INDIAN COUNCIL OF MEDICAL RESEARCH | NATIONAL INSTITUTE FOR RESEARCH IN REPRODUCTIVE AND CHILD HEALTH

वार्षिक प्रतिवेदन
Annual Report
2024-2025

आई सी एम आर - राष्ट्रीय प्रजनन एवं
बाल स्वास्थ्य अनुसंधान संस्थान

ICMR - National Institute for Research
in Reproductive and Child Health

राष्ट्रीय प्रजनन एवं बाल स्वास्थ्य अनुसंधान संस्थान

National Institute for Research in Reproductive and Child Health

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From the Desk of the Director...

It is with great pride that I present the Annual Report of the ICMR-National Institute for Research in Reproductive and Child Health for 2024-2025. This report is a brief compilation of our endeavors for research, capacity building, and services for better reproductive and child health.

The year was remarkable as it witnessed the institute becoming one of the stakeholders in three national health research priority projects envisioned by the Director-General, ICMR, to address recalcitrant health issues in our country, such as anemia, tuberculosis, and cancers. The institute has also been serving as one of the major research sites in an important implementation research study aimed at identifying modalities to improve the coverage and quality of comprehensive healthcare services through health and wellness centers.

Last year, the honorable minister of state for health and family welfare- Dr Bharati Pawar Ji laid the foundation stone of Model Rural Health Research Unit (MRHRU) at Vani, Nashik. I am happy to share that the construction work of the building is on full swing and will be completed soon. I also take this opportunity to thank Maharashtra State Health Department for generously making their infrastructure available to us for research and services under this new MRHRU facility as an interim agreement. The facility has become a major nodal point for training in snakebite envenomation in the country. Also, MRHRUs at Dahanu and Vani initiated population-based health surveys to assess the local-level estimates of the key indicators of common communicable diseases, non-communicable diseases, and reproductive, maternal, child health and nutrition in rural and tribal communities. This is a very important initiative to capture longitudinal changes in the incidence and risk factors of various communicable and non-communicable diseases, reproductive and child health, and nutrition.

Our research on Polycystic Ovary Syndrome (PCOS) demonstrated that targeting glucose and redox metabolism may hold promise for improving oocyte and embryo quality in Assisted Reproductive Technology (ART) settings. Further investigations revealed a coordinated interaction between epitranscriptomic and epigenetic mechanisms in granulosa cells, potentially contributing to the disrupted follicular microenvironment of PCOS. Initial findings indicate mitochondrial dysfunctions associated with mitochondrial variants and metabolic dysregulation in the follicular fluid from women with PCOS. These leads have furthered our understanding of the molecular underpinnings of PCOS.

Extensive studies were conducted in the domain of endometriosis research. A multicentric clinical study reiterated the urgent need for an integrated care model tailored to the Indian context. We also uncovered differential distribution patterns of endometrial stem cells across various subtypes of endometriotic lesions. A mechanism that endows endometriotic cells with a fitness to survive in a highly inflammatory environment was also deciphered. Also, we demonstrated a modulation in the uterine microenvironment, especially in specific immune cell types, in response to sterile inflammation.

We continued our efforts to gain more insights into the HOXA10-mediated transcriptional network governing epithelial cell integrity. Also, our work demonstrated that estrogen receptor α, via the paternal epigenome, influences key developmental pathways during embryogenesis. The epigenetic etiology of varicocele-associated infertility was also discovered in clinical cases.

Our multi-omics approach to vulvovaginal candidiasis revealed perturbations in host and pathogen pathways, underscoring the complexity of disease progression. We also validated molecular dynamics simulations as a rapid and reliable tool for toxicity screening of antimicrobial peptides, paving the way for safer therapeutic development. The potential of microbiome

modulation to preserve gut mucosal immunity was uncovered. Further, we continued our efforts to support 'Aatmanirbhar Bharat' in different capacities. In the reporting year, we, along with ICMR-NICPR, Noida, and AIIMS, New Delhi, participated in the validation of indigenous HPV tests for cervical cancer screening (i-HPV) under the guidance of Dr Neerja Bhatla. The HPV test kit (Truenat-HR-HPV-Plus) was found to have non-inferior clinical performance. The kit has shown great promise for clinical utility in LMIC settings. Another study conducted by the Health Technology Assessment (HTA) resource hub demonstrated that point-of-care testing for Hemophilia A and Von Willebrand Disease using an indigenous assay is more cost-effective than standard methods.

In addition to our research accomplishments, which included 83 publications in peer-reviewed national and international journals, and our scientists and students bringing many laurels to the institute, we continued to contribute towards capacity building through advanced training initiatives. We were invited by the Bill & Melinda Gates Foundation to organize a course on conception and contraception for capacity building in South East Asia, and we successfully organized this course in collaboration with international faculty. As in the previous year, we organized two intensive training programs sponsored by the Department of Health Research (DHR), each spanning four weeks. One focused on 'Precision Medicine: Promise and Practice', and the other on 'Applications of Genetics in Preconception, Prenatal and Pediatric Care'. These courses were thoughtfully designed for clinicians and researchers from medical colleges across India, equipping them with cutting-edge knowledge and practical tools to translate genomic science into clinical practice.

As we are spreading our wings by engaging in more research and capacity building activities, our administrative cadre is striving hard to cope with increased administrative and financial demands. Fortunately, we could recruit some administrative posts at the entry level.

I would like to express my sincere appreciation to Dr Rajiv Bahl, Secretary, Department of Health Research, Government of India, Director General, ICMR, for his visionary leadership and continued encouragement. His guidance has been instrumental in steering our institute toward impactful and translational research. I also extend my deep gratitude to the Additional Director General Dr Sanghmitra Pati; Senior Deputy Director General (Administration) Mrs Manisha Saxena; Deputy Director General (Administration); Assistant Director General (Administration); and the Head and staff of the Reproductive, Child Health & Nutrition Division at ICMR for their steadfast support and cooperation throughout the year. I also thank all the members of our Scientific Advisory Committee for their constructive input to our research programs.

As we reflect on the breadth and depth of our scientific endeavors this year, I extend my heartfelt gratitude to our dedicated scientists, students, and technical staff. I also acknowledge the very valuable support extended by our Senior Administrative Officer, Accounts Officer, and their teams. Their commitment and hard work drive us to our mission of health for all. I also thank our collaborators and funding agencies for their valuable support. Together, we remain steadfast in our pursuit of knowledge that transforms lives and strengthens the health systems of our nation.

Dr Geetanjali Sachdeva
Director

FEMALE INFERTILITY AND ASSOCIATED REPRODUCTIVE DISORDERS

1. FEMALE INFERTILITY AND ASSOCIATED REPRODUCTIVE DISORDERS

1.1 PON1 Expression, Activity and its Relationship with Oocyte and Embryo Quality in Women with PCOS undergoing Assisted Reproductive Techniques *(Partly Funded by Board of Research in Nuclear Sciences)*

Principal Investigator	:	**Srabani Mukherjee**
Co-Principal Investigator	:	D Modi
Project Associates	:	A Naigaonkar, Sushma Khavale, Gayatri Shinde
Collaborator	:	Indira Hinduja, PD Hinduja Hospital, Mumbai
Duration	:	2014-2023

Glucose is a quintessential metabolite for the development of oocyte and embryo. Granulosa cells (GCs) absorb and metabolize glucose and provide essential intermediates to the oocyte. This metabolic interaction between GCs and oocyte is influenced by gonadotropins and insulin, both of which are often disrupted in women with polycystic ovary syndrome (PCOS). These women experience hormonal, metabolic, and reproductive challenges, leading to difficulties in conceiving due to compromised oocyte and embryo quality. This compels women with PCOS to opt for assisted reproductive technologies (ART) for pregnancy. Further, the process of follicle and oocyte maturation is an energy-demanding phenomenon with high metabolic activity. Therefore, Reactive Oxygen Species (ROS) generation is inevitable which has to be tightly regulated by the antioxidant system.

This study seeks to investigate the dynamics of glucose metabolism and redox metabolism within the follicular environment to evaluate their potential as markers for oocyte/embryo quality and ART outcome. We previously demonstrated increased oxidative stress (OS), downregulated glycolysis and upregulated pentose phosphate pathway (PPP) along with lower CX43 transcript in the GCs of women with PCOS (Annual report 2023-24, pp. 1-2). In the reporting year, we assessed pyruvate levels in follicular fluid (FF) and GCs. These levels were found to be lower in women with PCOS (Fig. 1A&B). This suggested that downregulated glycolysis in GCs, and this may hamper the oocyte/embryo quality in PCOS. Connexin37 (CX37) levels in GCs were also found to be significantly lower in women with PCOS (Fig. 1C). Also, the expression of NRF2, a master redox regulator and its nuclear translocation was found to be higher in the GCs from women with PCOS (Fig. 2A&B). This may be in response to higher OS. NRF2 regulates G6PDH (rate limiting enzyme for PPP reported in Annual report 2023-24, pp. 1-2) and hence it is possible that NRF2 may have a role in metabolic reprogramming observed in GCs from PCOS group. Transcript levels of DNA repair enzyme OGG1 (8-oxoguanine DNA glycosylase 1) were also found it to be upregulated in GCs from women with PCOS, which goes in line with our previous observation of higher oxidative DNA damage (Annual report 2023-24, pp. 2). Our data strongly suggest that glucose metabolism and redox metabolism could be the potential targets to improve oocyte/embryo quality for women with PCOS in ART settings.

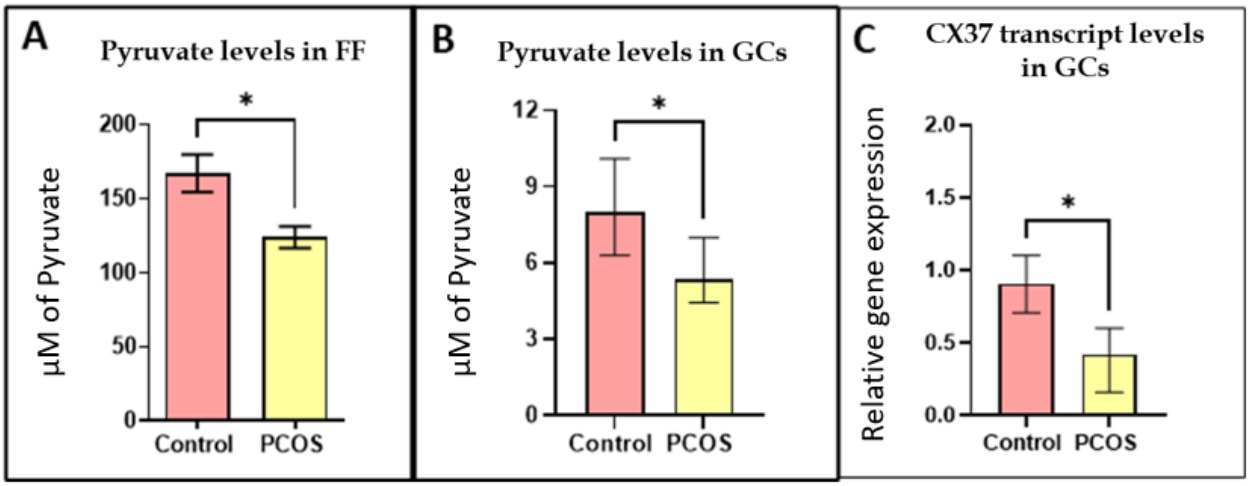

Figure 1: Levels of pyruvate in follicular fluid (A) and granulosa cells (B) of controls (n = 16) and women with PCOS (n = 10), Transcript levels of connexin 37 in granulosa cells (C) of controls (n = 12) and women with PCOS (n = 12), represented as mean ± SEM, *P<0.05 is significant.

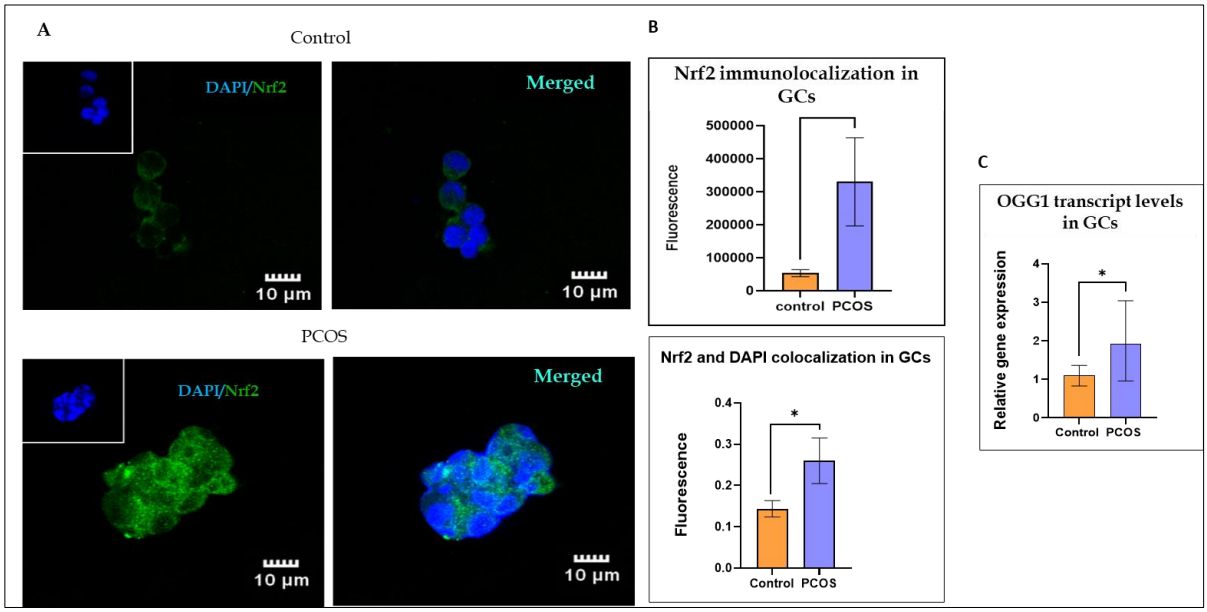

Figure 2: Representative images displaying immunolocalization of NRF2 (A) bar graphs showing the fluorescence intensity and colocalization of NRF2 and DAPI (B) in the GCs of controls (n = 4) and women with PCOS (n = 4), bar graph showing transcript levels of OGG1 (oxidative DNA damage repair enzyme) in the granulosa cells (C) of controls (n = 12) and women with PCOS (n = 12), represented as mean ± SEM, *p<0.05.

1.2 Integrated Analysis of Gut Microbiome and Metabolome in Women with Polycystic Ovary Syndrome *(Partly Funded by Department of Biotechnology)*

Principal Investigator	:	**Srabani Mukherjee**
Co-Principal Investigator	:	V Bhor
Project Associates	:	Komal Khade, R Patel
Collaborator	:	Anushree Patil
Duration	:	2023-2027

The pathophysiology of PCOS is complex and multifactorial. Studies conducted in rodent PCOS model and women with PCOS have shown a level between gut microbiota dysbiosis conducted and PCOS pathophysiology, offering new therapeutic interventions. The present study aims to understand gut dysbiosis and changes in gut metabolites in women with PCOS which has not been explored extensively in Indian women. To assess the gut microbiota composition, we carried out amplicon metagenomics using the Illumina MiSeq sequencing platform. Significant changes were observed in gut microbiota composition between PCOS and control group, as evident from altered beta diversity index. Differential abundance testing using Wilcoxon rank sum test and ANCOMBC2 revealed significant alterations of gut microbiota at class, order, family, genus and species levels. Increased abundance of *Ligilactobacillus ruminis* and *Collinsella species* was observed in PCOS. These were previously reported to be associated with ulcerative colitis and high BMI (Fig. 1). Spearman correlation analysis between significantly altered taxa and clinical features in women with PCOS revealed several significant correlations with gonadotropins and SHBG. We also assessed the levels of fecal short chain fatty acids (SCFAs), major gut microbial metabolite. Butyric acid, a multipotent SCFA, was significantly low in PCOS group (Fig. 2A). The disorder of gut microbiota could affect stability of intestinal barrier, leading to inflammation. Results showed that plasma level of zonulin, a gut barrier integrity marker was significantly elevated in women with PCOS, compared to controls, suggesting compromised gut integrity and increased intestinal permeability (Fig 2B). We further predicted differential functional profiles of the gut microbial communities by using Deseq2 (Fig. 2C). Altered gut microbiota in women with PCOS alters multiple metabolic pathways like cholesterol synthesis, vitamin K synthesis, amino acid metabolism etc. Gut microbiota dysbiosis and its correlation with gonadotrophins and SHBG indicates complex interaction of gut microbiota in PCOS pathophysiology. It is accompanied by alterations in microbial function, affecting host physiological function via its metabolites. The role of gut microbiota in PCOS pathophysiology needs further evaluation using multi omics techniques. Currently investigation of gut metabolites in conjunction with gut microbiota composition using shotgun metagenomics is ongoing.

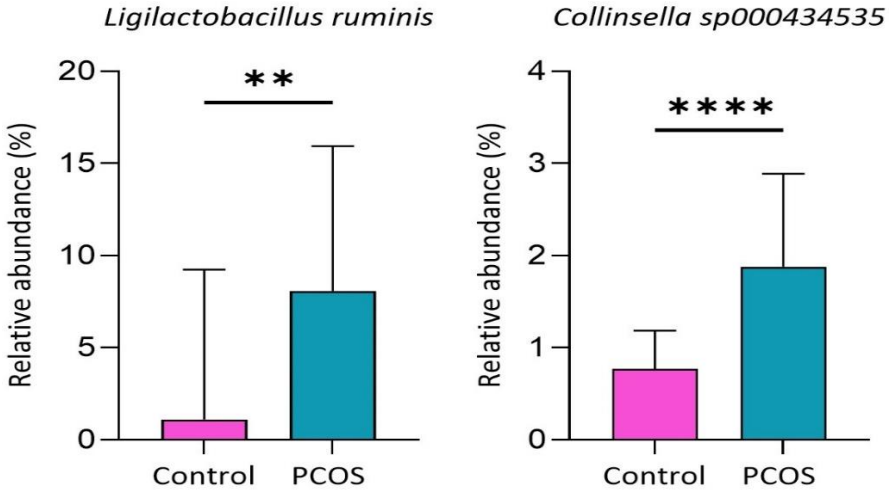

Figure 1: Relative abundance (percentage) of differentially abundant taxa in control and PCOS groups, identified using Wilcoxon rank-sum test and ANCOM-BC2

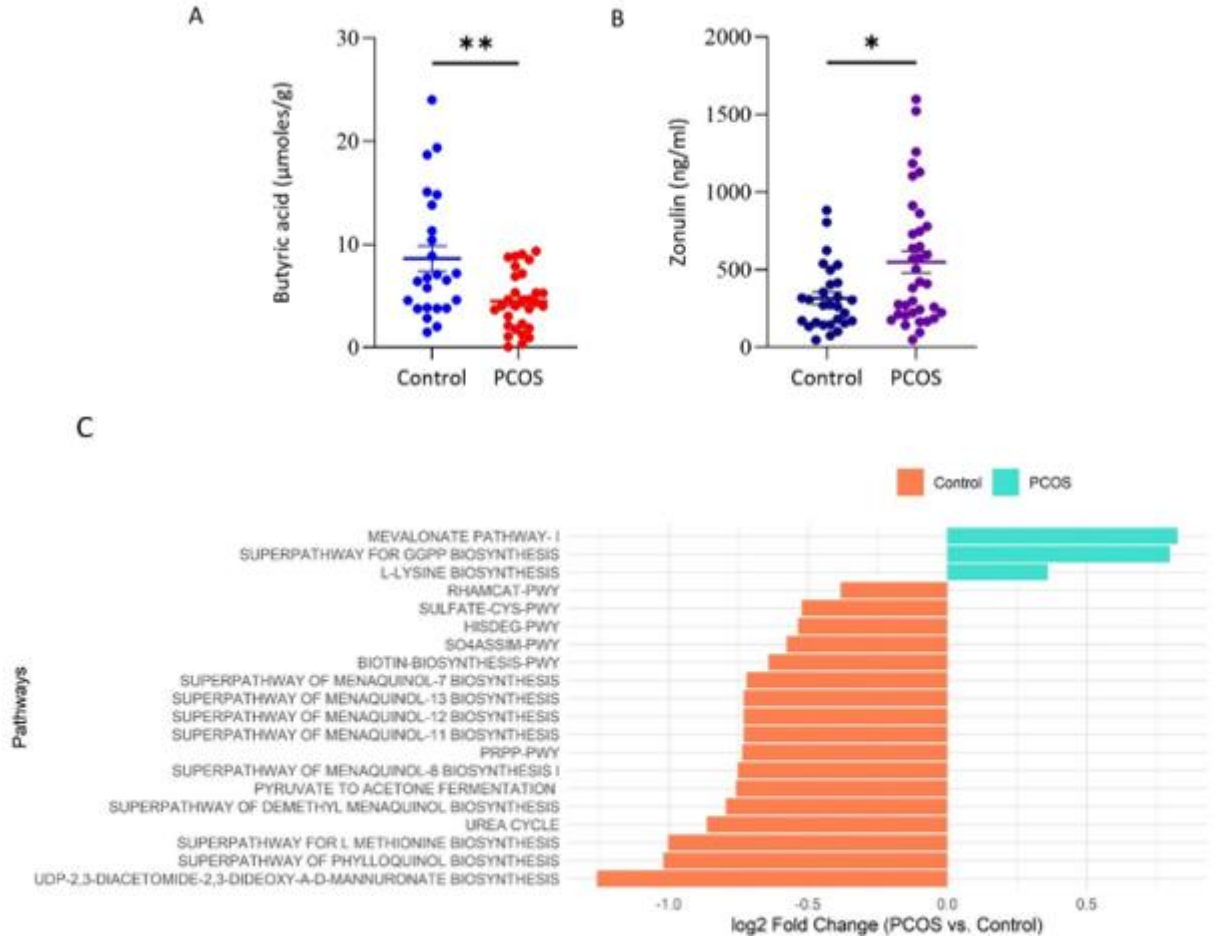

Figure 2: A) Levels of butyric acid estimated using HPLC in fecal samples. B) Plasma zonulin levels determined by ELISA. C) Differentially enriched gut microbial pathways in women with PCOS and controls. Pathways enriched in the PCOS group (right) have positive log2 fold change, while those enriched in the control group (left) have negative log2 fold change.

1.3 Assessing the Coagulation and Fibrinolytic System as Contributors of Thrombotic State in Polycystic Ovary Syndrome

Principal Investigator	:	**Srabani Mukherjee**
Co-Principal Investigator	:	B Kulkarni
Project Associates	:	Roshan Dadachanji, Gayatri Shinde, Sushma Khavale, Nanda Joshi
Collaborators	:	Anushree Patil, B Kulkarni
Duration	:	2021-2026

PCOS is a common cause of anovulatory infertility in women of reproductive age. Women with PCOS are at a higher risk for cardiometabolic disorders like obesity, diabetes, and cardiovascular disease. Prothrombotic conditions have also been reported in these women, possibly due to imbalances in coagulation and fibrinolytic markers. These conditions may contribute to cardiometabolic perturbations and reproductive anomalies like anovulation and recurrent miscarriage. Previously we have reported that women with PCOS have significantly higher circulating levels of hemostatic factors such as tissue factor, plasminogen activator inhibitor-1, tissue plasminogen activator enzyme, and plasminogen, reduced antithrombin levels and thrombin time readings (Annual report 2022-2023, pp. 4-5; Annual report 2023-2024, pp. 4-5). In the reporting year, significantly decreased fibrinogen and significantly increased TAFI levels,

but comparable urokinase-type plasminogen activator levels were found in women with PCOS compared to controls. Overall, PCOS women exhibit both procoagulant and hypofibrinolytic states. Further, we continued our study on genetic polymorphisms of thrombophilia related genes in PCOS. We have previously shown that C677T polymorphism of MTHFR, and -675 4G/5G polymorphism of PAI-1 do not influence PCOS risk in Indian women (Annual report 2022-2023, pp. 4-5; Annual report 2023-2024, pp. 4-5). This year we report for the first time to the best of our knowledge that that the -455G/C and -149C/T, but not -249C/T polymorphisms, in the promoter region of Fibrinogen beta chain (FGB) gene were significantly associated with a lowered risk of PCOS development in Indian women considering the dominant model (Fig. 1). Further, we genotyped the factor V Leiden 1691G-A polymorphism (rs6025), in F5 gene on chromosome 1q23. However, we did not find any association with PCOS risk, indicating that this may not be a strong contributing factor to PCOS or its associate cardiometabolic concerns. Alterations in the ratio of coagulation to fibrinolytic factors have also been demonstrated to affect critical ovarian processes such as ovulation. We observed that the transcript levels of SERPINE1 (or PAI-1), PLAT (Plasminogen activator, tissue type) CTSB (cathepsin B), FGG (fibrinogen gamma) were significantly reduced in the granulosa cells of PCOS women compared to controls. On the other hand, transcript levels of SERPINE2, SERPINB2, and Factor 3 (F3) levels were similar in the two groups (Fig. 2).

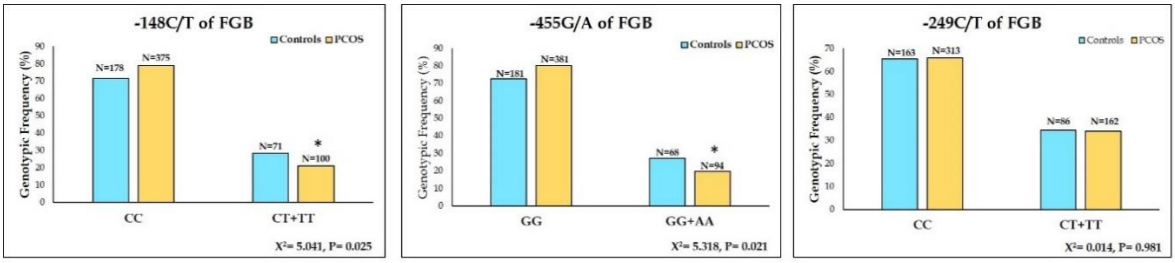

Figure 1: Genotypic distribution of promoter polymorphisms of FGB in controls and women with PCOS

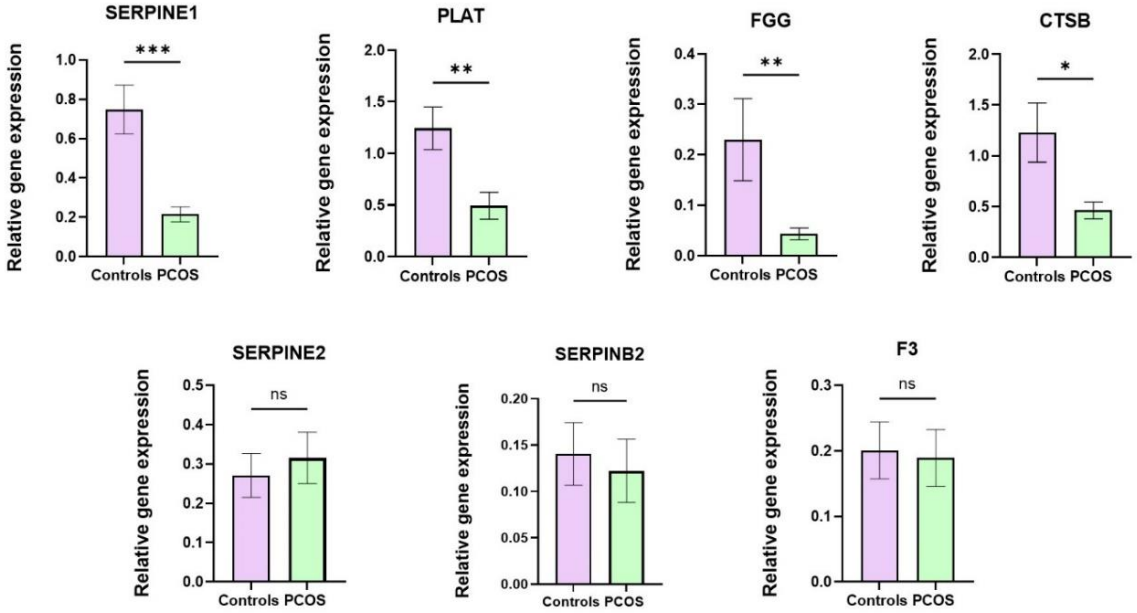

Figure 2: Relative expression of hemostatic parameters in granulosa cells. Transcript expression of key hemostatic factors in granulosa cells was studied by real-time PCR. Bar graphs represent relative transcript levels of antioxidant genes between controls (n=14) and women with PCOS (n=14). Analysis was carried out by Mann-Whitney U test and represented as mean+ SEM. *p<0.05, **p<0.01, ***p<0.001

1.4 Exploring the Epigenetic Alterations Regulating miRNA Expression in Women with Polycystic Ovary Syndrome

Principal Investigator	:	**Srabani Mukherjee**
Co-Principal Investigator	:	Pallavi Shukla
Project Associate	:	Snehal Bhingardeve
Collaborators	:	Sadhana Desai, V Mangoli, Richa Jagtap
Duration	:	2020-2026

Polycystic Ovary Syndrome (PCOS) is a complex disorder that affects the endocrine, metabolic, and reproductive functions and is a leading cause of anovulatory infertility. Recent studies highlight the significant roles of several epigenetic mechanisms such as DNA methylation and non-coding RNAs, particularly microRNAs (miRNAs), in shaping gene expression patterns associated with PCOS. We previously (Annual report 2022–23, pp. 5–6) reported a potential epigenetic interplay between DNA methylation and miRNA expression that may influence gene regulation and impact key cellular processes in PCOS. Notably, RNA modifications add an additional layer of regulatory complexity, however their role in PCOS pathogenesis remains largely unexplored. Among these, N6-methyladenosine (m6A), a prevalent and reversible modification in eukaryotic mRNA, is known to affect ovarian development and oocyte maturation. Recognizing its potential significance in ovarian function, we focused on investigating global m6A levels and the expression of m6A regulatory genes in ovarian granulosa cells (GCs) from women with PCOS. We assessed the global m6A methylation levels and analysed the expression of core m6A regulatory components categorized as “writers”, “erasers” and “readers” in the GCs from 23 women with PCOS and 23 matched controls. In addition, we explored potential regulatory interplay between m6A modifications and miRNAs. Our results revealed increased global m6A levels in GCs from women with PCOS (Fig. 1A). The transcript levels of m6A “writers” (METTL3, METTL14, WTAP, and VIRMA) was found to be increased and the expression of the "erasers" FTO and ALKBH5 were found to be decreased in the GCs of women with PCOS compared to controls. Furthermore, expression of m6A "readers" (YTHDF1, YTHDF2, YTHDF3, and YTHDC1) were found to be altered in PCOS (Fig. 1B, 1C, 1D). To investigate potential upstream regulators of m6A-modifying enzymes, we utilized miRTarBase, a curated repository of experimentally validated miRNA–target interactions. We identified miR-20b and miR-607 as miRNAs targeting METTL3 and FTO, respectively. Further, miR-20b and miR-607 showed inverse trend in terms of their expression compared to their respective target genes, suggesting a potential miRNA-mediated mechanism contributing to the elevated m6A levels observed in the GCs of PCOS (Fig. 2). Collectively, our findings demonstrate increased global m6A methylation in PCOS, likely driven by altered expression of m6A-modifying enzymes under miRNA regulation. These results underscore a coordinated interaction between epitranscriptomic and epigenetic mechanisms in granulosa cells, potentially contributing to the disrupted follicular microenvironment characteristic of PCOS.

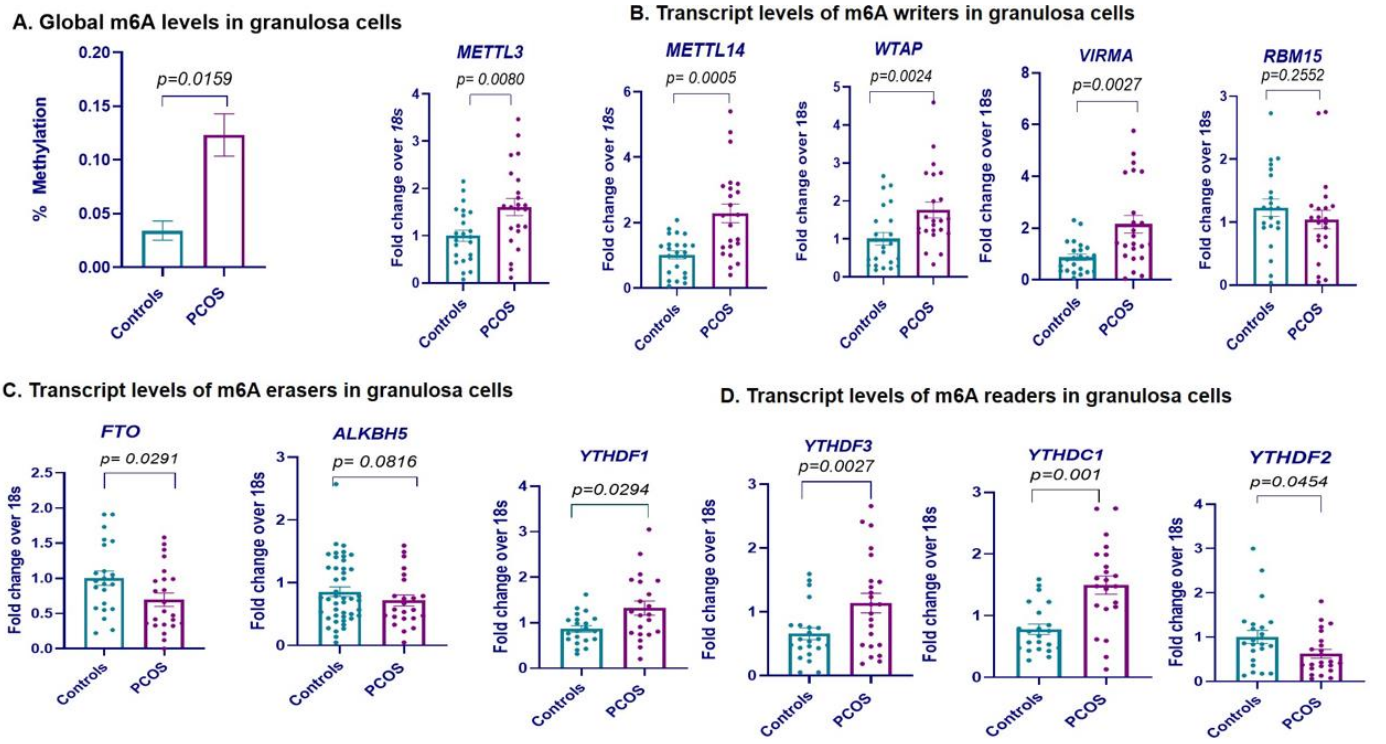

Figure 1: Global m6A levels and transcript levels of m6A regulators in granulosa cells obtained from controls (n=23) and women with PCOS (n=23) Percent global m6A levels (A); transcript levels of m6A writers METTL3, METTL14, WTAP, VIRMA and RBM15 (B); transcript levels of m6A erasers, FTO and ALKHB5 (C); transcript levels of m6A readers, YTHDF1, YTHDF3, YTHDC1 and YTHDF2 (D). Data for each group are represented as mean±SEM, statistical significance was calculated by Mann-Whitney U test. p-value < 0.05 was considered statistically significant.

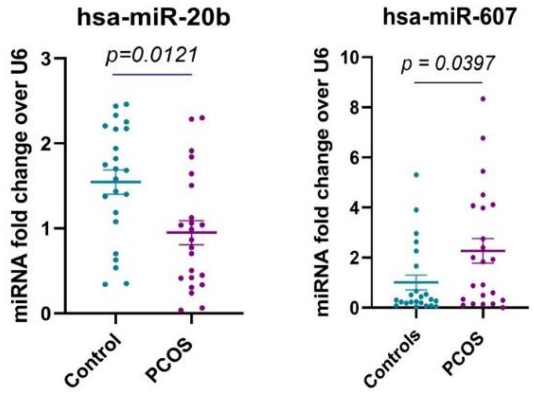

Figure 2: Transcript levels of miRNAs targeting m6A regulators in the granulosa cells of controls (n=23) and women with PCOS (n=23). Data for each group is represented as "mean±SEM". Statistical significance was calculated by Mann-Whitney U test. p<0.05 was considered statistically significant.

1.5 Unravelling Pathogenetic Mechanisms of Polycystic Ovary Syndrome by Whole Exome Sequencing *(Partly Funded by Department of Science and Technology)*

Principal Investigator : **Srabani Mukherjee**
Project Associates : Medini Samant, Roshan Dadachanji, Sushma Khavale, Gayatri Shinde, Nanda Joshi
Collaborators : Anushree Patil, Beena Joshi
Duration : 2017-2026

Polycystic Ovarian Syndrome (PCOS) is a multigenic complex disorder. Various approaches such as familial studies, candidate gene studies, and genome-wide association studies (GWAS) have identified numerous genetic loci associated with PCOS in different populations but no universal susceptibility maker has been identified. Exome sequencing can identify disease-causing variations in the protein-coding regions of the genome. The current study aims to comprehend the role of functional variants in PCOS using whole exome sequencing (WES) approach, which is not well explored in Indian women. We performed WES in eighty-five well-characterized women diagnosed with PCOS using the Agilent SureSelect CREV2 platform. Variants were annotated using ANNOVAR and used for further analysis. Screening of the WES data yielded a total of 5,33,628 variants which included 50.8% non-synonymous, 43.75% synonymous, 1.6% non-frameshift, 1.1% frameshift indels, 0.7% stop-gain, 0.05% stop-loss, and 2% unknown variants. Among these, 29,551 variants were classified as rare (gnomAD v2.1.1 minor allele frequency MAF<0.01). These variants were further filtered based on quality check parameters and pathogenicity for further analysis. VarElect tool prioritized genes associated with PCOS, and Chi-square test was used to compare allele counts between PCOS group and South Asian ancestry individuals in the gnomAD v2.1.1 database. A significant association of 234 rare pathogenic nonsynonymous variants were identified in 201 genes with PCOS in our study (Fig. 1). Pathway analysis of the genes harboring these variants identified several biologically relevant pathways, including steroid hormone biosynthesis, ovarian steroidogenesis, insulin resistance, and the PI3K-Akt signaling pathway, implicated in PCOS pathophysiology (Fig. 2). Variants of the steroidogenesis pathway were validated by Sanger sequencing including rs368902124 (CYP19A1), rs143286842 (IGF1R), and rs555458296 (BMP-6). In-silico protein stability analysis by DUET indicated that variants in CYP19A1 and IGF1R genes destabilized the folding of their corresponding proteins. Enrichment analysis of disease terms from 201 genes having rare variants according to DisGeNET revealed obesity, cardiovascular disorders, diabetes and metabolic syndrome among the top significantly enriched pathologies (Fig. 2). Furthermore, an in-depth literature review revealed that 160 of the 201 genes identified by us have not been reported for their association with PCOS, indicating a substantial set of new candidate genes having a role in the disorder. Further analysis is ongoing to identify polymorphism and rare variants present according to PCOS phenotypes.

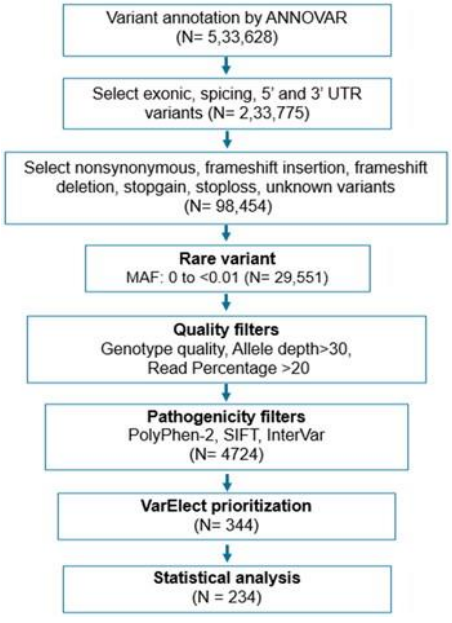

Figure 1: Workflow for variant filtration and analysis

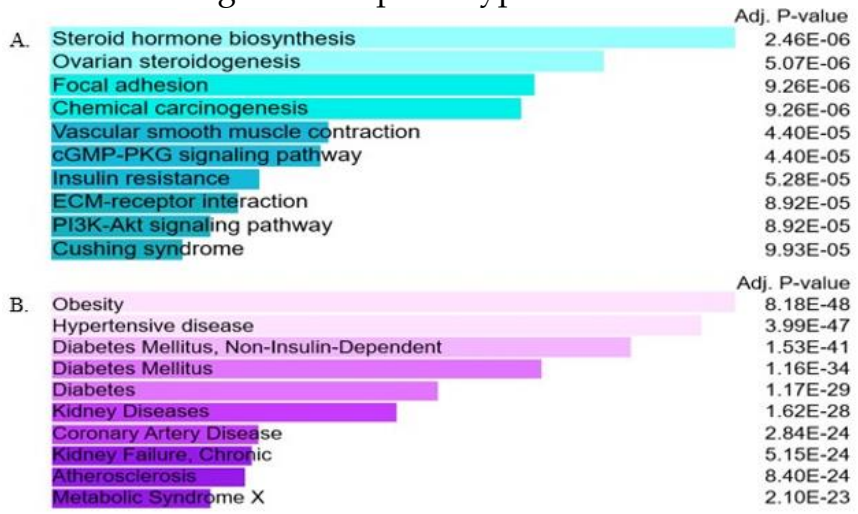

Figure 2: Pathway analysis of the genes harbouring rare variants identified in women with PCOS using Enrichr A. Enrichment analysis of pathways of 201 genes having rare variants according to KEGG pathways B. Enrichment analysis of disease terms of 201 genes having rare variants according to DisGeNET

1.6 Analysis of Mitochondrial DNA Sequence Variants in Polycystic Ovarian Syndrome Women with Insulin Resistance

Principal Investigator	:	**Pallavi Shukla**
Co-Principal Investigator	:	Srabani Mukherjee
Collaborators	:	Anushree Patil, Beena Joshi
Duration	:	2018-2025

Role of mitochondria in the etiopathophysiology of Polycystic Ovary Syndrome (PCOS), a common cause of infertility is not understood fully. In the current year, analysis of mitochondrial dysfunction data was carried out according to 4 different PCOS phenotypes, on the basis of advanced Rotterdam criteria based on Hyperandrogenism (HA), Ovulatory Dysfunction (OD), and Polycystic Ovary morphology (PCO) as follows: Frank/Classical PCOS(HA+OD+PCO) (n=118), Non-PCO PCOS (HA+OD) (n=42), Ovulatory PCOS (HA+PCO) (n=11) and Normoandrogenic PCOS (OD+PCO) (n=59). Quantification of mtDNA copy number, a biomarker of mitochondrial dysfunction in Frank PCOS (1.06 ±0.027) showed a significant reduction in copy number as compared to Non-PCO PCOS (n=42) (1.18 ± 0.051) (p=0.0418). This suggests that mitochondrial dysfunction is aggravated in full blown frank/classical PCOS phenotypes and may have greater metabolic impairments despite lacking poly cyst morphology when compared to non-PCO phenotype. More studies are required in larger samples to arrive at definite conclusion.

1.7 Study of Maternally Inherited Mitochondrial DNA Variants in Women with Polycystic Ovarian Syndrome *(Partly Funded by Indian Council of Medical Research)*

Principal Investigator	:	**Pallavi Shukla**
Co-Principal Investigators	:	Srabani Mukherjee, Anushree Patil
Project Associates		Samia Palat Thariyal, Jyotsna Khithani
Collaborators	:	Anushree Patil, V Patil
Duration	:	2021-2026

Polycystic Ovary Syndrome (PCOS) is a complex endocrine and metabolic disorder and one of the leading causes of infertility among women of reproductive age. Despite multiple genome-wide association studies (GWAS), nuclear genetic variants identified so far account for only a small proportion of the heritability observed in PCOS, suggesting the involvement of non-Mendelian inheritance mechanisms. Mitochondrial DNA (mtDNA), which is exclusively maternally inherited, has emerged as a potential contributor to the unexplained genetic component of PCOS. Notably, familial aggregation is frequently observed, with 3%–35% of women with PCOS reporting a maternal history of the disorder, implicating mtDNA in its pathogenesis. This study investigates mitochondrial dysfunction in daughters belonging to Group I (PCOS Mothers–PCOS Daughters), Group II (Non-PCOS Mothers–PCOS Daughters), and Group III (Non-PCOS Mothers–Non-PCOS Daughters). Our findings revealed a significant decrease in mitochondrial membrane potential (MMP) in daughters with PCOS (Group I + Group II) (n=22) compared to non-PCOS control daughters (Group III) (n=13) (p=0.0091). Additionally, mitochondrial reactive oxygen species (mtROS) levels were significantly increased in PCOS daughters (Group I + Group II) (n=28) relative to non-PCOS control daughters (Group III) (n=13) (p=0.014). These preliminary results indicate mitochondrial dysfunction in PCOS, potentially associated with mtDNA variants.

A B

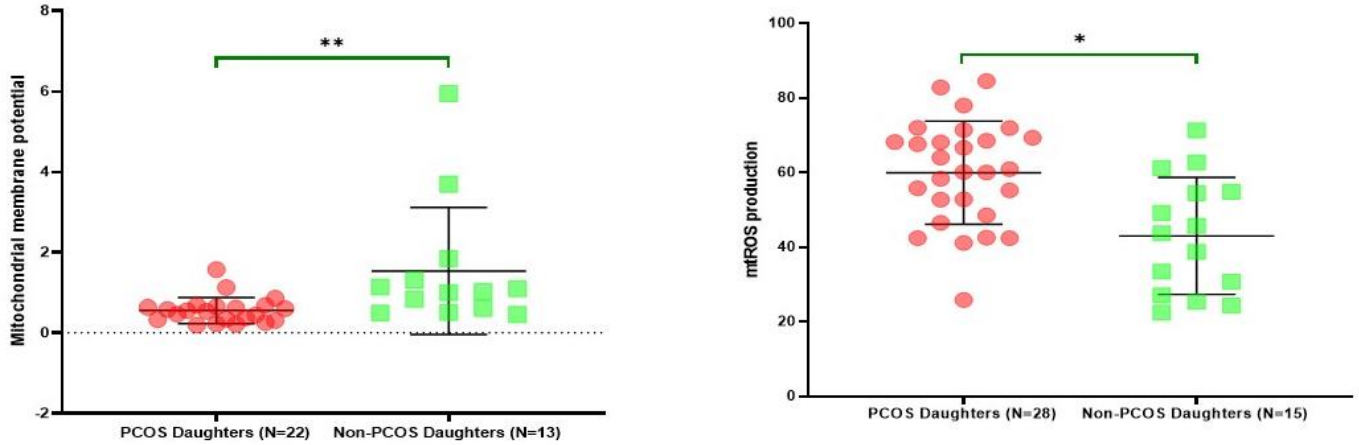

Figure 1: (A) Mitochondrial Membrane Potential (MMP) was decreased in daughters with PCOS compared to non-PCOS control daughters (p= 0.0091). (B) Mitochondrial Reactive Oxygen Species (mtROS) levels were significantly increased in PCOS daughters relative to non-PCOS control daughters (p= 0.014)

1.8 Study of Epigenetic Factors involved in Mitochondrial Dysfunction in Obese Polycystic Ovarian Syndrome Women

Principal Investigator	:	**Pallavi Shukla**
Co-Principal Investigators	:	Srabani Mukherjee
Collaborator	:	Anushree Patil
Duration	:	2019-2027

Polycystic ovary syndrome (PCOS) a leading cause of infertility among women of reproductive age. Two types of PCOS phenotypes are widely known, overweight/obese (35-60%) and lean with different biochemical, hormonal, and metabolic profiles among the two phenotypes. Menstrual disturbances and infertility are more common in obese PCOS women than in lean PCOS women. Obese PCOS women have a greater risk of Type 2 Diabetes, impaired glucose tolerance and endometrial hyperplasia than in lean PCOS and need to be treated more rigorously. Hence, there is a need to understand how obesity leads to PCOS or vice-versa and the pathogenic mechanism underlying obese PCOS phenotype. Obesity may trigger mitochondrial epigenetic changes leading to mitochondrial dysfunction (MD). In this reporting period, our studies demonstrated mitochondrial membrane potential (MMP) significantly reduced in obese PCOS women (n=42) than in obese non-PCOS women (n=10) ($p<0.0001$) and in lean PCOS women (n=13) than in lean non-PCOS women (n=20) (Fig. 1A). Further, mitochondrial ROS (mtROS) was significantly increased in obese PCOS (n=67) vs obese non-PCOS group (n=12) ($p=0.0002$) and lean PCOS (n=16) vs lean non-PCOS (n=21) group ($p<0.0001$). However, no significant difference in MMP and mtROS was observed between obese and lean PCOS phenotype. Further studies need to be conducted in large sample size, particularly lean PCOS women, obese and lean non-PCOS control women to arrive at a definitive conclusion.

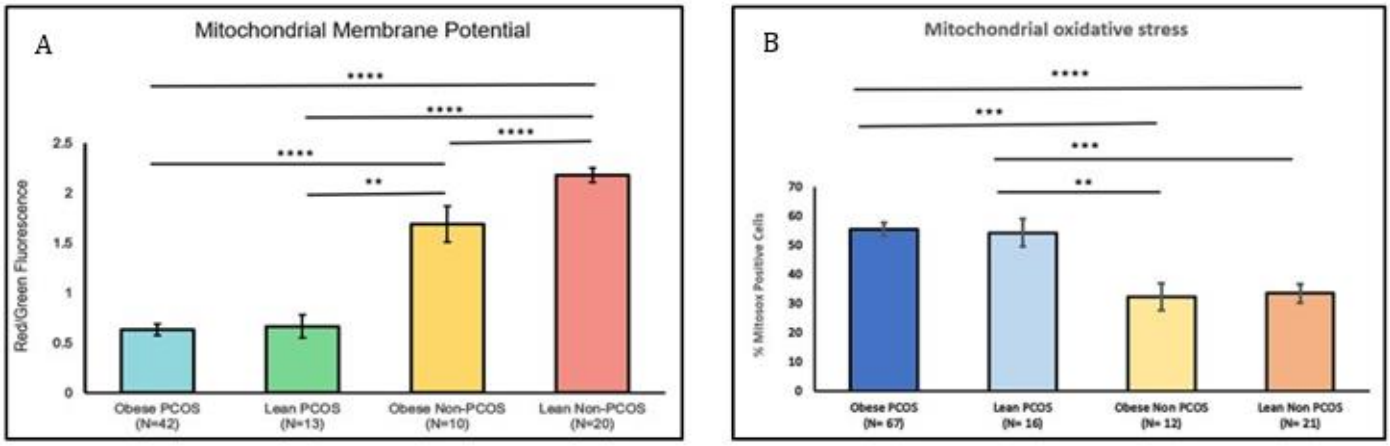

Figure 1: (A) Mitochondrial Membrane Potential (MMP) is significantly reduced in obese PCOS compared to obese non-PCOS and also in lean PCOS compared to lean non-PCOS group. (B) Mitochondrial ROS is significantly increased between obese PCOS compared to obese non-PCOS and in lean PCOS compared to lean non-PCOS group.

1.9 Understanding the Role of Antioxidants in Endocrine Disrupter-Induced Polycystic Ovary Syndrome (PCOS) like Condition

Principal Investigator	:	**V Dighe**
Project Associates	:	B Saha, S Jadhav, P Salunke
Duration	:	2024-2027

Polycystic Ovary Syndrome (PCOS) is an endocrine, metabolic disorder in women of reproductive age. This disorder leads to other conditions like infertility, endometriosis, hyperinsulinemia, and hyperandrogenism. A high-fat diet and endocrine disruptors are some of the key factors responsible for causing PCOS in women. BPA is an EDC known for its widespread application and persistence in human body. Antioxidants like Eugenol (anti-inflammatory), Curcumin, Vitamin C, Vitamin E, Q10, etc. have the potential to down-regulate oxidative stress and inflammation caused by PCOS and improve hormonal balance. We hypothesize that exposure to BPA alone or in combination with a high-fat diet (HFD) leads to PCOS-like conditions in rats. Previously, we attempted to develop a PCOS rat model using HFD and BPA. The rat model showed irregular estrous cycles, decreased serum prolactin levels, and increased glucose intolerance, serum testosterone, and LDL levels (Annual report 2023-2024, pp. 12-13). In this reporting year, other parameters such as serum luteinizing hormone (LH) and follicle-stimulating hormone (FSH) levels, were assessed along with ovarian histomorphology. LH levels were significantly elevated in the HFD+BPA group compared to control or BPA-treated group (Fig. 1A). FSH levels were significantly decreased in the HFD+BPA group compared to control and BPA-treated groups (Fig. 1B). LH: FSH ratio was significantly increased in the HFD+BPA group as compared to all other groups (Fig. 1C). Cystic follicle and atretic follicle counts were significantly higher in all treated groups than the control (Fig. 1E&F). Corpus luteum count was significantly reduced in all treated groups than in the control group (Fig. 1G). Inflammatory cytokines and levels of oxidative stress markers are being estimated.

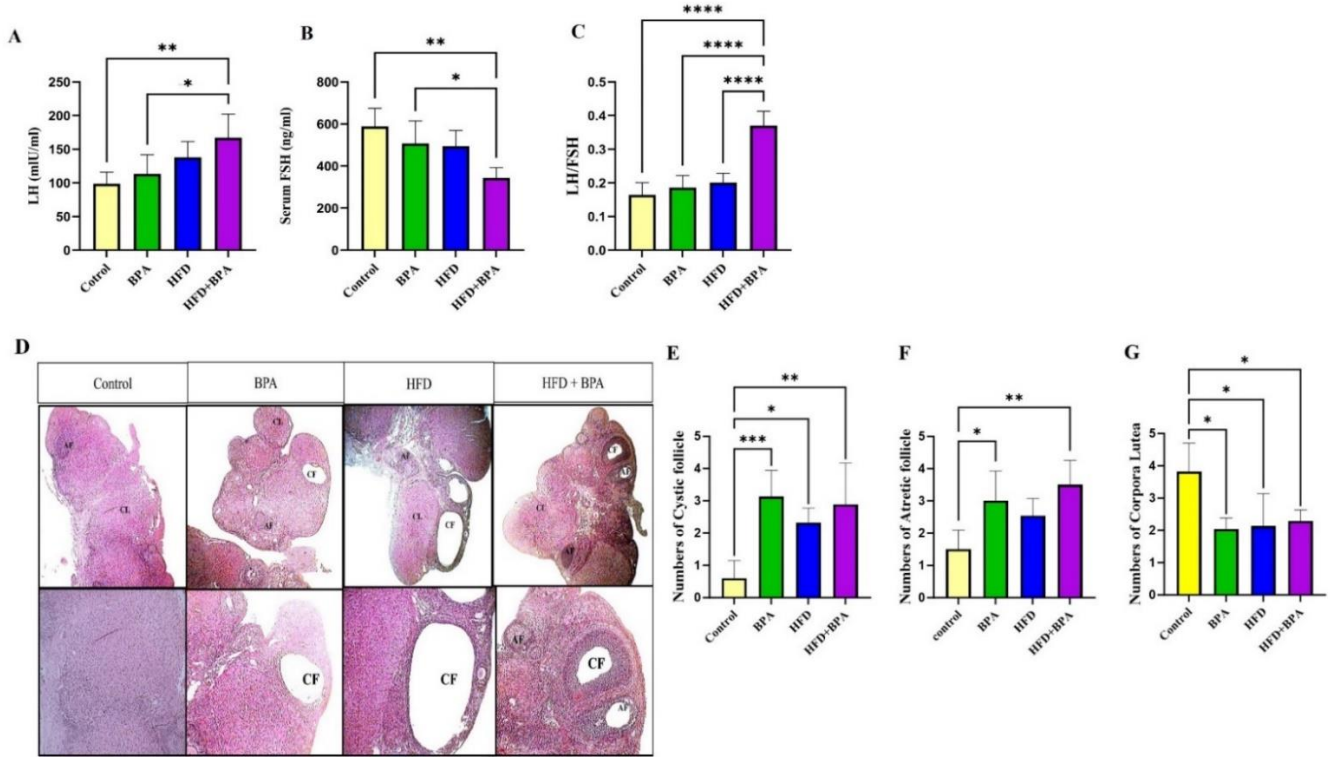

Figure 1: Effect of exposure to BPA and high-fat diet during prepuberty to adulthood in rats. (A) Total LH (mIU/ml), (B) Total FSH (ng/ml), (C) LH: FSH ratio, (D) Ovarian histology, (E) Total cystic follicle count, (F) Total atretic follicle, (G) Total corpora lutea. Bars represent the mean ± SD. *p≤0.05, **p≤0.005, ***p≤0.0005, ****p≤0.00005 (n=6)

1.10 Centre for Product Development: Development of Recommendations and Algorithms for Multidisciplinary Management of Polycystic Ovary Syndrome (PCOS) in the Indian Health Care System *(Partly Funded by Indian Council of Medical Research)*

Principal Investigator : **Anushree Patil**
Co-Principal Investigators : Rama Vaidya
Project Associate : Nupoor Limaye
Collaborators : Jayashree Joshi, Ashwini K Raut, Shobha Udipi, Medical Research Centre, Kasturba Health Society (KHS-MRC)
Duration : 2019-2024

The objectives of the study are to review the existing guidelines and management practices for PCOS and develop multidisciplinary recommendations (clinical and operational) and easy-to-use algorithms for the management of PCOS for the Indian health care system; and to pilot test recommendations with health care providers for user-friendliness. The draft guidance was revised in light of the 2023 International Evidence-based Guidelines for the assessment and management of Polycystic ovary syndrome (PCOS). This involved a thorough review of the guidance material and international recommendations. To achieve this, a series of meetings were held with the KHS-MRC, in parallel, ongoing tasks included the pilot testing of the revised guidelines with the healthcare providers to gather feedback and to understand the feasibility, acceptability, and training needs in PCOS management. A specialized tool for this pilot testing was developed, aimed at validating the effectiveness, utility, and user-friendliness of the guidelines. A meeting was held with the District Health Officer and Medical Officers of Palghar to facilitate the validation of this tool through a Continuing Medical Education (CME) session

for further improvement and finalizing the recommendations. A CME and stakeholder consultation of recommendations for the diagnosis and multidisciplinary management of PCOS in the Indian healthcare system, was conducted by ICMR- NIRRCH in joint collaboration with KHS-MRC at Govardhan Eco Village, Wada, for all medical officers of Palghar District, including specialists, DHO, Civil surgeon, THO, CHO. According to 88 (45.1%) of 210 participants, recommendations for PCOS are not available in healthcare system. 143 (69.4%) participants reported that PCOS is a public health problem in their practice area. Majority of healthcare providers referred women with PCOS to a higher facility for management for various reasons such as menstrual complaints, obesity management, dermatological manifestations, psychological concerns, endometrial biopsy, hyperandrogenism, counselling, USG, infertility management, non-availability of medicines for the treatment, nonavailability of specialists and lack of training. 165 (79.3%) participants stated that the sections of the recommendations for multidisciplinary management of PCOS in Indian healthcare system developed by ICMR-NIRRCH and KHS-MRC were clear and comprehensible. According to 199 (82.9%) participants the document has covered all the relevant aspects to provide practical guidance. 207 (86.3%) participants found case studies helpful and informative. 187 (89%) participants found the Recommendations for management of PCOS feasible to implement. The findings of the opinions of healthcare providers are useful in gaining deeper insights regarding implementation of the recommendations for multidisciplinary management of PCOS in the healthcare system.

1.11 Delineating Pathogenesis of Obese and Lean PCOS Phenotype using Integrated Transcriptomics and Proteomics Approach *(Funded by Department of Health Research)*

Principal Investigator : **Pallavi Shukla**
Co-Principal Investigators : Srabani Mukherjee, Anushree Patil
Project Associate : Shreya Joshi
Collaborator : Anushree Patil
Duration : 2023-2026

Polycystic Ovary Syndrome (PCOS) is a complex endocrine disorder affecting women of reproductive age and is associated with obesity, insulin resistance, and subfertility. Up to 35–60% of women with PCOS are obese. Menstrual disturbances, anovulation, and infertility are more common in obese PCOS women than in non-obese PCOS women. This study aims to delineate the underlying pathogenic differences between obese and lean PCOS women using integrated blood plasma transcriptomics and proteomics approach. Obesity was considered if BMI ≥ 25 kg/m^2 and women with BMI 18.5-22.9 kg/m^2 were considered as lean (according to Indian revised guidelines for Body Mass Indices). A total of 117 women were recruited for the study, comprising 57 women with PCOS and 60 women without PCOS, in accordance with the Rotterdam Criteria. Among the PCOS group, 33 participants (28.2%) were classified as obese, while 11 participants (19.3%) were classified as lean. In the non-PCOS group, 12 participants (20%) were categorized as obese, and 25 participants (41.6%) were categorized as lean. Interim analysis of hormonal profile analysis performed in some women with obese and lean PCOS phenotype as well as obese and lean controls showed that the SHBG is significantly increased in lean PCOS compared to obese PCOS. Testosterone and total HDL levels were significantly increased in obese non-PCOS compared to lean non-PCOS controls. The recruitment of participants is going on and plasma samples are being stored for transcriptomic and proteomics studies.

1.12 Prospective Evaluation of Etiological Factors, Trajectory of Comorbidities and, Efficacy and Safety of Various Therapeutic Agents among Indian Women with Polycystic Ovary Syndrome (PCOS): A Multicentric ICMR-PCOS Cohort Study Phase II *(Funded by ICMR - Indian Council of Medical Research)*

Principal Investigator : **Anushree Patil**
Project Associates : Srabani Mukherjee, Pratibha Kokate, Anamika Akula, Shobha Banage
Collaborators : Padmaja Samant Mavani, N Mayadeo, A Shukla, Amita Athavale, Ajita Nayak
Duration : 2023-2028

Polycystic Ovary Syndrome (PCOS), the complex and commonest endocrinopathy in reproductive age grouped women, has attracted significant attention from multiple specialities in recent years, owing to its diverse clinical and metabolic ramifications. A need for the proposed study emerges from the fact that nationally representative data about the prevalence of PCOS, long-term follow up of various comorbidities associated with PCOS (impaired glucose tolerance (IGT), non-alcoholic fatty liver disease (NAFLD), hypertension (HT), obesity, cancers etc), is negligible. To address these issues, ICMR adopted a systematic way to address these issues by formulating a National Task Force study in a phased manner (Phase I, II & III). In this direction this Multicentric ICMR-PCOS Cohort Study Phase II was proposed which is aimed to address these issues through following objectives: Development/maintenance of PCOS cohort and longitudinal evaluation of various comorbidities associated with PCOS (abnormal glucose tolerance, NAFLD, HT, obesity, sleep disorders, cardiovascular risk, cancer, psychiatric disorders etc.) in this cohort. This prospective study in collaboration with Seth GS Medical College and KEM Hospital was initiated in January 2024. The cohort will include women having symptoms suggestive of PCOS (oligomenorrhea, hyperandrogenism and polycystic ovary morphology (PCOM) either together or alone) for follow up to understand their evolution. These women will be examined for the trajectory of comorbidities, intercurrent health events, treatment received, therapeutic responses to various interventional modalities etc initially for a period of five years to be extendable by another 5 years. Total 71 participants have been recruited under this study till March 2025 (45 PCOS women and 26 control). All the participants were asked their medical history such as menstrual cyclicity, weight trajectory, hyperandrogenism features, physical activity, drug intake, quality of life, psychiatric comorbidities using appropriate validated questionnaires, wherever appropriate. Participants were evaluated for anthropometry measurements such as height, weight, BMI, waist hip ratio. In PCOS group 30 participants were married and 15 were unmarried girls. 15 participants had grade I fatty liver and one participant had grade II fatty liver. In healthy control group 23 were married and 3 unmarried girls. Only six participants had USG and two participants had grade I or grade II fatty liver. After approval of KEM ethics all these cases were evaluated for fibro scan. Data was also collected for quality of life using PCOS QOL questionnaire, Short Form Health Survey questionnaire (SF-36), Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM IV scale), and Epworth sleepiness scale at baseline.

