conducting vaccination and general treatment respectively. Recapping of needles was practiced by 18.9% of the respondents which may be one of the reasons of needle prick injury, which was strongly prohibited in human practice. Sixty-five percent of the respondents worried about zoonotic disease while working. Eighty-eight percent of the veterinarians of total respondents experienced the stress of different level, ranging from mild (24.2%), moderate (38.6%) to extremely stressful (25.3%) condition. Assessment of stress among the field veterinarians was carried out only on the basis of questions and no scale was included. Veterinarians from Gujarat and Maharashtra had risk of injuries, both animal and non-animal related.

Urban air quality assessment using remote sensing and GIS.

Result showed that PM₁₀ concentration (655µg/m³) was observed higher in samples collected from industrial area. The concentration was observed higher than the prescribed limit (100µg/m³) by NAAQS. Other pollutants' concentrations *i.e.*- Ammonia, SO₂, NO₂ and CO₂ were observed higher in commercial area whereas, ozone concentration was found higher in residential area of Ahmedabad. However, all values were under NAAQS prescribed limit. Secondary health data received from urban health centres showed increased cases of Acute Respiratory Infections in north and south zone of Ahmedabad during the period of October 2018 to January 2019.



Fig. 5: Urban air quality.

Respiratory morbidities in school children of critically polluted industrial area of Gujarat.

A total number of 515 students were enrolled in the study. Height, weight, blood pressure measurement was carried out among all students, and Pulmonary Function Test (PFT) of 61 students was performed. Result of air monitoring data revealed that NO_2 , SO_2 , O_3 , Ammonia and VOCs levels were observed within limit whereas, during the school hours $\text{PM}_{2.5}$ concentrations (within classroom) was observed higher than USEPA prescribed guideline value.



Fig. 6: Study in school children in Gujarat.

An explorative study of determinants of occupational injuries in child and adolescent workers and development of a suitable intervention approach.

A cross sectional study addressing occupational injury was carried out involving child and adolescent workers of four major informal sectors with intervention approach to identify human and workplace factors as well as to undertake intervention through health education. About twenty-five percent of study subjects were of less than 16 years age and majority of workers were working in present job for more than one year. Back pain, joint pain and headache during or after

work were major work related morbidity in study subjects. About half of subjects perceived their workload to be moderate to heavy. This study examined the occurrence of injuries in last one year period. It was observed that in about 75% injuries, limbs were affected. Superficial injuries/fracture/dislocation (55.7%) and sprain/strain (32.8%) were the major effect of such injuries. As far as causation is concerned, fall of object (27.3%) and wrong movements (66.7%) was major concern. So far, as involvement of equipments/agencies is concerned, in most of the injuries (87%), involvement of small tools was observed. The observation highlights that lack of job training, lack of safety training, lack of protective devices, lack of expertise to deal with small tools are major predictors of the injuries of the study subjects. While examining heat exposure of study subjects at work, centre found that moderate level heat stress was present in most of the work places, hence, contribution of such heat stress in injury occurrence may not be ruled out. Injury occurrence is multifactorial in causation, hence, multivariate analysis was sought for better understanding the role of different individual variables. Habit of workers (OR 2.123, 95% CI 1.162 – 3.879) and perception of pain and discomfort (OR 1.932, 95 % CI 1.076 – 3.471) was the significant predictors of such injuries in totality. When analyzed, the role of such factors on injury occurrence, excluding the ‘Perception of pain or discomfort’ from the logistic regression model, observed that smoking/chewing habit and gender remained as significant predictors. This time however, ‘Perception of work load’ became a significant factor (OR 2.733, 95% CI 1.06 -7.04). In brickfield workers, it was found that persons having perception of pain and discomfort (OR 13.044, 95 % CI 2.194 – 83.122) were at significant risk. In construction workers, age of the subject (OR 1.470, 95 % CI 1.01 – 2.175) was found to be a significant risk factor. In farming sector, study found that perception of pain or discomfort (OR 5.986, 95 % CI 1.305 – 27.468) had a significant risk. In garment sector habit of workers was proved to be a significant factor. Postural analysis was carried out by OWAS, REBA, RULA techniques. Working postures adopted in most occasions are not ergonomically optimum. Work postural stress combined with unskilled use of tools has been the cause of injuries in many occasions. An assessment of knowledge of participants (pre and post intervention) was undertaken by interviewer

administered questionnaire. Enhancement of knowledge following awareness activity was evident.

Association of chronic environmental organophosphorus pesticide exposure with neurodegenerative diseases: Case control study in rural West Bengal

This study aims to predict association of chronic environmental OP pesticide exposure with neurodegenerative diseases by utilizing a comprehensive paradigm of symptom-based validated screening for Dementia, Depression and Parkinson's disease; epidemiological information and estimation of biomarkers of pesticide exposure, viz., AChE, BChE, PON1 levels among indirectly exposed (general population) and directly exposed (occupational, agricultural workers) population groups in rural West Bengal. This study is of particular relevance in West Bengal as it is the fourth most populous state in India and with nearly 69% (as per 2011 census) population living in rural areas, agriculture remain the chief occupation in West Bengal. The state has consumed 3,710 metric ton chemical pesticides during the year 2008 – 2009; fourth highest in India after Uttar Pradesh, Punjab, Haryana and Tamil Nadu. Although the state is actively promoting organic farming, use of pesticides and retention of pesticide residues in farm produce is a concern for the health and well-being and thus, economic development of West Bengal.

Trained project staffs have commenced screening of subjects from October 2018 among directly exposed population in a high pesticide exposure block (Galsi II) of Bardhaman district, a district with high agricultural productivity in West Bengal. Samples were drawn from subjects 50 years and above of either sex, continuously living in the area for at least last five years. Till date, n=294 subjects have been screened and n=43 (14.60%) participants have been identified as “cases”.

Consortium on Vulnerability to Externalizing Disorders and Addictions [c-VEDA]

Till date, the ROHC (E) group has achieved its recruitment target and recruited and completed behavioral characterization on n=1501 subjects. Acquisition of blood samples for epigenetic analyses and urine samples for environmental toxicology has been accomplished in n=1008 and n=975 subjects, respectively. First follow up assessment after 12 months of recruitment has been completed in n=233 participants. The first quality control check on collected data has been carried out on first 300 subjects and following are the salient features.

- Completed assessments: 300 (16% of the cVEDA sample)
- Gender distribution: 45% males, 55% females
- Distribution among age bands: 55% C1 (6-11 years), 35% C2 (12-17 years), 10% C3 (18-23 years)
- There is a high rate of completion across questionnaire; data follows a consistent pattern on comparison between males and females and among the three age bands.
- Depressive disorders as measured by MINI are approximately 4%.
- Data on the measures for externalizing disorders, follows expected age and gender patterns. However, mean scores at ICMR-ROHC (E) site seem to be lower than other sites, and some of these are statistically significant.
- Low findings on morbidity measures may be due to the initial tribal population sampled where community bonding is stronger and mental health problems; substance use and help-seeking behaviour are low.

Analysis of environmental toxins has been initiated with plasma lead and urinary arsenic and metabolites of volatile organic compounds (from exposure to traffic exhaust in urban areas and biomass fuel smoke in rural areas). Till date, anonymized biological samples from all sites have been analyzed for metabolites of volatile organic compounds (urine, n=631), urinary arsenic (n=713) and plasma lead (n=759). Different levels

of exposure have been detected across sites. Environmental samples from coal mine areas have detected significant presence of volatile organic compounds. ICMR-ROHC (E) study group has also acquired 3T brain MRI resting state scans for n=48 participants from coal mine site.

Assessment of urinary biomarkers for detection of Chronic Kidney Disease of unknown etiology (CKDu) among industrial workers.

This project assessed the CKDu in 134 industrial workers (41 females and 83 males) using estimated Glomerular Filtration Rate (e-GFR) with MDRD equation. The levels of kidney function and stage of kidney disease was defined using KIDGO (Kidney Disease: Improving Global Outcomes) guidelines. The results of the study found that the 43.3% workers had normal (GFR >90), 52.2% workers had mild loss (GFR 89 to 60) and 4.5 % workers had moderate loss (59 to 45) of renal function. No cases of severe loss (GFR 44 to 15) and kidney failure (<15) was found among these subjects. Further, novel urinary biomarkers will be assessed in industrial workers who have normal as well as altered kidney function so as to find out the sensitivity and specificity of selected biomarkers.

A study to evaluate work schedule pattern on the development of Metabolic Syndrome (MetS) and Insulin Resistance (IR) with adipokines measurement among industrial workers.

This study evaluated the effect of work schedule pattern (day, rotation & night shift) on the development of Metabolic Syndrome (MetS) and Homeostasis Model Assessment Index-Insulin Resistance (HOMA-IR) with adipokines measurement among industrial workers. The parameters of MetS, HOMA-IR and adipokines (Adiponectin, leptin and leptin/Adiponectin ratio) were compared with day shift, rotation shift and night shift workers. The MetS was assessed by using the definition of the International Diabetes Federation. Insulin Resistance (IR) was assessed by using the HOMA-IR. The levels of serum insulin, Adiponectin and leptin were done by using ELISA methods. The levels of MetS, HOMA-IR, Leptin and Leptin/Adiponectin ratio (LAR) was

increased in night in rotation shift workers when compared to day shift workers. The level of serum Adiponectin was decreased in night shift workers when compared to day shift workers. The study results indicate that individuals who had shift work is susceptible to increased MetS, IR, leptin, LAR and decreased concentration of Adiponectin and need intervention strategies to diminish the risk of health problems due to shift work.

Identification of emerging microbial dermatitis and lung diseases among tannery workers in Southern India.

A total of 114 tannery workers participated in the study, which consisted of 89 male participants and 25 female participants. These workers were in pre-tanning, tanning and post tanning sections of the tanneries. Past 6 months clinical history revealed that 42% (n=49) of the workers suffered with skin disorders such as allergic contact dermatitis, eczema, psoriasis, vitiligo, fungal ring worm infection, bacterial skin infections etc. About 9.6% (n=11) of the participants suffered from fungal dermatitis. Both dermatophytic fungi (3.5%) and non-dermatophytic fungi were isolated from the samples. About 5% of the participants suffered from secondary bacterial skin infections. Bacterial as well as fungal lung infections were identified in 5% of participants. Klebsiella pneumonia and Streptococcus pneumonia were isolated from the sputum samples. Pulmonary Function Test (PFT) revealed that significant number of participants have restrictive type of respiratory morbidity. Further lab investigations are under progress.



Fig. 7: Microbial dermatitis.

Application of statistical tools using spatial modelling method to assess the health effects of pollutants in Bangalore city.

Health data were collected from PHC centres located near sensitive zone for the period of June 2017 to August 2018. The demographic details of patients such as name, age, sex and history of disease were collected. It was observed that 9085 cases were registered during the study period, in which 2685 were males and 6400 were females. Irrespective of age and nature of diseases, females were reported more. About 1683 (19%) cases of respiratory illnesses like cold, fever, cough and asthma were registered out of 9085. 353 diabetic cases and 854 hypertension cases were registered. Diseases like body ache, abdomen pain, viral fever, worm infection and dog bite cases were also recorded. Gastritis and general weakness are defined as other diseases. An attempt will be made to evaluate spatiotemporal analysis, focusing the levels of pollutants viz., SO₂, NO₂, PM₁₀ & PM_{2.5} for the period of 2017 to 2018 in the PHC areas covered so far.

Personal and biological monitoring of workplace pollutants and their potential health effect indices assessment in fuel filling station workers.

Total 92 participants (Exposed=67 participants, 46 Males & 21 Females and Control=25 participants, 21 Males & 4 Females) were covered in this phase. Major health complaints recorded was headache, cough and nausea. Estimated VOC's ranged from BDL to 0.7 ppm. The haemoglobin levels in female workers were less than the normal. About 37% (n=6) of female workers were anaemic. Microcytic hypochromic anaemia was detected in 25% (n=4) of female workers. The testosterone level in female workers were higher than the reference ranges whereas IL-3 level were higher in both male and female subjects compared to control population. It was observed that the maximum

mean concentration of 8-OHdG was recorded in female subjects which was slightly higher than the control group. The elevated frequency of micronuclei was observed in exposed workers. The statistically significant DNA damage in PBMC was recorded in exposed male workers compared to control group of workers. Total 50 study participants were analyzed for GST (Glutathione S Transferases) null genotype. Among fuel filling station workers, higher frequency of homozygous GSTM1 null genotype (35% in Males and 30.8% in Females) was identified. GSTT1 null genotype was recorded only in female workers (15.4%). In 5% male workers null genotype was noticed in both the GST family genes.

Occupational health assessment survey among asphalt associated job workers in India

Total 141 participants (Exposed-78, 67 Males & 11 Females, Control-63, 41 Males & 22 Females) were covered so far in this study. Major health complaints such as back pain, headache, tiredness and burning, eye irritation were noticed. Estimated PM₁₀ dust in road paving work place was 27-241 µg/m³. In asphalt mixing work area, it was 64.7-1699 µg/m³. Highest VOC's detected in road pavers during saval cleaning with diesel activity was 2.37 ppm. VOC's of 0.44 ppm was observed in tar loading to vehicle work activity of Asphalt mixing work area. Eosinophils count among exposed group was slightly higher than normal range. The level of Bilirubin, SGOT and SGPT of liver function were higher among exposed group. Iron Storage Status (Ferritin) in female workers was lower compared to control population. Increased level of oxidative injury markers (8-OHdG and 8-Isoprostane) was recorded in exposed group than the control group. The elevated frequency of micronuclei was observed in exposed workers. The statistically significant DNA damage in PBMC was recorded in exposed workers compared to control group of workers.



Fig. 8: Asphalt industry workers.

Monitoring of Pesticide Residues at National Level.

A total 814 samples were collected and analysed. None of the Pesticide residues were found in milk and water samples. The pesticide concentration in the majority of samples analysed were well within the pesticides prescribed limits (MRL) set by Prevention of Food Adulteration (Govt. of India). Total 10% of the samples are detected and 1 % of the sample were above the MRL. Therefore, majority of the food commodities are safe for human consumption. Moreover, this results can also be used to understand the quality of food commodities and to evaluate the possible health risk associated with their consumption.

Multi-Centric Task force Project “Study to assess the exposure and Health Effects of Pesticides”

The aim of this study is to assess the health status of the population in areas with high and low pesticide usage (5 selected areas) and to estimate the levels of pesticide residues in blood and urine. Also, to study the potential toxicity and health hazards with pesticide exposure. From these calculations, it is possible to judge whether their exposures are below or above hazard limit. The pesticide determination

method has been developed and validated for pesticides in serum sample, the results are described as follows. The calibration curves were constructed using different concentrations of OCs, SPs, OPs and Carbamate against the peak area of the individual analytes. The linear regression analysis was performed on the plots of the calculated concentrations versus expected concentrations. The unknown sample concentrations were determined by using linear regression analysis of the calibration plots that provided slopes and intercepts. The correlation coefficients (r^2) > 0.99 were obtained for OCs, SPs, OPs and Carbamate throughout the study within the acceptable range. The representative calibration curve of OCs, SPs, OPs and Carbamate was obtained. The recovery studies were conducted for OCs, SPs and OPs from serum matrix. The recovery range for OCs, SPs and OPs were 70 – 96 %, 76.7 – 100 % and 70 – 95 % respectively. The performance of the method recovery was within acceptable limits (70-120 %) for routine analysis. The repeatability of values for same spiked serum sample was carried out. The percentage for standard deviation obtained was in the range of 2 – 25%. The performance range for standard deviation is within the acceptable limits (20-30%) for routine analysis. The analysis will be initiated as soon as the sample is collected and received from participating sampling centre.

Public Health

- Identified serum club cell protein (CC16) along with silica dust exposure history may be useful as a suitable biomarker for early detection of silicosis, which perhaps is the first of its kind in South-East Asia. Earlier, confirmed silicosis cases were never subjected and their serum CC16 levels were never evaluated as done in this study.
- “Scaling up of the implementation of essential interventions for occupational health in BOHS through Primary Health Care system” shall assist in understanding the present knowledge, attitude and practices among the PHC health professionals. Such data would be utilized by governing agencies for focused intervention

for designing policy framework based on the primary healthcare system in India.

- NIOH researched for best possible chemical spot assay for detection of lead. With the positive results in in-vitro settings, centre has developed the usable prototype for transdermal patch which has been applied to healthy volunteers and lead recycling units' workers. The results are suggestive for its possible beneficial use in occupational lead exposure condition for early and onsite detection of lead in sweat.
- The synergistic application of remote sensing with *in-situ* ground level measurement of air pollutants and secondary health data is helpful in developing the air quality map. This data is also helpful in identifying the potential zone of air pollution related human health hazards.
- Initiated Associate Fellow of Industrial Health (AFIH) course at ICMR-NIOH along with its regional centres. Associate Fellow of Industrial Health (AFIH) is a three months full time Post Graduate Certificate course in Industrial Health approved by Directorate General Factory Advice Service & Labour Institutes (DGFASLI), Ministry of Labour & Employment, Govt. of India. On completion of course, an examination will be conducted by DGFASLI and successful candidates will be awarded Associate Fellow of Industrial Health (AFIH) which will fulfill the requirements in terms of additional qualification for Factory Medical Officers of Hazardous Process Industries as required under the Factories (Amendment) Act 1987.
- Poisoning cases reported at the ICMR-NIOH poison Centre on the day to day basis from different hospitals of Ahmedabad, based on which people are getting treatment at different government hospitals in the city.
- Poison Information Centre at ICMR-NIOH (NIOH-PIC) established in the year 1993, is one of the five WHO recognized poison centers in India. NIOH-PIC has been involved in public health related services like

laboratory based investigations of poisoning cases, toxico-vigilance, teaching and training of health professionals related to poisoning cases. Centre also collects epidemiological data with special emphasis on poisoning cases in relation to occupational health and the data is provided to WHO. In the year 2018, a total of 479 poisoning cases were referred to PIC-NIOH. The male to female ratio was 2:1 (Males-319 and females-160) indicating that males are more prone to poisoning compared to females. 20% cases (99 cases) were admitted in severe clinical condition. 44% of the cases (211 cases) were moderately severe and 31.1% (149 cases) were with mild severity. 2.2% cases (11 cases) were not severe at all. 9 cases were fatal at the time of admission. Centre investigated cholinesterase activity in blood samples by testing the plasma as well as RBC cholinesterase activity which are the most reliable markers for acute organophosphorus poisoning. Out of 479 cases tested, 34.23% (164 cases) were known to use organophosphorus/carbamate pesticides for poisoning. The chemicals used for poisoning was not known in 41.13% cases (198 cases). However, various House hold chemicals, rodenticides, drugs, mosquito repellents and others like alcohol, Bhang/Dhatura, bleaching powder were found to be used in 24.4% cases (117 cases) reported including 1 case of snake bite.

The exposure to poison was through oral route in 94.15% cases (451), followed by inhalation in 2% (10) cases, dermal exposure in two cases, Injection in 3 cases. The circumstances of poisoning were suicidal in majority of cases (85.38%) whereas accidental poisoning accounts for 6.0% cases and 4 cases were homicidal. The poisoning cases were categorized according to the occupation of subject who consumed poison. 18.78% were house wives (90 cases), this was followed by unskilled workers 13.15% (63 cases) and farming allies (11%, 53 cases), and 10% (47 cases) were students. A significant number (13.51%, 63 cases) were from people with government/pvt job. 5.2% cases (25 cases) were drivers.

The highest level of incidence was observed in the age group of 15-45 years (87%) and found to decline thereafter. Very less incidence was observed in these patients of the age 1-14 years (less than 0.16%). Educational status of patients was found to be inversely related to incidence of poisoning. In 52.19% of the cases, the patient had education up to primary level. The number of poisoning cases were very less (5.4%) among those patients with educational qualification of graduation. A significant number of poisoning cases (17.32%) were from uneducated population. The educational status of 15 patients was not known. In short, poisoning with suicidal tendencies with the use of pesticide/insecticide in young population is very common in India.

ICMR-NATIONAL INSTITUTE FOR RESEARCH IN ENVIRONMENTAL HEALTH, BHOPAL

Development of a mito-epigenetic carcinogenic risk assessment model for environmental chemical exposures: A pilot study.

This study is attempting to develop and validate a mito-epigenetic model of carcinogenic risk assessment for environmental chemical exposures in subjects exposed to highly reactive environmental pro-oxidants. Blood samples from 16 subjects exposed to broad chemical class of pro-oxidants *in utero* and 26 age and gender matched healthy controls were collected. A higher frequency of damaged sites in mitochondrial DNA of exposed individuals was recorded. The complex nature of lesions observed at fragment 14898-155 bp, 1404-3946 bp and 3734-6739 bp regions of the mitochondrial genome suggested recruitment of an active repair machinery. Detection of higher levels expression of DNMT1 further confirmed the recruitment of DNMTs to the damaged sites leading to differential mtDNA methylation in coding regions of displacement loop, tRNA phenylalanine, 12S and 16S rRNA and cytochrome b. In addition, methylation of nuclear DNA (5-methylcytosine) along with methylation and acetylation of histone

3 and 4 showed marked variations in the exposed group with respect to controls. The study is continuing.

Aberrant circulating epigenomic signatures: Development and validation of minimal-invasive biomarkers for trans-generational monitoring of air pollution associated cancers.

This collaborative study with IIT-Khadagpur is being carried out in three different tiers of cities, categorized as low-risk (Sagar, Nayagarh and Mandla); mid-risk (Bhopal, Bhubaneswar and Jaipur); and high-risk (Delhi, Raipur and Gwalior) air pollution areas based upon ambient air quality. Circulating levels of methylated DNA, post-translational histone H3 and H4 modifications, expression profiles of nuclear transcription factors and status of epigenetic modifiers are being currently examined. Relative expression analyses of select panel of 88 gene loci revealed alterations in the CDK2/4, CDKN1B/2B, RASSF1, COL4A2, FOXO3, BIRC2/3, NRAS, PIK3R1, BCL2, NF κ B1, CCND1, SKP2 and ITGAV gene transcripts regulating cell cycle, inflammation, cell survival, apoptosis and cell adhesion. In order to fully comprehend the patho-physiological implications, functional characterization of the isolated epigenomic signatures is in progress. Profiling of 26 different plasma metabolites in low-risk, mid-risk and high-risk areas is being done. The study is under progress.

Development of quantum dots based nano-biosensors for detection of circulating cell free miRNAs in environmental associated lung carcinogenesis.

The primary objective of this Indo-Russian joint collaborative project is to develop a novel non-invasive nano-biosensor based on the integration of semi-conductors via bio-chemical modeling to detect defined species of circulating cell-free miRNAs in lung cancer. Currently, evaluation of specificity and sensitivity of novel nano-constructs against 21 defined circulating miRNAs is in progress using control settings. The validation of the

expression profiles is being carried out following *in vitro* experimental protocols. Quantum dot based-nanobiosensors have been synthesized and characterized. After surface modification by site-click chemical conjugation, the emission spectra is being analyzed by flow cytometry. The study is under progress.

Biochemical Basis of Pathogenesis of Chronic Obstructive Pulmonary Disease.

This study, completed during the year, attempted to identify potential proteases in stable COPD patients vis-a-vis healthy individuals. Blood samples from 35 stable COPD patients and 15 healthy subjects were collected and profiling of 7 proteases *viz.* Dipeptidyl peptidase-4, Cathepsin K, Cathepsin L, Caspase 3, Matrix-metalloproteinase-2, Matrix-metalloproteinase-9 and neutrophil elastase was done. Analysis of differential protein expression, using LC-MS, indicated differential expression of some proteins in COPD patients as compared to controls. Matrix-metalloprotease-2, Neutrophil elastase, Carboxy peptidase B2 had higher expression while PZP, A2MG, PI16, SOCS-3, had lower expression in COPD patients compared to healthy individuals. Dipeptidyl Peptidase IV (DPPIV), a serine exopeptidase enzyme, was found significantly decreased in stable COPD cases compared to healthy people.

Population based long term epidemiological study on health effects of Bhopal toxic gas exposure.

This long term epidemiological study has been continuing since 1985 wherein the available persons belonging to the originally assembled cohort of toxic gas exposed and unexposed persons in 1985, are being surveyed for morbidities and mortalities following the original protocol. During the reporting year, 55th round of survey was completed (Jan-Dec 2018). In this round, a total of 12,177 exposed individuals belonging to 4,871 families and 3,461 unexposed individuals belonging to 1,583 families were surveyed, revealing 22.8% and 16.9% morbidity in the two groups respectively.

A cross-sectional study on current Health status of gas affected individuals of Bhopal: Phase I-Data triangulation to understand health status of gas exposed survivors of Bhopal

This study, completed during the year, documented the pattern of morbidities with particular reference to the intensity of exposure, disease chronicity among gas exposed survivors in Bhopal through data mining, triangulation and linking of the available 3 major data bases related to the health of gas exposed survivors *viz.* Bhopal Memorial Hospital & Research Centre (BMHRC: 2010-2016), Gas Rahat Hospitals (Jan 2015-May 2017) and NIREH data base of long term epidemiological study (2011-2016). After data cleaning, three data bases were merged to form a single master list and disease profile of 30,195 gas exposed survivors was prepared. It was revealed that 29,426 patients (97.5%) were suffering from chronic morbidities, either singly (80.2% subjects) or in combination (19.8% subjects-for 10 conditions), and only 769 individuals (2.5%) suffered from any acute condition. With about 21% of all hospitalizations/visits to health facilities by the gas survivors being related to the cardiac problems, cardiovascular system emerged as the leading cause of morbidity followed by ophthalmology (14.1%), respiratory (11.3%), digestive (9.0%) and genitourinary (5.9%) systems. Chronic ischemic heart disease was the leading cardiovascular morbidity (41% of all cases of cardiovascular morbidities) followed by hypertension (23% of all cases of cardiovascular morbidities) among the gas survivors. Prevalence of morbidities, by and large, did not show any specific pattern/gradient with the exposure intensity i.e. severely, moderately and mildly exposed areas.

Effectiveness of institutional versus domiciliary implementation of standard pulmonary rehabilitation module in Bhopal gas exposed survivors having COPD.

This study, completed during the year, evaluated the effectiveness of pulmonary rehabilitation in the management of COPD cases in two different settings *viz.* under supervision in a health facility

and unsupervised at domestic level. A total of 180 COPD subjects were recruited and randomized into two groups i.e. institutional group and domiciliary group and given pulmonary rehabilitation as per the protocol. Two rounds of six-monthly follow up of the study subjects were done. In 6-minutes walk test both the groups recorded improvement of distance walked, with significantly higher ($p < 0.001$) improvement recorded in Institutional than domiciliary group. No significant difference in the FEV1 values at first follow up (after 6 months) was noted compared to baseline in both the groups. However, at second follow up (after 12 months) a significant reduction ($p < 0.001$) in the FEV1 values in the domiciliary group compared to baseline was noted. On the other hand, the Institutional group maintained the baseline value of FEV1. Improvement in quality of life, as assessed by SGRQ score, and functional exercise capacity was found significantly higher after 12 months of pulmonary rehabilitation in Institutional group as compared to Domiciliary group.

Cytogenetic profiling of patients with Chronic Kidney Disease : Evaluation of genomic Instability.

In this ongoing study, cytogenetic profiling of gas exposed and unexposed individuals with chronic kidney disease is being done through conventional and molecular cytogenetic techniques. So far, blood samples from 416 study subjects (Group I: MIC exposed CKD patients - 151; Group II: non-exposed CKD patients -121; Group III: Exposed non-CKD patients -134; Group IV: Normal healthy adults-10) have been collected and micronuclei assay and chromosomal aberration assays have been completed in 311 and 287 subjects respectively.

Prevalence of Chronic Kidney Disease in severely exposed cohort populations in Bhopal.

In order to answer the issue of perceived higher prevalence of chronic kidney disease (CKD) in the gas exposed survivors, this short term study, completed during the year, estimated the prevalence of CKD in the severely exposed cohort population of long term epidemiological study of ICMR-NIREH. In a sample of 215 from the study cohort, selected using systematic sampling technique taking family as a sampling unit, the prevalence of chronic kidney disease was found to be 16.2% as compared to reported national prevalence of 16.8%.

Characterization of prevailing chronic respiratory morbidities among severely gas exposed population of Bhopal.

This study, initiated in February 2018, is characterized by the respiratory morbidities in severely exposed cohort members of the ongoing Long term population based epidemiological study of NIREH using validated INSEARCH questionnaire followed by evaluation of lung function by spirometry and Forced Oscillation Technique (FOT). Wheezing (29.0%), morning breathlessness (40.0%), breathlessness on exertion (86.3%) and on dust exposure (61.6%), coughing at night (29.9%) and at morning (24.3%), and phlegm in morning (24.3%) were the most common respiratory symptoms among the study participants. The proportions of normal, obstructive, and low FVC in spirometry were 50%, 22%, and 28% respectively. The study is continuing as per schedule.

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. Major highlights of various programmes undertaken by ICMR in the area of non-communicable diseases during the year 2018-19 are given below.

INTRAMURAL RESEARCH

ICMR-NATIONAL INSTITUTE OF CANCER PREVENTION AND RESEARCH, NOIDA

Empowering health care providers to update knowledge and skills in the area of Cancer prevention through ECHO

Online training programs (Beginners and Advanced) on oral, breast and cervical cancer screening, along with tobacco cessation were organized using ECHO platform. A total of 230 participants, including gynecologists, radiation oncologists, dentists, public health specialists, medical social workers and lab technicians were trained in these programs.

Implementation of population based cancer screening in North East region of India.

ICMR-NICPR has implemented operational framework guidelines for cancer screening in 2 districts in the state of Assam viz; Cachar district and Tata tea garden Dibrugarh. This is the first pilot project in the country implementing the cancer screening guidelines released by the MoHFW. Training of ASHAs and project staff was undertaken at both the sites. At Cachar, 12929 subjects were screened and abnormalities detected on screening were appropriately managed. A mobile application for screening to be used by medical officers was developed. Field visits and procurement of requisite equipments has been undertaken at Dibrugarh.

Development of DNA vaccine constructs against India specific HPV-16 variant : enhancement of Immunogenicity of L1 constructs and characterization of T-cell epitope based E6/E7 constructs.

Persistent infection with high risk Human Papillomavirus (HR-HPV) is an established factor for the development of cervical cancer, especially HPV-16 followed by HPV 18. In previous study, centre identified major variations in L1 and E6 / E7 in HPV-16 and their impact on immunogenicity. Work is under progress to develop the epitope based vaccine construct and its characterization

PUBLIC HEALTH

- **Facilitation of Roll out of population based screening program for prevalent cancers by Government of India**

ICMR-NICPR has been identified as one of the nodal centers for training of master trainers to implement this program. During the period, various workshops and hands-on training programs for cervical, breast and oral screening for different cadres of health care providers were organized at NICPR in collaboration with NHRDC.



Fig. 1: Training of master trainers in cancer screening at ICMR-NICPR, Noida.

WHO-FCTC Smokeless Tobacco Knowledge Hub at NICPR

It compiled and released the 'Report on Global Smokeless Tobacco Control Policies and their Implementation' in April 2018 and to assist/guide them in implementing these measures. This report is the first ever compilation of the global progress made in implementing smokeless tobacco control policies in respect of the WHO Framework Convention on Tobacco Control. The report includes contributions and inputs from more than 60 national and international experts working in the field of tobacco control.

The Hub also organized seven webinars to disseminate knowledge on various aspects of smokeless tobacco usage and control delivered by

national and international experts. The webinars witnessed global participation. This activity was funded by Government of Norway through WHO FCTC Secretariat, Geneva.



Fig. 2: Release of 'Report on Global Smokeless Tobacco Control Policies and their Implementation', Apr 2018, ICMR-NICPR, Noida.

- **National Tobacco Testing Laboratory** was formally inaugurated at NICPR on 31st May 2018. This is a state-of the art laboratory intended to provide scientific inputs for implementation of directives of WHO Framework Convention on Tobacco Control (FCTC) in the South-East Asia Region; contribute to technology validation and assist Government of India in development and monitoring of strategies for harm reduction of tobacco products.

All the major instruments, environmental chamber, continuous flow analyzer, gas chromatography, near infrared analyzer quantum neo and smoking machine have been successfully installed. Various smokeless and smoked tobacco products such as Pan Masala, Zarda, Khaini, Tuibur, Kiwam, Dohra, Gul, Cigarettes, Bidies and Hukkah samples etc. would be analyzed for the estimation of toxic contents. An Instrument-specific training program for scientific and technical staff of the three NTTLS in the country was organized at NICPR from 25th to 27th March 2019.

- **Setting up of Population based Cancer Registry** at NICPR to cover Distt. Gautam Budh Nagar, U.P. to generate reliable data on the magnitude and patterns of cancer and

to undertake epidemiological studies based on results of registry data. Data collection in required format is in progress from various medical establishments in GB Nagar district. The registry has established linkages with HBCR, AIIMS and health promotion clinic, NICPR to capture the data of incident cancer cases.

ICMR-NATIONAL CENTRE FOR DISEASE INFORMATICS AND RESEARCH, BENGALURU

CANCER

Population Based Cancer Registries (PBCR)

This is the regular and long term activity of NCDIR under its National Cancer Registry Program (NCRP). PBCRs provide information on the incidence rates, burden and trends of cancer in the population. During 2018-19, three PBCRs were added to the existing 36 PBCRs under NCRP at Sher-I-Kashmir Institute of Medical Sciences, Srinagar, Jawaharlal Nehru Medical College, Aligarh and Indira Gandhi Institute of Medical Sciences, Patna.

PBCRs at Jawaharlal Nehru Medical College, Aligarh and Indira Gandhi Institute of Medical Sciences, Patna are the PBCRs that have been set up along the river course of Ganga.

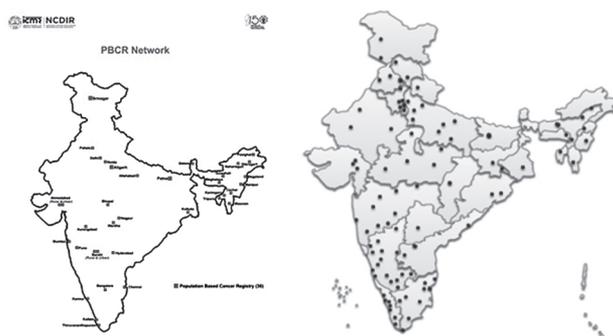


Fig. 3: Network of Population and Hospital Based Cancer Registries.

Hospital Based Cancer Registries (HBCR)

This is another long term ongoing activity which involves recording patient identifying information,

diagnostic details, clinical stage and treatment for all the proved malignant cases diagnosed in a particular hospital. During 2018-19, 21 new HBCR centres have been registered under the network of NCDIR-NCRP which is the repository of data. Under the 12th Five Year plan, the Regional Cancer Centres Scheme was renamed as Tertiary Cancer Care Centres/State Cancer Institutes (TCCC/SCI) and Ministry has identified 70 hospitals across the country to be funded. During this period, NCRP established HBCRs at two hospitals, Vivekananda Cancer Hospital, Latur and State Cancer Institute, Guwahati with funding support from MoHFW.

As on 31st March 2019, there are a total of 229 HBCRs under NCRP. A series of workshops/meeting were held during the year to train the investigators and the project staff working at the above registries in order to improve the quality.

Patterns of Care and Survival Studies (POCSS)

The primary purpose of hospital-based cancer registries is assessing patient care. Clinical stage-based survival and treatment-based survival are some of the key parameters for such assessment. Because of the challenges in obtaining follow-up parameters, a separate study on patterns of care and survival is being conducted at NCRP. As of March 2019, 28 TCCC/SCI/RCCs and 34 HBCRDM & SoR centres are transmitting data for the POCSS study. The study has been extended to Cancers in Childhood, Lymphoid and Hematopoietic Malignancies, other Gynaecological Malignancies except cervix and being undertaken at Chennai, Bangalore, Thiruvananthapuram, Delhi and Mumbai. The proforma and software has been designed and being deployed in all the centres and data collection to begin in all the centres.

A study on Patterns of Care and Survival Studies (POCSS) on Gall Bladder Cancer (GBC) in Indian Hospital Based Cancer Registries has been initiated in 2018-19 with the objective to determine detailed pattern of care (diagnosis and management), estimate demographic (Overall) survival and to identify the epidemiological, clinical and health system determinants of survival and estimate their

effect.

Development of an atlas of cancer in Haryana State

This project was sanctioned by Department of Health Research (DHR) under the scheme “Inter-Sectoral convergence and Coordination for Promotion and Guidance on Health Research” in December 2015 with the objective to get to know the similarities and differences in patterns of cancer across this state of the country in a cost-effective way, using recent advances in computer and information technology transmission. The project was undertaken in partnership of Office of DGHS, Haryana State Government. The project has provided district wise cancer statistics for Haryana. Besides creating awareness and strengthening cancer registration till CHC/PHC level, the data obtained through the project is both from urban as well as rural areas of Haryana state. The project has been completed on 31 March 2019. Few important findings of the project are highlighted in the following graphs and the maps.

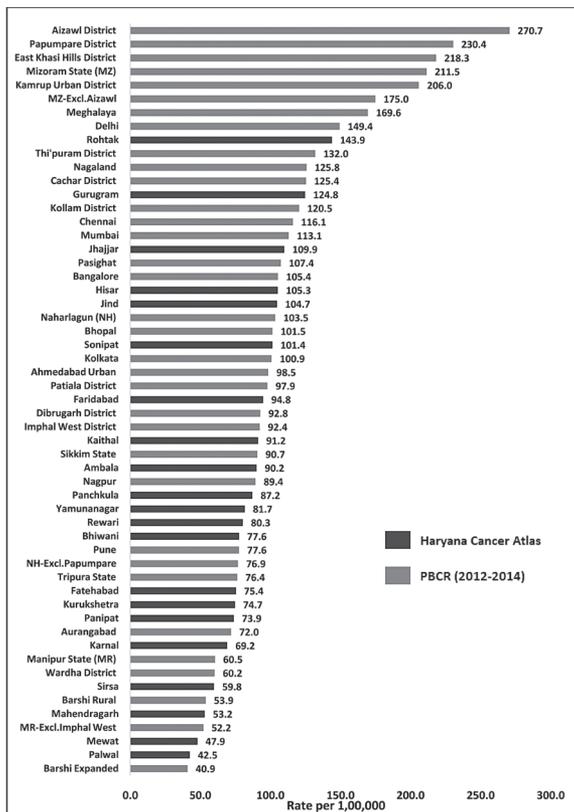


Fig. 4: District wise Comparisons of AAR* with that of selected PBCRs under NCRP. All Sites (ICD-10:C00-C96) - Males - (2016-2017).

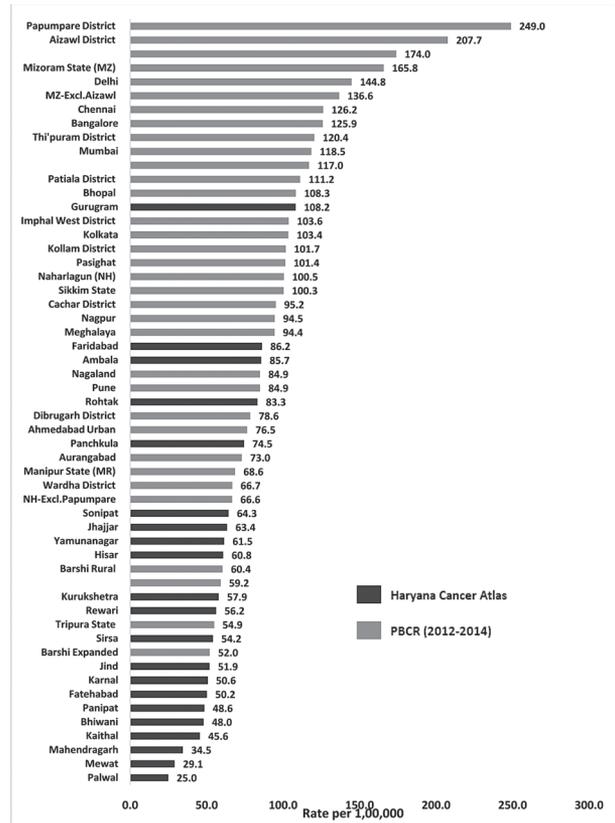


Fig. 5: District wise Comparison of AAR* with that of selected PBCRs under NCRP. All Sites (ICD-10:C00-C96) - Females - (2016-2017). *AAR- Age Adjusted Incidence rate

Males

- Rohtak district of Haryana with highest AAR comes in ninth position with AAR of 143.9/100,000 for all sites of cancer
- Nineteen districts of Haryana showed the AAR above Pune PBCR which had the lowest AAR of 77/100,000 but below that of Aizawl PBCR which is highest (270.7/100,000).

Females

- The Gurugram district of Haryana with highest AAR comes in fourteenth position with AAR of 108.2/100,000 with all PBCRs in India.
- Among urban PBCRs, eleven districts had a higher AAR than that of Tripura state (lowest AAR 54.9/100,000)
- Twelve districts had AAR above that of Barshi Expanded PBCR, which in females was 52.0/100,000

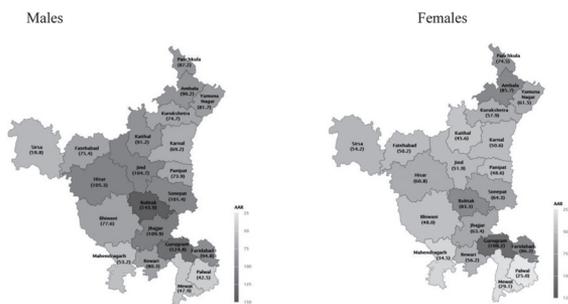


Fig. 6: District wise distribution of MAAR*- All Sites (ICD-10:C00 – C96) –(2016-2017).

*MAAR -Minimum Age adjusted incidence rate

- Districts with rates less than that indicated are given lighter shades.
- A belt of higher incidence of cancer is seen over Hisar (105.3), Rohtak (143.9), Jhajjar (109.9) Gurugram (124.8), Jind (104.7) and Faridabad (94.8) for males
- The relatively higher rates within the state are in tandem with incidence rates seen in PBCRs of neighbouring state/UT/districts of Delhi (149.4) and Patiala (97.9) which has been functional since 1988 and 2014 respectively
- For females similar belt with relatively higher rates within the state is seen.
- District of Ambala (85.7) also shows higher rates for females. The rates of these districts falling in the belt were comparable with Delhi (144.8) and Patiala (111.2) for females.

Population Based Cancer Survival on Cancers of Breast, Cervix and Head & Neck

The project has been initiated with the aim of generating reliable data on population based cancer survival in cancers of the breast, cervix and head and neck cancers and to know wherever feasible survival based on clinical stage/extent of disease across the Population Based Cancer Registries (PBCRs). Core proforma has been designed and the PBCR software has been appended for collection of the survival information. The revised software has been deployed in 23 registries with training for the staff out of the proposed 26 PBCRs. 12 PBCRs have started collecting follow-up data.

Cancer Samiksha, a data visualization portal shows the point of presence of Hospital Based Cancer Registries (HBCRs) and Population Based Cancer Registries (PBCRs) in the map of India, cancer statistics, allows online analysis, provides dashboard, generates tables and charts for further analysis. The location of centres contributing to the Karnataka and Haryana Cancer Atlas are also depicted in the respective state maps. A feedback window seeking opinions and suggestions from the users was provided for improvement. It can be accessed from www.ncdirindia.org/cancersamiksha. Recent infographics on cancer statistics have been added.

STROKE

Development of Population Based Stroke Registry(PBSR) in different regions of India

Population Based Stroke Registries have been established in the following five centres in one geographical area from the north, south, east, north east and west regions of India with the main objective to generate reliable data on the magnitude and incidence of stroke.

1. Institute of Medical Sciences, Banaras Hindu University, Varanasi
2. Tirunelveli Medical College, Tirunelveli, Tamil Nadu
3. SCB Medical College and Hospital, Cuttack, Odisha
4. Silchar Medical College, Cachar, Assam
5. Govt. Medical College & Associate Group of Hospitals, Kota

The staff from these centres have been trained at NCDIR and the centres have mapped the sources of registration in their respective areas. Data collation and transmission through the PBSR software module has started in January 2018 and is ongoing.

National Stroke Care Registry Programme: Development of Hospital Based Stroke Registries(HBSR) in Different Regions of India

The project has been initiated with the objective to generate reliable data on pattern of stroke and

pattern of care and treatment for stroke from major hospitals that treat stroke patients in India. Core form for HBSR has been revised as per the suggestions given by the experts and a procedure manual has been developed for the same. Development of HBSR data entry software module in open source Java platform has commenced. Data entry page template has been designed in html format. A sensitization workshop was held on ICMR- National Stroke Care Registry Programme regarding development of HBSR during the XIII Indian National Stroke Conference, Ahmedabad on 17th March 2019.

CARDIOVASCULAR DISEASES

A Study on the Magnitude and Pattern of Causes of Heart Failure-a feasibility study

The study has been initiated with the aim to understand the pattern of causes of heart failure, outcomes among attending and hospitalised patients in different geographies of India. The core proforma and the procedure manual have been finalized in consultation with the experts and sent to the centres. Work on data collection software has been completed and will be deployed. The centres are collecting the data in core forms.

List of study centres:

No.	Name of the Institution	City and State	Geography
1.	Indira Gandhi Medical College and Hospital	Shimla, Himachal Pradesh	North
2.	JLN Medical College and Associated Group of Hospital	Ajmer, Rajasthan	North West
3.	Sri Jayadeva Institute of Cardiology	Mysore, Karnataka	South West
4.	Tirunelveli Medical College	Tirunelveli, Tamil Nadu	South
5.	All India Institute of Medical Sciences (AIIMS) Bhubaneswar	Bhubaneswar, Odisha	East

MORTALITY

Implementation of NCDIR electronic Mortality software (NCDIR e-MOR) in hospitals of the National Cancer Registry Programme (NCRP) network in North East India

NCDIR electronic mortality (NCDIR e-Mor) software has been developed by the NCDIR team. The software captures information on all causes of deaths as per National list of the Office of Registrar General of India. The project aims to strengthen Medical Certification of Cause of Death (MCCD) reporting in hospitals through training, quality checks to avoid mode of dying and guide doctors in recording the underlying cause of death and report deaths. Sensitization workshop was conducted on 15th March 2018 where the Head of the Institutions and Principal Investigators of 8 centres from North East and few representatives of Chief Registrars of Births and Deaths from North East states were present. The training workshop was conducted on 22nd June, 2018 at Dr. B. Borooah Cancer Institute, Guwahati for the staff in registered Hospitals in the North East states.

The following centres are registered for implementing the project:

2017-18		
Sl. No.	State	Name of the Hospital
1-3	Assam	Dr. B. Borooah Cancer Institute, Guwahati
		Silchar Medical College, Silchar
		Cachar Cancer Hospital and Research Hospital, Silchar
4	Nagaland	Naga Hospital Authority, Kohima
5	Mizoram	Civil Hospital, Aizawl
6	Sikkim	STNM Hospital, Gangtok
7	Arunachal Pradesh	Bakin Pertin General Hospital, Pasighat
		Tomo Riba Institute of Health and Medical Science, Itanagar
8	Manipur	Regional Institute of Medical Sciences (RIMS), Imphal
2018-19		
9-11	Nagaland	Zion Hospital and Research Centre, Dimapur
		Christian Institute of Health Sciences & Research, Dimapur
		Eden Medical Centre, Dimapur

12	Mizoram	Mizoram State Cancer Institute, Aizawl
13	Sikkim	Central Referral Hospital, Gangtok

Implementation of NCDIR electronic Mortality software (NCDIR e-Mor) – strengthen Medical Certification of Cause of Death

The project was initiated on 01-12-2018. Six hospitals have registered to implement the NCDIR e-Mor software.

Sl. No.	State	Name of the Hospital
1	Punjab	Government Medical College & Rajindra Hospital, Patiala
2	Andhra Pradesh	Andhra Medical College, Vishakapatnam
3	Kerala	Malabar Cancer Centre, Kannur
4	Telangana	MNJ Institute of Oncology & Regional Cancer Center, Hyderabad
5	West Bengal	Peerless Hospitex Hospital and Research centre limited, Kolkata
6	Karnataka	St. John's Medical College Hospital, Bengaluru

NCD SURVEILLANCE

National NCD Monitoring Survey- 2017-18

The ICMR-NCDIR has implemented the survey at the behest of the Ministry of Health and Family Welfare, Govt of India to monitor the progress made at the national level towards achieving the national NCD targets by 2025. It has been undertaken in partnership and collaboration with AIIMS Delhi, National Institute of Medical Statistics (NIMS) New Delhi, National Institute of Epidemiology (NIE) Chennai AIIMS Bhopal, AIIMS Jodhpur, AIIMS Bhubaneswar, National Centre for Disease Control New Delhi, Assam Medical College Dibrugarh, BJ Government Medical College Pune, National Institute of Nutrition Hyderabad, AMCHSS Sree Chitra Tirunal Institute of Medical Sciences, Kerala and National Institute of Epidemiology Chennai.

The survey was implemented during October 2017 - May 2018. The data collected has been synced and cleaned for quality checks. The quality data thus obtained was subjected to analysis and the results

of the factsheet and the final report have been presented to the TWG members following a 3-day workshop on “Data analysis and Report writing” was conducted for all the survey implementing agencies PI’s and Co-PI’s. The factsheet of 21 NCD indicators and the final factsheet of NNMS 2017- 2018 have been submitted to the Ministry of Health and Family Welfare, Govt of India. The Technical working group meeting held on 24th of January 2019 discussed the final draft report with results, executive summary and recommendations for approval.

National Burden of Non communicable Diseases and associated risk factors - Cancer working group

The project aims to estimate burden of cancer and its associated risk factors in India. The draft report has been submitted to the TAC committee. The suggested recommendations following the submission are being implemented and the same were resubmitted and discussed in the National Technical Advisory Committee meeting during March 2019.

BIOETHICS

Common forms for Ethics Committee

Currently, in India, different formats are being followed by various Ethics Committees (EC) in the country, for the ethical review of proposals submitted. This was causing difficulties especially, when multi-centric research studies were to be conducted using common protocols. To address the felt need, ICMR had prepared draft EC forms and checklists for use by Ethics Committees. Further, the forms were field tested at 5 institutes across the country to evaluate the structural and functional ease in translating a research protocol into ethics committee review format. The evaluation used a mixed methods approach of a quantitative survey using a structured questionnaire and a qualitative assessment using in-depth interviews with researchers and member secretaries of ethics committees and qualitative analysis was coordinated by Sree Chitra Tirunal Institute for

Medical Sciences and Technology (SCTIMST), Thiruvananthapuram. The results of the study helped to revise the common EC forms and finalize for use across the country. The forms were revised based on the results of the pilot study and finalized during the ethics advisory committee meeting held on 10th and 11th September, 2018 at ICMR-NCDIR, Bangalore. The comments from experts who attended the consultation meetings at NCDIR, Bangalore and THSTI, Faridabad were also reviewed and incorporated in the form wherever necessary. The “Common EC forms for ethics committee review” were released at NCDIR on 7th December 2018. These forms are available free for download in PDF and word formats.

Ref:- ICMR, 2018 Common Forms for Ethics Committee Review – available at <http://www.ncdirindia.org/ETHICS/CF/index.html>

An International FERCAP Survey entitled “A Survey of What Information Research Participants Would Like to Know in Informed Consent Forms in Biomedical Research”

A multicentric, cross-sectional, descriptive survey was simultaneously carried out in 7 member countries of Forum for Ethical Review Committees in the Asian and Western Pacific region (FERCAP). ICMR Bioethics Unit, NCDIR, Bangalore coordinated this multicentric study in India which was conducted at five centres for three months from June 1 to August 31, 2017. Four regional centres were identified for the survey in different parts of the country, the centres involved in the study were (NIRT, Chennai (South); NIRRH, Mumbai (West); SGPGI, Lucknow (North) and NICED, Kolkata (East)). A common anonymous, paper-based, structured and self-administered questionnaire was used at the sites to collect information from research participants. The study concluded that the research participants would like to be informed of the ICF elements required by ethical guidelines and regulations; however, the importance of each element varied with the region.

The outcomes of this survey study will be beneficial to both investigators and ethics committee members as the study results provide important insights about the Informed Consent Form (ICF) that will guide the investigators to develop better and more suitable ICFs for their biomedical research studies as well as help the ethics committee members when they assess ICFs during the ethical review and approval process.

Handbook on ICMR National Ethical Guidelines for Biomedical and Health Research Involving Human Participants.

The handbook has been drafted by ICMR to provide stakeholders such as students, researchers and ethics committees with a simple and precise document which is adapted from the “National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, 2017”. The handbook provides a summary of the guidelines and was released by Dr Shekhar C Mande, Secretary DSCIR and DG CSIR during the Symposium on Gandhi & Health @150 at ICMR Headquarters, New Delhi on 26th March 2019. This handbook will be very handy for use by students, clinicians and scientists and is expected to improve the ethical conduct of research in India.

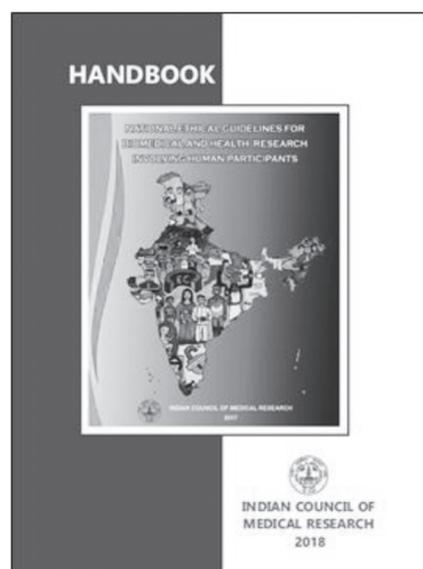


Fig. 7: Handbook on ICMR National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, 2017.

Bioethics webpage:

A dedicated webpage with bioethics resources and updates has been developed. It would improve the access of various stakeholders and other national and international agencies to ICMR Bioethics

unit and its activities. Webpage will also serve as a means to disseminate the tools and instruments such as National Ethical Guidelines, Common Ethics committee forms and other relevant policy documents.



Fig. 8: Bioethics webpage in NCDIR website.

BASIC MEDICAL SCIENCES

The Basic Medical Science division coordinated intramural research in the field of basic medical sciences at the National Institute of Pathology (NIOP), 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. Nanomedicine, Haematology, Biochemistry, Pharmacology, Physiology, Human genetics, Stem cell research, Genomics, Allergy, Immunology, Translational Neuroscience, Drug development initiative. The division also coordinated NAC-SCRT secretariat and Standing committee on national list of essential medicines (NLEM).

INTRAMURAL RESEARCH

ICMR-NATIONAL INSTITUTE OF PATHOLOGY, NEW DELHI

Comparative study of Genetic, Clinical and Epidemiological factors of Breast Cancer in Indian population.

The genomic basis of breast cancer in Indian women is being evaluated in a multicentric task force project. The work done so far includes transcriptome profiling of 24 pairs of tissue samples (tumour and adjacent normal) from mastectomy and lumpectomy specimens. Cases were classified according to molecular classification after immunohistochemistry for Ki67, ER, PR and Her2neu and FISH where Her2neu by IHC was 2+. More number of samples will be collected and

transcriptome profiling and data analysis will be done.

Molecular profiling of invasive urothelial carcinoma.

The tissue samples of bladder tumour and adjacent normal appearing tissue as well as urine were being collected from the urology ward. Transcriptome profiling of 8 pairs of tissue samples has been done. Data is being analysed but preliminary analysis shows that Cancer testis family genes are upregulated in invasive cancer.

***In vitro* evaluation of effect of PKCε silencing on tumor invasiveness in urothelial cancer.**

Urothelial cancer cell lines (T24 and 5376) were obtained and PKCε and ζ silencing experiments were carried out. The kinase activity assay showed significant decrease in both PKC isoforms (ε and ζ) in both cell lines after transfection. PKCε and ζ gene expression was reduced significantly in T24 cells after transfection but the reduction was not statistically significant in 5376 cell line. The expression of downstream pathways genes involved by PKCε and PKCζ were evaluated after silencing and compared with the expression before silencing.

A pilot study to determine causes of death in under-five children in a tertiary hospital in Indian using the MITS technique.

Minimally Invasive Tissue Sampling (MITS) technique has been applied to sample tissues and biofluids from U5 (under five) children after

consent was obtained from parents. The samples collected include CSF, blood, Nasopharyngeal and rectal swab. Tissues collected include liver, kidney, spleen, brain, left and right lung, heart. Both pathological and microbiological study is being conducted on these post-mortem samples to assign cause of death.

Table 1. Cases performed between Jan 18, 2019 to March 31, 2019

Cases	Still Birth	U-5 Neonate (0-28 days)	U-5 (28days-5years)
Total Cases approached	06	17	08
No. of Cases eligible for Inclusion	06	15	06
No. Cases with Successful Consent administration	05	08	02
No. Cases with Consent not obtained	01	07	04

Genome wide analysis of genetic alterations and gene expression profile in hormone sensitive and hormone refractory prostate cancer.

Array comparative genomic hybridization and analysis were performed in prostate tissue samples. Array analysis detected higher frequencies of genomic aberrations in malignant tissues. Genomic loci at chr14 involving ADAM6, LINC00226 were observed to be amplified in all tissue samples. Furthermore, gain/amplifications in ZIC4, ZIC1, GDI1 and loss/deletions in ANTXRLP1, ANTXRL, PTEN, RNLS genomic loci were found to be associated with prostate cancer aggressiveness.

Molecular regulation of mTOR signaling in acute lymphoblastic leukemia.

Acute Lymphoblastic Leukemia (ALL) is caused by the uncontrolled clonal proliferation of immature lymphoid cells. The Aim of the study is to identify the regulatory molecules of mTOR signaling in acute lymphoblastic leukemia. mTOR expression in T-ALL cell lines was found to be upregulated in both the cell lines. Since Jurkat cells demonstrated much higher mTOR expression, it was used for further experiments.

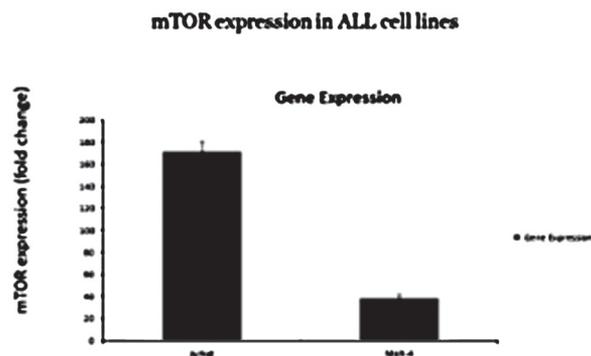


Fig. 1: mTOR expression in T-ALL cell lines.

Jurkat cells were seeded in 6-well plate and were treated with different concentration of rapamycin for 48 hrs. Cell viability assay was done using trypan blue. Number of live cells were plotted against concentration of drug. IC₅₀ was found to be at 10uM.

The results highlight the importance of mTOR signaling in poor clinical response in ALL patients. Also, it was found that combination of conventional chemotherapeutic drugs with rapamycin has more impact on hyper activated mTORC1 and mTORC2 signaling in T- ALL cell line.

Role of IL-8 Signalling in Glioblastoma Progression.

Glioblastoma Multiforme (GBM) is one of the most vascular neoplasms characterized by robust micro vascular proliferation. Formation of vessels in tumors may take place by several mechanisms, most of which are endothelial cell-dependent while one mechanism named vascular mimicry is endothelial cell independent. In the present study, we investigated the potential of targeting IL-8/CXCR1 axis with pharmacological antagonist on VM formation in vitro.