Table 1: Recruitment details

Profile	Number Screened	Number Enrolled
PCOS Women	100	45
Control Women	56	26
Total Participants	156	71

1.13 Unravelling the Metabolic Nexus in the Granulosa Cells of Women with PCOS *(Funded by Department of Health Research)*

Principal Investigator : **Srabani Mukherjee**
Co-Principal Investigator : Pallavi Shukla
Project Associates : Manisha Kumari, A Naigaonkar
Collaborator : Sadhana Desai, Fertility Clinic and IVF Centre
Duration : 2023-2026

The quality of oocyte is largely influenced by follicular microenvironment which comprises of granulosa cells (GCs) and follicular fluid (FF). Folliculogenesis is a metabolically active process, hence any metabolic imbalance in the follicular microenvironment can affect oocyte competence. The metabolic co-operation between granulosa cells and oocyte is very important as oocyte has limited capacity to utilize larger metabolites. GCs metabolize larger metabolites and supply energy substrates to oocytes. Few studies have been carried out to explore the metabolome of FF. However, the metabolome of GCs has not been studied yet. Therefore, the present study aims to investigate the metabolic dysregulation in the follicular microenvironment of women with PCOS. We have recruited 15 women with PCOS, diagnosed by Rotterdam criteria and 16 control women. Metabolomics of FF was investigated using H1-NMR. Our preliminary data by multivariate statistical analysis using supervised classical model Partial Least Squares Discriminant Analysis (PLS-DA) showed distinct separations between metabolite profiles of PCOS and controls (Fig. 1). A total of 52 metabolites were identified. Using univariate t-test, we found significantly altered metabolites viz., valine, glucose, lactate, glycine, betaine and leucine (FDR<0.05) between PCOS and control suggesting perturbed amino acid and carbohydrate metabolic pathways (Fig. 2). More samples are being analysed by NMR. These identified metabolites can be further explored for their potential as biomarkers for predicting oocyte quality and IVF outcomes in PCOS. Preliminary data analysis indicates metabolic dysregulation in FF of women with PCOS. Further the genes encoding the metabolites found dysregulated in the follicular microenvironment will be assessed for their expression at transcript level.

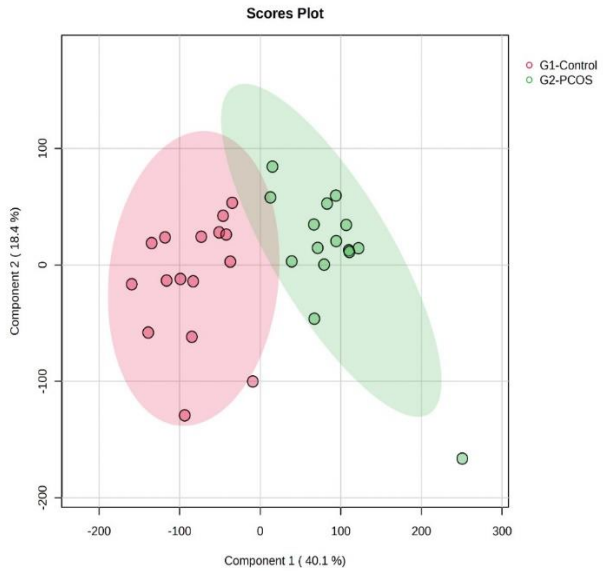

Figure 1: Score plot obtained by PLS-DA of MetaboAnalyst for follicular fluid samples from control and PCOS cases. The ellipses showing 95% confidence limits of a normal distribution for each group.

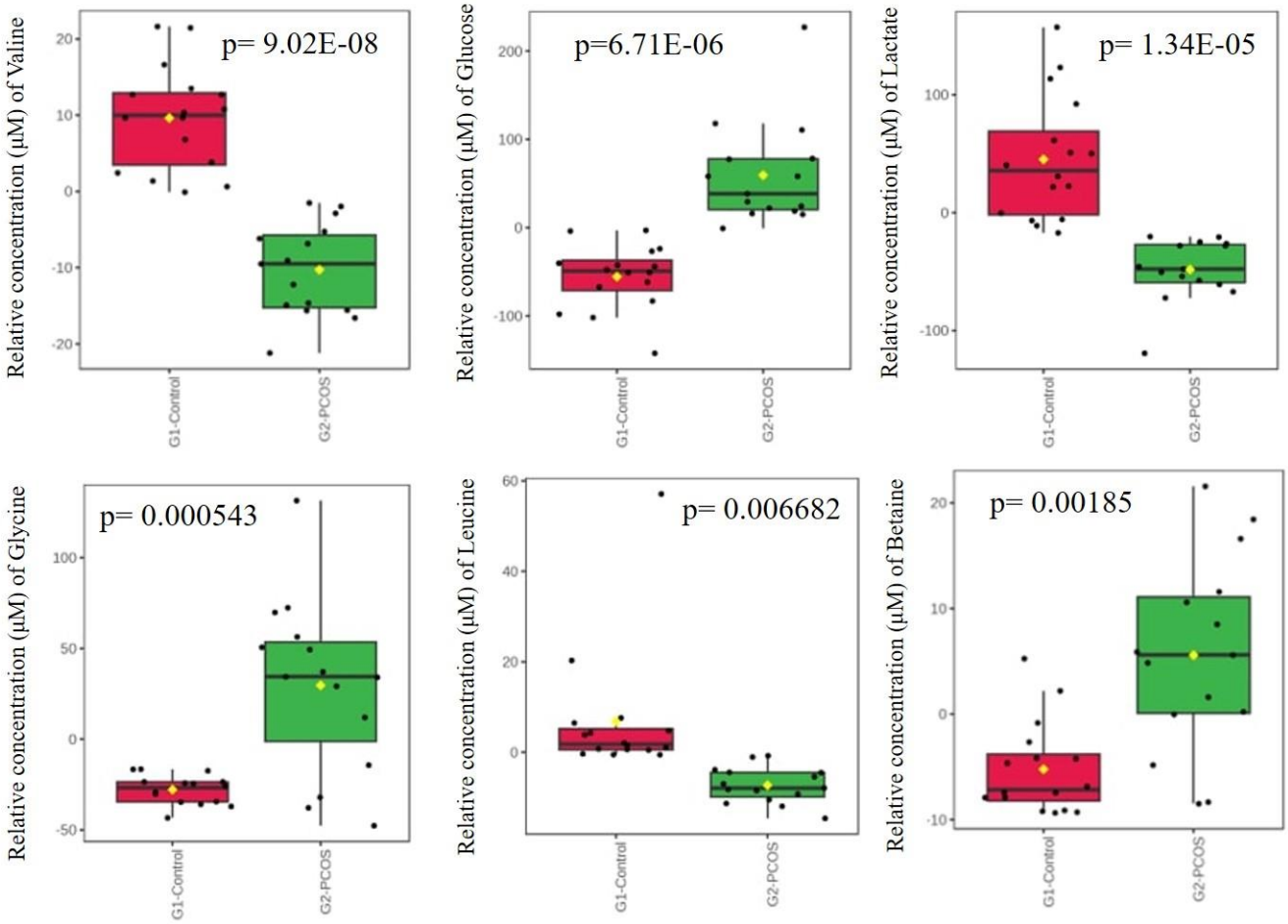

Figure 2: Comparison of relative concentrations of valine, glucose, lactate, glycine, leucine and betaine between control (n=16) and PCOS (n=15) samples. The results are presented as box whisker plots showing statistically significant difference (FDR<0.05) in metabolite concentrations obtained by Student's t-test using MetaboAnalyst

1.14 Clinical Phenotypes and Genetic Regulation of Endometriosis in Indian Women (ECGRI study) *(Partly Funded by Department of Biotechnology Wellcome India Alliance)*

Principal Investigator	:	**R Gajbhiye**
Mentor	:	Grant Montgomery, Institute for Molecular Biosciences, University of Queensland, Australia
Supervisor	:	Smita Mahale
Project Associates	:	Geetanjali Sachdeva, H Munshi, Sandhya Anand, Akshata Shetty, Ashwini Patel, Arti Kushwaha, Kiran Kharsodiya, Tabassum Khan, Naffifa Rehman, Sheetal Dubey, Sindhya Raju, Teesta Banerjee, Sakshi Gangurde, Nayana Barada, Narayani Bhat, Namita Naik, Priya Ingle
Collaborators (Epidemiology)	:	Gita Mishra, School of Public Health, University of Queensland, Australia R Dikshit, Director, Center for Cancer Epidemiology, Tata Memorial Center, Mumbai

Clinical Collaborators : P D Mahapatra, Spectrum Clinic & Endoscopy Research Institute, Kolkata
A Humne, Department of Obstetrics & Gynaecology, Government Medical College, Nagpur
C Shembekar, Omega Hospital, Nagpur
K Padate, Dr Kedar's Maternity, Infertility and Surgical Hospital, Endoscopy and IVF Center, Goa
N S Pande, Worli Hospital For Women, Worli, Mumbai
Deepali Kale, Nowrosjee Wadia Maternity Hospital, Mumbai
N Mahajan, Topiwala National Medical College & B. Y.L. Nair Charitable Hospital, Mumbai
M Shah, Naval Maternity Endoscopy & Infertility Center, Mumbai & Solapur
A Ganatra, Progeny IVF Center & clinic for women, Mumbai
S Kumta, Fortis Hospital, Mulund West, Mumbai
P L Sankhwar, King George Medical University, Lucknow
S Shekhar, AIIMS Jodhpur
P Phukan, Assam Medical College, Dibrugarh
B John, Credence Hospital, Trivandrum
R Mohan, Government Medical College and SAT Hospital, Trivandrum
M V Pai, Kasturba Medical College, Manipal, Sikkim Manipal Institute of Medical Sciences, Gangtok, Sikkim
Rekha Upadhya, Kasturba Medical College, Manipal
Nilaj Bagde, AIIMS Raipur
Swati Mahobia, Sai Baba Nursing Home, Raipur, Chhattisgarh

Duration : 2019-2025

Endometriosis is a chronic, estrogen-dependent condition affecting 6-10% of women of reproductive age, leading to pelvic pain, subfertility, and dysmenorrhea. It impacts 247 million women globally, with ~42 million in India. The disease's etiology remains unclear, although factors such as age at menarche and shorter menstrual cycle length are associated with an increased risk. Endometriosis has three subtypes: superficial peritoneal (SUP), ovarian endometrioma (OMA), and deeply infiltrating endometriosis (DIE), with potential regional and ethnic variations. Genome-wide association studies (GWAS) have identified genetic risk factors, but no studies have investigated their relevance in the Indian population. The objectives of the study are as follows: 1. To identify and characterize endometriosis subtypes in different geographical regions of India 2. To identify the clinical, epidemiological, environmental, and lifestyle factors associated with different endometriosis subtypes in India 3. To investigate the genetic risks associated with endometriosis in the Indian population. ECGRI is the largest study on endometriosis in India, utilizing standardized recruitment methods (WERF-EPHect). A total of 1775 endometriosis cases and 1775 controls were recruited from 18 study sites across India. Clinical data analysis demonstrated the geographic differences in endometriosis lesion types in the Indian population. Endometrioma (59%) is the most common lesion type reported in Indian women followed by DIE (28%) and SUP (12%). There is an average delay of 8.8 years in the diagnosis of endometriosis. The first symptom of endometriosis was reported in 37% of cases during the adolescence period while 77% had symptom onset before the age of 30 years. The common presenting symptoms were Pain (73%) and Infertility (46%). Dysmenorrhea was most

frequently reported in DIE (88%). Hormonal use, heavy bleeding, irregular cycles, and short cycle length (<24 days) are significantly associated with endometriosis compared to controls. Underweight women (BMI ≤18.5) are at higher risk of endometriosis, especially DIE. Fibroids co-occur in over one-third (34.3%) of cases, Adenomyosis (10.6%) and PCOS (4.5%) also frequently co-exist with endometriosis. More than 2 comorbidities were present in 37.5% of endometriosis cases vs 3.2% in controls. A high prevalence of comorbidities is reported in women with endometriosis. Amongst these common comorbidities are: Gynecological disorders (50.6%), Autoimmune conditions (18.6%), Musculoskeletal disorders (13.5%), and psychiatric conditions (11.6%). Environmental exposures (e.g., pollution, passive smoking, smokeless tobacco) are associated with increased risk. Evidence supports multisystemic impact—beyond the reproductive tract. The study suggested the urgent need for an integrated, multidisciplinary care model for the management of endometriosis in India.

1.15 Omics of Serum Exosomes in Endometriosis: An Attempt to Identify a Possible Biomarker (*Partly Funded by Indian Council of Medical Research*)

Principal Investigator	:	**D K Das**
Co-Principal Investigator	:	Geetanjali Sachdeva
Project Associate	:	Kanchan Sharma
Collaborators	:	V Salunke, Shinjini Pande, Nalini Speciality Hospital, Mumbai
Duration	:	2022-2027

Endometriosis is a chronic estrogen-dependent disorder that affects approximately 10% of women of reproductive age. Women with endometriosis exhibit symptoms like dysmenorrhea, dyspareunia, cyclic pelvic pain and secondary infertility. Definite diagnosis of endometriosis is carried out using laparoscopic examination, an invasive procedure. Therefore, there is a need to develop a simple non-invasive technique that can identify/diagnose the recurrence of the disorder. In this study, women aged 20-45 years with endometriosis (with adenomyosis and/or uterine fibroid) have been recruited. In the previous year, differential miRNAome of blood samples from 4 cases and 4 control participants. A total of 56 differential miRNAs have been identified, of which 32 were downregulated and 24 upregulated in women with endometriosis compared with controls. In the reporting year, validation of 25 differentially abundant miRNAs has been carried out using custom miRNA array (Qiagen Inc, GmBH). The expression of miR-196b-5p was similar in cases and controls, hence, it was considered as the reference for the relative quantification of other miRNAs. The validation was carried out in 28 controls and 25 cases. Abundance of 13 miRNAs (miR-223, miR-191, miR-30c, miR-628, miR-450, miR-93, miR-485, miR-708, miR-210, miR-145, miR-150, miR-199a, and miR-125) did not differ between the two groups, and abundance of the remaining 12 miRNAs was significantly different between the groups. Heat map of 12 significant miRNAs in cases and controls is depicted in Fig 1. Out of 12 miRNAs, expression of miR-3960 and miR-365a was significantly upregulated. Among downregulated miRNAs, miR-369 and miR-148 showed the highest statistical significance, followed by miR-409, miR-200a, miR-30a, miR-6852, miR-181, miR-144, miR-143 and miR-30b (Fig. 2). Based on the statistical significance levels, we again shortlisted one upregulated miRNA (miR-3960) and two downregulated miRNAs (miR-369 and miR-148) for evaluation of diagnostic potential. The analysis on the diagnostic potential of statistically significant miRNAs is ongoing.

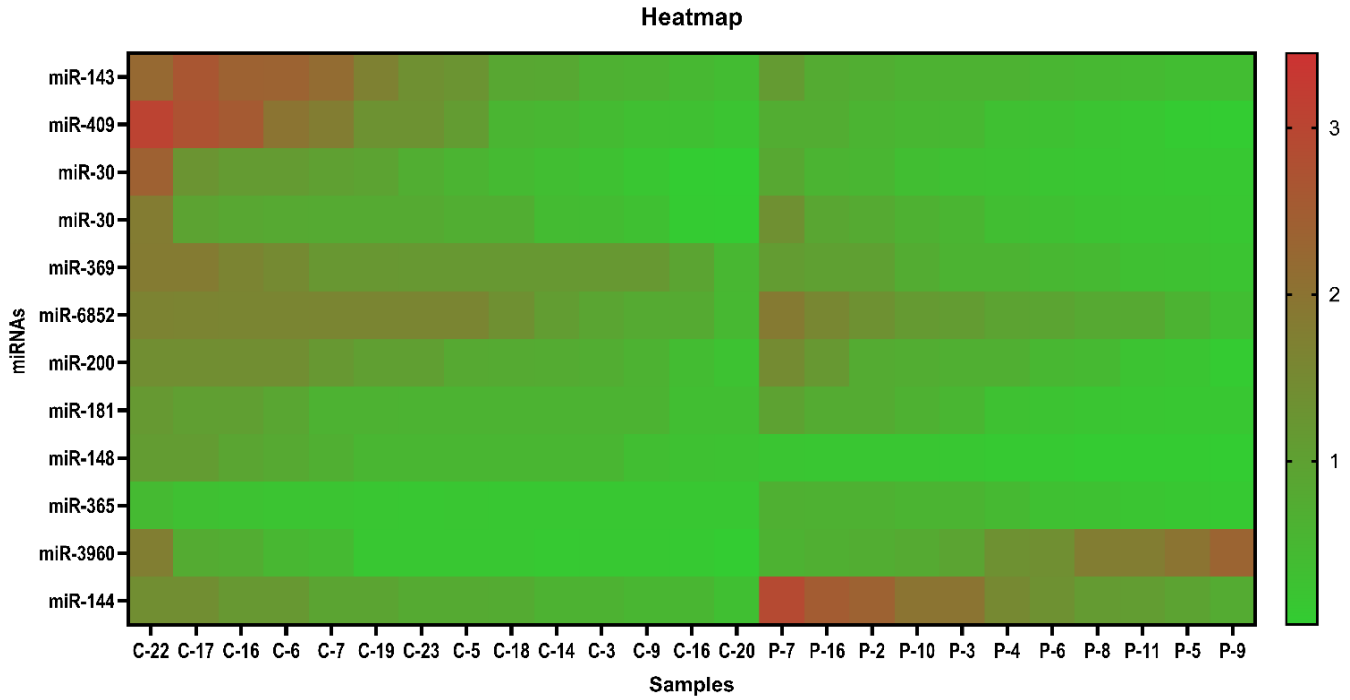

Figure 1: Heat-map of validated significant miRNAs in endometriosis patient samples compared to controls. Control samples have been designated as 'C' and patients as 'P'.

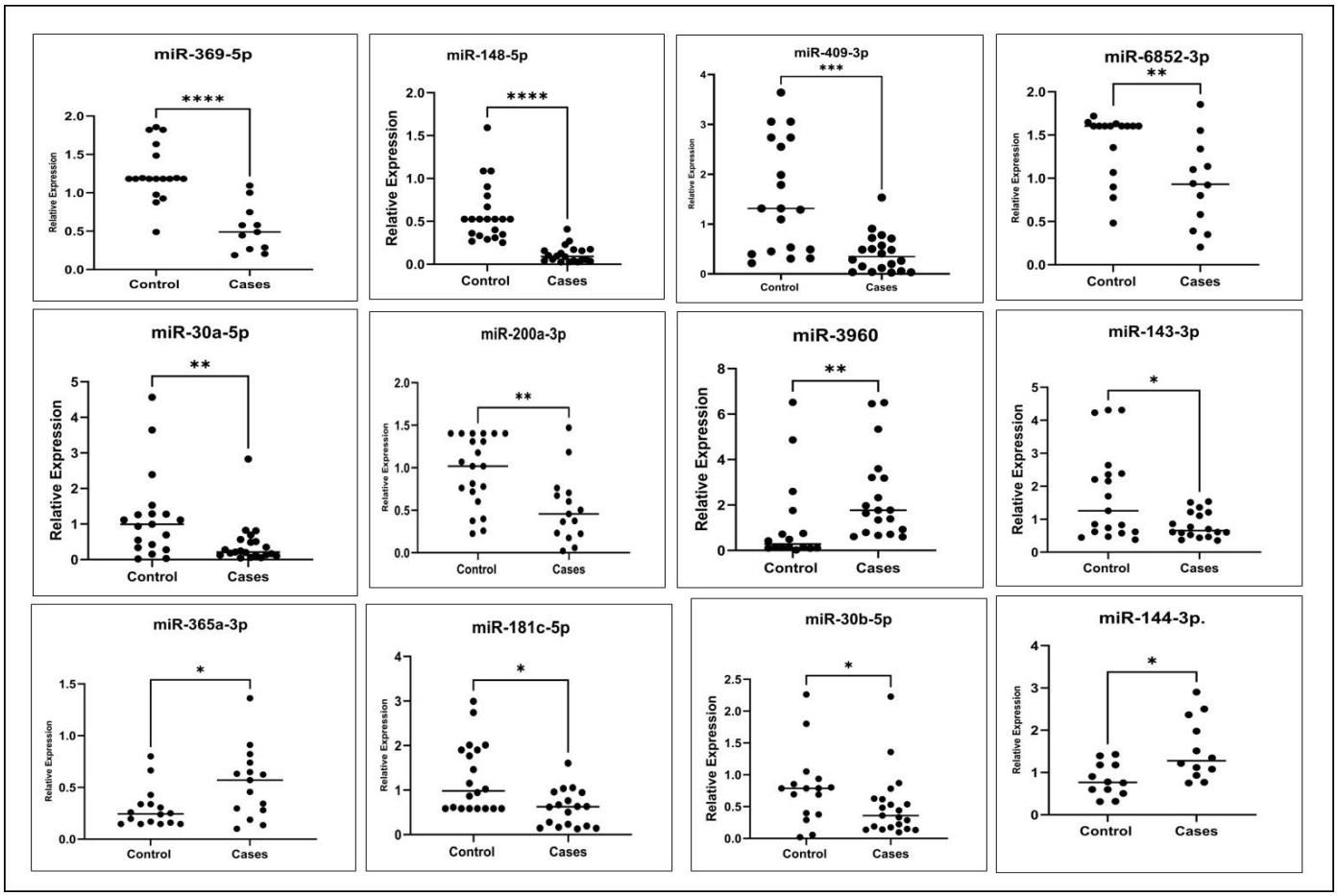

Figure 2: Expression of 12 miRNA in endometriosis patients (n=25) and controls (n=28). Statistical analysis was done using a nonparametric Mann-Whitney test. Significance of the difference in abundance of each miRNA is displayed as * (*<0.05; **<0.01; ***<0.001; ****<0.0001)

1.16 Human Endometrial Stem Cells and their Possible Role in the Etiology of Endometriosis *(Partly Funded by Department of Biotechnology)*

Principal Investigator	:	**D K Das**
Co-Principal Investigator	:	Geetanjali Sachdeva
Project Associate	:	Mousumi Bal
Collaborators	:	V Salunke, Shinjini Pande, Nalini Speciality Hospital, Mumbai
Duration	:	2023-2028

Endometriosis (EM) is a chronic, estrogen-driven disorder where tissue resembling the endometrium grows outside the uterus. The endometrium itself is highly regenerative, and the `Stem Cell Theory` suggests that retrograde menstruation carrying endometrial stem cells may seed ectopic lesions like ovarian endometrioma (OMA), superficial peritoneal endometriosis (SUP), and deep infiltrating endometriosis (DIE). This study aims to investigate the potential role of tissue-resident endometrial stem cells in the pathophysiology of the disease. In this reporting year, we assessed endometrial stem cell populations (endometrial Mesenchymal Stem Cells; eMSCs, Side Population; SP, endometrial Epithelial Stem/Progenitor Cells; eEPCs) in ectopic lesions (DIE, OMA) and paired eutopic endometrium (EUE) from 37 women with endometriosis (with adenomyosis +/ fibroids) and 11 control samples (EUC) from women without endometriosis but with adenomyosis +/ fibroids. The eMSCs have been identified using International Society for Cells and Gene Therapy (ISCT) criteria. The gating strategies included selection of singlet, live cells using 7AAD, MSC negative markers (CD45, CD34, CD14, CD19, HLA-DR), followed by SUSD2+ (universal eMSCs marker) cells. Further, analysis was conducted to assess the percentage of CD73, CD90, CD105, and HLA- ABC positive cells within SUSD2+ cells. A co-expression of two positive markers, CD146 and CD140b, was used to identify pericyte eMSCs within $CD45^-$ and $CD31^-$ cells (Fig. 1B). The gating strategies for SP included singlets, live cells, and $CD45^-$ cells, followed by ABCG2+ cells (Fig. 1C). eEPCs populations were identified based on singlets, live cells, $CD45^-$ cells, followed by dual eEPCs markers, N-cadherin and SSEA-1 (Fig. 1D). Key findings revealed distinct cellular profiles between DIE and OMA. OMA lesions had significantly higher pericyte-eMSCs ($CD146^+$ $CD140b^+$) than DIE, which are critical in promoting the vascularization of cystic lesions. While DIE showed significantly higher frequency of junctional eEPCs (N-cadherin- SSEA-1+) that would support the formation and maintenance of glandular structures within invasive lesions (Fig. 2A). Eutopic endometrium from women with endometriosis (EUE) had significantly more SUSD2+ eMSCs than controls (EUC), confirming an altered endometrial stem cell composition than control endometrium (Fig. 2B). When comparing ectopic lesions to paired eutopic endometrium, deep basalis eEPCs (N-cadherin+ SSEA-1-) were significantly more abundant in DIE and OMA (Fig. 2C & 2D). Interestingly, immunophenotypic characteristics of SUSD2+ eMSCs revealed that eutopic endometrium (EUE, EUC) retained more than 80% positivity for typical MSC markers (CD73, CD90, CD105, HLA-ABC), suggesting a more preserved MSC phenotype. However, variable expression of these markers was noted in SUSD2+ eMSCs of ectopic lesions (DIE, OMA) (Fig. 2E). This altered immunophenotypic characteristics in eMSCs may be attributed to the change in the microenvironment in the ectopic site. This study highlights differential distribution of endometrial stem cells in the different subtypes of endometriotic lesions. These inferences open up opportunities for further research to investigate whether a differential preponderance of various endometrial stem cells has any functional implications in the formation of lesions of specific subtypes.

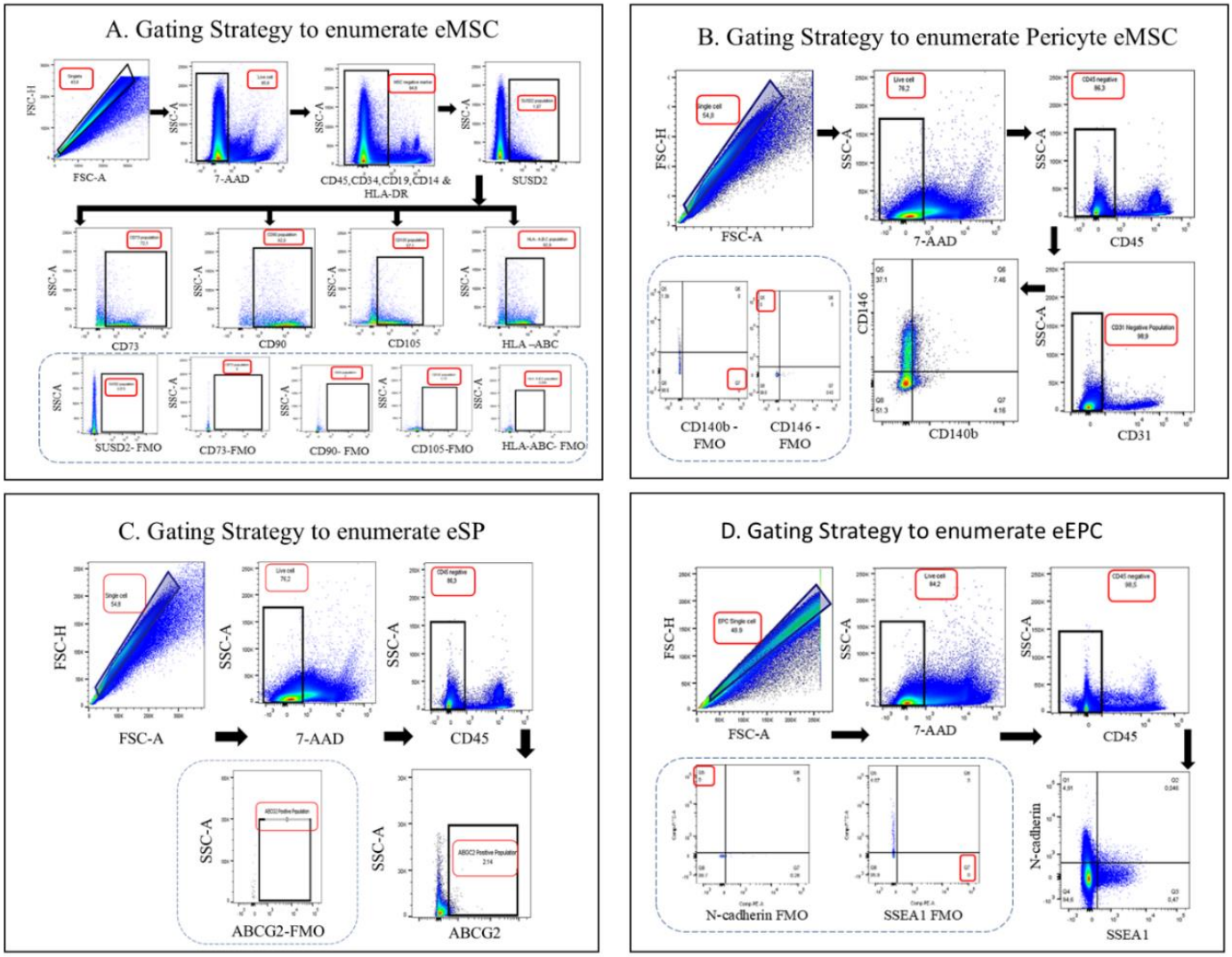

Figure 1: Enumeration of Endometrial Stem Cells in ectopic lesions and eutopic endometrium. (A) Flow cytometry strategy for quantifying endometrial Mesenchymal Stem Cells (eMSCs) in single cell suspensions. Single cells were selected based on forward area versus forward height, followed by live cells (7-ADD), and MSC negative markers (CD45, CD34, CD14, CD19, HLA-DR). Further SUSD2 were gated for typical MSC markers CD90, CD73, CD105, HLA-ABC (B) Flow cytometry strategy for quantifying pericyte eMSCs in single cell suspensions. Single cells were selected based on forward area versus forward height, live cells (7-ADD), followed by sequential gating for CD45 and CD31 negative markers, to which double positive markers CD146 and CD140b were analysed. (C) Flow cytometry strategy for quantifying endometrial Side Population was based on the singlet subset, live cell, CD45^{-}cell population, and cells expressing ABGC2. (D) Flow cytometry strategy for quantifying endometrial epithelial progenitor/stem cells (eEPCs) was analysed using the following events: singlet subset, live cell (7-ADD), CD45^{-}. Further dual positive markers N-cadherin and SSEA-1 expressing cells were enumerated. The unstained control and FMO control were run with compensation to determine the negative population and positive population respectively.

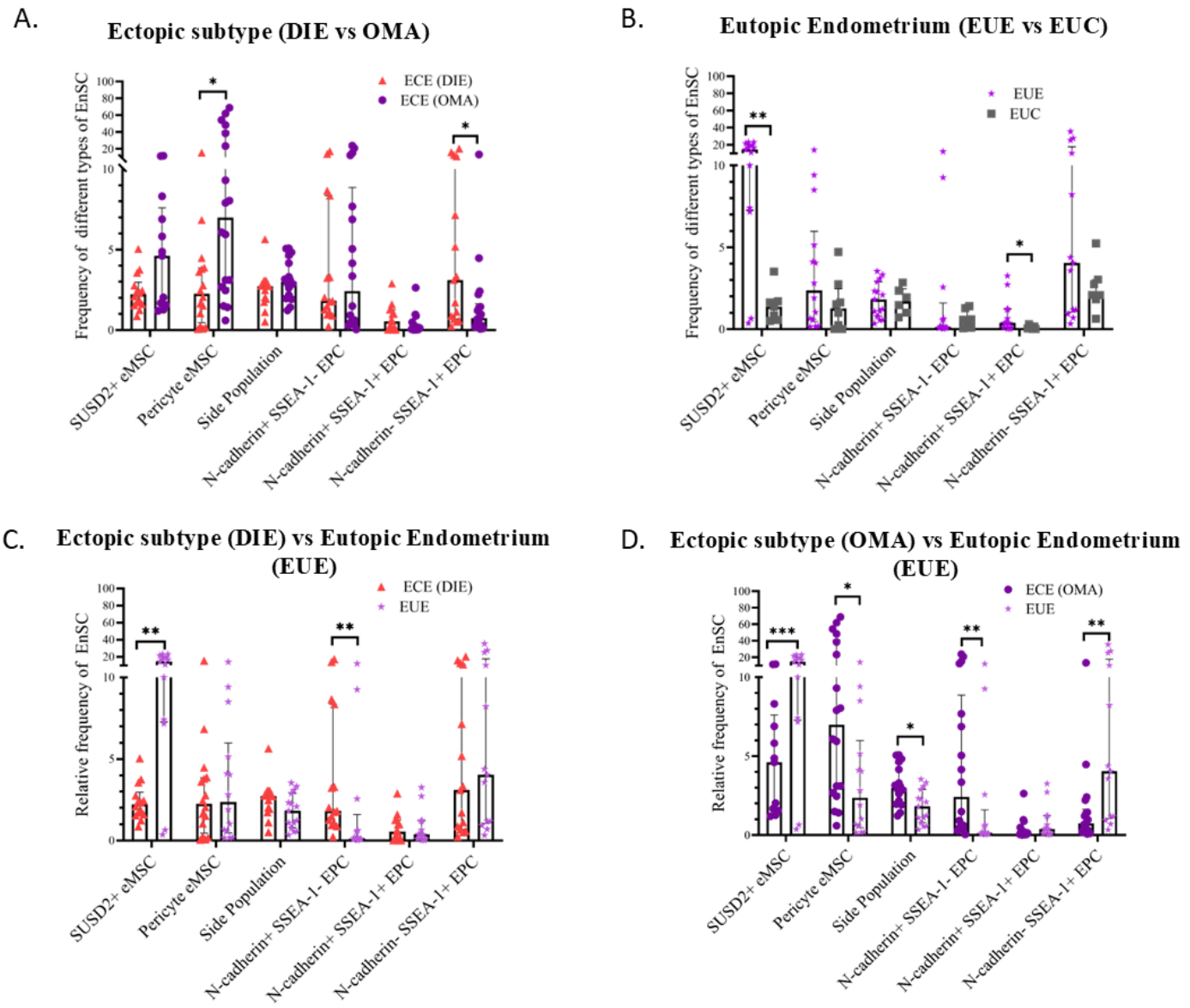

Figure 2: Proportion of tissue-resident Endometrial Stem Cells in ectopic lesions and eutopic endometrium of women with endometriosis. Median interquartile frequency and distribution of cells expressing endometrial stem cell markers (eMSCs, SUSD2+; pericyte eMSCs, CD146+ CD140b+; Side Population, ABCG2+; and eEPCs, N-cadherin+/- SSEA-1+/-) in deep infiltrating endometriosis (DIE), and ovarian endometrioma (OMA) in women with endometriosis (A); in eutopic endometrium of endometriosis (EUE), and eutopic endometrium of control women (EUC) (B); in DIE, and eutopic endometrium of endometriosis (EUE) (C); OMA and EUE (D). Statistical analysis was conducted using the Mann-Whitney test. Significant differences are indicated by the p-value at the top of the graph (*p<.05, **p < .01). (E) Frequency of typical MSC markers CD73, CD90, CD105, and HLA-ABC on SUSD2+ eMSCs population of DIE, OMA, eutopic endometrium of endometriosis (EUE), and eutopic control endometrium (EUC). All the data are represented on the median with the interquartile range. Statistical analysis was conducted using Kruskal-Wallis and Dunn's multiple comparisons tests. Significant differences are indicated by the p-value at the top of the graph (*p<.05, **p < .01, ***p<0.001, ****p<0.0001).

1.17 Investigating the Contribution of DNA Damage, Repair and Demethylation in Pathogenesis of Endometriosis *(Partly Funded by Department of Biotechnology)*

Principal Investigator	:	**Geetanjali Sachdeva**
Co-Principal Investigator:		R Gajbhiye
Project Associates	:	Itti Munshi, U Chaudhari
Collaborators	:	A Mangeshikar, Jaslok Hospital, Mumbai
		Pratima Thamke, MGM Hospital, Navi Mumbai
Duration	:	2022-2027

Endometriosis is a gynaecological condition wherein the eutopic endometrial like cells form endometriotic lesions in the abdominal cavity. Endometriotic lesions can be present on the surface of the peritoneal wall, ovary or the rectum. Endometriotic lesions are known to have higher DNA damaging stimulus (oxidative stress, inflammation and proliferative stress). Studies have reported genomic instability and presence of mutations in the endometriotic lesions from women with endometriosis. In the previous Annual report 2022-2023 pp. 16-17, we reported an upregulation in the expression of genes involved in DNA damage response (DDR) in the stromal cells from the ectopic lesions compared to their eutopic counterparts. MBD4 (Methyl CpG Binding Domain 4), a glycosylase protein and part of the base excision repair machinery, was found to be upregulated in the stromal cells of ectopic lesions compared to their eutopic counterparts. The expression of MBD4 was found to be upregulated following induction of oxidative damage in the endometrial stromal cells. To elucidate the effect of MBD4 on DDR, MBD4 was silenced in T HESC (endometrial stromal cell line) using morpholinos. MBD4-silenced stromal cells exposed to oxidative stress (10μM, 8 hrs) showed reduced expression of γH2AX, ATM and pATM compared to stromal cells transfected with scrambled morpholino. Further, an increase in percentage DNA in the head and a reduced percentage DNA in the tail was observed in MBD4-silenced stromal cells exposed to oxidative stress compared to control (Figure 1A-C). These investigations reveal that MBD4 regulates DNA damage response events upstream to recruitment of γH2AX on damaged sites in the genome.

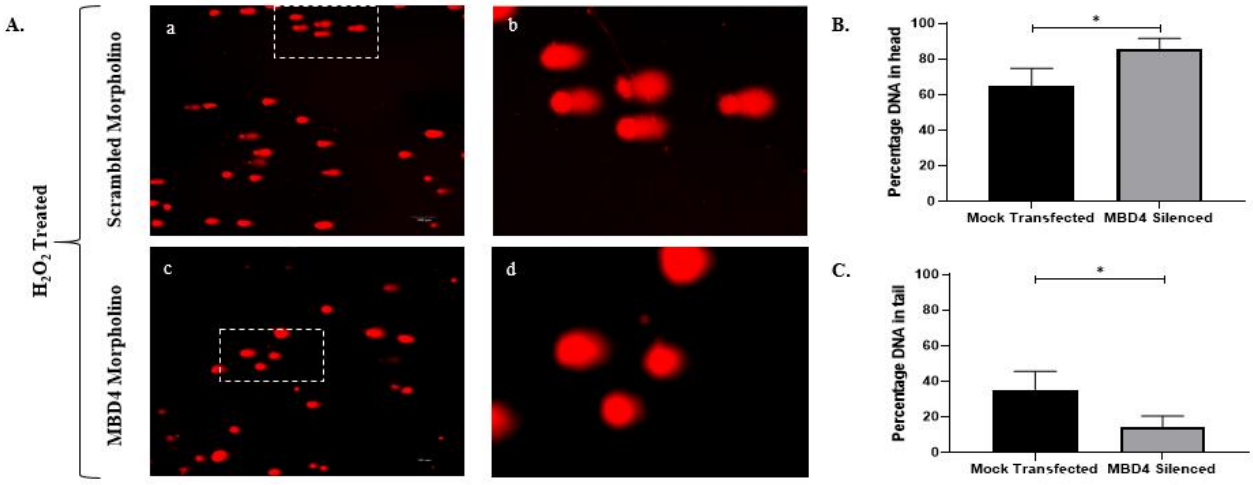

Figure 1: Effect of MBD4 depletion on DNA damage response in endometrial stromal cells exposed to oxidative stress. Panel A represents DNA comets in control and MBD4-depleted cells exposed to oxidative stress. b and d are the zoomed areas of the insets shown in sub-panels a and c, respectively in panel A. Graphical representations of percentage DNA in head and tail are depicted in panels B and C respectively. Shapiro-Wilk test was used to assess normality of the data. Unpaired t-test was used for comparison of the percentage DNA in heads and tails (* $p<0.05$).

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

Principal Investigator	:	**U Chaudhari**
Co-Principal Investigator	:	Geetanjali Sachdeva
Project Associates	:	A Khandvilkar, SM Metkari
Collaborators	:	Vandana Bansal, Deepti Tandon
Duration	:	2022-2027

The endometrium is highly influenced by ovarian steroids hormones. Endometrium undergoes proliferation, differentiation, and breakdown during each human menstrual cycle. However, the post-menstrual endometrial repair occurs simultaneously during endometrial breakdown, independent of support from ovarian hormones. Damage Associated Molecular Patterns (DAMPs) are molecules released extracellularly during physiological or pathological damage of cells. Extracellular DAMPs act as cytokines and induce inflammatory responses that promote tissue repair. The aim of the present study is to understand the role of DAMPs (HMGB1) and their receptor (RAGE) in endometrial breakdown and repair. To study the mechanisms of endometrial breakdown and repair, we have established the Rat Model of Induced Menstruation (Annual Report 2019-2020, p. 18). Using the same rat model, we have previously reported the involvement of the HMGB1-RAGE axis in endometrial breakdown (Annual Report 2022-23, p. 18-19) and re-epithelialization (Annual Report 2023-24, pp. 24-25). Inflammatory stimulus during menstruation recruits immune cells in the endometrium milieu. Recruited immune cells in the endometrium play important role in the endometrial breakdown and repair. In the reporting year, the frequency of neutrophils during endometrium breakdown and repair was assessed in Rat Model of Induced Menstruation using flowcytometry. Rats were sacrificed at different timepoints (n=6 each) after progesterone withdrawal i.e., 0h (T0), 8h (T8), 24h (T24), and 48h (T48). There was a significant increase ($p < 0.05$) in the neutrophil frequency at T8 when the endometrial breakdown was initiated compared to T0. The neutrophil count further increased significantly ($p<0.0001$) at T24 during the complete breakdown stage compared to T8. However, when the endometrium was completely repaired at T48, the frequency of neutrophils decreased significantly ($p<0.0001$) compared to at T24 (Fig. 1). Increased neutrophils frequency during active breakdown (8 and 24hrs) indicate their role in tissue breakdown and low frequency at 48 hrs indicate their role in resolution of inflammation and complete repair of endometrium. Further studies are going on to assess the effects of HMGB1-RAGE axis inhibition and its role in neutrophils recruitment during endometrial breakdown and repair.

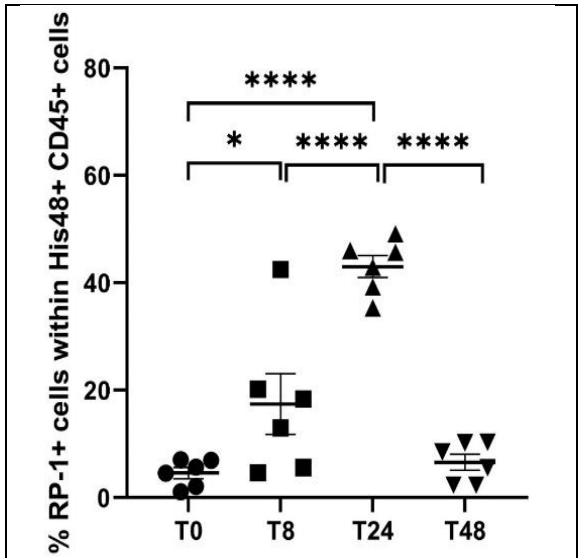

Figure 1: Percentages of RP-1+ cells (neutrophils) within His48+ CD45+ cells in the endometrium of Rat Model of Induced Menstruation sacrificed at time points 0h (T0), 8h (T8), 24h (T24) and 48h (T48) post-progesterone withdrawal (n=6 each). Data are expressed as mean±SEM. One-way ANOVA with Tukey post-hoc testing was used for multiple group comparisons. p-value of *≤ 0.05, ****<0.00001

1.19 Uterine Alarmins and their Relevance in Implantation *(Partly Funded by Women Scientists Scheme-A (WOS-A)*

Principal Investigator	:	**Geetanjali Sachdeva**
Co-Principal Investigator	:	SK Adiga, Kasturba Medical College, Manipal
Project Associates	:	U Chaudhari, V Patel, SM Metkari, RR Katkam, Rithika Rajendran, Sheetal Singhania
Collaborators	:	P Narayan, Anjali M, Kasturba Medical College, Manipal
Duration	:	2022-2027

Embryo implantation is a critical step in pregnancy during which a competent embryo establishes physical contact with a receptive endometrium. One of the major components of this connection is the uterine immune system that protects the semi-allogeneic fetus from immune rejection. Uterine immune cells viz, uterine natural killer (uNK) cells, macrophages, dendritic cells and regulatory T (Treg) cells assume a more tolerogenic function implantation and failure to do so result in implantation failure or early embryo loss. Immune cell function may be influenced by several types of stimuli, one of which is a family of endogenous molecules known as alarmins or Damage Associated Molecular Patterns (DAMPs). These are chemically divergent cellular molecules that can elicit an immune response by being secreted actively or released passively into the extracellular space, thereby leading to an inflammation. Increased systemic levels of DAMPs such as high mobility group box – 1 (HMGB1), S100 proteins and uric acid have been associated with pregnancy pathologies. Our laboratory had identified the presence of HMGB1 and S100A8 in the human uterine fluid (Annual Report 2010-11, pp 25-26). Furthermore, it was also demonstrated that excess of HMGB1 in the uterine lumen in the peri-implantation phase led to implantation failure in rats (Annual Report 2013-14, pp. 23-24). The present study is being conducted to determine the effects of excess of HMGB1 on the uterine immune profile. We previously demonstrated that intrauterine administration of recombinant HMGB1 (rHMGB1) in the peri-implantation phase altered the frequencies of activated M2 (anti-inflammatory) macrophages, uNK and Tregs. In the reporting year, we strived to decipher whether co-administration of rHMGB1 with its inhibitor glycyrrhizin rescued embryo implantation. To accomplish this objective, we administered glycyrrhizin (0.4 µg, 0.8 µg or 1.2 µg per 15µL) along with rHMGB1 (0.8µg/15µL) in one horn of Wistar rats on day 3 post coitum (p.c.). 0.8µg/15µL rHMGB1 alone was administered in the contralateral horn. Glycyrrhizin (0.8 µg/15µL) co-administered with the same concentration of rHMGB1 abrogated the effect of excess of HMGB1 in the uterine lumen (Fig 1).

Flow cytometric analyses of the uterine immune cells revealed that co-administration of glycyrrhizin with rHMGB1 restored the frequencies of activated M2 macrophages (CD45+CD11b/c+CD68+CD163+CD86+MHCII+; Fig. 2A) and uNK (CD45+DBA-lectin+; Fig. 2B) that were altered due to excess of HMGB1 in the uterine microenvironment during the peri-implantation phase. The frequency of Tregs (ratio of CD4+Foxp3+CD25+ to CD4+; Fig. 2C) did not change significantly in the animals that were administered glycyrrhizin along with rHMGB1. Thus, co-administration of glycyrrhizin with HMGB1 abrogated the effects of excess of HMGB1 on the immune profile during implantation.

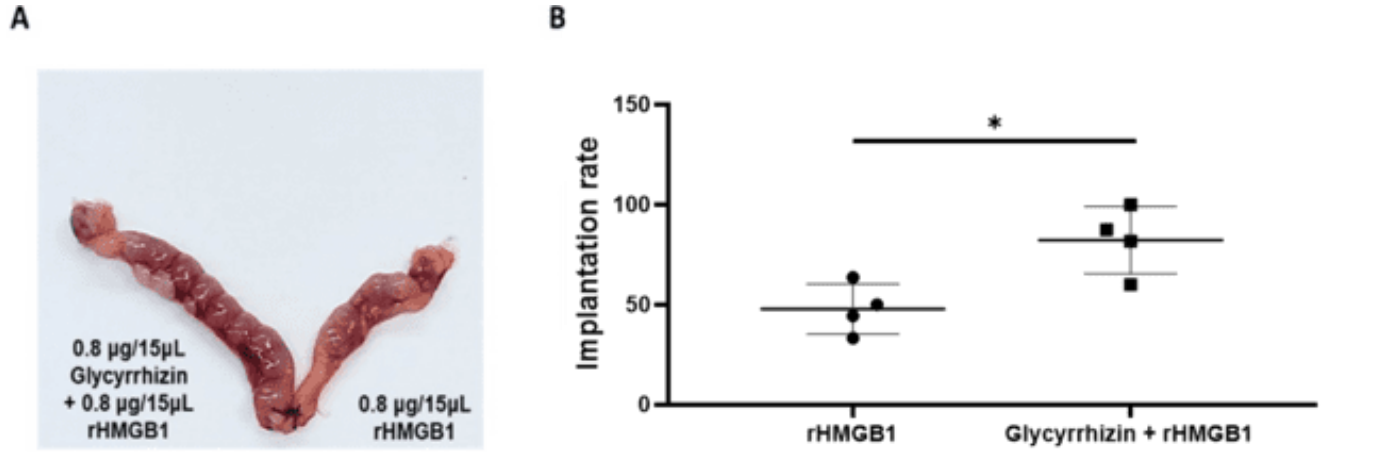

Figure 1: Effect of intrauterine administration of glycyrrhizin (0.8 µg/15µL) with rHMGB1 in the uterine horn on embryo implantation as observed on day 10 p.c. (panel A). The contralateral horn was administered with HMGB1 (0.8 µg/15µL) alone. Implantation rate in each horn was determined by calculating the ratio of number of implantation sites to the number of corpora lutea (panel B). * in panels B (p=0.0165) indicates statistical significance of the difference between the two groups.

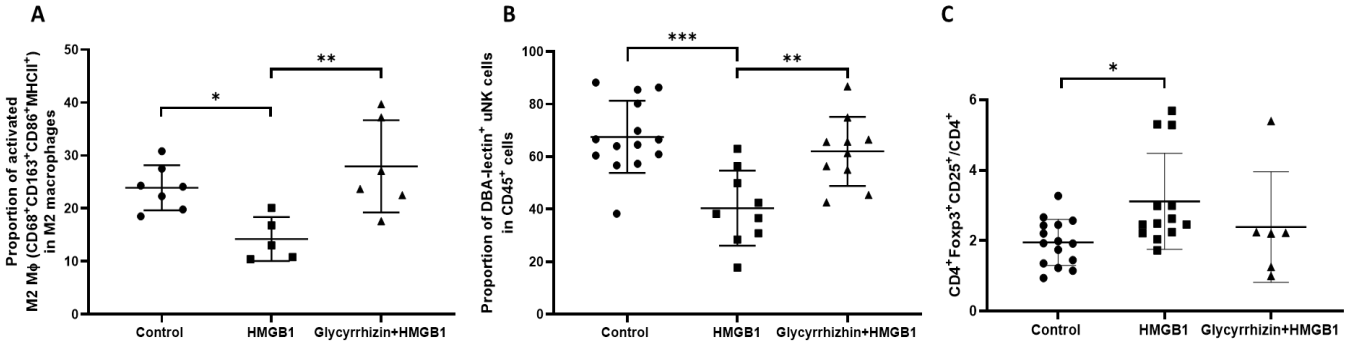

Figure 2: Frequencies of activated M2 macrophages (panel A), uNK (panel B) and Tregs (panel C) in the uterus of animals that were treated with saline, rHMGB1 or glycyrrhizin+rHMGB1 on day 5 p.c. * in panels A (p=0.0402 and 0.0054), B (p=0.0002 and 0.0049) and C (p=0.0224) indicate statistical significance of the difference between the two groups.

1.20 Comprehensive Assessment of Women Diagnosed with Spontaneous Premature Ovarian Insufficiency *(Partly Funded by Institutional Intramural)*

Principal Investigator	:	**Deepti Tandon**
Co-Principal Investigators	:	S Pande, Shaini Joseph
Project Associates	:	Anushree Patil, Shahina Begum, Deepak S, Anamika Akula
Collaborators	:	R Ravindrum, Consultant Clinical Immunologist, Mumbai D Bhenki, Obstetrician Gynaecologist Infertility Specialist, Mumbai
Duration	:	2023-2026

A three-year longitudinal study is being undertaken to identify those with spontaneous premature ovarian insufficiency (POI) and probable POI among women with complaints of amenorrhoea, oligomenorrhoea attending gynecological and infertility OPD. Women diagnosed to have POI in the past two years and attended infertility clinic are also being enrolled. Probable POI cases diagnosed prospectively will also be included in this study. A cohort of 14 women diagnosed with spontaneous POI have been recruited for this study. Their mean age is 30.4± 4.01 years. Among them, 78.6% (11) are married, 14.3% (2) is unmarried and 7.1% (1) separated.

Socioeconomic distribution analysis showed that 35.7% (5) belonged to the lower middle class, 35.7% (5) to the upper lower class, and the remaining 28.6% (4) to the upper and upper middle classes. As for lifestyle factors, one participant (7.1%) reported smoking, and two participants (14.3%) reported alcohol consumption. The mean age of menarche among these women was 13.5 ±1.6 years. All participants 100%(n=14) reported amenorrhea with only withdrawal bleeding. Associated symptoms included hot flushes in 42.9% (6), vaginal dryness in 35.7% (5), hair loss in 57.1% (8), and changes in skin pigmentation in 35.7% (5). Additionally, 28.6% (4) reported joint pain, and 14.3% (2) experienced night sweats. Sleep disturbances were reported by 35.7% (5), and 35.7% (5) also experienced decreased sexual desire. Clinically, 14.3% (2) of the participants exhibited goitre, while 7.1% (1) presented with webbing of the neck. The mean BMI of the participants was 26.3 kg/m^2 ± 3.2. Hypothyroidism was diagnosed in 14.3% (2) of the participants, and hypertension in 7.1% (1). 71.4% (10) of the participants are nulligravida. Genetic evaluation was conducted for 13 patients, revealing that 30.8% (n=4) had a normal karyotype, while 7.7% (n=1) exhibited Turner syndrome (45XO). Additionally, three patients displayed polymorphic variations such as 46XX,14ps; 46XX,9qh+; and 46XX,1qh+1. Microarray analysis identified pathogenic abnormalities in 15.4% (n=2) of the women and for rest results are awaited. Testing for Fragile X mutation was normal in 35.7% (5) women and for rest results are awaited. Autoimmune profile evaluation indicated that 28.6% (n=4) tested positive for antinuclear antibodies, all at a titre of 1:100. Notably, all 14 participants tested negative for antiovarian antibodies. The cohort is currently undergoing further follow-up.

1.21 Identification of HOXA10-driven Genetic Networks in the Endometrium *(Funded by Department of Biotechnology (DBT))*

Principal Investigator : **D Modi**

Project Associates : A Bhide, Saee Patil

Duration : 2024-2027

HOXA10 is a homeobox gene essential for uterine development and in the adult uterus, HOXA10 is indispensable for endometrial differentiation for receptivity and embryo implantation. HOXA10 expression is altered in women with infertility, recurrent implantation failures, endometriosis, and even endometrial cancer. However, the mechanisms by which HOXA10 controls receptivity and its altered expression lead to these endometrial pathologies is not understood. The project aims to uncover the genetic networks operated by HOXA10 in endometrial cells. In the reporting year we have generated human endometrial cell lines overexpressing and knockdown for HOXA10. A tetracycline inducible HOXA0 construct and a previously validated shRNA constructs against HOXA10 were transfected in human endometrial epithelial and stromal cell lines. Stable clones have been generated with the altered levels of HOXA10. Using an in-house generated and knockout validated polyclonal anti-peptide antibody, we employed CUT&RUN of human endometrial cell to identify the chromatin occupancy of HOXA10. We identified 69,990 high-confidence binding sites of HOXA10 in estrogen and progesterone-treated endometrial epithelial cells. Analysis of the top 10,000 peaks revealed that most HOXA10 binding events occurred in intergenic and intronic regions, with a subset mapping to promoters and transcription start sites (TSSs). Analysis of the top 5,000 peaks revealed a significant enrichment for binding motifs of multiple transcription factors, including CTCF, ERα, ERβ, STAT3, STAT5A/B, SMAD2, SMAD3, FOXA2, FOXO1, KLF4, KLF5, and KLF9. Given the essential role of estrogen signaling and FOXA family of genes in the uterine epithelium, our results support the idea that HOXA10 acts as part of a larger transcriptional network governing epithelial function.

1.22 Deciphering the Immunomodulatory Roles of Homeobox A10 in the Endometrium during Embryo Implantation (*Partly Funded by Department of Biotechnology*)

Principal Investigator	:	**DN Modi**
Co-Principal Investigator		Nupur Mukherjee
Project Associates	:	Babita Negi, Ramya Singh Bal
Collaborator	:	S Chauhan, CSIR-CCMB, Hyderabad
Duration	:	2021-2025

The success of embryo implantation depends on genetic and cellular interactions which must be executed during window of implantation. Immunomodulation in the endometrium is a central event as the system has to prepare itself for accommodating the semi-allogenic blastocyst along with continuous maternal surveillance against the pathogens. Studies have shown that embryo implantation is characterized by an increase in inflammatory cytokines and recruitment of immune cells in the endometrium. Despite this, the classical inflammation reaction does not take place and the fetus is retained suggesting the controlled inflammation during embryo implantation. How this inflammation is controlled during implantation remains unclear. IL-1β processing is driven by inflammasomes (oligomeric multi-protein complexes) and is impeded via autophagy degradation. Therefore, an equilibrium between autophagy and inflammasome is important for controlling inflammation. Immunity-related GTPase M1 (Irgm1) negatively regulates inflammasomes by blocking the oligomerisation of inflammasome components and activating autophagy. Here we hypothesize that the interplay between inflammasome and autophagy to regulate inflammation during embryo implantation can be marinated by Irgm1. Thus we aim to investigate the role of Irgm1 in the process of embryo implantation. To achieve this, the fertility of Irgm1 knockout mouse was checked through litter size and number of days taken to conceive by comparing with wild-type mice. Previously, we had reported that the knockouts showed significantly reduced litter size and took minimum three times longer to conceive than the wild-type indicating they are sub-fertile. Moreover, 10 % of knockouts were found to be infertile. Histological analysis of the knockouts was carried and we observed defective implantation cup formation along with defective decidualization zone suggesting they have implantation defect (Fig. 1). Further, the effect of loss of Irgm1 on receptivity was checked using receptivity marker ERα, ERβ, HOXA10 and β-catenin. Increased expression of the receptivity markers was observed in the knockouts indicating their altered receptivity profile (Fig. 2). Thus, Irgm1 does play a role in embryo implantation. Further studies related to inflammasome expression in the knockouts are ongoing.

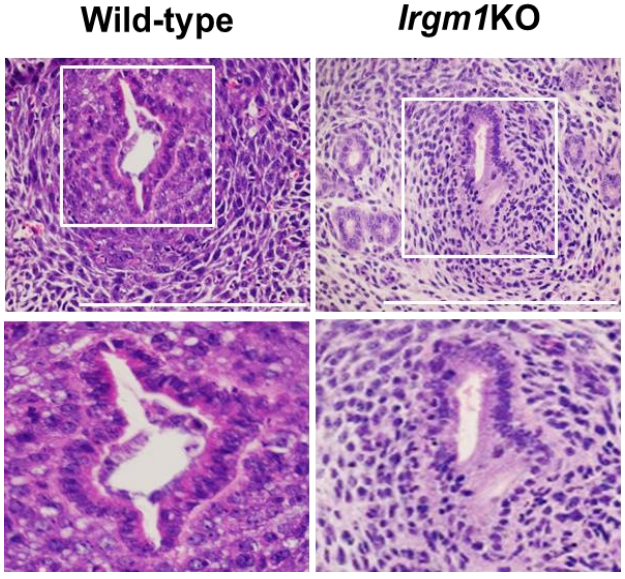

Figure 1: Histological differences in the endometrium of wild-type and Irgm1 knockout mice at implantation site on day 5. HE was performed on the day 5 paraffin embedded tissue sections of wild-type and Irgm1 knockout mice uterus. Bar: 100 µm; n=3.

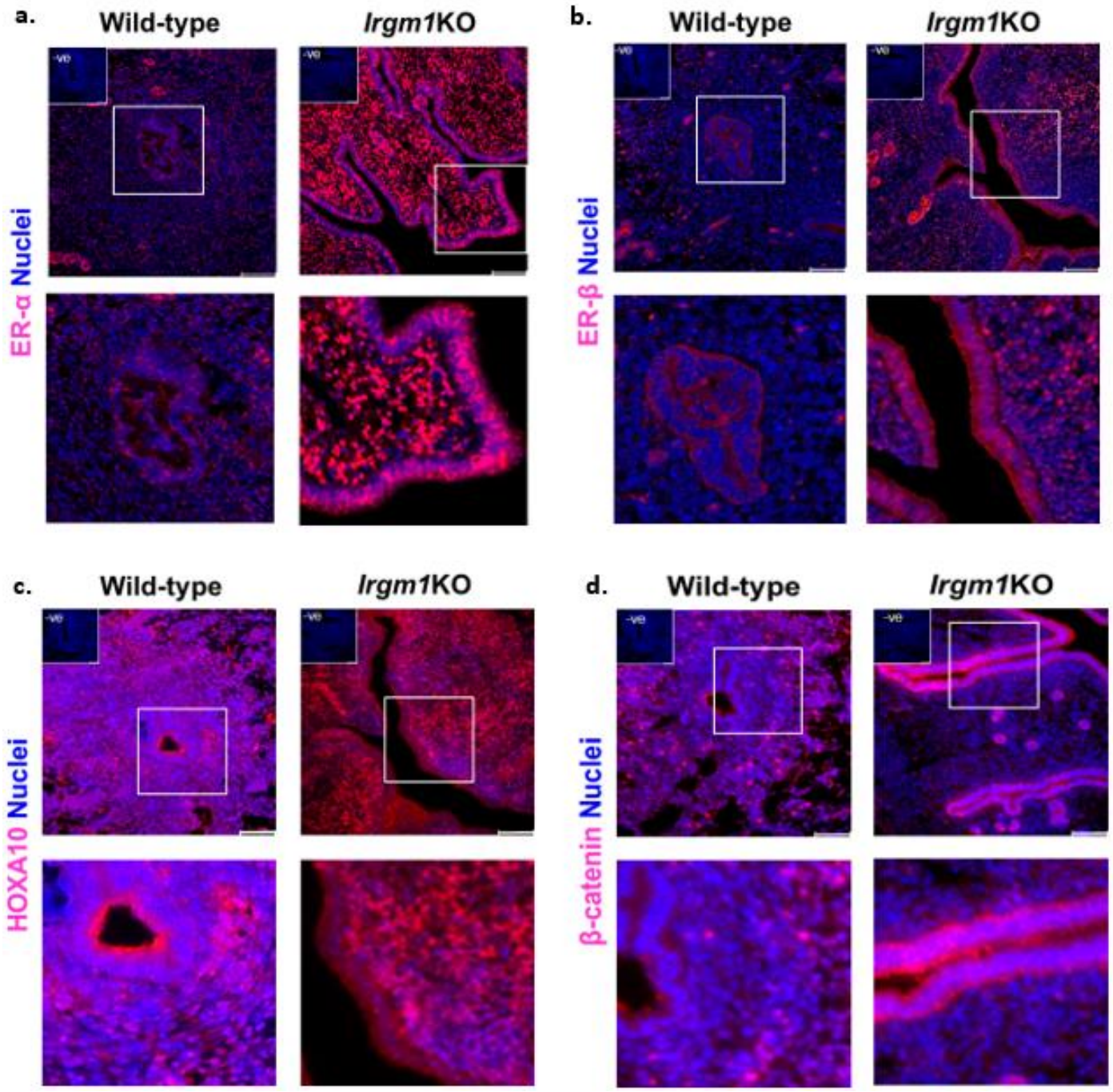

Figure 2: Receptivity marker expression in day 5 wild-type and Irgm1KO. Immunolocalization of ERα (a), ERβ (b), HOXA10 (c) and β-catenin (d) in wild-type day 5 and Irgm1 KO day 5 paraffin embedded tissue sections of mice uterus (n=3); Bar: 100 µm.

MALE INFERTILITY AND ASSOCIATED REPRODUCTIVE DISORDERS

2. MALE INFERTILITY AND ASSOCIATED REPRODUCTIVE DISORDERS

2.1 Unravelling Sperm Epigenetic Landscape Regulated by Estrogen Receptors in Adult Male Rats

Principal Investigator : **Kushaan Khambata**
Duration : 2020-2026

Estrogen through its receptors (ERα and ERβ) plays an important role in regulation of various aspects of spermatogenesis and male fertility. To study the roles of ERs in male fertility, rat models have been established wherein treatment with selective ERα against 4,4´,4´´-(4-Propyl-[1H] pyrazole-1,3,5-triyl) (PPT) and ERβ against 2,3-bis(4-hydroxyphenyl)-propionitrile (DPN) for 60 days leads to decreased fertility in adult male rats resulting in pre- and post-implantation embryo loss. Since epigenetic marks such as DNA methylation in the sperm play a crucial role in embryogenesis, the present study aims to investigate the effects of estrogen signaling via ERα and ERβ on sperm DNA methylome in rat models. Whole genome bisulfite sequencing (WGBS) revealed 4653 differentially methylated genes (DMG) in PPT and 314 DMG in DPN treated groups. Majorly, the DMGs were involved in the developmental processes. It was noted that developmental process was the major ontology enriched by DMGs in both PPT and DPN treated groups. DNA methylation aberrations, specifically in the developmental genes, were validated in the sperm samples (Annual report 2022-2023, pp. 31-33). In the reporting year, the DNA methylation and gene expression of the validated developmental genes were investigated in resorbed embryos sired by control and ER agonist treated male rats. Most of the genes showed the same trend of DNA methylation aberrations in the resorbed embryos as observed in sperm from the treated group; indicating that they were passed on from sperm to the developing embryo. Expression of these genes was also found to be affected in the resorbed embryos sired by PPT and DPN treated rats as compared to resorbed embryos (Fig. 1). For PPT, developmental genes such as Cdkn1c, Gab1, Peg3, Igf2r, Sfmbt2, were down-regulated and Tgfb1, Bmp4, Myc, WT1, and Hoxc10 and were up-regulated indicating that the aberrant methylation can alter the expression of these genes. Specific developmental pathways found enriched on ontology analysis after PPT treatment were further investigated. Expression of DMGs involved in MAPK, Tgfβ, Wnt, Notch, and Hedgehog, and Scf-cKit signaling pathways was evaluated in resorbed embryos. In MAPK signaling pathway expression of most of the DMGs such as the ligand Fgf4, and the receptors Fgfr2 and Egfr, as well as the downstream signaling proteins such as Sos and Raf1 were up-regulated (Fig. 2A). In the Tgfβ signaling pathway, expression of the genes encoding the receptors Tgfbr2 and Bmpr2 were up-regulated, while that of the downstream transcription factors Smad3 was down-regulated and Smad4 was up-regulated (Figure 2B). In the Wnt signaling pathway, expressions of the ligands Wnt5a, Wnt7a and the receptor Fzd8 and Ror2 were up-regulated, the co-receptor Lrp5 was down-regulated and adapter protein Skp1 was up-regulated (Fig. 2C). Expression of the gene for ligand Jag2 was down-regulated and the receptor Notch1 was up-regulated; while the downstream transcriptional regulators such as Ncor2 and Maml1 were up-regulated (Fig. 2D). In the ligand Hedgehog signaling pathway, Shh and Sufu for the were down-regulated. In contrast, the transcription factor Gli1 was up-regulated and Ccnb1 was down-regulated (Fig. 2E). In the Scf-cKit signaling pathway, down-stream regulators such as Src, Lyn and Jak2 were affected (Fig. 2F). The above results indicate that estrogen receptor α regulates sperm epigenome and this has implications on various developmental pathways during embryogenesis.

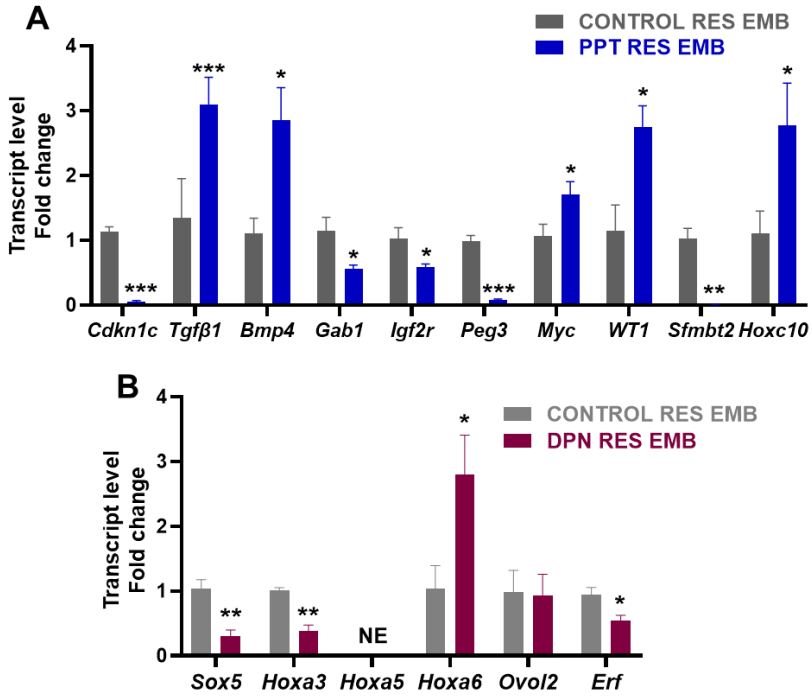

Figure 1: Expression of developmental genes in resorbed embryos sired by control, PPT (A), and DPN (B) treated male rats. N=8 in three groups. * indicates p<0.05, ** indicates p<0.01, and *** indicates p<0.001.

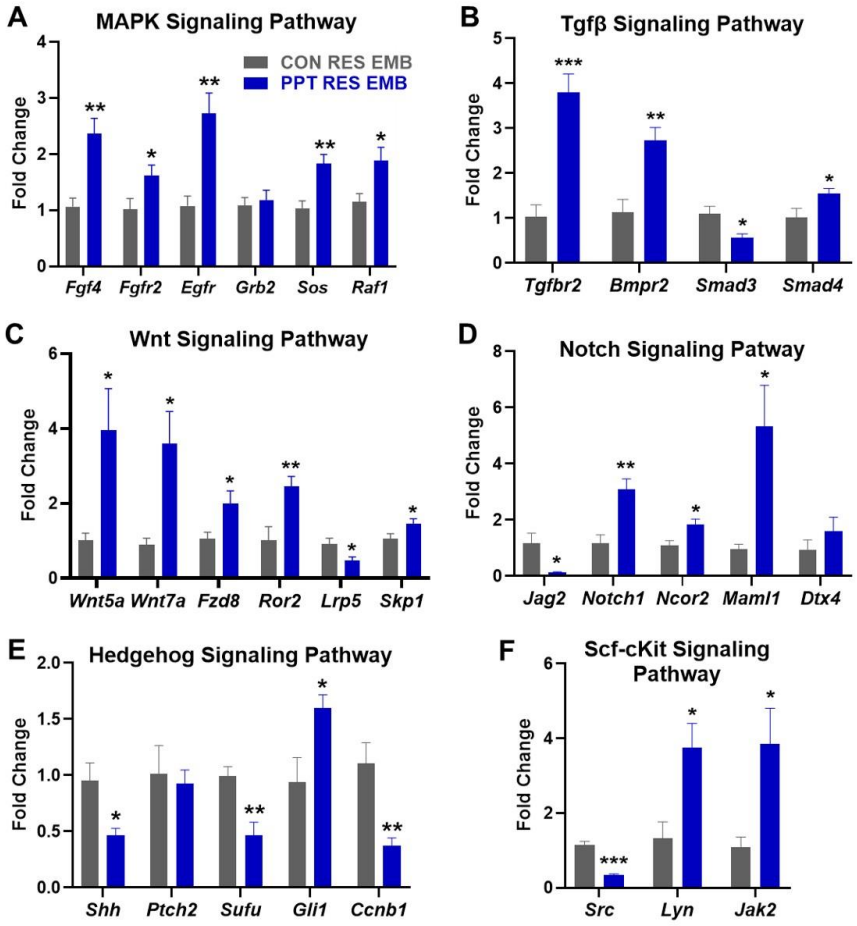

Figure 2: Expression of genes involved in MAPK (A), Tgfβ (B), Wnt, (C) Notch (D), and Hedgehog (E) and Scf-cKit (F) signaling pathways in resorbed embryos sired by control and PPT treated male rats. N=8 in both groups. * indicates p<0.05, ** indicates p<0.01, and *** indicates p<0.001.

2.2 Implications of Gonadotropin and their Receptor Gene Variants in Male Infertility

(Partly Funded by Institutional Research Grant)

Principal Investigator : **P Kuppusamy**
Project Associates : R Gajbhiye, S Pande, DVS Sudhakar, Shagufta A Khan
Collaborators : P Kothari, V Kulkarni, Consultant Andrologists
D Kale, G Desai, Nowrosjee Wadia Maternity Hospital, Mumbai
J Shah, Kamala Polyclinic and Nursing Home, Mumbai
Duration : 2022-2026

Globally, 49 to 180 million couples are affected by infertility, and of these 3.9% to 16.8% couples are from India. More than 10% of couples worldwide and about 10-15% of Indian couples consult for infertility problems. About 40% of Infertility cases are contributed by male factor alone. A comprehensive physical examination, complete medical history and adequate laboratory testing are essential components of the initial evaluation of men being assessed for infertility. Male reproductive hormones are key regulators for germ cell development and its regulation. The present study assessed andrological and endocrinological factors associated with the semen quality in the Idiopathic infertile men. This study is an ongoing longitudinal cohort of infertile men attending tertiary care hospitals in Mumbai. A total of 72 infertile cases with complete profile of physical examination and laboratory data, for semen profiles and hormone analysis were considered for analysis.

Table 1: Study characteristics of infertile and fertile men

Description of Study	Infertile men			Fertile men	
Sample size (n)	72			91	
Age (years)	33.7 ± 3.7			34.6 ± 4.0	
Anthropometric measurements					
Height (cm)	170.1 ± 7.6			166.8 ± 5.8	
Weight (kg)	72.4 ± 12.4			71.3 ± 13.9	
BMI kg/m²; (mean, SD)	24.8 ± 3.9			25.6 ± 4.4	
Fertility status	**Primary infertility**		**Secondary infertility**	Parity 1	Parity >1
Proportion %, n)	81.9 (59)		18.1 (13)	42.5 (37)	57.5(50)
Andrological evaluation	Normal genital: 62.5% MTV: 18.1 ml	Testicular hypotrophy: 23.6%; MTV: 9.9 ml	Soft testes: 5.6%; MTV: 13.4 ml		
Seminogram Volume (ml)	2.6 ± 1.5			3.2 ± 1.5	
Mean Testicular volume (MTV) & sperm conc.	MTV (ml)	Sperm Conc. (10^6/ml)	% (n=72)	Sperm. Conc. (10^6/ml)	
Normozoospermia	22.2 ± 10.2	34.7 ± 25.4	13.9	62.7 ± 39.4	
Mild	19.3 ± 4.4	12.7 ± 1.4	12.5		
Moderate	17.7 ± 5.1	7.8 ± 2.1	15.3		
Severe	13.7 ± 4.9	1.3 ± 1.4	58.3		
Total motility (%)	23.4 ± 19.6			67.1 ± 17.0	

Out of 72 cases, majority of them had primary infertility (81.9%). Around 33.3% of men had comorbidities. According to spermiogram: narmozoospermia, mild, moderate, and severe oligozoospermia were found to be 13.9%, 12.5%, 15.3%, and 58.3% irrespective of motility and morphological abnormalities. A decreasing trend in mean testicular volume (MTV) of infertile men was observed among narmozoospermia (22.2 ml), mild (19.3 ml), moderate (17.7 ml), and severe oligozoospermia (13.7 ml). As per the clinical evaluation report, 62.5% of men had normal genital

findings with MTV of 18.1 ml, followed by 23.6% of men having testicular hypotrophy with MTV of 9.9 ml, and 5.6 % of men having soft testes with MTV of 13.4 ml. A sharp increasing trend in serum levels of FSH and LH were found, depending on the sperm count abnormalities. However, moderate oligozoospermic men had lower levels of serum Testosterone and SHBG, and higher levels of serum Inhibin-B and estradiol as compared to mild and moderate oligozoospermic men. Our preliminary observation indicates that idiopathic infertile men having moderate oligozoospermia with low testosterone and high estradiol may be considered for empirical medical therapy using SERMs to improve sperm count.

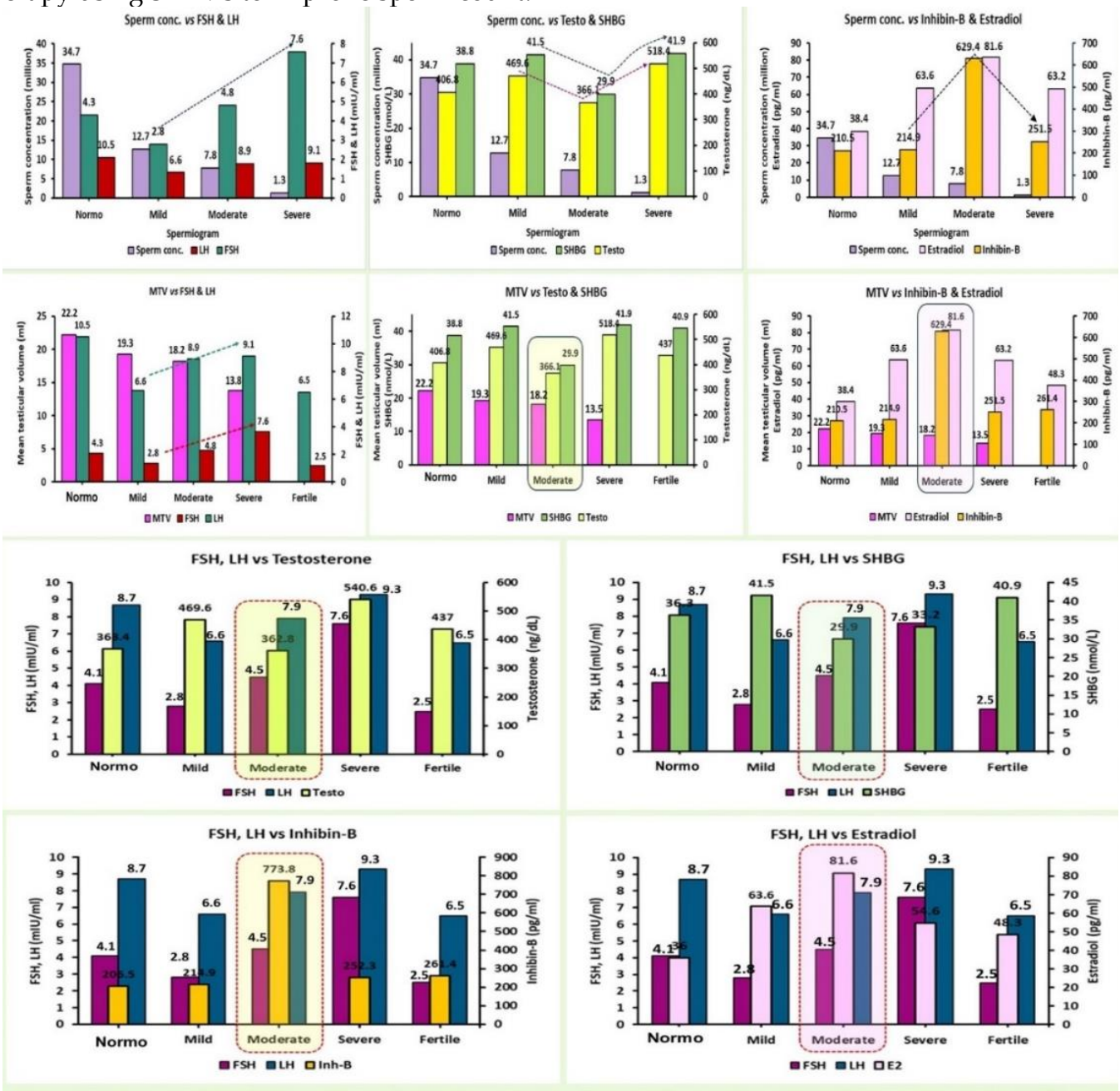

Figure 1: Pattern and distribution of reproductive hormone levels according to sperm concentration and testicular volume in infertile and fertile men

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

Principal Investigator	:	**Bhakti R Pathak**
Project Associates	:	Vaidehi Miya, Antara Banerjee, Ananya Breed
Duration	:	2018-2025

Cysteine RIch Secretory Proteins (CRISPs) form tight complex with Prostate Secretory Protein of 94 amino acids (PSP94) in human seminal plasma. Apart from semen, they are present in body secretions highlighting their role in innate immunity. Interestingly, in prostate tumorigenesis, the expression of CRISP3 is upregulated while that of PSP94 is downregulated. This inverse correlation has been linked to poor prognosis in patients with prostate cancer. However, their precise role, alone or in complex, in the prostate tumor microenvironment remains unknown. In Annual report 2023-2024, pp. 42-44, we identified P2RX7, an ATP-gated ion channel, to be upregulated when CRISP3 was silenced in prostate cancer cell line. P2RX7 receptor is important in the NLRP3 inflammasome pathway and our data suggested that exogenously added rhCRISP3 suppressed P2RX7 expression and ATP induced cytotoxicity in PC3 cells. Interestingly, the presence of hPSP94 in combination with rhCRISP3 abrogated this effect. Considering that P2RX7 is predominantly expressed in immune cells, we extended our investigations to THP1 macrophages and observed similar results. To further support these findings, we evaluated RNA Seq data from 50 prostate adenocarcinomas and adjacent normal tissues available in TCGA database and observed an inverse expression pattern of CRISP3 and P2RX7 (Fig. 1A, 1B). We further stratified the data into three groups based on CRISP3 expression in tumors as compared to adjacent normal i.e. i) upregulated CRISP3 by ≥1.5 folds, ii) negligible change in CRISP3 and iii) downregulated CRISP3 by ≤0.5 folds (Fig. 1C). A significantly negative correlation was observed between CRISP3 with P2RX7 in the first subgroup (ρ = -0.8064, p-value: <0.0001) (Fig. 1C) suggesting CRISP3 to be a negative regulator of P2RX7. Activation of P2RX7 induces stress followed by IL-1β secretion. Therefore, we evaluated alterations in the stress response and IL-1β release due to rhCRISP3 and/or hPSP94 pre-treatment. Total cell lysates from PC3, pretreated with rhCRISP3 alone (1 µg/mL) and in complex with hPSP94 (1 µg/mL) followed by stimulation with 2 mM ATP for 1 hr were subjected to the Proteome Profiler stress array containing 26 stress markers (Fig. 2A). Downregulated JNK phosphorylation and upregulated CITED2 expression were observed upon rhCRISP3 treatment as compared to untreated cells (Fig. 2A). This was subsequently validated in PC3 cells and THP1 macrophages suggesting dampening of stress response due to downregulated P2RX7 (Fig. 2B and 2C). Interestingly, presence of rhCRISP3 in combination with hPSP94 did not alter JNK phosphorylation or CITED2 expression suggesting its role in regulating CRISP3 mediated signalling. IL-1β levels were also measured in the culture supernatant using ELISA. PC3 cells liberated very low IL-1β when stimulated with ATP, therefore, THP1 macrophages were used in this experiment. THP1 macrophages, either untreated or pretreated with rhCRISP3, hPSP94 or hPSP94+rhCRISP3, treated or untreated THP1 macrophages were primed with 1 µg/mL LPS for 3 hrs followed by stimulation with 2 mM ATP for 1 hr where rhCRISP3 treatment significantly reduced IL-1β release compared to untreated or hPSP94-treated controls (Fig. 2D). Notably, this suppressive effect of rhCRISP3 on IL-1β secretion was abolished when rhCRISP3 was administered in combination with hPSP94, thereby strengthening our observations.

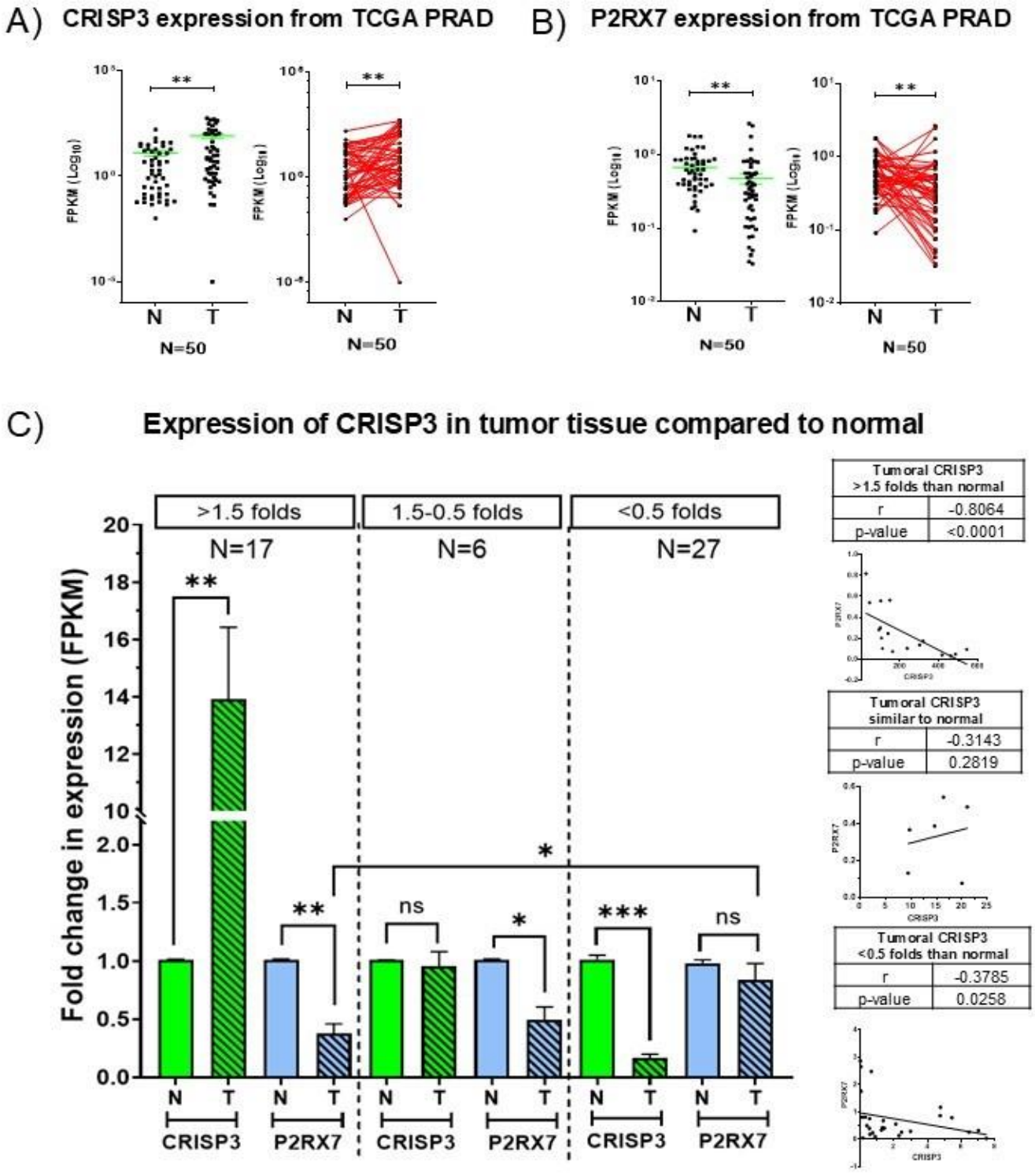

Figure 1: CRISP3 modulates expression of P2RX7 in prostate tumor cells FPKM (Fragments Per Kilobase of transcript per Million mapped) reads of A) CRISP3 and B) P2RX7 of 50 prostate tumors (T) and adjacent normal tissues (N) were extracted from The Cancer Genome Atlas and represented as a dot plot and paired scatter plot. C) Patients were stratified based on level of fold change in CRISP3 expression with respect to adjacent normal as indicated. For each subgroup, correlation analysis by Spearman correlation was performed. A significant negative correlation was observed for high CRISP3 expressors. Statistical analysis was performed by student's t test and represented as '*' for $p<0.05$, '**' for $p\leq0.01$, '***' for $p<0.001$, ns for non-significant

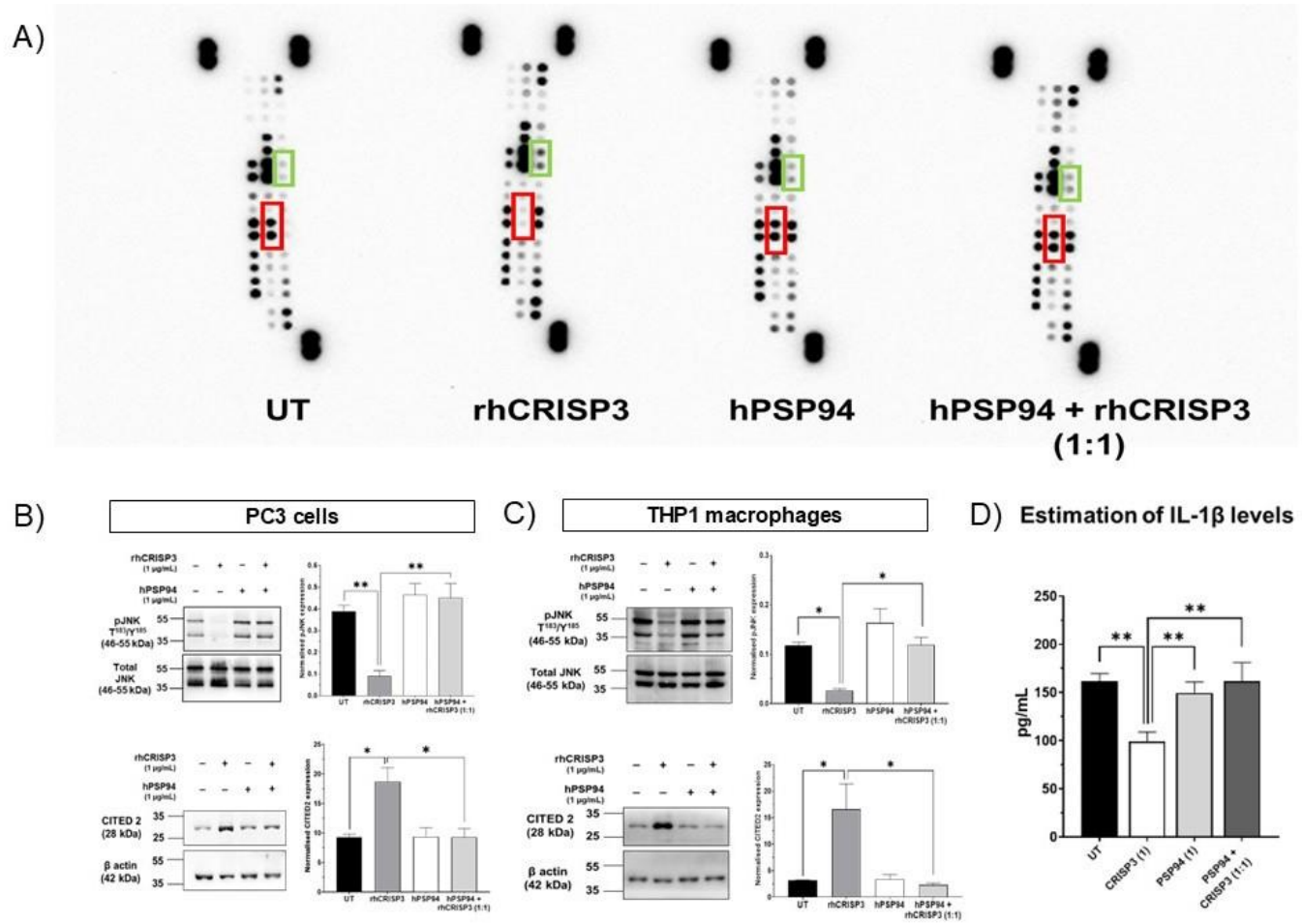

Figure 2: CRISP3 abrogates ATP induced stress response and IL-1β secretion via P2RX7 A) Proteome profiler human cell stress array was incubated with total lysates from PC3 cells pretreated with indicated proteins followed by 2 mM ATP treatment. Significant difference across two spots corresponding to CITED2 (marked in green box) protein and phosphoJNK (marked in red box) was observed for CRISP3 treated cells. Validation of JNK phosphorylation and CITED2 was carried out in B) PC3 and C) THP1 macrophages by immunoblotting. For densitometric analysis, signals for pJNK in total cell lysates were normalized with total JNK while that of CITED2 were normalized with β-actin. D) THP1 macrophages were subjected to the indicated treatments. IL-1β released post treatment, was quantitated by ELISA and plotted as a bar graph. The concentration of proteins used for treatment is indicated in parenthesis (µg/mL). Experiments were repeated thrice and the data shown is from a representative experiment. Statistical analysis was performed by one-way ANOVA and represented as '*' for $p < 0.05$ '**' for $p \leq 0.01$ and '***' for $p < 0.001$.

2.4 Identification of New Male Infertility Genes in Obstructive Azoospermic Men with Congenital Bilateral Absence of Vas Deferens *(Funded by DBT)*

Principal Investigator	:	**R Gajbhiye**
Project Associates	:	R Shah, V Kulkarni, DVS Sudhakar, V Dighe, Shagufta Khan
Duration	:	2019-2023

Congenital Bilateral Absence of the Vas Deferens (CBAVD) contributes to 2-3% of all male infertility cases and is responsible for 25 % of cases of obstructive azoospermia. The objectives of the study are (i) to identify and characterize new candidate male infertility genes in obstructive azoospermic men with CBAVD; (ii) to identify the genes in CBAVD men having Unilateral Renal Anomalies

(URA); and (iii) to investigate the role of the Adhesion G Protein-Coupled Receptor G2 (ADGRG2) gene and other new male infertility genes (identified from objectives 1 and 2) in Indian men with CBAVD We performed whole exome sequencing (WES) of genome from 16 men of whom 9 were men with CBAVD, 4 were men with CBAVD and URA, 3 were men with Congenital Unilateral Absence of Vas Deferens (CUAVD), and 1 individual had CUAVD and URA phenotype. We identified a novel, pathogenic missense variant (p.Thr569Ile) in the ADGRG2 gene in two individuals with CBAVD phenotype. The variant p.Thr569Ile was absent in the gnomAD v4.0.0 database and is predicted to be pathogenic by most of the Metascore in silicon predictors. Of the 14 individuals with CUAVD/CBAVD phenotype (with normal kidneys), we identified CFTR pathogenic variants by exome sequencing in 28.5% of individuals (n=4). To summarize, we identified an ADGRG2 variant in 14% (n=2) of CUAVD/CBAVD individuals with normal kidneys. A total of 13 (68.4%) CUAVD/CBAVD individuals with or without renal agenesis did not show any pathogenic variants in known genes for their respective phenotypes. However, using in-house exome data analysis pipelines we identified candidate genes for isolated CUAVD/CBAVD and CUAVD/CBAVD with renal agenesis.

2.5 Delineating the Role of Human β-Microseminoprotein in Male Reproduction *(Partly Funded by Indian Council of Medical Research)*

Principal Investigator	:	**Dhanashree Jagtap**
Co-Principal Investigators	:	Bhakti Pathak, Priyanka Parte, D Modi
Project Associates	:	B Kulkarni, V Pawar
Collaborators	:	R Gajbhiye, V Kulkarni, Anushree Patil, Deepti Tandon A Phadke, SRL Dr Avinash Phadke labs
Duration	:	2023-2026

Beta-microseminoprotein (β-MSP) is secreted by prostate and is found in human seminal plasma and on spermatozoa. Aim of the study is to delineate the role of β-MSP in male reproduction. During the reporting period, difference in β-MSP levels in human seminal plasma and spermatozoa of fertile (22 normozoospermic) individuals were investigated. β-MSP concentration was expressed as relative abundance (percentage of total protein concentration). In seminal plasma, the relative abundance of β-MSP was found to be 0.6%, whereas in lysed spermatozoa (after three washes) was 0.0083%. These results indicate that β-MSP in seminal plasma is acquired by spermatozoa and exists in both loosely and tightly bound forms. This dual binding may have implications for the role of β-MSP in sperm capacitation and acrosome reaction. For identification of interacting partners of β-MSP on spermatozoa, standardization of immunoprecipitation of sperm lysate from normozoospermic samples using anti-β-MSP followed by LC-MS/MS was carried out in the previous year (Annual report 2023-2024, pp. 44-45). In the reporting year, immunoprecipitation of sperm lysates from asthenozoospermic and oligoasthenozoospermic samples using anti-β-MSP followed by LC-MS/MS and proteomic analysis was carried out. The unique proteins identified in each group were subjected to WebG salt analysis for function prediction. β-MSP interactome analysis identified a total of 240 proteins in normozoospermic individuals, 253 proteins in asthenozoospermic individuals, and 121 proteins in oligoasthenozoospermic individuals. Comparative analysis from these seminogram-specific proteomes identified 159, 178 and 98 unique proteins from normozoospermic, asthenozoospermic and oligoasthenozoospermic groups respectively (Fig. 1 A-D). Functional enrichment analysis of the unique identified proteins from above 3 groups using WebGestalt showed highest functional coverage for proteins involved in sperm motility (Fig. 1E).

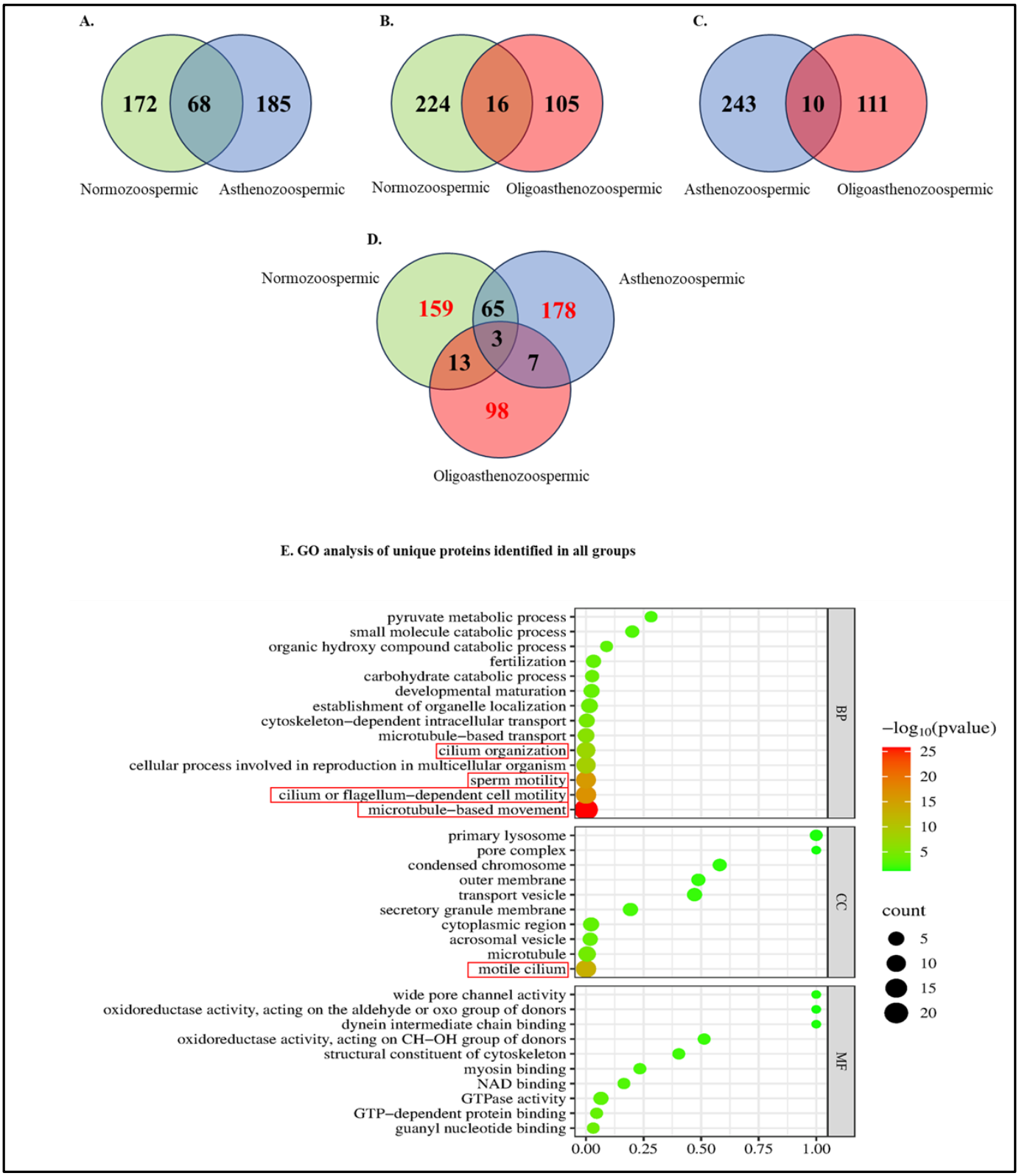

Figure 1: Identification and functional enrichment of β-MSP interacting proteins across different seminograms. Venn diagram depicting the comparative analysis illustrating identification of unique and differentially expressed proteins among normozoospermic, asthenozoospermic, and oligoasthenozoospermic groups (A-D). WebGestalt analysis of the unique proteins identified in the normozoospermic, asthenozoospermic, and oligoasthenozoospermic samples predicted various Biological Processes (BP), Cellular Components (CC), and Molecular Functions (MF) (E). Proteins associated with sperm motility were found to have highest coverage (highlighted in red).

2.6 Unravelling the Sperm Epigenetic Landscape in Infertile Men with Clinical Varicocele *(Partly Funded by **Institutional** Research Grant)*

Principal Investigator	:	**Dipty Singh**
Project Associates	:	Deepshikha Arya, Nafisa Balasinor, R Gajbhiye, Kushaan Khambata, Deepti Tandon
Collaborators	:	P Pawar, Lokmanya Tilak Municipal General Hospital P Kothari, Nair Hospital
Duration	:	2020-2025

Varicocele condition is often associated with infertility in men. Varicocele affects spermatogenesis via several distinct mechanisms. Of these elevated oxidative stress has been implicated as a key factor in varicocele induced male infertility. High oxidative stress during spermatogenesis may lead to aberrant epigenetic modifications in spermatozoa. This study aims to evaluate sperm genome wide DNA methylation signatures by Whole-Genome Bisulfite Sequencing (WGBS) before and after antioxidant treatment and before or after varicocele repair in men with varicocele. Thirty healthy fertile men and 50 infertile men with clinical varicocele (Grade I-III) have been recruited. Varicocele patients were followed-up and semen samples (n=25) were collected after 3 months of treatment. The varicocele group exhibited significantly reduced semen parameters compared to the control group. Although improvements were observed in a subset of men following both treatment modalities, varicocelectomy proved to be more effective than antioxidant therapy in enhancing sperm parametersWGBS of sperm genomic DNA was analysed to identify differentially methylated CpG (DMC) sites before those with and without varicocele. Five samples from each group were pooled and submitted for WGBS. Alignment was done with hg38 (Homo sapiens) reference genome. Differentially Methylated Cytosines (DMCs) were identified with >25% methylation change and with a Q-value <0.05. Upon further analysis, a total of 6414 DMCs and 1484 differentially methylated genes (DMGs) were obtained (Annual report 2024, pp. 41-44). The DMGs H2AX, BCR, SPATA6L, PRKN, SOD2, CDKN1B, P2RX7, NF1, KIT, RAI14, and BCL2 are involved in processes such as spermatogenesis, cell cycle regulation, cell differentiation, reactive oxygen species ROS metabolic regulation, heat response, and mitochondrial regulation. DMCs within genes relevant to spermatogenesis, sperm function and sperm mitochondria regulation were validated for their methylation levels in the study population by pyrosequencing. The DMC H2AX was significantly hypermethylated, and CDKN1B and BCR were significantly hypomethylated in the varicocele group (Fig. 1). However, after 3 months post treatment, no significant restoration was observed in any of these DMCs (Fig. 2). The present results suggest that varicocele treatment modalities did not help in restoring the altered DNA methylation levels of differentially methylated CpG sites within the genes. The present study unravels the genome-wide sperm DNA methylation landscape of clinical varicocele cases, and suggests that current varicocele treatments are not highly effective in restoring sperm DNA methylation. It also provides deeper insights into the epigenetic aetiology of varicocele-associated male infertility.

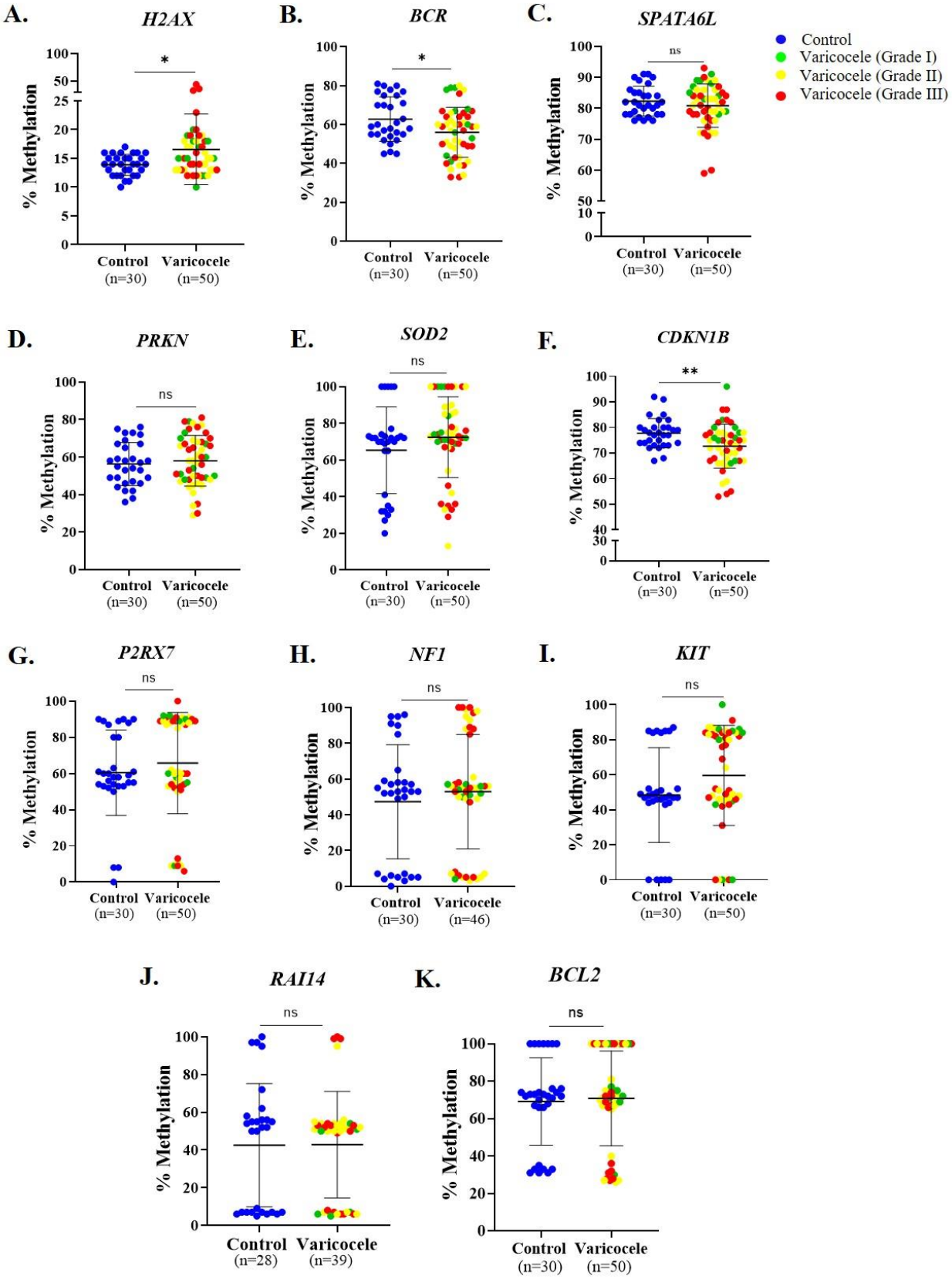

Figure 1: Methylation status of selected DMCs within genes (A) H2AX, (B) BCR, (C) SPATA6L, (D) PRKN, (E) SOD2, (F) CDKN1B, (G) P2RX7, (H) NF1, (I) KIT, (J) RAI14 and, (K) BCL2 in sperm from control and varicocele groups. Mean±SEM. (*p≤0.05, **p≤0.01), ns: nonsignificant.

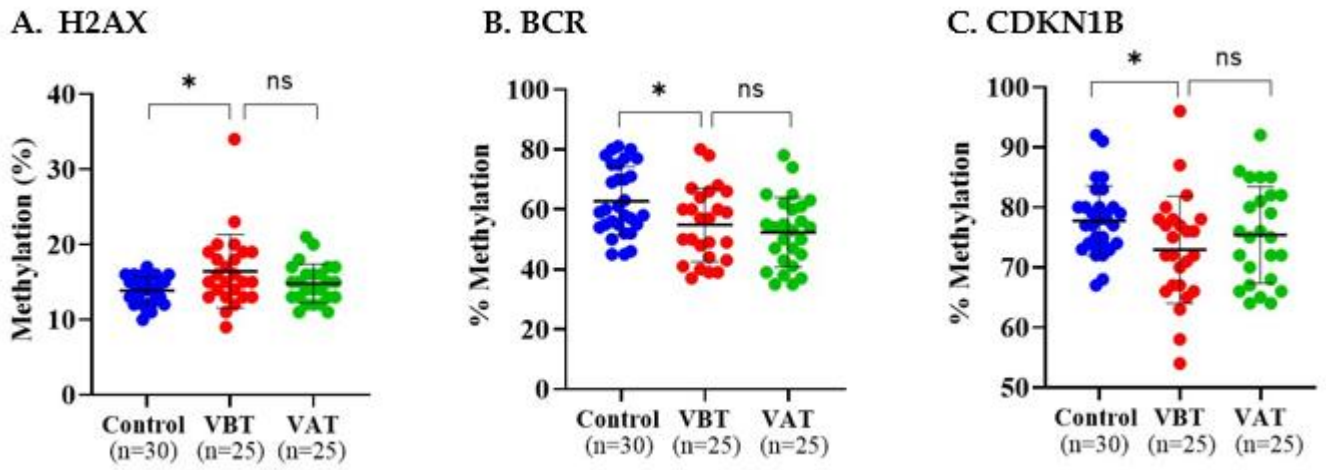

Figure 2: Methylation status of altered DMCs in the varicocele group after treatment in comparison with the control group and before treatment within gene (A) H2AX; (B) BCR; and (C) CDKN1B. No significant methylation restoration observed after treatment. Mean±SEM. (*p≤0.05). VBT: Before Treatment, VAT: After Treatment, ns: non significant

2.7 Therapeutic Potential of Epigallocatechin-3-gallate for Improving Sperm Quality, Fertility and Pregnancy Outcomes in a Murine Model of Endocrine Disruption *(Partly Funded by Indian Council of Medical Research)*

Principal Investigator	:	**Dipty Singh**
Co-Principal Investigator	:	Kumari Nishi
Project Associates	:	Deepshikha Arya, Shobha Sonawane, Anushruti Singh, Nayanika Roy
Duration	:	2023-2026

Exposure of Cypermethrin (CYP), a widely used insecticide and known Endocrine Disrupting Chemical (EDC) during adulthood or sensitive windows of foetal development, has detrimental effects on male reproductive functions and foetal outcomes. Epigallocatechin-3-gallate (EGCG), a major polyphenol in green tea, has been reported to have protective effects against reproductive toxicity. In our previous study, we observed that EGCG supplementation significantly helps in restoring the testicular damage and perturbed semen parameters in CYP-exposed F1 offspring indicating the beneficial role of EGCG on the male reproductive system (Annual report 2020-21, pp. 123-124). During the reporting year, molecular mechanisms of EGCG in restoring the damage induced by CYP reproductive were studied. For this study, pregnant dams (F0) were orally administered with corn oil or CYP (25 mg/kg BW/day) once daily from gestation day 6 to postnatal day (PND) 22. At PND 60, control and CYP exposed F1 male rats were further divided into vehicle control and EGCG (10 mg/kg BW/day) treatment groups and orally administered with these doses once daily for another 60 days. VASA protein is primarily present in all cell types of germ cells in adult rats except elongated spermatid. It is involved in germ cell proliferation and function. The immunolocalization studies of VASA in rat testis showed intactness of different germ cells in control whereases CYP group showed sloughing of germ cells in the lumen indicating detrimental effects of CYP exposure. EGCG supplementation to CYP exposed adult F1 male rats for 60 days showed intact germ cell associations similar to control group indicating its therapeutic effects (Fig. 1). Further, flow cytometry studies revealed an increase in the number of elongated and elongating spermatids in CYP group compared to control group indicating spermiation failure. The 4N and S-phase population were unaffected and 2N population was decreased in CYP group compared to

control. Round spermatids (RS) population was significantly decreased in CYP group as compared to control and this effort was abrogated by EGCG supplementation to CYP rats (Fig. 2(I)). CYP-exposed rats exhibited increased testosterone and estradiol levels which were observed to be significantly decreased by EGCG supplementation. FSH and LH levels were non-significantly altered in all the treatment groups, whereas prolactin levels were found increased in only EGCG and CYP exposed groups. The prolactin level was decreased significantly after EGCG supplementation in F1 male rats that had perinatal CYP exposure (Fig. 2(II)). Further studies to evaluate the effect of EGCG supplementation on the fertility of CYP exposed F1 male rats are underway.

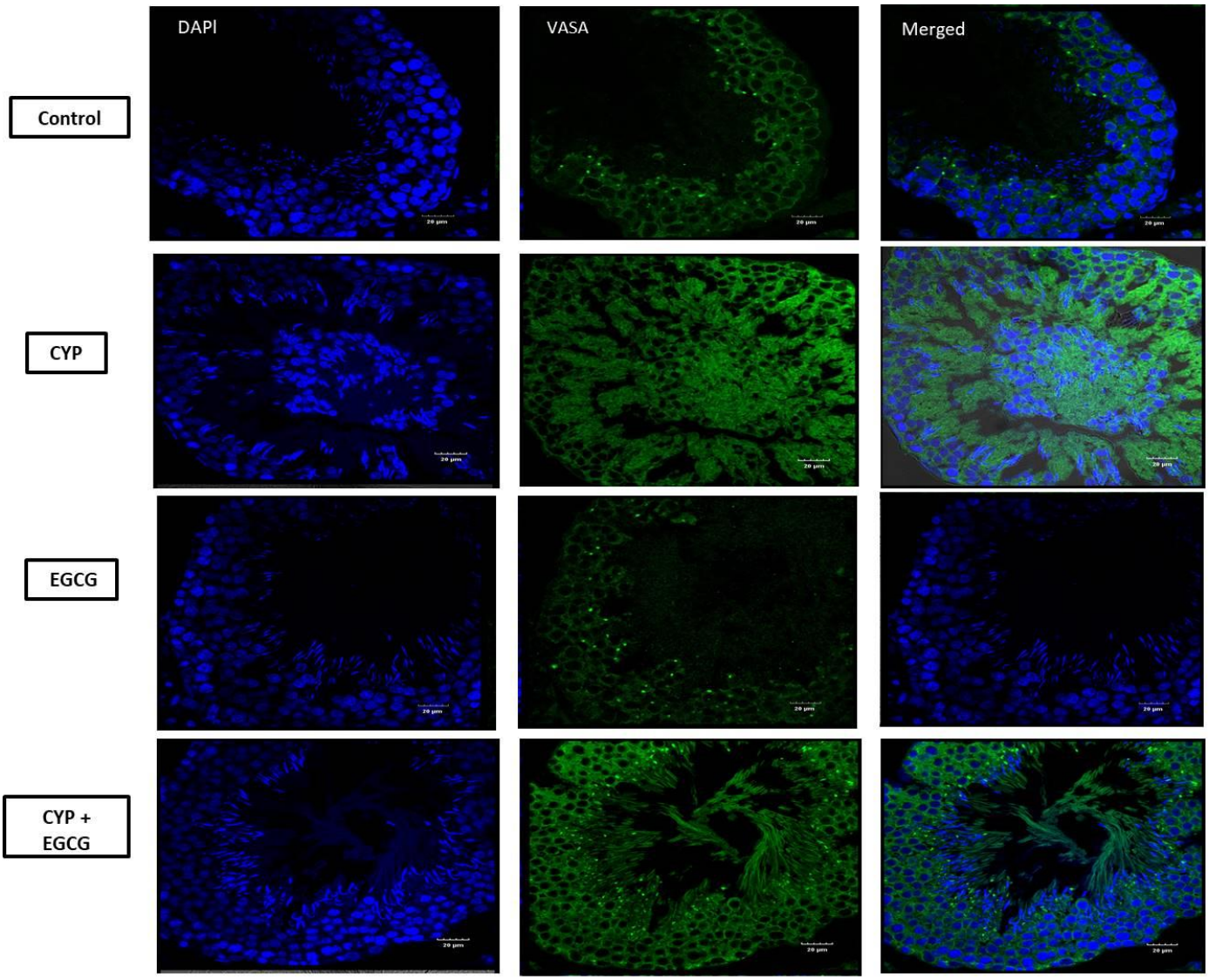

Figure 1: Immunolocalization of the germ cell marker VASA (green) in testicular sections of F1 male rats at PND 75 upon perinatal exposure to CYP. EGCG supplementation for 60 days in CYP-exposed adult F1 males restored germ cell integrity. Nuclei were counterstained with DAPI (blue). Magnification: 60×; Scale bar = 20 µm.

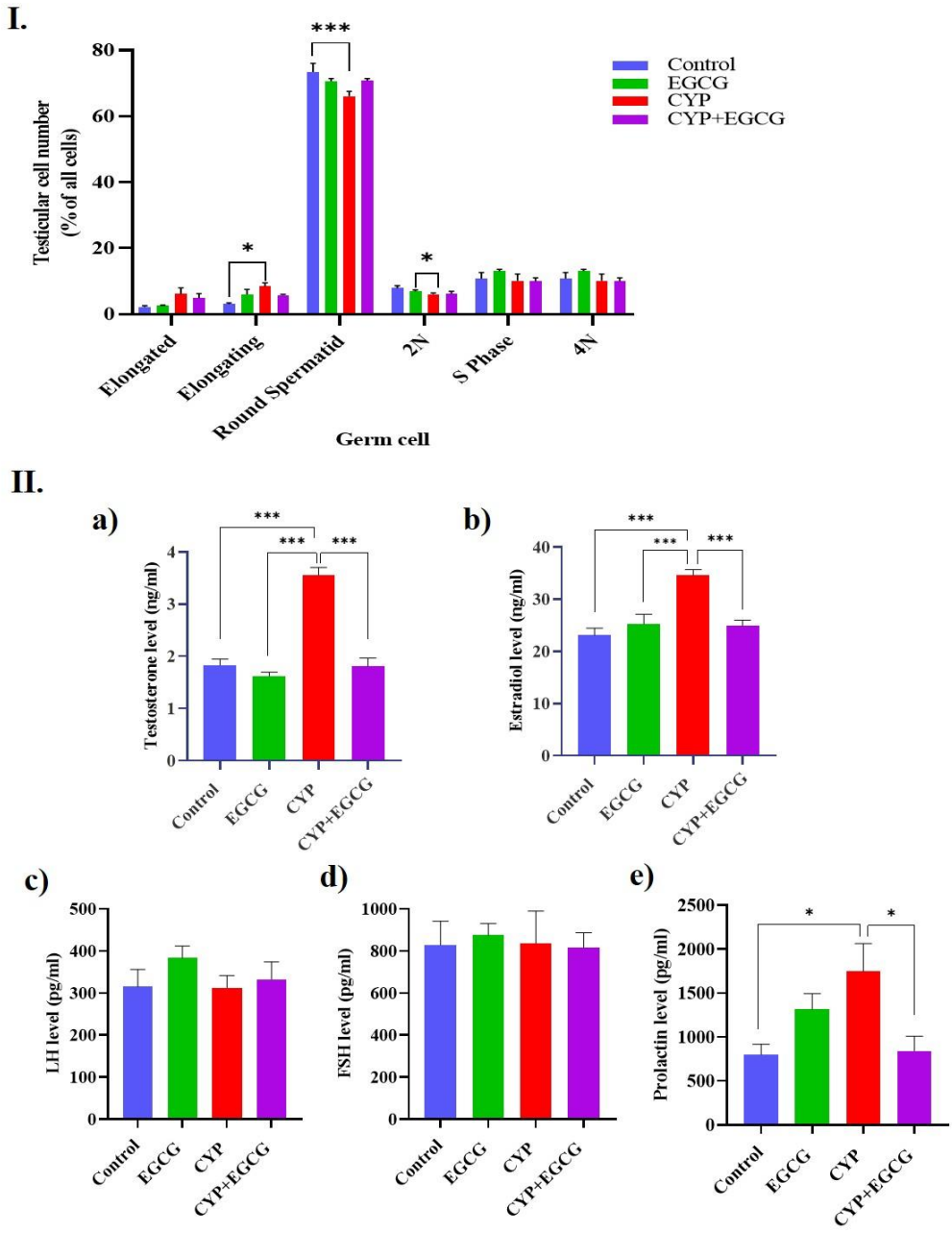

Figure 2: (I) Effect of EGCG on testicular germ cell populations (Mean ± SE, n=6), *p ≤ 0.05, ***p ≤ 0.0001. (II) Serum a) testosterone, b) estradiol, c) LH, d) FSH and e) prolactin levels in control, EGCG, perinatally exposed CYP and CYP+EGCG exposed male rats. Mean ± SE (n=6). *p ≤ 0.05, **p≤0.001.

2.8 Investigation of Potential Chemotactic Metabolites in the Follicular Fluid

Principal Investigator	:	**Priyanka Parte**
Project Associates	:	Durva Panchal, M T More
Collaborators	:	Grishma Desai, Nowrosjee Wadia Maternity Hospital, Mumbai
		Priyanka Vora, Ankoor Fertility Clinic, Mumbai
Duration	:	2019-2024

Building on our previous findings (Annual report 2023-2024, pp. 52-54) that ovulatory-phase oviductal fluid (OV-OF) exhibits stronger sperm chemoattraction than pre-ovulatory oviductal fluid (Pre OV-OF), we aimed to characterize the OV-OF metabolite profile using Liquid Chromatography-

Tandem Mass Spectrometry (LC-MS/MS). Hydrophilic and hydrophobic metabolites from rat PreOV-OF and OV-OF were extracted using the Metabolite, Protein, Lipid Extraction (M-PLEX) protocol. Metabolomic profiling was done using hydrophilic interaction liquid chromatography (HILIC-MS/MS) and reversed-phase liquid chromatography (RPLC-MS/MS) in both positive and negative ion modes. Our analysis revealed several metabolites with potential roles as odorants, odorant receptor (OR) agonists, leukocyte chemoattractants, or fertility modulators. Odorants and odorant-like metabolites are gaining importance for their role in guiding sperm behavior, particularly through interaction with ORs, which were first identified on human sperm (Flagel et al., 2015). Given this, we identified few metabolites that were significantly increased during ovulation and had prior evidence supporting their function as odorants. These were subjected to molecular docking analysis against all known sperm-expressed ORs to predict receptor-binding affinities and potential interactions. Among these, 3-phenylpropyl isovalerate (CIV) emerged as the top candidate ligand, exhibiting the highest binding affinity with the sperm-expressed odorant receptor OR10J1 (−8.5 kcal/mol), indicating a strong ligand–receptor interaction. To experimentally validate the docking predictions, chemotaxis assays were conducted to assess sperm responses to CIV gradients. Prior to evaluating chemotactic responses, we assessed the potential cytotoxic effects of CIV on sperm. Capacitating sperm were incubated with different concentrations of CIV (0.1mM, 1mM, and 10mM), and sperm motility and viability were evaluated at 10-, 20-, 30-, and 45-min post-incubation. At all tested concentrations and time points, both sperm motility and viability remained comparable to the media control, indicating that CIV did not exert cytotoxic effects or impair sperm motility (Fig. 1A and 1B). To evaluate the chemotactic potential of CIV, capacitating sperm were exposed to gradients of 0.1 mM, 1 mM, and 10 mM CIV. Sperm migration showed no significant increase in the percentage of cells moving along the ascending gradient (Fig. 2A), nor in their mean straight-line velocity (VSL), compared to the media control at any tested concentration (Fig. 2B). These findings indicate that, despite the high *in silico* binding affinity of CIV for the sperm-expressed odorant receptor OR10J1, the compound does not elicit a chemotactic response under the assay conditions. In parallel, we evaluated whether CIV modulates intracellular calcium dynamics, a key regulator of sperm function. Capacitating sperm were loaded with Fura-2AM and exposed different concentrations of CIV (0.1 mM, 1 mM, and 10 mM). A significant increase in intracellular calcium levels ($[Ca^{2+}]_i$) was observed at 0.1 mM CIV compared to the DMEM control group (*$p < 0.05$), indicating calcium influx (Fig. 2C). No such response was noted at 1 mM or 10 mM, suggesting a concentration-dependent effect. Although 0.1 mM CIV did not induce chemotaxis, the observed calcium influx implies a potential role in other calcium-dependent sperm processes, such as capacitation or the acrosome reaction that warrants further investigation.