Since IL-8 exerts its effect through two of its cognate receptors CXCR1 and CXCR2, both of which have been shown to play significant role in GBM previously, study used chemical antagonist of CXCR1 and CXCR2 (Reparixin-l-lysine) to block this axis and check its effect on VM formation. (Fig 2). These results indicate strong anti-VM potential of targeting IL-8/CXCR1/CXCR2 axis in GBM cell line.

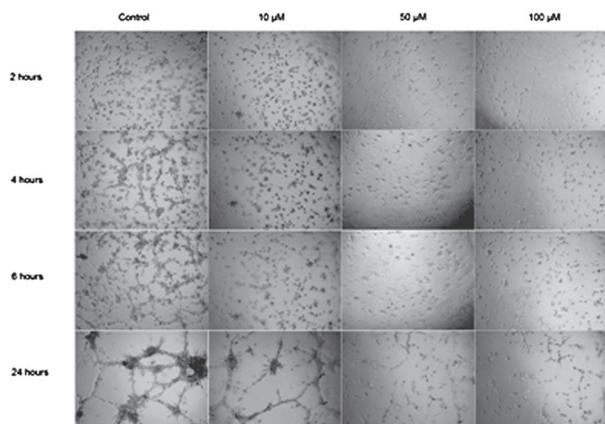


Fig. 2: Tube formation assay: Effect of Reparixin-l-lysine (chemical antagonist for CXCR1 and CXCR2) at different concentration and at different time interval on tube formation capacity of U-87MG cell line.

Autoantibody Response and Identification Of Tumor-Associated Antigens In Gallbladder Carcinoma - Immunoproteomics Approach.

Early diagnosis is important for improved treatment of Gallbladder Carcinoma (GBC) patients, leading to the increased survival rate. Here, centre has applied Serological Proteome Analysis (SERPA), an immunoproteomics approach for detection of Tumor Associated Proteins (TAPs) eliciting humoral response in GBC patients with early stages. Liquid Chromatography- Tandem Mass Spectrometric analysis (LC-MS/MS) led to identification of proteins from the immunoreactive spots, including Annexin A1 (ANXA1), and Heat Shock Protein 60 (HSP60), Arginase-1, Vimentin. Dot blot assay for two of the identified proteins, ANXA1 and HSP60 using individual blood plasma samples (30 cases and 20 controls), showed 33% and 66% sensitivity to detect early stages of GBC, respectively. The study showed that a combination of ANXA1 and HSP60 may be included in the panel of markers for detection of GBC at early stages.

Proteomic Analysis of Plasma Exosomes to Identify Circulatory Biomarkers for Gallbladder Carcinoma.

Extracellular Vesicles (EVs) are microvesicles, secreted by all cell types and contain various bioactive molecules - miRNA, mRNA, DNA, proteins, lipids. In this study, centre has analyzed

plasma-derived EVs with an aim to detect circulatory biomarkers to detect GBC cases. Total EV protein was extracted to identify proteins with altered levels in GBC. Mass spectrometric analysis led to identification of 57 proteins having altered level in GBC. The clinical verification of functionally relevant proteins using ELISA/ Western blot analysis is in process.

TUBERCULOSIS

FDA approved drugs and nanoparticles inhibit biofilm formation and enhances the efficacy of anti-TB drugs.

Mycobacterium tuberculosis (*M.tb*), like other bacterial pathogens, creates an ecosystem of biofilm formed by several proteins including the cyclophilins. The study showed that the *M.tb* cyclophilin peptidyl-prolyl isomerase (PpiB), an essential gene, is involved in biofilm formation thereby making *M.tb* tolerant to anti-mycobacterial drugs (Fig 3). The study showed interaction between PpiB and US FDA approved drugs (cyclosporine-A and acarbose) by *in-silico* docking studies. Cyclosporine-A and Gallium Nanoparticle (GaNP) additionally disrupted *M.tb* H₃₇Rv biofilm formation. Co-culturing *M.tb* in their presence resulted in 2-4 fold decrease in dosage of anti-tubercular drugs- isoniazid and ethambutol. Comparison of the cyclosporine-A and acarbose binding sites in PpiB homologues of other biofilm forming infectious pathogens revealed that these have largely remained unaltered across bacterial species. Targeting bacterial biofilms could be a generic strategy for intervention against bacterial pathogens.

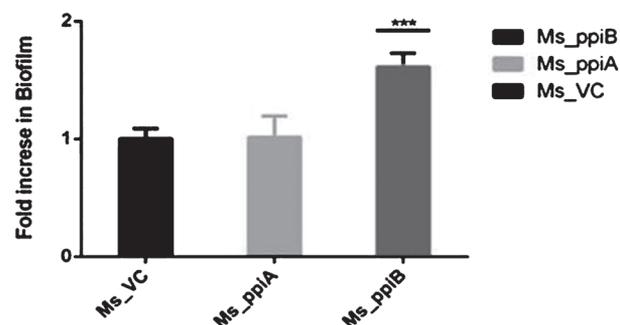


Fig. 3: *Mycobacterium tuberculosis* PpiB is involved in Biofilm formation.

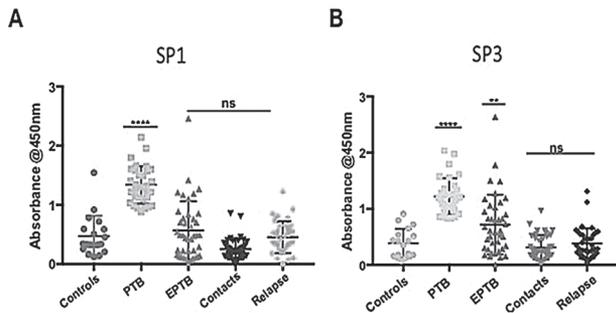


Fig. 8: SP1 and SP3 induce strong B cell immune response in tuberculosis patients.

PCR based NAAT assays based on Genes Specific to Mycobacterium tuberculosis.

Nucleic Acid Amplification Test (NAAT) is a highly sensitive molecular technique based on Polymerase Chain Reaction (PCR) and helps in the detection of low density microbial infections. The study aimed to design a Nucleic Acid Amplification Assay (NAAT) for the diagnosis of *M.tb* based on the genome sequences which are unique to *M.tb*. A pilot study to determine the specificity of these four Signature Sequence (SS) probes on clinical samples were carried out and compared with other WHO approved methods. All samples underwent PCR with SS probes as well as IS6110, while 158 samples went through GeneXpert and 103 samples were subjected to culture. Only 28 of the 31 sputum smear positive samples turned out to be culture positive which gave a sensitivity of about 90%. Signature Sequence probes gave the highest sensitivity of 96% as compared to commonly used GeneXpert, was the highlight of this study (Fig 9).

	PCR with IS6110	GeneXpert	Culture	PCR with SS sequences
Smear Positive Cases (Sensitivity)	77%	93%	90%	96%

Fig. 9: Sensitivity analysis of the SS probes as compared to the other test.

LEISHMANIASIS

Studies on mechanism of resistance towards artemisinin in Leishmaniadonovani.

Artemisinin, isolated from *Artemisia annua*, has demonstrated effectiveness in experimental models of leishmaniasis. AS-R parasites showed up-regulated expression of genes of unfolded protein response pathway including methyltransferase domain containing protein (HSP40) and flagellar attachment zone protein (prefoldin), that are reported to be associated with ART resistance in *Plasmodium falciparum* malaria.

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.

The current chemotherapy for post-kala-azar dermal leishmaniasis, faces major hurdle as drugs are costly and show resistance with passage of time leading to therapeutic failure or relapses. The study aims at effectively monitoring the drug efficacy in terms of parasite clearance and restoration of various immunological parameters. Confirmed cases of PKDL[n= 10;macular (n=3), papular (n=4) and nodular (n=3)]were included, of which 4 patients were put on treatment with Miltefosine (MIL) monotherapy, 2 on Liposomal Amphotericin-B treatment (LAmB) and 4 were administered combination therapy consisting of MIL and LAmB. Parasite load was estimated in slit aspirate and blood at different time points of treatment. The median parasite load at pre-treatment stage was 364 parasites/μL of slit aspirate which declined to 25 parasites/μL and finally regressed to 6 parasites/μLat post-treatment stage. [Fig-10]. Parasite DNA was detectable in 7 out of 10 blood samples at pre-treatment stage. Only in two cases, the parasite load was seen at mid-treatment stage. No parasite was detected at post treatment stage. Further, efficacy of different drug regimen in terms of parasite clearance will be ascertained by pooling data from larger number of cases.

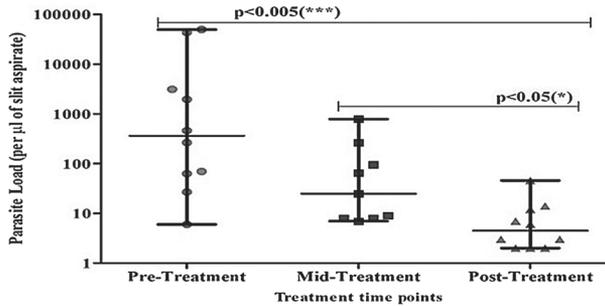


Fig. 10: Parasite kinetics in slit aspirate of PKDL patients. The parasite load has been estimated at pre, mid and post treatment stages using real time quantitative PCR. The load has been shown as median value with range.

DEVELOPMENT OF DIAGNOSTICS FOR INFECTIOUS DISEASES.

Development of multiplex loop mediated isothermal amplification assay (m-LAMP) for differential diagnosis of PKDL and Leprosy.

Centre has developed a LAMP assay for a rapid and accurate diagnosis of leprosy with high sensitivity and specificity compared to conventional histopathology based methods. Further, we have developed a multiplex (m)-LAMP assay for differential diagnosis of Leprosy and PKDL that are co-endemic diseases with similar clinical presentation using real-time fluorometer. The m-LAMP was rapid with mean amplification time of 15:23 minutes; analytical sensitivity of 1fg for *Leishmaniadonovani* and 100fg for *Mycobacterium leprae*. The distinct mean T_m values of $90.32 \pm 0.22^\circ\text{C}$ for *M.leprae* and $88.68 \pm 0.05^\circ\text{C}$ for *L. donovani* allowed differentiation of the two organisms in m-LAMP. The diagnostic sensitivity of m-LAMP with confirmed cases of Leprosy and PKDL was 100% (95% confidence interval (CI) - 91.19% to 100.00%) for detecting PKDL and 95% for leprosy (95% CI- 83.08% to 99.39%).

MALARIA

Novel quantitative isothermal fluorescence based rapid detection method for the diagnosis of malaria.

This study is aimed to develop a rapid, quantitative molecular assay for diagnosis of Malaria. A set

of six LAMP primers targeting specific repeat sequence for *P. vivax* and 18S rDNA region for *P. falciparum* was designed. Analytical sensitivity of the LAMP assay was found to be 71 parasites/ μl and 20 parasites/ μl , respectively. Multiplex LAMP assay was established to detect co-infection cases of *P. vivax* and *P. falciparum* simultaneously in a single reaction according to the annealing temperature.

ANTIMICROBIAL RESISTANCE

Phenotypic and genotypic characterization of polymyxin (colistin) resistant Gram-negative bacteria isolated from patients with blood stream infections.

Screening of colistin resistant ($\text{MIC} \geq 2 \mu\text{g/ml}$) isolates, identified *Klebsiellapneumoniae* and *Acinetobacterbaumannii*. *A. baumannii* (n=6) isolates exhibited multidrug resistant and extensively drug resistant phenotype, with colistin MICs ranging from $8 \mu\text{g/ml}$ to $\geq 128 \mu\text{g/ml}$. Colistin resistant in *A. baumannii* isolates was majorly attributed to base mutations in chromosomally encoded genes *pmrB*, *pmrC*, *lpxA*, and *lpxC* genes involved in lipid A modification. All the isolates were negative for plasmid mediated resistance due to *mcr*-genes. Identification of diverse mutations imparting colistin resistance, highlights emergence of discrete resistance response to the rampant use of colistin.

Study on matrix metalloproteinases and their inhibitors in women with *Chlamydia trachomatis*-associated ectopic pregnancy.

The expression of selected Matrix Metalloproteinases (MMPs)/ Tissue Inhibitor of Matrix Metalloproteinases (TIMPs) genes is being evaluated in *C. trachomatis*-infected tubal Ectopic Pregnancy (EP) patients. Ct604 was found to be the predominant *C. trachomatis* *hsp60* gene in tubal tissue of EP women.

Immunogenetic study on enzymatic antioxidants in *Chlamydia trachomatis*-associated spontaneous aborters.

Infection with *C. trachomatis* is associated with adverse obstetric outcomes including recurrent spontaneous abortion. MicroRNAs (miRNAs) expressed by the interaction between *Chlamydia* and host may regulate the inflammatory process and level of pathology. It was, therefore, proposed to investigate the expression profile of selected circulating miRNAs in Recurrent Spontaneous Abortion (RSA) patients by qRT-PCR analysis found to be infected with *C. trachomatis*.

Study of HLA-DR3 and/ or DQ2 restricted CD4+T cells in Type 1 diabetes in North India.

The study is being carried out to identify HLA-DR3 and/or DQ2 restricted GAD65 peptide epitopes which might be responsible for activating auto-reactive CD4+ T cells leading to autoimmune response against pancreatic islet β cells in T1D patients. We have developed a tagged SNP based PCR method to identify HLA-DR3/DQ2 positive individuals; this was validated by PCR-SSP (Sequence Specific Priming) method. The PBMCs from HLA-DR3/DQ2 positive patients and healthy controls have been cultured with multiple pools GAD65 peptides and CD4 T cells are being studied for intracellular cytokines like IFN γ , TNF α , IL17 and IL10. A data on smaller number of patients show the pro-inflammatory immune response by CD4 T cells against GAD65 peptides. More number of study subjects will be recruited for meaningful conclusion of the study.

BIOINFORMATICS AND ENVIRONMENTAL TOXICOLOGY

dbGAPs – Data analysis.

Analytical reports on gene ontology terms and pathways for genes listed in dbGAPs have showed altered genes are majorly associated in immunity and inflammation. It also revealed genetic variations on specific genes uniquely associated with psoriasis subtypes. Twenty hub genes playing vital role in psoriasis pathogenesis are identified as potential therapeutic targets.

FGFR1 as potential biomarker for developmental defects.

Microarray gene expression analysis showed the dysregulated genes between smoker and non-smoker umbilical cord samples. Further, network and module analysis revealed FGFR1 to be the seed gene and potential biomarker for developmental defects in new-borns.

pLBW webserver for low birth weight prediction.

The web-server is based on the maternal characteristics and blood PAHs concentration. The models were developed using Support Vector Machine, Random Forest, Artificial Neural Network, *etc.* algorithms in SVM^{light} and Weka software. The models integrated in the server could predict potential IUGR new born with blood pesticide concentration.

Immunoassay Kit Development for Chlorpyrifos Detection.

In silicologation of linkers with chlorpyrifos and molecular docking based binding affinity & simulation towards Bovine Serum Albumin, Human Serum Albumin and Ova albumin have been performed. With subsequent experimental validation and kit development, it would be highly useful for mass screening.

In silico fungal drug target identification.

In silico target identification through genomics, pathway and network analysis has been completed. Systems biology based analysis and experimental evaluations are on-going (MIC test completed, Resistant strains of *Candida* need to be acquired for silencing of selected genes through siRNA).

Developing prediction server for molecular subtyping of psoriasis from transcriptome data.

Differential Gene Expression analysis and network analysis have been completed.

TiD v2.0.

An automated tool for drug target mining from whole proteome of bacteria and fungi was developed that can complete target mining within 2hrs.

Laboratory Information Management System.

It would be useful for online reporting of histopathology, cytology, electron microscopy and microbiology laboratory test reports generated at NIP. The reports can be assessed by patients and doctors directly. This will add improved efficiency, cost reduction and compliance in patient care. LIMS architecture developed and hosted over institute LAN.

Clinical Decision Support System.

Initiated developing histopathology image knowledgebase as part of extramural project "Clinical decision support system to identify histogenesis in cases of carcinoma with unknown primary (CUP)".

Training Programmes -M.Sc. and B.Tech (Biotech)

- Dissertation on Exploration of Hub Genes and Key Pathways of Psoriasis Using Transcriptome Analysis by B.Tech student from Amity University, Bareilly.
- To study genetic expression of IL-36RN as potential marker in psoriasis pathogenesis by M.Sc. Student from Jamia Hamdard, New Delhi. (On-going)
- Construction of atom based 3-D QSAR model using p-values of pesticides by M.Sc. Student from Jamia Hamdard, New Delhi. (On-going)

ICMR-NATIONAL INSTITUTE OF IMMUNOHAEMATOLOGY, MUMBAI

Centre of Excellence for diagnosis, management, and research of Primary Immune-deficiency disorders.

This project was initiated in Feb 2017 and centre established the state of art facilities for evaluation of suspected cases of PIDs. One of the important tests that have been standardized this year has been 3 laser 12 colour lymphocyte subset analysis

enabling us a comprehensive analysis of various T, B and NK cell subsets simultaneously.

In the last one year, centre has evaluated total of 879 suspected cases of PID; of these 100 cases were diagnosed for specific PIDs. Over the years, centre has established a large cohort of specific PIDs and has helped to develop specific algorithms for Indian PID patients. The centre had published last year algorithms for CGD and SCID suitable for Indian population. The centre has also performed molecular characterization of diagnosed PIDs using various techniques including Sanger sequencing, gene scan, Long-range PCR and targeted NGS. Prenatal diagnosis was provided to 7 affected families. Apart from this, 5 research projects on the different PIDs which include HLH- a disorder of immune dysregulation, ALPS, INF- γ -IL-12 loop defects causing MSMD and LAD-I have also given us very useful information on these specific PIDs.

Satellite centre for Hemoglobinopathies at Chandrapur.

This centre has been established since 2015 in the TB Hospital premises near GMC, Chandrapur as the prevalence of haemoglobinopathies is very high in central India. Comprehensive diagnosis facilities including HPLC and molecular diagnosis have been established at the center and it is currently running programmes like population screening, antenatal screening, newborn screening, and antenatal diagnosis. A total of 570 SCD, 81 Sickle/ β thalassemia, and 34 β -Thalassemia major cases have been enrolled and provided comprehensive management. Under antenatal screening programme, a total of 9564 pregnant women were screened and 330 women were found to be sickle cell trait and 12 were sickle cell anemia (SS) while 17 were β -thalassemia trait and provided genetic counseling. Newborn screening programme has identified 85 sickle cell heterozygous and 4 sickle cell homozygous babies.

Molecular characterization of undiagnosed cases of congenital hemolytic anemia using a multigene next-generation sequencing panel.

Molecular characterization of 45 cases of severe transfusion dependent anemia cases was done by targeted next-generation sequencing and discovered many new genetic defects such as Hexokinase deficiency, Novel *CI5ORF41* gene mutation causing CDA type Ib first time in Indian populations. Several novel mutations were detected in pyruvate kinase gene, 5 new cases of R347H mutation in glucose phosphate Isomerase gene and 3 novel mutations in pyrimidine 5' nucleotidase gene. The prenatal diagnosis was successfully offered to glucose phosphate Isomerase deficient patients.

Study of Genotypes, Phenotypes and search for new genes in patients of Fanconi anemia with no mutations in known genes.

The breakthrough in the present study is that the FANCL gene mutation is the second frequent

mutation gene in Indian FA patients. The haplotype analysis from SNP array data revealed that the FANCL mutation as a founder mutation in the Indian population.

DNA analysis of blood group antigens.

This project helped in establishing simple molecular methods for genotyping Colton, Dombork, Indian, Diego, Cartwright, Miltenberger blood group system antigens. The study standardized molecular methods for screening antigens of Dombork and Diego blood group systems, which will enable to know the frequency of these antigens for the first time in the Indian population. The database of antigen typed regular blood donors will be prepared. This will help us to prepare reagent red cell panels for identification of clinically significant antibodies against these blood group antigens.



Fig. 11: World Immunology week was celebrated on 26th April 2018 at B. J. Wadia Childrens Hospital.



Fig. 12: Conference on “Upcoming avenues for elimination for Viral Hepatitis in India” was organized to celebrate World hepatitis day on 29th July 2018.



Fig. 13: Swachh Bharat Abhiyan drive at Mumbai High School, Lalbaug in July, 2018.



Fig. 14: Two-day symposium and one-day flow-cytometry workshop on the diagnosis of PID was organized at ICMR-NIIH from 5th to 7th September 2018.



Fig. 15: An Outreach Programme under the banner of India International Science Festival & Expo was organized on 25th September 2018.



Fig. 18: 5th International Conference of Primary Immunodeficiency disorders - ICPID was organized from 9th-11th March 2019.



Fig. 16: 1st NIIH Diamond Jubilee Oration was awarded to Dr. Navin Khattry, ACTREC on 26th November 2018.



Fig. 19: Dr. H. M. Bhatia Oration for the year 2019 was awarded to Dr. Anand Deshpande, Hinduja Hospital on 11th Feb 2019.



Fig. 17: The 20th INDO US Flow-cytometry workshop- for diagnosis of Primary Immune-deficiency disorders was organized from 7th-8th March 2019.

ICMR-NATIONAL INSTITUTE OF TRADITIONAL MEDICINE, BELAGAVI

TRADITIONAL MEDICINE

Evaluation of anti-inflammatory and analgesic activities of *Plumbago zeylanica* L. root paste in osteoarthritis of knee joints.

A single centric, open clinical trial was conducted with an objective to evaluate the analgesic and anti-inflammatory activities of *Plumbago zeylanica* L. Root Paste in Osteoarthritis of knee joints. In this trial, the patients were randomly assigned into 3 groups and the affected joints were subjected to topical application of root paste of Chitraka (*Plumbago zeylanica* L.) followed by fomentation with hot water bag for a period of 7 days, twice in a day. The patients were evaluated and assessed on days 0, 8, 22 & 37. The VAS Score was used to assess the subjective parameter of pain; while WOMAC Scale was used to evaluate the osteoarthritis of knee: including pain, stiffness, and physical functioning of the joints. The objective parameters were walking velocity, tenderness, crepitus, knee circumference and range of movements. As per the IEC suggestions, safety parameters (Hematological parameters, Renal Function Tests and Liver Function Tests) were carried out on Day 0, 22 and 37. Based on the clinical findings, the following observations were made.

Majority of the subjects showed reduction in symptoms and were able to perform routine activities with more ease after topical application. Greater improvement was observed in parameters like swelling, pain, and tenderness, that too more in Mild group, in comparison to the Moderate group. After the topical application of the root paste, increase in joint mobility was found owing to improved walking velocity. The safety parameters obtained were within normal limits which indicate the drug safety.

Preclinical evaluation of safety and efficacy of the decoction of the plant RMRC-BM IP_156

for anti-diabetic activity and characterization of active compound(s).

A decoction of leaves of a plant RMRC-BM IP_156, a lead from a local traditional practitioner for the management of type 2 diabetes, (widely distributed all over India) is being validated scientifically. The efficacy of decoction was tested in chemically induced diabetic rat model and the lyophilized decoction showed prominent anti-hyperglycemic activity including diabetic complications.

Evaluation of Add on Efficacy & Safety of an Ayurvedic Formulations in the management of Dengue Fever & prevention of its complications-A Double Blind Clinical Study.

The study was carried out in KLE hospital; the dengue patients were recruited based on inclusion and exclusion criteria approved by the ethical committee. The patients were divided into two groups after baseline screening. In the trial group, the patients received trial formulation whereas the other group received standard dengue care. This study showed that trial formulation can shorten the duration of illness, reduce the severity of symptoms and prevent the development of severe complications like Dengue hemorrhagic fever and dengue shock syndrome.

ICMR-Networking Centre for Product Development & Rational Use of Medicine.

The project has been initiated and is in progress.

Screening and development of antimalarial drug of herbal origin through target-based drug development approach.

Based on the available literature, two medicinal plants viz., RMRC-NTD-M1 and RMRC-NTD-M2 were tested for antimalarial activity. The hydroalcoholic extract of leaves of RMRC-NTD-M1 showed 65.45% inhibition of *Plasmodium falciparum* Transketolase (P_{TK}). Methanol extract of leaves of RMRC-NTD-M1 and RMRC-NTD-M2 showed 92.85% and 70.55 % inhibition of the enzyme while ethyl acetate extract of the latter plant showed 86.91 % inhibition. Ethyl acetate extract of

bark of plant RMRC-NTD-M2 showed 88.33% inhibition and hence more potent than other extracts. Thus, both the plants showed potent inhibition activity against *PfTK*. On the basis of enzyme *PfTK* inhibition, the extracts of the plant which showed very high activity were tested for anti-malarial activity using *P. falciparum* (strain 3D7, chloroquine sensitive strain) *in vitro*. The hydro-alcoholic extract of leaves of RMRC-NTD-M1 showed 114.35% inhibition of the parasite with EC50 4.17 µg/ml. Ethyl acetate extract of bark of RMRC-NTD-M2 showed 46.71% of the parasite with EC50 1.94 µg/ml. Further, these extracts were fractionated and out of 90 fractions of hydro-alcoholic extract of leaves of plant RMRC-NTD-M1, 6 fractions showed more than 90% anti-malarial activity. Fraction HA4 showed highest level of activity (124.23% growth inhibition with EC50 0.52 µg/ml), while fraction G3 showed slightly lesser activity (97.90% growth inhibition with EC50 0.63 µg/ml. Fraction EA1 of ethyl acetate extract of bark of the plant RMRC-NTD-M2 showed 97.46 % with EC50 0.66 µg/ml. Thus, both the plant extracts showed potent antimalarial activity against *P. falciparum* in “*in vitro*” assays. The toxicity studies were carried out using zebra fish (*Danio rerio*) embryo model and the results showed that hydroalcoholic extract of leaves of RMRC-NTD-M1 showed LC50 100 µg/ml and ethyl acetate extract of bark of RMRC-NTD-M2 showed LC50 10 µg/ml. Thus, both the plants showed potent antimalarial activity and need to be studied further.

INFECTIOUS DISEASES

Validation of rapid point of care immunological diagnostics for lymphatic filariasis.

A prototype lateral-flow point of care (POC) for detecting antifilarial antibodies was developed and evaluated for its efficacy in detecting the infection in individuals residing in filariasis endemic communities. Currently available filariasis diagnostics are imported, expensive (Rs.400 per test) and not available in adequate numbers to cater to the huge needs of GPELF. The centre has developed PoC prototype using an antigen

for detecting filarial specific antibodies which, in preliminary tests, has shown good differentiation between infected (microfilaria positive) and uninfected individuals. Furthermore, these test kits will be indigenous, less expensive and can be produced in adequate numbers. Unlike the tests available, the proposed test will specifically detect the most recent exposure/infection, which is the need of the global LF elimination programme.

Immunomodulation by Parasitic Macrophage Migration Inhibitory Factor in Type 1 and Type 2 Diabetes animal Model.

The objective of this project is to investigate the immunomodulatory effects of Macrophage Migration Inhibitory Factor of *W. bancrofti* (Wb-MIF) in type 1 and 2 diabetes. So far, wild type Wb-MIF2 protein and mutant type protein of wb-MIF2 was purified successively and checked for purity on 12% SDS-PAGE. The purified protein was checked for its enzymatic activity and found to be active against its substrate. In order to study its effect on signaling pathways Wb-MIF2 was treated to RAW 264 macrophage *in-vitro*, glucose uptake assay was done on differentiated adipocytes *in-vitro* and the cell lysate was subjected to phosphoproteomics study. Phosphoproteomics study showed that wb-MIF2 protein activated a total of 980 proteins in macrophage cells, out of which 69 proteins are hyperphosphorylated and 153 are hypophosphorylated. Wb-MIF2 was tested *in vitro* on adipocytes to check the glucose uptake by using 2NBDG assay and found that wb-MIF 2 in comparison of control cells showing significant results.

Vector surveillance for ZIKV/JEV in selected high risk areas in India (ZIKA).

The Zika virus has emerged as a global public health concern. Its rapid geographic expansion is attributed to the success of *Aedes* mosquito vectors, but local epidemiological drivers are still poorly understood. This study was conducted to detect the prevalence of zika virus in *Aedes* mosquitoes collected from 4 sites (Mysore, Mangalore, Bijapur

and Belagavi). These were pooled (10 mosquitoes/pool) and detected for the presence of ZIKA, Dengue and Chikungunya infections. RNA from 365 mosquito pools were tested for the presence of viral RNA by real time PCR assay. None of the samples were positive for zika. However, 3 (2 Bijapur and 1 Belagavi) and 8 vector samples were positive for dengue and chikungunya (4 Mangalore, 2 Bijapur and 2 Belagavi), respectively. These studies indicated that the areas from where the vectors were collected viz., Mangalore, Bijapur, Mysore and Belagavi did not have the transmission of zika virus, while transmission of dengue and chikungunya is going on.

TRIBAL HEALTH

Workshops on Augmenting Local Resources for Primary Healthcare and Better Livelihood in Tribals (Supported by NASI, Allahabad).

Initial sensitization workshop was conducted at ICMR-NITM, Belagavi on 2nd and 3rd August, 2018 for selected tribal representatives and volunteers from four selected tribes viz. Siddi, Bedar, Lambani and Danagar Gowli from Karnataka. The health conditions among each tribe were listed out through Free-Listing and were prioritized based on need of Local traditional Medicines. Further, field level workshops have been conducted for Siddis and Gowlis (20th-21st December, 2018), Lambani (15th and 16th February, 2019) and Bedar (16th and 17th May). The field level workshops addressed the common prioritized health conditions, mapping of available resources for prioritized disease conditions and their usage for tribals for their better livelihood.

Assessment of nutritional status and health seeking behaviour among Siddi tribe in Karnataka.

Siddi tribe is of African origin and have settlements in jungles of Western Ghats of Dharwad and Uttara Kannada districts in Karnataka. Malnourishment and anaemia are prevalent in the community, especially in children and women. In the present study, detailed investigations on nutritional status

among tribal community in this region were carried out. Till date, the investigation was carried out among 1229 Siddi subjects of different age-groups. The BMI indicated that 73.85% of the children (452 out of 612 subjects) are severely thin, within 'underweight' category as per WHO standards (2015). The haemoglobin estimations in children of the age group 12 to 14 years and in adult women category, indicated about 29.56% moderate anaemia and 25% with mild anaemia. As there are no systematic studies available on the nutritional status among Siddi tribe of Karnataka, the current study is expected to provide baseline to understand the health perspectives among Siddi tribe in the changing context of food pattern and nutrition.