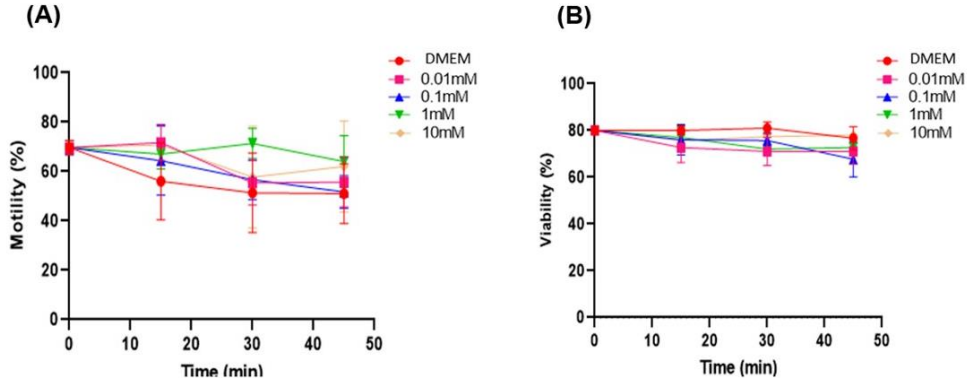

Figure 1: Sperm motility and viability following incubation with 3-phenyl-propyl isovalerate (CIV). Capacitating sperm were incubated with CIV at concentrations of 0.01mM, 0.1mM, 1mM and 10mM. Sperm motility (A) and viability (B) were assessed at 15-, 30-, and 45-min post-incubation. Data represent the mean ± SD from three independent experiments

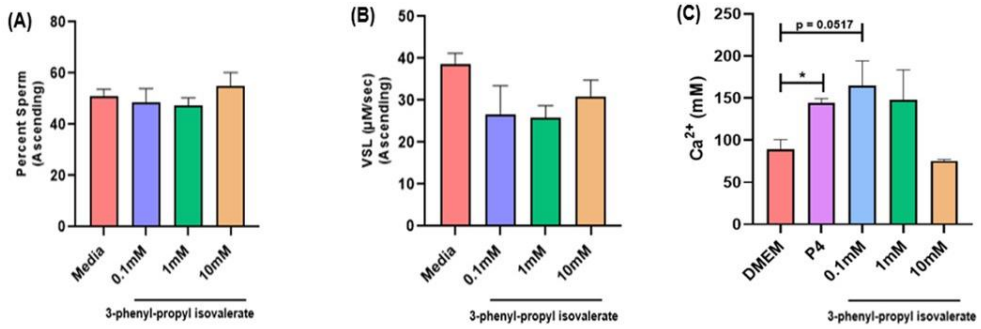

Figure 2: Chemotactic and calcium signaling responses of sperm to 3-phenylpropyl isovalerate (CIV). (A) Percentage of sperm migrating in the ascending direction toward gradients of CIV at 0.1 mM, 1 mM, and 10 mM, compared to the media control. (B) Mean straight-line velocity (VSL) of sperm moving up the CIV gradient at each concentration. (C) Intracellular calcium responses (expressed as 340/380 nm fluorescence ratio) following stimulation with CIV. Progesterone (10 µM) was used as a positive control (P4), and DMEM served as a vehicle control. Data are presented as mean ± SEM and are representative of three independent experiments.

2.9 Investigating Sperm 5hmC Landscape in Male Infertility and Recurrent Pregnancy Loss *(Partly Funded by Department of Biotechnology)*

Principal Investigator	:	**Kushaan Khambata**
Co-Principal Investigators	:	Priyanka Parte, Dipty Singh, R Gajbhiye, Deepti Tandon, Anushree Patil, S Pande, Shagufta Khan
Project Associate	:	Aarthi Prakashan
Collaborators	:	Vandana Bansal, Grishma Desai, M Pai, Nowrosjee Wadia Maternity Hospital, Mumbai
Duration	:	2024-2027

DNA methylation is an important mechanism by which sperm conveys its epigenetic information for embryo formation. Most of the sperm DNA methylation studies have been conducted in the context of 5-methylcytosine (5mC). However, several recent reports have indicated that sperm genome has also stable 5-hydroxymethylcytosine (5hmC) marks and that the paternal genome is more hydroxymethylated as compared to the maternal genome. The physiological role of this 5-hydroxymethylation mark in the sperm DNA remains to be elucidated. It is now commonly accepted that altered sperm methylome can lead to male infertility. However, in all these studies DNA methylation marks were studied by the traditional bisulfite sequencing methods, which cannot distinguish the 5mC and 5hmC marks. Hence, the sperm DNA methylation profiles studied so far are a cumulation of both these marks. Since 5mC and 5hmC have distinct genomic distribution and regulatory roles, there is need to investigate the 5hmC profiles independently in these conditions. There are very few studies investigating the sperm 5hmC marks in the context of male infertility and none exists for recurrent pregnancy loss (RPL). Hence, the present study aims to investigate the 5hmC marks at global and genome-wide level along with the DNA methylation and demethylation machinery in sperm in conditions of male infertility and RPL. Healthy men who have fathered a child in past 1-2 years were included in control group. Infertile men (with normal or abnormal semen parameters) who are unable to conceive for more than 1 year were included in Infertile group; while men whose wives are undergoing more than 2 consecutive miscarriages were included in RPL group. So far, 33 participants have been recruited in control group, 61 in infertile

group with 12 in normospermic (NS) infertile (i.e. unexplained infertility), 11 in asthenozoospermia (AS) group and 38 in oligoasthenozoospermia (OAS) group. Participants in RPL group are still being recruited. Sperm concentration and total counts were lower in OAS group as compared to control (Fig. 1A-B). Total and progressive motility and sperm mitochondrial membrane potential were reduced in AS and OAS groups (Fig. 1C-E). Percentage of sperms with DNA fragmentation (as detected by TUNEL assay) and defective chromatin compaction (CMA3 positive sperms) were higher in NS, AS and OAS (Fig. 1F-G), while percentage of sperms with histone retention (aniline blue positive sperms) were increased in OAS group (Fig. 1H). Further participant recruitment and epigenetic studies are underway.

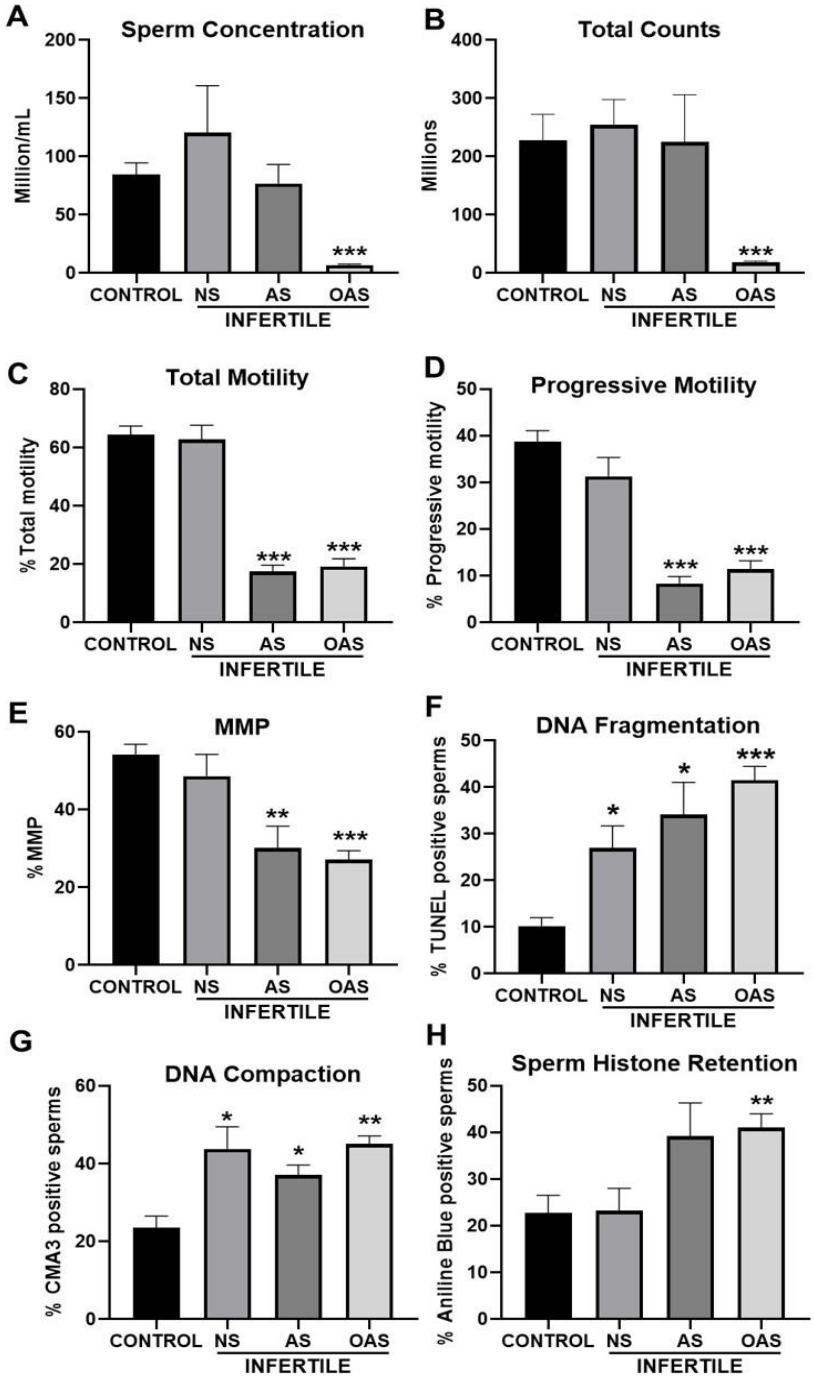

Figure 1: Semen Analysis Parameters. Sperm concentration (A), total counts (B), total (C) and progressive motility (D), sperm mitochondrial membrane potential (MMP) (E), DNA fragmentation (F), compaction (G) and sperm histone retention (H) in control (n=33) and infertile subgroups of normospermic (unexplained) infertile (n=12), asthenozoospermic (n=11) and oligoasthenozoospermic (n=38).

MICROBES, PATHOGENS AND REPRODUCTIVE HEALTH

3. MICROBES, PATHOGENS AND REPRODUCTIVE HEALTH

3.1 Evaluating the Inflammatory, Microbiome Profile and Co-infections in Women Diagnosed with Treatment Failure, Relapse or Recurrent Bacterial Vaginosis *(Partly Funded by Indian Council of Medical Research Extramural Grant)*

Principal Investigator	:	**Deepti Tandon**
Co-Principal Investigators	:	V Bhor, Kiran Munne, Clara Aranha
Project Associates	:	Anushree Patil, Shahina Begum, Rachna Dalvi
Collaborator	:	K Mali, N Mayadeo, Jyotsana Divedi, V Wani
Duration	:	2023-2026

This prospective study was jointly initiated in February 2023 by ICMR-NIRRCH, KEM Hospital, and the Brihanmumbai Municipal Corporation. The study, spanning over three years, aims to evaluate co-infections, longitudinal changes in vaginal microbiome profile and inflammatory profile, and factors influencing adherence to treatment among women experiencing relapse, recurrence, or treatment failure following standard bacterial vaginosis (BV) treatment. Recruitment is being conducted from two ICMR-NIRRCH family welfare clinics, the ICMR-NIRRCH infertility clinic, KEM Hospital, and Haji Mohammad Haji Sadu Municipal Maternity Home (BMC). A total of 541 patients have been recruited as of March 31st, 2025. The data analysis was carried out for 500 patients. Sociodemographic data of all the recruited participants were recorded. Based on Nugent scoring at first visit, 166 (33.2 %) patients are classified as BV, 172 (34.4%) as intermediate, and 162 (32.4%) as the normal group. The patients were treated with syndromic management with antibiotics at the time of recruitment (F0). These 166 BV patients are followed further at six time points (F1 to F6) at different intervals: 7 days, 1 month, 3 months, 6 months, 9 months, and 1 year, respectively. The numbers of BV patients followed up are 82.5%(n=137), 72.8%(n=121), 53.6%(n=89), 36.7%(n=61), 30.1%(n=50), and 23.4%(n=39) respectively from F1 to F6. The BV participants who were near to or completed their follow ups, were classified into two broad groups called treatment responders comprising Remission 17 (10.2%) group and Treatment non-responders with Relapse 17 (10.2%), Recurrent 3 (1.8%) and treatment failure 5 (3.01%) groups in response to the syndromic management based on their Nugent score and clinical symptoms. To evaluate coinfections in this cohort, total of 221 (44.2%) women had candidiasis, out of which 145 were identified in culture only and 8 in Gram stain only and 68 in both. Different *candida* species and their percentage prevalence are shown in the Fig. 1 and 2 respectively. Amongst those women with BV (n=166), 100 (60.24%) had candidiasis. This cohort of BV patients was also classified based on the *Candida* detection during their follow up visit. In 166 BV positive samples, 160 samples were subjected for multiplex PCR assay for coinfection. Out of these 119 (74.4%) patients had STI co-infection. Multiple infections are common in STI condition. Indeed, we observed dual, triple and four infections in the cohort. The prevalence of different STIs is depicted (Fig. 2). Cytokine profiling using multiplex ELISA was performed on cervico-vaginal lavage samples collected at baseline (F0) and post-treatment (F1), as well as from approximately 35 participants at various follow-up time points, categorized based on treatment response. Additionally, next-generation sequencing of the 16S rRNA V3-V4 amplicon regions was conducted on three time-point samples from these 35 patients to assess similarities and differences in microbial composition across participant groups. The study is currently ongoing.

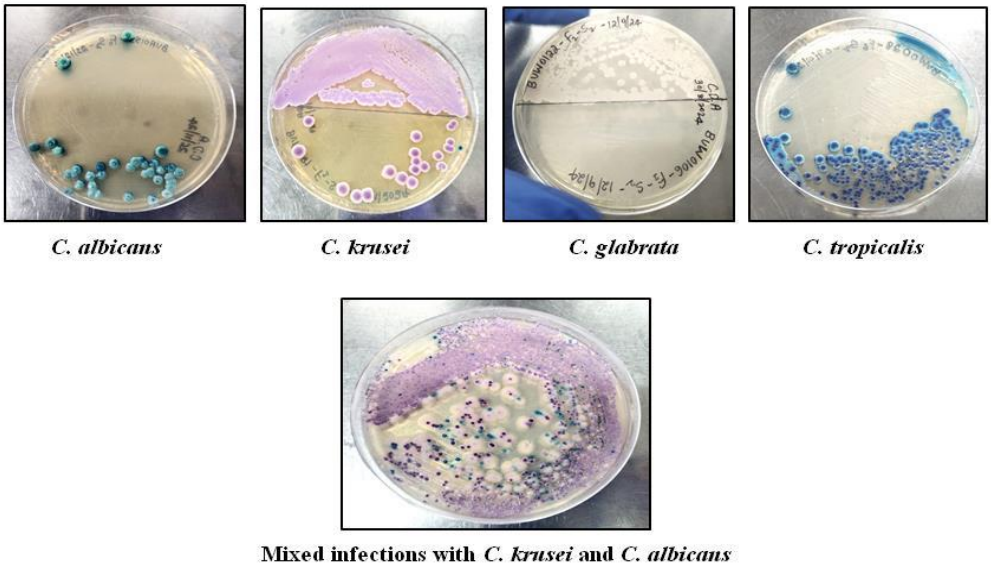

Figure 1: Different species of *Candida* on differential agar

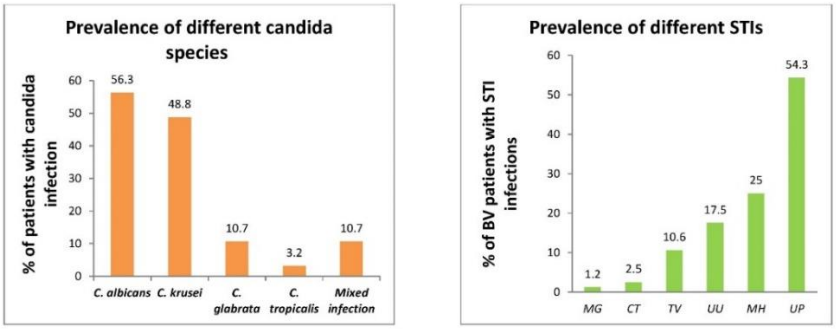

Figure 2: Graphs depicting the prevalence of *Candida* and STI co-infections

3.2 Integrated Analyses of Genomic Scale Metabolic Models and Omics Profiles to Capture the Host-Pathogen-Environment Interplay of *Candida* sp. *(Partly Funded by Science and Engineering Research Board)*

Principal Investigator	:	**Susan Thomas**
Co-Principal Investigators	:	Taruna Madan, KV Venkatesh
Project Associates	:	Kshitija Rahate
Duration	:	2021-2024

Candida spp. are opportunistic pathogens existing in humans as commensals under healthy host conditions. They have the ability to cause superficial (candidiasis) as well as deep-seated infections (candidemia) in virtually every organ of the human body. The increasing burden of *Candida* infections worldwide found this pathogen a prominent place on the fungal priority pathogens list released by the World Health Organisation in 2022. Increasing resistance to the limited array of antifungal drugs available to effectively tackle these infections makes *Candida* spp. a significant public health challenge. The present study aims to understand the host-pathogen interactions in the human vaginal niche conditions at the global level using multi-omics analyses. In the previous year, an *in vitro* model of host-pathogen interactions in vulvovaginal candidiasis (VVC) was generated by co-culture of human vaginal epithelial cell line (A-431) and *C. albicans* (CAL) in conditions mimicking the vaginal niche. In the reporting year, complete proteomic (LC-MS/MS), metabolomic (LC-MS/MS) profiles of the host (A-431) and pathogen (CAL) grown in co-culture were generated and compared to that of monocultures at

the end of 3 hours and 6 hours. This multi-omics data revealed several metabolic, immune, disease and signaling pathways to be perturbed in the host as well as the pathogen indicating their role in VVC progression (Fig. 1 and 2).

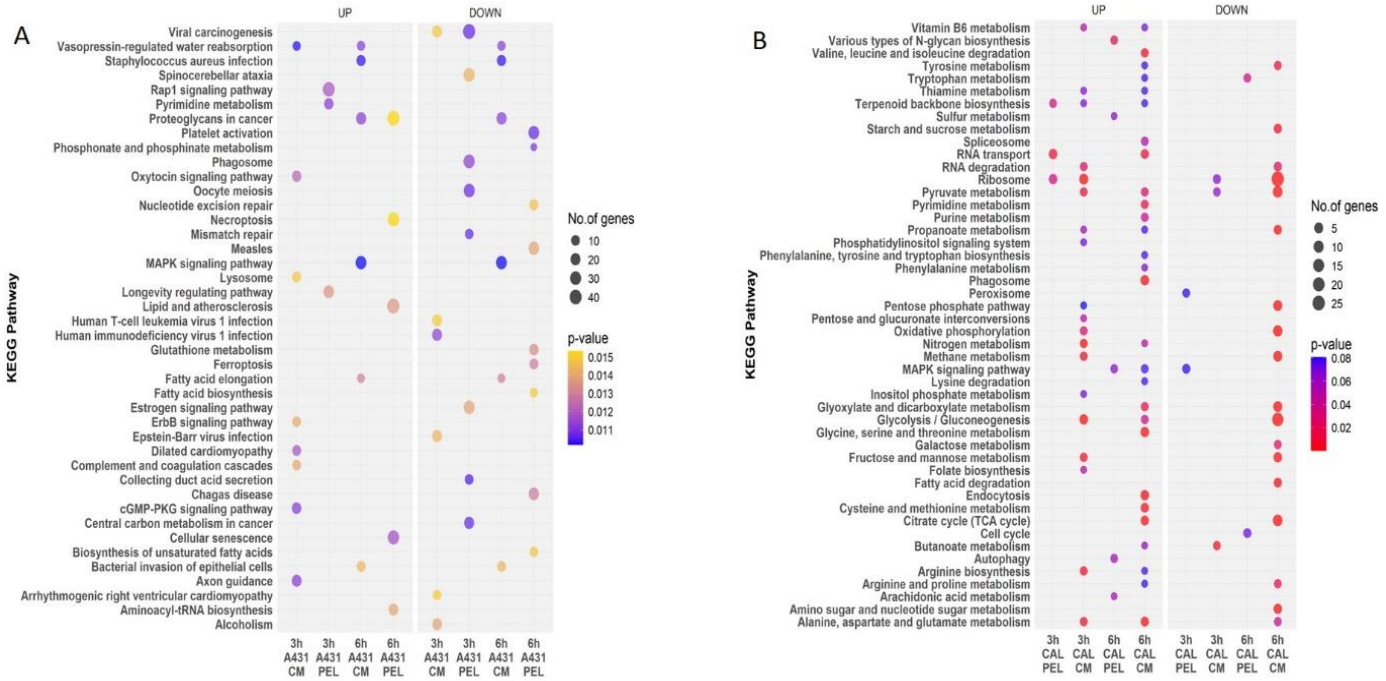

Figure 1: Pathways enriched in (A) Host cell line: A-431; (B) Pathogen: *C. albicans*, after untargeted proteomics analysis

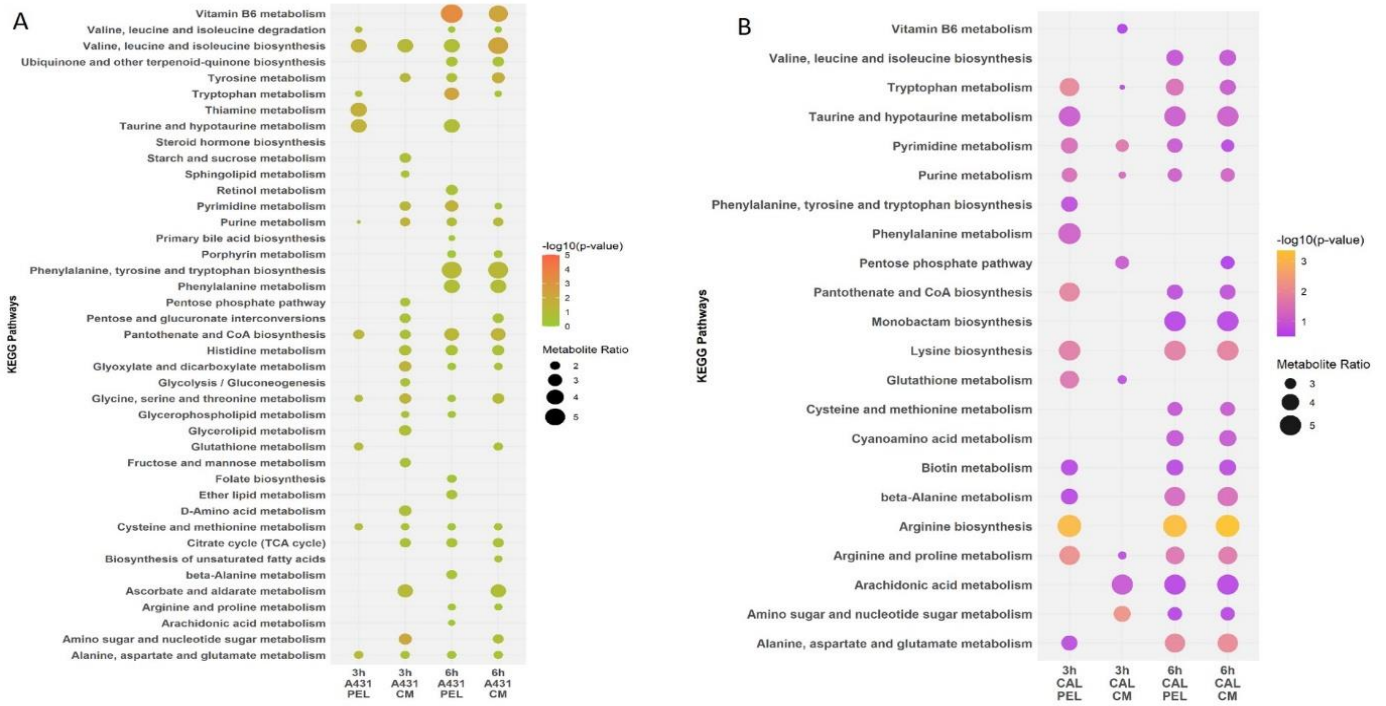

Figure 2: Pathways enriched in (A) Host cell line: A-431; (B) Pathogen: *C. albicans*, after untargeted metabolomics analysis

3.3 Exploring the Association of Cervico-vaginal Microbiome with Transient and Persistent High-Risk HPV Infection and Cervical Precancerous Lesions

Principal Investigator	:	**Kiran Munne**
Co-Principal Investigators	:	Anushree Patil, V Bhor
Project Associates	:	Anamika Akula, Deepti Tandon, Shahina Begum
Collaborators	:	Sharmila Pimple, S Biswas, Tata Memorial Hospital, Mumbai
Duration	:	2023-2026

Persistence of the Human Papillomavirus (HPV) is essential for the development of high-grade cervical intraepithelial neoplasia and cervical cancer and factors that correlate with higher persistence rates include age, parity, immunodeficiency, smoking, oral contraceptives and *Chlamydia trachomatis* infection. Emerging evidence indicates that cervicovaginal microbiota plays a substantial role in the persistence or regression of HPV and subsequent disease. This prospective observational cohort study was planned with an objective to study the association of cervicovaginal microbiome with transient and persistent high-risk HPV infection. Cohort of high risk HPV positives and negatives enrolled in a previous completed study on screening of cervical precancers and cancers by molecular HPV method are being followed for persistence or clearance of HPV infection and changes in vaginal microbiota. During the reporting year, follow up camps were organised for women previously screened for cervical precancers and cancers and total 41 participants have been recruited at Mumbai and Dahanu sites. Their socio-demographic and clinical history have been recorded in case record forms. HPV samples and PAP smears were sent to Tata Memorial Hospital for reporting. Based upon the previous and this study (at least 1-year gap) the participants have been classified as persistent HPV (n=9), transient HPV (n=19) and HPV-negative group (n=13). The samples will be tested for microbiome analysis by sequencing and cytokine assay.

3.4 Gut Microbiome - Immune Signatures of HIV-TB Coinfection

Principal Investigator	:	**V Bhor**
Project Associates	:	P Devadiga, Nandini Kasarpalkar, Shilpa Bhowmick, V Patel, Taruna Gupta, Nupur Mukherjee, Kiran Munne
Collaborators	:	Vidya S Nagar, Priya Patil, Grant Medical College and JJ Group of Hospitals Jayanthi Shastri, Sachee Agrawal, TN Medical College and BYL Nair Hospital
Duration	:	2021-2025

HIV infection increases susceptibility to active tuberculosis (TB), primarily due to reactivation of latent TB infection (LTBI). Our previous work suggests that gut microbiome dysbiosis and immune dysregulation are likely to be important contributors to this reactivation. Integrin α4ß7, the gut-homing receptor and alternate HIV receptor, facilitates the migration of immune cells to Gut-Associated Lymphoid Tissue (GALT) and plays a role in HIV acquisition, pathogenesis, and reservoir formation. Altered expression of integrin α4ß7 in the context of HIV and/or LTBI may disrupt gut immune cell trafficking and function. Although gut microbiota are linked to immune activation in HIV and TB infection independently, the manner in which they affect gut homing immune cells during HIV-TB coinfection remains unclear. In view of this, we aimed to profile α4ß7+ i.e. gut homing immune cell subsets in HIV-infected individuals with LTBI and active TB (aTB), and to examine their association with gut microbiome composition. A total of 77 ART naïve HIV infected individuals i.e. HIV infected individuals with either latent, HIV+LTBI+ (n=30) or active TB infection, HIV+ aTB (n=17) or without coinfection, HIV+LTBI- (n=30) were recruited as study participants from J J Hospital and Nair Hospital. The gut microbiome composition of all study participants was determined by 16S rRNA sequencing

while the frequency of gut homing naïve and memory T cell subsets was characterized by multi-parametric flow cytometry. A significant increase in the frequency of integrin β7+ terminally differentiated 2 CD8+ T cells (TD2) was observed in individuals from the HIV+LTBI+ group compared to those in the HIV+LTBI- group (Fig 1b).

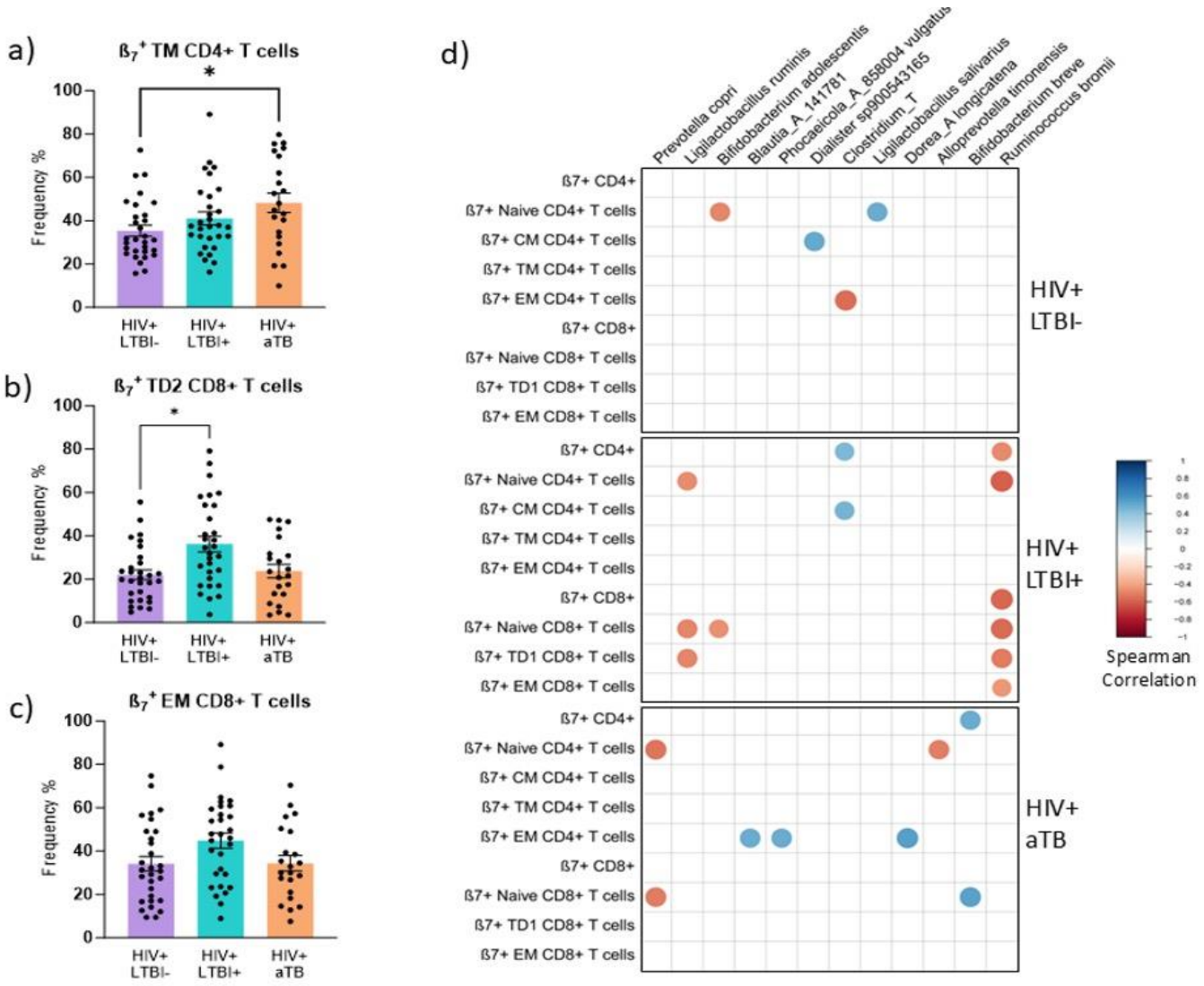

Figure 1: Gut-homing memory T-cell frequencies and their correlations with gut microbiota. (a) Mean ± SEM frequency of transitional memory CD4⁺ T cells expressing integrin β7 across HIV+LTBI- (n = 30), HIV+LTBI+ (n = 30) and HIV+ aTB (n = 17) groups. (b) Mean ± SEM frequency of terminally differentiated 2 CD8⁺ T cells expressing integrin β7 in the same groups. (c) Mean ± SEM frequency of effector memory CD8⁺ T cells expressing integrin β7 across study groups. For panels a–c, differences between groups were assessed by Kruskal–Wallis test with Dunn's post-hoc correction; $p < 0.05$. (d) Spearman correlation heatmap depicting associations between integrin β7⁺ T-cell subsets and the relative abundance of dominant gut microbial taxa in each group; only correlations with $p < 0.05$ are shown.

Further, the frequency of integrin β7+ transitional memory (TM) CD4+ T cells was significantly higher in HIV+ aTB group compared to the HIV+LTBI- group (Fig. 1a). Group specific significant correlations were observed between gut homing immune cells and microbiota with a higher number of correlations (Fig. 1d) found in HIV+LTBI+ group compared to other groups. A significant negative correlation specific to HIV+LTBI+ group was observed between abundance of *Ruminococcus bromii* with frequency

of all integrin β7+ expressing CD8+T memory cell subsets (r= –0.43 to -0.57) as well as integrin β7+ naïve CD4+ T cells (r = -0.60). Only Clostridium sp. showed a positive correlation with integrin β7+ CM CD4+ T cells (r = 0.47) in HIV+LTBI+ group. In HIV+aTB group specifically, integrin β7+ effector memory (EM) CD4+ T cells correlated positively with *Blautia sp*. (r = 0.49), *Phocaeicola vulgatus* (r = 0.50) and *Dorea longicatena* (r = 0.54). Taxa like *Prevotella copri* correlated negatively with integrin β7+ naïve CD4+ (r = -0.53) as well as CD8+ (r =-0.52) T cells. These findings suggest that the HIV+LTBI+ group exhibits a higher frequency of gut-homing TD2 $CD8^+$ T cells, which may lead to recruitment of cytotoxic $CD8^+$ effector cells to the gut mucosa in disease states. These patterns point to a nuanced, disease severity specific crosstalk between the gut microbiome and gut mucosal T cell migration in HIV/TB co-infection These results highlight potential benefits of targeted microbiome modulation to preserve gut mucosal immunity.

3.5 Longitudinal Cohort Study of Lactating Women to Assess Impact of SARS-CoV-2 Exposure and Vaccination on Systemic and Vertically Transferred SARS-CoV-2 Specific Immunity in the Mother-Infant Dyad *(Partly Funded by Indian Council of Medical Research)*

Principal Investigator	:	**V Bhor**
Co-Principal Investigator	:	V Patel
Project Associates	:	Gauri Bhonde, Sindoora Balan, Hajra Ansari, P Devadiga, Pranita Nikam, Dhanashree Jagtap
Collaborator	:	Purnima Satoskar, Nowrosjee Wadia Maternity Hospital
Duration	:	2023-2025

Lactation represents a distinct physiological phase in women, affecting their vulnerability to SARS-CoV-2 infection. Maternal immunity is essential for protecting newborns against COVID-19, making it critical to understand how immune protection is transferred from mother to infant. This study investigates the characteristics and mechanisms of SARS-CoV-2-specific maternal immunity transmission—through cord blood, peripheral blood, and breast milk—taking into account both natural infection and vaccination history. During the reporting period, a total of 97 pregnant women admitted at Nowrosjee Wadia Maternity Hospital, Mumbai, for delivery and recruited as study participants were subjected to assessment of anti-SARS-CoV-2 specific humoral immunity. All the study participants were vaccinated against SARS-CoV-2, with the majority having a history of natural infection. Venous blood, cord blood and breast milk samples were obtained from these women, post-delivery. The samples were processed to obtain plasma in case of venous blood and cord blood (VBPL and CBPL respectively) and supernatant in case of breast milk (BMSN) and batch processed for quantitation of antibody levels by ELISA. All the study participants tested positive for anti-SARS-CoV-2 IgG antibodies, regardless of whether they had a confirmed history of infection or vaccination. This broad seropositivity underscores a robust humoral response postpartum in the study population.

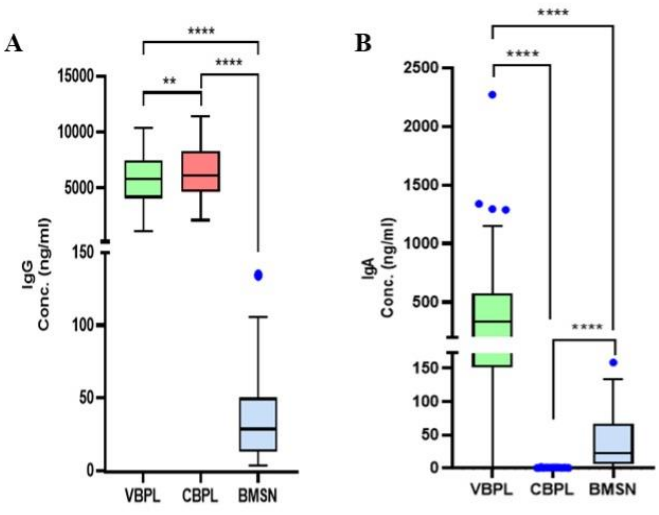

Figure 1: Levels (ng/ml) of anti-SARS-CoV-2 IgG and anti-SARS-CoV-2 IgA in venous blood plasma, cord blood plasma, & breast milk supernatant samples at baseline (n=97); Statistical significance was calculated by Dunn's multiple comparisons test; *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$; and ****, $p < 0.0001$.

Notably, none of the participants was seronegative. This points to a widespread level of prior exposure or vaccine-induced seroconversion. This is supported by the consistent detection of IgG antibodies not just in VBPL and CBPL, but also in BMSN, which is a less commonly analyzed sample in the context of serological testing. Higher levels of anti-SARS-CoV-2 IgG were detected in cord blood and peripheral blood compared to breast milk (Fig. 1a). However, cord blood had the highest levels of anti-SARS-CoV-2 IgA followed by venous blood and breast milk had almost negligible levels (Fig. 1b). These observations underscore the durability and persistence of antibody-mediated immunity even two to three years following initial exposure. Importantly, the data indicate that lactating mothers can provide a certain degree of immunological protection to their infants through breast milk. However, the magnitude of this passive immunity appears to be lower than the levels observed in maternal peripheral and cord blood, highlighting a differential transfer of immunity across compartments. While the results of this cross-sectional analysis immediately post-delivery are insightful, longitudinal analysis over the exclusive breast feeding period are likely to contribute to a better understanding of the maternal-infant immunity against SARS-CoV-2 and also possibly inform vaccination strategies in future.

3.6 Evaluating the Utility of Molecular Workflow for Establishing Microbial Profile and Antimicrobial Resistance for Neonatal Sepsis in a Tertiary Care Setting in Maharashtra

(Funded by ICMR Intramural)

Principal Investigator	:	**Kiran Munne**
Co-Principal Investigator	:	Suchitra Surve, V Bhor
Project Associates	:	Sharmila Kamat, Shahina Begum, P Venkateshwaran, M Periyappa
Collaborator	:	Sudha Rao, Dhruv Mamtora
Duration	:	2025-2027

Sepsis is the third leading cause of neonatal mortality in developing countries. Despite advances in clinical research in this area, we still lack accurate diagnostic tools for neonatal sepsis, complicating the management of this condition. Reports of multidrug-resistant bacteria causing neonatal sepsis in developing countries are increasing, particularly in intensive care. This study is planned with an aim to study the utility of molecular workflow for establishing microbial profile and antimicrobial resistance for neonatal sepsis. 16S rRNA PCR will be used for the rapid detection of the bacterial cause of neonatal sepsis. This will be followed by identification of microbial profile and antibiotic resistance genes by sepsis flow chip assay and NGS (nanopore sequencing), which will be compared with the blood culture results. The study will provide the insight regarding the rapid and comprehensive detection of agents causing neonatal sepsis by molecular methods, which can lead to shorter antibiotic courses, and NICU stays. The project has been recommended for intramural funding and will be initiated after receipt of funds.

3.7 Development of Nucleic Acid Amplification (NAAT) Based Test for Detection of Common Vaginal Infections Leading to Preterm Births

(Partly Funded by ICMR-Medical Young Innovation Fund)

Principal Investigator	:	**D Modi**
Collaborators	:	Purnima Satoskar, Nidhi Bala, Nowrosjee Wadia Maternity Hospital, Mumbai
Duration	:	2021-2024

A systematic review and meta-analysis was done to identify various infections and their relation to preterm births. The search terms included preterm delivery, bacterial vaginosis, vaginal infection, Mycoplasma, sexually transmitted infections, *Gardnerella vaginalis*, *Klebsiella pneumonia*, *Chlamydia trachomatis*, *Lactobacillus iners*, Group B *Streptococci*, *Escherichia coli*, *Enterococci* and microbiome. Based

on this we selected common bacterial organisms related to preterm delivery. The vaginal microbiome plays a key role throughout the life of women. It is also a critical determinant of successful pregnancy and health of the newborn. The vaginal microbiota is mainly dominated by lactobacilli which protects the woman from other bacterial infections. Any alteration or reduced dominance of lactobacilli species leads to dominance by opportunistic infections. This leads to preterm birth (>37 wks) stillbirth or death of the neonate perinatally. Approximately 15 million pre-term deliveries have been estimated during 1990-2010 worldwide, wherein India constituted 24% of these with the highest percentage of PTB. Though, traditional microbiological methods are "gold standard", they are time-consuming and have inadequate efficiency in evaluating patients with bacterial vaginal infections. Thus, We have developed assays for the detection of common vaginal infections that lead to preterm births. The Nucleic Acid Amplification (NAAT) based multiplex PCR assay for the identification of common microorganisms associated with preterm births. Based on systematic review and meta-analysis, we developed multiplex PCR assay after synthesizing primers against specific genes of the microorganisms. Thereafter, the primers of *Lactobacillus iners*, *Klebsiella pneumoniae*, *Escherichia coli*, Group B *Streptococcus* (GBS) and *E. faecalis*, *G. vaginalis*, *Chlamydia trachomatis*, *M. hominis*, *S. aureus*, *M. genitallium*, *N. gonorrhoeae*, *Ureaplasma urealyticum* were individually standardized in a singlet PCR at different temperatures. All were amplified at their respective molecular size. We standardized and optimized the multiplex PCR from the standard strains of microorganism's DNA. This study is a translational research project where previous laboratory findings are translated in the form of technology and validated for its clinical utility. This assay will be a positive step for identifying affected patients. The multiplex PCR data indicates that out of 100 samples *L. inners* 30%, *G. vaginalis* 16%, *K. pneumonia* 17, *E. coli* 13%, *E. faecalis* 8%, *S. aureus* 7%, GBS 7%, *M. hominis* and *Chlamydia trachomatis* 1%. This multiplex PCR is sensitive, accurate, less time consuming and helps to detect vaginal infections in pregnant women in India. This work has generated novel information on vaginal infections in the Indian perspective and enhance ante- natal screening in the clinical setting, improve pregnancy outcomes and leads to better maternal and child health.

3.8 National Network Project for ICMR-National Institute for Research in Reproductive and Child Health *(Funded by Department of Biotechnology)*

Principal Investigator	:	**Susan Thomas**
Co-Principal Investigators	:	Shahina Begum, Suchitra Surve
Project Associates	:	Priyanka Sahajwani, D Gandhi, Ulka Gawde, Sailee Shahane, S Shinde
Collaborators	:	Ira Shah, Bai Jerbai Wadia Hospital,Mumbai Sushma K, St. John's National Academy of Health Sciences, Bangalore Tulika Goswami, Mahanta, Assam Medical College, Dibrugarh Chandrakanta, King George's Medical College, Lucknow Suyash Awate, Indian Institute of Technology-Bombay, Mumbai
Duration	:	2023-2028

This is a registry-based study to capture information related to childhood Tuberculosis (TB) from four different geographical areas. The receipts of fund for sites were at different time points based on submission of document and availability of funds at DBT. ICMR-NIRRCH has successfully completed the development of the Electronic Patient Record (EPR)-based software system. The software is now ready to be tested across all participating study sites. Once the testing phase is completed, it will be implemented for regular use in recording new cases. Furthermore, all previously documented cases that were recorded using paper-based Case Record Forms (CRFs) will also be entered into the system, ensuring a comprehensive and centralized digital database of study participants. Meanwhile, all sites are working with paper-based CRF and storing it safely at respective study sites. At King George's Medical University (KGMU), Lucknow, 81 participants have been enrolled since July 2024, with 11

deaths and 70 participants under monthly follow-up. Bai Jerbai Wadia Hospital (BJWH), Mumbai, has enrolled 65 drug-sensitive and 8 drug-resistant pediatric TB patients, with 2 excluded due to latent TB diagnoses. St. John's Hospital (SJH), Bangalore, received project funds in August 2024, facilitating the commencement of all necessary activities. Recruitment of project staff began on December 9, 2024, and to date, three participants have been enrolled. Assam Medical College (AMC), Dibrugarh, received funding in December 2024, resulting in delays in participant recruitment due to budget constraints. Thus far, two participants have been enrolled and are currently under follow-up. The Indian Institute of Technology-Bombay is analyzing retrospective radiological data from KGMU, covering 38 TB and 155 non-TB chest X-rays.

3.9 Evaluation of HIV-1 Subtype C Infection Dynamics, Therapeutic Responses and Reservoir Distribution *In vivo* (*Partly Funded by DBT and India Alliance DBT Wellcome Trust)*

Principal Investigator : **V Patel**
Project Associates : Snehal Kaginkar, Ashashree Sahoo, Tejaswini Pandey, P Gurav, Jyoti Sutar, A K Singh, Leila Remling-Mulder, Ella Barnett, S Panickan
Collaborator : R Akkina, University of Colorado, Fort Collins, USA
Duration : 2023-2025

While HIV-1 subtype C (HIV-1C) is the most prevalent and widely distributed subtype in the HIV pandemic, nearly all current prevention and therapeutic strategies are based on work with the subtype B (HIV-1B). HIV-1C displays distinct genetic and pathogenic features from that of HIV-1B. Thus, treatment approaches developed for HIV-1B need to be suitably optimized for HIV-1C. A suitable animal model will help delineate comparative aspects of HIV-1C and HIV-1B infections. Here, we used a humanized (human hematopoietic stem cell, hu-HSC) mouse model to evaluate HIV-1C infection, disease progression, response to anti-retroviral therapy (ART) and viral rebound following therapy interruption. A limited comparative study with a prototypical subtype B virus was also performed. Viral infection, immune cell dynamics, acquisition of anti-retroviral therapy (ART) resistance and anatomical reservoir distribution following extended and interrupted therapy were compared. In comparison, lower early plasma viremia was observed with HIV-1C, but with similar rate of CD4+ T cell depletion as that of HIV-1B. Viral suppression by ART was delayed in the HIV-1C infected group with evidence, in one case, of acquired class wide resistance to integrase inhibitors, a critical component of current global therapy regimens. Also, HIV-1C infected animals displayed faster rebound viremia following ART interruption (ATI). Disparate patterns of tissue proviral DNA distribution were observed following extended ART and ATI suggestive of distinct sources of viral rebound. In this preliminary study, discernible differences were noted between HIV-1C and B with implications for prevention, therapeutics and curative strategies. Results also highlight the utility of the hu-HSC mouse model for future expanded studies in this context. Pursuant to the successful publication of our results in the internationally peer-reviewed journal 'Frontiers in Immunology' we have initiated the development of a humanized mouse model in the Institute which will be an invaluable tool to pursue HIV eradication and cure strategies as well as human immune dysfunction in other communicable and non-communicable diseases.

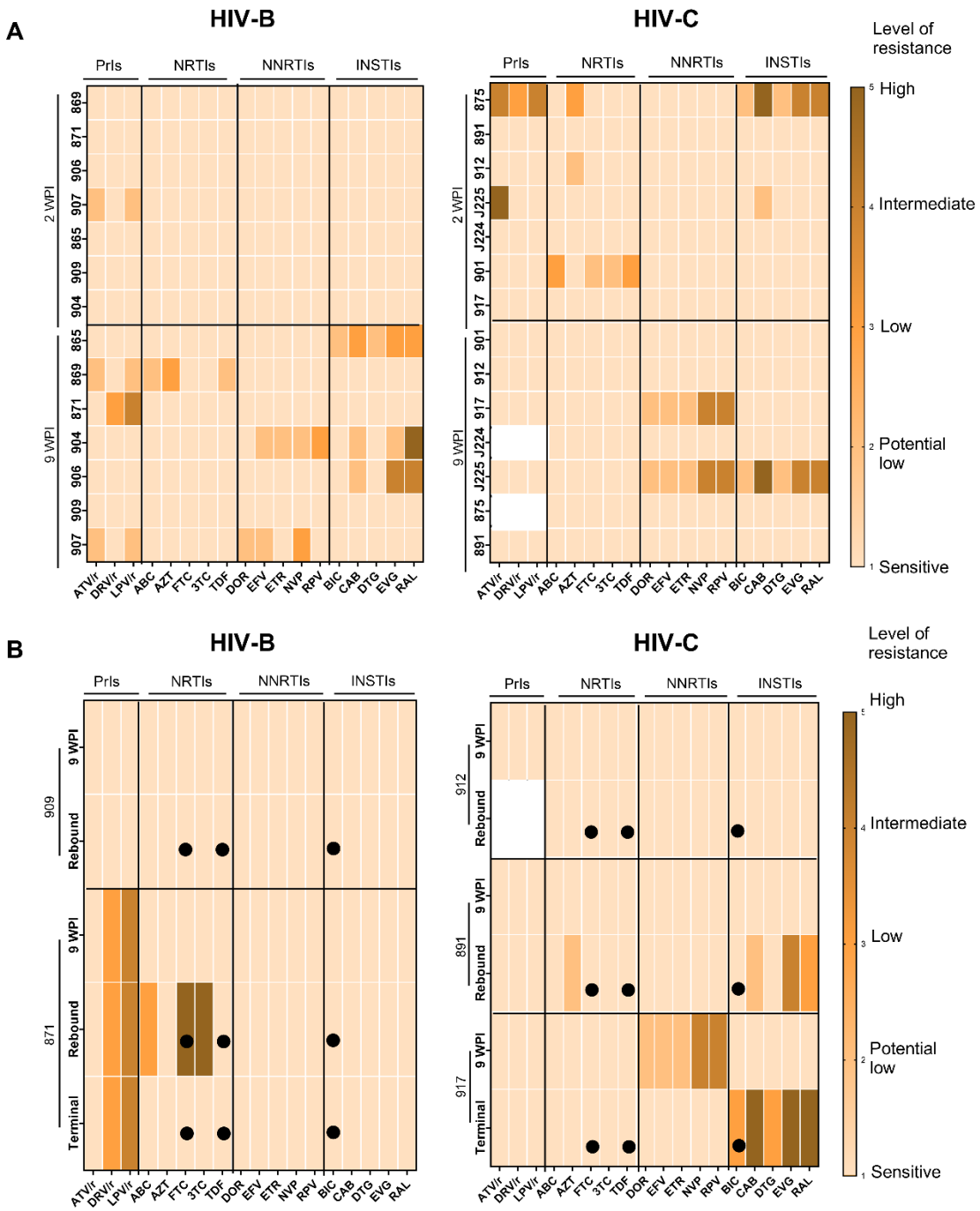

Figure 1: Assessment of drug resistance mutations in circulating viruses during pre-treatment and post-ART. Colour key indicates level of resistance with lighter to darker shades representing sensitive (no resistance), potential low level, low level, intermediate level and high level of resistance. (A) Heatmap of pol sequences indicating presence and level of DRM conferred resistance to classes of antiretroviral Protease Inhibitors (PrIs), Nucleoside Reverse Transcriptase inhibitors (NRTIs), Non-Nucleotide Reverse Transcriptase Inhibitors (NNRTIs) and Integrase Strand Transfer Inhibitors (INSTIs) with drugs on the X axis and animal IDs on the Y axis during infection phase (B) Heatmaps of longitudinally sampled animals from HIV-B (909 and 871) and HIV-C (912 and 891) groups in treatment release arm, and HIV-C animal 917 that received uninterrupted therapy. For each animal, ART drugs are listed on the X-axis and time points for DRM analysis are shown on the Y-axis along with animal IDs. Solid circles indicate the drugs administered during therapy.

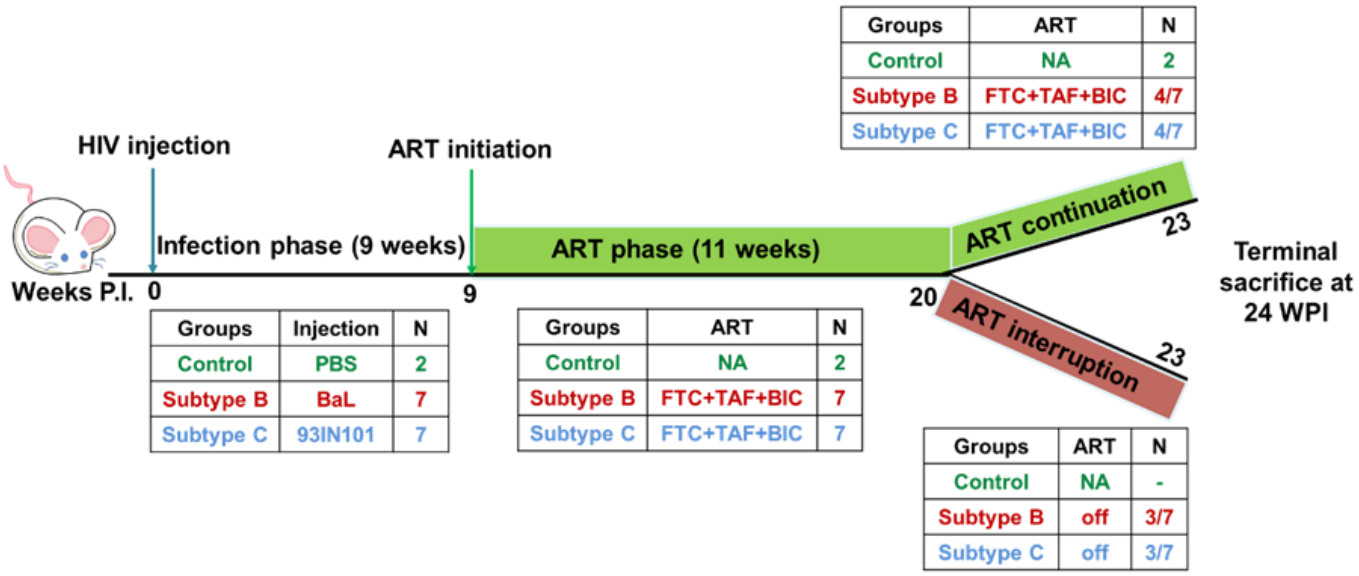

Figure 2: Schematics of experimental design: HIV infection was monitored in hu-mice for a total of 23 weeks. Hu-mice were classified into 3 groups. Uninfected (control, n=2), subtype B infected (HIV-B, n=7), subtype C infected (HIV-C, n=7). The study was divided in 3 phases. In the pre- anti-retroviral therapy phase (ART), up to 9 weeks post infection (WPI) was allowed to occur in the absence of ART. ART phase was initiated at week 9 in viremic mice and continued for 11 weeks i.e. 20 WPI. After ART phase, animals were divided into two study arms. In the ART continuation arm, 4 mice from HIV-B and HIV-C each were continued on ART for a further three weeks. In the second arm, the ART interruption arm, 3 mice from HIV-B and HIV-C each, were released from ART and monitored for viral rebound for 3 weeks. The study was terminated for all animals at 24 WPI.

3.10 Hospital-Based Surveillance of Acute Encephalitis Syndrome *(Funded by Indian Council of Medical Research)*

Principal Investigator : **V Bhor**
Co-Principal Investigator: V Patel
Project Associates : Anamika Dwivedi, Shreya Peddakolmi, Aishwarya Hankare, Nayana Ingole, Kasturba Hospital, Mumbai
Jayanthi Shastri, Centre for Excellence in Immunology Research, TN Medical College and BYL Nair Hospital, Mumbai
Collaborators : Uma Sundar, N D Karnik, H Bharote Lokmanya Tilak Municipal General Hospital and Lokmanya Tilak Municipal Medical College, Mumbai
Duration : 2023-2025

Advances in laboratory diagnostics have greatly enhanced the understanding of the infectious aetiologies of Acute Encephalitis Syndrome (AES) globally. However, these diagnostic tests are not widely utilized in many public sector clinical settings in India. Significant gaps thus remain about the knowledge and understanding of the burden, aetiologic spectrum, and risk factors associated with AES occurring in different epidemiological zones of the country. This study aims to characterize the infectious causes of AES among patients in heavily affected regions of India through a network of 21 tertiary care government teaching hospitals and their affiliated Virus Research and Diagnostic Laboratories (VRDLs) in India. The study site for Mumbai is Lokmanya Tilak Municipal General Hospital and Lokmanya Tilak Municipal Medical College (LTMGH and LTMMC), Sion Mumbai Sample collection commenced on 6th October 2024, following ethical

approval from the institutional ethics committees of ICMR-NIRRCH and LTMGH and LTMMC. Patients aged 1 year to < 65 years with high fever (>38˚C, duration not more than 5-7 days) and altered sensorium were enrolled in the study. Following screening and upon receipt of informed consent/assent/parental consent as applicable, a total of 53 participants were recruited. Out of these 10 were children and 43 were adults, with a male:female ratio of 37 : 16. The majority of patients belonged to the lower strata of society. Whole blood, EDTA blood, CSF and throat swab were collected from all the participants. A standardized testing algorithm employing both serological and molecular techniques for the diagnosis of a wide range of possible aetiologic agents of infectious AES was followed. Pathogens were grouped according to their reported incidence in decreasing order of priority. Pathogens of the highest priority - Malaria, Japanese Encephalitis, Scrub Typhus, Dengue, Chikungunya, and Measles are identified in level 1 through IgM ELISA. Level 2 comprised of pathogens such as HSV, Enterovirus, Varicella Zoster virus, Pneumococcus, *H. influenzae*, *Meningococcus*, Group B Streptococcus, E. coli detected through Biofire Meningitis/Encephalitis panel testing and Leptospira was detected based on IgM ELISA and PCR. The samples were processed for Mycobacterium tuberculosis under level 3 using GeneXpert at the clinical site while PCR based level 4 testing was performed for detection of Enterovirus from throat swab samples of the participants. Samples from 10% of the patients negative for the above mentioned pathogens will be subjected to NGS (Level 5) to identify infectious causes of AES, if any. Out of 53 patients, 15 tested positive for Leptospira, 2 for Chikungunya, 2 for *Mycobacterium tuberculosis*, 3 for *Streptococcus pneumoniae*, 1 for *Streptococcus agalactiae*, 1 for *Klebsiella pneumonia*, 1 for *Varicella zoster* virus and 1 for Malaria. However, etiology was unknown in 27 cases and further investigations will be conducted according to the study protocol. The lack of conclusive etiological identification in a majority of cases underscores the necessity for enhanced diagnostic capabilities and comprehensive surveillance to effectively address AES in India.

MATERNAL HEALTH

4. MATERNAL HEALTH

4.1 Impact of Mukta Shukti Bhasma and Saubhagya Shunti in Reversal of Bone Mineral Density among Lactating Women Consuming Traditional Diet Foods in Maharashtra: A Randomized Controlled Preliminary Clinical Study *(Partly Funded by CCRAS, Ministry of AYUSH)*

Principal Investigators	:	**Lalita Savardekar** **R. G. Reddy, CCRAS-CARI**
Co-Principal Investigators	:	Daksha Shah, Mangala Gomare, Vandana Bansal, S Timmanpyati, Vaishali Chandanshive, S Mohite, D Singh, A Jain
Project Associates	:	Shweta Hardas, Shilpa Chaudhary, Radhika Vora, Tanvi Gelye, A Shaikh, P Kumar, Yasashwi Wadekar, Neera Mehta, K Chavan
Collaborators	:	L Bhurke, A Avahad, CCRAS-CARI Pallavi Mundada, CCRAS-Delhi
Duration	:	2023-2026

In phase 1, 15 FGDs were conducted with 117 participants from Konkan, Marathawda and Vidarbha regions. Traditional dietary food recipes, food taboos were collected from them. Information about the local customs and cultural beliefs practiced by the region specific postpartum & lactating women was obtained from the FGD participants. Salient findings of the data captured from the FGD are as follows: • Green leafy vegetables like methi, shepu; condiments like ova, til; dry coconut, kharik, types of porridges namely methi, haleem, rava, laddoos like methi, haleem, were consumed alternately but on daily basis. • Consumption of non-vegetarian items - soups like mundi, paya, chicken, mutton, khekhada, dry bombil rasa were as per financial status. These were consumed by post-partum women to strengthen the bones and help in rejuvenating during the Sutika Paricharya. Non-vegetarian foods were consumed by postpartum women from some communities only after 13th day (baby is put in cradle), till then the mother was made to consume only soft rice, sugar, milk & ghee. • Galactogogues like poppy seeds, fenugreek (seeds/ leafy vegetable), bajri four (bhakri /porridge), hot potency food items (garlic) were consumed. It was mandatory practice that the lactating mother should have watery consistency foods, has to crush the jowar, bajra bhakri in rasa or dals and then consume. Wheat roti was replaced by jowar and bajra bhakri, and in summer nachani bhakri was consumed. • Consumption of fruits is not recommended during the first six months of lactation. However, once the baby begins consuming complementary foods, the mother starts incorporating limited fruits like apples into her diet. Freshly made foods and timely eating was a rule, no left over foods of morning for afternoon was allowed to be served to lactating mothers. It was important that the mother is kept happy and mental stress is reduced as it decreases milk supply and thereby affects baby. • Dhuri, kajal, udhar vesthanam (tight clothing over abdomen), massage with oil for mother and baby was a practice, which was not informed/ refuted to the doctors at follow up (vaccination etc.) • It was a rule that the lactating mother could eat till she reaches satiety, hence her food portions are unlimited. Dietary recommendation on daily basis for vegetarian and non-vegetarian consuming lactating women representative of different regions of Maharashtra is under preparation. One hundred and eighty-two recipes collected and 5 draft recipe booklets prepared. For phase II, clinical trial recruitment initiated with two participants in March 2025.

4.2 Transgenerational Effects of Paternal Hypertension on Fertility and Pregnancy Outcome: An Epigenetic Approach

Principal Investigator	:	**Kumari Nishi**
Co-Principal Investigator	:	Dipty Singh
Project Associates	:	Reshma Gaonkar, S Mandavkar
Duration	:	2022-2025

Hypertension, a common lifestyle disorder in men of reproductive age, is associated with impaired sexual function and fertility. Observational studies in humans have linked hypertension to reduced fertility. Nitric oxide (NO) is a highly reactive free radical that acts as a potent vasodilator of vascular smooth muscles and regulates blood pressure. The Nω-Nitro-L-arginine-methyl ester (L-NAME) is used to induce hypertension in animal models (pharmacological "NO-deficient hypertension" model) which targets the nitric oxide synthase (NOS) pathway. L-NAME, a competitive inhibitor of nitric oxide synthase, impairs nitric oxide (NO) production, leading to endothelial dysfunction, disrupted pressure natriuresis, activation of the renin-angiotensin system, and increased oxidative stress, ultimately causing hypertension. The L-NAME model of male hypertension was developed using a dose of 10 mg/kg bw (L10) or 20 mg/kg bw (L20) for 3-weeks. The control group (L0) was given drinking water (Annual report 2022-23, pp. 70-72; 2023-24, pp. 75-77).

Present study investigated the effects of paternal L-NAME exposure on the reproductive health of the F0 generation and its subsequent impact on the F1 generation in rats. Male were divided into three groups: Groups I and II were treated with L-NAME at doses of 10 and 20 mg/kg/day, respectively, for a 21-day period., while Group III served as a control. After 60 days of treatment cessation, males were paired with normotensive females. In treated males, reduced sperm count, abnormal sperm morphology, disturbed hormonal balance, and defects in spermatogenesis were observed (Annual report 2023-24, pp. 75-77).

Histological analysis revealed sloughing of germ cells and spermatid failure. The fertility assessment of F0 male rats treated with L-NAME was done. No change in number of copulated females and copulation index were found in F0 generation rats compared to control. There was an increased percent post-implantation loss observed in the L10 group compared to control. The F1 male offspring of hypertensive males and normotensive females were evaluated after weaning at 12 weeks of age. The F1 generation exhibited alterations in NO and SOD levels, reduced sperm count, changes in testosterone and estradiol hormone levels, and impaired spermatogenesis compared to controls (Fig. 1). Testicular histopathology showed germ cell sloughing and spermatid failure (Fig. 2). This study demonstrates that L-NAME-induced hypertension in males can cause germline changes with adverse reproductive effects transmitted to the next generation. These findings highlight the long-term reproductive risks associated with L-NAME induced hypertension.

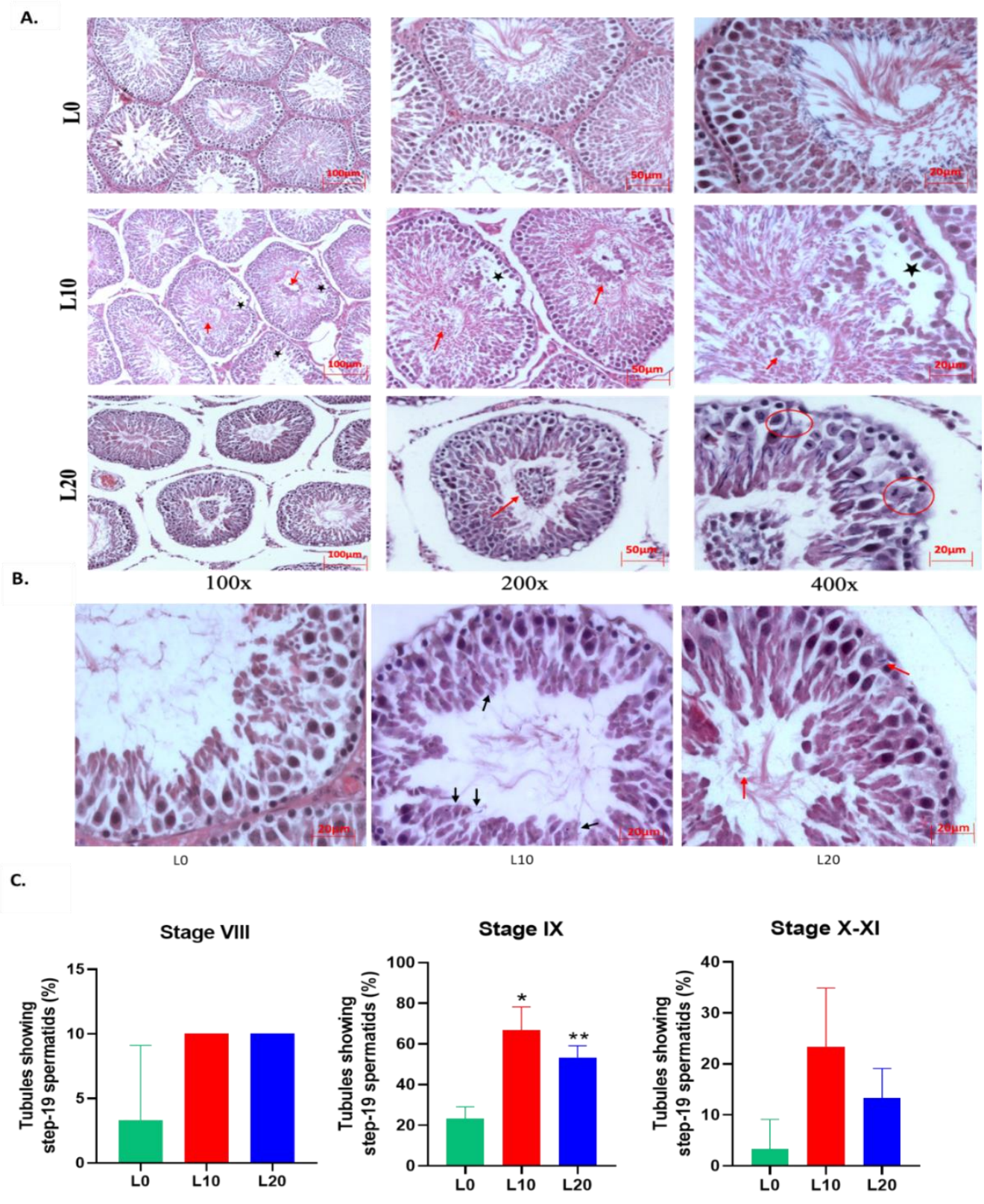

Figure 1: Histopathological changes assessed by hematoxylin and eosin staining in adult testis of F1 sired by normotensive females impregnated by hypertensive male rats. (A) Red circle indicates Step-19 spermatid lagging; star indicates germinal epithelial atrophy; Red arrows indicate sloughing of germ cells (B) Stage IX showing step-19 spermatid lagging. Arrow showing step-19 spermatid; (C) Stage-wise number of lagging/retained spermatids per tubule at stages VIII-XI. Control(L0) v L10, L20; ***p≤ 0.001, **p≤ 0.01, *p≤ 0.05. Values are mean ± SEM.

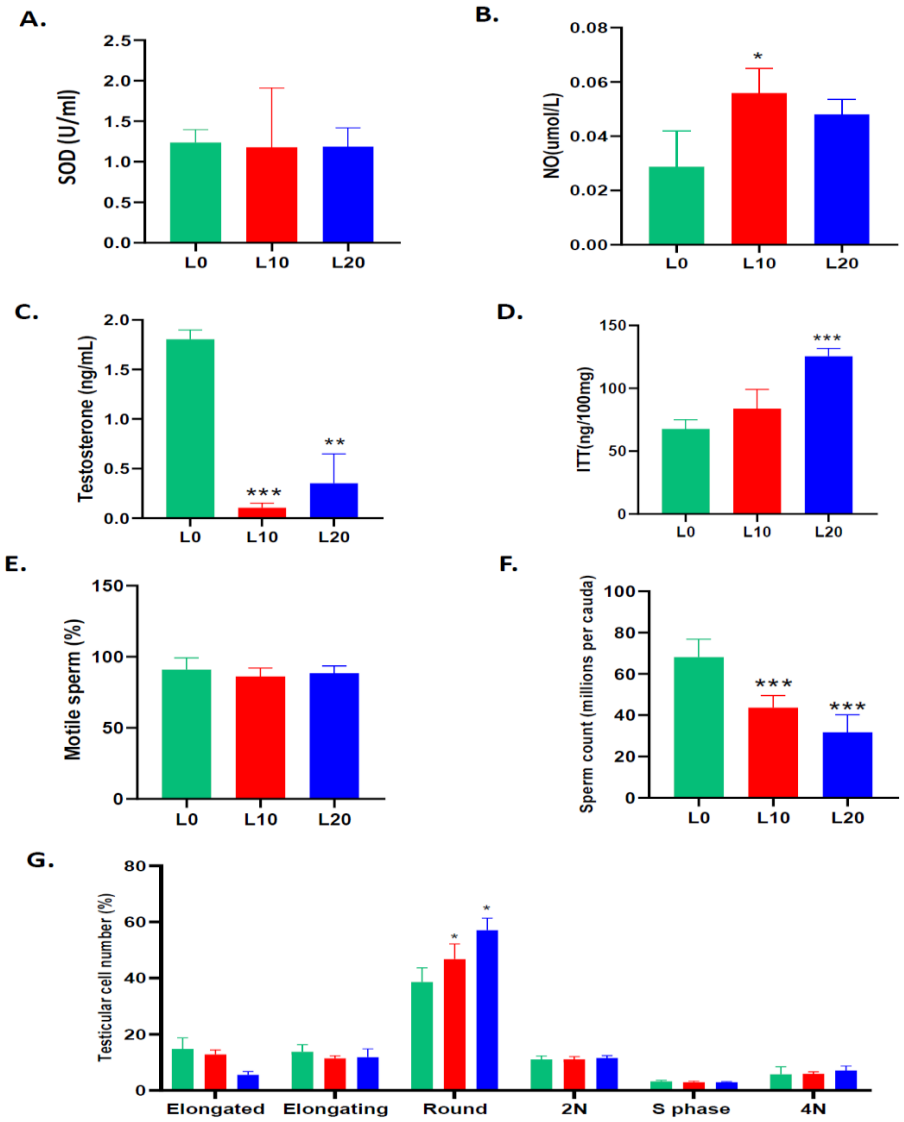

Figure 2: Serum superoxide dismutase activity (SOD) (A), serum nitric oxide (NO) levels (B) in F1 males of L10 and L20 group compared to control (L0). Serum testosterone levels (C) and intratesticular testosterone levels (D) in F1 males from L10 and L20 groups. Sperm parameters (E, F) and flow-cytometric analysis of testicular cells (G) in F1 and control male rats. ***P≤ 0.001, **p≤ 0.01, *p≤ 0.05. Values are mean ± SEM.

4.3 Machine Learning Algorithms for Voice-based Detection of Psychological Stress and Postpartum Depression *(Partly Funded by ICMR-AI Cell)*

Principal Investigator	:	**Susan Thomas**
Co-Principal Investigator	:	Shahina Begum
Project Associate	:	Ulka Gawde
Collaborators	:	TS Jaisoorya, S Ganjekar, Paulomi Sudhir, Shobha Meera, National Institute of Mental Health and Neuro Sciences, Begaluru
Duration	:	2023-2025

Mental disorders account for 7% of the global disease burden and 19% of years lived with disability, with India facing an 84.5% treatment gap due to stigma, distance, and cost. Early detection of mental

health issues in postpartum mothers is essential, as untreated depression can negatively impact both mother and child. Voice-based technology, by analyzing vocal features, offers a low-cost and scalable solution for real-time remote screening, with significant yet largely unexplored potential in the Indian context. This clinical case-control study aims to develop machine learning models using voice data to detect psychological distress and postpartum depression in the Indian population. Fig. 1 illustrates workflow adapted for the study. Recruitment of postpartum mothers is ongoing at NIMHANS, with 184 participants screened and enrolled to date. In parallel, 525 college students were screened at the same site, and 400 were enrolled. Voice recordings were completed for all enrolled participants, comprising two language sub-groups: 200 Kannada-speaking and 200 English-speaking individuals. De-identified voice datasets with extracted features were analyzed at NIRRCH. Based on K-10 scores (≥20 indicating distress; <20 indicating healthy), 200 participants were classified as distressed and 200 as healthy. Several machine learning algorithms, including Support Vector Machines (SVM), Random Forests (RF), Naïve Bayes, Artificial Neural Networks (ANN), k-Nearest Neighbours (kNN), C5, and CART, were trained and tested using multiple data splits (70–30, 80–20, 85–15). Performance was evaluated separately for Kannada, English, and combined datasets. The kNN model performed best for Kannada (accuracy: 0.67), while RF yielded the highest accuracy for English (0.60) followed by the combined dataset (0.65). Model optimization through hyperparameter tuning is currently in progress.

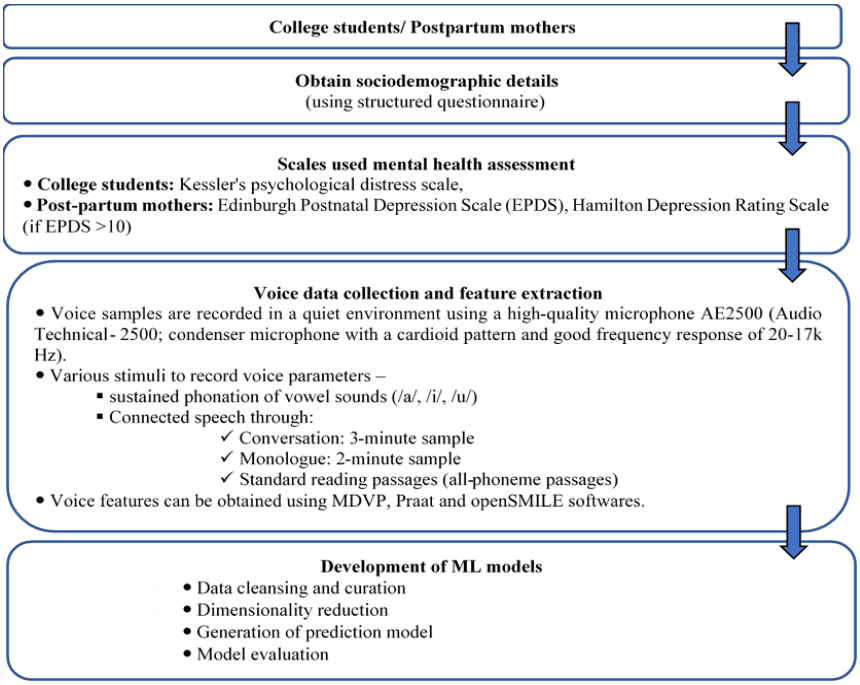

Figure 1: The workflow adapted for study

4.4 Evaluation of Synergistic Impact of Nano-curcumin and Alpha-Linolenic Acid on Pathophysiology of Pre-eclampsia *(Partly Funded by Indian Council of Medical Research)*

Principal Investigator	:	**V Dighe**
Co-Principal Investigator	:	Taruna Madan
Project Associates	:	A Tiwari, Shruti Desai
Duration	:	2022-2025

Pre-eclampsia (PE) is pregnancy-induced hypertension associated with proteinuria in mothers, leading to fetal growth restriction. PE is associated with higher maternal oxidative stress,

inflammation and altered fatty acid metabolism. Curcumin and Alpha-linolenic acid (ALA) have anti-inflammatory and antioxidant properties, respectively, and have been investigated individually for their effects on pre-eclampsia. The present study aims to investigate the synergistic impact of ALA and Nanocurcumin (NC) in a preeclamptic rat model as well as in normotensive pregnant Wistar rats. Earlier, we reported that curcumin, nano-curcumin, ALA and a combination of nano-curcumin ALA are safe as a dietary supplement in pregnancy. We found no significant alterations in physiological parameters, such as hormone profiles, oxidative stress markers, organ histopathology, and growth and developmental parameters of offspring up to the F2 generation (Annual Report 2023–2024, pages 84-86). During the reporting year, we developed and characterized a novel LPS+ L-NAME-induced PE Wistar rat model, which was subsequently used to evaluate the synergistic effect of NC and ALA as a prophylactic dietary supplement for preventing PE in an animal model. To develop the PE model, four groups of animals were inducted: Group-I: control (saline I.P.), Group II: LPS (from GD 3 to GD 8-2 µg/kg-BW), Group III: L-NAME (300 mg/l in drinking water from GD-12 to GD-20 ad-libitum), Group IV: a combination of LPS (increasing doses from 20 µg/kgbw to 100 µg/kgbw) and L-NAME (300 mg/litter in drinking water ad-libitum) from GD-12 to GD-20. A significant increase in systolic blood pressure and diastolic blood pressure (Fig. 1A&B), increased oxidative stress (Fig. 1D), and increased level of inflammatory cytokines was observed in LPS + L-NAME treated animals. Offspring survival (Fig. 1C), and growth parameters such as body weight and anogenital distance (AGD) were also found to be negatively impacted in LPS and L-NAME combination treated groups. Serum biochemistry of GD-20 pregnant Wistar rats showed that the L-NAME treated group and LPS and L-NAME combination treated group had significantly low LDL levels correlating with preterm and low birth weight, mimicking human-like conditions.

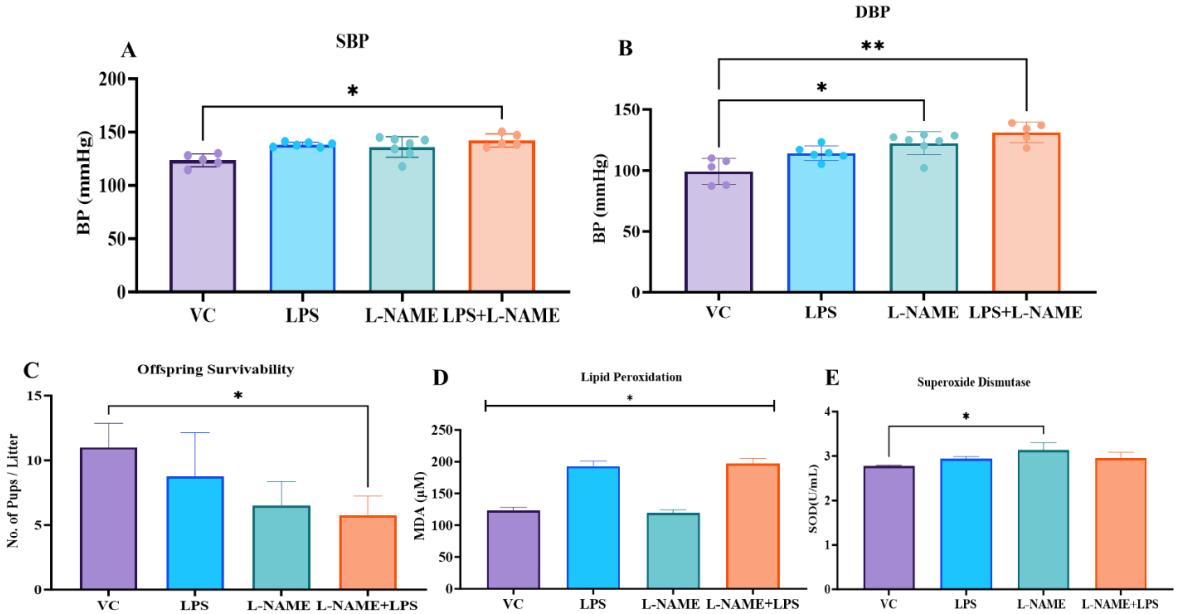

Figure 1: Model development, (A)LPS+L-NAME combination treatment elevated systolic blood pressure in treated pregnant rats as compared to the control. (B)L-NAME alone and LPS+L-NAME combination treatment elevated diastolic blood pressure in treated pregnant rats as compared to the control. (C) L-NAME with LPS severely reduced the survival of offspring after birth. (D) LPS and LPS+ L-NAME combination-treated groups showed increased lipid peroxidation as compared to the control. (E) L-NAME treated group showed significantly elevated levels of SOD as compared to the control group. Values are expressed as Mean ± SD. Statistical analysis was carried out by Kruskal-Wallis test followed by Dunn's multiple comparisons test. *-p<0.05, **-p<0.005, ***-p<0.0005 and ****-p<0.00005 (Abbreviations: VC-Vehicle Control, PE-Preeclampsia, NC-Nanocurcumin, ALA-Alpha Linolenic Acid)

Further LPS + L-NAME-induced PE Wistar rat model was selected for the main study. Female Wistar rats were divided into five groups and were primed 14 days prior to conception with the following doses: Group I: Vehicle Control, Group II: Disease Control (PE), Group-III: PE + NC (400 mg/kgbw/animal/day), Group IV: PE+ ALA (150 mg/kgbw/animal/day) and Group V: PE + ALA (150 mg/kgbw) + Nano-curcumin (400 mg/kgbw/animal/day) treatment. Dosing of NC and ALA was continued till post-natal day 21. The PE group showed a decrease in monocytes and hematocrit percent, MCV, and percent lymphocytes, while an increase in percent neutrophils and neutrophil to monocyte ratio as compared to the control group. SBP and DBP were found to be significantly elevated in the PE group, while the treated groups (NC, ALA, NC+ALA) showed that blood pressure was comparable to the control group (Fig. 2A). Offspring weight in preeclamptic group was significantly reduced compared to the vehicle control (Fig. 2 C-F).

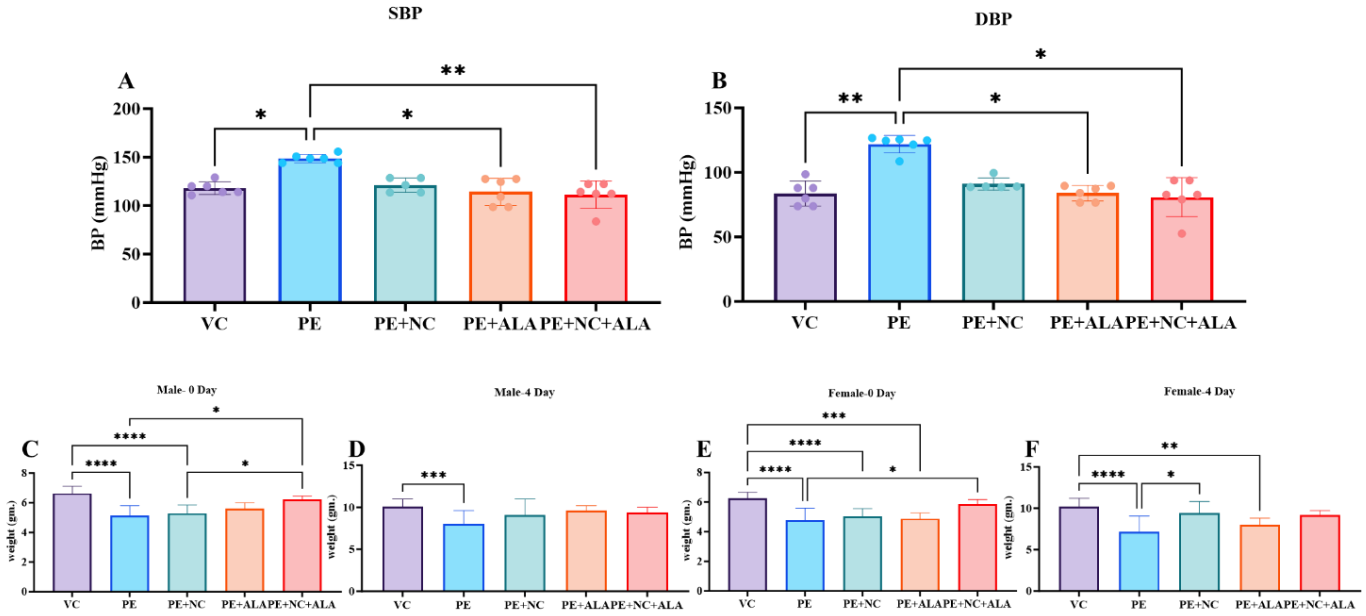

Figure 2: PE Preventive therapy, (A) Systolic blood pressure in PE group was found to be significantly elevated as compared to the vehicle control; PE treated with ALA and PE treated with NC+ALA groups. (B) Diastolic blood pressure in PE group was found to be significantly elevated as compared to the vehicle control; PE treated with ALA and NC+ALA groups. (C, D, E & F) Preeclamptic group showed significantly reduced offspring weight at 0-day and 4-day time points in both male female offsprings compared to the vehicle control. Values are expressed as Mean ± SD. Statistical analysis was carried out by Kruskal-Wallis test followed by Dunn's multiple comparisons test. *-p<0.05, **-p<0.005, ***-p<0.0005 and ****-p<0.00005 (Abbreviations: VC-Vehicle Control, PE- Preeclampsia, NC-Nanocurcumin, ALA-Alpha Linolenic Acid)

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

Principal Investigator	:	**Dipty Singh**
Project Associates	:	Delna Irani, Nafisa Balasinor, Anushree Patil, Deepti Tandon
Collaborators	:	Vandana Bansal, Nowrosjee Wadia Maternity Hospital, Mumbai
Duration	:	2018-2024

Recurrent Pregnancy Loss (RPL) is a condition characterized by the consecutive loss of two or more clinically recognized pregnancies prior to the 20th week of gestation. Globally around 1-2% women experience RPL and RPL prevalence is reported to be higher (7.46%) in the Indian population.

Known contributory factors are majorly of maternal origin. Approximately 50% of the cases are termed idiopathic recurrent pregnancy losses (iRPL). Endocrine disrupting chemicals such as phthalates have been reported to affect pregnancy outcomes and sperm quality. Di-(2-Ethylhexyl) phthalate (DEHP) and Diethyl phthalate (DEP) have been designaled as primary pollutants by the USA Environmental Protection Act (EPA). Within the body, these parent phthalates are metabolized and are converted into their respective monoester metabolites. These metabolites are then excreted mainly into urine and feces. Although these compounds have a short half-life, a small fraction of these compounds get stored into fatty tissues due to their lipophilic nature and orchestrate a state of constant exposure. Multiple studies have reported increased phthalate exposure in cases of infertility and sub-fertility by indirect estimation in the urine. Some studies have reported higher levels of urinary phthalate in women experiencing iRPL as compared to the fertile cohort. Investigating circulatory phthalate levels would be of a higher significance, as it is this fraction which can carry out the action of endocrine disruption. There have been no published reports on the phthalate levels in male partners of iRPL couples. To address the possible association of phthalate exposure with the incidence of iRPL, we estimated the circulatory phthalate levels in both partners of iRPL couples and that of fertile couples. In this case-control study, a total of 60 fertile couples and 75 iRPL couples were recruited. The parent phthalates DEHP and DEP and their respective metabolites Mono-2-ethylhexyl phthalate (MEHP) and Monoethyl phthalate (MEP) were estimated in blood serum by LC-MS/MS in control (n=50 couples) and iRPL (n = 70 couples) groups. In iRPL men, a subset of the population had higher DEHP, MEHP and DEP levels (Fig. 1A, B, C) and serum MEP was found to be significantly higher (Fig. 1D).

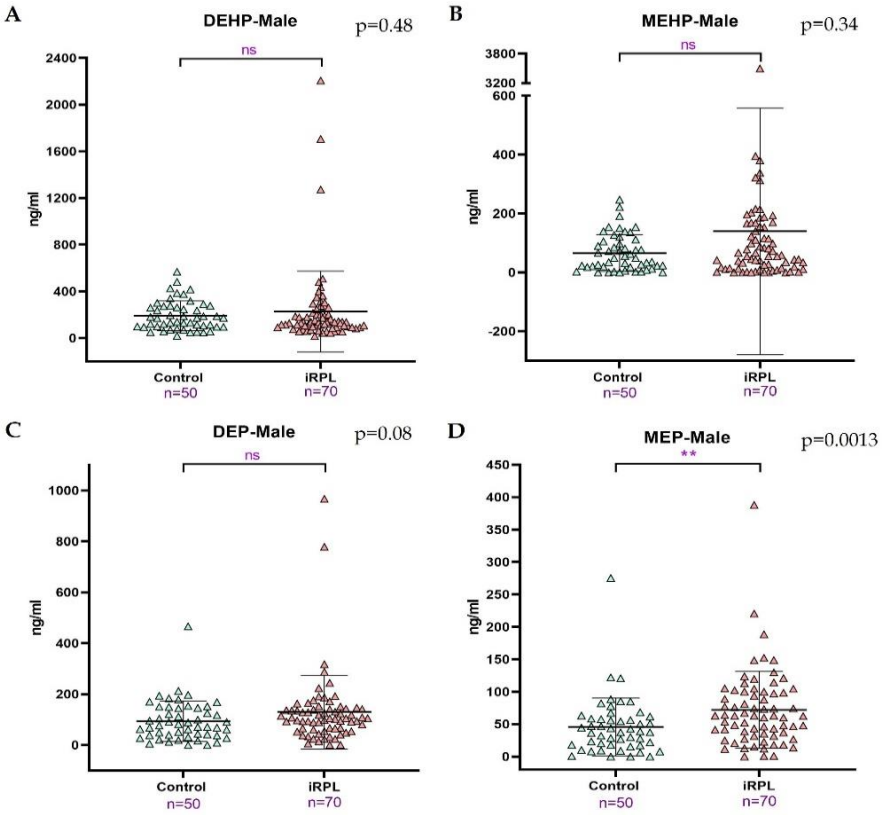

Figure 1: Levels of circulatory phthalates (ng/ml) in male partners of Control (n=50) and iRPL (n=70) couples. (A) DEHP, (B) MEHP, (C) DEP, (D) MEP. Mean ± SD. ns: non-significant, **p<0.01.

In iRPL women, no significant difference could be observed in serum DEHP levels (Fig. 2A). Serum MEHP and DEP were found to be significantly higher in the iRPL female partners as compared to control (Fig. 2B, C). A subset of the population had higher MEP levels (Fig. 2D). Owing to the

endocrine disruption and ROS production property of phthalates, their ability to act as agonists or antagonists to steroid hormone receptors and their effects on gametogenesis; these compounds could possibly impact gamete quality of both male and female partners of iRPL cases. Also, due to the ability to cross the placental barrier. These compounds may impact embryo development and lead to early embryo loss.

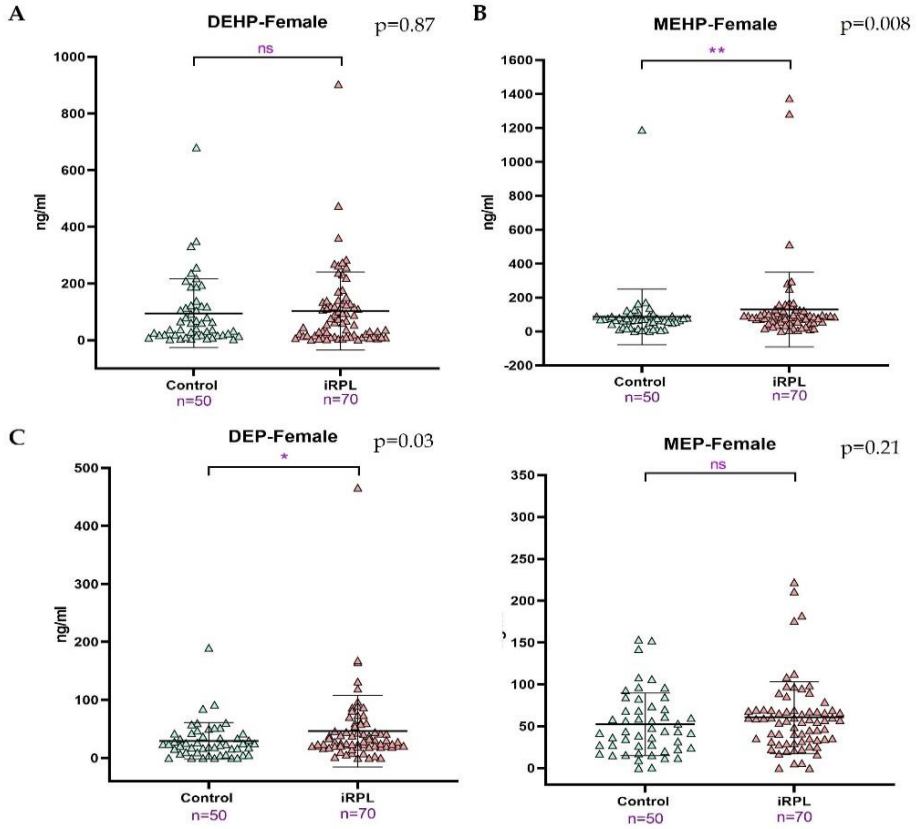

Figure 2: Levels of circulatory phthalates (ng/ml) in female partners of Control (n=50) and iRPL (n=70) couples. (A) DEHP, (B) MEHP, (C) DEP, (D) MEP. Mean ± SD. ns: non-significant, *p<0.05, **p<0.01.

4.6 Evaluating the Role and Proteolytic Processing of Trop1 and Trop2 in Normal Placentation and Placental Pathologies *(Partly Funded by Department of Biotechnology)*

Principal Investigator	:	**Bhakti R Pathak**
Project Associates	:	A S Pawar, Antara Banerjee, Ananya Breed, Madhulika Bajaj, D Modi
Collaborators	:	Pooja Bandekar, A Pawar, Nowrosjee Wadia Maternity Hospital, Mumbai
Duration	:	2021-2026

Trop2 (Trophoblast protein 2) and EpCAM are widely studied in various cancers, however, their role in placental biology is largely unexplored. Both of these protiens are type-1 transmembrane proteins with a large extracellular domain that undergoes proteolytic processing by a membrane serine protease, matriptase. We investigated the expression patterns of these two proteins at specific gestational time points in the rat (Annual report 2021-2022, pp. 78-79) and human placentas (Annual report 2023-2024, pp. 88-89). Further, the expression profiles of EpCAM and Trop2 were assessed in the different zones of the rat placenta (Annual report 2022-2023, pp. 81-82), and their immuno-localization was determined in the human placenta (Annual report 2023-2024, pp. 88-89). In the reporting year, the co-expression analysis of EpCAM, Trop2, and other trophoblast subtype-specific markers (cytokeratin-7 and HLA-G) in the human placental cell digests derived from second-

trimester and term placentas was undertaken by flow cytometry. To confirm the trophoblast identity of Trop2-positive cells, we conducted co-staining with cytokeratin-7 (pan-trophoblast marker). The total trophoblast cell population in the placental cell digests marked with CK-7 was observed to be ~16%, whereas the population positive for Trop2 and CK-7 positive was ~7% in the second trimester placenta, indicating that not all trophoblast subtypes expressed Trop2. In term placental digests, ~20% of the total trophoblast cell population was marked with CK-7, and ~16% were positive for both Trop2 and CK-7. Notably, ~80% of the trophoblast subtypes showed its co-expression in the term placenta. It was also observed that not all Trop2 positive cells are positive for EpCAM, indicating that there could be mutually exclusive populations expressing only one of these two proteins. Importantly, a negligible fraction of cells co-expressed HLA-G, a marker for extravillous trophoblasts (EVTs), and Trop2, suggesting that Trop2 negative population marks the EVTs. Comparison of median fluorescence intensity between the second trimester and term placenta did not show a significant difference, suggesting that Trop2 and EpCAM expressions do not change from mid-gestation to the end of gestation. Further, the effect of Trop2 overexpression on the placental invasion was evaluated by generating Trop2-expressing stable clones in HTR-8/SVneo (a known extra-villous trophoblast cell line) (Fig. 2). The empty vector clone and parental HTR-8/SVneo cells were used as negative control (Fig. 2A). Transwell invasion assays were performed using Trop2 clones 5 and 9 which showed a significantly higher invasion upon Trop2 overexpression than parental cells (Fig. 2B). These results indicate that probably silencing of Trop2 expression during differentiation of cytotrophoblasts to EVTs is needed to prevent uncontrolled invasion of EVTs.

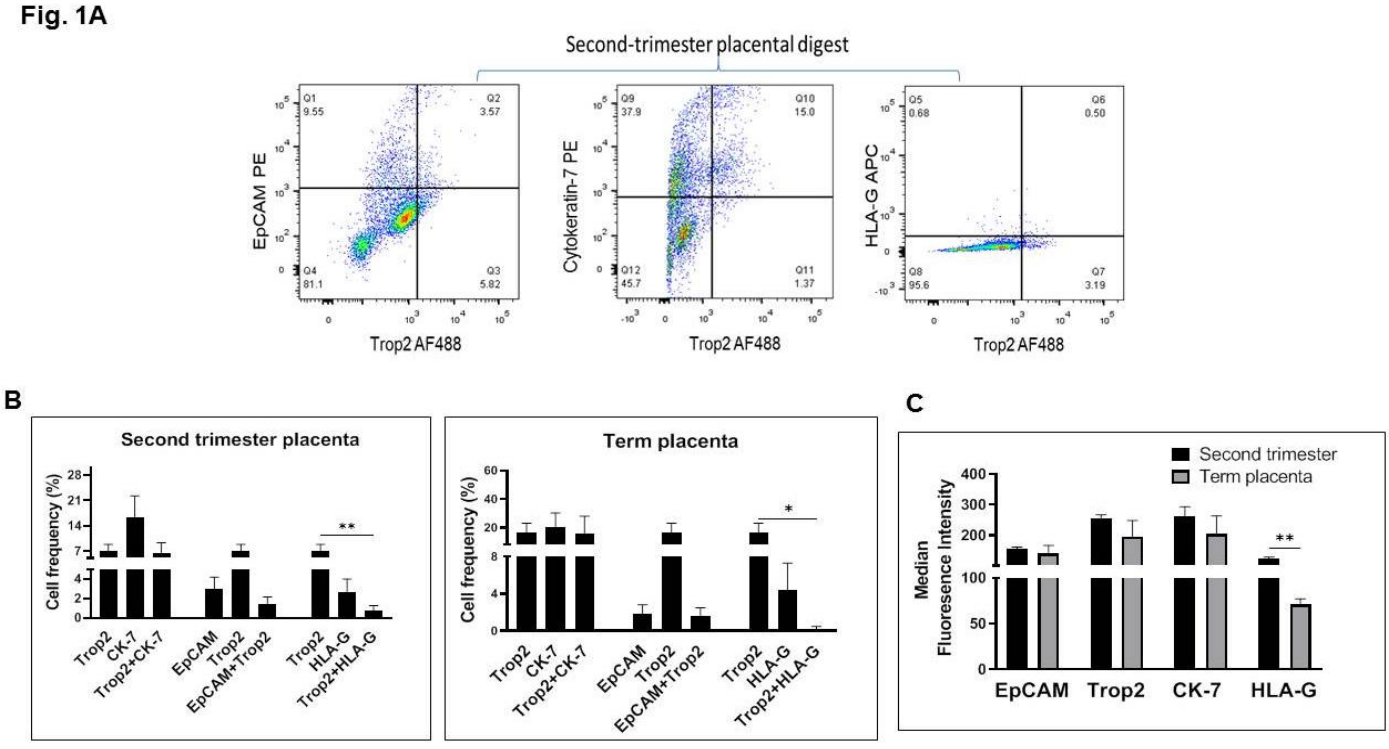

Figure 1: Flow cytometric analysis of Trop2 and EpCAM in the human placental digests derived from second-trimester and term placental tissues. (A) Representative images showing the percentage positivity of double-positive cells of the second-trimester placental digests are displayed in the upper right quadrant. (B) The graph illustrates the percentage positivity of placental cells only expressing Trop2 and EpCAM, trophoblast markers (CK-7 and HLA-G), and co-expressing Trop2 with CK-7, EpCAM, and HLA-G in the second trimester and term placenta (mean ± SEM). (C) Median Fluorescence Intensity (MFI) was determined to evaluate the expression of targets in the isolated placental cells of the second trimester and term placentas. The data are representative of observations from three placentas.

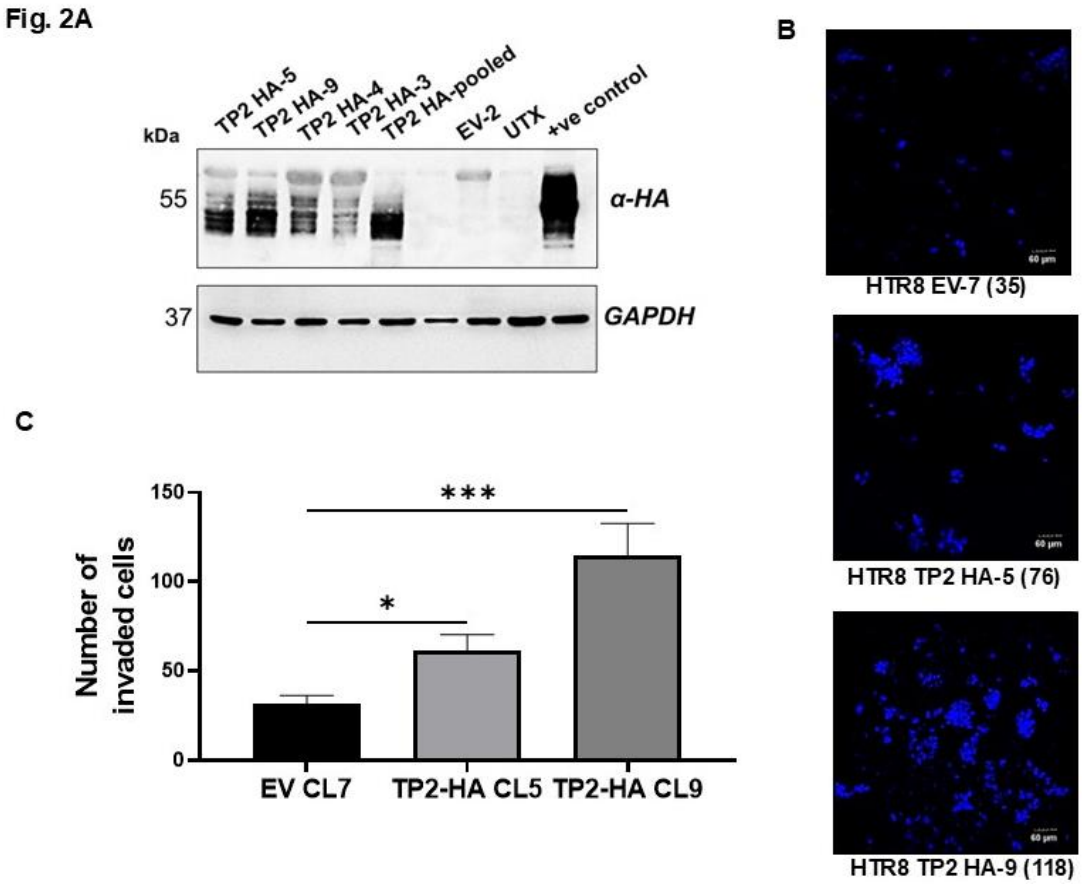

Figure 2: Effect of Trop2 overexpression on the invasive ability of HTR-8/SVneo cells. A. Overexpression of Trop2 in HTR-8/SVneo cells was assessed by immunoblotting using the anti-HA antibody (upper panel) and loading control by anti-GAPDH antibody (lower panel). HTR-8/SVneo cells transfected with only an empty vector served as a negative control. HEK-293 transfected with Trop2-HA served as a positive control. B. The invasive ability of HTR-8/SVneo cells expressing Trop2 HA clones and empty vector clone (control) was detected using a transwell assay. Invaded cells were stained with DAPI and counted under the fluorescent microscope. The number of invaded cells in four random microscopic fields was counted at 20X magnification, and a representative image is shown. B. Bar graphs depicting the averaged results from two replicates. Data is represented as mean±SEM. *$p < 0.05$, ***$p < 0.001$.

4.7 Investigating the Role of Endocannabinoid System in First Trimester Chorionic Villi of Women Experiencing Recurrent Spontaneous Abortions (*Partly Funded by ANRF*)

Principal Investigator	:	**Kumari Nishi**
Project Associate	:	Sharon D`souza
Collaborators	:	Vandana Bansal, Nowrosjee Wadia Maternity Hospital, Mumbai Padmaja Samant, GS Medical College and KEM Hospital, Mumbai
Duration	:	2023-2026

Endocannabinoid system (ECS), a lipid signalling system, is involved in neuromodulation and also other physiological processes. Several studies have indicated involvement of endocannabinoids in the placental development. Our study aims to investigate the role of ECS which comprises of -cannabinoid receptors i.e. CB1 and CB2 (CBRs); regulatory enzymes involved in synthesis and degradation of their endogenous ligands -Anandamide and 2-arachidonoylglycerol in Recurrent Spontaneous Abortions (RSA). In order, to understand the effects of endocannabinoids on

migration, invasion and adhesion on placental cells, in vitro experiments were carried out. HTR/SVneo8 cell line was used to obtain the non-toxic concentrations of the receptor agonists and antagonists i.e. NADA -CB1 agonist; HU308- CB2 agonist, AM251-CB1 antagonist, SRR144528-CB2 antagonist using MTT assay as well as its effects on proliferation using BrDU assay. Fig. 1: A, B shows effect of dose concentration of CB1, CB2 agonist and antagonist ranging from 1-10 ng/ml plotted against percentage cell viability and proliferation activity. There was no significant effect of the given concentration on the cell viability and proliferation, indicating the given concentration is non-toxic to HTR8/SVneo8 cell lines. Based on these observations, this range of dose concentration was used for further experimentation. To study the endocannabinoid pathway, gene expression studies of placental cell lines and human chorionic villi were done. Placental cell lines were treated with 10ng/mL of CB1, CB2 agonist and antagonist and expression of the ECS metabolic pathway genes (DAGLB, MGLL) was studied. DAGLB and MGLL showed reduced expression in the treated group as compared to the control group (Fig. 1. C). The study also includes investigating the expression of ECS in chorionic villi of women experiencing RSA (undergoing dilation and curettage procedure) and women undergoing medical termination of pregnancy with no identifiable medical problem (control). Gene expression studies in chorionic villi samples of control and RSA samples were carried out (Fig. 1. D). A non-significant increase in TRPV6 (a calcium channel) and DAGLB expression was observed in RSA samples compared to control, whereas non-significant reduction was observed in CNR1 compared with control. MGLL when compared to control group showed significant increase in RSA group. Migration studies showed reduced migration in treated groups whereas an increase in the invasion was observed in treated group compared to control group. Further experimentation to study the role of endocannabinoids are still ongoing.

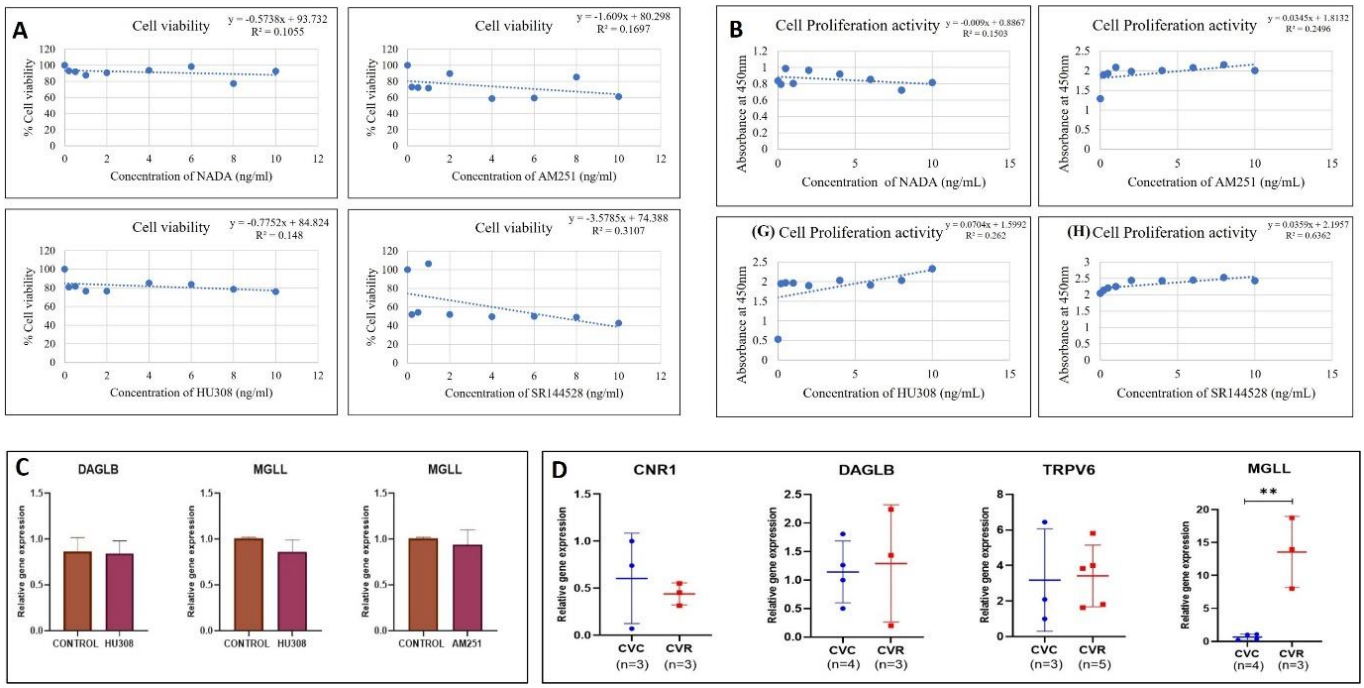

Figure 1: (A) MTT assay showing concentration of respective agonist (NADA: a CB1 agonist; HU308; a CB2 agonist) antagonist (AM251; a CB1 antagonist of HU308, SR144528, an CB2 antagonist) against percentage cell viability. (B) BrDU assay showing concentration of respective CB1, CB2 agonist and CB1, CB2 antagonist at 450nm. (C) Relative gene expression of DAGLB, MGLL in HTR-8/SV neo cell lines treated with 10ng/mL of NADA, AM251, HU308, SR144528 and untreated group. D: Relative gene expression of TRPV6, MGLL, CNR1, DAGLB in chorionic villi samples of control and RSA.

Table 1: Results from migration and invasion assay of HTR-8/SV neo cell lines when treated with 10ng/mL of CB1, CB2 agonist and antagonist each along with untreated (control) group.

Treatment	Cells migrated	% migration	Cells invaded	% invasion
CB1 agonist-NADA	8	0.08	8	0.08
CB2 antagonist-AM251	107	1.07	0	0
CB1 agonist- HU308	95	0.95	9	0.09
CB2 antagonist-SR144528	88	0.88	0	0
Untreated	133	1.33	0.07	0.07

4.8 Molecular Analysis of HLA-G in Pregnant Tribal Women and its Role in Infectious Etiologies Modulating Intrauterine Inflammation - A Prospective Cohort Study

(Funded by Indian Council of Medical Research)

Principal Investigator : **KC Itta**
Co-Principal Investigator : VM Bhor
Project Associates : Anushree Patil, Ragini Kulkarni, SK Mishra
Collaborators : B Hengne, Sub-district Hospital, Dahanu, Palghar District
PN Dhodi, Sub-district Hospital, Kasa, Palghar District
A Gadag, Primary Health Center, Ashagad, Dahanu
Smita Bari, Primary Health Center, Gholwad, Dahanu
Duration : 2023-2026

The role of HLA-G in mediating maternal–fetal immune tolerance, while potentially contributing to immune escape mechanisms that reduce the mother's ability to combat infections, remains under investigation. Identifying the HLA-G genotype is key to understanding this dual role in pregnancy. The present study focused on the molecular analysis of HLA-G and associated infections in a cohort of pregnant tribal women, examining its potential impact on pregnancy outcomes. A total of 326 participants aged 18 to 35 years were enrolled, primarily from the Warli tribe (87.1%), followed by Malhar Koli (8.8%), Dubla (2.4%), Dhodi (0.3%), and Konkani (1.2%). Most Warli participants were 18-20 years, and 45% were married. Among 700 blood samples collected, sHLA-G levels were analyzed using ELISA in 154 (first trimester), 104 (second trimester), and 81 (third trimester), with interquartile ranges (IQRs) of 47.5, 43.2, and 29.2 U/mL, respectively. Of the 549 samples tested for infections using IgM ELISA, 46% (253) were positive, with infection rates peaking in the third trimester (64.1%). The most common infection was Chlamydia (18.9%), followed by Toxoplasma (11.8%), CMV (4.9%), and HBsAg (2.36%), while HSV, HIV, and HCV showed the lowest prevalence. Next-Generation Sequencing (NGS) of 173 samples revealed HLA-G*01:04:01 as the most frequent allele (51.6%), commonly occurring with a deletion genotype. For the 14-bp insertion/deletion polymorphism, 50.3% of individuals were heterozygous, 40% homozygous for the deletion, and 9.3% carried the insertion. In total, seven novel HLA-G alleles (3.9%) were identified, three of which have been officially named by the WHO. Two were intronic variants: HLA-G*01:01:01:34 (G→A in intron 3) and HLA-G*01:06:01:02 (C→T in intron 4). The third, HLA-G*01:24:02, located in exon 5, involves a G→A substitution that causes a nonsynonymous mutation (GCT→ACT), changing the amino acid at position 304 from alanine to threonine (Fig. 1). This variant is considered a silent variant of HLA-G*01:24:01. Since exon 5 encodes part of the transmembrane region, this change may affect the protein anchors to the cell membrane. Miscarriages occurred in 5.78% (10/173) of participants, with average gestational age of 9.77 weeks. sHLA-G levels ranged from 16.88 to 103.72 U/mL, with higher concentrations observed in the G*01:01:01 and G*01:01:03 (ins/del) genotypes, particularly in women with co-infections of Chlamydia and Toxoplasma. Further detailed analyses are ongoing to assess the association between sHLA-G levels, HLA-G genotypes, and pregnancy outcomes.

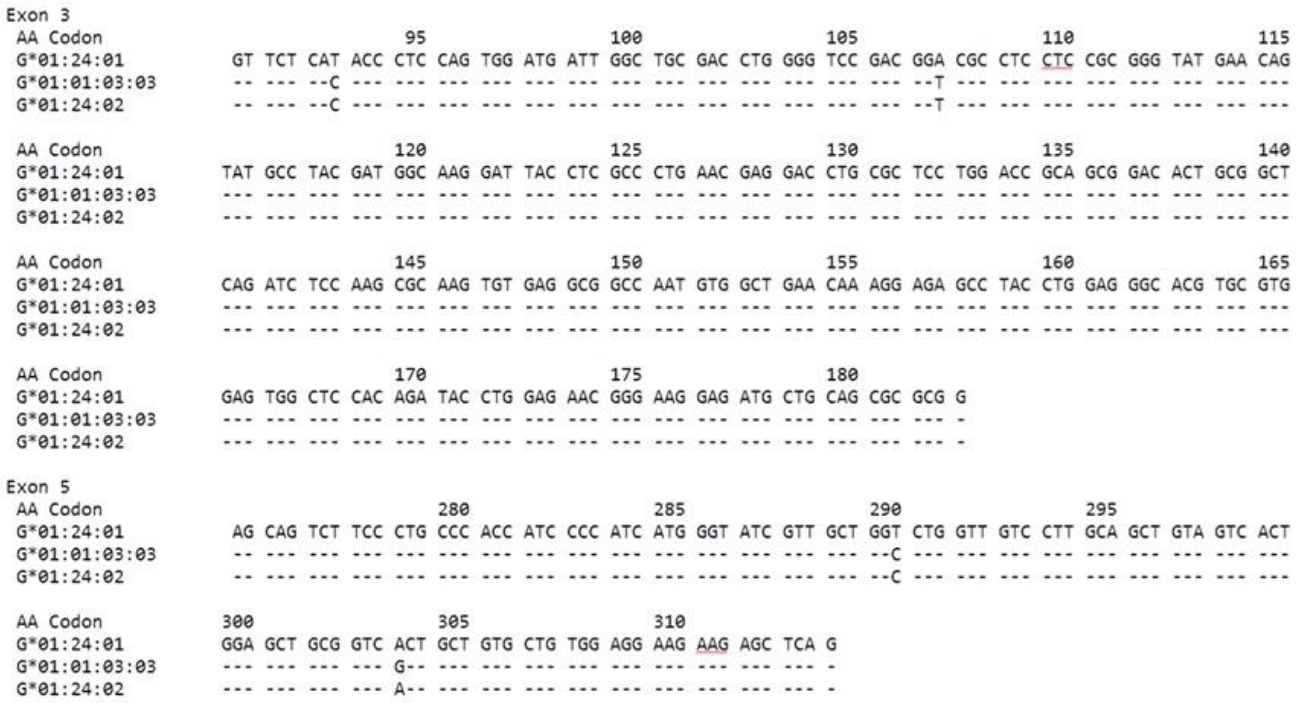

Figure 1: Alignment of the sequence of exons 3 and 5 of HLA-G*01:24:01 with the sequence of HLA-G*01:01:03:03 and HLA-G*01:24:02. HLA-G*01:24:01 and HLA-G*01:24:02 differ by three synonymous substitutions, two in exon 3, codon 93 CAC>CAT both encoding Histidine, codon 107 GGA>GGT both encoding Glycine, and one in exon 5 codon 290 GGC>GGT both encoding Glycine. HLA-G*01:24:02 is a silent variant of the HLA-G*01:24:01. Dashes (-) indicate nucleotide identity with the HLA-G*01:24:02 allele. The numbers above indicate the codon position.

4.9 Urinary PLGF as a Predictive Marker for Preterm Delivery with SGA Infant: Evaluating the Efficacy and Attempting Development of Point-of-Care Device *(Funded by ICMR)*

Principal Investigator	:	**Bhakti R Pathak**
Project Associates	:	Ananya Breed, Deeksha Jadhav, Swapna Deopurkar, Anushka Gore, Dhanashree Jagtap, Antara Banerjee, Shahina Begum, Anushree Patil
Collaborators	:	Archana Bhosale, Madhuri Mehendale, Lokmanya Tilak Municipal Medical College and General Hospital, Sion, Mumbai Pooja Bandekar, Nowrosjee Wadia Maternity Hospital, Parel, Mumbai Bharati Singh, A Kotnis, AIIMS, Bhopal
Duration	:	2024-2027

PLacental Growth Factor (PLGF) levels serve as indicator of appropriate placentation. PLGF levels in blood peak at 26-30th week of pregnancy and decrease thereafter. Low levels of PLGF in blood are associated with risk of preeclampsia. However, in the recent years, low PLGF levels have been shown to be associated with low birth weight of babies. PLGF levels in blood correlate with that in urine and hence determining urinary PLGF can be a non-invasive method to predict delivery of SGA (Small for Gestational Age) infants. Our pilot study on urinary PLGF in 28th to 32nd week of gestation in 203 pregnant women showed strong association between low PLGF and SGA infants delivered preterm. The current study is a case-control study to evaluate urinary PLGF in women delivering preterm with SGA and AGA (Appropriate for Gestational Age) infants and determine the sensitivity and specificity of urinary PLGF as a predictive marker for preterm deliveries with

SGA infants. We have received ethics approval from the institute and 2 collaborating sites (LTMGH, Sion and AIIMS, Bhopal). Participant recruitment was initiated in November 2024. In the reporting period, 519 participants were recruited and spot urine samples were collected at two different time points 25th-28th week of gestation and 29th-32nd week of gestation. Participants were followed till their delivery and medical records (baby birth weight, gestational age at the time of delivery, mode of delivery, sex of the foetus etc) were noted down for 107 participants. 28.03% deliveries were preterm. Of these, 9.34% delivered SGA infants and 18.69% delivered AGA infants. Week wise distribution of study participants is indicated in Fig. 1.

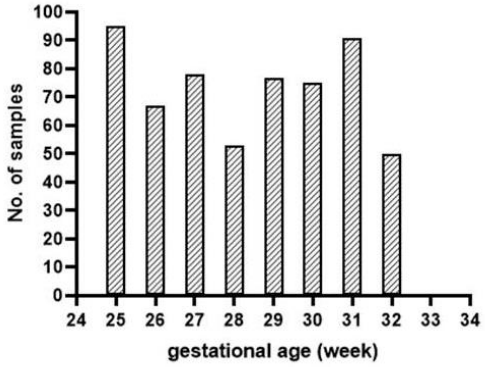

Figure 1: Bar graph depicting gestational week wise distribution of recruited participants

4.10 Increasing Access to Postpartum Contraception by Linking Family Planning and Infant Vaccination Services *(Funded by NIH, USA)*

Principal Investigator	:	**Shahina Begum**
Project Associates	:	Tejal Patel, Deepali Ukande, Bhawana Pakhare
Collaborators	:	Sarah Averbach, Anita Raj, A B Rabin, University of California, San Diego
Duration	:	2023-2025

Infant vaccination programs are a promising practice to integrate postpartum family planning, reducing service burden while improving access. This is especially relevant in India, where women have unmet need in the first postpartum year. The hypothesis of the study was that the integrated family planning services to routine community-based infant vaccination services provided by front-line Indian health workers would increase access to and uptake of modern postpartum contraception and enhance contraceptive use. A total of 286 postpartum women within 12 weeks not currently using any modern contraceptive methods were included in the cluster randomized trial. Women (n=143) at intervention clusters received an individual counselling by ANM at infant vaccination visits plus modern contraceptive provision if desired, while control group (n=143) received the standard of care i.e. referral to public health centers. Outcomes included contraceptive use at six month follow up survey. The study group was more likely to use a modern contraceptive method at six months postpartum compared to controls (50% vs 38%, p=0.06). The difference in contraceptive use was not statistically significant, however the power of the study was found to be 48% indicating a large sample should be considered to find the significant outcomes. However, the study demonstrates the feasibility of family planning services integrated into routine infant vaccination services in rural India. The study is completed.

4.11 Establishment of Centre for Maternal and Child Health Genetics *(Funded by Department of Biotechnology)*

Principal Investigator	: **S Pande**
Co-Principal Investigators	: Shaini Joseph, Manisha Madkaikar
Project Associates	: Juili Bharankar, Khushbu Shirsat, Priya Tripathi, Sakshi Patil, Neha Minde, Shiny Babu, H Gawde
Collaborators	: Sudha Rao, Pooja Bandekar, Vandana Bansal, Ketki Kulkarni
Duration	: 2024-2027

The DBT-NIDAN Kendra at Genetic Research Center enrolled and counseled of 71 families from major municipal and tertiary care hospitals and special care centers across Mumbai. These families presented with a diverse spectrum of clinical conditions including infertility, recurrent pregnancy loss, congenital anomalies, suspected hereditary disorders, etc. Comprehensive genetic evaluation was initiated to support preconception and prenatal planning, emphasizing early risk identification and informed decision-making. A total of 197 genetic tests including karyotyping, whole exome sequencing (WES), fluorescent in-situ hybridization (FISH), microarray analysis were conducted etc. Karyotyping for 136 individuals revealed significant structural variations, including a Robertsonian translocation and chromosomal inversions, which proved essential for counseling in cases of infertility and familial Down syndrome. FISH confirmed mosaicism in one case of Down syndrome and ruled out common chromosomal anomalies in others. Whole exome sequencing proved instrumental in identifying pathogenic and likely pathogenic variants in cases with monogenic disorders. Among 35 individuals tested, actionable variants were detected in genes such as TMEM260, DOCK8, PRF1, PKD1, HMBS, and DYRK1A. These findings facilitated personalized reproductive counseling and management strategies for high-risk couples. Haemoglobinopathy screening, conducted as standard care in collaboration with the ICMR-NIIH, screened 99 individuals, with 3% identified as carriers of hemoglobinopathies such as β-thalassemia and Hb Hofu trait.

4.12 Heterogeneity of Gestational Diabetes Mellitus Based on Insulin Resistance Measured by Glucose Disposition Index *(Partly Funded by ICMR Intramural Grant)*

Principal Investigator	: **U Chaudhari**
Co-Principal Investigator	: Geetanjali Sachdeva
Project Associates	: Nikita Sharma, Rupal Shah, Balaji Jamdare, Sadeep Sawant
Collaborators	: A Pawar, Trupti Nadkarni, Puja Bandekar, Nowrosjee Wadia Maternity Hospital, Mumbai D Mamtora, Bai Jerbai Wadia Hopspital for Children, Mumbai
Duration	: 2023-2027

Any degree of glucose intolerance first diagnosed during the second or third trimester of pregnancy is called as Gestational Diabetes Mellitus (GDM). GDM affects 10% to 14% pregnancies worldwide

with a higher prevalence in South Asian Women. Currently, GDM is considered as homogeneous condition and GDM women are treated as one-size-fit-all approach. Studies have shown that despite the initiation of GDM treatment immediately after diagnosis, the odds of adverse maternal and neonatal outcomes are significantly higher compared to normal pregnancy. Evidences from Caucasian population have shown heterogeneity in the pathophysiology of GDM. GDM is associated with defect insulin sensitivity, or have defect in insulin secretion. However, data on the heterogeneity of GDM among South Asian population are lacking. Understanding GDM heterogeneity in different ethnic group may help in tailor-made interventions for prevention of adverse maternal and neonatal outcomes in GDM. The aim of this project is to assess pancreatic β cell function, metabolic characteristics and subtype in GDM based on insulin sensitivity and secretion. Oral glucose tolerance test (75g) was conducted in pregnant women n=257 during 24th to 28th weeks of gestation. Blood was collected at fasting 0 h and at 30 min, 60 min and 120 min after post glucose load. In women with GDM, defect in insulin secretion (Stumvoll estimate) or sensitivity (Matsuda Index) were assessed based on the below 25th percentile of women displaying normal glucose tolerance (NGT). In this cohort 30 women (12%) were diagnosed with GDM. Subtyping of GDM revealed predominately 60% women with defect in insulin sensitivity, 10% GDM women with defect in insulin secretion, 13% with mixed defects and remaining 13% were unclassified without any defect (Fig.1). The study is ongoing to characterize metabolic signatures of different subtypes of GDM.