Optimising forest benefits whilst minimising impacts of emerging zoonotic diseases: co-developing an interdisciplinary tool for forests in India.

This project aims to improve the economic development, health and welfare of the people, including tribal communities, who depend on forest ecosystems in India by developing a novel interdisciplinary tool to understand how forests can be used sustainably to maximize ecosystem benefits whilst minimising exposure to zoonotic disease. The framework will be developed initially for Kyasanur Forest Disease Virus that causes debilitating and fatal haemorrhagic disease in forest communities. The project will scope out how the framework could be generalised to understand trade-offs between infectious disease burdens, trade, and forest ecosystem benefits in different global contexts. Earth observation of different landscape mapping has been done for Kyasanur Forest Disease Virus (KFDV) affected areas in Karnataka and Kerala by collecting tick samples from both infected and uninfected areas, which includes different habitats like forest, crop matrix and household area. The collected samples were subjected to ecological, morphological and molecular analysis. The earth observation mapping has been carried out which helps for predicting the epidemiology of KFDV and other zoonotic

diseases. The decision-support tool to be developed in the study will help the health department to improve target vaccination and communication efforts towards the forest communities.

EXTRAMURAL RESEARCH

CLINICAL PHARMACOLOGY

Drug Testing Advisory Board (DTAB) sub-committee reviewed Fixed Dose Combination as per Supreme Court order. Sub-committee recommended banning of 343 FDCs. Report was accepted by Govt. of India and banning order issued.

DSMC for bedaquiline conditional access program through RNTCP for multidrug resistant tuberculosis. Bedaquiline has been administered to 600 patients. Efficacy safety was reviewed by DSMC, risks and minimization strategies were identified and implemented. Bedaquiline has been rolled out to 1000 patients. The DSMC helped in ensuring safe effective use of bedaquiline.

Centres for Advanced Research (CAR) have been funded and are working on important areas e.g. prescriptions for elderly, antibiotic stewardship, pharmacogenetics personalized medicines for haematological diseases, pharmacodynamics, pharmacokinetics of anti-infectives, vector borne diseases anti-malarials, capacity building of young investigators for clinical research. Plan for developing National Virtual Centre for Clinical Pharmacology with network of centres for rational use of Medicines (RUMC) and centres for Product Development (PDC) has been approved. 15 RUMC and 5 PDC have been established and work started.

Rational use centers are developing an online program for prescribing skills training, learning and assessment for interns. This involves prescription research for evaluating specific problems which will provide input to developing the training assessment program.

The Product Development Centers will evaluate potential products developed by ICMR funded

projects in colleges/ICMR centers/centre for advance research. Centres will carry out clinical trials for developing national guidelines/programs, for New drugs eg phytopharmaceuticals, (as per CSIR MOU) and industry initiated studies.

PHYSIOLOGY

A study on dectin 1 and Toll Like Receptors (TLR) at the interface of beta glucan and macrophage interaction: a mechanistic study of immunomodulatory activity of B glucan using leishmaniasis as an immunosuppressive disease model was conducted at Dept. of Molecular Biology and Bioinformatics, Tripura University. The study reveals that Zymosan is more potential than barley beta glucan in inducing anti-leishmanial activity in murine macrophages. It may be concluded that beta glucan is a potential immunomodulator in host macrophages against leishmania infection and it induces Th1 cytokine response and suppresses Th2 cytokine response to combat with *L. donovani* infections in host macrophages. Therefore, beta-glucans can be further explored to develop newer therapeutic strategy against immunosuppressive infectious diseases.

A study on assessment of Cognitive and oxidative status in thyroid dysfunction patients and correlation with Event Related Evoked Potential & EEG with brain mapping was carried out at Jawaharlal Nehru Institute of Medical Sciences (JNIMS), Porompat, Imphal with the aim to assess the cognitive & oxidative status in thyroid dysfunction patients by using event related potentials, EEG and study the topographical differences between normal controls and thyroid. The findings are suggestive of cognitive slowing which after treatment improves though statistically not significant. QEEG findings along with EEG source analysis are suggestive of involvement of pre-frontal, frontal & temporal areas in hypothyroid patients while parietal, temporal & limbic lobes were involved in hyperthyroid patients.

A study on Prevalence and Risk factors of Obstructive Sleep Apnea-Hypopnea syndrome

(OSAHS) in rural Indian population: A community based cross sectional study was conducted at Mahamta Gandhi Institute of Medical Science, Sewagram.

In this cross-sectional community based prevalence study which was conducted in two stages, a total of 4713 subjects aged 18-65 years were screened by screening questionnaires and modified Berlin questionnaire in first stage. A total of 345 individuals were subjected for polysomnography (PSG) study in second stage of the study. Their socio-demographic, anthropometric and polysomnographic feature were studied. It was found that the prevalence of OSAHS was 3.07% in rural Indian population between 18-65 years of age. The variables which significantly affected the presence of OSAHS such as age more than 40 years, male gender, positive family history, habitual smoking, habitual drinking, body mass index, neck length, neck circumference, percentage predicted neck circumference waist circumference, systolic blood pressure, fasting blood sugar, triglyceride and low density lipoprotein can be considered as significant independent risk factors for OSAHS.

MEDICINAL PLANTS

A study on evaluation of *in-vitro* and *ex-vivo* antimycobacterial activity of selected plants traditionally used in tribal medicine against MDR mycobacterium tuberculosis isolate and their active fractions investigation was done at National Jalma Institute for Leprosy and other Mycobacterial Disease, Agra. The most significant anti-TB activity of plants were identified in *Berberis aristata*, *Curcuma casesia*, *Cyperus rotundus*, *Glycyrrhiza glabra*, *Hedychium coronarium*, *Holarrhena antidysentria*, *Mallotus philippensis*, *Mesua ferra*, *Nardostachys jatamansi*, *Orchrocarpus longifolius*, *Plumbago zeylanica* and *Sphaeranthus indicus*. The present investigation supports the potential role of plants used by tribal healers. The knowledge may be useful for process and product development. The research could yield more information to improve the existing therapeutic

practices after isolation of pure compound/s, study of safety parameters and *in vivo* anti-TB activity.

Identification and mechanism of action of antidiabetic principles from the leaves and fruits of *Coccinia indica* W&A, a traditional antidiabetic plant conducted at S.J., Entomology Research Institute, Loyola College, Chennai. The main aim of this research was to investigate the scientific basis and strong mechanistic evidence for the traditional use of *Coccinia indica* in type 2 diabetes, T2D and to define the antidiabetic activity of the extracts/fractions/components of the leaves and fruits of *Coccinia indica* and discover potential antidiabetic drug(s) useful for the treatment of T2D in the community.

PHARMACOLOGY

Total number of Adhoc and fellowship proposals

	Ongoing	Approved
Fellowships (SRF/RA)	7	132
Adhoc Projects	230	40

Effect of berbamine on pancreatic transcription factor and insulin signaling proteins in high fat diet/streptozotocin induced diabetic rats conducted at Annamalai University, Annamalainagar. The insulinotropic effect of berbamine was significant at 100 mg/kg b.w. than other two doses (50 and 200 mg/kg b.w.). At this effective dose (100 mg/kg b.w.), berbamine curtailed oxidative stress by improving the levels of enzymic and non enzymic antioxidants in diabetic treated rats. The above findings were supported by immunohistochemical and histopathological studies. The effect of berbamine was compared with the standard drug, metformin.

Effect of spinal cord contusion injury on male reproductive and sexual health: A novel therapeutic approach using *Mucuna pruriens* (Linn.) Seed Extract carried out at Dr. A L Mudaliar PG Institute of Basic Medical Sciences, Chennai. The ethanolic extract of *M. pruriens* has the potential to improve male sexual behaviour. *M. pruriens* is useful as a

sexual invigorator in spinal cord injured males. Exploring the possibility of neural connection repair as a therapeutic target mediated through Androgen Receptor (AR) is a bright project. With SCI, there is increased possibility of disturbance of circuitry. *M. pruriens* has shown beneficial effects through AR expression in nerve regeneration and preservation of endothelial dysfunction and corpus cavernosum from fibrosis.

Allergy, Biochemistry, Human Genetics and Immunology

Total number of Adhoc and fellowship proposals

	Ongoing	Approved
Fellowships (SRF/RA)	89	91
Adhoc Projects	36	31

In view of the role of ICMR as outlined in the National Policy on rare diseases in India, to support research in the area of rare disease, a Task Force on rare diseases is initiated.

Department of Health and Family Welfare (Drugs Regulation section), MoHFW, Govt. of India has constituted a Standing National Committee on Medicines (SNCM) to review and revise The National List of Medicines (NLEM), 2015 under the chairmanship of DG, ICMR and Sect., DHR. Division is facilitating the committee in preparing detailed guidelines and procedures for revision of NLEM.

Clinical and molecular evaluation of inherited arthropathies and multiple vertebral segmentation defects.

Successfully characterized 138 families with a genetic arthropathies or a MVSD clinically and radiographically. Mutation spectrum in *WISP3*, *MMP2* and *FLNB* has been delineated for Indian patients. Furthermore, identified exons 2 and 5 as mutational hotspot for *WISP3*, which could help in establishing diagnostic strategy for Indian patients with PPD. The research work has identified mutation in *EXOC6B* and *ARSK* as a cause of spondyloepiphyseal dysplasia with joint laxity and

dislocatin and with novel bracydactyly syndrome respectively. These are likely to be new genes causing arthropathy. The present work is likely to help in molecular diagnosis and prenatal diagnosis for Indian families with an arthropathy or MVSD.

Genetic screening in a large family with Primary Open Angle Glaucoma.

Family history is one of major cause of the disease; therefore, analysed two big South Indian families with POAG. Based on the bioinformatics analysis, 85 genes were targeted including the known candidate genes in 16 samples and the genes chosen from the analysis of previous exome data from the five samples. Based on case-control enrichment and co-segregation, two novel variants in *ARHGEF40* and *NCAM1* gene were identified. Three variants in *PLK4*, *KIR2DS4* and *SSTR1* were identified through low frequency analysis. Pho guanine nucleotide exchange factors Gene family protein (*ARHGEF12*) has been implicated in the risk of glaucoma by increasing intraocular pressure through RhoA/ RhoA kinase pathway. In addition, Neural Cell Adhesion Molecule (*NCAM*) participates in the optic nerve changes associated with elevated intraocular pressure.

Insulin Gene VNTR Polymorphism in Kashmiri Women with Polycystic Ovary Syndrome.

Results confirm that these loci should not be considered major contributors to the pathogenesis of this prevalent disorder. However, genotype comparisons of *INS VNTR* and *IRS 1* polymorphism showed association with metabolic markers like HOMA IR, BMI and fasting glucose. These SNPs could play a contributory role in pathophysiology and risk of PCOS. The breakdown of PCOS in various sub groups can actually help understanding role of genetic variants in triggering specific phenotypes. The SNPs need to be checked with other SNPs in different unselected population groups to confirm if SNPs act in tandem with epigenetic modifications and other exogenous factors.

Anatomy, Anthropology, Hematology and Nanomedicine

Total number of Adhoc and Fellowship Proposals recommended for the year 2019:

	Ongoing	Approved
Fellowships (SRF/RA)	71	77
Adhoc Projects	3	30

Task Force for Nanomedicine

The task force for nanomedicine would focus on the exploratory research based on specific need for clinical application, defining the novelty and superiority over the current practice including cost effectiveness. Research for translation on demonstrated proof of the concept with a plan for preclinical &/Clinical trial would also be

emphasized. There were 443 concept proposals received in the various sub-categories:

- i. Nano-drug delivery
- ii. Nano-enabled point of care devices
- iii. Nano-biosensor
- iv. Nano-enabled system for Regenerative Medicine & Wound Healing
- v. Nano-immunotherapeutics& Nano-adjuvant
- vi. Imaging & Theragnostics
- vii. Nano-enabled emerging technologies like, Photodynamic Therapy (PDT), Nanorobotics etc.

Out of total 80 full submissions received, 17 were accepted for funding w.e.f. year 2019.

REGIONAL MEDICAL RESEARCH CENTRES

To deal with health problems of the regional and marginalised population, ICMR has established a total of 5 Regional Medical Research Centres at Port Blair (Andaman Nicobar), Bhubaneswar (Odisha), Jodhpur (Rajasthan), Dibrugarh (Assam) and Gorakhpur (UP). The effort 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 2018-19 is mentioned below.

INTRAMURAL RESEARCH

ICMR-REGIONAL MEDICAL RESEARCH CENTRE, BHUBANESWAR

RMRC, Bhubaneswar was established in 1981 under the 6th five-year plan period to undertake research activities in both communicable and non-communicable diseases, human resource development programme and in establishing strong linkage with State Health Department in finding solutions to the regional health problem. The centre in the past three decades has worked effectively towards identifying regional health problems and contributed significantly in evaluation & implementation of government health programme & policies.

Regional Virology Research & Diagnostic Laboratory

The centre has been upgraded to Regional Laboratory for virology research and diagnostics

and catering service to Chhattisgarh and Andhra Pradesh in addition to Odisha.

- The centre is rendering diagnostic services to the referral cases from various medical colleges, tertiary hospitals, and IDSP.
- The VRDL of the centre is recognised as apex referral lab for Dengue, Chickunguniya and JE by NVBDCP and state referral lab for diagnosis of H1N1 cases.
- The unit is also investigating the various outbreaks of viral aetiology.
- Diagnostic facility was provided to more than 45,000 patients suspected of viral illness admitted to different secondary/ tertiary care hospitals of the state.
- The observations on clinical presentation and viral agent identification improved the clinical diagnosis by the physicians of the region through information sharing and publications.
- Part of laboratory network for enhancing diagnostic capabilities for surveillance, outbreaks and epidemics investigations of high-risk group of viral pathogens causing viral hemorrhagic Fevers.
- The laboratory is a part of different national/ CDC/WHO surveillance network in the state like Measles, Rubella, Dengue, ZIKA, Respiratory viruses including antiviral susceptibility in H1N1 cases.
- During 2018-19 around 30 outbreaks were investigated suspected for viral origin including Dengue, Chickunguniya and Hepatitis.

- The centre is supporting training and technical man power development in the state as well as state and medical colleges of Chattishgarh and Andhra Pradesh for laboratory detection of different viral diseases and outbreak investigation.

NATIONAL REFERENCE LABORATORY FOR TUBERCULOSIS

- NABL accreditation obtained for the NRL for Tuberculosis in August 2018
- A total of 3142 presumptive MDR TB cases were tested for diagnosis of MDR TB from ten districts of Odisha and three North eastern states (Meghalaya, Sikkim and Nagaland). Out of 3142 specimens received, 2516 specimens were tested by LPA and 27 (1.1%) were detected as MDR TB patient and referred to DR TB sites for DOTS Plus treatment.
- A total of 2654 samples were tested by GeneXpert; out of which 529 were found as MTB positive among which 29 specimens were found as Rifampicin resistant, which were referred to districts for DOTS Plus treatment initiation.
- A total of 513 specimens of patients suspected for XDR-TB were subjected to 2nd line LPA; of which 18 were XDR and 134 were found resistant to Fluoroquinolones .
- A total of 418 specimens of MDR-TB patients on DOTS Plus treatment were processed for follow up culture.
- In 2018 a total of 261 presumptive TB & 106 follow up sample were tested at DMC out of which 28 and 11 are AFB positive respectively.
- Provided technical support for establishment of nine TB containment laboratories in eight states

REGIONAL HUB FOR HEALTH TECHNOLOGY ASSESSMENT

- The centre is one of the 6 regional hubs for the Health Technology Assessment and catering

services to 4 states - West Bengal, Bihar, Jharkhand in addition to Odisha.

- Working on current assignment on Diagnostic Validation and Health Technology Assessment of 'SOHUM' Neonatal Hearing Screening Device
- The device 'Sohum' was designed by the School of International Biodesign (SIB) startup, Sohum Innovation Labs India Pvt. Ltd. by Dept. of Biotechnology (DBT), GoI, 2017.
- The assigned proposal has been approved by the Technical Appraisal Committee (TAC) of HTAIn, Ethical Committee of ICMR-RMRC, and Odisha State Ethical Committee. Permission and necessary information has been also obtained from the concerned stakeholders.
- All the necessary tools required for the data collection has been developed and validated.
- More than one third of the data has been collected for Out of Pocket Expenditure (OOPE) among the targeted facilities and sampled population.
- Two systematic reviews have been registered in Prospero and are in final stage of submission.
- Further, the SOHUM device has been also validated in the community settings for the feasibility study.

MRHRU, TIGIRIA

- A baseline household survey was conducted during this period on Socio-demographic & Morbidity status of various villages in and around the MRHRU.
- The household survey on Socio-demographic & Morbidity status was conducted at Baliput village, Tigiria block of Cuttack June – July'2018 to identify the different health problems prevalent in that locality.
- Among 1009 study participants, 188 (18.6%) had chronic illnesses (83% with single disease and 17% having multi-morbidity).

- Facility level data collection of CHC Tigiria and CHC Bindhanima was conducted on February'2019.
- The ten most common health problems for seeking OPD care were found to be URTI, Ophthalmic diseases, Gastroenteritis, Hypertension, gynaecological conditions, Skin & VD, Parasitic diseases and Injuries & Wounds.
- A cohort is being developed in Tigiria block with representation of rural and tribal population.

Anthrax in Odisha: A roadmap for elimination

- Knowledge Attitude Practice (KAP) analysis study on Anthrax was carried out in 4 most effected indigenous population dominated district (Koraput, Rayagada, Malkangiri and Sundargarh) of Odisha.
- The study involved household survey, FGDs, IDIs of the stakeholders.
- 557 households covered in 4 endemic districts.
- 49 IDIs and 11 FGDs were conducted with officials representing various stake holders.
- 20% and 48% of the respondents never heard about Anthrax disease and were unaware of the mode of transmission.
- About 18% of the respondents were found to consume dead animals.
- Butchering and deskinning of dead animal accounted for majority (36%) of the Anthrax cases (88) interviewed.
- Awareness among the respondents, Interdepartmental coordination and a proper vaccination programme were identified as main roadblocks in control & management of Anthrax in these districts.

Japanese Encephalitis Virus infection in Malkangiri District: Pre & Post Vaccination Period

- A network has been established between Regional Medical Research Centre and district health system for AES/JE diagnosis which include sample collection, sample transportation and reporting. RMRC, Bhubaneswar has been recognized as apex laboratory for the diagnosis of JE by the state government.
- From total 2263 villages, 41 villages were selected using PPS sampling method.
- From each village, 10 households were selected by systematic sampling method and those houses where more than one child in age group between 1 and 15 were there, only one child was selected by KISH selection method
- Total of 410 children were enrolled for the vaccination survey
- The survey revealed that 96.71% children between the age group of 9 month to 15 years have received JE vaccine

Prevalence of asymptomatic malaria infection below 5 years and mode of transmission in Kalahandi district of Odisha

- Malaria is responsible for the greatest public health problems in Odisha and the study was carried out with a objective to determine the prevalance of asymptomatic Plasmodium infection below 5 year children and to determine the per man hour density and transmission potential of vectors in Kandhamala district of Odisha.
- Phiringia, Khajuripada, Kajamandi Nuagaon, Tumudi Bandha and Daringibadi blocks of Kandhamal district were selected based on the API.
- A total of 130 slides were collected from under five children and RDT was done for all.
- Only one case was positive for RDT and blood slide examination in Phiringia Block.

- Similarly, 168 samples were collected from Khajuripada block and none were found positive.
- 218 samples were collected from Tumudibandha and five samples were found to be positive by both RDT and blood slide examination.

Strengthening the existing ICDS-MIS cell integrating components of ICT-Real time monitoring & supporting convergent action plans of the National Nutrition Mission (NNM) in Odisha

- State level inception was conducted explaining salient points through video conference,
- Four batches of ToT of ICDS supervisors, CDPO's and Programme Officers and DPMs conducted for 136 participants of 15-high burden district and trained on measuring anthropometric parameters besides supportive supervision, monitoring of nutritional indicators and preparation of context specific convergent nutrition action plans.
- The concurrent monitoring team analyzing the ICDS data generated through e-pragati and RRS and cross validated with primary field data duly collected by administering checklists in the Anganwadi centers.
- The teams have visited 4 districts (Sambalpur, Khordha, Dhenkanal, Koraput), 11 blocks, 15 sectors and 27 Anganwadi centers and findings shared with WCD department.
- Currently working on identifying key indicator, base line status, bottlenecks and suggested specific action for multi sector convergent nutrition action plan.
- Analysis of the blue print of the ICDS MIS cell structure incorporating best practices, capacities and HR and annual costs of running the same study of MIS systems of line departments such as H&FW, PR&DW,

RWSS, S&ME at state and district levels is being done.

Study on Mid-Day Meal programme in Odisha: Impact Evaluation

- The study covered 11, out of 30 districts across division in Odisha covering 362 schools under 112 clusters, 37 blocks.
- Total 51414 children aged 6-14 years covered, 48.7% of them are boys and 52.3% girls
- Enrolment of girls students are high in every category i.e. SC (50.3%), ST (50.4%), and others (51.5%).
- More than 70% of schools have functional kitchen cum store and 9.1% schools depends on central kitchen. Only 28.2% schools use LPG for cooking. Food safety is maintained in majority schools.
- Many schools are not maintaining records and registers such as Bank pass-book (61.9%), Cash book (50.3%), Guard register (49.2%), Stock & consumption (65.7%), Visitors/Observation (38.1%). Awareness on objectives and entitlement of MDM is poor among school teachers.
- Potable water is available in 88% of MDM schools, 2.5% samples tested coliform positive, depend mainly hand pump, bore wells and tap water.
- Toilet facility is there in 97%, while 75% of them are currently in use and 69% of schools have separate toilet facility.
- Assessment of nutritional status revealed that 22% of children (15886) in MDM schools are underweight and 31% are stunted, while 9% are overweight or obese.
- Mean haemoglobin is 11.5 g/dl, 58% are anaemic and 22%, 34.7% and 0.1% are mildly, moderately and severely anaemic.
- Overall, there has been significant improvement in quality of MDM programme

implementation and monitoring services by stakeholders.

Diseases profiling of Primitive Vulnerable Tribal Group of the state

- The study was conducted from 1st July, 2018-28th February, 2019 in 17 Micro project areas of PVTGs in Odisha.
- In this study, it was found that there was 64.2% wasting (weight for height) with 40.1% in severe category and 52.1% stunting (height for age) compared to 37.1% severe category among the under-five children.
- Stunting was high among the girls of this age group than the boys.
- Around 73.2% were underweight (weight for age) out of which 51% of them had severe malnutrition. Likewise, in the age group of 6–18 years, centre found 43.7% stunting and 60% wasting with higher proportion of girls malnourished.
- Iron deficiency anaemia is a matter of great concern and the PVTG women are worst affected with 75% prevalence.
- Sickle cell anaemia is also an issue in Saora, LAngia Saora, Paudi Bhuiyan, Kutia Kondha, Dongoria Kondha, Didayi and Juang PVTG groups. In fact, skin-disease (10.4%) and syphilis (4%) were more prevalent among the Lodhas.
- Hypertension (29% in Kharia, Mankidia) and diabetes (12% amongst Lodha) have arrived with other Non-Communicable Diseases (NCD) but the burden of infectious diseases such as malaria (Asymptomatic:45.3% in Kutia Kondha, Kondhamal 40% in Paudi Bhuiyan, Sundargarh; Symptomatic: 12% Kutia Kondha, Kalahandi), acute respiratory infections (33% in Paudi Bhuiyan, Anugul; 20% Paudi Bhuiyan, Sundargarh; 20.7% in Bonda; 19.4% in Saora), skin infections (14.1 % in Saora, Tumba; 12% in Saora, Gajapati;

11.2% in Dongaria Kondha, 10.4% in Lodha), diarrhoea (3.8% Paudi Bhuiyan, Sundargarh) and intestinal parasitism remains high compared to NCDs .

- Study also observed that Rh-negative blood type is a problematic factor among the pregnant women of Chutkia Bhunjia PVTG which may be properly addressed by the local PHCs.

Feasibility of using two simple tools for improving documentation during childbirth in Peripheral health facility

- Two simplified tools viz. “prashav sheet” and “still birth case sheet”, developed by maternal health division, ICMR, were pilot studied to assess the feasibility and effectiveness of the tools in labour room documentation.
- Labour room documentation improved in the intervention sites.
- The still birth case sheet was found to be quite useful and effective to find the possible or associated risk factors with the still birth, which can be addressed later.
- The partograph portion in prashav sheet was found to be easy and well appreciated.
- Adherence to partograph plotting and its completeness improved after intervention.
- Effectiveness with respect to early detection of any complication and prompt management was found to be better in intervention facilities.
- The simplified discharge sheet was user friendly and less time taking.

HRD for health research in the area of health informatics

- DHR, has sanctioned a project entitled "Human Resource Development for Health Research in the area of Health Informatics" under HRD scheme.
- Focusing towards the objective, the centre had organized 45 days training programmes on

different modules which were attended by 25 participants (representatives from state health officials, clinicians, research scholars and scientists) per programme.

- The topics that were focused in the programme were Evidence Synthesis and Systematic Review, Economic Evaluation of health programmes, Qualitative Research Methods, SPSS/STATA, Development of disease registry, Principles of Project Management and M&E, Principles and Practice of Implementation Research, National Ethical Guidelines for bio-medical Research, Health Communication, Biomedical Informatics, Research Methodology, Scientific paper Writing (Basic and Advanced), Referencing/literature survey/bibliography.
- The training was disseminated by renowned health professionals/scientists of the country.

PUBLIC HEALTH

Outbreak Investigation

The centre has supported both field and laboratory investigation for management of outbreak due to pandemic H1N1, ChikV, Dengue, JE, Chandipura, Measles, Rubella, Chicken Pox and Hepatitis A, E reported in the region by immediate diagnosis and recommendation for control, within minimum turnaround time. The reports were provided to respective authority within 6-24 hours in emergency/outbreak situations. During 2018-19 around 30 outbreaks were investigated for jaundice, chickenpox, AES/JE, Dengue and Measles. The scientists from the centre have been part of the central team deputed as Emergency Medical response for investigation and containment of Avian Influenza in Odisha.

Supporting programme implementation through research

The centre is involved in various projects on evaluation of government programme and policies. Mid-day Meal programme evaluation is being carried out with support of Dept. of School & Mass Education, Govt. of India. The centre is also involved in health impact assessment of Pradhan Mantri Ujjwala Yojna (PMUY). The centre has been designated as apex laboratory for JE diagnosis by the state government and has been supporting the various programmes of NVBDCP, IDSP and implementation of RNTCP. The Health Technology Assessment of a neonatal hearing impairment device, SOHUM is being carried out prior to its introduction into RBSK. The centre has 2 field units in tribal dominated districts of Rayagada & Kalahandi, an outpatient facility which is attending patients and dispensing free drugs and a Model Rural Health Research unit in Tigriria and is currently developing a cohort population (including rural, urban & tribal) for various studies and intervention for improving the health condition.

Organised data systems and platforms for research

The library of the centre has been upgraded to National Information Centre for Public Health Research. The library of the centre is acting as knowledge resource centre and catering service to various medical colleges, hospitals, academic and research institution. The centre has been undertaken various projects on documenting the health profile of Primitive Vulnerable tribal group of the state. The centre is also working on developing human resource for Public Health informatics. A rare disease registry is also being developed by the centre.

UNITS OF RMRC



Fig. 1: Field unit in Rayagada.



Fig. 2: Out-patient facility.



Fig. 3: Model Rurl Health Research unit, Tigriria.

OUTBREAK INVESTIGATIONS



Fig. 4: Dengue Outbreak Investigation.



Fig. 5: Part of central team for Emergency Medical Response for Avian Influenza outbreak.

FIELD STUDIES



Fig. 6: FGD In Sundargarh.



Fig. 7: IDI with DFO, Koraput.



Fig. 8: Nutrition Survey.



Fig. 9: Disease profiling of PVTG.



Fig. 10: TB-nutrition study.



Fig. 11: Diagnostic validation of SOHUM device.



Fig. 16: Diarrhoea conclave with NGO & stake holders.



Fig. 12: Qualitative IDI with SN at DHH Kalahandi.



Fig. 17: Photography competition to commemorate 150th Birth Anniversary of Mahatma Gandhi.

COMMUNITY OUTREACH & AWARENESS PROGRAMMES



Fig. 13: India International Science Festival.



Fig. 14: 2nd edition of Odisha Vikash Conclave (OVC)-2018.

STRENGTHENING OF HEALTH RESEARCH CAPACITY



Fig. 15: ICMR-IIT KGP-IIM MedTech Internship programme, 2018

ICMR-REGIONAL MEDICAL RESEARCH CENTRE, PORT BLAIR

RISK REDUCTION/ ELIMINATION OF INFECTIOUS DISEASES

Effectiveness and operational feasibility of mass DEC fortified salt as a supplementary intervention to mass drug administration towards elimination of the lone foci of diurnally subperiodic *Wuchereria bancrofti* in Andaman & Nicobar Islands

Diurnally sub periodic form of *Wuchereria bancrofti* is endemic only in five islands of the Nancowry group of islands. Although 6 rounds of mass administration of DEC and Albendazole under the programme to eliminate lymphatic filariasis has been carried out, microfilaraemia (*Mf*) rate > 1% still existed in the islands. The effectiveness and feasibility of DEC fortified salt (DEC +Iodine) as a supplementary measure to MDA to achieve LF elimination was assessed. MDA was supplemented with DEC-iodine double fortified salt in 12 villages (Study arm) while MDA alone was continued in

the remaining 14 villages (control arm). One-year salt distribution could reduce *Mf* prevalence below 1% in all the 12 villages (Study arm). In the control arm *mf* persisted with more than 1% in 4 out of 14 villages. Antigenemia prevalence in the age class 2-3 years in the DEC salt arm was reduced to zero from baseline 59 prevalence of 0.7%.