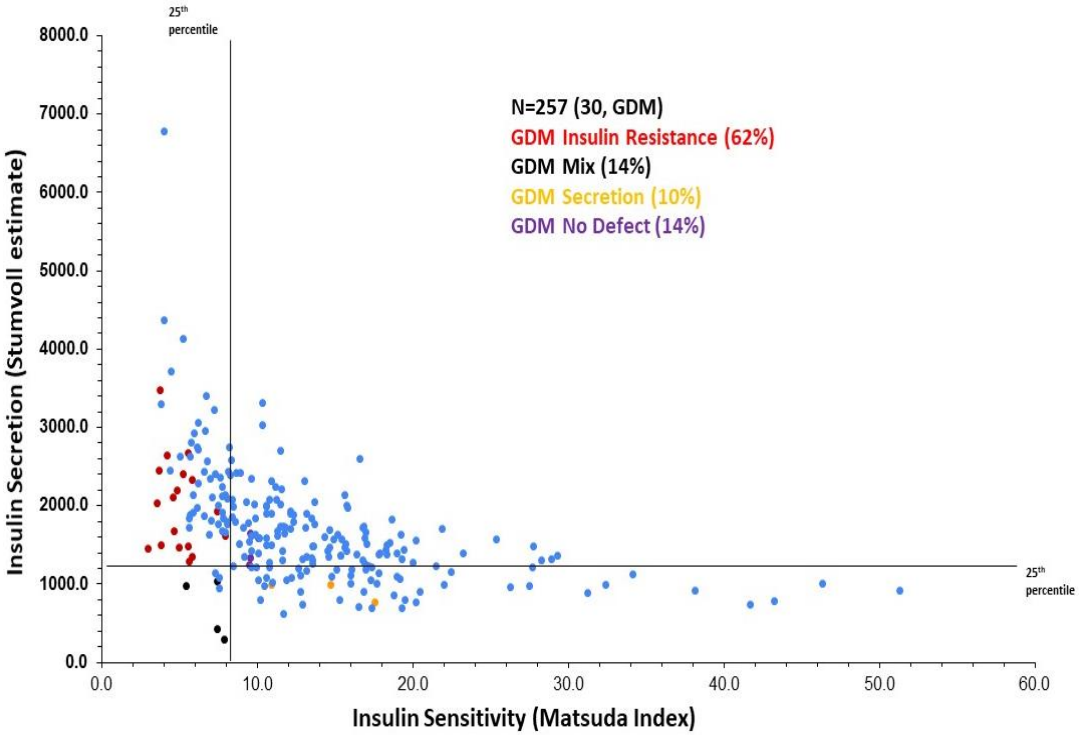

Figure 1: Hyperbolic relationship between insulin secretion and insulin sensitivity in women with normal glucose tolerance and GDM. Physiological subtyping of GDM was defined based on the insulin secretion and sensitivity indices below 25th percentile of women displaying normal glucose tolerance (NGT, n=220, blue circles). In this cohort (n=257), 30 (11.5%) women were diagnosed with GDM. The blue circles represent women with NGT. Based on Matsuda Index and Stumvoll first phase insulin estimates below 25th percentile, women with NGT the GDM were classified into physiological subtypes i.e. insulin-resistant GDM (n=18, 62%, red circles); insulin deficient GDM (n=3, 10%, yellow circles); mixed (n=4, 13%, black circles); and unclassified (n=4, 13%, purple circles).

CHILD HEALTH

5. CHILD HEALTH

5.1 Comprehensive Genetic Evaluation of Fetus in Antenatally Detected Abnormal Pregnancies with Fetal Malformations: Outcomes, Benefits and Limitations - a Pilot Study *(Funded by ICMR)*

Principal Investigator : **S Pande**
Co-Principal Investigator : Shaini Joseph, D Das
Project Associates : Juili Bharankar, Neha Minde, H Gawade, Shiny Babu
Collaborator : Vandana Bansal, Nowrosjee Wadia Maternity Hospital, Mumbai
Duration : 2021-2025

This pilot study aims at understanding and developing a workflow for genetic diagnosis for USG detected fetal malformations. Products of Conception (POC) samples of malformed fetuses were processed. Histopathology reports identified abnormalities in 18 cases. Chromosomal abnormalities, identified by karyotype or FISH were identified in eight cases. In eight cases, pathogenic deletions/ duplications were identified by chromosomal microarray. Whole Exome Sequencing (WES) carried out for POC samples identified pathogenic variants in two cases. Novel variants of uncertain significance were identified in 29 cases out of total 100 cases.

5.2 Assessment of Neonatal Screening Approaches for Sickle Cell Disease and the Effect of Early Intervention in Management of the Disease in Tribal Populations –Research cum Intervention Study

Coordinating Centre : ICMR-National Institute of Immunohaematology (NIIH)
Principal Investigator : Prabhakar Kedar, Anita Nadkarni
Co-investigator : Manisha Madkaikar, ICMR-NIIH, Mumbai
Site Principal Investigator : **Suchitra Surve**
Site Co-Principal Investigator : **Ragini Kulkarni**
Site Co-Investigators : S Bodade, Civil Surgeon, Palghar District
B Hengne, Sub district Hospital, Dahanu
D Suryavanshi, District Health Officer, Palghar District
P Dhodi, Sub district Hospital, Kasa
Project Staff : Yugali Kore, Arati Patil, Jidnyasa Kore, Shweta Dubey
Ajinkya Gawad, S Solanki, Y Jadhav
Duration : 2019-2024

Primary objectives of the study are: (i) to undertake a newborn screening program for Sickle cell anemia (disease) in tribal populations of different states for early detection; (ii) to understand the magnitude of the problem; (iii) to understand the barriers for undertaking such program; and (iv) to measure the benefit of early comprehensive care of affected babies. Secondary objective is to evaluate the genotypic and phenotypic correlation to understand role of genetic modifiers for disease severity. This prospective study as a part of the multicentric study, was implemented at Dahanu block of Palghar District at Sub-district hospital, Dahanu and Kasa, PHCs through Model Rural Health Research Unit (MRHRU) Dahanu over a period of five years. This study was implemented through 7 centers across the country (Maharashtra Centers, Gujrat, Tamilnadu, Orrisa, Madhya Pradesh and Rajasthan). Considering the prevalence of 1% for sickle cell disease and 10% for sickle cell trait, approximately 2000 newborns were required to be screened per year to

identify 100 Sickle cell disease (SCD) newborns during the study period at each center to give cohort of approximately 700 SCD newborns in 7 centers.
The newborns in SDH Dahanu and Kasa were enrolled in the study. High-Performance Liquid Chromatography (HPLC) was performed to diagnose the disease. After confirmed diagnosis, samples of mother, father and sibling were also taken. Since the start of the project i.e. from 2nd December 2019 to 31st March 2023, a total of 7786 babies were screened for SCD. Of which, 41 babies were found to have Sickle cell disease. Pneumococcal vaccine was given to diseased babies through UIP. Typhoid vaccine and Meningococcal vaccine were given. Medicines such as Pentid, Folic acid, A-Z syrup were started in 21 diseased babies. Hydroxyurea was commenced in 13 babies. Total 661 trait babies were diagnosed. So far 345 babies have been followed up at 6 weeks for confirmation of diagnosis and family screening. Report handover and genetic counselling were done for the families of sickle cell disease and trait babies. Babies having SCD are being followed up by haematologists at the monthly Anemia OPD organized at SDH Dahanu by Comprehensive Thalassemia Care Centre, Borivali and IAP, Palghar in collaboration with ICMR-NIRRCH. A dissemination meeting was conducted on 23rd August 2024 to discuss findings of the multicentric ICMR project and sustainability considerations of newborn screening for sickle cell disease and follow up in Palghar.

5.3 Mission Program on Paediatric Rare Genetic Disorders (*Funded by DBT)*

Principal Investigator	:	**S Pande**
Co-Principal Investigator	:	Shaini Joseph
Project Associates	:	Neha Minde, Tanvi Raj Agarbattiwala, Amisha Kumar, Shiny Babu, H Gawde
Collaborators	:	DVS Sudhakar, Suchitra Surve
Duration	:	2022-2027

One hundred and twelve pediatric patients attending the Genetic Research Center OPD were evaluated for genetic defects by conventional diagnostic techniques. Chromosomal abnormalities in eight cases were identified in children with short stature, disorders/differences of sex development (DSD), Autism, dysmorphism and developmental delay. FISH diagnosed eight cases with Di-George, Downs, Angelman, Prader-Willi syndrome or DSD. Twelve cases were reported to have microdeletions/duplications and were solved by Chromosomal Microarray. Two cases of Duchenne muscular dystrophy were diagnosed by MLPA. Whole Exome Sequencing (WES) data analysis of 50 cases identified pathogenic variants in 16 cases and variants of uncertain significance were identified in eight cases. Analysis for the remaining cases is ongoing.

5.4 Genetic and Biochemical Characterization of Mitochondrial Oxidative Phosphorylation (OXPHOS) Disorders in Children

Principal Investigator	:	**DK Das**
Project Associate	:	Debolina Saha
Collaborators	:	Shilpa Kulkarni, Sonam Kothari, Bai Jerbai Wadia Hospital for Children, Mumbai
Duration	:	2021-2026

Oxidative Phosphorylation (OXPHOS) disorders are a wide group of heterogeneous disorders caused mainly due to dysfunctions in single or multiple OXPHOS components. Various diseases

such as MELAS, LHON, NARP, Leigh syndrome etc. are caused by mtDNA and nuclear DNA mutations. We previously assayed the mitochondrial enzyme activity in muscle and buccal swab samples from patients with Mitochondrial Disorders (MD). In the reporting year, a subset of MDs, Leigh syndrome (LS) was analysed for genetic and biochemical defects. LS a subacute necrotizing encephalopathy, is a rare inherited mitochondrial disorder with a global prevalence of 1 in 40,000. Classical magnetic resonance imaging shows focal and bilaterally symmetrical necrotic lesions in the basal ganglia and brainstem. A total of seven clinically confirmed LS cases (S13, S18, S20, S24, S31, S47 and S50) were identified in the reporting year. MRI findings showed patient S24 having small focal areas of restricted diffusion involving bilateral subthalamic nuclei. Patient S47 showed diffused restriction involving bilateral caudate and putamen, suggestive of extrapontine myelinolysis like Leigh's syndrome. MRI was suggestive of diffused increase in cerebral atrophy with increase in dilatation of ventricular system, cortical sulci, extra cerebral cerebrospinal fluid (CSF) spaces, and basal cisterns in S50. Bilateral thalami were also atrophied with atrophied brainstem. Patient S13 showed generalized mild cerebral atrophy evident by prominence of lateral ventricles and extra ventricular CSF spaces. Polyploidal mucosal thickening in bilateral maxillary sinuses as well as in bilateral ethmoidal air cells were observed in S20. In S18, MRI findings had shown symmetrical white matter and gray matter involvement with dorsal brain stem involvement. Patient S31 had shown altered signal intensity in the posterior 2/3rd of bilateral putamen. Respiratory chain enzyme analysis identified isolated complex deficiency in 2 patients and rest of the patients had shown multi-complex deficiencies. Patient S18 & S31 had isolated complex deficiency in Complex I (40%) and Complex III (31.8%) respectively. S13 had shown deficiency in Complex II and III. Patient S20 had shown the presence of multi-complex deficiency in complex I, II and complex III. All four complexes were deficient in patient S24 with residual enzyme activities below 40%. Complex I & III were observed to be deficient in S47 & complex I, III and IV were observed to be deficient in S50 (Table 1).

Table 1: Respiratory chain enzyme activities in LS patients. Residual enzyme activities (expressed in %) of patients compared to controls in buccal swabs of LS patients. Deficiencies in mitochondrial complexes are marked in red; N indicates normal enzyme activity

Mitochondrial complex	**Percentage deficiency in patients (Buccal Deficiency <40%)***						
	S13	**S18**	**S20**	**S24**	**S31**	**S47**	**S50**
Complex I	N	40%	**17.30%**	**15.10%**	N	**32.30%**	**19.20%**
Complex II	**37.50%**	N	**28.50%**	**22.20%**	N	N	N
Complex III	**26.50%**	N	**7.50%**	**4.40%**	**31.80%**	**8.80%**	**28.10%**
Complex IV	N	N	N	**24%**	N	N	**5.50%**

Genetic analysis of seven patients showed presence of variants in mitochondrial genome, leading to missense variants in MT-ND6 and MT-ATP6 genes; nuclear encoded mitochondrial genes harbored multiple genetic variants in ECHS1, SURF1, TTC19 and TPK1 genes. Two variants in MT-ATP6 and TTC19 genes were found to be novel variants in our study. Long Range-PCR analysis revealed the presence of multiple large deletions in mtDNA in 5 patients. Further MD simulation analysis of the missense variants in MT-ATP6, MT-ND6 (Fig. 1), ECHS1 and TPK1 genes (Fig. 2) were carried out using I-Taesser and PyMol. Genetic variants in MT-ATP6 and ECHS1 were found to be pathogenic, and benign variants were in MT-ND6 and TPK1 genes (Table 2). Samples collection and data analysis of this study have been completed.

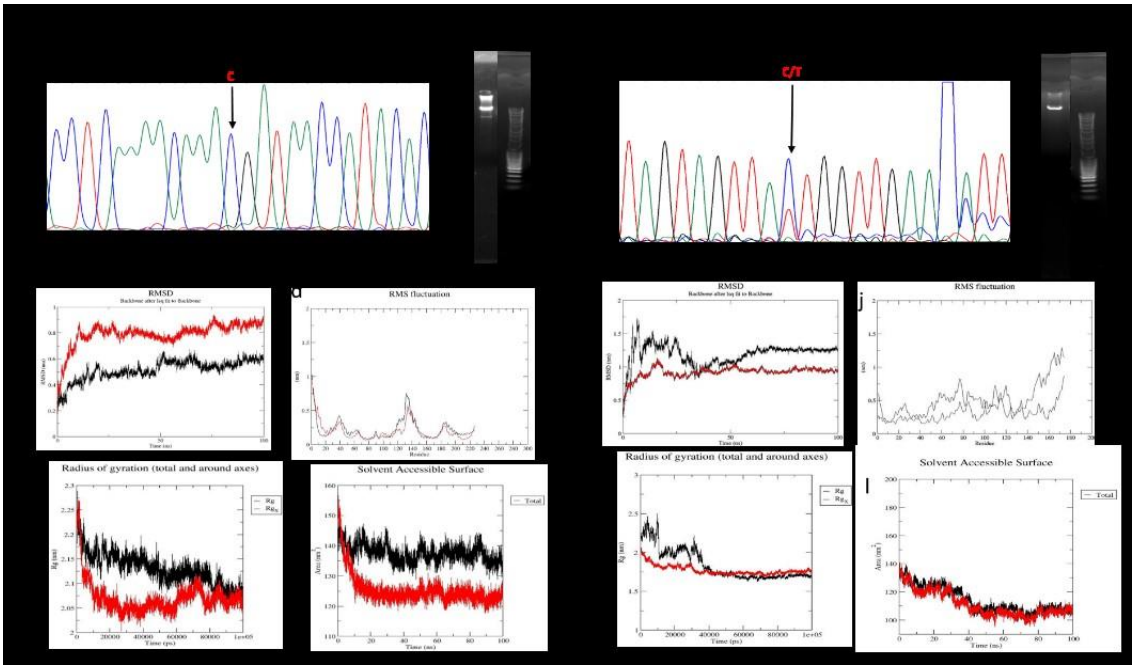

Figure 1: Sequence chromatogram, Long-range PCR and MD simulation studies of genetic variants identified in Leigh syndrome patients (a) YP_003024031.1:p.Met57Thr in MT-ATP6 gene; (b) LR-PCR showing multiple deletions; (c-d) showing structural instability and fluctuations in RMSD and RMSF plot; (e-f) showing fluctuations in Rg and SASA; (g) YP_003024037.1:p.Thr156Ile in MTND6 ; (h) LR-PCR showing no multiple deletions; (i-j) RMSD & RMSF showing fluctuations leading to structural instability; (k-l) showing no significant changes in Rg and SASA. The mutant residues in all chromatograms are depicted with arrows and in all MD simulation plots, red denotes wildtype and black denotes mutant.

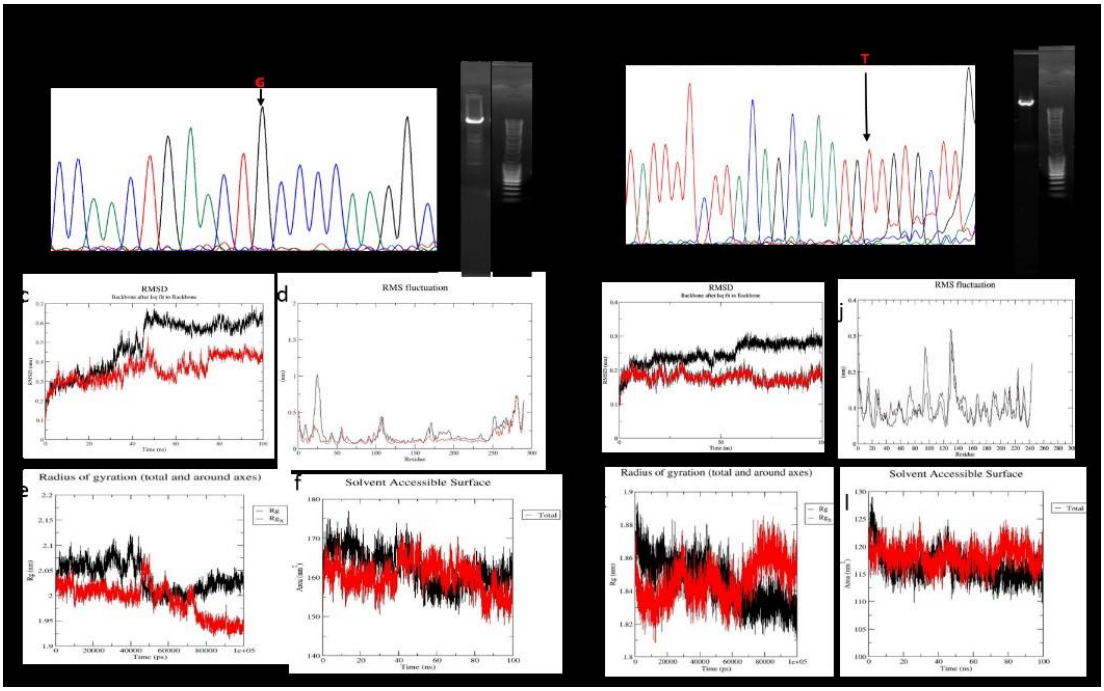

Figure 2: Sequence chromatogram, Long-range PCR and MD simulation studies of genetic variants identified in Leigh syndrome patients. (a) NP_004083.3:p.Arg54Cys in ECHS1 gene; (b) LR-PCR showing multiple deletions in S18; (c-d) showing mild fluctuations in RMSD and RMSF plot; (e-f) showing fluctuations in Rg and SASA; (g) NP_071890.2:p.Asp207Val in patient S47; (h) LR-PCR showing no multiple deletions in S47; (i) RMSD showing mild fluctuations leading to structural instability; (j-l) showing no significant changes in RMSF, Rg and SASA. The mutant residues in all chromatograms are depicted with arrows and in all MD simulation plots, red denotes wildtype and black denotes mutant.

Table 2: Details of pathogenicity of genetic variants identified in Leigh syndrome cases

Patient ID	Gene	Genetic variant	Zygosity	Novel/ known	PolyPhen-2	CADD score	MAF (South Asian)
S50	**MT-ATP6**	**chrM:8696T>C (p.Met57Thr)**	**Homoplasmic**	**Novel**	0.99 (probably damaging)		N/A
S31	**TTC19**	**NM_017775.4:c.903T>A (p.Tyr301Ter)**	**Homozygous**	**Novel**	Termination	N/A	N/A
S13	MT-ND6	chrM:14207G>A (p.Thr156Ile)	Heteroplasmic	rs879217937	0.375 (Benign)		0.00 (N/A)
S18	ECHS1	NM_004092.4(ECHS1):c.160C>T (p.Arg54Cys)	Homozygous	rs758723288	1 (probably damaging)	31	1.1E-05
S20	SURF1	NM_003172.4:c.532_535	Homozygous	rs105751	Termination	33	1.1E-05
S24		del (p.Asn178GlufsTer9)		7942		31	1.1E-05
		NM_003172.4:c.758_759 del (p.Thr253SerfsTer38)	Homozygous	rs782349178			
S47	TPK1	NM_022445.4: c.620A>T (p.Asp207Val)	Homozygous	rs747262651	0.05 (Benign)	17.62	7.7E-05

5.5 Exploring Clinical and Therapeutic Relevance of Novel Biomarkers among the Children Presenting with Idiopathic and Incomplete Precocious Puberty at Tertiary Hospital, Mumbai *(Partly Funded by Indian Council of Medical Research)*

Principal Investigator : **Suchitra Surve**
Co-Principal Investigators : Antara Banerjee
Sudha Rao, Bai Jerbai Wadia Hospital for Children, Mumbai
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Duration : 2021-2024

Central Precocious Puberty (CPP) is the condition where girls reach sexual maturation at an early age due to premature reactivation of the hypothalamic-pituitary-gonadal axis leading to GnRH secretion. Central PP is the most common and idiopathic CPP (ICPP) contributes to 90% of the cases in girls Precocious puberty is associated with adverse outcomes such as risk of short stature, polycystic ovary syndrome, diabetes mellitus-1, metabolic disorders in later life. Its most detrimental effect is psychosocial stress. Some individuals present with incomplete puberty such as premature thelarche (PT), wherein the risk of disorder development is not significant and hence, a clear distinction is needed when managing these similar variants (ICPP and PT) of precocious puberty. Currently, there exists no definitive test to differentiate between ICPP and incomplete variants of PP and lack of a conclusive diagnosis may cause a delay in initiation of treatment, thus affecting health outcomes. Therefore, there is a need of exploring newer biomarkers as adjuvant markers and correlation with clinical phenotypes for a conclusive diagnosis of ICPP and PT. Increasing evidence points towards the utility of the neuropeptides upstream to GnRH such as Kisspeptin-10 (Kp-10), Neurokinin B (NKB) and Neuropeptide Y (NPY) for the diagnosis of ICPP and PT. We explored the clinical and therapeutic relevance of Kp-10, NKB and NPY. Study participants were recruited at the collaborating BJ Wadia Hospital for Children, Mumbai and

Abhyudaya Nagar Clinic of ICMR-NIRRCH over a period of 3 years. 40 heathy age-matched controls who met the inclusion criteria, were recruited after screening of 250 girls. Out of the 86 precocious puberty cases, 57 girls meeting inclusion criteria were recruited as PP cases, of which 33 and 23 were confirmed ICPP and PT cases respectively, and one case remains to be classified. Given below are the representative results where the circulating level of Kp-10, NKB, NPY were evaluated among the 40 prepubertal control participants, 33 ICPP cases and 23 PT cases. As reported previously (Annual report 2023-24, pp. 97-99) a significantly higher level of Kp-10 was detected in ICPP cases ($p=0.0002$) and PT cases ($p<0.0001$) as compared to control participants. However, there was no significant difference in the Kp-10 levels observed between the ICPP cases and PT cases ($p=0.7380$). We observed that basal LH levels were lower in girls with PT as compared to ICPP but their values were not discriminatory between the two groups. Thus, we hypothesized that the ratio of Kp-10 to LH might aid in discriminating between the two groups. Towards this, we calculated the ratio of Kp-10/LH (Fig. 1B) in each patient in both groups and observed that a majority of PT cases had a higher index as compared to ICPP cases. This ratio termed as Kp-10/basal LH index was subjected to Receiver Operating Characteristic (ROC) analysis as shown in Fig. 1C. A cut-off of <4.07 led to the segregation of ICPP cases from PT cases with a specificity of 86.96% and sensitivity of 72.73% towards identification of ICPP below this index.

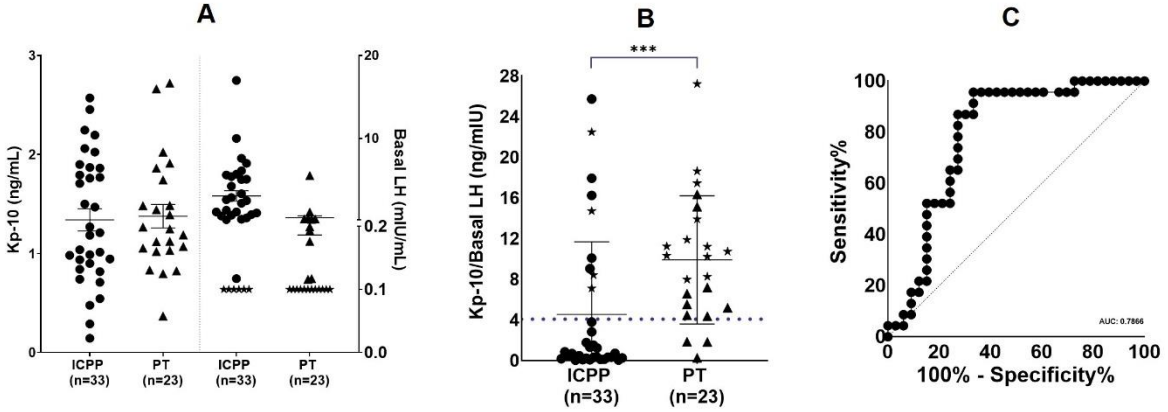


Figure 1: Assessing the ability of Kp-10/basal LH index (B), to differentiate ICPP and PT cases (Data represents median values with interquartile range). All assays were performed in duplicates, where circles represent ICPP cases and triangles represent PT cases. As seen in (A), some ICPP and PT cases exhibited basal LH values of 0.1 mIU/ml (represented by stars) but had distinct Kp-10 values. Hence, suggesting the unreliability of using basal LH or Kp-10 parameters individually for differentiating ICPP and PT. Upon calculating the ratio, the majority of PT cases exhibited higher indices in comparison with ICPP cases as seen in (B), enabling a marked segregation of the ICPP cases from PT cases. The receiver operating characteristic curves of Kp-10/basal LH (C), had an area under the curve 0.7866 (95% CI: 0.6633-0.9099, p= 0.0003).

5.6 Delineation of the Role of Isoforms of Kisspeptin in Mammalian Reproduction *(Partly Funded by Science and Engineering Research Board)*

Principal Investigator : **Antara Banerjee**
Project Associates : Aishwarya Chakraborty, Dhanashree Jagtap, B Kulkarni
Duration : 2022-2024

The signaling of the neuropeptide kisspeptin (KISS1) through kisspeptin receptor (KISS1R) triggers the secretion of gonadotrophin-releasing hormone in the hypothalamus, thus inducing puberty. KISS1-KISS1R interaction also modulates other reproductive functions such as ovulation, implantation and placentation, menopause in females; and spermatogenesis in males. KISS1 is a product of the KISS1 gene which undergoes proteolytic processing from an initial 145 amino acid

peptide to give rise to 54-mer (Kp-54), 14-mer (Kp-14), 13-mer (Kp-13) and 10-mer (Kp-10) isoforms, each sharing a common C-terminal decapeptide sequence. Not much is known about the physiological significance of these KISS1 isoforms. Thus, a detailed investigation into understanding the signaling profiles of each of these KISS1 isoforms downstream to KISS1R activation is being undertaken in this study. CHO cells stably expressing wild type KISS1R were stimulated with vehicle or 4mM of each of the isoforms of kisspeptin for 1 hour, following which the cell lysates were prepared. Global proteomic alterations were assessed by LC/MS analysis (N=3). All samples were processed and RAW files generated were analyzed with Proteome Discoverer (v2.5) against the Uniprot Human database. As per the pathway analysis, a higher proportion of the upregulated genes in Kp-10 stimulated cells were related to metabolism of lipids (Fig. 1A) and in Kp-54 stimulated cells, highest proportion of upregulated genes was found to be involved in the biological process of reproduction (Fig. 1B). To validate the mass spectrometry data for Kp-10 by immunoblotting, two differentially expressed proteins involved in the IP3 lipid signaling pathway were chosen, viz Synaptojanin1 (SYNJ1) and SAC1 like phosphatidylinositide phosphatase (SACM1L). Total cell lysates of KISS1R expressing cells stimulated with different KISS1 isoforms were probed with indicated antibodies (Fig. 2). SYNJ1 is a Type II phosphoinositide 5-phosphatase crucial for synaptic vesicle recycling. It dephosphorylates the inositol ring at the 5th position on its substrates PIP2, PIP3, IP3 and IP4 (Krajnik et al., 2020). Its primary substrate is PIP2, a prominent signaling lipid involved in membrane trafficking. SACM1L is another integral membrane protein phosphatidylinositide phosphatase that hydrolyzes PIP molecules and is localized to the endoplasmic reticulum (Bethesda, 2004). The higher SYNJ1 production in Kp-10 stimulated cells corroborated with the proteomics data (Fig. 2A). However, in case of SACM1L, Kp-13 exhibited higher production as compared to Kp-10, in contrast to the data obtained by mass spectrometry. Validation for other target proteins is ongoing.

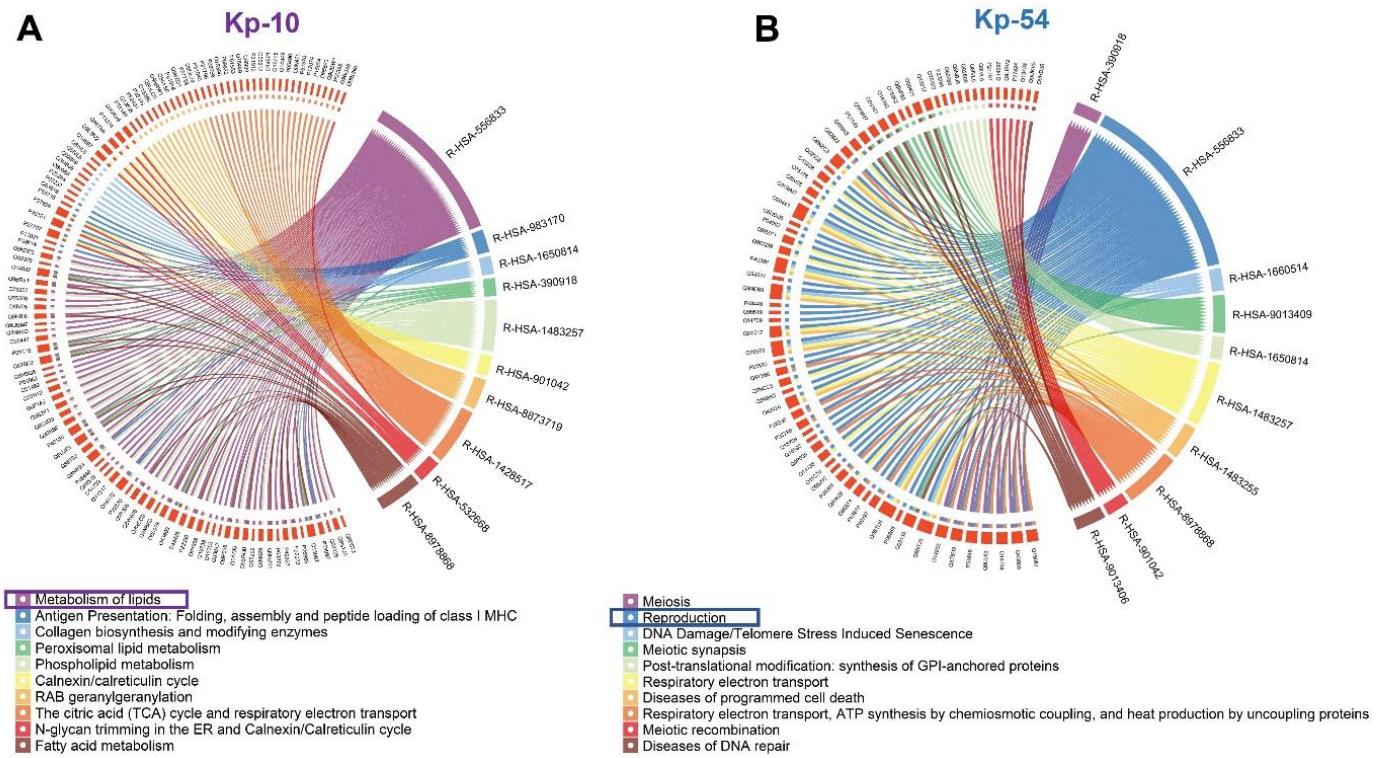


Figure 1: Reactome analysis indicating upregulated pathways post stimulation of KISS1R expressing cells with A) Kp-10 or B) Kp-54

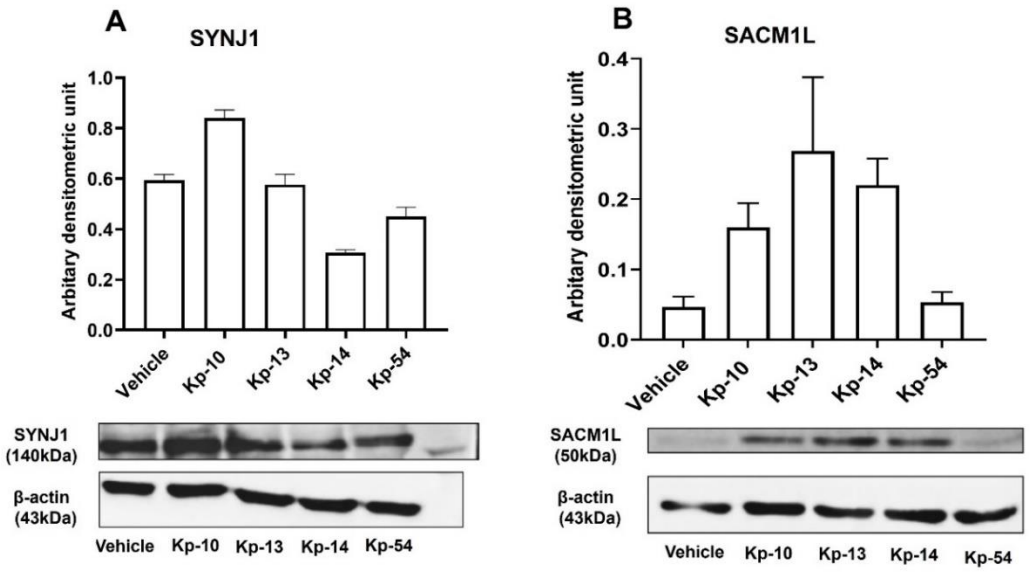


Figure 2: Western Blot and densitometric analysis of SYNJ1 (A) and SACM1L (B) proteins in KISS1R expressing cells stimulated with vehicle or kisspeptin isoforms. Bar graphs represent the densitometric value of the respective proteins normalized to beta actin levels obtained from three independent experiments, representative blots have been shown in the lower panel.

5.7 Study of Kisspeptin Receptor Oligomerization and its Functional Significance *(Partly Funded by Board of Research in Nuclear Sciences-DAE)*

Principal Investigator	:	**Antara Banerjee**
Co-Principal Investigator	:	Bhakti Pathak, Dhanashree Jagtap
Project Associate	:	Vidhi Rathod
Collaborator	:	Vidita Vaidya, Tata Institute for Fundamental Research, Mumbai
Duration	:	2023-2026

The neuropeptide kisspeptin-1 (KISS1) and its cognate G-Protein Coupled Receptor (GPCR), the kisspeptin-1 receptor, KISS1R, are central players in the induction of puberty and are key regulators that influence the entire reproductive lifespan of an individual. KISS1R is a class A G-protein coupled receptor (GPCR) belonging to the rhodopsin family. Analogous to other members of this family, it can be postulated that KISS1R also forms homo di/oligomers. This seems likely due to the evidence from clinical case studies of KISS1R mutations and KISS1R knockout data wherein the heterozygous forms of the mutations are not deleterious probably due to functional rescue of the mutant receptor by oligomerization with its wild type counterpart. However, this awaits experimental validation. The present study aims to delineate the homo di/oligomerization potential of KISS1R using in vitro model systems. Towards the same, Flag and HA epitope tagged KISS1R constructs were transiently co-transfected in CHO cells followed by their detection using the respective anti-tag antibodies. By employing complementary techniques of co-immunoprecipitation and imaging FRET analysis by acceptor photobleaching method, constitutive homo-oligomerization of KISS1R was demonstrated. Given the importance of transmembrane 7 domain (TM7) of KISS1R in formation of heterodimers with G-protein coupled estrogen receptor (GPER), a deletion mutant of TM7 (TM7del, from amino acid residues 306-328) was generated using Wild Type (WT) Flag-tagged KISS1R as a template. The TM7 deletion of KISS1R hampered its oligomerization as seen in co-immunoprecipitation studies (Fig. 3A). A densitometric analysis of the IP/input (normalise) bands seen in Western Blot was carried out for triplicate data and a 0.588-fold decrease was

observed for TM7del KISS1R IP with respect to WT KISS1R (Fig. 3B). Further, FRET by acceptor photobleaching method using directly conjugated fluorophores against epitope tags was carried out. A total of 30 cells had a robust FRET efficiency of 40.63 ± 1.63% indicating that the WT KISS1 receptors were within 10 nm of each other (Fig. 3C). A diminished FRET efficiency of 0.819±3.49% was observed in TM7del KISS1R which was statistically significant with respect to WT KISS1R ($p<0.001$) (Fig. 3E). This corroborated the results of co-immunoprecipitation studies and confirmed the importance of TM7 in contributing to the KISS1 receptor oligomer interface. Further, the naturally occurring heterozygous mutants of KISS1R, namely, R38P, P46Q, S125L and R198G implicated in delayed puberty in literature, were chosen for functional studies. The positions of the four naturally occurring heterozygous mutations in KISS1R are indicated in Fig. 4. Interestingly, all the four residues, R38, P46, S125 and R198 were conserved across the KISS1R sequence in closely related mammalian species, mouse, rats, rhesus monkeys and chimpanzees; substantiating the importance of these residues in KISS1R function. These mutations were subjected to the DynaMut2 web server that carries out in silico prediction of the effect of missense variations on protein stability and dynamics. Results indicated the mutations P46Q, S125L and R198G to be destabilising with the mutation at the R198 position being the most deleterious one.

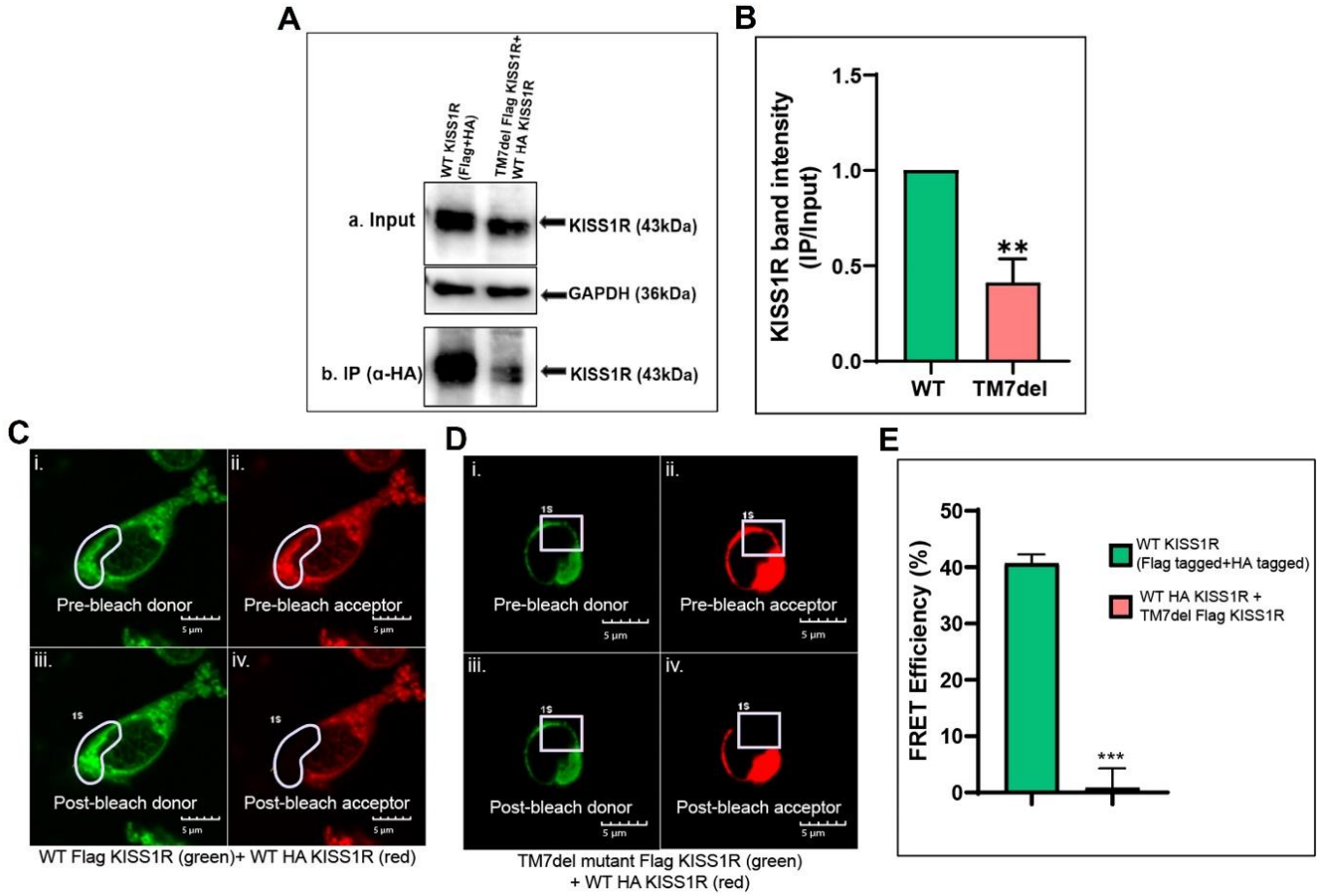
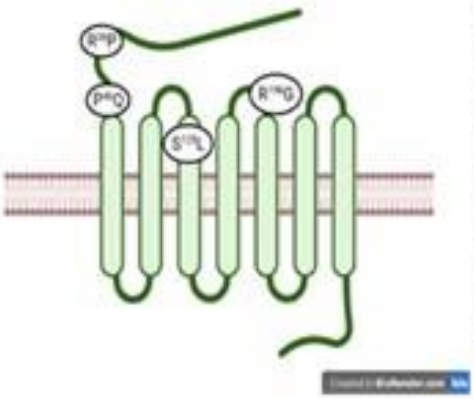


Figure 1: Role of TM7 domain of KISS1R. A) Representative western blot depicting impaired homo-oligomerization of KISS1R due to TM7del mutation. B) Densitometric quantification of the Western blot co-immunoprecipitation bands from three independent experiments. The KISS1R CoIP band intensities of WT and TM7del were normalised with their respective inputs (IP band/Input band). C) Homo-oligomerization of WT KISS1R demonstrated by FRET by acceptor photobleaching. Confocal images of CHO cells co-transfected with Flag and HA-tagged KISS1R (1:1) stained with Alexa Fluor Flag-488 (donor) and Alexa Fluor HA-555 (acceptor), respectively. Pre-bleach images of donor and acceptor fluorescence were captured with 547 and 633 lasers. A Region of Interest was selected and acceptor fluorescence was photo-bleached with 633 nm laser. Post-bleach images were captured and analysed for FRET efficiency. D) Impaired homo-

oligomerization of TM7del mutant of KISS1R demonstrated by FRET via acceptor photobleaching. Confocal images of CHO cells co-transfected with Flag-tagged TM7del mutant KISS1R and WT HA-tagged KISS1R (1:1) stained with Alexa Fluor Flag-488 (donor) and Alexa Fluor HA-555 (acceptor), respectively; Scale bar = 5 µm. E) Graph depicting the decrease in % FRET efficiency in TM7del mutant KISS1R in comparison to WT KISS1R. Data represents mean±SEM of at least 30 cells. **p< 0.01, ***p<0.001 with respect to WT, Unpaired student's t-test.



KISS1R mutant	$\Delta\Delta G^{stability}$ (kcal/mol)	Predicted Stability Change by DynaMut2
$R^{38}P$	0.79	Stabilising
$P^{46}Q$	-0.49	Destabilising
$S^{125}L$	-0.6	Destabilising
$R^{198}G$	-0.75	Destabilising

R^{38} (Extracellular domain)																		
Human	A	S	D	G	P	V	P	S	P	R	A	V	D	A	W	L	V	P	L
Mouse	A	S	D	D	P	G	S	A	P	R	P	L	D	A	W	L	V	P	L
Rat	A	S	D	G	P	G	S	A	P	R	P	L	D	A	W	L	V	P	L
Rhesus monkey	A	S	D	G	P	V	P	A	P	R	A	V	D	A	W	L	V	P	L
Chimpanzee	A	S	D	G	P	V	P	S	P	R	A	V	D	A	W	L	V	P	L
P^{46} (Extracellular domain/Transmembrane domain I)																		
Human	P	R	A	V	D	A	W	L	V	P	L	F	F	A	A	L	M	L	L
Mouse	P	R	P	L	D	A	W	L	V	P	L	F	F	A	T	L	M	L	L
Rat	P	R	P	L	D	A	W	L	V	P	L	F	F	A	A	L	M	L	L
Rhesus monkey	P	R	A	V	D	A	W	L	V	P	L	F	F	A	A	L	M	L	L
Chimpanzee	P	R	A	V	D	A	W	L	V	P	L	F	F	A	A	L	M	L	L
S^{125} (Transmembrane domain III)																		
Human	K	F	V	N	Y	I	Q	Q	V	S	V	Q	A	T	C	A	T	L	T
Mouse	K	F	V	N	Y	I	Q	Q	V	S	V	Q	A	T	C	A	T	L	T
Rat	K	F	V	N	Y	I	Q	Q	V	S	V	Q	A	T	C	A	T	L	T
Rhesus monkey	K	F	V	N	Y	I	Q	Q	V	S	V	Q	A	T	C	A	T	L	T
Chimpanzee	K	F	V	N	Y	I	Q	Q	V	S	V	Q	A	T	C	A	T	L	T
R^{198} (Extracellular loop 2)																		
Human	A	Y	C	S	E	A	F	P	S	R	A	L	E	R	A	F	A	L	Y
Mouse	T	Y	C	S	E	A	F	P	S	R	A	L	E	R	A	F	A	L	Y
Rat	T	Y	C	S	E	A	F	P	S	R	A	L	E	R	A	F	A	L	Y
Rhesus monkey	A	Y	C	S	E	A	F	P	S	R	A	L	E	R	A	F	A	L	Y
Chimpanzee	A	Y	C	S	E	A	F	P	S	R	A	L	E	R	A	F	A	L	Y

Figure 2: KISS1R heterozygous mutants R38P, P46Q, S125L and R198G. A) Positions of the four naturally mutations R38P, P46Q, S125L and R198G in human KISS1R. B) Multiple sequence alignment depicting the conservation of the residues R38, P46, S125 and R198 in KISS1R sequences across humans and the closely related mammalian species, mouse, rat, rhesus monkeys and chimpanzees. C) In silico prediction of the impact of the KISS1R mutations on protein stability using DynaMut2. The Gibbs Free Energy (ΔΔG) values for the mutants P46Q, S125L and R198G indicate that these mutations are destabilizing in nature.

REPRODUCTIVE CANCERS

6. REPRODUCTIVE CANCERS

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

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Project Associates : Junita Desouza, SM Metkari, V Patel, U Chaudhari
Collaborators : G Bakshi, S Menon, M Pal, N Sable, Tata Memorial Hospital, Mumbai
S Patwardhan, A Joshi, G Fernandes, GS Medical College & KEM Hospital, Mumbai
Duration : 2021-2027

GPER1 (G-protein coupled estrogen receptor 1), a non-conventional estrogen receptor, belongs to the family of G- protein coupled receptors spanning seven transmembrane domains. GPER1 is known to have physiological and pathological roles and cell-context dependent functions. In prostate cancer (PCa), GPER1 activation resulted in inhibition of proliferation *in vitro* and *in vivo*. However, GPER1 is not well researched for its role as a potential target for chemoprevention in PCa. Previously, we demonstrated that prostates displaying high-grade intraepithelial neoplasia (HGPIN) have a higher GPER1 expression and those with well-differentiated carcinoma (WDC) have a lower GPER1 expression compared to respective age-matched control prostates (Annual report 2022-2023, pp 113). We also demonstrated that GPER1 activation using G1 prevented disease progression in TRAMP mice from HGPIN to poorly-differentiated carcinoma (PDC) (Annual report 2023-2024, pp 115). In the reporting year, we investigated whether GPER1 expression is epigenetically regulated. Methylation analysis of 5 CpG sites spanning the GPER1 promoter and flanking regions revealed a decrease in the percent methylation in the prostate GPER1 in TRAMP mice displaying HGPIN and an increase in the animals displaying WDC, compared to respective age-matched control mice (Fig. 1). Further, to assess the specificity of GPER1 action in tumor inhibition, TRAMP mice at the HGPIN stage were treated with G1 (2.0 mg/kg body weight) alone and in combination with G15, a GPER1 antagonist. G1 treatment prevented the progression of a precancerous stage (HGPIN) to carcinoma stage as observed earlier. However, when G1 was given in combination with G15 (4.0 or 10 mg/kg body weight), the protective effect of G1 was abrogated in TRAMP mice. Histological analysis demonstrated that animals treated with G1 (2.0 mg/kg body weight) and G15 (4.0 mg/kg or 10.0 mg/ kg body weight) had prostatic histology similar to that observed in vehicle-treated TRAMP mice (Fig. 2). These studies reiterate the significance of GPER1 in the contect of prostate cancer pathogenesis.

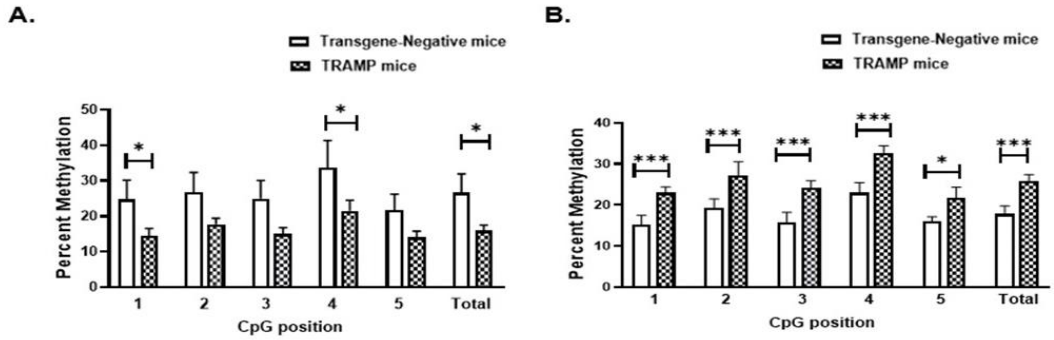

Figure 1: Site-wise and total promoter methylation analysis of the GPER1 promoter in the prostates of A) 2-month-old TRAMP mice displaying HGPIN and B) 4-month-old displaying WDC, (n=4 each). Data were checked for normality by Shapiro-Wilk test and analyzed using One-way ANOVA with Tukey's post-hoc test. *$p < 0.05$, ****$p < 0.0001$.

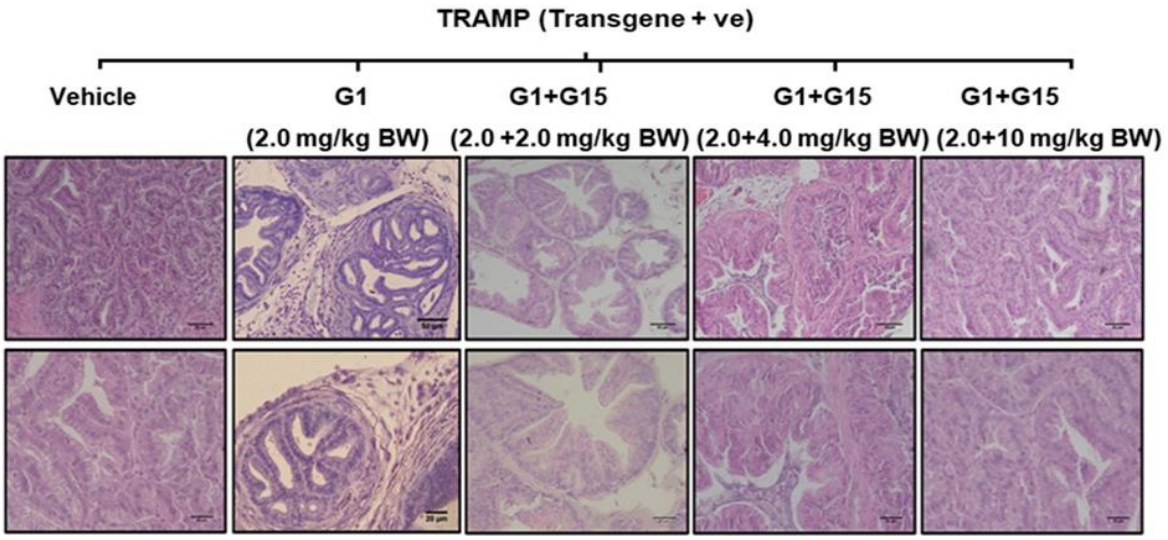

Figure 2: Haematoxylin and Eosin-stained histological sections of prostates from TRAMP mice treated with Vehicle (5% DMSO) or G1 (2.0 mg/kg BW) alone or in combination with G1 (2.0 mg/kg BW) and G15 (2.0, 4.0 or 10 mg/kg BW) [scale bar: 50 µm (top panel) and 20 µm (bottom panel)]. BW: Body Weight.

6.2 Utility of Estimating Serum PSP94 Levels in Management of Patients with Raised PSA in Clinical Setting: A Multicentric Study *(Partly Funded by ICMR)*

Principal Investigator	:	**Dhanashree Jagtap**
Co-Principal Investigators	:	A Arora, Bhakti Pathak, Antara Banerjee, G Prakash, Tata Memorial Hospital, Mumbai S Addla, Apollo Hospital, Hyderabad Ginil P, Amrita Institute of Medical Science, Kochi G Sharma, Medanta Hospital, Gurugram G Das, Dr Bhubaneswar Borooah Cancer Institute, Guwahati
Project Associates	:	B Kulkarni, A Sarma, Durga Chougule, Jui Wadwalkar
Duration	:	2024-2027

Prostate Secretory Protein of 94 amino acids (PSP94) has emerged as promising serological marker along with Prostate Specific Antigen (PSA) for differential diagnosis of benign prostatic hyperplasia (BPH) and prostate cancer (PCa). The aim of the study is to ascertain the utility of estimating serum PSP94 levels in management of patients with raised PSA in clinical settings at multiple centers across India. In the previous year (Annual report 2023-2024, pp. 116-117), we had purified PSP94 from seminal plasma. Twenty rats and four rabbits were immunized with PSP94 protein to generate polyclonal antibodies. High titre of anti-PSP94 antibodies were obtained in rats and rabbits (1:80000 and 1:320000) respectively. Newly generated anti-PSP94 antibodies in rabbit and rat were evaluated using previously standardized protocol of in-house PSP94 sandwich ELISA (Mhatre et al, 2014). In-house ELISA to detect PSP94 was standardized using 2%BSA as blocking agent, capture antibody at 1:5000 dilution and detection antibody at 1:2500. In the reporting year, 5 study sites across India were identified for participant recruitment namely Tata Memorial Hospital, Mumbai; AIMS, Kochi; Apollo Cancer Institute, Hyderabad; Medanta hospital, Gurugram and Dr. BBCI, Guwahati. The study has been registered with CTRI (CTRI/2024/11/076259) and in the reporting period, 69 patients (AIMS-Kochi n=35, Medanta-Gurugram n=22, Apollo-Hyderabad n=10, Dr. BBCI-Guwahati n=2) have been recruited and the study is ongoing.

6.3 Role of Toll-like Receptors and TLR Agonists in Modulating Response to Chemotherapy in TNBC Patients *(Partly Funded by NIRRCH intramural fund)*

Principal Investigator : **Nupur Mukherjee**
Co-Principal Investigator: Taruna Madan, Uddhav Chaudhari
Project Associates : Rushigandha Salunke
Collaborator : Shalaka P Joshi, Tata Medical Hospital, Mumbai.
Duration : 2019-2025

Global disease burden of breast cancer (BC) is ever increasing. Triple Negative Breast Cancer (TNBC), a subtype of breast cancer, accounts 15-20% of all the BC. TNBC lacks hormone receptors (ER/PR/Her2) and these patients are frequently associated with rapid metastasis and tumor recurrence. Accumulating studies have highlighted the immunogenic potential of TNBC tumors thus making immunotherapy as a promising option for treatment. Members of TLR (Toll-like receptor), a family of pattern recognition receptors (PRR), have been associated with pathogenesis of multiple cancers. However, the role of TLRs in progression of TNBC remains to be explored. Thus, in the present study we have developed and characterized a murine syngeneic TNBC model to understand the role of TLRs in TNBC pathogenesis. Briefly, the 4T1 cells (murine TNBC cell line) were injected into the 4th inguinal mammary gland via nipple by intraductal surgery Tumors became palpable within 7 days post injecting the 4T1 cells. The tumor volume and body weights were monitored biweekly up to 4 weeks, wherein progressive increase was observed in the tumor volume. Tumor tissues were subjected to histopathological analysis for confirming the tumor stages in comparison with human BC stages (Fig. 1).

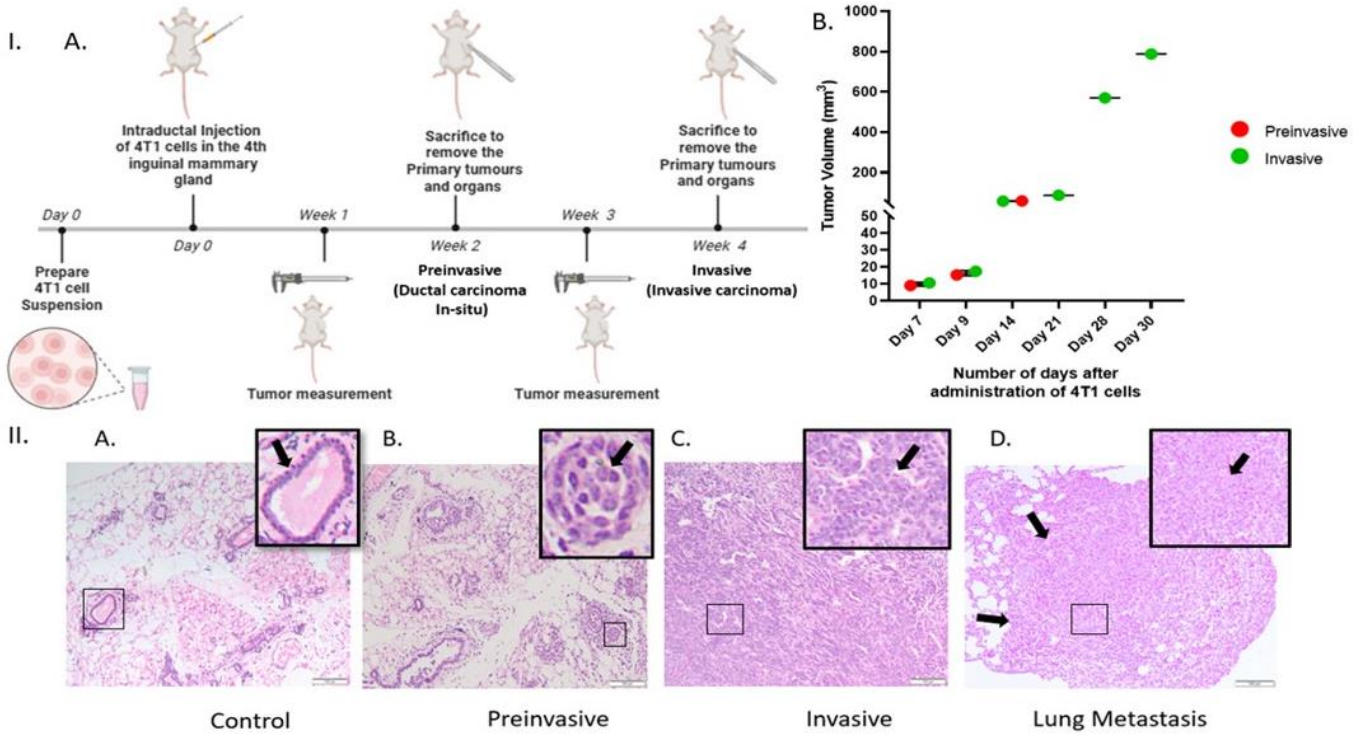

Figure 1: Development of 4T1 induced murine syngeneic TNBC model. I. A. Pictorial representation of timeline used for development of TNBC mouse model. B. Tumor volume measured at day 7, day 9, day 14, day 21, day 28 and day 30 post injection of 4T1 cells. II. Representative Images for H&E-stained tissues for A. Control breast tissue B. Ductal Carcinoma In-situ (Preinvasive) C. Invasive Carcinoma (Invasive) D. Breast tumor cell metastasis in Lungs of animals with invasive carcinoma.

The stages were confirmed for ductal carcinoma in situ (DCIS) (preinvasive) and invasive carcinoma (IC) (invasive) were further used for its characterization of markers for tumor cell proliferation, invasiveness, and epithelial content. A progressive loss of alpha smooth muscle actin expression (αSMA) (Fig. 2E-H), increase in proliferative cell nuclear antigen (PCNA) and Cytokeratin (CK) expression were observed as the tumor progressed from DCIS to IC (Fig. 2 A-D, I-L). We found that the frequency of cells expressing TLR9 significantly increases as the tumor progresses from preinvasive to invasive stage with subcellular localization (Fig. 2 M-P). Further we plan to use this model to study the cell type specific expression of TLR9 and other TLRs (3,4,6) in progressive stages of TNBC and understand the role of TLRs in TNBC.

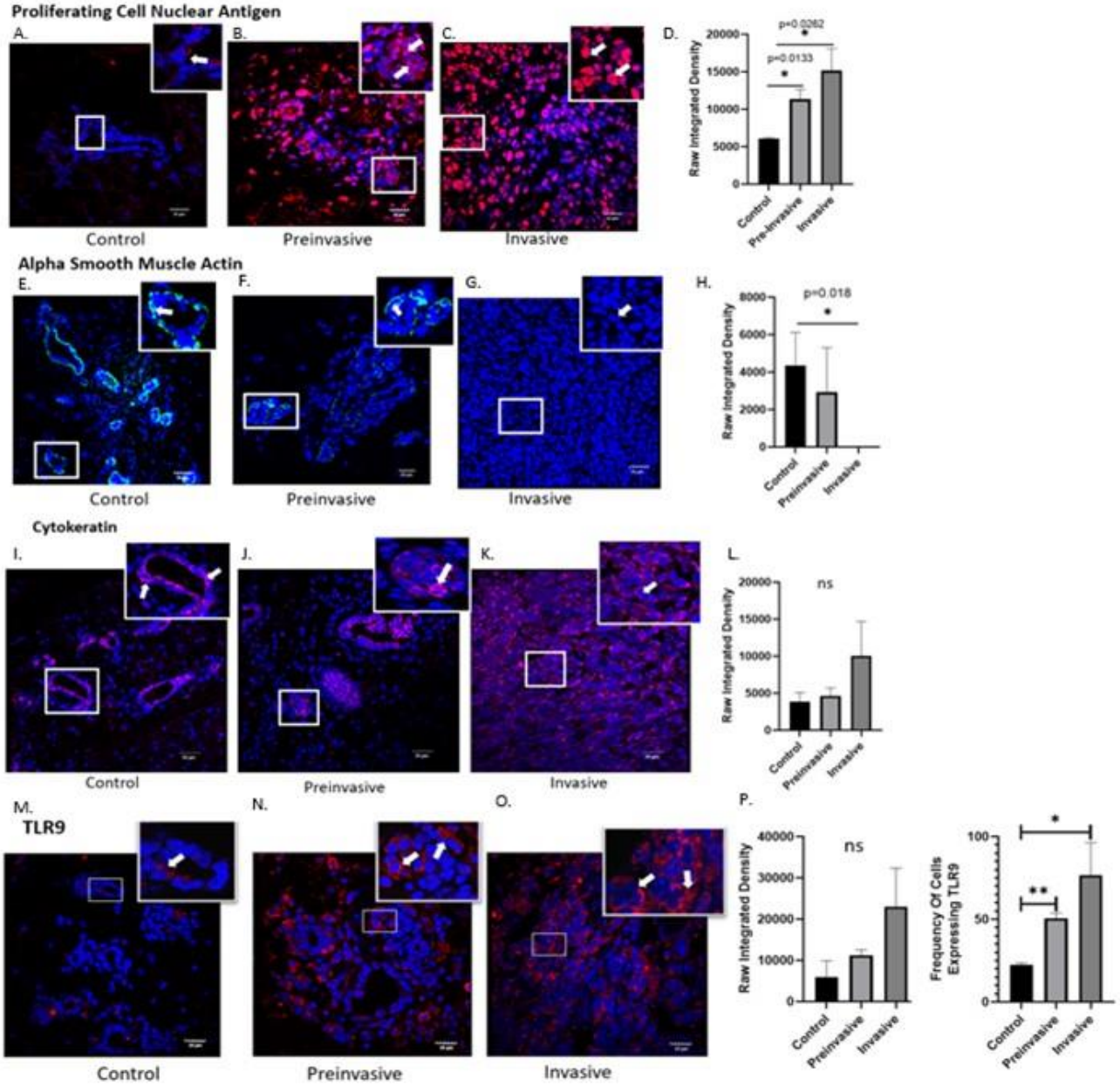

Figure 2: Representative immunofluorescence images of murine control mammary tissue, preinvasive and invasive breast tumor tissue. Panels A-C represent immunolocalization of and Panel D respresents densitometric analysis of immunoreactive PCNA. Panels E-G represent immunolocalization of and Panel H respresents densitometric analysis of immunoreactive αSMA. Panels I-K represent immunolocalization of and Panel L respresents densitometric analysis of immunoreactive cytokeratin. Panels M-O represent immunolocalization of and Panel P respresents densitometric analysis of immunoreactive TRL9.