Spatial and temporal variations of potential malaria vector(s) and associated species of Anopheles in Andaman and Nicobar Islands

A study was conducted to identify the anopheline fauna and assess the status of malaria vector(s) in Andaman & Nicobar Islands. The study was conducted in 3 villages each from each of the 9 tehsils. Nicobar district recorded the highest density both for culicines and anophelines. Anopheline per-dip density was 2.38, 2.74 and 4.43 in three districts during the 3rd cycle and 3.72, 2.86 and 4.72 in the 4th cycle. Anopheline immatures were recorded from 23 different habitats types. Pupal stage of anophelines were found in nine habitats of South Andaman which included; cess pool, pond, rainwater pool, tyre print, mangrove swamp, kutchra drain, dam and stream margin. A total of ten anopheline species were identified. A new molecular form of *An. barbirostris* was identified from Andaman and Nicobar Islands, which was closely related to *Anopheles barbirostris* form A (A3).

Investigation and containment of the post-flood outbreaks of leptospirosis in Kerala, August-September 2018

A team from the Centre was deputed to Kerala to carry out research and public health activities during the post-flood outbreaks of leptospirosis in Kerala during August 2018 as per the requirements of the state health department. The team established facilities for laboratory diagnosis of leptospirosis at field unit of ICMR-NIV, Alappuzha. Based on MAT titres Australis, Canicola and Icterohaemorrhagiae were the common infecting serogroups. The team also helped in monitoring the outbreak trend and participated in public awareness programmes for implementation of the control strategies. A coverage

evaluation survey for doxycycline prophylaxis and an evaluation of the effectiveness of doxycycline prophylaxis in preventing leptospiral infection, disease and death were conducted by the Centre, NIE and DHS, Kerala. A preliminary analysis of the data on efficacy of doxycycline prophylaxis showed that the strategy had an efficacy of 98.6% (95% CI: 89.9, 99.8) and the prevented fraction in the population was 48.4% (95% CI: 40.6, 50.0).

HEALTH AND NUTRITION OF MARGINALIZED COMMUNITIES

Health and nutritional status of Jarawas

A study was conducted to assess the present health and nutritional status of the Jarawa population. A total of 382 Jarawas were contacted and among them 204 were males and 178 were females. The sex ratio was 872.5 (95% CI: 818.9, 915.0). Out of the 72 children in the age group 0-59 months, 45 (62.5%) had BMI within normal range, five (6.9%) had severe thinness and four (5.6%) thinness. Out of the 141 school aged children (60 – 228 months of age) and among them 114 (80.9%) had normal BMI, 13 (9.2%) had thinness and 14 (10%) were overweight or obese. Out of the 169 adults, 36 (21.3%) adults had thinness, 22 (13%) were overweight or obese. Anaemia prevalence was 70% (163/233). Prevalence of hypertension was 2.2%. Serum cholesterol levels >200gm/dL was seen in 11 (5.0%) and triglyceride > 200 mg/L in 6 (2.7%). HDL levels < 40 mg/dL was prevalent in 73 (33.2%) of the Jarawas.

Health and nutritional status of Onges of Little Andaman

A health and nutritional survey was carried out among the Onges of Little Andaman. The present population of Onges consists of 118 individuals, 63 males and 55 females with an overall sex ratio of 878 females per 1,000 males. Out of the 21 pre-school children, 17 (81.0%) had normal BMI for their age and gender while two (9.5%) each were overweight and obese. Out of the 44 school aged children, 28 (63.6%) had BMI within normal range for their age and gender. While 15 (34.1%)

children had thinness, one boy was overweight. There were a total of 53 Onges adults above the age of 19 years. While 28 (52.8%) of the Onges had normal BMI values, 21 (39.6%) were underweight and 4 (7.6%) were either overweight or obese. Anaemia prevalence was 60.2% and hypertension prevalence was 15.5% (15/58). Four (4.9%) of the 92 Onges screened had cholesterol level > 200 mg/dL and none had triglyceride level > 200 mg/dL. HDL levels < 40 mg/dL were observed in 38 (41.3%) of the Onges.

ECOLOGY AND ENVIRONMENTAL MICROBIOLOGY

Developing the model of *Anopheles* mosquito breeding parameters and their physico-chemical determinants and application of the model for environmental monitoring of risk *Anopheles* breeding in the context of Global Climate Change

The project is funded by the DST under the National Mission on the impact of climate change on health of the tribal communities residing in the island of Car Nicobar. The objective of the study was to develop a model to predict risk of *Anopheles* breeding. A total of 683 observation in 21 types of water habitats were made. The analysis identified eight variables as significantly associated with the risk of *Anopheles* breeding. A multiple binary logistic regression yielded a model with four predictor variables. A pH \geq 8.3, dissolved oxygen \geq 16, nitrite \geq 0.026 and ammonia \geq 0.36 were found to be protective against breeding risk. The study yielded statistical models for risk of breeding as well as *Anopheles* immature abundance. But these models need refinement before evaluating their predictive abilities.

Study of *in vivo* leptospiral biofilms and their role in transmission and pathogenesis, chronicity of leptospirosis

Centre's earlier studies have demonstrated formation of Leptospiral biofilms and observed abundantly from paddy field surface water, stagnated rain water bodies, domestic sewer and walls of urban sewage canals. A preliminary study was conducted

in vitro using the strains recovered earlier from the patients with varying clinical syndromes to identify the strains capable of forming biofilms. Among the 24 isolates/strains studied for ability to form biofilm, 10 (41.6%) isolates/strains were capable of forming biofilm *in vitro*. Six isolates were obtained from mild case of illness and among these 2 (33.3%) were able to form biofilm *in vitro*, whereas among the 18 isolates obtained from severe cases, 8 (44.4%) showed the ability to form *in vitro* biofilm. The results indicate that *in vitro* biofilm forming strains are more likely to produce severe disease than strains incapable of forming biofilms *in vitro*.

BASIC AND APPLIED RESEARCH

Whole genome sequencing to understand virulence factors of infecting Leptospiral serovars /strain with varied clinical manifestations

A total of 40 leptospiral strains were included in the study, of which 39 were recovered from the patients with varying clinical syndromes. Whole genome sequencing of all 40 leptospiral strains has been completed raw reads were assembled and developed *de novo* contigs. Development of scaffolds has been initiated. The data generated from the strain isolated from sheep which had history of fever with jaundice was analysed along with set of whole genome data available on database from different genera of leptospires showed that the strain is closely related to *Leptonema*. The species under the genera *Leptonema* is considered as non-pathogenic. However pathogenic status of this genus could not be ruled out as several intermediate species (consisting of strains both pathogenic and non-pathogenic) have been reported in the recent past. In this study centre reported for the first time isolating strains belonging to *Leptonema* from sheep, pig and rat.

Phytochemical investigation and anti-malarial activity evaluation of medicinal plants used by indigenous tribes of Andaman and Nicobar Islands

The centre recently undertook studies on the prevailing traditional health practices in different

island groups. As a part of this, crude extracts from 15 medicinal plants were tested for malarial activity, of which 8 indicated anti-malarial potential. Five of these plants were further analysed to identify the pharmacologically active compounds. A total of 12 compounds were isolated from hexane extract of plant AN-K-511. The full structural information of the isolated compounds was obtained by various physical and spectroscopic methods, including, IR, UV, low and high-resolution mass spectroscopy, and ¹H, ¹³C NMR including 2D NMR methods (COSY, NOESY, HMQC, and HMBC). Out of twelve active compounds obtained, six tested for anti malarial activity and one compound showed activity.

Characterization of proteins involved in the adhesion of *Leptospira* to epithelial cells and macrophages and their function

In this project, we are aiming to identify interacting molecules on real time basis by cross linking and identifying the molecules that take part in interaction. This will make it easy to know the role of these molecular interactions. A total 2957 proteins were identified which accounts 78.79% of the *Leptospiral* proteins. Fractionation using Trion X-114 was found efficient in enriching cytoplasmic proteins in the aqueous fraction, inner membrane protein in the pellet fraction and OMPs in the detergent fraction evidenced from their abundance in the respective fractions in tune with their predicted functional correlation. Only 19.66% of the predicted proteins were found abundant in the outer membrane. This shows that though 89.4% of OMPs expressed and available in the cell, only 17.57% were found abundant on the outer membrane. The presence of those OMPs on outer membrane may be limited in response to their requirement on the membrane. This scenario also will be considered in further analysis wherever the interacting partner is OMP.

PUBLIC HEALTH

- Generated evidence for the effectiveness and feasibility of supplementing mass drug administration of DEC and albendazole with

replacement of iodized salt with salt double fortified with DEC and iodine in hastening the reduction in microfilaraemia rate and thereby, elimination of lymphatic filariasis in Nancowry group of islands, the only focus of diurnally subperiodic *W. bancrofti* filariasis in India.

- For the first time in the country, centre carried out a comprehensive health and nutritional survey among the isolated tribe, Jarawas. The survey showed that the tribe is suffering from high prevalence of anaemia and that hypertension and dyslipidaemias are starting to become prevalent among the adults.
- Health and nutritional profile of three tribes viz., Onges, Andamanese and Shompen were updated with the results of recent surveys among them. These recent surveys showed that Shompen under-five children no longer have high prevalence of under-nutrition as was reported earlier. However, about 45% of the adults are either overweight or obese. IgG antibodies against measles and rubella were observed in older children and adults indicating natural infection with these viruses.
- A statistical model of Anopheles breeding risk based on physico-chemical parameters of the habitats was developed. The model showed that a pH \geq 8.3, dissolved oxygen \geq 16, nitrite \geq 0.026 and ammonia \geq 0.36 were found to be protective against breeding risk.
- A study on biofilm forming ability of *Leptospira* strains revealed that the severity of the disease caused by these strains showed that *in vitro* biofilm forming strains are more likely to produce severe disease than strains incapable of forming biofilms *in vitro*.
- Whole genome analysis showed that a strain that morphologically resembled *Leptospira* and isolated from a sick sheep was actually *Leptonema*, which was thought to be non-pathogenic. This is the first report of isolating strains belonging to *Leptonema* from sheep, pig and rat.

- Phytochemical investigation and anti-malarial activity of medicinal plants used by indigenous tribes of Andaman and Nicobar Islands identified with newer compounds in their crude extracts and showed antimalarial activity .

ICMR-DESERT MEDICINE RESEARCH CENTRE, JODHPUR

DMRC, Jodhpur has been working for two major research projects viz; Early Detection of Breast Cancer and Sickle Cell Anaemia. Other studies are mainly on Iodine Deficiency Disorder among pregnant women and estimation of the burden of TB among the tribal population and malnourished children

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 Govt And ICMR- Desert Medicine Research Centre, Jodhpur.

The aim of the study is 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 2018-19; a total of 25258 women from Jalore, Pali and Jodhpur districts have been covered and information about awareness about signs and symptoms and risk factors of breast cancer were collected. A total of 17529 women have also been imparted training for breast self examination. A total 229 suspect cases of Breast Cancer have been identified and cases have been recommended to consult PHC Medical Officer.

Sickle Cell Anaemia

Sickle cell disease is a group of genetically transmitted blood disorders. Probable estimate of magnitude of the problem of sickle cell disorders in the state of Rajasthan shows that it is a significant health problem. Present study is being carried out in the three blocks of the Tribal Sub Plan (TSP) areas reported high prevalence in our studies i.e.

Sajjangarh block of Banswara district, Kotra block of Udaipur district and Abu Road block of Sirohi District. Bhils are found predominant in Sajjangarh block of Banswara district whereas Garasiya tribe mostly residing nearby areas of Gujarat border i.e Kotra and Abu Road blocks. The screening work is being carried out jointly with Medical & Para medical staff of State Medical & Health Department, Udaipur. Total 36709 individuals have been screened so far out of which 4949 (13.48 %) individuals found confirmed positive cases.

Consumption pattern of food and food products/ items high in fat, salt and sugar among selected cities/ towns and rural population of India

The project was initiated with the objective to assess the consumption pattern of food and food products/ items high in fat, salt and sugar, from organized and unorganized sectors. Jaipur is one of the study sites under this multi-centric study, being carried out at 16 locations in the country and coordinated by Division of Nutrition, ICMR, New Delhi. A total of 947 and 620 households have been covered so far in Jamwa Ramgarh block and Chomu block, respectively of Jaipur district. The anthropometric parameters of the individuals residing in all 1567 houses have also been taken.

Iodine Deficiency Disorder (IDD)

ICMR has initiated a task force study on "Assessment of Iodine status among pregnant women in selected districts of India" during 2017 at 10 locations in the country. DMRC, Jodhpur is one of the participating centres of longitudinal study under which Jaisalmer District, Rajasthan is being covered. So far, the centre has recruited 223 pregnant women in first trimester and is being followed. Around 698 blood samples and 698 urine samples of pregnant women and 698 salt samples from their houses have been collected and analysed. Dietary intake and food frequencies of all the pregnant and lactating individuals has been carried out. Anthropometry of all the pregnant and lactating individuals has been conducted. The height & weight of the infants was taken.

Systematic pulmonary TB case finding among severely malnourished children admitted to Nutritional Rehabilitation Centres.

The objective of the study was to evaluate the current implementation of PTB screening and diagnostic efficiency in selected NRCs and also to estimate the prevalence of PTB amongst children admitted to NRCs. Study has so far detected 2 bacteriologically confirmed cases by cartridge based nucleic acid amplification test among 42 admitted children so far. Study will enroll 915 children in total and screen for PTB as per guidelines.

Estimate the burden of TB among the tribal population and develop an innovative health system model to strengthen TB control in the tribal areas of Rajasthan.

The study has been implemented in 4 phases including phase 1 - situational analysis, phase 2 – qualitative study, phase 3 – quantitative survey and phase 4 – intervention study in 8 villages in state. So far, first 3 phases have been covered in 3 villages. During the study, 5 bacteriologically confirmed TB cases were detected over and above the passively detected cases of TB in these villages by RNTCP.

ICMR-REGIONAL MEDICAL RESEARCH CENTRE, GORAKHPUR

Diagnostic services for suspected Japanese Encephalitis (JE) cases from eastern Uttar Pradesh.

Centre undertakes 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 during (1st April 2018 to 31st March 2019) were investigated for detection of anti-*Japanese encephalitis (JE)* virus specific IgM (anti-JE IgM), anti- *Orientia tsutsugamushi* IgM (anti - OTs IgM) and Dengue NS-1 antigen (DEN

NS-1 Ag) by ELISA assays as per the ICMR recommendations.

A total of 1884 clinical specimens (CSF and Serum) was collected from 1009 AES cases. Anti-JE IgM, anti-OTs IgM and DEN NS-1 Ag positivity were documented in 159 (15%), 474 (47%) and 55 (5.6%) AES cases respectively. In 11 AES cases, neither serum nor CSF was available for testing. (Table 1)

In addition, centre received specimens of suspected cases of Viral Encephalitis (VE) (n= 1830), which were tested as per AES diagnostic protocol. Anti-JE IgM positivity was found to be 12% of the cases, anti-OTs IgM (29.6%) and DEN NS-1 Ag positivity was documented in 6.9% of cases (Table 1). Of the 1830 cases, 227 suspected cases converted to AES during their hospital course.

2018- 2019 (No cases)	Specimens Type	Total samples received and tested	Anti-JE IgM Positivity (%)	Anti-OTs IgM Positivity (%)	DEN NS-1 Ag Positivity (%)
AES (1009)	CSF	910	72 (7.91%)	379 (41.6%)	--
	SERUM	974	150 (15.4%)	447 (45.9%)	55 (5.6%)
Suspected VE (1830)	CSF	477	31 (6.5%)	133 (27.9%)	--
	SERUM	1799	220 (12.2%)	521 (29.0%)	127 (6.9%)

Etiologic investigations in clinical specimens collected from Acute Encephalitis Syndrome (AES) cases from Eastern Uttar Pradesh.

ICMR recommended algorithm entitled "Laboratory testing algorithm for AES in India" to be followed to investigate the other viral /bacterial causes of AES. As per clinical presentation, laboratory finding and algorithm, virological diagnosis in CSF samples were done by PCR assay and were found positive for Herpes simplex virus (HSV)-1 (0.86%), Varicella Zoster virus (VZV) (0.86%), Parvovirus P4 (2.43%), while EBV, CMV, HSV-2/7, Parvovirus B19 were not detected in any of the cases. Results of the cases with rash, tested positive for Enteroviruses (0.81%) and flaviviruses (0%) (Table 2). Whole blood sample of OTs IgM seropositive cases was

tested by PCR and were found positive in 27.5%. Rickettsia (spotted fever group) was detected by PCR in 12.72% of the whole blood specimens of JE/ OTs/ Dengue negative AES cases with rash and thrombocytopenia. CSF samples from the selected JE negative cases suspected of bacterial infection (meningeal symptoms) also were investigated for *Streptococcus pneumoniae*, *Neisseria meningitidis* & *Haemophilus influenzae* by multiplex PCR, one case found positive for *S. pneumoniae*. These findings suggest a major contribution of OTs and other rickettsial agents in the non-JE AES cases occurring in the region.

Table 2: Summary of the diagnostic finding of AES cases during 2018

Etiology	Samples	Test	Positive / total samples	% Positivity
Flaviviruses (JEV, DENV, WNV, Zika, etc.)	CSF	RT-PCR	0/33	0%
Parvo P4	CSF	PCR	1/41	2.43%
Parvo B19	CSF	PCR	0/41	0%
HSV 1	CSF	PCR	1/116	0.86%
HSV 2	CSF	PCR	0/116	0%
CMV	CSF	PCR	0/116	0%
VZV	CSF	PCR	1/116	0.86%
EBV	CSF	PCR	0/116	0%
Enterovirus	CSF	RT-PCR	1/122	0.81%
<i>O. tsutsugamushi</i>	Blood	PCR	121/439	27.56%
Rickettsial	Blood	PCR	14/110	12.72%
<i>N. meningitidis</i>	CSF	PCR	0/43	0%
<i>S. pneumoniae</i>	CSF	PCR	1/43	2.85%
<i>H. influenzae</i>	CSF	PCR	0/43	0%
MTB	CSF	PCR	0/12	0%

Epidemiological and clinical correlation of acute encephalitis syndrome cases with JE, non-JE viral and other AES associated etiologies from eastern Uttar Pradesh.

JE, OTs and other Rickettsia and Dengue have emerged as the associated causes with about 60% AES cases investigated during 2018. Maximum AES cases were reported from Gorakhpur district (274) followed by Kushinagar (166), and Deoria (158). AES cases began to rise from the month of July, peaked during the months of August to October and decline in the incidence of cases was noted in the month of November as the similar pattern shown in previous years. The most affected population was in the range of 1-5 years (337) followed by 5-10

years (261) of the age group. Of these cases, JE was reported maximum from Gorakhpur (34) followed by Kushinagar (18). Similarly, Scrub typhus (ST) was reported maximum from Gorakhpur (135) followed by Deoria (82) and Kushinagar (69). Children of age group 1-5 year (156) were affected maximum by ST and cases peaked during the months of August to November. In AES cases, Dengue positivity was mostly documented during the months of September (23) and October (15). Azithromycin was given to 899 out of 1017 AES patients. Children who received azithromycin were less likely to die of AES (Yates Corrected Chi squared value: 5.66; p- 0.017).

Isolation, identification and genetic characterization of viruses isolated from acute encephalitis syndrome cases from eastern Uttar Pradesh.

Virus isolation is regarded as the 'gold standard' in the investigation of viral etiologies as well as genetic characterization of viruses. Fifty four serum specimens collected from Dengue fever cases admitted to Gorakhnath hospital, Gorakhpur, were all positive for Dengue NS1 antigen. These serum samples were attempted for virus isolation in Porcine Stable kidney (PS) cells. Moreover, 11 serum specimens collected from suspected viral encephalitis cases from BDR medical college, Gorakhpur and positive for anti-Dengue IgM were also attempted for virus isolation. None of the cultures showed any cytopathic effect till the fourth passage.

Etiological investigations of non-AES referred cases from Gorakhpur region.

Apart from diagnostic services to referred AES cases, centre also provides diagnostic services to non-AES referred samples from BRD Medical College and other hospitals from Gorakhpur and nearby districts. Based on the clinician recommendation, 140 clinical specimens (79 CSF, 46 serum, 4 blood, 5 throat swab, 4 skin swab and 2 urine) were investigated for JE, OTs, DEN, HSV, VZV, CMV. Anti-JE IgM antibodies were detected

in 5.26 % (2/38) of Serum and 1.49% of CSF (1/67), anti-OTs IgM in 7.89% of sera (3/38) and 4.47 % of CSF (3/67) specimens, while Dengue NS1 was diagnosed in one serum (1/38). The CSF of 67 patients was subjected for molecular diagnosis for HSV-1/2, VZV and CMV. Blood, serum and urine specimens were detected positive for CMV in one patient. In addition, VZV was detected in skin swab (n=2), throat swab (n=2), and serum (n=1) samples tested.

Setting up of AES Cell at Baba Raghav Das Medical College, Gorakhpur.

AES cell was established on recommendations of ICMR to streamline the process of clinical specimen collection, distribution for different investigations and storage for future research on AES cases. Genetic characterization of ST and rickettsia was carried out to define the prevalence and circulation of different strains and to define their genetic relationship. OTs IgM positive whole blood samples were processed for PCR targeting the 56 kDa gene specific primers of OTs, and PCR positive samples were further reconfirmed by nucleotide sequencing. The percentage positivity was 27.56% (121/439) in whole blood specimens. Further the PCR positive samples were selected for genetic analysis to know the prevalent genotype of OTs in the Gorakhpur region. The phylogenetic analysis was carried out using sequences retrieved in our study along with global reference sequences downloaded from NCBI Gen Bank database. The sequence analysis confirmed Gilliam genotype is the most prevalent genotype in this area comprising about 95.1% (79/83) and the karp genotype is about 4.81% (4/83) of OTs (Fig 18). The percentage nucleotide identity is >99.95% in-between the sequences of the Gilliam genotype isolated in this study. (Fig 18).

In addition to it, 110 selected cases of OTs IgM / PCR negative with the sign of a rash and multi organ involvement were investigated for Spotted Fever Group (SFG) of rickettsia with primers targeting the 23s-5s Inter genomic region of rickettsia. The PCR result found that 12.72% (14/110) cases

were positive and sequence analysis followed by preliminary blast result showed the prevalence of *R. conorii* in most of the cases.

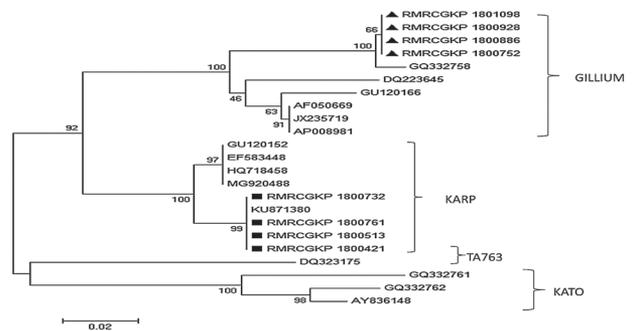


Fig. 18: Phylogenetic tree of *Orientia tsutsugamushi* based on the nucleotide sequences of the 56-kDa cell surface antigen gene.

Genetics of susceptibility to encephalitis in Japanese encephalitis virus infected children from Uttar Pradesh.

The clinical outcome of the disease is influenced by factors involving host, virus and environment. Polymorphisms in the genes coding for various molecules involved in the immune response against JEV might affect their expression and functioning and may be associated with susceptibility to encephalitis in JEV infection. To find out polymorphisms in genes coding for pattern recognition receptors and inflammatory mediators and receptors, a total number of 312 healthy controls without any history of encephalitis and 148 encephalitis cases positive for JEV were recruited from villages in blocks of Gorakhpur, Deoria, Maharajganj, Kushinagar and Sant Kabir Nagar. Patients were followed up for assessing post JE disability as well as a large spectrum of the behavioral disturbance. The frequency of *TNFA* -308 G/A [Odds Ratio (95%CI); 2.14 (1.10-4.16)], *CCL2* -2518 G/G [1.89 (1.07-3.33)] genotype were significantly higher in JE cases as compared to controls. *CCL2* -2518 G/G genotype associated with JE was of recessive mode (GG/G vs. A/A + A/G). A higher frequency of heterozygous genotype of *CCR5* Δ 32 mutation was observed in JE cases but the difference was not significant. The results suggest that G/A genotype of *TNFA* -308 and G/G genotype of *CCL2* -2518 might be associated with susceptibility to Japanese encephalitis.

Establishment of a Health and Demographic Surveillance System [HDSS], Gorakhpur, Uttar Pradesh.

Establishment of HDSS helps to monitor demographics of the population and provides a well characterized denominator for complex observational and interventional epidemiological studies. Findings of HDSS will generate evidence for making holistic policies for this region. Such data collected over the years will be valuable because of its longitudinal nature.

Reducing the burden of AES due to scrub typhus through the empiric treatment of acute febrile illness with doxycycline/ azithromycin: An implementation research study

Scrub Typhus (ST) is the major etiology of AES outbreaks, accounting for >60% AES patients while Japanese encephalitis virus accounted for <10% cases. While most infections are asymptomatic, few children develop febrile illness and small proportion progress to AES. Hence early administration of appropriate antibiotics is crucial. Indian Council of Medical Research had recommended the state health authorities to provide empiric doxycycline/azithromycin (EDA) treatment to children with acute undifferentiated febrile illness (AUFIs) attending peripheral health facilities in Gorakhpur and Basti divisions during August–November, when AES cases peak. Centre estimated the effectiveness of EDA treatment in Gorakhpur district.

Medical Officers (MO) and pharmacists from all the PHCs/CHCs in the three blocks (Bhathat, Campiergunj and Jungle Kaudia) were sensitized about etiology of AES in the region, the rationale of EDA strategy, an algorithm for treatment of AUFIs including dosage of doxycycline/azithromycin by weight as well as age. All AUFIs aged ≤15 years, after their consultation with MOs were enrolled and followed up telephonically on the third and fifth day to collect information about clinical status including recovery, improvement or worsening of the clinical condition. At public health facilities, 801 (86%) were prescribed doxycycline/

azithromycin. The compliance to prescribe EDA ranged between 76.4% to 92.7% across three health centres. Of the 725 AUFIs followed up, 621 (86%) had received EDA. Six of the 621 AUFIs who received EDA and five of the 124 who did not receive EDA progressed to AES with cumulative incidences of 0.96% and 4.8% respectively. The effectiveness of EDA strategy was 79.9% (95% CI: 35.4–94).

EDA treatment to children with AUFIs in peripheral health facilities between August and October could prevent progression to AES due to ST. For reducing the burden of ST-AES in the region, it is necessary to sensitize health professionals in public as well as private sector before the outbreak. It is also necessary to monitor the implementation of this strategy including the drug resistance.

ICMR-RMRC DIBRUGARH

CANCERS

Germline mutation spectra of *BRCA1* and *BRCA2* genes in multi-ethnic breast cancer patients from N.E. region based on direct sequencing.

It was found that out of 24 exons of *BRCA1*, only 5 exons (7, 16, 18, 22 & 24) had clinically important mutation, while 3 exons (3, 13 & 23) had silent mutation which are not clinically important. Two novel mutations in *BRCA1* gene were observed in North East India.

Study on molecular epidemiology and risk factors of gastric cancers in Tripura and Nagaland.

Detection of mutation spectra in key tumor suppressor and proto-oncogenes have shown that there is population specific mutation patterns in gastric cancer cases from Tripura and Nagaland.

Screening & early detection of oral, breast & cervical cancers in Dibrugarh District, Assam. A demonstration project in TATA Tea gardens.

Till date, 2500 subjects have been enrolled in the study. Based on their risks score, pre-cancerous

lesions evaluation will be done at their TATA Central Hospital, Chabua & the confirmed cases shall be referred to AMCH, Dibrugarh for further management.

CARDIOVASCULAR DISEASES

Effectiveness of diet and lifestyle intervention through IEC tools with Angan wadi centres as the centre of knowledge dissemination for hypertension (including hypercholesterolemia and diabetes) risk reduction – a cluster randomized controlled trial.

The study was carried out in 12 clusters to assess the impact of lifestyle intervention for reduction of risk associated with hypertension, hypercholesterolemia and diabetes.

Health system preparedness for interventions for diabetes, hypertension, chronic respiratory diseases and cardiovascular diseases and deaths due to non-communicable diseases (NCD) among the tribal population in India.

It was observed that in the northeast, overall non-communicable diseases including cardiovascular diseases, cancer, diabetes are leading causes of death. Among the communicable diseases, tuberculosis was the commonest cause of death.

Establishment of health and demographic surveillance system in Dibrugarh district, Assam (Dibrugarh – HDSS).

This study was launched on 17th January 2019 with the objective to establish population-based health and demographic surveillance system for epidemiological and programmatic evidence/intervention in Dibrugarh district, Assam.

MALARIA

Malaria Evolution in South Asia (South Asia-ICEMR)-Phase II.

After completion of the first phase work, visits were carried out in the 7 different states of north east India to select the main hot foci of malaria prone areas to set up the base camp for field work.

Novel malaria surveillance system along international borders to North-east India using mobile platforms (MoSQUIT).

Deployment of mobile based app was completed in 3 international border areas of Northeast India. So far, 3799 records have been obtained from Tripura, 2906 from Assam and 139 from Arunachal Pradesh.

A pilot study to see the feasibility and impacts of novel personal protectants on the Jhumias of a selected malaria endemic zone of Tripura along with the entomological studies.

In this study, several issues with malaria surveillance and vector control measures associated with malaria risk among the Jhum cultivators in Tripura were observed and the findings of background studies were conveyed to the national programs and state health departments.

Monitoring of insecticide resistance in malaria vectors in endemic states of India.

Entomological survey was carried out in 91 sites from collectively 19 districts of 7 northeastern states. The primary vectors of malaria in N.E. states viz., *An. minimus* and *An. baimaii* were found to be susceptible to DDT 4%. *An. baimaii* collected from Pangbalkawn locality in Kolasib district of Mizoram was susceptible to 5% malathion, 0.05% deltamethrin, 1% fenitrothion, 0.05% lambda-cyhalothrin and 0.75% permethrin. *An. nivipes/philippinensis* was found to be susceptible to 4% DDT, 5% malathion, 0.05% deltamethrin, 1% fenitrothion, 0.05% lambda-cyhalothrin and 0.75% permethrin.

Bionomics of malaria vector(s), sibling species composition and to establish their role in malaria transmission in North East Region of India.

Entomological surveys were conducted in 15 villages from 4 districts of Meghalaya and Tripura. Primary malaria vector i.e., *An. minimus* and *An. baimaii* mosquitoes were present in the study areas (density: 8-12 number of mosquitoes per night survey). Breeding habitat of 9 *Anopheline* species revealed that *An. annularis*, *An. jeyporiensis*, *An.*

vagus, *An. hyrcanus*, *An. kochi*, *An. splendidus* were found prevalent in the study sites during the peak transmission period *i.e.*, June-August. *An. baimaii* type of *An. baimaii* complex were prevalent in Meghalaya and Tripura. Allele specific PCR shows that *An. minimus* complex comprised of *An. minimus*, *An. varuna* and *An. Jeyporiensis*.

Operational feasibility of additional interventions for accelerated malaria control in areas with Jhum Cultivators in Tripura.

This is a newly initiated ICMR funded project in collaboration with State Health Dept, NVBDCP, VRDL, Tripura and NESAC, Shillong aiming towards extensive control of malaria in very high malaria endemic areas to get them into pre-elimination phase, with a set of low cost interventions targeted and customized for Jhum cultivating areas with overall strengthening of malaria surveillance and public health system .

MICROBIAL DISEASES

Study on impact of climate change on seasonality and distribution of insect vector borne viral and Rickettsial diseases in North-East India: A remote sensing and geographical information system approach.

A total of 347 JE cases have been reported from Dibrugarh during 2013 to 2017. To assess the impact of the climate variables on the occurrence of JE cases, time lagged (3 month) correlation between meteorological factors and occurrence were used. Logical relations were found with rainfall except in the year 2015 which recorded high rainfall (approximately 1577.85 mm cumulative) but only 32 JE cases were reported. The localities with distribution of hot spot and cold spot of JE case abundance were identified with the Z-score computed by Getis-Ord Gi.

Study of Genetic diversity and drug resistance pattern of *Mycobacterium tuberculosis* in the tribal state of Sikkim.

This study revealed 56 different spoligotypes circulating in Sikkim and Beijing genotype was

most dominant (61.9%). Beijing genotypes were associated in MDR TB. Mutation patterns of MDR strains from Sikkim was also worked out.

Estimate the burden of TB among the tribal population and develop an innovative health system model to strengthen TB control in the tribal areas of Meghalaya, Manipur, Nagaland and Tripura.

A community based study was carried out in the tribal dominated areas of Meghalaya, Manipur, Nagaland and Tripura to estimate prevalence of TB and understand TB treatment seeking behavior of tribals. Highest prevalence of TB was found in tribal from Nagaland.

Rickettsial diseases in the states of Nagaland, Meghalaya and Mizoram in NE India: epidemiology, disease burden and vectors.

Rickettsial diseases have been found to be widely prevalent in the states with Scrub typhus being predominant (18%, N= 986) followed by Spotted fever group rickettsia (8.6%, N=986) and Typhus group rickettsiae (3.7%, N=986) in the three states. Potential vectors of rickettsial diseases *viz.*, *Haemaphysalis* spp, *Rhipicephalus* spp, *Boophilus* spp, *Ctenocephalides felis*, *Dermacentor* spp, *Hyalomma* spp, *Leptotrombidium* spp, *Xenopsylla* spp and *Pulex irritans* have been identified from the endemic areas of the study states.

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.

Effectiveness of a single dose of the JE vaccine has been found to stabilize around 70% after a period of 7 years (Sivasagar) and 5 years (Dibrugarh) post vaccination. Vaccination has brought down the number of JE cases in both the districts. However, the incidence rate (IR) is maintained around 5 in the adult population in both the districts. Vaccine coverage among controls in both the districts is found to be low (~33-40%).

To study the virulence factor and adhesins of uropathogenic *Escherichia coli* (UPEC) isolates

from pregnant women with urinary tract infections.

In order of frequency *fimH* was the most common virulence gene detected (64.3%) followed by *iutA* (43%), *papC* (28.6%) *sfa/foc* (21.4%), *iucC* & *fimA* (14.3%), *afaC*, *hlyF*, *ibeA* (7.1% each) among *E. coli* obtained from UTI cases.

Influence of maternal microbiome (vaginal, breast milk, cord blood and amniotic fluid) and immunogenic factors for survival, growth and immune modulation of premature neonates via gut microbiota establishment.

The present study is mapping the dynamicity of neonatal gut-microbiome establishment throughout the lactation period among vaginally delivered and C-section neonates and its correlation with maternal microbiome.

Role of accessory gene regulator (*agr*) operon and virulence markers of *S. aureus*, causing endogenous invasive infections.

So far, 7 nasal isolates of *S. aureus* with their paired invasive isolate from same patient were subjected to PFGE to identify the similar clones. Of these, identical colonizing and pathogenic strains were found in 12 paired strains and were processed for RNA isolation and downstream processing.

Enhancing Biorisk mitigation awareness in public health community and creating laboratory networks for enhanced diagnostic capabilities to deal with surveillance and outbreaks of high-risk group viral pathogens causing viral hemorrhagic fevers and respiratory infections.

So far, 2773 (Males: 1350; Females: 1423) samples of acute RTI cases screened for respiratory viruses showed overall positivity of 34.9% (969/2773). Maximum detection was Rhinovirus (10.4%) followed by RSV (6.40%) & Influenza-A (5.73%). The co-infection of two or more respiratory viruses was detected in 7.95% (77/969) of them.

Establishment of a network of laboratories for managing epidemics and natural calamities.

So far, the Regional VRDL have performed 41,227 tests for 12,931 samples and investigated 33 nos. of outbreaks. Presently the laboratory has developed facility for diagnosis of 41 different viral infection and 15 non viral pathogens. The most prevalent virus was found to be respiratory virus viz. Influenza A virus and RSV. Scrub Typhus and *S. pneumoniae* were found to be the most prevalent non-viral agents identified.

Vector surveillance for ZIKV in selected high risk areas in India.

In this study, a total of 6229 adult *Aedes* mosquitoes were collected from the four study sites. [Pasighat: 2253; Dimapur: 1902; Guwahati: 1597; Tura: 477]. No evidence of presence of ZIKV/DENV was found in the screened pools by first stage RT-PCR. During this study DENV-1, 2 and 3 were detected from Northeast India and altogether 54 pools were found positive for DENV.

Assessment of the acute gastroenteritis pathogens among hospitalized children below 5 years of age in Dibrugarh and Dimapur.

The overall prevalence of rotavirus diarrhoea was highest (67.1%), followed by Adenovirus (45.9%), *Shigella/enteroinvasive E coli* (43%), *Norovirus* GII (17.9%), *Campylobacter jejuni/coli/lari* (10.1%) and Astrovirus (5.9%). The most common co-infection was caused by rotavirus and adenovirus (28.1%) and by rotavirus together with *Shigella spp/enteroinvasive E coli* in 26.6% (108/406) of the subjects tested. Triple co-infection of rotavirus with adenovirus and *Shigella spp/enteroinvasive E coli* was seen in 5.9% (24/406) subjects.

A systematic study of Acute Encephalitis Syndrome (AES) in North-eastern states of India for clinical, etiological and epidemiological aspects.

On the basis of an algorithm developed for the diagnosis of AES cases, serological screening of 3035 blood samples was done. The screening revealed that 23.82% (n=3035) were positive for JE, followed by scrub typhus (14.21%; n=2286);

spotted fever group rickettsiae (11.46%; n=2286); *Leptospira* (4.1%; n=2286); typhus group rickettsiae (1.57%; n=2286). West Nile (WN) positivity was detected in 3.78% (n=3035).

OTHER PROJECTS

DBT-ICMR animal house facility for Biotechnology Research in North-eastern Region.

The objective of the project is to develop an advanced animal house facility for housing small laboratory animals, accessible to all the Northeastern states of India for biomedical / biotechnology research .

OUTBREAK INVESTIGATIONS

Malaria outbreak investigation in Dhalai district of Tripura.

It was conducted in September-October 2018 and report was submitted to State Health authority pointing out the possible causes of the outbreak with suggestions for immediate and long term control measures, from which a number of them have been or going to be implemented by the State as well as RMRC projects in the State in collaborative manner.

Hepatitis B investigation at Anjaw District of Arunachal Pradesh (6th -10th Aug 2018).

A team from Regional VRLD, RMRC Dibrugarh, visited Anjaw district of Arunachal Pradesh from 6-10 August 2018 following request received from state health authorities to investigate Hepatitis B infection in the district. The team could investigate 317 cases; (176 cases in Hayuliang and 141 cases from Hawaii) and found all cases to be asymptomatic. On request of health authorities of Arunachal Pradesh, plasma viral load testing provided free of cost to 310 patients (As service on request by State).

Outbreak of Dengue Fever in Dimapur, Nagaland (Sept 2018).

A team from Regional, VRDL, Dibrugarh investigated a dengue fever outbreak in Sep 2018 in Dimapur Nagaland. A total of 345 cases were detected to be positive for dengue and there was no reported mortality. The team also performed a house to house survey and collected 20 samples of fever which were found to be positive for either NS1 Ag or IgM. The circulating serotype of dengue circulating was found to be Serotype-I.

SUPPORTING FACILITIES

During the period under report, the National Institute of Epidemiology (NIE) at Chennai and the National Institute of Medical Statistics (NIMS) at New Delhi provided statistical assistance to various ICMR institutes. 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 ISRM Division strived to move the organization towards new goals of technology and digitization.

INTRAMURAL RESEARCH

ICMR-NATIONAL INSTITUTE OF EPIDEMIOLOGY, CHENNAI

INDIA HYPERTENSION CONTROL INITIATIVE (IHCI)

ICMR, in collaboration with state health departments, MoHFW, WHO and Resolve to Save Lives - Vital Strategies initiated a project in 25 districts to strengthen the hypertension treatment component of National program for Prevention and Control of Cancer, Diabetes, CVD and Stroke (NPCDCS). The strategies to improve hypertension treatment coverage and blood pressure control included (a) Standard treatment algorithm (b) Capacity building at all levels (c) Availability of

protocol drugs (d) Patient cohort monitoring and (e) Decentralization for BP measurement and drug dispensing at sub-center level. The program is currently being implemented in 800+ health facilities in Punjab, Maharashtra, Madhya Pradesh, Telangana and Kerala and 2,80,000 hypertension patients have been initiated on treatment.

HIV SENTINEL SURVEILLANCE IN SOUTHERN INDIA

In the current round of HIV surveillance, 1,00,322 blood samples from antenatal women from 251 sentinel sites and 3171 blood samples from Prisoners from 12 sites across the states of Tamil Nadu, Andhra Pradesh, Telangana, Karnataka, Kerala, Orissa and Pondicherry were collected. The lab testing at the concerned state Laboratories are in progress.

Surveillance for pneumonia and Invasive Bacterial Diseases (IBD)

Surveillance for pneumonia and IBD has been ongoing in 6 sites to determine the serotype profile and subsequent replacement of serotypes of *S. pneumoniae* in under-five children with pneumonia and IBD. During 2016-18, a total of 1216 suspected pneumonia, 671 suspected meningitis and 312 suspected sepsis were enrolled. Based on the various laboratory test, *S. pneumoniae* (n=51) was the commonest cause for pneumonia and other IBD cases in children aged between 1 to 59 months, followed by *H. influenzae* type b (n=8) and *N. meningitidis* (n=8). During the study period, 12 different serotypes were identified which includes

14 (5 nos), 6B (2 nos), 1 (2 nos), 10A (2 nos), 2, 19 F (4 nos), 9V (2 nos), 33A; 5 (2 nos), 7B, 6A, and 15C.

Congenital Rubella Syndrome surveillance (CRS) in India

Hospital based surveillance for congenital rubella syndrome has been established in five sentinel sites to estimate the burden of CRS. During 2016-18, a total of 645 suspected CRS patients were enrolled, 20% of whom were laboratory confirmed CRS. CRS surveillance is being expanded to additional 10 sites

Indian Network of Population-Based Surveillance Platform for Influenza and Other Respiratory Viruses among Elderly (INSPIRE)

The surveillance data indicate that the prevalence of Acute Respiratory Illness (ARI) among elderly population was 7% and 3.7% during phase-1 and phase-2. The incidence of influenza during these periods was respectively 1.7 and 0.6 per 1000 person weeks.

Integrated Road Traffic Injury Surveillance system (IRIS) Chennai, Tamil Nadu

As a part of ICMR Task force study, hospital-based surveillance of Road Traffic Injuries (RTIs) was established at a major public sector referral facility (Rajiv Gandhi Government General Hospital – RGGGH; since 31 Oct 2018) and a private sector referral facility (Sundaram Medical Foundation Hospital – SMFH since 14 Feb 2018) in Chennai, Tamil Nadu. As on 30 April 2019, a total of 2077 and 140 RTI cases enrolled at RGGGH and SMFH respectively. Community-based surveillance was established at the sub-urban locality (Ayappakkam) since 1 Feb 2019 and 38 RTI cases have been recorded in this site covering 1357 households.

Surveillance of Acute febrile illness, Acute respiratory illness at district and sub-district hospital

Hospital based surveillance of Acute Febrile Illness (AFI) and Acute Respiratory Illness (ARI) was established at a district Headquarters Hospital and

2 sub-district hospitals in Tamil Nadu. Between October 2016 and March 2019, 8500 cases were enrolled in the three hospitals and overall proportion of infections detected were Dengue (11%), Scrub typhus (11.7%), Leptospirosis (7.7%), Influenza A (7.1%), Influenza B (13.3%), Malaria (1.3%) and enteric fever (0.8%).

In-Country assessment for Elimination of Mother to Child Transmission of HIV and Syphilis in India

An assessment for elimination of mother to child transmission of HIV and Syphilis has been initiated in 19 Indian states. The assessment covers the following components: (a) Programs and services (b) Data quality (c) Laboratory and (d) Human rights and community engagement.

Impact of Measles and Rubella (MR) Vaccination campaign on population Immunity (IMRVI)

A project to estimate the seroprevalence of measles and rubella before and after MR vaccination campaign has been initiated in 9 states. The seroprevalence of measles before MR campaign was 63%, 68%, 53%, and 71% in Assam, Maharashtra, Punjab and Uttar Pradesh respectively. The corresponding sero-prevalence of rubella was 32%, 46%, 39% and 42% respectively.

A Multicentric Study to estimate the seroprevalence of Dengue Virus infection in India

A survey to estimate the seroprevalence of dengue was conducted in 15 Indian states covering 60 districts and 240 clusters (120 rural and 120 urban). The overall seroprevalence of dengue in India was The overall seroprevalence of DENV infection in India based on testing of sera from 12,300 individuals, was 48.7% (95% confidence interval 43.5-54.0)

Dengue in India: A systematic review and meta-analysis

A systematic review and meta-analysis of dengue in India indicated that the prevalence of lab confirmed

dengue infection among clinically suspected patients: 38.3% (95% CI: 34.8%–41.8%).

Sero-prevalence of IgM and IgG antibodies against Nipah among close contacts of laboratory confirmed NiV case

A sero-survey of 279 close contacts of laboratory confirmed patients of Nipah during the outbreak in Kerala indicated three individuals with subclinical infections.

Assessment of health impacts among the nearby residents of thermal power stations at Ennore, North-Chennai, Tamil Nadu

A total of 1217 (M-560; F-657) participants were recruited. Spirometry tests were done for 522 (M-288; F-234) individuals. Self-reported morbidity indicates that Diabetes followed by hypertension and respiratory diseases are found high.

Rotavirus Vaccine Impact Assessment Study

Hospital based surveillance for Acute Gastroenteritis (AGE) among under five children and Intussusception (IS) among under 2 year old children was established at the Institute of Child Health and Hospital for Children, Chennai. Between August 2017 and March 2019, 677 children with AGE and 79 cases of IS were enrolled and rotavirus positivity was 30.6% and 1.5% respectively. Rotavirus associated AGE was highest among children below 2 years of age 29.7%.

Rapid assessment of coverage of Doxycycline for prevention of Leptospirosis

Coverage among individuals with history of exposure to dirty/ contaminated water (n=119) was 48.7% (36.9 – 60.5). Nearly 95% of those who consumed Doxycycline reported of taking one or more than one dose in the week previous to survey.

A Systematic assessment of acute viral hepatitis and chronic liver diseases in Northeast India with special reference to strengthening of laboratories in the region

A project to systematically study the prevalence, potential risk factors, virological profile and

molecular characterization associated with Hepatitis Viruses (HAV, HBV, HCV, HDV and HEV) in all eight northeast states of India has been initiated. This study will also help in strengthening the laboratory capacities (VRDLs/hospital sites) for diagnosing of these hepatotropic viruses in the entire North Eastern region.

Health systems preparedness and deaths due to non-communicable diseases among the tribal population in India

Verbal autopsy was done for 5292 deaths across twelve districts with 50% or more tribal population (eight north eastern states, Odisha, HP, A and N and MP). Overall, non communicable diseases accounted for most of the deaths (66%) followed by infectious diseases (15%), injuries and suicide (11%), and not elsewhere classifiable (9%). Centre surveyed 177 health centres in 12 districts including 156 PHCs and 21 district hospital in the study. The doctors were available in most health facilities. The major gaps for managing NCD were lack of training, inadequate availability of drugs, lack of diagnostic facilities, lack of information systems for NCD patients and poor utilisation of health facilities for NCD treatment.

Concurrent evaluation of Human Papilloma Virus (HPV) vaccine program and (HPV) and vaccine acceptance among adolescent girls in Punjab

A survey of 1800+ 7th and 8th standard school girls vaccinated with HPV one dose and two doses in 2016 and 2017 was completed in Bhatinda and Mansa districts.

PUBLIC HEALTH TRAINING PROGRAMS

- **Master of Public Health (Epidemiology and Health Systems)**

11th cohort of the MPH with 11 scholars was recruited during 2018. A total of 246 health officers from 26 Indian States/Union Territories have graduated.

- **MSc (Biostatistics)**

MSc Biostatistics program has enrolled 25 students in three batches. In the first cohort 3 students have graduated.

- **Online course on Health Research Fundamentals**

2402 students were enrolled in the 7th batch. Till date, 20,266 students have been enrolled for the course since 2016 and 95% qualified the written examination.

- **Noncommunicable disease Epidemiology Fellowship**

NIE initiated a two year NCD epidemiology fellowship program with 5 five fellows.

- **India Epidemic Intelligence Service Programme (EIS)**

The Southern hub of EIS program was established at NIE during 2018. Five officers from Telangana (2), Kerala (1) and Tamil Nadu (2) are undergoing the program in the first cohort.

ICMR-NATIONAL INSTITUTE OF MEDICAL STATISTICS, NEW DELHI

The Clinical Trials Registry – India (CTRI) is a national online register for registering clinical trials being conducted in India. CTRI is a Primary Registry of the WHO's International Clinical Trials Registry Platform (ICTRP), it also registers trials being conducted in countries which do not have a Primary Registry of their own. CTRI registers all types therapeutic area trials, i.e. interventional, observational bio-availability/bio-equivalence, surgical, lifestyle, devices, Ayurveda, herbal etc. In line with the global mandate, the CTRI has also moved towards only prospective registration from 1st April 2018. The CTRI has 18345 clinical studies registered till 31st March 2019.

The BOD-NCD Methodology group was initiated on 20th September 2017 as one of the working

groups of the BOD-NCD study at ICMR in the Division of Non-Communicable Diseases. The primary objective of the project was to generate evidence-based, valid and comparable national and sub national estimates of the disease burden and risk factors. The estimates were derived for 2015 using an indigenous algorithm based on available mortality data from RGI-SRS cause of death statistics. Disease burden estimates for India, Urban-Rural and the following 19 (Jammu and Kashmir; Punjab; Delhi; Haryana; Uttar Pradesh; Rajasthan; Chhattisgarh; Bihar; Jharkhand; Madhya Pradesh; Gujarat; Maharashtra; West Bengal; Odisha; Andhra Pradesh; Tamil Nadu; Kerala; Karnataka; Assam; Other North Eastern States) and all remaining states was estimated.

ICMR-NIMS is designated as the nodal Institute by NACO to provide estimates of HIV burden of India and its states since 2003. As part of the HIV estimation 2017 process, the following activities were undertaken during the reporting period like Preparation of HIV estimation technical report 2017, constitution of National Working Group Committee for District level HIV estimation, finalisation of methodology for district level estimation, data management and analysis of HSS data 2017. India HIV Estimation 2017 technical report was published and is available on NACO and ICMR-NIMS website.

A project on comparing methods of assigning causes of death supported by MoHFW and WHO to field test the WHO harmonized verbal autopsy tool and compare PCVA and CCVA methods. The study findings will be utilised for recommending the methodology of a routine national verbal autopsy programme for ascertaining the cause of death in India.

A study entitled, 'Evaluation of Impact of Antiretroviral Therapy under National AIDS Control Programme in India for 8 Northern States funded by NACO through ICMR-NARI' is ongoing at ICMR-NIMS to assess the impact of ART on the health (e.g. illness profiles, hospitalization, incidence of TB and deaths, quality of life) of

people living with HIV (PLHIV) taking treatment in NACO supported ART Centres (ARTC) in India. Primary and secondary data collection has been completed.

A study on gender inequity in health seeking behaviour and utilization of health services among Santhal tribes of Jharkhand was undertaken. The findings of study indicate low utilization of health services and gender differentials in treatment seeking behavior among these tribes. For seeking treatment for general illness, about one third of tribal people visited government service providers, 42% visited private health service providers and 22% used traditional methods for treatment. For treatment of chronic illnesses, half of the tribes visited government health service providers, one third visited private health service providers and 16% used traditional methods. Two-thirds of ill persons delayed seeking treatment for more than 2 days (> 2). Majority (70.0%) had to travel more than 10 kilometres for seeking treatment from government health services.

A research project on ‘Improvement in the utilization of Reproductive and Child Health services through male participation among the Saharia Tribes in Gwalior district, Madhya Pradesh’ has been completed. Study findings indicate that Saharia men were unaware of health care needs of the pregnant and lactating women. The practices and beliefs in the community and the low level of knowledge regarding ANC/PNC and safe delivery process prevent them from participating in the maternal and child health care activities. Feasibility study conducted for testing the Behaviour Change Communication model developed during the study for engaging men in RCH services showed potential of being acceptable by the community and capacity of being integrated with the current programme.

The project entitled, ‘Quality of care in maternal and newborn health in Rural India: a multilevel modelling’ is ongoing to understand quality of care provided to the mother exclusively and quality of care provided to the newborn while evaluating the impact of care on newborn mortality.

TRAINING AND CAPACITY BUILDING

Capacity Building in Survey Research Methodology

A three day training programme was organized for faculty and researchers at ICMR-NIMS during 8-10 October, 2018 in collaboration with Institute of Applied Statistics and Developments Studies, Lucknow. Forty participants attended the workshop.

BIOMER 2018 - Biostatistical Methods in Medical research

A total of 30 participants attended the four-day workshop that focussed on interactive learning sessions on research methodology and hands on training on statistical softwares.

Statistical methods in health data analytics using R

Thirty participants attended workshop that focused on R Programming in statistical analysis of health data.

Public Health Relevance

- The CTRI brings all clinical trials to public domain which empowers patients to participate in relevant clinical trials pertaining to their conditions particularly life-threatening diseases. It is a free and online searchable database in the country which can be tapped by academicians, researchers, social activists and parliamentarians among others.
- HIV estimates and prevalence data would help in identifying regions with high disease burden which in turn assists the programme strategies for control, treatment and prevention of disease.
- Disease burden estimates helps in identifying major data gaps and guide policy actions. State level disease burden estimates would aid in addressing the health inequalities between

states and help the governments to take appropriate measures to provide health care services.

- Studies on tribal health in Madhya Pradesh and Jharkhand states would suggest appropriate health care delivery programmes to tribal community.



Fig. 1: Community Training Programme for Male Saharia Tribes of Dabra block, Gwalior.



Fig. 2: Dr V K Paul, Member NITI Ayog was awarded P P Talwar Oration award on 14th June 2018. Prof B Bhargava, Secretary, DHR and DG ICMR, presided over the function.



Fig. 3: Prof Srinath Reddy, President Public Health Foundation, chief guest, NIMS-ICMR Foundation day celebration lighting the lamp. Prof B Bhargava, Secretary, DHR and DG ICMR, presided over the function.



Fig. 4: Prof. Srinath Reddy delivering lecture, Back to the future with Bayes: Probabilities in a world of uncertainties on the occasion of ICMR-NIMS Foundation day celebrations, 2019.

EXTRAMURAL RESEARCH

Socio-Behavioural & Health Systems Research (SBHSR) Division

During this year, the Socio-Behavioural & Health Systems Research (SBHSR) Division has funded some ad-hoc projects on understanding and strengthening of health systems in the country, as well as on understanding the social and behavioural determinants of health. In addition, two national task force projects on road traffic injuries are progressing well. The Division has initiated processes of national task force projects on health care issues among scheduled tribe population.

An intervention study on community engagement in control of vector-borne diseases has been concluded in Kerala's Alappuzha municipality. This study demonstrated the way the community intervention contributed to eco-bio-social factors to control vectors and its sustainability and scaling up. The study explored the possible ways to engage the community and suggested to include community engagement in state public health policy as the main crust to control vector-borne diseases. The Municipality of the Alappuzha scaled-up this intervention to other parts of the town.

Impact of an intervention programme on symptom management among advanced cancer patients and their family caregivers was assessed. The multi-component interventional package included

yoga, physical exercise, counselling sessions and individualized education. The study demonstrated that a structured education on symptom management will improve the patients' quality of life. It further demonstrated the promotion of non-pharmacological methods of pain management and the role played by family caregivers in supporting terminally ill cancer patients.

A pilot study was conducted in the Alwar district of Rajasthan to assess and manage mental health problems through frontline health workers. The study was to create an enabling environment for health seeking for mental health issues among the rural community. Feasibility of using Global Mental Health Assessment Tool (GMHAT) was assessed. Frontline health workers are able to use GMHAT. The GMHAT accessibility, ease of use and adding value to clinical decision making are important factors in determining its usefulness in the routine practice of frontline workers. The frontline health workers not only diagnosed but sought expert advice through Skype video calling.

A quasi-experimental study to determine the impact of capacity building of nursing students on sexuality, reproductive and sexual health using the life skills approach on their personal and professional perceptions and competencies was concluded in Karnataka. Through this, students developed a neutral attitude and gained appropriate skills to deliver key and tailor-made information to their clientele on reproductive and sexual health. Prevention of hypertension and associated co-morbidities was promoted through the involvement of primary health care providers. In this community-based intervention, the intervention was provided at two levels - primary healthcare providers and patients diagnosed with hypertension and associated co-morbidities. Hands-on training for clinical measurement of different physiological parameters was given. They were further trained on motivational counseling to bring about desired behaviour change. Change in knowledge, attitude and skills of primary health care providers are reported. This study has an implication on the National Programme for Prevention and Control

of Cancers, Diabetes, Cardiovascular Diseases and Stroke.

A study on the work-related stress amongst the police officers was conducted in Uttarakhand. It evaluated the police officials' experiences with relation to the support received by them and assessed the implication of work-related stress on the health. Work overload is one of the stressors amongst the police officials. Absence of social and personal life because of long and odd working hours and burden of additional work is the major issue. This study warranted effective stress mitigating measures among police officials.

The Division has supported the testing of self-help yoga manual for caregivers of schizophrenia patients living in the community. This single-blind randomized controlled study tested the feasibility of a self-help audio-visual yoga manual. Results show a significant decrease in the burden of the caregivers who practised the self-help manual. Manual found to be feasible to use by the caregivers even though its effectiveness could not be ascertained due to high attrition.

A study on advancing equity in primary health care has been progressing in Telangana state. This study examined the social determinants of health and established the chain of causality between social determinants and equity in the context of community participation initiatives. A detailed and thematic plan to explore reasons for health inequity owing to cultural norms conditioning health practices has been developed. Another study on bridging education and adolescent mental health among teachers in Karnataka identified the level of mental health literacy and referral practices among high school teachers. It also assessed the stakeholder's views on providing interventions through schools. There is a need to identify means to address the existing gap in information. School teachers have been expected to form an effective means of bridging this gap. Cognitive and psychosocial intervention for persons with dementia has been initiated during the current year. Cognitive stimulation therapy is adopted. Another study on

evaluation of the effect of select Indian classical music *ragas* on electrophysiological parameters and salivary stress markers has been initiated as a randomized control trial. Effect of these *ragas* on the autonomic functions and brain waves of subjects is being assessed.

Under socio-behavioural research, self-rated health, stress, personality, social supports and self-regulation is being studied among elderly men and women from different social classes as a prospective study. It implies that the social disadvantaged elderly needs better attention on welfare programmes, especially in health care services. Situation Analysis of health services for sexual assault survivors in Karnataka has been initiated with the objective to assess the adequacy and quality of health services provided for sexual assault survivors at district hospitals of Karnataka. The study revealed that the hospitals have prioritized on the collection of forensic evidence over gender sensitivity. Lack of privacy and uniformity in obtaining the consent, haphazard case formats and documentation of cases are reported. Health care providers had no training and orientation towards appropriate forensic evidence collection and testimony in court, provision of emotional support to sexual assault survivors and management of child victims and physically/ mentally challenged sexual assault survivors.