6.4 Identification of Circulating microRNA Signatures as Diagnostic Markers for Early Stage and Metastatic Breast Cancer *(Partly Funded by Indian Council of Medical Research)*

Principal Investigator	:	**Sadhana M Gupta**
Project Associates	:	Puja Kumari, Shreya Thakkar
Collaborators	:	J Anam, Surgical Specialty Oncology Hospital V Maniar, Mumbai Oncocare Hospital
Duration	:	2021-2024

The aim of this study is to identify circulating microRNA (miRNA) profiles in sera of breast cancer (BC) patients to aid in the development of diagnostic markers for early detection of BC. BC patients are classified into four molecular subtypes, Luminal A (ER+, PR+, HER2−), Luminal B (ER+, PR−, HER2±), HER2-positive (ER−, PR−, HER2+) and Triple Negative (ER−, PR−, HER2−), with 30 participants assigned to each group. So far, 110 breast cancer patients and 30 healthy controls have been recruited. Next Generation Sequencing (NGS) was carried out to identify the differentially abundant miRNAs. NGS data analysis of 50 serum samples (40 BC patients and 10 healthy controls) revealed that, out of 1527 differentially expressed microRNAs, 17 miRNAs displayed statistically significant difference. These miRNAs were validated for their abundance in the sera of 80 BC patients and 30 healthy controls by real-time PCR. The results indicated significant differential abundance (reduction) of three miRNAs- hsa-miR-200a-3p ($p=0.0005$), hsa-miR-125b-5p ($p=0.0418$) and, hsa-miR-4306 ($p<0.0002$) in the sera of BC patients compared to healthy controls, confirming the NGS data (Fig. 1A-C). These miRNAs exhibited lower expression in tumor tissues also compared to adjacent normal tissues, hsa-miR-200a-3p ($p=0.0258$), hsa-miR-125b-5p ($p=0.0008$) and hsa-miR-4306 ($p=0.0342$) (Fig. 1D-F). Further, receiver operating characteristic (ROC) curve analysis indicated diagnostic potential of hsa-miR-4306 (AUC=0.803, 95% CI: 0.711–0.895, $p<0.0001$) and hsa-miR-200a-3p (AUC=0.801, 95% CI: 0.703–0.899, $p<0.0001$). Further, we identified targets of miRNAs- hsa-miR-200a-3p, hsa-miR-125b-5p and, hsa-miR-4306 using miRTarBase database. Database for Annotation, Visualization and Integrated Discovery (DAVID) Gene ontology analysis revealed enrichment of key biological processes viz transcriptional regulation, phosphorylation, and RNA polymerase II-mediated transcription and molecular functions- protein binding, DNA-binding transcription factor activity, and sequence-specific double-stranded DNA binding (Fig. 2). The Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis indicated significant enrichment in pathways associated with cancer metastasis and progression- AMPK, MAPK, Ras, ErbB, mTOR, Notch, Hippo, and Wnt signaling (Fig. 2). Genes such as CTNNB1, YAP1, WWTR1, and GSK3B were identified as shared targets associated with Hippo and Wnt signaling pathways. hsa-miR-200a-3p targets CTNNB1, YAP1, and WWTR1; hsa-miR-125b-5p targets WWTR1; and hsa-miR-4306 targets GSK3B. The expression of target genes was found to be elevated in tumor tissues by qRTPCR, however the difference was not significant. The study is currently ongoing, with continued recruitment and follow-up of patients to reach the target sample size. Further analyses is being carried out to evaluate the prognostic and predictive potential of these miRNAs in relation to treatment outcomes.

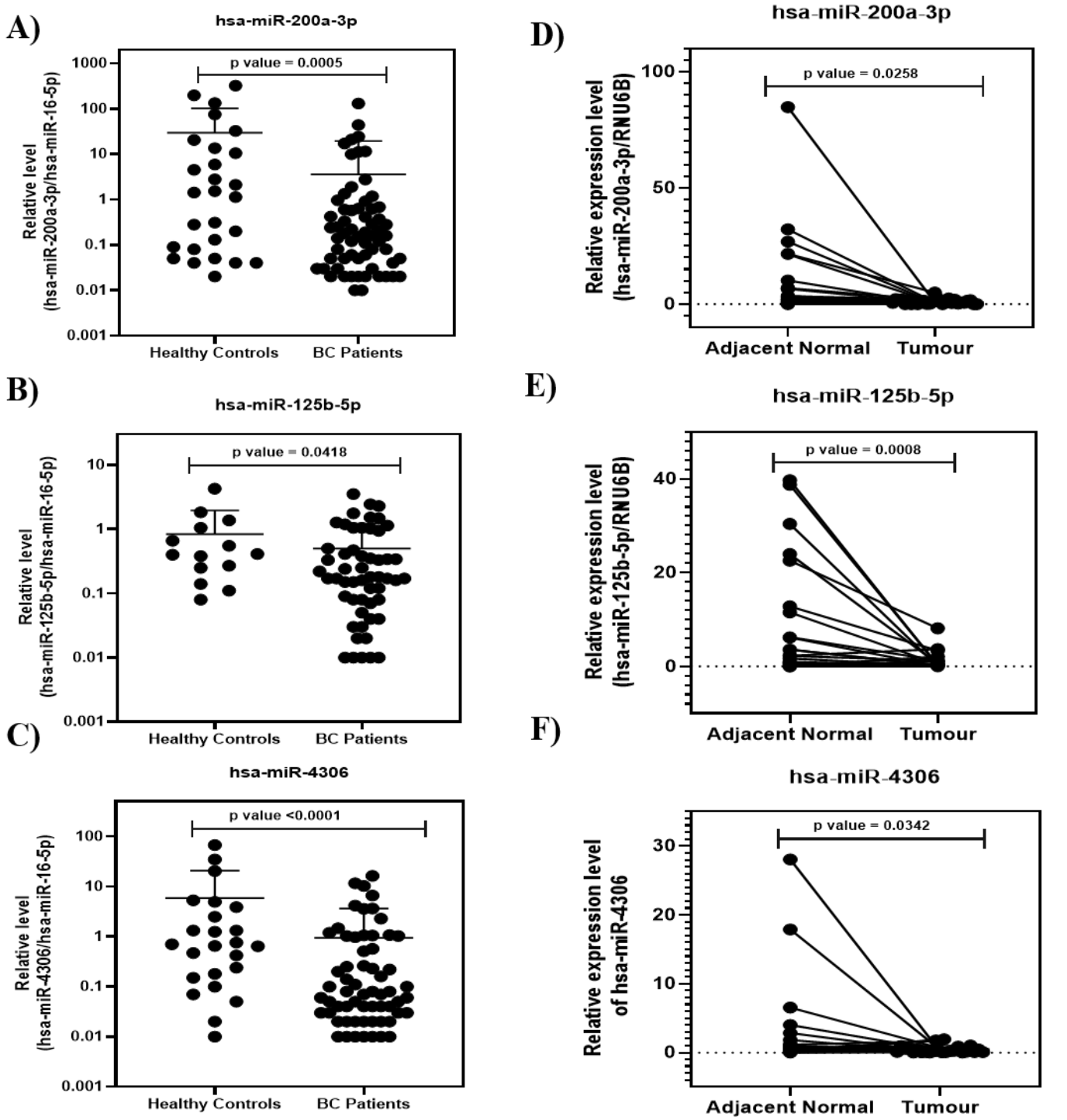

Figure 1: Relative abundance of miRNAs hsa-miR-200a-3p, hsa-miR-125b and, hsa-miR-4306 in the sera of BC patients (n=80), compared to healthy controls (n=30) (Fig. 1- A-C) and tumor tissues compared to adjacent normal tissues (n=42) (Fig. 1- D-F). $p<0.05$ was considered statistical significant.

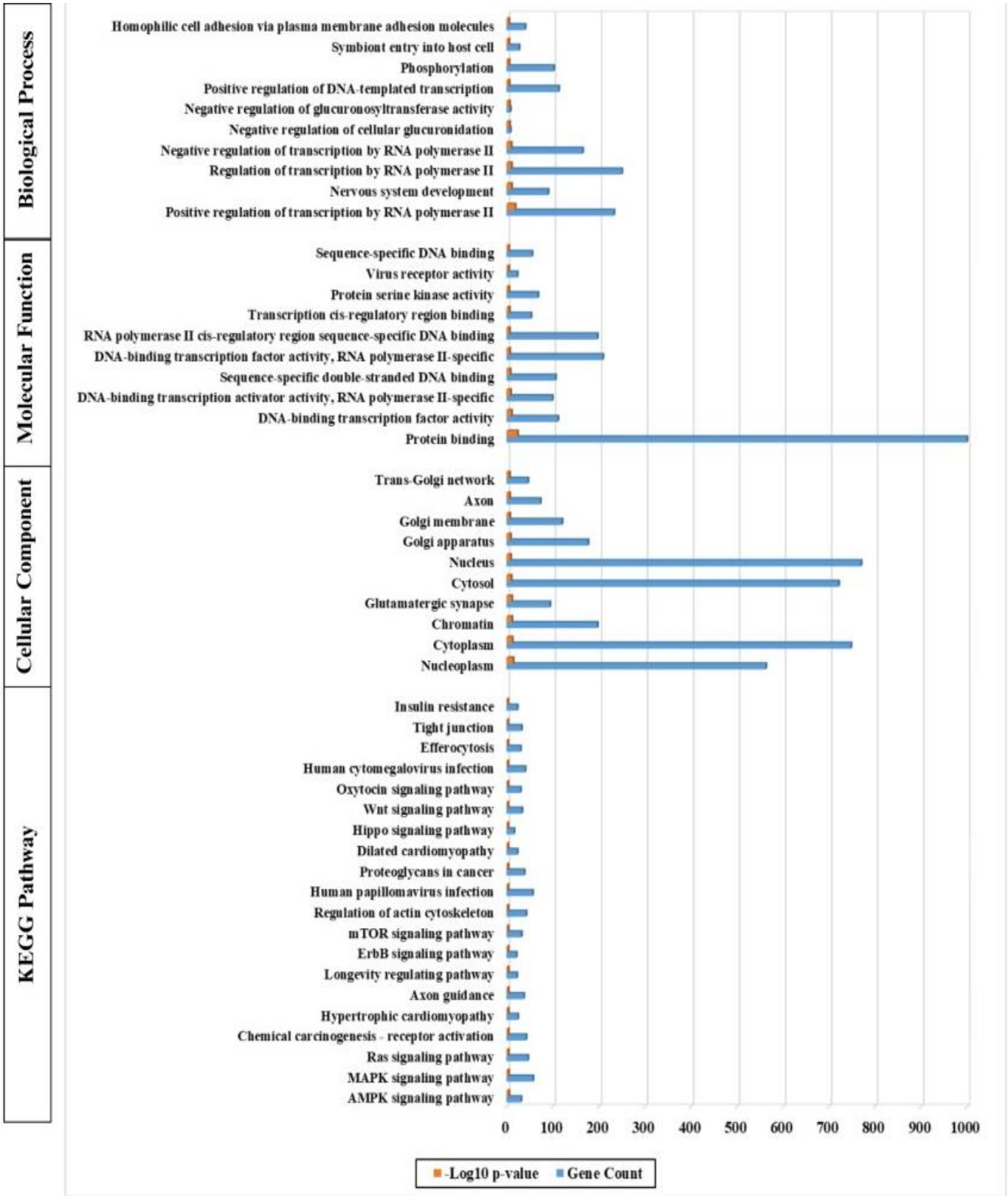

Figure 2: Functional enrichment analysis demonstrating 10 most significant GO terms for Biological Processes, Molecular Functions, and Cellular Components, 20 most significantly enriched KEGG pathways

6.5 Deciphering the Placental-Breast Epithelial Cell Cross-Talk in pregnancy Associated Breast Cancer *(Partly Funded by DST SERB)*

Principal Investigator	:	**Nupur Mukherjee**
Co-Principal Investigators	:	Geetanjali Sachdeva, U Chaudhari
Project Associate	:	P Chavan
Collaborators	:	Vandana Bansal, Norwojee Wadia Maternity, Hospital, Mumbai Shalakha Joshi, Tata Memorial Centre, Mumbai
Duration	:	2023-2026

Pregnancy-Associated Breast Cancer (PABC) is a subtype of Breast Cancer (BC) diagnosed during pregnancy or within two years postpartum. Incidence of PABC is rising in urban settings due to women delaying the age of first pregnancy. Pregnancy-associated changes in the maternal system have been previously shown to potentially play a role in BC pathogenesis. The key contributing factor is the placental tissue secretions which affect physiological functions in the mother such as breast tissue remodeling to prepare the breast tissue for lactation. Accumulating studies have shown that placental secretome can significantly alter BC cell phenotype and function (cell proliferation, invasion, and migration). We have previously observed that placental secretome can alter BC cell proliferation and clonogenic abilities. However, molecular mechanisms involved in the process are not clearly understood. In the present study, the involvement of placental cell supernatants on regulation/activation of Wnt/β-catenin signaling was investigated. BC cells (MDA-MB-231 cells) exposed to HTR-8 and BeWo (trophoblast cells) conditioned media was used as in-vitro model to mimic PABC like condition. This model was used to screen β-catenin expression in MDA-MB-231 cells treated for 72 hrs with placental supernatant of HTR-8 and BeWo cells (at different dilutions: 25%, 50% and 100%). In untreated MDA-MB-231 cells, the localization of ß-catenin was observed predominantly in plasma membrane (Fig. 1A).

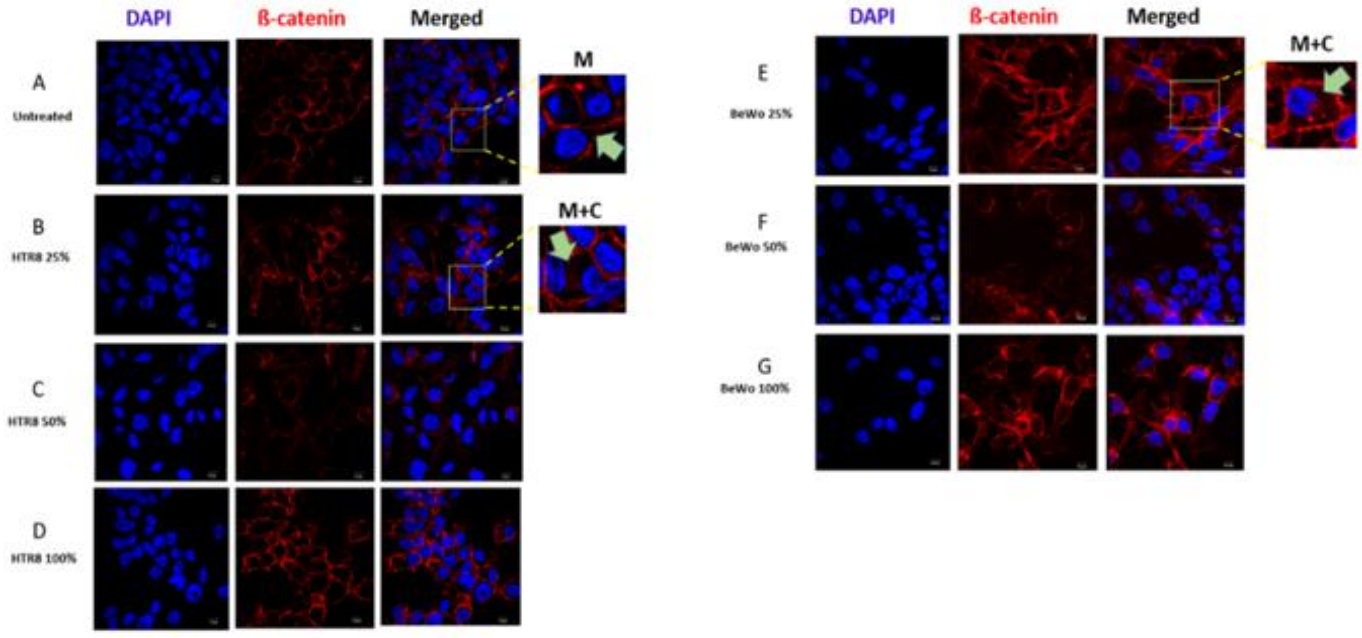

Figure 1: The β-catenin expression in HTR8/BeWo treated MDA-MB-231 cells (M: Membrane expression; M+C: Membrane and Cytoplasmic expression). Expression of β-catenin (red), detected by immunofluorescence imaging, in MDA MB 231 cells treated with placental cell supernatants with varying concentrations of conditioned medium: complete medium (A) untreated, (B) HTR8 CM 25%, (C) HTR8 CM 50%, (D) HTR8-CM 100%, (E) BeWo CM 25%, (F) BeWo CM 50%, (G) BeWo CM 100%. The experiment was done in triplicates.

No significant changes in the expression of ß-catenin was observed in HTR8 treated MDA-MB-231 vs untreated control (Fig. 2A-C). Elevated expression of β-catenin was observed in the MDA-MB-231 cells exposed to BeWo-derived conditioned medium (Fig. 1E, 1F & 1G) with an increased cytoplasmic expression of β-catenin in treated cells. Significantly higher intensity of ß-catenin expression was observed in BeWo treated MDA-MB-231 cells compared to HTR8 treated MDA-MB-231 cells (Fig. 2D) thereby indicating an activation of Wnt/β-catenin signaling in BC cells in response to placental cell supernatants. We plan to further investigate the expression of additional genes associated with Wnt/β-catenin signaling pathway that might be regulated by placental cell supernatants in BC cells. We believe that outcome of this study will aid in developing novel therapeutic targets for treating pregnancy associated breast cancer.

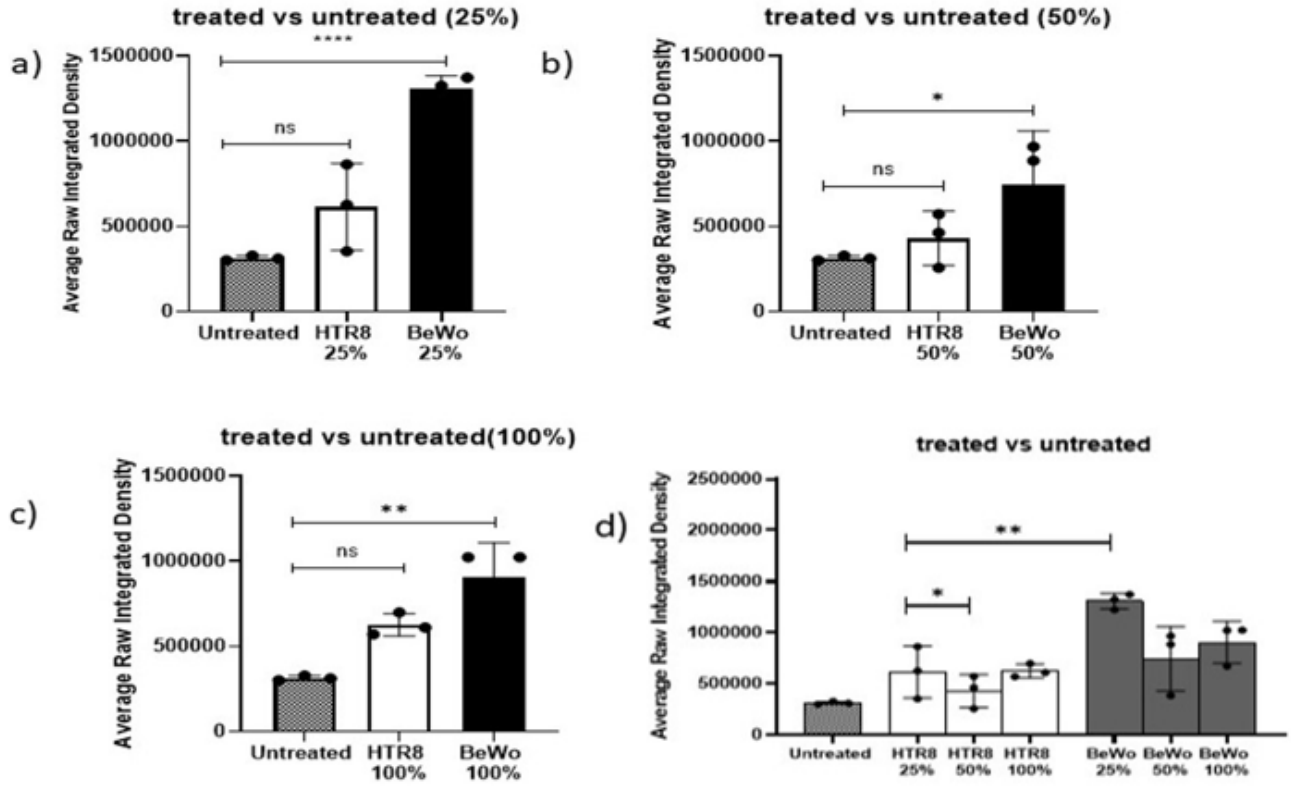

Figure 2: Intensity analysis of ß-catenin localization in treated vs untreated MDA-MB-231 cells. Average raw integrated density/cell treated with (a) 25%; (b) 50%; (c) 100%; (d) immunolocalization of ß-catenin in MDA-MB-231 cells treated with conditioned media from different placental cell types.

6.6 Develop Multicellular 3D Tumor Model of Metastatic Breast Cancer as a Platform to Test Novel Therapeutic Drugs *(Funded by DHR International fellowship for Young Biomedical Scientists 2024)*

Principal Investigator : **Nupur Mukherjee**
Co-Principal Investigator : J Prakash, Advanced Organ Bioengineering and Therapeutics Lab, University of Twente, Netherlands
Duration : 2024-2024

Tripe Negative Beast Cancer (TNBC) is a highly metastatic subtype of breast cancer. Most of the women diagnosed with TNBC develop lung metastasis during the course of their treatment. Specific treatment options for BC patients with lung metastasis is very limited and often associated with poor prognosis. The study was focussed on establishment and characterization of multicellular in-

vitro 3D model of human breast lung metastatic tumor that can be used as platform to test novel therapies for treating metastatic breast cancer. 3D-multicellular microtissues were consructed using human breast cancer cell line (MDA MB 231 or MM231), human lung fibroblasts (HPF) and PMA differentiated monocytes (THP1) using established protocol in Dr J Prakash's lab (Pednekar et al 2021). Organoid like structures were observed to be formed from day 3 onwards. A steady increase in size of BC (MM231) organoid monoculture was observed from day 1 to day 7 (Fig. 1).

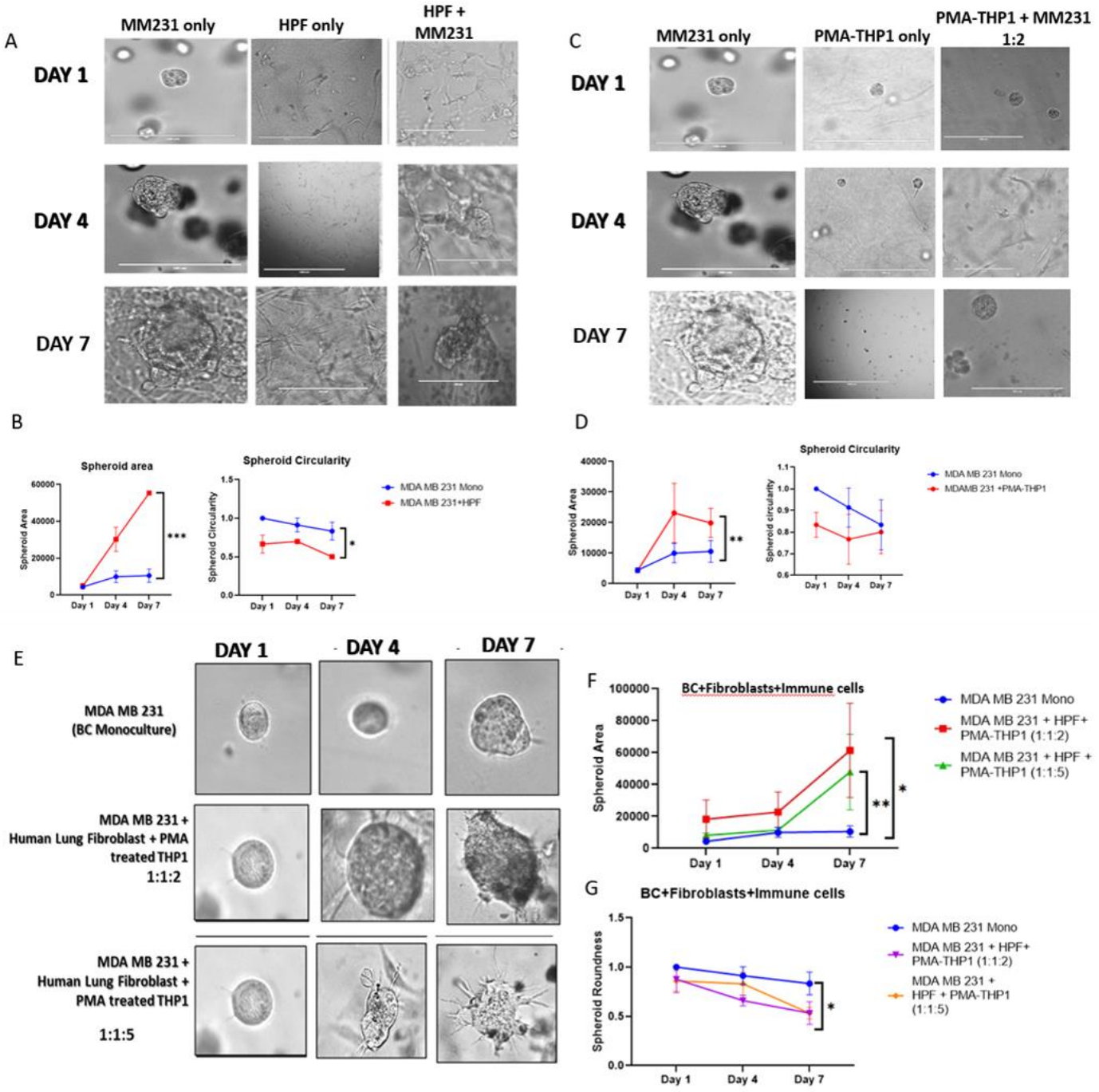

Figure 1: Tumor characteristics of breast tumoroids cultured with human lung fibroblasts, differentiated human monocytes and invasive human breast tumor cells. (A-B) Projected area and circularity of breast tumoroids generated from co-culture of BC (MDA MB 231) cells with lung fibroblasts (HPF); (C-D) Projected area and circularity of breast tumoroids generated from co-culture of BC cells with differentiated monocytes (THP1); (E-F) Projected area and circularity of breast tumoroids generated from tri-culture of BC (MDA MB 231) cells with lung fibroblasts (HPF), and differentiated monocytes (THP1).

Interestingly, in presence of pulmonary lung fibroblasts or monocytes, a significant increase ($p<0.001$) in the size of the breast tumors were observed (Fig. 1A-D). A simultaneous decrease in tumor circularity of BC tumoroids was observed when co-cultured with fibroblast or differentiated monocytes indicating an increase in invasive potential of breast tumor cells in presence of lung fibroblasts or monocytes. To further understand the significance of molecular cross-talk between BC organoids with lung stromal tissue components, a triculture was established with BC/lung fibroblasts/macrophages in ratio of (1:1:2, representing low immune cell enriched tumor and 1:1:5, representing high immune cell enriched tumor). The BC organoid size is significantly higher in the BC tumors with high density of immune cells compared to the ones having low density immune cells (Fig. 1E-G). This indicates that the molecular cross-talk between BC cells with fibroblasts/immune cells is promoting breast metastatic progression. The number of viable cells also increased in presence of lung fibroblasts while BC organoids co-cultured with just immune cells showed an overall decrease in total number of viable cells (determine by LIVE/DEAD immunostaining assay). This indicates a potential inhibitory role of immune cells in metastatic breast cancer progression. Further staining the tumors with epithelial/fibroblast cell specific markers showed that duct like structures formed by the BC tumoroids by Day 7 (Fig. 2). Also changes in extracellular matrix (ECM) density, expression of ECM proteins like FAP/Fibronectin/Vimentin were also observed in the multicellular BC model. In addition, upregulation in immunomodulatory genes such as IL6/CD163 was also observed in the in-vitro tumoroid model of metastatic breast tumor. A 3D metastatic breast tumor model may serve as a platform to test novel therapeutic drugs for treating breast cancer patients.

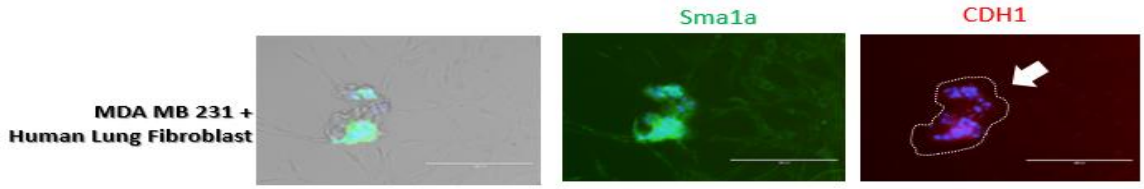

Figure 2: Immunostaining of metastatic breast tumoroids with Sma1a (fibroblast cell marker) and CDH1 (epithelial cell marker) in Day 7 breast tumoroids.

6.7 Pragmatic Stepped Wedge Cluster Randomization Trial to Evaluate the Screening of Clinical Breast Examination through Health Education Interventions in Rural Maharashtra *(Partly Funded by DHR)*

Principal Investigator	:	**Shahina Begum**
Co-Principal Investigator	:	R K Prusty
Co- Investigators	:	Anushree Patil, M Bhise
Project Associates	:	Supriya Shivaji Utale, Darshika Sanjeev Sonawane
Collaborators	:	Government of Maharashtra
Duration	:	2023-2026

The objective of this study is to form a sustainable, community-based outreach initiative that utilizes Accredited Social Health Activists (ASHAs) to promote breast cancer awareness. In addition, the study aims to train Auxiliary Nurse Midwives (ANMs), Lady Health Visitors (LHVs), and mid-level care providers to perform Clinical Breast Examinations (CBEs) at the primary healthcare level. A key component of this initiative is the creation of an efficient referral system to ensure timely

diagnosis and treatment of breast cancer cases. The study employs a Stepped Wedge Cluster Randomized Trial (SW-CRT) design, wherein each subcentre is treated as a cluster. A total of 500 women between the age group of 30-55 years were selected from the Junner block of Pune district in Maharashtra. The goal is to evaluate the impact of the intervention on changes in women's knowledge and the utilization of breast cancer services over a specified period. Baseline data collected from the participants reveal that although awareness of the symptom "painless lump in the breast" is relatively high, with 77% of women recognizing it as a sign of breast cancer, knowledge of other symptoms remains significantly low. Only 15% of women identified "pulling in of the nipple" as a potential indicator of breast cancer. Approximately one-fifth of the participants, or 21%, were aware that symptoms such as dimpling of the breast skin, ulceration, and changes in breast shape could also be associated with breast cancer. About one-third of the women recognized that pain in the breast region and redness of the breast skin might indicate the presence of breast cancer, with 33% awareness for each symptom. Regarding risk factors, the baseline data showed that more than half of the participants agreed or strongly agreed that the use of tobacco (61%) and not breastfeeding a child (57%) are associated with an increased risk of developing breast cancer. However, knowledge of most other known risk factors for breast cancer was generally low among the participants, as reflected in the accompanying data (Fig. 1). The findings also indicated that most women held positive attitudes towards breast cancer treatment and were willing to participate in prevention programs. They also expressed supportive social norms regarding discussions and actions around breast cancer. Despite these encouraging attitudes, awareness of preventive practices, particularly breast self-examination (BSE), was notably poor among the participants. At present, the intervention phase of the study is ongoing.

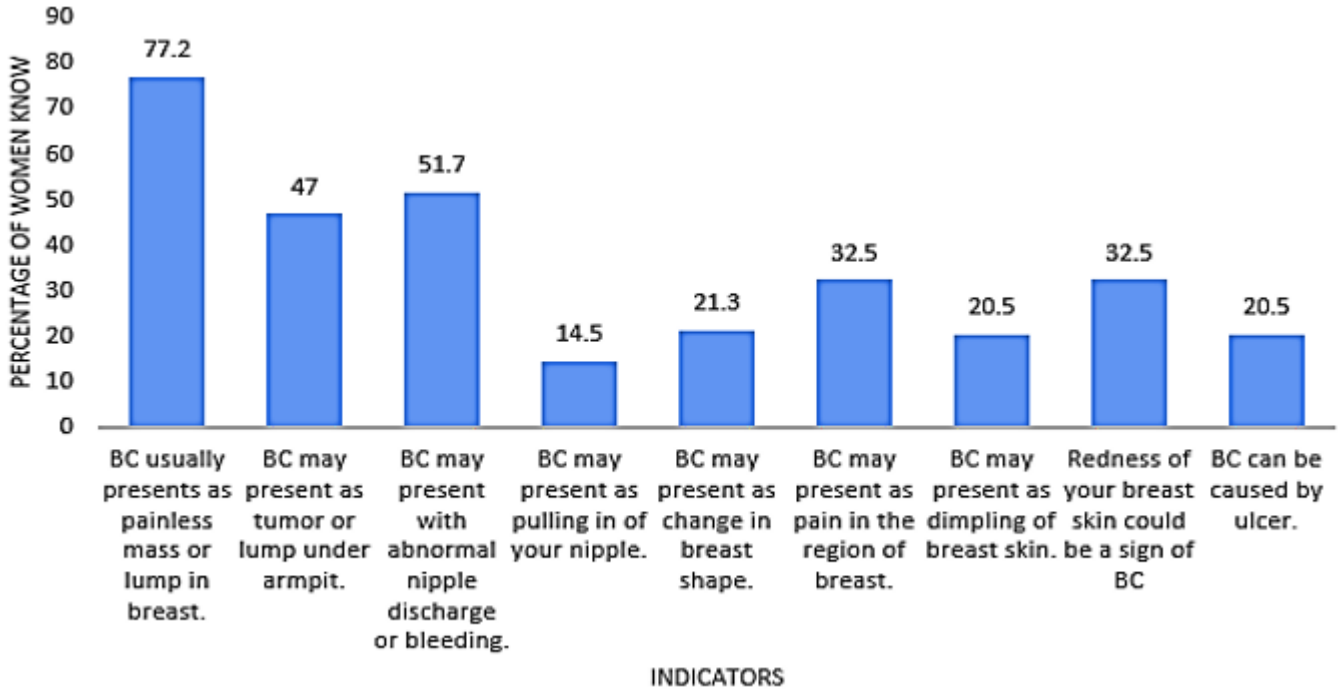

Figure 2: Knowledge of breast cancer signs and symptoms among the participants

6.8 Analysis of Molecular Cargo and Paracrine Effects of Extracellular Vesicles Secreted by Ovarian Cancer Cells

Principal Investigator : **Bhakti R Pathak**
Project Associates : Meghali Borkotoky, Ananya Breed, Dhanashree Jagtap, Antara Banerjee
Duration : 2021-2027

Late diagnosis and development of chemo-resistance are the two most common hurdles in management of ovarian cancer. Extracellular Vesicular (EV) cargo derived from tumor cells plays a crucial role in cellular communication, promoting tumor progression and metastasis. However, there is limited in-depth analysis of EV cargo from ovarian cancer that can be potentially used in the diagnosis and/or prognosis and treatment of ovarian cancer. This study aims to characterize the proteomic and transcriptomic profiles of EVs from ovarian cancer cells under different conditions and also to evaluate their paracrine effects and uptake mechanisms. Towards this, we compared molecular cargo of EVs from 2D and 3D grown ovarian cancer cells and mouse model of ovarian cancer. Earlier, we reported comparison of proteomic profiles of EVs liberated from 2D and 3D grown ovarian cancer cells (Annual report 2023-2024, pp. 122-123). We compared the proteome cargo of EVs derived from 2D and 3D grown ovarian cancer cells (OVCAR4). We also validated one of the differentially abundant proteins of EVs derived from 3D culture via immunoblotting (in OVCAR4 and OVCAR5 human HGSOC cell lines), referred then as 3D-EV-1 which is Ferritin Heavy Chain (FTH). In the reporting year, EVs isolated from 2D and 3D grown ID8, a mouse origin ovarian cancer cell line, were evaluated by immunoblotting (Fig. 1A). Though 2D as well as 3D grown cells showed presence of FTH, it was highly enriched in the EVs isolated from the 3D grown cells than 2D grown cells. Densitometric analysis revealed ~ 3 fold increase in FTH levels in 3D cell lysates and ~50 fold increase in 3D derived EVs. ID8 cells were then used to generate ovarian cancer ascites model by intraperitoneal injection into 4-6 weeks old female C57BL/6 mice. After about 90–120 days, mice developed peritoneal bloating due to ascites accumulation in the abdomen. Ascetic fluid was collected by paracentesis and used for EV isolation. EVs were characterized for classical EV markers CD9, CD81, and CD63. Unlike EVs from 2D and 3D cultures of ID8, EVs from ascites showed the presence of only CD63, while CD9 and CD81 were either low or undetectable (Fig. 1C). FTH was present in both, ascitic cells and EVs from ascites. Since cellular component of ascites contains tumor cells as well as immune cells and mesothelial cells, exact contribution of EVs from each population cannot be ascertained.

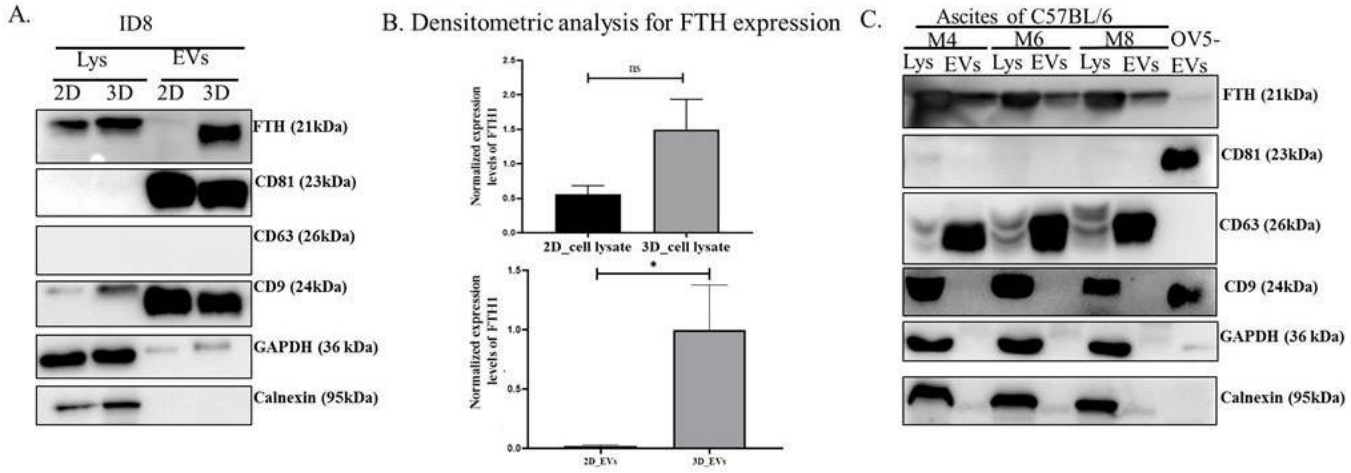

Figure 1: A) Immunoblots for 2D & 3D grown ID8 cells and EVs show enriched presence of classical EV markers CD9 & CD81 and absence of ER marker calnexin. EVs from 3D grown cells of ID8 showing an enriched presence of FTH. GAPDH was used as a loading control for cell lysates B) Densitometric analysis of the immunoblots shown in A. For lysates, expression levels were normalized with GAPDH and for EVs it was normalized with CD81. Significance of the difference between the groups was tested by unpaired t-test (p-value * < 0.05, n=3, ns = non-significant) C) Characterization of ascetic fluid derived EVs from three C57BL/6 mice (M4, M6 and M8) by immunoblotting for EV markers and FTH presence. OV5 2D grown cells derived EVs were taken as positive controls for EV markers CD9 and CD81 and negative control for CD63

ID8 syngenic model was then used to study the impact of cisplatin treatment on ascites re-accumulation (Fig. 2A). It was observed that mice treated with two doses of cisplatin (5 mg/kg, once per week) showed a twofold slower re-accumulation of ascites compared to saline-treated controls (Fig. 2B). EVs from cisplatin-naive and exposed ascites will be isolated and further subjected to proteomics analysis to investigate treatment-induced changes in the EV cargo including FTH.

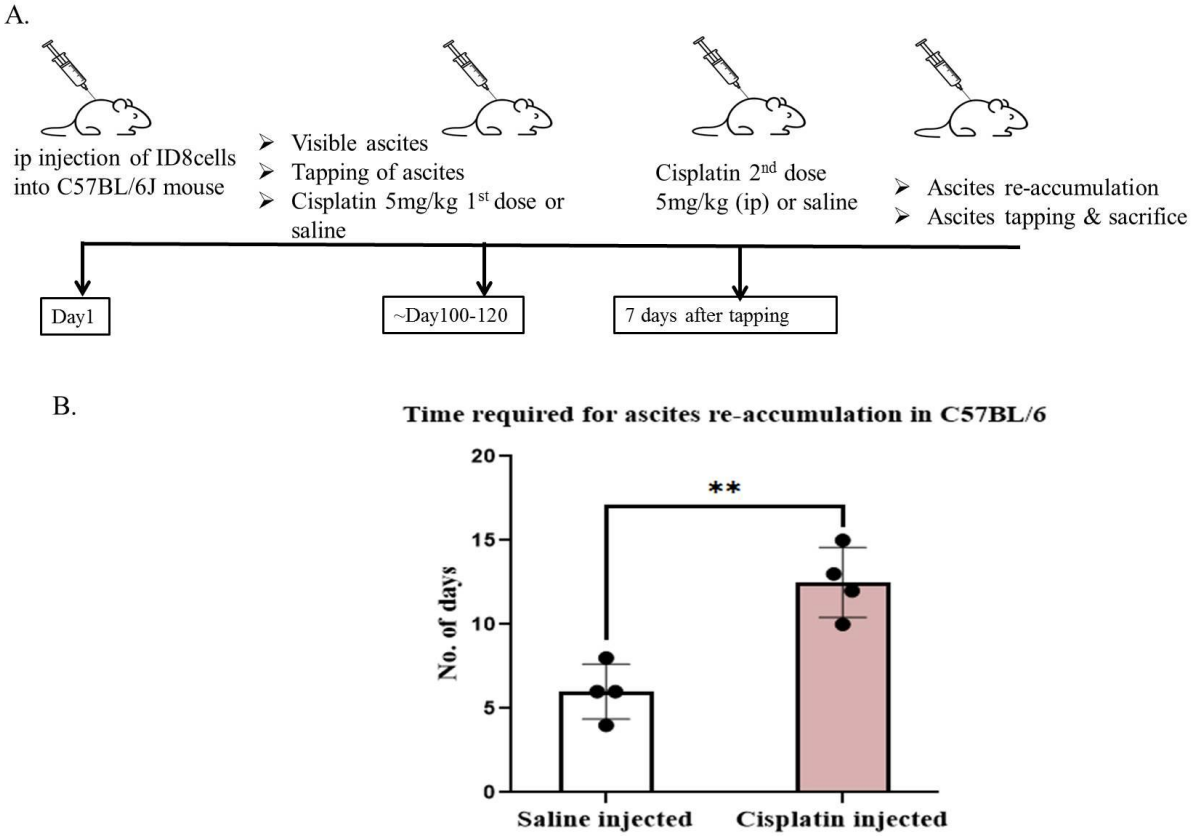

Figure 2: A) Schematic representation of generation of ID8 syngeneic model and cisplatin or saline treatment B) Bar graph depicting time taken for ascites accumulation after cisplatin or saline injection in C57BL/6 mice. Statistical significance was assessed by unpaired t-test (**p-value < 0.005, n=4)

6.9 Validation Study of Indigenous HPV Tests for Cervical Cancer Screening (i-HPV) *(Funded by BIRAC)*

Principal Investigator	:	Neerja Bhatla
Site PI	:	**Anushree Patil**
Co-Principal Investigators	:	Kiran Munne, V Bhor
Project Associates	:	RutujaWakchaure, Sunaina Yadav
Collaborators	:	Seema Singhal, Pranay Tanwar, Shalini Singh, Showket Hussain, Partha Basu, A Baena, Mary Luz Rol, WHO-IARC
Duration	:	2023-2025

The study was planned for cross-sectional validation of indigenous HPV assays. The biobank at the International Agency for Research on Cancer (IARC), WHO has samples from women aged >30 years collected in PreservCyt (Hologic) medium during the multicentric study of cervical cancer screening with HPV testing and assessment of triage methods in Latin America: the ESTAMPA

(EStudiomulticéntrico de TAMizaje y triaje de cáncer de cuellouterino con pruebas del virus del PApilomahumano; Spanish acronym) study. These samples have known HPV, cytological and histopathological status. Our technical partners at IARC provided blinded aliquots. It was aimed to validate an indigenously developed point-of-care HPV test that can detect at least the 7 most common oncogenic strains included in the nonavalent HPV vaccine, namely, HPV 16, 18, 31, 33, 45, 52, and 58. The test is likely to have an efficacy comparable to already FDA-approved HPV tests to detect high-grade cervical intraepithelial neoplasia (CIN2+). Such a Make-In-India initiative will be cost-effective for our country and other LMICs and will be suitable for a single visit approach. Primary objectives of the study are to compare the concordance of hrHPV detection by indigenously developed HPV tests with bio-banked samples tested with Cobas HPV test (Roche), and to also assess their performance for detection of CIN2+ disease compared to the Cobas HPV test. Secondary objectives are to determine type-specific agreement between the indigenously developed HPV tests and Cobas HPV test, and to assess the inter-laboratory assay variability. During the reporting period, three indigenously developed point-of-care HPV tests HPV-Q (Genes2Me), PathoDetect 7 and 14 (Mylab), Truenat HPV-HR (Molbio) were validated by AIIMS Delhi; ICMR-NIRRCH, Mumbai; and ICMR-NICPR Noida respectively. 1100 Samples from ESTAMPA CRI participants were analysed by each indigenous platform, including 100 histopathology proved CIN2+ cases (enrichment set). Inter-laboratory testing of 500 samples was done with MolBio Truenat Platform at ICMR-NIRRCH. The results were uploaded on the RedCap platform and the data were analysed. Samples from 1000 screened women who were screened by Cobas HPV test, were randomly selected, of which 13% of samples corresponded to HPV-positive women. Among HPV-positive women, about 40% would have a diagnosis of any cervical neoplasia (i.e., CIN1+) at enrolment, with about 25 cases of histopathology proved CIN2+. Additionally, 100 samples were provided from women in whom there was a histopathology diagnosis of CIN1+, of whom more than 50% had CIN3+ (Fig. 1). Samples from HPV-negative CIN2+ cases (n= 8) were included in the enrichment set. Thus a total of 1100 samples from ESTAMPA CRI study participants were analysed by each indigenous platform, including 100 histopathology proved CIN2+ cases (enrichment set).

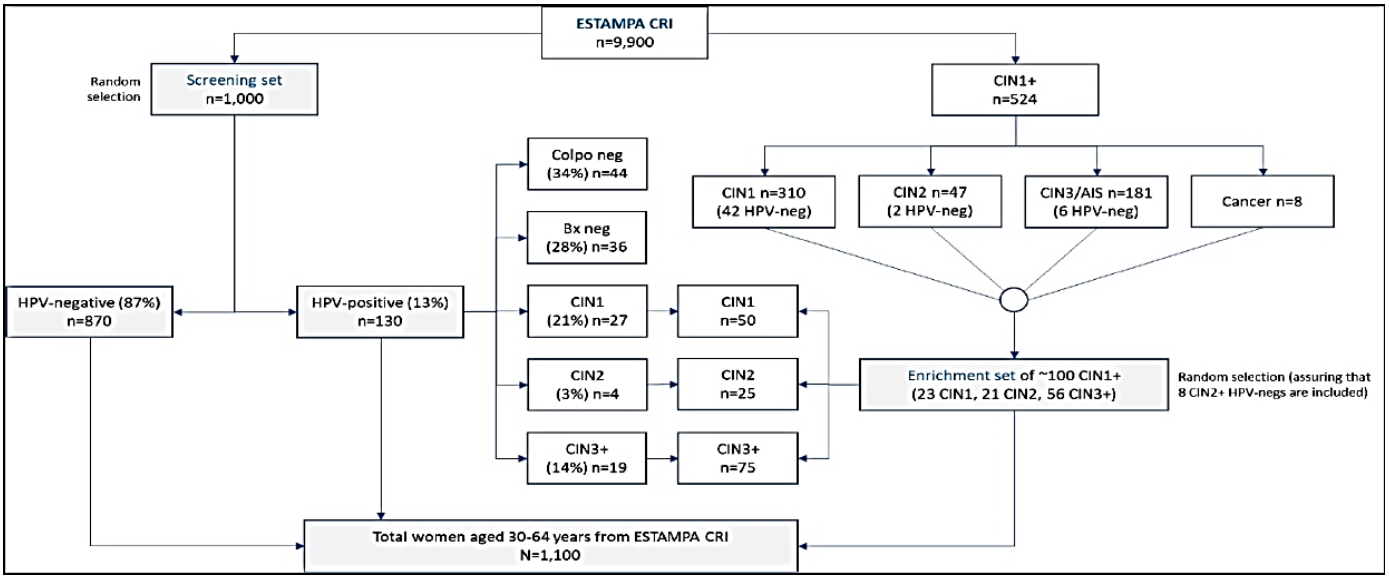

Figure 1: Description of samples used from ESTAMPA Costa Rica (ESTAMPA CRI) study for the iHPV study.

HEALTH TECHNOLOGY ASSESSMENT AND DRUG DISCOVERY

7. HEALTH TECHNOLOGY ASSESSMENT AND DRUG DISCOVERY

7.1 Health Technology Assessment to Determine Cost-effectiveness of Hydroxyurea Oral Suspension as Prophylaxis for Management of Sickle Cell Anemia in Children *(Funded by DHR HTAIn)*

Principal Investigator	:	**Beena Joshi**
Project Associates	:	Pooja Gund, A Padhan, Tejal Warekar, Nikita Phadtare
Collaborators	:	Manisha Madkaikar, Dipty Jain, Ragini Kulkarni
Duration	:	2024-2025

In India, approximately 40,000 sickle homozygous births are estimated every year. Children with Sickle Cell diseases (SCDs) start to have signs of the disease during the first year of life, including repeated bouts of illness, majorly caused by vaso-occulsion such as pain, hand foot syndrome, severe anemia needing blood transfusions, bacterial infections, most common being acute chest syndrome, acute symptoms of abdominal pain, breathlessness, splenic sequestration requiring blood transfusion or splenectomy throughout their life. Symptomatic management includes pain management, treating infections, hydroxyurea treatment as well as blood transfusion and hydration as per the need. Evidence shows Hydroxyurea (HU) is a safe and effective treatment for complications such as pain crisis, acute chest syndrome and strokes. HU is safe for all children starting from 9 months to 18 years with Sickle cell anemia, regardless of the form (liquid or capsule) or how it's dosed (by weight). While in India 500 mg capsules or 200 mg dispersible tablets of hydroxyurea are available, the biggest challenge is availability of its suspension form for effective use in pediatric patients. Due to unavailability of low-dose HU tablets/capsules, initiating a low/standard-dose treatment is a tedious task for the service providers. Hence in India, the healthcare providers initiate HU therapy to only symptomatic SCD children due to fear of toxicity and the as lack of availability of pediatric dose. To address this issue, the Akums Drugs and Pharmaceuticals Limited has produced India`s first homegrown oral indigenous Hydroxyurea suspension for the treatment of sickle cell disease in children for less than 1% cost of the global products. In the wake of the availability of this new treatment, this study was designed to evaluate the cost-effectiveness of hydroxyurea oral suspension compared to hydroxyurea capsule as prophylaxis for the management of SCD in children and Out-of-pocket expenditure (OOPE) incurred for management and treatment of SCDs in pediatric patients using Hydroxyurea. More than one third of the study population (37%) experienced a catastrophe due to OOPE incurred for treatment and management of SCDs. Major source of financing OOPE was through savings and borrowings from family and friends reported at 71%. The median OOPE incurred for SCD management including and excluding hospitalization was INR 8333 IQR range (4583-18248) and INR 7016 IQR range (4073-12405) respectively. An economic evaluation through Markov model using societal perspective with a time horizon of 5 years was developed. The cost included both health system cost and OOPE incurred due to the treatment. The study is completed and waiting for Technical Appraisal Committee (HTA In) approval. Cost effectiveness analysis showed that although the hydroxyurea oral suspension costs @ 600 rupees per 100 ml (₹ 2,32,78.74 crores) and capsules cost is @ 2.5 rupees per capsule (₹ 1,63,50.86), the suspension delivers better health outcomes by averting 633620 DALYS and gaining additional 9504 life years for the cohort of 1375213 children. The Incremental Cost-Effectiveness Ratio (ICER) was ₹1,08,983.67 per DALY averted, which is well below India's willingness-to-pay threshold of ₹2,35,108, making the intervention cost-effective.

Table 1: Results of the Markov model in terms of costs and outcomes

Cohort size: 1375213	**Intervention** (for the cohort for five years)	**Comparator** (for the cohort for five years)
Total Cost	₹23,278.74 crore	₹16,350.86 crore
Total DALY	39,724,779	40,359,508
Total Life Years	7,582,987.80	7,573,483.58

Table 2: Budget Impact Analysis

Parameters	**HU suspension (INR)**	**HU capsule (INR)**
Total Health system cost for providing medication to children of 2-7 years with SCD	Rs. 9344	Rs. 1097
Incremental Health system cost of HU suspension vs HU capsule for the entire cohort	Rs. 8247	

7.2 Assessment of RMNCAH+N Service Delivery Costs, Work Patterns and Efficiency of Primary Healthcare Teams at Ayushman Arogya Mandirs *(Partly Funded by UNICEF)*

Principal Investigator : **Beena Joshi**
Project Associates : AK Padhan, Tejal R Varekar
Collaborator : S Prinja, PGIMER, Chandigarh`
Duration : 2024-2024

The Ayushman Bharat – Health and Wellness Centre (AB-HWC) programme, launched by the Government of India in 2018, seeks to revolutionize the country`s primary healthcare system by operationalizing 150,000 Ayushman Arogya Mandirs. These centres provide Comprehensive Primary Health Care (CPHC), covering preventive, promotive, curative, rehabilitative, and palliative services. The initiative marks a significant shift from selective to holistic care, aiming to address the dual burden of non-communicable diseases (NCDs) and reproductive, maternal, neonatal, child, and adolescent health (RMNCAH). By decentralizing care delivery and promoting wellness at the community level, AB-HWCs contribute to India's commitment to Universal Health Coverage (UHC) and the Sustainable Development Goals (SDGs). Despite substantial progress in service expansion, there remains limited evidence on the cost efficiency and time utilization within this restructured model of care. To bridge this gap, a cross-sectional study using a mixed-method approach was conducted across 12 randomly selected HWCs (including both Sub-Health Centres and PHCs) in Maharashtra. Cost data were gathered using both top-down and bottom-up methods, capturing inputs such as human resources, infrastructure, drugs, equipment, and operational overheads. In parallel, time-motion studies and time allocation interviews were carried out with Community Health Officers (CHOs) and Auxiliary Nurse Midwives (ANMs) to understand their work patterns. Technical efficiency was assessed through Data Envelopment Analysis (DEA), comparing input utilization to service delivery outputs. The cost analysis of HWCs in Maharashtra reveals that annual cost of for delivering RMNCAH+N program at Sub-Health Centre (HWC-SC) is approximately ₹18.56 lakh per HWC-SC, while the cost per PHC-HWC is at ₹1.10 crore. The major cost drivers for both facility types are human resources, accounting for over 75% of the total costs. Drug procurement, lab diagnostics, and patient benefit schemes also contribute significantly, particularly at the PHC level. In terms of time analysis, CHOs/Mid-Level Health Providers (MLHPs) spent the majority of their weekly time (87.8%) at the facility, while only 12.2% spent on outreach activities. ANMs/Village Health Nurses (VHNs) spent 64.1% of their time at the facility

and 35.9% in outreach, highlighting their critical role in community-based service delivery. In terms of CHO/MLHPs` weekly productive time revealed that 30.2% spent on direct service delivery, while 24.7% used for record keeping, 4.2% on group activities, and a substantial 41.1% on supporting tasks. CHOs and ANMs distribute their productive time across various CPHC service packages based on their roles. CHOs primarily focus on non-communicable disease (NCD) screening and management, outpatient care for minor ailments, reproductive health, and pregnancy-related services. Meanwhile, ANMs allocate more time to maternal and child health, immunization, adolescent care, and national health programs. Both cadres spend relatively less time on elderly care, palliative services, and emergency care, indicating these areas are still emerging in primary care settings. This distribution reflects a complementary approach to comprehensive primary healthcare delivery at the Ayushman Arogya Mandirs.

7.3 Health Technology Assessment of Point of Care Test Kit for Hemophilia and Von-Willebrand Disease (vWD) Screening Developed by ICMR-NIIH *(Funded by DHR HTAIn)*

Principal Investigator : **Beena Joshi**
Project Associates : Pooja Gund, A K Padhan, Tejal R Varekar, Nikita Phadtare
Duration : 2024-2024

Global prevalence of Hemophilia A (HA) is estimated at 1 in 10,000 and in males, it is 1 in 5000. India is reported to have 1,40,000 Hemophilia cases, but only 27,000 are registered with Hemophilia Federation of India (HFI). Von Willebrand Disease (VWD) affects 1% of the general population. In India, this translates to 1 crore cases. There are only a few comprehensive diagnostics facilities in our country. Even coagulation screening facilities are unavailable in many district hospitals and medical colleges. Many labs do not have facilities to diagnose VWD, and patients are often misdiagnosed with Hemophilia A. With this background, a ground-breaking development has arisen from the ICMR-National Institute of Immunohaematology in Mumbai - a straightforward, rapid, and cost-effective diagnostic kit catering to Hemophilia A and VWD. Remarkably, this marks the world's first such a kit. The kit employs a lateral flow immunoassay (LFIA) for testing, enabling its use at Primary Health Centers (PHCs) without the need for specialized expertise. The proposed kit does not need any technical expertise or equipment and results can be read in 10 min after application of plasma or whole blood. The study was structured to answer the policy question put forward by the Ministry to estimate the cost per test by the POC kit for diagnosis of HA and VWD. The study identified the cost per test for the POC test kit. The cost was estimated for testing all individuals presenting with symptoms and signs of HA and VWD at public health facilities. As the disease is not endemic or prevalent in a specific population group, the estimated proportion of entire population within the 0-40 year age group was considered. The cost per test was identified for this population. The study was undertaken from Health Systems' perspective. The study findings revealed that the cost per case tested and cost per case detected using the POC for diagnosis of HA/VWD is lower than Standard of care test. The total cost saving in both the scenarios of POC test kit as compared to the SOC test is more than INR 42 crores (100% coverage). In the cohort, the POC test kits were able to additionally diagnoses more than 70,000 cases of HA and 10,000 cases of VWD which would have been missed using the current standard of care regimen. Thus, availability of highly effective Point-of-Care test Kit for Hemophilia A and Von Willebrand Disease developed by ICMR NIIH, would improve access to screening of bleeding disorders and early detection. This kit should be made available across all levels of public health care system. There is a need to formulate standard treatment workflow for diagnosis of patients using the POC test kit and referral following detection for Hemophilia A and Von Willebrand Disease.

7.4 Estimating health system costs for introducing indigenous HPV vaccine for adolescent girls in Maharashtra *(Funded by DHR HTAIn)*

Principal Investigator	:	**Beena Joshi**
Project Associates	:	A Padhan, Pooja Gund, Tejal Warekar, Nikita Phadtare
Collaborator	:	State Health System Resource Centre, Government of Maharashtra
Duration	:	2024-2024

Cervical cancer remains a significant public health concern, particularly in low- and middle-income countries. Globally, it is the fourth most common cancer among women, with India contributing nearly one-fifth of the new cases each year. Persistent infection with high-risk human papillomavirus (HPV) types, especially HPV 16 and 18, is the primary cause of cervical cancer. While preventive vaccines such as Gardasil and Cervarix have been available for over a decade and proven to be safe and effective, their uptake in India has been limited, particularly within the public health system. This study estimates the incremental cost of HPV vaccine introduction in Maharashtra to inform national scale-up and support sustainable, evidence-based implementation. A normative costing approach was used to estimate the incremental costs of introducing the HPV vaccination program in Maharashtra from the state government's perspective. Cost data were sourced from measles rubella vaccination guidelines, government reports, and multiple secondary datasets, including Rural Health Statistics, UDISE+, and the Population Projection Report (2011–2036). Costs were categorized by activity and input type, and the cost per dose delivered was calculated. One-way sensitivity analysis was conducted to test the robustness of estimates by varying input costs by ±20%. The incremental cost for two doses (100% coverage) for cohort (9-14 yrs. adolescent girls) including both vaccine and vaccinator cost is Rs 10,354,710,899 costing Rs 1917.31 cost per case. The incremental cost for two doses (100% coverage) for cohort (9-14 year adolescent girls) without vaccine and vaccinator cost is Rs 1,04,679,389 costing Rs 19.38 cost per case. Vaccine delivery accounted for the largest share of non-vaccine costs, followed by reporting and monitoring. Training, IEC activities, and microplanning also made substantial contributions. One-way sensitivity analysis shows delivery costs (including vaccine transport and cold chain) has highest impact for incremental cost followed by consumables and injection safety. Reporting and monitoring, as well as training, IEC, and micro-planning, showed moderate impact on costs.