An evaluation study on *Janani Suraksha Yojana* (JSY) under NRHM is going on in Karnataka, Tamil Nadu and Andhra Pradesh States. Findings indicate a huge increase in institutional deliveries in the high performing states and this can be attributed to the immense popularity of the JSY. A high level of awareness about JSY among mothers is reported. Few cases of home deliveries are reported and the reasons were found to be 'convenience of delivering at home' and 'normalcy of pregnancy. It is concluded that in order to reach the stated goal of total institutional deliveries, more capacity needs to be created in the health system to cater to the JSY induced demand.

A study on care within and outside home for school-age children with insulin dependent diabetes mellitus was undertaken. Care practices at home were observed to be 'good' in only 30% of families and care practices at home for boys was observed to be better than girls. Treatment, socio-emotional needs of the child and academic and extra-curricular activities aspects of care at home were significantly important in reducing the stress associated with type 1 diabetes among young children. Mother's education was an influencing factor for reducing stress levels among children. Cognitive behavioural-based intervention in a group setting for tobacco cessation is being assessed among tobacco users visiting a tobacco cessation clinic in Delhi. The intervention group showed the increased score on treatment effectiveness, behavioural strategies of coping and also improvement in their motivation.

Health systems research on road traffic injuries (RTIs)

The Division is supporting two national task force projects on road traffic injuries. The first study has established an electronic-based comprehensive and integrated RTI surveillance system in five places in India, viz., Chennai, Chittoor, Tehri-Garhwal, Delhi and Jaipur. It established both passive and active surveillances comprehensively to capture all RTI and related deaths in a particular geographical area. The study demonstrated the feasibility of establishing the system within the public health system. It can be taken over by the government for scaling-up. Advocacy efforts are to be made. Epidemiological data has been collected through this system from all the sites and it is being analysed.

The second task force project is to standardize structured evidence-based intervention for safety, efficacy and quality of post-crash pre-hospital and in-hospital trauma care services to improve the outcome in RTI victims. This study is implemented in five cities, viz., Bengaluru, Delhi, Karamsad, Lucknow and Thrissur. An Android-based trauma registry is developed under this project to collect pre and post-intervention trauma-related data. The intervention on prehospital care included education

and training for prehospital care and prehospital notification, standardized hospital selection, a mandatory checklist for persons attend RTI and prior notification of arrival. Another interventional activity undertaken was educating and training the first-responders for prehospital notification. The training included the American Heart Association's basic life support training and certification. The intervention was made to ensure the availability of ambulances to transport the critically injured patients according to prior set criteria. The list of all the qualifying hospitals per type of injury or the injured patient was made available to the first-responders and posted in the ambulances. It was ensured that the recipient hospital will be notified about patient's basic injuries and vitals while en-route so that the receiving hospital has enough time to assemble a team which is ready to receive and treat the patient immediately upon arrival. This is to optimally utilize the golden hour. The in-hospital intervention included the strengthening of the quality of care within the hospital, through relevant quality improvement activities. These activities included trauma quality improvement training for key clinicians followed by mentoring of developing the necessary structures and processes to conduct regular morbidity and mortality meetings, preventable death reviews, audit filters and risk-adjusted benchmarking of key performance indicators. AIIMS Trauma Assessment and Management (ATAM) course was conducted in all participating centres.

In addition to the above task force projects, Division has supported twelve ad-hoc projects on different issues of the RTIs. Some studies aimed to study the health systems' responsiveness and availability. One study is to understand the effectiveness of first aid care package on knowledge and quality of first responders care provided by auto rickshaw drivers. Another study is developing an IT-enabled tool for automatic accident detection and road safety support system for reshaping transportation in smart cities. Immobilization and evacuation of RTI victims are studied in Delhi. An epidemiological study of maxillofacial trauma in a tertiary teaching

hospital is progressing. One of the projects is assessing communication barriers in reaching service facilities. Quality of life and economic burden of persons who met with road traffic accidents are studied in Tamil Nadu and Karnataka states. Another study is exploring the correlations in livelihood status and support systems among road injury victims.

DIVISION OF INNOVATION & TRANSLATION RESEARCH (ITR)

Intellectual Property Rights

Patents Portfolio

Patents filed: A total of 7 patents applications were filed during Fiscal Year 2018-2019 with the Indian Patent Office. Out of these, five are from intramural institutes and two from extramural. One PCT application was filed during this period with 4 National phase applications in USA, China and Brazil. One design and three copyright applications were filed.

Patents Granted: During this period, 6 patents (3 Indian and 3 international patents) has been granted. A total of 19 patents (13 Indian and 6 international patents) were maintained and 9 International patent applications were maintained.

Technology Transfer through in-house efforts

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. One technology on LAMP assay has been transferred to company.

Collaborations

MoU between ICMR and SCTIMST was executed on 27th Feb 2019 for strengthening the scientific relation of both institutes. The objective of MoU is cooperation and collaboration in planning and conducting validation through clinical trials of various medical devices, biomaterials and in-

vitro diagnostics devices/kit being developed by SCTIMST.

Letter of consent was executed between ICMR and Biotech Consortium India limited (BCIL), New Delhi, on 15th March, 2019. As per LOC, the ICMR and BCIL will cooperate for working together for the improvement and packaging of technologies and their successful transfer to industry for commercial exploitation and socio-economic benefits.

Indian Council of Medical Research (ICMR) has licensed through BCIL, the technology for Shigella vaccine developed by ICMR-National Institute of Cholera and Enteric Diseases (NICED), Kolkata for further development and commercialization to MSD Wellcome Trust Hilleman Laboratories Pvt. Ltd., New Delhi on April 23, 2019 at the ICMR Headquarters. The agreement was executed between ICMR, NICED, Biotech Consortium India Limited (BCIL) and MSD Wellcome Trust Hilleman Laboratories Pvt. Ltd.

For strengthening the commercialization activities of ICMR's technologies, the council has collaborated with Federation of Indian Chambers of Commerce and Industry (FICCI) for both national and international commercialization of health technologies. A workshop was organized on Converting Research into Value through Technology Transfer and Commercialization 11-16 November 2018, Goa. The main objective of the workshop was to orient the scientists on the importance of technology commercialization and how to convert research into value through tech transfer. Realizing the need to accelerate and sustain the progress, the workshop covered three perspectives i.e. private sector involvement, Government involvement & international perspective.

ICMR has collaborated with WISH Foundation for the development of public health innovation. ICMR technologies most suitable for PHCs are being identified for validation in the WISH operated public health centres. A joint working group may be constituted to take forward the various shared agendas of collaboration.

ICMR Centre for Innovation and Bio-Design (CIBioD)

The CIBoD will create a platform for collaboration of clinicians and domain experts to share the idea and evolve the innovative and patent-oriented research. The CIBioD will operate 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. The research will be 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.

IMPacting Research Innovation and Technology (IMPRINT)

This is a flagship national initiative of the Government, launched by the President, Prime Minister and Human Resource Minister on November 5, 2015. Healthcare is one of the 10 technology domain identified under the IMPRINT. ICMR along with MHRD has provided support to 25 projects in healthcare domain. The projects range from Bioresorbable Drug Eluting Coronary Stents, Artificial Pancreas for Closed Loop Blood Glucose Control of Type-1 Diabetic Patients and Development of Microneedle Array for Paediatric Applications.

Uchhatar Avishkar Yojana (UAY)

The Uchhatar Avishkar Yojana (UAY) was launched to promote industry –specific need-based research so as to keep up the competitiveness of the Indian industry in the global market. The UAY is a joint collaboration between MHRD, participating ministry and industry. During 2017-18, 10 projects were funded by ICMR. These research projects are designed to provide path breaking new knowledge. All projects under UAY scheme are ongoing.

Drone for vaccine delivery: last mile coverage

The national immunization program continues to face challenges in terms of making safe and potent vaccines available in remote areas. A 2013 study from India found that two thirds of vaccines were damaged by freeze exposure in the cold chain between State stores and administration sites across ten States. Technologies like Drones can be used to cover the gaps in cold chain system. In view of this, ICMR and IIT KGP have initiated a project ‘Drones for Vaccine Delivery: last mile coverage’. The overall aim is to develop a drone system that can be instructed to fly autonomously using GPS points to sites administering immunization under National program in far flung remote areas and deliver vaccine payload under temperature controlled condition. The drone technology being developed at IIT KGP has successfully tested landing on fiducial marker based landing pads.

MedTech Internship: Clinical, Technology and Management Emersion

ICMR in collaboration with IIT KGP and IIM Ahmadabad organize MedTech summer Internship program since 2016. Sixteen medical-technology-business interns were trained in year 2018 in a strategic area of health (maternal and child health). The interns observe the clinical facility, physician, frontline health worker and/or a patient for a period of one week at MRHRU, Tigiria and/or SCB Medical College, Cuttack, AIIMS Bhubaneswar. The MRHRU and medical college provided support for medical technology need assessment. The IIT KGP faculty guided the interns through the process of technology development whereas the IIMA faculty helped in mentoring the business model development part of the technology. The observations collected during their stay at MRHRU/ Medical College were useful in building new ideas or reshaping the initial project proposal. This was followed by design development for identified technology at ICMR institute, IIT KGP and IIM A laboratories. The interns were also trained in evaluation of the Intellectual Property, regulatory compliance, stakeholder validation, methodology

for preclinical and clinical testing of the prototype or methodology for validation of the health system model and marketing strategy.

The ideas on which this year’s interns worked included backrest cum squat-stool to help pregnant female during delivery and decreasing pain, device for early screening of congenital heart defects in neonates and metallic degradable fracture fixation devices. Since inception, MedTech internship has seen a significant growth.

New Outcomes

- Developed a Smartphone based optical microscope for clinical application.
- Completed development and optimization of a non-contact device for online monitoring of neonatal and maternal jaundice.
- Field and Laboratory based validation of Mobile Lab (Labike & Suitcase model) against Gold standard methods found that the machine is conforming gold standards for routine biochemical tests required for screening of Non communicable diseases.
- Anirban Mukherjee from Department of electrical engineering, Indian Institute of technology, kharagpur developed one Smart phone enabled spirometer and respiratory sound-based point of care system.
- Developed a Design for fabrication of a novel scoop stretcher for full body immobilization during causality transfer.
- Completed Preclinical evaluation of safety and efficacy of the decoction of the plant successfully with patent filing RMRC-BM IP_156 for anti-diabetic activity and characterization of active compound (s).
- Evaluated analgesic and anti-inflammatory activities of *Plumbago zeylanica* L. Rootpaste in osteoarthritis patients successfully and filed patent.

- Completed tests on live cell electro-spinning with biomimetic polymers for bioengineered bone constructs at Centre for healthcare sciences and technology, Indian Institute of Engineering Science and Technology, Howrah, West Bengal.
- Completed Research and product development Pre-clinic, clinical evaluation of low cost indigenous single use safety syringe with passive spring actuated needle stick injury & revise prevention mechanism
- Quantified correlation between visual outcomes and biomechanical changes in cornea in vivo after refractive surgery (LASIK and PKK)
- Studied the structure and blood flow in chorioretinal complex of human using optical coherence angiography successfully.
- Completed development of differential synchronous fluorescence-A new paradigm for probing oxidative stress and inflammation using serum samples successfully with patent filing.

RESEARCH METHODOLOGY CELL

Research Methodology cell (RMC) has been established in ICMR in year 2010. The objective is to create awareness about the various research methodologies being used globally in different fields of medical science to new researchers, especially those belonging to state medical colleges and other academic institutions located in the periphery of different states.

Capacity building Workshops

Four research methodology workshops were conducted against the call for concept proposals to identify young and middle level faculty/researchers from North –South zones of the country, where 380 concept proposals were received and screened based on the novelty, applicability and justification for research; work carried out and competence of PI; work proposed to be carried out in three years and

infrastructure, staff available, grants received, and previous publication if any in the area of proposed research. Proposals were selected keeping in mind local/ regional / national health priorities related to communicable diseases, non-communicable diseases, maternal and child health, health system research, and behavioral research.

The RMC division then proposed to develop the shortlisted concept proposals into full length proposals with the mentorship of Experts by conducting hands on training and workshops for duration of three days.

Southern zone

- First workshop was conducted at National Institute of Epidemiology (NIE), Chennai from 2nd -4th May 2018 with 46 participants from various medical colleges, universities and health research institutions from the south zone regions of Karnataka, Tamil Nadu and Kerala. Most of the proposals reviewed in the workshop were from medical colleges (64%) and universities (18%) (Fig. 5).

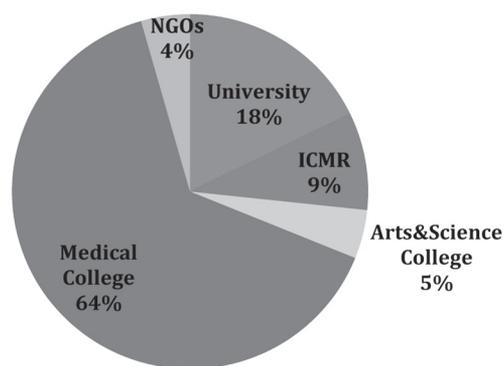


Fig. 5: Type of Institutions in the Research Methodology workshop at NIE, Chennai on 2nd -4th May 2019.

- Following second workshop was conducted at National Institute of Nutrition (NIN), Hyderabad from 20th -22nd June 2018. A total of 46 participants from Telangana and Andhra Pradesh belonging to various medical colleges, Institutions and Hospitals with specialization in different areas like Neurology, Biochemistry, Community Health, Nursing, Pathology, Pharmacology, Surgery,

Epidemiology, Physiotherapy, Microbiology, Gynaecology, General medicine, paediatrics etc were mentored.

Northern zone

- The third workshop was conducted for the 33 participants of Delhi zone, from 6th-8th August 2018 at the ICMR Hqrs.
- The fourth workshop was conducted at PGIMER, Chandigarh from 18th -20th Nov 2018, for 28 participants belonging to Haryana, Uttar Pradesh, Uttarakhand, J&K and Himachal Pradesh.

Western- Eastern zone

A call for concept proposals to identify young faculty/ researchers working in government medical colleges and health research institutions from Western & Eastern zones of India was initiated from 1st February to 31st March 2019.

RESEARCH METHODOLOGY CELL PROJECTS

Monitoring and Surveillance of Hypertension Control in Urban Slum through Community Ownership Program.

Hypertension prevalence is 32% among adult population with an overall prevalence of 15% among general population. The non-compliance rate was 75.7% which drastically came down to 35% after community catalyst activist's involvement.

Molecular mechanisms of antibiotic resistance in Pseudomonas spp. Causing Ocular infections.

Keratitis and endophthalmitis were the key infections in the study. Antibiotic Susceptibility data was confirmed by performing Kirby-Bauer method according to CLSI guidelines for all the isolates. Efflux pump activity was observed using the EtBr cartwheel Assay for all the isolates and 20 isolates showed high efflux activity out of 73. Multidrug resistant strains and drug resistant strains (XDR) among selected strains was observed.

Descriptive study to assess cancer burden, level of delays in cancer management and socio-economic impact of cancer on the family.

The project was conducted to assess the cancer burden in 3012 follow up cases over a period of one year where cases were 54% females and 46% males . 68% of rural population was affected compared to 32% of the urban. The maximum cases in females involved breast (20%), Cervix (8%) and ovary (3%) whereas in males, mouth (13%), Oesophagus (8%), Larynx and Lungs (4%). It was observed that the causative substance in males was smoking tobacco (30%), alcohol (21%) and chewing tobacco (6%). Most of the cases (26%) were diagnosed at Stage IV and only 6% in Stage I. The maximum cases belonged to the age group 60-67 years (23%) followed by 44-59 years (20%) and 7% in the age group of 68-75 years. It was observed that in 30% cases, the family delayed in first consultation and initiation of right management. This data can be used to prioritize delivery of services and improve screening and supportive services. Poverty and high cost of treatment for breadwinners has a major socio-economic impact.

Epidemiology of Infertility in a rural area of Odisha and need for simplified management approach

The study covered 33 villages with 3300 households reporting 167 infertile couples, accounting to 5% prevalence which was much less than anticipated 10%. Most of the couples (44%) visited private facilities while rest 38% sought consultation from government health care facilities. Hence, development of simplified approach to tackle various aspects of infertility at appropriate level of health care can pave way to propose a model centre using hub and spoke model for dealing with issues related to infertility in resource poor settings.

An epidemiological study of goitre in females of a non iodine deficient coastal area of Kerala.

1611 women in the age group of 20-60 years, permanent residents of coastal area were examined for goitre along with relevant history. 84% of the

women had Grade 0 goitre, 11% grade 1 and 5% grade 2 on physical examination of the neck.

DIVISION OF HUMAN RESOURCE PLANNING & DEVELOPMENT

FELLOWSHIPS

- **JRF (Junior Research Fellowship)** -ICMR JRF fellowship exam 2018 was conducted on July 22, 2018 in collaboration with Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh at 12 Centres *viz.*, Bengaluru, Bhopal, Bhubaneswar, Chandigarh, Chennai, Delhi, Guwahati, Hyderabad, Kolkata, Mumbai, Srinagar (J&K) and Varanasi. In 2018, a total of 144 JRF (122 Life Sciences and 22 Social Sciences) were selected.
- **ICMR Centenary PDF (Post-Doctoral Fellowship)**- ICMR offers 50 PDF fellowships every year for working in 26 ICMR Institutes/ Centres with state-of-art R&D facilities. A total of 151 PDF's proposals were received by the Division during 2018-19, 107 were shortlisted as per the eligibility criteria for personal discussion, out of which 49 PDFs were selected and were approved for funding.
- **MD-MS/Ph.D. Fellowship**- The programme is designed to identify young medical graduates with brilliant academic records for pursuing postgraduate qualifications and to motivate them to opt for career in research. The selection of the candidates is made on the basis of a competitive National level examination consisting of a written test conducted at 3 or 4 Centres in the country. Under this programme, the selected medical graduates are provided financial assistance for 4-5 years and a total of 25 fellowships are available per year. 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 University (SRMU), Chennai.

During 2018-19, out of 15 allotted slots, a total of 13 candidates were selected (KGMU- Five, NIMHANS- Three and SRMU- Five).

ICMR Chairs for Sr. retired medical/biomedical teachers/scientists

- **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. At present both the Biomedical and Clinical Chairs are ongoing.
- **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. Presently, all the five Chairs are occupied.
- **STS (Short Term Studentship)**- During the year 2018-19, a total of 7245 MBBS students registered from all over the country, out of which 4535 MBBS students had sent their proposals,

which were reviewed by Scientists/Experts in the concerned subject areas from ICMR Hqrs. and 26 ICMR institutes. Out of which, 1219 students had qualified for carrying out the STS-2018 research project. Finally, a total of 1043 students had successfully submitted the STS 2018 report. After successful review, 882 students were approved for studentship. The State-wise proposal submission, proposal selection, report submission, report selection and the States/UTs participated in STS-2018 are given in Fig. 6.

There was an increase in selection (13%) from different medical colleges. This included 373 Medical Colleges of India.

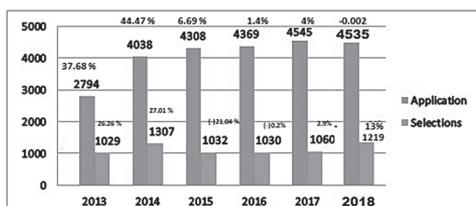


Fig. 6: Five-year (2013-2018) data of STS applications received/selections.

1. **Nurturing Clinical Scientists (NCS) Scheme-** A new scheme of ICMR “Nurturing Clinical Scientists Scheme” is being instituted to foster high quality research opportunities. Fresh MBBS/BDS candidates within two years of completing their degree are eligible to apply (Interns/MD/MS/MDS are NOT eligible) in the cutting edge areas of Fundamental Basic/Clinical Research in communicable and non communicable diseases, and reproductive health including nutrition *etc.* at MCI/DCI recognized medical/dental colleges/ICMR network of Institutes/Centres, among others. Special focus will be on fundamental research in priority areas identified by ICMR from time to time, keeping in mind the National Health Policy 2017.

The selected candidates will enroll themselves for pursuing Ph.D./MPH in any UGC recognized University/MCI/DCI recognized medical/dental colleges/institutes. The applicants will have to

submit a Concept Note of the research work (1000 words only) to be undertaken for pursuing Ph.D./MPH to ICMR for the same. All the selected candidates will undertake the ICMR-NIE Certification e-Course on Health Research Fundamentals (detailed information of the e-Course available on: http://nie.gov.in/niecer/niecer_page.htm). Applications will be accepted twice a year *i.e.* by June 30 and December 31. A total of eight Clinical Scientists were selected for 2018.

2. **ICMR-Emeritus Scientist (IES)-** Scientists, who have retired or are about to retire and who hold/have held before their retirement, the posts of the status of a Professor/Associate Professor in a Medical College or of Director/Deputy Director, in a Institute of an all India character or scientists with comparable scientific experience and achievements in an organization of the Council and have been actively engaged in biomedical research of a high standard are eligible for appointment as IES. In total, 29 applications have been received for IES. Out of these, 7 applications were considered for the award in the Expert Committee meeting held in October 2018.

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 improve visibility and accessibility of their research work to larger research audience as it is mandatory to publish one paper in an indexed journal. Out of 515 thesis proposal received, 101 proposal awarded financial assistance for the year 2018-2019.
- **International Travel Grant to non-ICMR scientists-** A total of 1465 applications were received, out of which 312 were approved for funding for period under report.
- **DHR-ICMR Funded Workshops on Clinical Training/Translational Research-**

The scheme of Seminars/Symposium/Conferences/Workshops was fixed by DHR-ICMR from April 2018 and a new scheme of DHR-ICMR Funded Workshops on “Clinical Training/Translational Research” was introduced. The applications were invited twice a year *i.e.* in June and December, until 2018 but now the applications are invited on a quarterly basis. During the period of June-December 2018, a total of 79 applications were shortlisted and only 56 were further approved for funding.

MISCELLANEOUS PROGRAMMES

ICMR Awards & Prizes- During the period under report total no. of applications received was 205 for 20 different Award/Prizes categories and 24 Scientists were awarded. Citation booklet was published by December 2018.

A total of 121 applications have been received for 2018-19 and in 28 different award categories, which are under evaluation and screening, including the One-time Award category was constituted “ICMR-NIN Centenary Year Oration Award for Excellence in Nutrition Research”, on the occasion of the ICMR-National Institute of Nutrition (NIN), Hyderabad Centenary Year (1918-2018).

THE INDIAN JOURNAL OF MEDICAL RESEARCH

The Indian Journal of Medical Research (IJMR), the flagship journal of Indian Council of Medical Research (ICMR) with national and international repute, is a monthly biomedical journal with an uninterrupted publication history of 105 years. The IJMR is brought out in two volumes, 12 issues every year and is covered by all global abstracting and indexing services. The IJMR is available full text, free on the internet (www.ijmr.org.in) with a searchable menu and IJMR Archive is available at <http://ijmr.in> with the full text of articles available free in PDF format since the inception (July 1913). Since January 2017 IJMR has also been made

available live on IJMR App both on Android and iPad devices.

The IJMR continued to publish quality original research articles in the area of biomedical research as well as review articles on topics of contemporary biomedical interest. Other regular sections such as Editorials, Commentaries, Research Correspondences, View Points, Perspectives, Systematic reviews & Meta-analyses, Clinical Images, Students’ IJMR and Book reviews were also published in addition to Policy Documents and Special Reports occasionally. The impact factor of IJMR for the year 2017 was 1.508 (Clarivate Analytics, 2018).

The number of submissions were more than two thousand during 2018-2019; 46 percent were from countries other than India. More than a thousand reviewers were involved in the peer-review process; 17 per cent reviewers were from foreign countries. A total of 213 articles were published during the year under report; 15 per cent articles were from foreign countries like China, Turkey, Iran, Egypt, Brazil, Saudi Arabia, Nigeria, USA, *etc.* Fig. 7 depicts the percentage of articles submitted, published and reviewers’ contribution from India and foreign countries.



Fig. 7: Indian and Foreign contribution in terms of per cent articles submitted, published, and reviewers participated in peer-review process during 2018-2019.

Two special issues and two supplementary issues were published in addition to regular issues during the year. A total of 213 articles were published; 41 percent were original research articles followed by 29 per cent review articles. The details are shown in Figure 8.

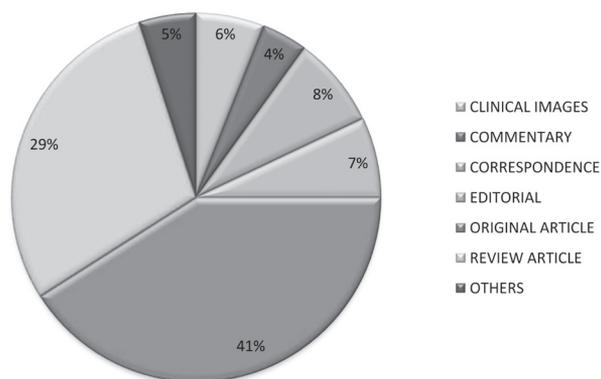


Fig. 8: Articles published under different categories (2018-2019).

A special issue on ‘Challenges in Control of Smokeless Tobacco Use’ was brought out in July 2018, guest editors were Drs. Ravi Mehrotra and Dharendra N. Sinha. In this special issue one View point, six review articles, three systematic reviews and four original articles were published. Another special issue on ‘Nutrition Research: Commemorative issue on 100 years of National Institute of Nutrition, Hyderabad’ was brought out in November 2018 with 18 review articles; guest editors were Dr R. Hemalatha and Dr G.S. Toteja (Fig. 9)

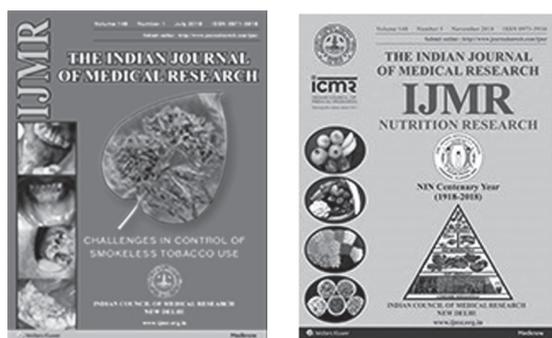


Fig. 9: Special issues published during the year.

A supplementary Issue entitled, “Reproductive Health with Emphasis on Strategy for Infertility” was brought out in December 2018. A total of 14 review articles and four original articles were published in this issue. To celebrate 150th birth anniversary of Mahatma Gandhi a commemorative issue (Collector’s edition) entitled, “Gandhi and Health @150: Footprints of ICMR’s century-long journey” was brought out as January 2019 supplementary issue (Fig. 10).



Fig. 10: Supplementary issues published during the year.

MEDICINAL PLANTS DIVISION

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 on Indian Medicinal Plants which serve as comprehensive, informative & reliable source of information providing information on new leads, thus helping in systematic and planned evaluation of Medicinal plants, including drug design, basic and applied research.



Fig. 11: During the year volumes 19 (with botanical names Pa-Phl) and 20 (with botanical names Pho-Pip) covering monographs on about 375 medicinal plants species carrying multidisciplinary information with 3900 citations were published.

Earlier, 18 volumes of Reviews on Indian Medicinal Plants (with botanical names starting with A-O) covering multidisciplinary research data on about 4576 plants, covering about 71586 citations were published. Each Monograph includes regional names of the medicinal plant, its sanskrit synonyms as well as the Ayurvedic description (wherever available), ethnobotanical studies, apart

from the habitat and the parts used, properties and uses on one hand, and the details of botanical, pharmacognostical, chemical, pharmacological and clinical data on the other, backed by complete references and bibliography on each aspect of the information cited, besides the colour photographs of important medicinal plants.

Quality Standards of Indian Medicinal Plants

During the year, the Quality standards on 30 medicinal plants were developed, monographs prepared, finalized, technically reviewed and published as Vol. 16 as part of series on “Quality Standards on Indian Medicinal Plants”.

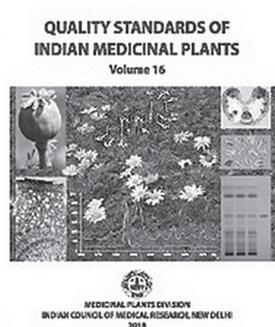


Fig. 12: Quality standard of Indian Medicinal Plants.

Earlier 15 volumes have been brought out containing quality standards on 519 plants. The monographs are on the pattern of WHO guidelines and focus on the diagnostic features and phytochemical studies, including markers besides having information on Pharmacological, clinical, toxicological aspects along with dosage, adulterants /substitutes etc. Monographs on another 30 plants are being finalized for 17th volume

Safety Review monographs on Indian medicinal plants

First volume of this series comprising 75 popular medicinal plants pertaining to their scientific evidence on efficacy and safety has been published in Year 2018. The monograph document comprises comprehensive published information mainly on historical use, pharmacopoeial status, preclinical general toxicity/safety, mutagenicity/genotoxicity, reproductive safety, adverse effects observed

in clinical trials, safety in pregnancy, safety in children, case reports and herb-drug interactions (if reported any). The document is helpful to prescribers, researchers, academicians, regulators, policy makers and drug industry that are dealing in the area of medicinal plants.

Inter-Ministerial Cooperation Program on Phytopharmaceutical Drug Development

This is a new inter-ministerial cooperation program through a MOU between CSIR, DBT and ICMR for promotion and facilitation of innovative research on ‘Phytopharmaceuticals’ by taking forward the leads already existing with CSIR, DBT and ICMR. Under this tri-partite inter-ministerial cooperation program, the development of Phytopharmaceutical drug has been planned initially in the area of pain management in terminal cancer, sickle cell anaemia, neuropathic pain, arthritis and paediatric epilepsy.



Fig. 13: Signing tripartite MOU between CSIR, ICMR and DBT of inter-ministerial cooperation program for promotion and facilitation of innovative research on Phytopharmaceuticals” in the country, event held on 31st December 2018.

Research Management, Policy, Planning and Coordination Division

This Division is engaged in work related to preparation of various policies, planning documents, write-ups on achievements, impact analysis, etc through coordination with various ICMR Institutes and stakeholders’ consultations. This year, it has coordinated major activities related to Gandhi & Health @ 150 and the preparation of providing technical inputs and assisting in releasing various important policy documents like NITI Aayog’s Ranking & Ratings of national S&T agencies, Trend Analysis of Resource Investment in Health & Health Research. The Division has also been instrumental in various activities like foundation

stone laying ceremony of a new Regional Medical Research Centre at Gorakhpur (UP). 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. It also coordinates activities of the Communications Unit 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.

- **Foundation Stone laying of RMRC Gorakhpur:** Foundation stone of RMRC Gorakhpur was laid by Hon’ble Chief Minister of UP, Shri Yogi Aditya Nath in the presence of Union Minister of Health and Family Welfare, Shri J P Nadda on 2nd September 2018.
- **New Logo and Brand Identity:** To enhance the visibility of ICMR, a new logo was designed as well as to address the need for uniformity of ICMR brand across its institutes and project ICMR brand as the apex health research organization, a comprehensive branding exercise was undertaken. Under this exercise, a brand identity manual which included a supplementary logo for ICMR and its 26 Institutes and a tagline was developed. The brand identity was launched by Dr. Balram Bhargava, DG, ICMR on 16th November 2018 which saw participation from all Institutes of ICMR.
- **Coffee Table Book and Animation Film:** As a celebration of ICMR’s century-long journey and in recognition of the work done by its researchers, the following collaterals were developed. These collaterals were launched by Shri J.P. Nadda, Union Health Minister, India on 2nd May 2018.
 - **Coffee Table Book:** Titled “Touching Lives”, the book was developed to highlight key contributions of several ICMR Institutes that have significantly improved lives and health conditions of communities across India.
 - **Animation Film:** Showcasing key contributions made by ICMR and its Institutes towards health research in India, an animation film was developed.
 - **Ranking & Rating of national S&T agencies:** The division represented ICMR in NITI Aayog’s initiative to review the ranking & rating system of various S&T organisations. The committee prepared the framework document for the assessment of S&T activities.
 - **Trend Analysis of Resource Investment in Health & Health Research:** An Expert Committee was formed on Enhancing Resource Investment in Health under the Chairmanship of Shri RatanWattal, Member Secretary, Economic Advisory Committee to the Prime Minister. The committee administered the responsibility of Sub Gr 1 on Trend Analysis of Resource Investment in Health & Health Research to ICMR. The division coordinated the expert discussions involving various stakeholders.
 - **Release of Special Edition of Indian Journal of Medical Research (IJMR) and Symposium on Gandhi and Health@150:** To commemorate the 150th birth Anniversary of Mahatma Gandhi, a 2 day symposium ‘Gandhi and Health@150’ was organized at ICMR Hqrs, New Delhi on 25th and 26th March, 2019. A special issue of IJMR on ‘Gandhi & Health@150’ was unveiled which was released by His Holiness the Dalai Lama on 20th March, 2019 at Dharamshala. This edition features articles on the health file of Mahatma Gandhi, his medical legacy, his virtues and their importance in the current health scenario followed by writings from the pens of ardent Gandhian followers and a special section that documents the role played

by ICMR and its 26 institutes over the last 100 years following Gandhian thoughts. During the 2 day symposium, there were following 5 Technical Sessions and 4 Panel Discussions, in which eminent speakers delivered informative talks and useful deliberations were made in the panel discussion.

Technical Sessions

- Insights of Mahatma : Gandhian Values & Philosophy towards a Healthy Nation
- Following the footsteps of Mahatma : Health, Hygiene, Nature Cure, Cleanliness and Sanitation
- Gandhi a Known Leader - Unknown Scientist Experiments with Diet and Dietetics
- Public Health Legacy of Gandhi / ICMR's Research linked to Gandhian Values and Philosophy
- Gandhi and Mental Health - Self, Wellbeing and Consciousness

Panel Discussions

- India's State of Health and Gandhi
- Swachh Bharat – The Gandhian Principle that is changing the face of India
- Make in India- Gandhi's Mantra for Health Innovation
- Gandhi and International Perspectives
- On the occasion, an exhibition was also displayed depicting Gandhian values and practices as well as his audio clips.



Fig. 14: Release of special issue of IJMR-Gandhi and Health@150.

- **Nodal Communications Officers Meeting:** The first Nodal Communications Officers meeting was organised with all the ICMR institutes to discuss the ongoing media activities, difficulties, challenges and proposed communications plans.
- **Workshop on developing effective policy briefs:** Two workshops on writing effective policy briefs were conducted at Bhubaneswar and Gorakhpur. Around 70 scientists were trained for enhanced biomedical communications. A policy brief on Anthrax has been published.
- **Crises Communications Workshop (3 Two-day trainings):** 53 scientists from 19 Institutes and HQ attended the two-day crisis communications workshop conducted in Delhi, Ahmedabad and Bhubaneswar.

The training workshop focused on:

- Understanding crisis and its management
- Crisis communications and management strategies in traditional and social media
- Government Policies on crisis management
- Learning from past crisis
- Managing crisis in real life scenarios
- **Media and Public Liaison Activities:** The PR unit organised Media Interaction with DG, ICMR to disseminate the research findings of projects (like CCMP, Odisha) and publications (like India State Level Disease Burden Initiative publications in The Lancet) and major launches (MERA India, Mission DELHI). The event and research findings were captured by leading media houses (both print and electronic). Also, the PR unit regularly monitors the media for recent health and ICMR in news and prepares a weekly report that is published on ICMR website.

Publication and Information Division

HINDI UNIT

ICMR PATRIKA

Continued to bring out the monthly Hindi 'ICMR Patrika'. The articles on major health topics were included in the ICMR Patrika. *Bharat mein Papilomavirus vaccine kaa pryog* (April-May, 2018); *Tamba : Swasthya par Iske Prabhav* (June, 2018); *Vishwa Pratirakshikaran Saptaah 2018* (July-August, 2018); *Bharat mein Cancer ki Sthiti* (Sept., 2018); *Bharat mein Mitti dvara Sancharit Helminth Sankramanon ki Sthiti* (Oct., 2018); *Mirgi : Vivah se Sambandhit ek mano-Vyavharik Samasya* (Nov., 2018); *Ketoenic Aahar : Vardan ya Abhishap?* (Dec., 2018); *Bharat mein Cancer Anusandhan : Chunautiyan aur Avasar* (Jan.- Feb., 2019); *Bharatiya Auyrvigyan Anusandhan Parishad Mukhyalaya mein 'Gandhi aur Swasthya@150' vishay par do-diwasiya Sangoshthi ka Ayojan* (March, 2019).

Varshik Prativedan 2017-18

Brought out the Hindi version of ICMR Annual Report 2017-2018 as *Varshik Prativedan 2017-18*.

Dissemination of Biomedical Information

ICMR carried out large number of education and extension activities during the year in different parts of India to disseminate the activities and achievements of ICMR at various platforms as well as to enhance the outreach of ICMR. The major outreach activities were as follows:

- **Vibrant North-East 2018** : a three day exhibition 'Vibrant North-East 2018' during 3rd to 5th May, 2018 at Guwahati.
- **Alluring Rajasthan Exhibition 2018** : organized by Sanasa Foundation during 18th to 20th July, 2018 at Inder Residency, Udaipur.
- **Govt. Achievements and Schemes Expo** : organized by NNS Events & Exhibitions Pvt Ltd, New Delhi during 27th to 29th July, 2018 at Pragati Maidan, New Delhi.
- **Vision Maharashtra** : a 3 day exhibition held during 3-5th August, 2018 at Pune. ICMR and its Institute National Institute of Virology, Pune showcased their activities and achievements through various posters and technologies developed. Sh Amar Sable, Hon'ble Member of Parliament visited the ICMR stall on 3rd August, 2018. A large number of people from all walk of life including school children, women, aged people, workers *etc.* visited the ICMR stall.
- **22nd National Exhibition** : a 4 day Exhibition held during 3rd to 6th August, 2018 at Milan Samity Maidan, Nimta, Belgharia, Kolkata. The ICMR and its two Institutes/Centres located at Kolkata *viz.* National Institute of Cholera and Enteric Diseases (NICED) and Regional Occupational Health Centre (Eastern) [ROHC(E)] showcased their activities and achievements through various posters and live demonstrations.
- **Mega Science, Technology & Industry Expo, IISF 2018** : a 3-day exhibition organized by *Vigyan Bharti* as a part of India International Science Festival 2018 during 5-8 October, 2018 at Railway Ground, Gomti Nagar, Lucknow. The ICMR and its two institutes *viz.*, ICMR- National Institute of Malaria Research, New Delhi and ICMR- National Institute of Nutrition, Hyderabad also showcased their achievements. The NIMR displayed live demonstration of various stages of mosquito vector, larvaevorous fishes, and different malaria parasites.



Fig. 15: Prof Balram Bhargava, Secretary, DHR & DG, ICMR in the ICMR Stall.

- **6th Government Developments & Policy Exhibition at Indore** : a 3 day Exhibition during 20-23 Oct., 2018 at Indore.
- **Rise in Jammu & Kashmir, 2018 at Jammu** : a three day Exhibition during 1-3 Nov., 2018 at Jammu.
- **14th Jatiya Sanhati Utsav-O-Bharat Mela -2018** : during 12-16 December, 2018 at Sonarpur, District South 24 Parganas, West Bengal. ICMR's Kolkata located 2 Institutes viz. NICED & ROHC (East) participated in this Exhibition.
- **Ujwal Himachal Pradesh 2018, Mega Exhibition** : a three day Mega Exhibition during 14th to 16th Dec., 2018 at the HPCA Cricket Stadium Campus, Dharmashala, H.P.
- **Pride of India Expo during 106th Indian Science Congress** : a 5 day exhibition during 3rd to 7th Jan., 2019 at Lovely Punjab University, Phagwara. The Science Congress was inaugurated by the Hon'ble Prime Minister of India Shri Narendra Modi on 3rd Jan., 2019. The Pride of India Expo was inaugurated by Dr Harsh Vardhan, Hon'ble Union Minister of Science & Technology and Earth Sciences on 3rd Jan., 2019 who visited the ICMR pavilion and interacted with the ICMR scientists.
- **9th Vibrant Gujarat Global Trade Show -2019** : a 5-day Vibrant Gujarat Summit 2019 during 18-22 January 2019 at Gandhinagar. The ICMR-NIOH displayed posters, instruments, brochures on various occupational health hazards.
- **Rajasthan Srajan 2019 National Expo & Seminar at Jhunjhunu** : ICMR-DMRC, Jodhpur participated in this Exhibition held during 25-27 Jan., 2019 at Jhunjhunu, Rajasthan.
- **Mharo Rajasthan 2019** : ICMR-NIOH, Ahmedabad participated in this 3-day exhibition during 13-15 Feb., 2019 at Jalore, Rajasthan.
- **Arogya Wellness Tourism Expo-2019** held during 21-24 Feb., 2019 at Thrissur, Kerala. The scientists from ICMR-NIRT, Chennai participated in this exhibition and showcased various research activities and achievements of the institute. A large number of people visited the ICMR stall.
- **Kutuhel Expo** held during 9-11 Feb., 2019 at Nagpur : ICMR's two Mumbai located institutes viz. ICMR- NIRRH, & ICMR-NIIH participated in this exhibition.
- **7th Government Development & Policies Expo- 2019** : a 3-day exhibition held during 22-24 Feb., 2019 at Faridabad.



Fig. 16: Dr Harsh Vardhan, Union Min of Sc. & Visitors in ICMR Stall.



Fig. 17: Technology in ICMR Stall

Health Conclave during 5th to 8th October, 2018 at Lucknow

ICMR Coordinated with DBT in organizing the Health Conclave with the theme **Life Style Diseases: Risk Factors and Preventive Strategies** as part of India International Science Festival (IISF) at Indira Gandhi Pratishthan, Gomti Nagar, Lucknow on 7th October, 2018.



Fig. 18: Prof Balram Bhargava lighting the lamp.

Prof. Balram Bhargava, Secretary to the Government of India, Department of Health Research and Director-General of Indian Council of Medical Research, New Delhi presided over this event and inaugurated the Health Conclave with lighting of lamp. Prof. Bhargava gave his key note address on “Value Conscious Innovations”.



Fig. 19: Prof Balram Bhargava giving his Key Note address.



Fig. 20: Audience in the Hall.

Prof Vasantha Padma Srivastava from the Neurology Department, All India Institute of Medical Sciences, New Delhi delivered a talk on “Stroke Prevention”. Prof Eesh Bhatia from Endocrinology & Metabolism Department of SGPGI, Lucknow spoke on “Diabetes: Rising Epidemic”. A lecture on “Cancer Prevention” was delivered by Prof Anurag Srivastava of Surgery Department, AIIMS, New Delhi. Prof S. C. Tiwari from Geriatric Mental Health of KGMU, Lucknow delivered a talk on “Stress and Depression”. Prof S. K. Dwivedi of Cardiology Department, KGMU, Lucknow delivered an interesting talk on “Myocardial Infarction”. Dr R. M. Acharya from Department of

Integrative Medicine, AIIMS, New Delhi delivered an informative lecture on “Life Style Intervention”. A large number of medical and nursing students and faculties from KGMU, SGPGI, Lucknow and nearby Medical Colleges attended the Health Conclave and took keen interest on these deliberations.

LIBRARY & INFORMATION SERVICES

The subscription to core bio medical e-journals like *Lancet*, *Science*, *Nature*, and *NEJM* for all ICMR Library & Information Centres has been continued under ICMR e - consortia. Subscription for full text electronic data base ProQuest Health & Medical Complete (which covers more than 3000+ full text and Archive volumes for the most of the titles are available from 1998 onwards) has been renewed for one more year for eight ICMR institutes including ICMR Hqrs.

ICMR has joined as a member of ERMED Consortia, an initiative taken by DGHS and MOHFW to develop nationwide electronic information resources in the field of medicine for delivering effective health care. The consortium will be coordinated through headquarter set up at the NML. It provides 244+ medical online e-journals access from five leading Publishers.

The subscription to J - Gate Plus has also been renewed for one year. Subscription to J - Gateplus is continued on the basis of satisfactory usage report. J-Gate provides access to millions of journal articles available online offered by 12,288 Publishers It presently has a massive database of journal literature, indexed from 45,047 e-journals with links to full text at publisher sites. The J-Gate @ ICMR is a customized solution for the ICMR Consortium to enable 30 members across India, to access consortia subscribed journals, individual library subscribed journals and full text journals available at J-Gate, through a single search discovery platform and a DDR (Document Delivery Request) functionality, for resource sharing among the consortia members.

INFORMATICS, SYSTEMS AND RESEARCH MANAGEMENT (ISRM) DIVISION

The division of ISRM has a mandate to nucleate and support informatics in medical research through focused programs and services. During the year 2018-19, the Division of ISRM worked in the areas of Data Management, Analytics, Dissemination, Networking and research management. The division provided wide range of services to the medical fraternity as well to the administration and finance. The Division also worked on strengthening collaborations with National and International organizations. Major programs and the achievements are given below.

DATA MANAGEMENT AND DISSEMINATION

Data Management Laboratory

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 23 programs of ICMR and other organizations. A few important programs for which the Division developed data collection and analysis portals include:

- 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).

- E-Partograph available at <http://epart.icmr.org.in>. It is a web and mobile based tool for monitoring progress of labour and for decision making for augmentation of labour, delivery by caesarean section and referral to a higher facility for further management.
- 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 coordinated signing of MoU between ICMR and National Digital Library of India (NDLI), an initiative of IIT Khargpur funded by Ministry of Human Resource Development (MHRD). The division developed websites for Health Technology Assessment (<http://htain.icmr.org.in>) and Standard Treatment Workflows (<http://stw.icmr.org.in>).

Integrated Research Data Platform

ICMR generates huge volumes of data through intramural and extramural research programs. Availability of research data in a timely and responsible manner to different stakeholders will accelerate research and improve public health. In order to improve access to data generated by programs of ICMR to different stakeholders, ICMR initiated a large scale collaborative program 'Integrated Research Data Platform' or IRDP. The Division actively contributed to IRDP program.

The program aims at organizing data generated from ICMR intramural and extramural program and develop an integrated research platform. Under the IRDP platform, each ICMR institute has nominated data coordinator and SOPs for Data Coordinators were released. Data sources from ICMR institutes have been catalogued.

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. At present the Centre is using resources for 21 service requests by medical professionals. The Centre has developed customized pipelines for making pangenomes, trios data analysis, association studies and rare variant identification. Information about the activities of the Centre is available at <http://genomics.icmr.org.in>.

Connectivity and Communication Services

The centre is managing internet and LAN connectivity at ICMR Headquarters and institutes of ICMR. During the year 2018-19, the Division strengthened network security and reliability through configuring vLANs, netting and firewall. The Division is also providing software based Video Conferencing Services to ICMR. The Division also managed email accounts of ICMR employees on 'icmr.gov.in' domain.

Electronic Research Management System: ePPMS system

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 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. ePPMS is a cloud service for Project proposal submission, evaluation and monitoring system. The main vision of ePPMS system is to provide Transparent & Centrally Controlled electronic Proposal Evaluation and Grant Disbursement to support R&D in various Institutions throughout the country.

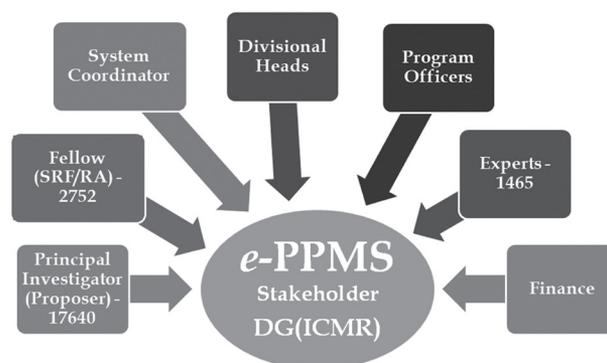


Fig. 21: Stakeholders of ePPMS system.



Fig. 22: Current ePPMS system.

During the period from 6th Nov 2018 till 7th Jan 2019, total 2636 concept proposals were received online and after evaluation by Technical Divisions, total 1056 concept proposals were shortlisted for submission of full proposal. Out of 1056, total 980 full proposals were received online, from which 429 full proposals were technically Approved after evaluation by Technical Divisions.

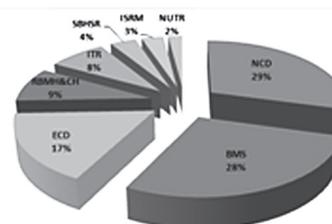


Fig. 23: Percentage Share of received adhoc concept proposals, Division wise- 2018-19.

Table 1: Top 20 Major Discipline wise received adhoc concept proposals- 2018-19.

Major Discipline	No. of proposals	% of proposals
Oncology	200	7.59
Translational Research	142	5.39
Cellular and Molecular Biology	108	4.10
Nanomedicine	85	3.23
Child Health	84	3.19
Tuberculosis & Chest Diseases	84	3.19
Biochemistry	82	3.11
Bioinformatics	82	3.11
Viral Diseases	82	3.11
Neurological Sciences	70	2.66
Pharmacology	61	2.31
Reproductive Health	55	2.09
Diabetes	54	2.05
Cardiovascular Diseases	53	2.01
Nutrition	51	1.94
Antimicrobial Resistance	49	1.86
Maternal and Child Health	47	1.78
Immunology	45	1.71
Oral Health	45	1.71
Genomics	44	1.67

During the year, Extramural Fellowship (RA/SRF) Proposal Submission opened for one month (1st -31st Jan 2019). During this period, total 1697 fellowship proposals were received online. Out of 1649 fellowship proposals, total 813 fellowship proposals were technically Approved after evaluation by divisions.

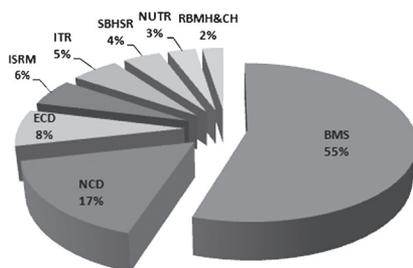


Fig. 24: Percentage Share of received SRF/RA fellowship proposals, Division wise- 2018-19.

Table 2: Top 20 Major Discipline wise received fellowship proposals- 2018-19.

Major Discipline	No. of proposal	% of proposal
Biochemistry	147	8.94
Cellular and Molecular Biology	136	8.27

Oncology	116	7.05
Bioinformatics	92	5.59
Nanomedicine	86	5.23
Immunology	73	4.44
Pharmacology	70	4.26
Nanotechnology	67	4.07
Molecular Biology	59	3.59
Translational Research	57	3.47
Nutrition	50	3.04
Medicinal Plants	40	2.43
Health Systems Research	38	2.31
Pharmacology and Toxicology	34	2.07
Human Genetics	32	1.95
Genomics	31	1.88
Public Health	24	1.46
Diabetes	23	1.40
Neuroscience	23	1.40
Stem Cell Research	22	1.34

Eight specified ‘Call for proposal’ programmes pertaining to certain priority areas were also launched during the year, which resulted in receipt of 1998 proposals online. These included a). Call for Submission of Concept Proposals for Task force in Nanomedicine (01-11-2018 to 30-11-2018 by BMS Division) (460 proposals), b). Task Force on Rare Diseases (26-12-2018 to 25-01-2019 by BMS Division) (440 proposals), c). Call for Proposals for participation in studies on Health Care Access among Tribal Population (12-12-2018 to 11-01-2019 by SBHSR Division) (356 proposals), d). Call for Proposals on Systematic Reviews in areas of National Health Priorities (05-02-2019 to 11-03-2019 by RBMH&CH Division) (325 proposals), e). Call for Submission of Concept Proposals on “Dengue Viral Disease (05-10-2018 to 07-11-2018 by ECD Division) (215 proposals), f). Call for Submission of Concept Proposals on “HIV/AIDS (12-10-2018 to 12-11-2018 by ECD Division) (93 proposals), g). Call for concept proposals for identifying Young and Middle level Faculty to participate in Research Methodology Workshop (01-02-2019 to 31-03-2019 by RMC Division) (91 proposals), h). Call for Proposals on Tribal Health Research (01-04-2018 to 13-04-2018 by ECD Division (18 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 <http://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.

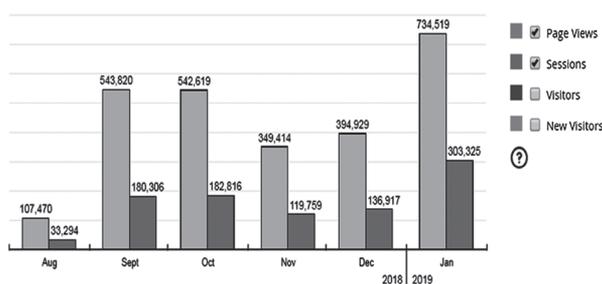


Fig. 25: Page Views/sessions Statistics of ICMR Website.

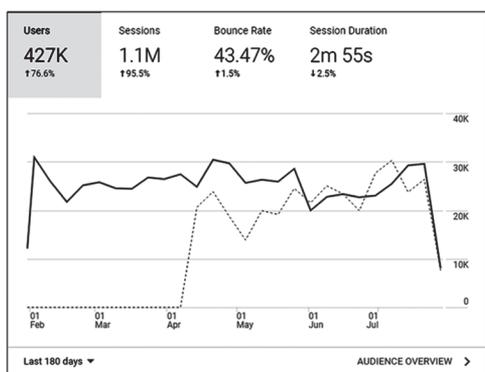


Fig. 26: Users Statistics of ICMR Website.

Management of ICMR Social Media sites

The division is working tirelessly to enhance the outreach of five Social Media Handles of ICMR- Facebook, Twitter, YouTube, Instagram and LinkedIn. The followers, likes, engagements of all Social Media Handles are increasing each day. On an average, 30-35 infographics and 4-5 banners per month were designed throughout the year. These infographics and banners were based on specific days of medical significance e.g. World TB Day, specific events like Antimicrobial resistance week

or specific causes like cancer awareness, Healthy nutrition campaigns, etc.

Table 3: Quarterly Outreach Data of ICMR Facebook for the year 2018-19.

Months	April	Jul	Oct	Jan	Mar
Total Likes	16,556	18,958	25,326	30,551	31,061
New Likes	2,215	2,506	2,492	2,062	189
Engagements	4,287	4,411	6,346	4,121	1,596
Page Reach	34,010	25,557	51,345	35,471	9,956

Table 4: Quarterly Outreach Data of ICMR Twitter for the year 2018-19.

Months	April	Jul	Oct	Jan	Mar
Total Followers	8,864	9,306	10,744	11,570	12,291
New Followers	442	457	294	409	408
Impressions	29,000	21,700	96,500	77,900	94,000
Mentions	545	536	678	1,118	691
Tweets	39	31	107	99	95
Retweets	2,084	2,107	1,987	1,981	1,861

Table 5: Quarterly Outreach Data of ICMR Instagram for the year 2018-19.

Months	Apr	Jul	Oct	Jan	Mar
Followers	254	307	566	891	1,059
Following	79	79	79	79	79
Posts	188	212	289	388	424

Table 6: Quarterly Outreach Data of ICMR You Tube for the year 2018-19.

Months	Apr	Jul	Oct	Jan	Mar
Total Subscriber	226	252	319	370	427
New Subscriber	26	23	11	22	27
Total Videos Views	92	190	138	659	467

Table 7: Quarterly Outreach Data of ICMR LinkedIn for the year 2018-19.

Months	Apr	Jul	Oct	Jan	Mar
Total Followers	590	681	1082	2,374	4,297
New Followers	77	91	102	974	1,056
Impressions	6,155	5,583	24,405	31,300	29,099

Management of Direct Benefit Transfer (DBT) Schemes

There are currently 6 Direct Benefit Transfer schemes from ICMR. Online team collects transaction data pertaining to direct benefit transfer schemes from online research management portal, technical divisions and Account section; then updates this information on the DBT portal every month. ISRM division integrated all the schemes with DBTApp so that MIS integration is possible.

Management of Public Financial Management System (PFMS)

During the year, a tremendous effort was made by ISRM division to implement and maintain complete PFMS module across ICMR Headquarters as well as its 26 Institutes/ Centres.

Management of ICMR Communication cell unit

Several meetings and workshops were organized at Headquarters and institutes of ICMR to disseminate the knowledge pertaining to scientific policy briefs,

scientific communication, crisis communication, social media management, and communication challenges.

Management of ICMR Annual Report

Compilation, editing, publishing, timely laying in parliament and distribution of Annual Report of ICMR was successfully achieved by the Division. Annual Report pertains to all activities- research as well as several Government of India initiatives as well as achievements of ICMR Headquarters as well as its 26 institutes & approx. 100 field units.



Fig. 27: ICMR Annual Report 2017-18.

ICMR INSTITUTES/CENTRES

ICMR INSTITUTIONAL NETWORK

1. ICMR National JALMA Institute for Leprosy & Other Mycobacterial Diseases
Dr. M. Miyazaki Marg, PO Box 101,
Tajganj, Agra - 282001
Uttar Pradesh.
2. ICMR National Institute of Occupational Health
Meghani Nagar, Ahmedabad - 380 016
Gujarat.
3. ICMR National Institute of Traditional Medicine
Belagavi, National Highway No.4,
Belagavi - 590010,
Karnataka.
4. ICMR National Centre for Diseases Informatics and Research
Nirmal Bhawan - ICMR Complex (II Floor), Poojanahalli Road,
Off NH-7, Adjacent to Trumpet Flyover of BIAL Kannamangala Post,
Bengaluru - 562 110
Karnataka.
5. ICMR National Institute for Research in Environmental Health
Kamla Nehru Hospital Building, Gandhi Medical College Campus,
Bhopal - 462 001
Madhya Pradesh.
6. ICMR Regional Medical Research Centre
Chandrasekharpur, Bhubaneswar - 751023
Odisha.
7. ICMR National Institute for Research in Tuberculosis
No.1 Sathiyamoorthy Road Chetput, Chennai - 600031
Tamil Nadu.
8. ICMR National institute of Pathology
Safdarjang Hospital Campus - 110029
New Delhi.

9. ICMR National Institute of Epidemiology
Second Main Road, Tamil Nadu Housing Board, Ayapakkam,
Near Ambattur - 600 077
Chennai.
10. ICMR National Institute of Medical Statistics
Post Box No. 4911, Ansari Nagar - 110029,
New Delhi.
11. ICMR National Institute of Malaria Research
Sector-8, Dwarka - 110077
New Delhi.
12. ICMR Regional Medical Research Centre, NE Region
Post Box No. 105, Dibrugarh - 786001,
Assam.
13. ICMR Regional Medical Research Centre
Gorakhpur
Uttar Pradesh.
14. 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.
15. ICMR National Institute of Nutrition
Jamai - Osmania (P.O.), Tarnaka,
Hyderabad - 500 007,
Andhra Pradesh.
16. ICMR National Institute for Research in Tribal Health
Nagpur Road, Garha, Jabalpur- 482 003,
Madhya Pradesh.
17. ICMR Desert Medicine Research Centre
New Pali Road, Jodhpur - 342 005,
Rajasthan.
18. National Institute of Cholera and Enteric Diseases
P-33, C.I.T. Road, Scheme XM Beleghata,
Kolkata.
19. ICMR National Institute of Immunohaematology
13th Floor, New Multi-storied Building, KEM Hospital Campus,
Mumbai - 400012,
Maharashtra.
20. ICMR National Institute for Research in Reproductive Health
Jehangir Merwanji Street, Parel,
Mumbai - 400 012,
Maharashtra.

21. ICMR National Institute of Cancer Prevention and Research (NICPR)
I-7, Sector - 39, Noida - 201301
Uttar Pradesh.
22. ICMR Rajendra Memorial Research Institute of Medical Sciences
Agam Kuan, Patna - 800007,
Bihar.
23. ICMR Regional Medical Research Centre
Post Bag No. 13, Port Blair - 744 101,
Andaman and Nicobar Islands.
24. ICMR Vector Control Research Centre
Indira Nagar - 605006,
Puducherry.
25. ICMR National AIDS Research Institute
G-73, MICD Complex, Bhosari, Pune - 411026
Maharashtra.
26. ICMR National Institute of Virology
20 A Dr Ambedkar Road, Pune - 411 001
Maharashtra.



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