7.5 Multi-omics Based Machine Learning Models for Detection of Metabolic Syndrome and its Components

Principal Investigator	:	**Susan Thomas**
Co-Principal Investigator	:	M Sudhakar
Project Associates	:	Karishma Desai, Indra Kundu
Collaborators	:	Taruna Madan, ICMR, New Delhi J Menon, Amrita Institute of Medical Science, Kochi
Duration	:	2022-2027

Metabolic Syndrome (MetS) is a complex disorder characterized by a cluster of metabolic abnormalities including obesity, hyperglycemia, dyslipidemia and hypertension. Its rising prevalence significantly contributes to global burden of non-communicable diseases. Precise molecular mechanisms linking individual or co-occurring components of MetS to its development remain largely unresolved. Current study aims to address this research gap by conducting a cross-

sectional study in Kerala. The study recruited treatment naïve individuals who are either healthy or have MetS or its components. Till date, 392 participants have been recruited of the proposed sample size of 450. A subset of collected plasma samples has undergone untargeted metabolomic profiling, with subsequent data analysis in progress.

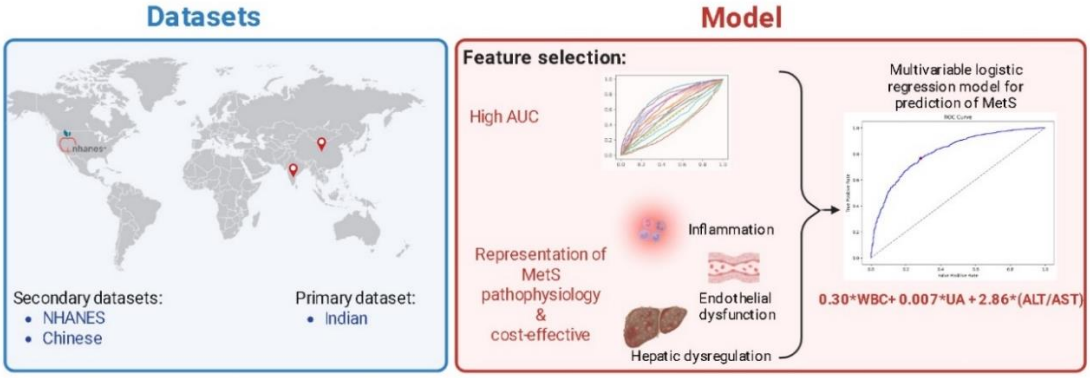

Figure 1: Development of a cost effective prognostic model for MetS. A multivariate logistic regression model is developed on NHANES dataset using three variale (WBC, UA, ALT/AST). The model is validated on Chinese and Indian datasets having an AUC greater than 0.7 in all test datasets.

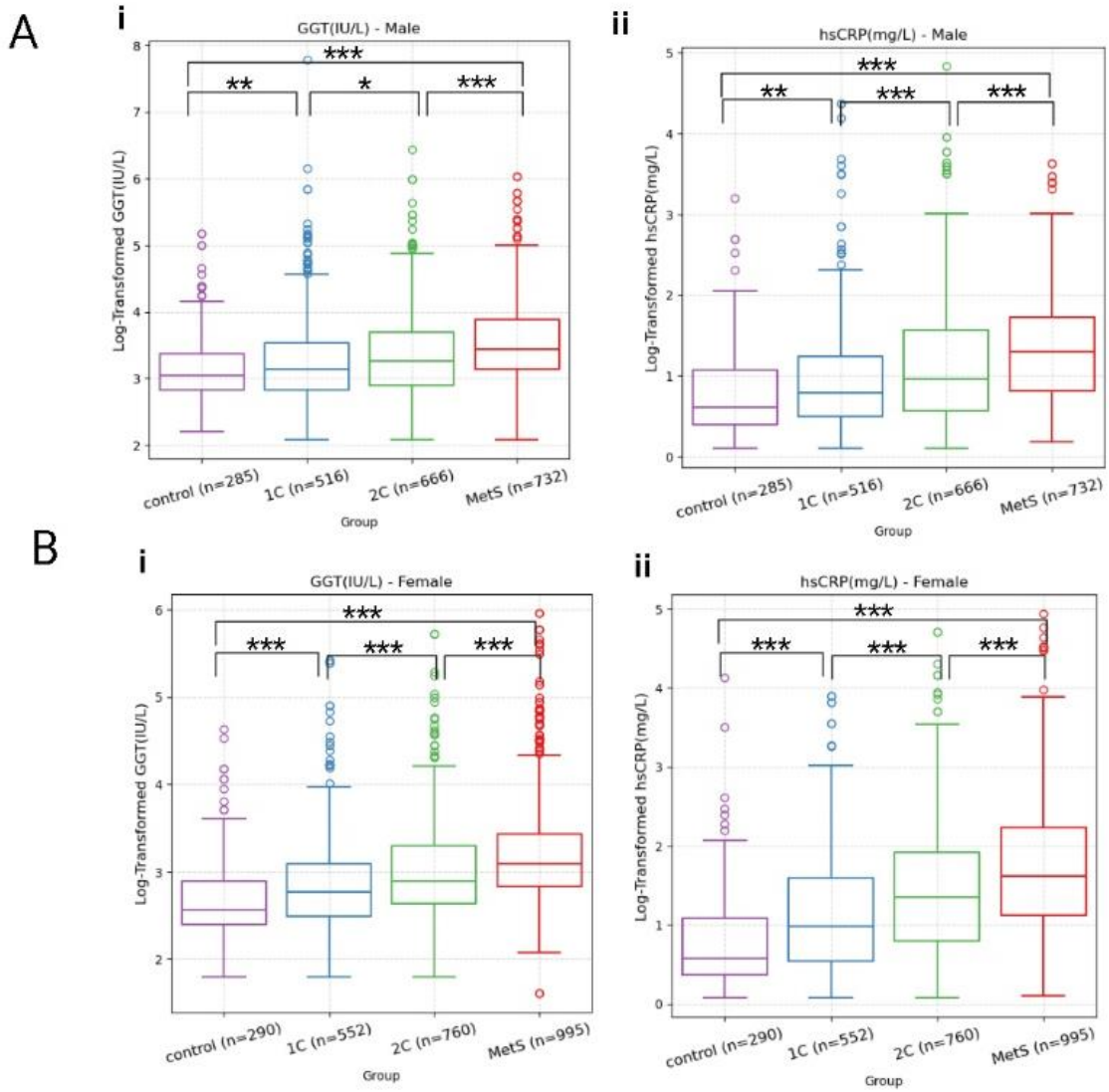

Figure 2: Box and wiskers plots of gender-based biomarker levels across MetS progression stages (Control, 1C, 2C, and MetS) for (A) Males and (B) Females. Biomarkers analyzed: (i) GGT, (ii) hsCRP. Statistical significance (KW test, median difference) is indicated as * $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$.

Concurrently, our group has utilized publicly accessible datasets to construct a risk prediction model aimed at differentiating MetS cases from controls, relying exclusively on routine, non-diagnostic biochemical measurements. We have developed a multivariate logistic regression based prognostic model that incorporates features representing three core aspects of MetS pathophysiology: systemic inflammation (white blood cell count, WBC), endothelial dysfunction (uric acid, UA), and hepatic dysregulation (alanine aminotransferase/aspartate aminotransferase, ALT/AST) (Fig. 1). The model relies on three routinely measured parameters commonly included in standard health check-up packages, making it both practical and cost-effective. By monitoring disruptions in these physiological processes, the model enables early prediction of MetS, which is demonstrated by the stratification of risk scores across different disease states. Due to the high prevalence of MetS, extensive research has focused on identifying relevant biomarkers. However, most studies have been conducted in varied populations and settings, lacking a unified comparison within a single dataset. In the reporting year, we conducted a comparative benchmarking evaluation of five well-established early MetS markers using a single dataset, aiming to assess their relative predictive power. Our findings highlight hsCRP and GGT as the most effective markers, demonstrating strong discriminatory ability across MetS severity stages: control, 1 component (1C), 2 components (2C) and MetS (Fig. 2).

7.6 Establishment of Bioinformatics and Computational Biology Centre (Centre for Advanced Research in Bioinformatics and Computational Biology for Woman and Child Health) *(Partly Funded by Department of Biotechnology)*

Principal Investigator	: **Susan Thomas**
Co-Principal Investigator	: RS Barai, ICMR-NIOH, Ahmedabad
Project Associates	: Ulka Gawde, P Chandra Sekar, C Kumar
Duration	: 2021-2026

Insect venom-derived antimicrobial peptides (AMPs) hold significant therapeutic potential, particularly for treating infections in vulnerable populations such as women and children. However, their clinical use is often limited by toxicity to mammalian cells. While conventional toxicity assessment methods are reliable, they are labor-intensive and time-consuming. Molecular Dynamics (MD) simulations using mammalian membrane models offer faster and more efficient alternatives for preliminary toxicity screening. In this study, we evaluated two mammalian membrane models multicomponent and realistic with distinct lipid compositions for their ability to predict the toxicity. A dataset comprising 30 AMPs (16 toxic, 14 non-toxic) from five insect families: anoplin, polybia, halictine, hyline, and macropin were used to perform MD simulations for 500 nanoseconds (ns) per peptide. A total of 21 microseconds (μs) of MD simulation data was produced in this study. Analysis of the MD trajectories revealed significant differences in structural stability and membrane interaction between toxic and non-toxic peptides, aligning with known experimental toxicity data. The assessment incorporated key structural and dynamic parameters (Fig. 1), including the distance between the centers of mass (CoMs) of the peptide and the membrane, Root Mean Square Deviation (RMSD), radius of gyration (RG), solvent-accessible surface area (SASA), and root mean square fluctuation (RMSF). The RMSD-based decision tree model, computed over the last 100 ns of each simulation, accurately differentiated toxic and non-toxic peptides with 90% accuracy, utilizing realistic membrane system. Importantly, all toxic peptides were correctly identified across all families when realistic models were applied. These

results underscore the utility of MD simulations as a fast and reliable method for early-stage toxicity screening of AMP, supporting the development of safer antimicrobial therapies.

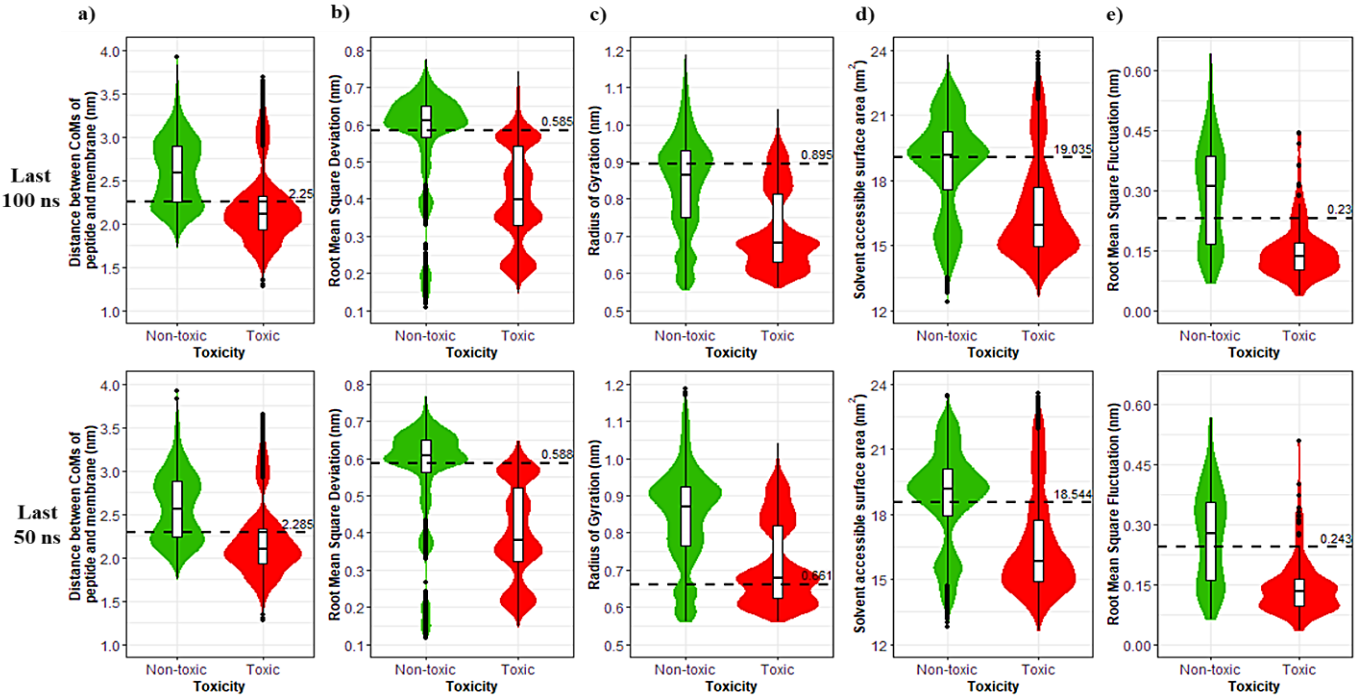

Figure 1: Violin plots with overlaid boxplots depicting the analysis of MD simulations trajectories with realistic membrane for parameters (a) Distance between Centers of Masses (CoMs) of peptide and the membrane, (b) Root Mean Square Deviation (RMSD), (c) Radius of Gyration (RG), (d) Solvent-Accessible Surface Area (SASA), and (e) Root Mean Square Fluctuation (RMSF) across last 100 ns, and last 50 ns timeframes. The red and green colors represent toxic and non-toxic AMPs respectively. The dotted line indicates the classification threshold derived from the decision tree analysis.

7.7 Exploring the Therapeutic Potential of Peptides Targeting Lysophosphatidic Acid Receptors in Ovarian Cancer *(Partly Funded by Department of Biotechnology)*

Principal Investigator	:	**V D Dighe**
Co-Principal Investigator	:	Taruna Madan
Project Associates	:	Bhavana Bhat, Yugandhara Jirwankar, Akanksha Nair, S Jadhav, P Salunke
Duration	:	2022-2025

Ovarian cancer is one of the leading female cancers affecting women globally. Lysophosphatidic acid (LPA), an onco-lipid, is elevated in the ascites of women with ovarian cancer, resulting in the overexpression of LPAR2 and LPAR3. The dysregulation in the LPA–LPAR3 interaction results in the activation of growth signaling pathways, cell proliferation, invasion, and metastasis in ovarian cancer. The present study aims to explore the therapeutic potential of the peptides targeting LPAR3 in ovarian cancer. Last year, we reported the specificity of the phages displaying LPAR3 binding peptide sequences by phage and cell-based ELISA using the M13 phage antibody. The specificity of the LPAR3 pep1 phage was confirmed to LPAR-3. (Annual Report 2023-24, pp. 133-134). In the current year, we reported the specificity of the LPAR3 Pep1 *in vitro* qualitatively by confocal microscopy and quantitatively by flow cytometry. The specificity was assessed using the FITC-labelled LPAR3 Pep1 in confocal and flow cytometry experiments. The human ovarian cancer cell line, OVCAR3, which is reported to express LPAR3 abundantly, was used to check the specificity; HepG2, a liver cancer cell line, and TM4, a Sertoli cell line, were non-ovarian cell lines. The LPAR3

Pep1 showed increased uptake in OVCAR3 compared to HepG2 and TM4 cell lines in the confocal microscopy analysis (Fig. 1). While for flow cytometry analysis, *in vitro* specificity of the FITC-labelled LPAR3 Pep1 was assessed in the OVCAR3 cell line, and the FITC-labelled Pep-N was used as a non-related peptide control. The LPAR3 Pep1 showed significantly increased uptake compared to Pep-N in OVCAR3 cells (Fig. 2). *In vitro* specificity studies confirmed the specificity of the LPAR3 Pep1 to the OVCAR3 cell line. *In vivo* specificity studies and functional studies are in progress.

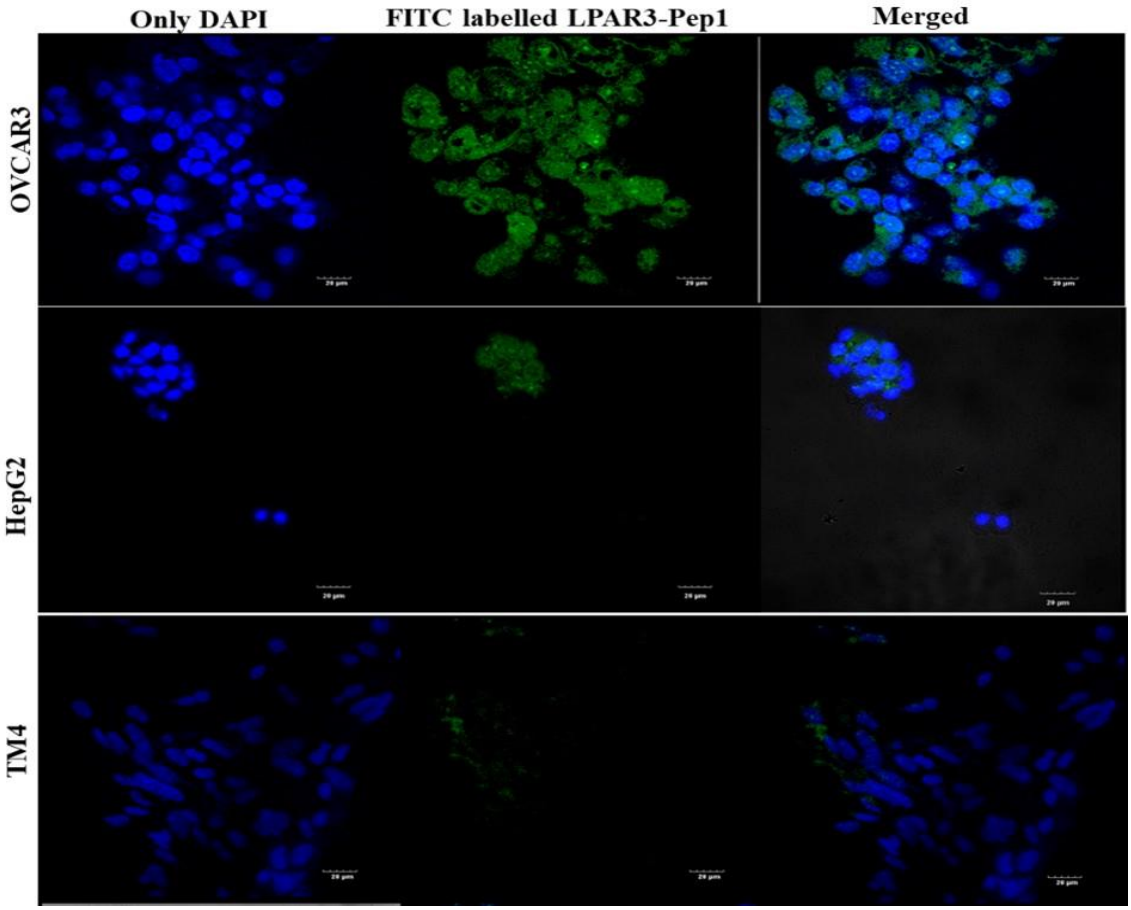

Figure 1: Uptake of FITC-labelled LPAR3 Pep1 in a human ovarian cancer cell line, OVCAR3, and two non-ovarian cell lines, HepG2 (a liver cancer cell line), and TM4 (a Sertoli cell line), were used. The cells were counterstained with DAPI. The images were obtained using a confocal microscope (60X magnification).

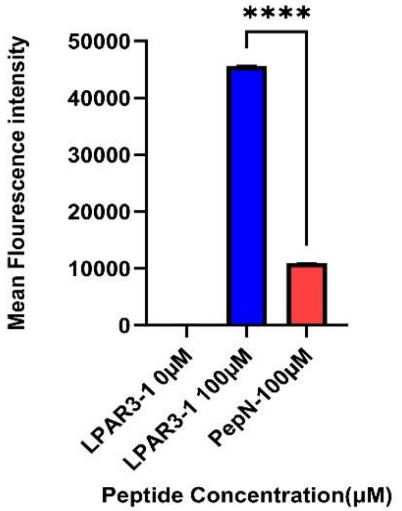

Figure 2: Uptake of FITC-labelled LPAR3 Pep1 and a control peptide (Pep N) as assessed by flow cytometry using the human ovarian cancer cell line, OVCAR3. (Bars represent mean±SD, **** p value≤ 0.0001)

7.8 Preclinical Study on Efficacy, Safety, and Toxicity of Swarna Prashan Regimen as Adjunct Therapy in Pediatric Acute Lymphoblastic Leukemia *(Funded by Central Council for Research in Ayurvedic Sciences)*

Principal Investigator	:	**V D Dighe**
Project Associates	:	Deep Jagani, Yugandhara Jirwankar
Collaborator	:	K Choudhary, Raja Ramdeo Anandilal Podar (RRAP) Central Ayurveda Research Institute, Mumbai
Duration	:	2023-26

Acute Lymphoblastic Leukemia (ALL) is the most common pediatric malignancy. Despite significant advancements, treatment toxicity, multiple adverse effects and relapse are most common causes of treatment failure. Ayurvedic formulations are sought as preferred complementary or alternative medicine (CAM) therapies. Swarna Prashan, a combination of Swarna Bhasma (SB), Honey and Ghee has been utilized as therapeutic agent in clinical disorders. Considering the immunomodulatory effects of gold-nanoparticles and colloids-based compounds in-vitro and in-vivo, Swarna Prashan may have immunotherapeutic potential in pediatric ALL. The objective of this study is to determine the efficacy, safety and toxicity of Swarna Prashan regimen as an adjunct therapy in pediatric ALL. *In-vitro* cytotoxicity of Swarna Bhasma on human leukemic cells MOLT-4 was assessed by MTT assay. It was found that Swarna Bhasma is safe for MOLT-4 cells up to the concentration of 5 mg/mL (Fig. 1A). The cytotoxicity of 5.0 mg/mL Swarna Bhasma with Ghee: Honey in 1:1 ratio was determined. However, the SB accumulated at the bottom of wells and the immiscibility of Ghee and honey resulted into inaccurate results. Thus, adherent cell line TM4 was used to determine cytotoxicity of Swarna Bhasma, Ghee and Honey. It was found that 5.0 mg/mL Swarna Bhasma with Ghee: Honey (1:1) diluted up to 1:15 is safe for cells (Fig. 1B).

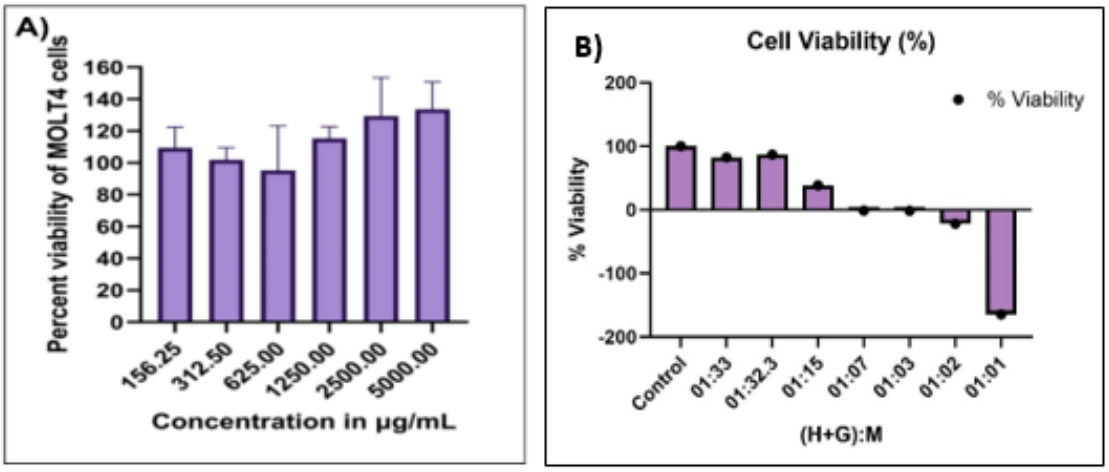

Figure 1: *In-vitro* cytotoxicity assessment of A) Swarna Bhasma and B) Swarna Bhasma with Ghee-Honey (1:1) on human leukemic cell line MOLT-4 by MTT Assay

In-vivo acute toxicity study of Swarna Prashan was performed in BALB/C mice. One group was treated with 50 mg/kg body weight SB in Ghee-Honey in 3:1 ratio, amd ampther group with SB in Ghee-Honey in 1:3 ratio. After 14 days, there were no significant changes in body weight as well as organ weight between control and SB-treated groups (Fig. 2A&B). The liver function profile of control and SB-treated groups was also similar (Fig. 2C). All the behavioral parameters observed

were normal for control and SB-treated groups (Fig. 2D). Thus, no significant acute toxicity from Swarna Bhasma with Ghee and Honey was observed. The evaluation of interaction of Swarna Prashan regimen with cytochrome P450 enzymes and enzyme-specific marker substrate metabolism in liver cell line and xenograft ALL mouse model generation is in progress.

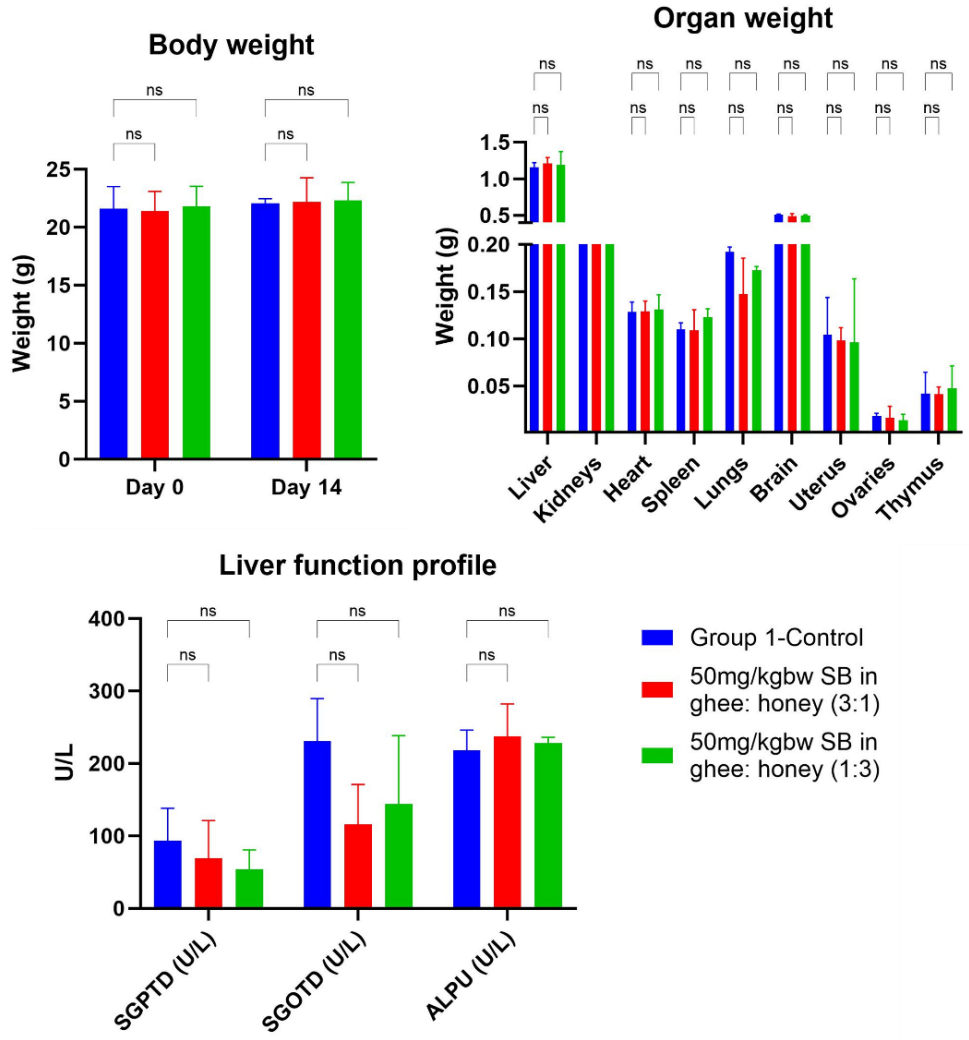

Figure 2: *In-vivo* acute toxicity study of Swarna Bhasma on BALB/C mice. Effect of Swarna Bhasma, Ghee and Honey on A) Body weight B) Organ wight C) Liver Function Profile [Blue – Control, Red – 50 mg/kg body weight SB + Ghee:Honey (3:1), Green - 50 mg/kg body weight SB + Ghee:Honey (1:3)]. ns indicates not significant.

7.9 Evaluation of Apocynin Efficacy in Bisphenol-A Induced Reproductive Toxicity

Principal Investigator	:	**V D Dighe**
Project Associates	:	Shilpa C Kerkar, S Jadhav, P Salunke, Y Kamble
Duration	:	2024-2027

Bisphenol-A (BPA) is widely used as an additive for the production of polycarbonate; epoxy resins that perturbates the hypothalamic– pituitary–testicle axis, modulates gene expression and enzymatic activity of testicular steroidogenesis. Pregnancy is a critical period where exposure of BPA can affect the fetal growth and development of the reproductive organs. Induction of oxidative stress by BPA may induce marked reproductive effects during prenatal, perinatal, and postnatal exposure. Lycopene has been shown to ameliorate reproductive toxicity in the offsprings of mice

exposed to BPA in-utero while Retinol acetate, a metabolite of vitamin A, has been shown to inhibit toxic effect of BPA on the developing reproductive system in male mice. However, there are no reports on the ameliorative effect of antioxidants on inflammatory damage caused by BPA-induced reproductive toxicity. One such herbal molecule, apocynin - a methoxyacetophenone, is found to have low toxicity and exhibits powerful anti-inflammatory and anti-oxidant effects. The present study investigates the protective effect of apocynin on BPA-induced reproductive toxicity in perinatal model. A pilot study was planned using wistar rats for perinatal model development. Dams were grouped as follows. G-I: Vehicle control (VC), G-II: 2.4 µg BPA/kg bw, G-III: 5 µg BPA/kg bw, and treated from GD6 to PND21 via oral gavage. After which the F1 animals were housed separately till sexual maturation. In males the period of testicular descend was delayed though not significantly, compared to the control group. Percentage body weight of F1 males did not show any significant difference compared to the control group (Fig. 1A). Computer Assisted Semen Analysis was performed and the sperm count of males sired by both G-II and G-III was found to be significantly lower compared to the control group (Fig. 1B). Testis weight of F1 males from G-III was significantly lower compared to those from G-II and control group while the epididymis weight of F1 males from G-II and G-III was significantly lower compared to the control group. Prostate weight was significantly increased in G-II sired F1 males compared to those from control group while it was found to be decreased in G-III, compared to G-II. (Fig. 1C). Serum protein levels of G-II and G-III were significantly higher compared to the control group (Fig. 1D). While FSH levels were significantly higher in F1 males from G-III compared to F1 males from G-II. Estradiol levels were significantly lower in G-III compared to control group. LH levels did not show any significant difference compared to control group (Fig. 2A-D). Preliminary results suggest that perinatal exposure of BPA at 2.4 µg or 5 µg BPA/kg bw caused reproductive toxicity.

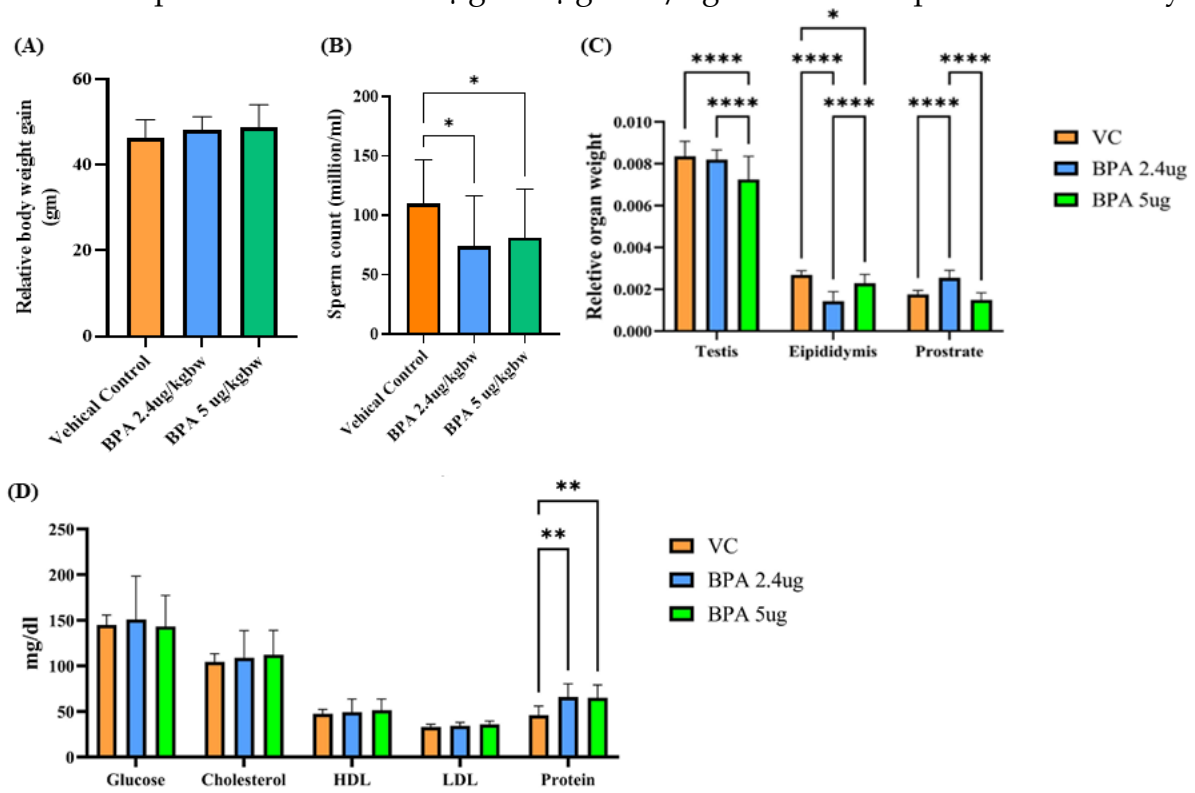

Figure 1: Effect of perinatal exposure of BPA on F1 males. (A) Percentage body weight gain, (B) sperm count, (C) relative organ weight, (D) Serum biochemical parameters (Glucose, Cholesterol, HDL and LDL) and (E) Total Protein. Bars represent mean±SD. *p ≤ 0.05, **p ≤ 0.005, ****p ≤ 0.00005.

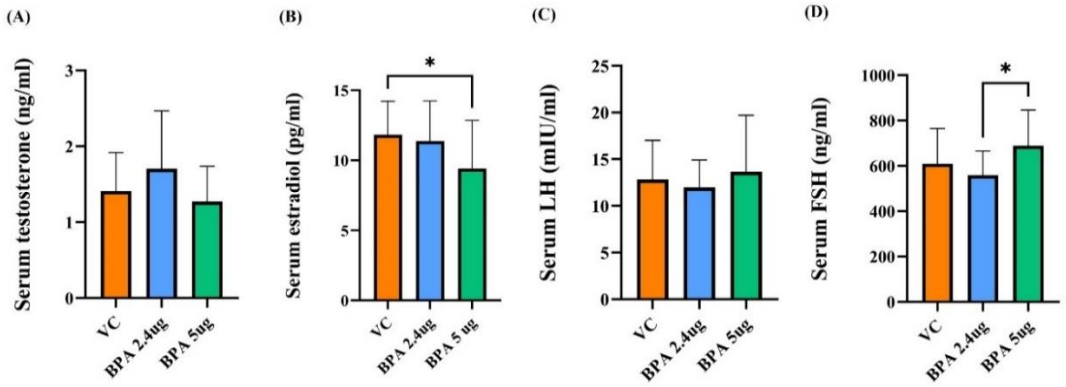

Figure 2. Effect of Perinatal exposure of BPA on F1 males. (A). Testosterone, (B). Estradiol, (C). LH, (D). FSH. Bars represent mean ±SD. *p ≤ 0.05.

7.10 Evaluation of Immunomodulatory and Anti-cancer Properties of Hydroxychavicol, a major Constituent of Piper Betel *(Funded by ICMR-DHR)*

Principal Investigator	:	**V D Dighe**
Project Associates	:	Amruta Gadade, S Ghuge
Collaborators	:	Sadhana Sathaye, Institute of Chemical Technology, Mumbai
Duration	:	2024-2027

Immunotherapeutic strategies have shown promising effects in addressing the high immune resistance and recurrence, commonly observed in lung adenocarcinoma. In this context, phytoconstituents with immunomodulatory properties are gaining research attention. Hydroxychavicol, a phenylpropanoid compound found in Piper betel, has demonstrated potential anti-cancer and immunomodulatory activities. A comprehensive investigation of these properties may offer novel insights for the effective management and potentially complete elimination of lung adenocarcinoma. This study investigates hydroxychavicol's impact on macrophage polarization, immune subset activation, and gene expression, along with its anti-cancer and antioxidant activity *in vitro*. In the reporting year Molecular Docking studies with immune checkpoints was performed using Molecular Operating Environment (MOE 2022) and all the protein structures were downloaded from RCSB PDB (www.rcsb.org). This study revealed strong binding affinities of Hydroxychavicol with key immune checkpoint proteins (e.g. PD-L1: –5.83 kcal/mol), suggesting potential immunotherapeutic relevance (Table 1). To evaluate the immunomodulatory potential of Hydroxychavicol, macrophages were used as a model. THP-1 monocytes were differentiated into macrophages using 80 ng/mL PMA. Increased CD68 expression by immunofluorescence staining confirmed successful differentiation ($p<0.05$) into macrophages (Fig. 1) and will be used to analyse the gene expression of CTLA-4, PD-1, PD-L1, etc.

Table 1: Molecular docking scores of hydroxychavicol with selected immune checkpoint proteins

Protein	PDB ID	HC-Docking Score
Adenosine A2A receptor	2YDO	-4.62
CTLA-4	5TRU	-4.51
PD-1	5WT9	-4.1
PD-L1	5N2F	-5.83
TIGIT	3Q0H	-5.11
TIM-3	7M3Z	-4.26

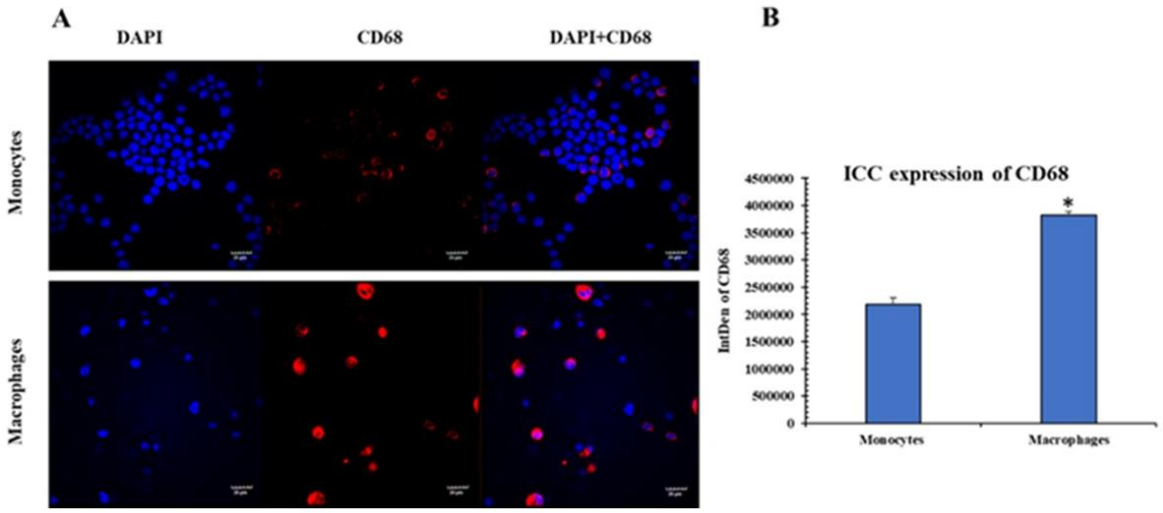

Figure 1: Immunofluorescence staining of monocytes and macrophages for CD68 for (60x). A) Confocal micrographs of THP-1, monocytes and macrophages (ICC) labeled CD68 (Red) and DAPI (blue) (B) Quantification of the immunolocalization of of CD68 in monocytes and macrophages using ImageJ software.

7.11 Identification and Characterization of Sertoli and Leydig Cell Homing Peptides *(Partly Funded by ICMR-DHR)*

Principal Investigator : **V D Dighe**
Co-Principal Investigator : Taruna Madan
Project Associate : Akanksha Nair
Duration : 2021-2024

In our previous studies, phage display screening led to the identification of 10 novel Sertoli Cell Homing Peptides (SCHPs) and Leydig Cell Homing Peptides (LCHPs). Among these LCHP1 and LCHP2 were validated. Building on these findings, LCHP3 and LCHP4 were quantitatively evaluated last year for their homing potential using flow cytometry and *in vivo* biodistribution. Flow cytometric analysis was performed using FITC-tagged LCHP3 and LCHP4 in TM3 (mouse Leydig cells), TM4 (mouse Sertoli cells). SH-SY5Y (neuroblastoma cells) was used as controls. TM3, TM4, and SH-SY5Y cells were incubated with 40, 80 or 160 µM of FITC-tagged LCHP3 and LCHP4; cells without peptide served as controls. LCHP3 (Fig. 1A(i)) showed the highest uptake in TM3 cells across all concentrations, followed by TM4, with minimal uptake in SH-SY5Y. LCHP4 (Fig. 1(A(ii)) exhibited maximum uptake in TM4, followed by TM3, and least in SH-SY5Y cells. LCHP3 showed better dose-dependent uptake and Leydig cell specificity than LCHP4, with minimal non-specific binding. Biodistribution studies (Fig. 1(B)) were performed using Cy5.5-labeled LCHP3 and LCHP4, 24 hours' post-injection in BALB/c mice, based on average radiant efficiency across organs. Both LCHP3-Cy5.5 and LCHP4-Cy5.5 exhibited moderate testicular accumulation, comparable to that of the control cardiac-targeting peptide (CTP), indicating restricted translocation across the blood-testis barrier (BTB). The highest accumulation for all three 3 peptides was observed in the liver, kidney, and spleen, suggesting physiological uptake and slower clearance in these organs. CTP-Cy5.5 showed greater accumulation in these tissues than LCHP3 and LCHP4, and significantly higher uptake in the heart, consistent with its targeting specificity. LCHP4 displayed slightly higher kidney accumulation than LCHP3. Minimal distribution was observed in the brain, seminal vesicle, and epididymis, indicating limited off-target penetration. In a parallel set of experiment, the testis-targeting efficiency of Adjudin-loaded nanoparticles (NPs) conjugated with SCHP1 was evaluated to assess SCHP-mediated

delivery. Histological analysis (Fig. 2) revealed that testicular damage was more significant in the Adjudin-NP-SCHP1 group (Panels I–K) than in the Adjudin-only group (Panels E–G). BALB/c mice (n = 5 per group) treated with SCHP1-conjugated Adjudin exhibited extensive disruption of seminiferous tubule architecture, including prominent vacuolization, luminal spaces devoid of spermatozoa, germ cell depletion, and epithelial disintegration. In contrast, the Adjudin-only group showed comparatively less architectural damage, indicating that SCHP1 conjugation enhanced testicular delivery of Adjudin, resulting in more effective germ cell depletion.

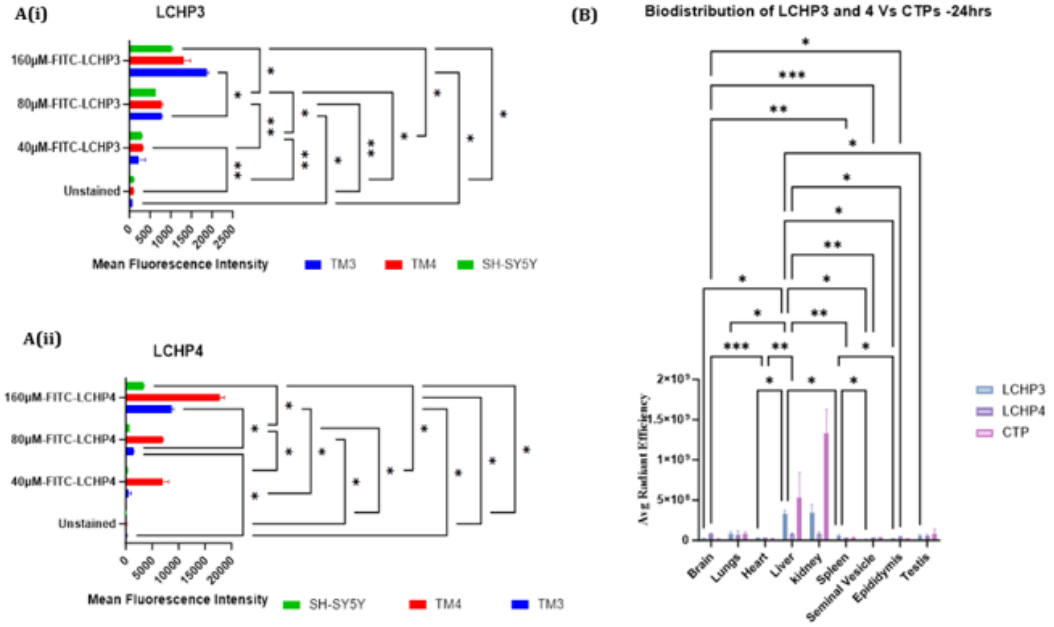

Figure 1: (A i&ii) *In vitro* uptake of LCHP3 and LCHP4 by TM3, TM4, and SH-SY5Y cells. Data are mean ± SD (n = 3). *p < 0.05, **p < 0.001, ***p < 0.0001. (B) *In vivo* biodistribution of LCHP3-Cy5.5, LCHP4-Cy5.5, and CTP-Cy5.5 in Balb/c mice via IVIS imaging. Data are mean ± SD (n = 3). *p < 0.05, **p < 0.001, ***p < 0.0001.

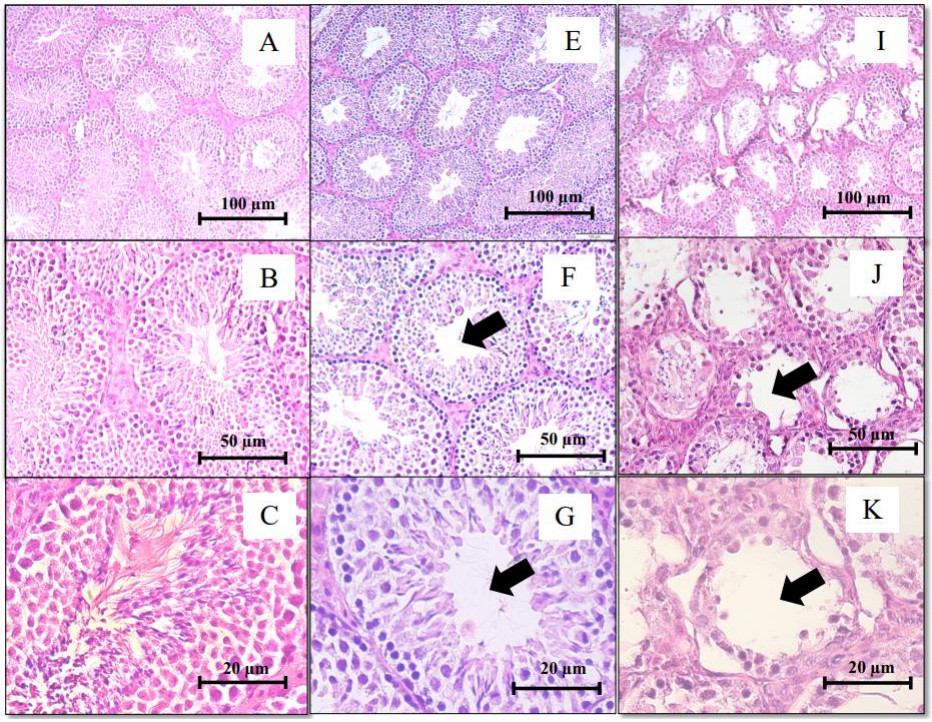

Figure 2: Histological assessment of testicular architecture after treatment with 100 mg/kgbw Adjudin-loaded nanoparticles conjugated with SCHP1. Representative H&E-stained sections are shown for the control group (A–C; 10×, 20×, 40×), Adjudin-only (E–G), and Adjudin-NP-SCHP1 (I–K).

HEALTH CARE RESEARCH

8. HEALTH CARE RESEARCH

8.1 Understanding Availability of Essential Diagnostic in Healthcare Systems Identifying Barriers and Facilitators *(Partly Funded by Indian Council of Medical Research)*

Principal Investigator	:	**Beena Joshi**
Coordinator	:	Kamini Walia, ICMR Headquarters
Project Associates	:	Ragini Kulkarni, Shahina Begum, Sakshi Rane, Iswarya Reddy, Nikita Phadtare
Collaborator	:	Government of Maharashtra
Duration	:	2023-2024

The National Essential Diagnostic List (NEDL) was developed in India to make availability of quality diagnostics an essential component of the health care system that is aspiring to provide universal access to affordable, accessible and good quality health servicesThe primary objective of this study is to assess the availability and quality of essential diagnostic services in Sub-Centres (SCs) and Primary Health Centres (PHCs) across selected Indian states, as per the National Essential Diagnostics List (NEDL). Maharashtra was one of the five states chosen for the study. A simple random sampling method was applied to select 10 districts within each state, with 8 PHCs and 8 Sub-Centers (HSCs) selected from each district. Districts were chosen using Probability Proportional to Size Systematic Sampling (PPSS), while PHCs and HSCs were selected using systematic and simple random sampling methods. Surveys were conducted by trained staff using structured questionnaires. Data on diagnostic test availability, infrastructure, procurement, and supply chain issues were collected and analyzed. Availability of essential diagnostics and equipment varied significantly by district. Nandurbar, Nagpur, Pune, Nashik, and Ratnagiri had relatively higher diagnostic capacity, with more than 75% of PHCs equipped with digital hemoglobinometers and glucometers. Advanced diagnostic equipments such as haematology analysers, ECG machines, and biochemistry analysers were limited, with only 9-25% of PHCs in select districts having them. Radiographers were available in 58-92% of healthcare facilities in districts such as Pune, Ratnagiri, and Nagpur. Some districts reported significant manpower shortages, particularly in Akola and Nandurbar, where over 50% of facilities lacked adequate staff. Lab technician posts were generally filled across districts, particularly in community health centers and district hospitals. More than 50% of PHCs in certain districts were equipped with critical diagnostic equipments and supplies. However, several essential supplies (e.g., KOH solution, Gram's iodine, and autoclaves) were either scarce or absent in many facilities. Infrastructure deficiencies wereobserved, with equipment shortages and inconsistent supply chain management reported across many districts. For instance, less than 15% of PHCs had incubators or rubber aprons, limiting their ability to deliver effective diagnostic services. The study reveals considerable variation in the availability and quality of diagnostic services across PHCs and SCs in Maharashtra. While some districts (e.g. Pune and Nagpur) performed relatively well in terms of diagnostic capacity, others, such as Parbhani and Akola, faced challenges due to shortages in equipment, manpower, and supplies. Strengthening the procurement and supply chain, improving infrastructure, and ensuring adequate staffing are critical for enhancing the diagnostic capacity in rural and underserved areas. The findings highlight the need for targeted interventions at the district level to improve diagnostic services and health outcomes.

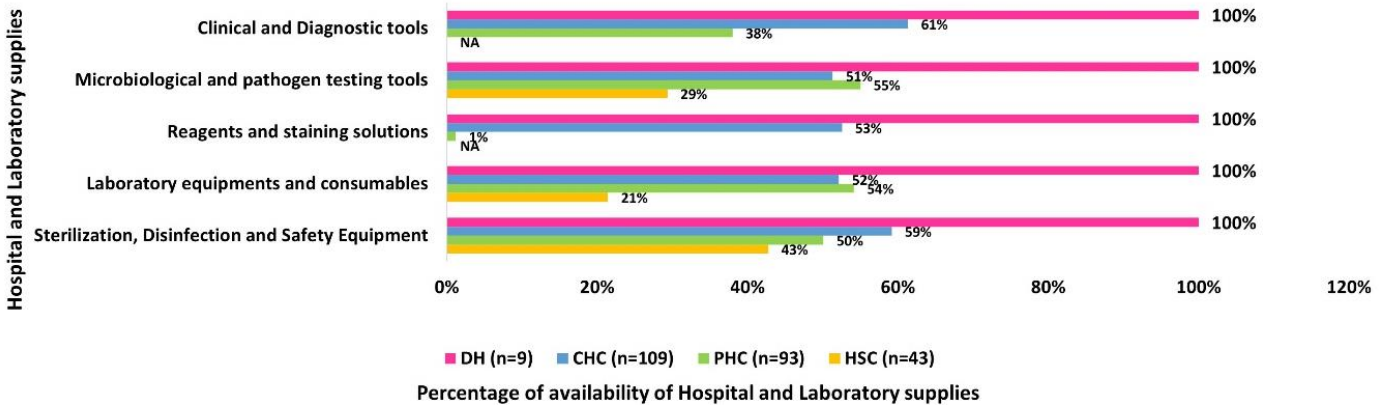

Figure 1: Availability of Hospital and Laboratory Supplies

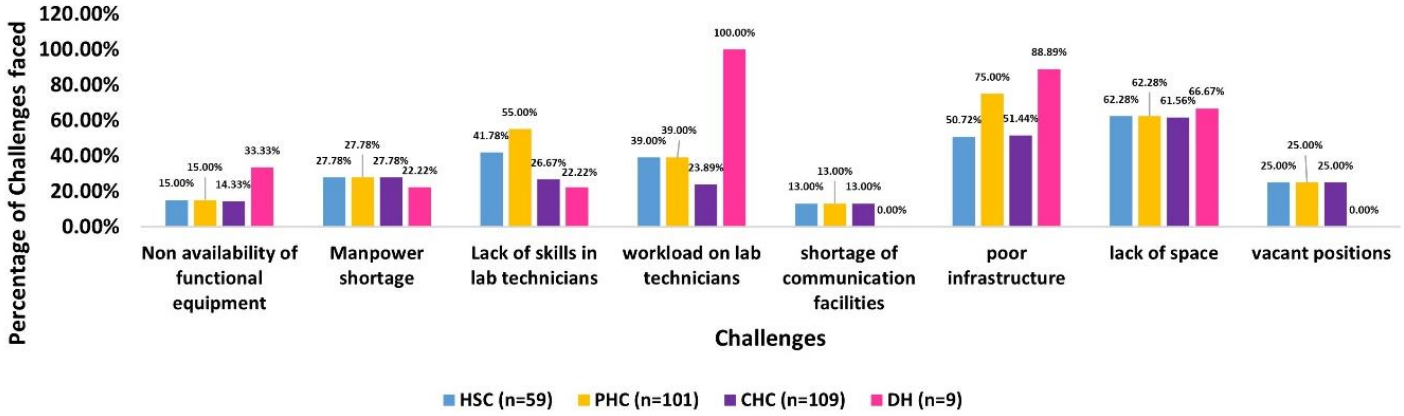

Figure 2: Challenges faced by health facilities in Maharashtra regarding provision of laboratory anddiagnostic services

8.2 Accelerating Efforts to End TB in India *(Partly Funded by Indian Council of Medical Research)*

Principal Investigator	:	**Bhavya M K**
Co-Principal Investigator	:	Beena Joshi
Project Associates	:	S Pandey, S Patel , H Surum, K D Khanjodiya, Manisha Bhoya, S Vilat, S Kharpade
Collaborators	:	Deepti Tandon, M Singh, Vinita Rajgar, V Garasiya
Duration	:	2023-2025

The study is a multicenter task force study of ICMR in collaboration with the Central TB Division. Ministry of Health and Family Welfare, Government of India. Each of the selected ICMR institutes is allocated a district in a state/union territory, with close collaboration with the State Tuberculosis Officer (STO). The study site for ICMR NIRRCH is the Dadra and Nagar Haveli district of Dadra Nagar Haveli and Daman and Diu Union territory. The first phase focused on rapid situational analysis to assess the program gaps and challenges of the current TB program in study district. All the health facilities were mapped. The patients registered in the last six months and patients registered prospectively, at the respective TB Units, were followed for treatment compliance, and their contacts were screened. Basic information (mapping of the infrastructure, facilities, and staff for TB under the State TB program) about the district has also been collected. Qualitative data were collected using In-Depth Interviews (IDI) and Focus Group Discussions (FGDs). IDIs were conducted among Health Care Workers (Medical officers, ANM, ASHA, MO, MPW) using a validated IDI guide. FGDs at the

patient level were conducted to understand the challenges faced by them in availing the treatment and their experience with National TB Elimination Program guidelines (NTEP). The Informed Consent Form (ICF), Participant Information Sheet (PIS), and tools were translated into the local language. Migration of patients was one of the major challenges faced by the health system. The community had basic awareness of TB. Stigma and fear of job loss restrict individuals from seeking treatment. In the second phase, community-based intervention strategies were implemented. The main focus of the intervention was community-based screening of high-risk populations, contact tracing, providing services as per NTEP guidelines and spreading awareness. A total of 80917(45,047 males & 35,870 females) (till 31st March 2025) have been screened for TB symptoms. 5,585 individuals (2882 males and 2703 females) were identified as symptomatic based on the NTEP criteria. For all symptomatic cases, X rays have been done with handheld X-ray machines and sputum samples have been taken for NAAT/ microscopy Testing. 12 cases were diagnosed with TB. A total of 59 close contacts of the diagnosed TB patients were traced and screened as part of contact investigation activities. Out of these, 17 individuals were found eligible for TPT (Tuberculosis Preventive Therapy) and were enrolled into the preventive care pathway. Along with the screening activities, awareness and IEC campaigns were carried out in the community at regular intervals. The study team developed IEC materials and launched on 24th March, TB day. Special screening camps were also organized in high-risk and vulnerable settings such as district jail facilities and selected industries where workers are at greater risk due to overcrowded living conditions and occupational exposure. Capacity-building initiatives have also been undertaken to strengthen the healthcare response at the district level. Training sessions for Medical Officers and Community Health Officers (CHOs) were successfully conducted, focusing on the latest guidelines in TB diagnosis, treatment, contact tracing, and preventive therapy. The study is ongoing.

Figure 1: TB Day Celebration and Launch of IEC materials on 24th March 2025, CHC Rakholi, Silvassa, Dadra Nagar Haveli

Figure 2: Capacity Building Session for Medical Officers and CHOs in Dadra Nagar Haveli on 5th October 2024

8.3 Development of Primary Health Care Models for Palliative Care, Elderly Care and Mental Health in Maharashtra *(Partly Funded by Department of Health Research)*

Principal Investigator	:	**Ragini Kulkarni**
Co-Principal Investigator	:	Kiran Munne
Co-Investigator		Bhavya MK
Project Associate	:	S K Mishra, Mrunali Dhak, Twinkal Solanki, N Raut, Saloni Patel, Anushree Mankar
Collaborators	:	S Choudhari, R Marad, S Patil
Duration	:	2023-2025

This project was developed with an aim to utilize the MRU/MRHRU network to undertake action research to collect data, identify gaps in health care delivery systems, design and evaluate the primary care model in pilot mode. The project is being implemented in collaboration with the Department of Health Research (DHR), regional ICMR institutes, state medical colleges, and selected MRUs/MRHRUs. MRHRU Dahanu has been selected as one of the study sites for this initiative The community based data collection has been done in redCAP app from households under selected Health and wellness centres, namely, HWC Gholwad 1, Bordi 4, Narpad, Vaki and Saravalli 1. Household surveys included general health status profiling including mental health, palliative and geriatric care services have been done by five IPEM field workers taking help from ASHA workers under the following four sections. i. Section I pertaining to the socio-demographic details of the family. ii. Section II pertaining to palliative care needs of any member of the family. iii. Section III filled for each elderly member (>60 years) in the family. It is based on the WHOICOPE questionnaire and the NPCDCS- CBAC questionnaire. The tool screens for cognitive decline, mobility, malnutrition, visual impairment, hearing loss, depressive symptoms, hypertension, diabetes and cancers. iv. Section IV pertaining to mental health. This tool screens for depressive disorder, anxiety disorder, psychoses, suicidal/self-harm behaviour, alcohol and tobacco addiction and child and adolescent behavioural disorders. Section 1 was administered to each adult member

of the family, while Section 2 was filled for family as a whole. The community based data collection has been completed with 25097 individuals covered for the community-based data collection from 5263 households (Table 1). The total number of beneficiaries identified from selected HWCs requiring services were for elderly care -572, mental health-26 and palliative care -702. The SWOT analysis based on in-depth interviews with Medical Officers, Community Health Officers, Staff Nurses, and ANMs from selected Primary Health Centres (PHCs) and Health and Wellness Centres (HWCs) have been completed. Qualitative data were analyzed using thematic analysis. Findings from the qualitative study indicate that while certain screening and intervention activities particularly in elderly care and Non-Communicable Disease (NCD) screening are being implemented at the field level, significant gaps remain. Areas such as mental health and palliative care require enhanced staff training and capacity building. Key challenges reported by healthcare providers include heavy workloads, insufficient staffing, and a lack of structured training and capacity-building programs. Additionally, the stigma associated with mental health issues presents a barrier to care and must be addressed through targeted community awareness initiatives.

Table 1: Individuals requiring Elderly Care, Mental Health and Palliative Care as identified during community based survey

HWC	Population collected	Total number of houses	Beneficiaries for Elderly Care	Beneficiaries for Mental health	Beneficiaries for Palliative Care
Aravalli 1	7797	1606	198	7	210
Vikki	4858	1053	14	4	45
Goliad 1	1737	410	75	5	81
Goliad 2	3373	733	225	5	215
Arpad	3161	740	17	1	48
Bordia	4171	721	43	4	103
Total	**25097**	**5263**	**572**	**26**	**702**

8.4 Equitable, Quality Universal Health Coverage Implementation Research Project for Optimizing Comprehensive Primary Health Care through Health and Wellness Centers (EQUIP-HWC) *(Funded by ICMR)*

Principal Investigator : **Beena Joshi**
C-Principal Investigator : N Ambadekar
Project Associates : Ragini Kulkarni, S P, Mukta Gadgil. S Deshmukh, Ru Wakode, Priyanka Dey, Kavita Gawali
Collaborators : Health Department, Pimpri Chinchwad Municial Corporation (PCMC), Pune
Duration : 2024-2026

The EQUIP Project commenced in May 2024 with an orientation session for the project staff about the project objectives and methodology and status of the PCMC health system. A baseline survey was undertaken, encompassing Facility Assessment, Exit Interviews, Key Informant Interviews, In-Depth interviews of HWC staff, Focus Group Discussions (FGDs) with different community groups, Urban Health ward Surveys and Household Survey in systematically sampled 4800 houses. The data were analysed and discussed in a brainstorming meeting held on 10th December 2024. Findings from the situational analysis were discussed with State officials, ICMR project Coordinator and with PCMC officials . Based on the gaps identified, Model Zero implementation strategy was drafted and discussed to strengthen the health system to optimise provision of 12 package of services. Due to shortage of space to establish new centers, the state developed a SOP to install Porta Cabins to run as

HWCs which were taken up by PCMC and got the technical and financial bids cleared. 20 such cabins are being installed across the municipal area. Field visits were carried out by the teams in collaboration with Medical Officers and interdepartmental personnel to address and close identified gaps. The project team facilitated the conduct of NQAS , reviewed the available IEC material at the IEC Bureau, conducted sensitisation of ASHAs and community awareness programs on the services of 12 package of services. Further, all HWC personnel at the District health and Family Welfare Training Center Pune were trained. The state had entrusted responsibilities of setting up few HWC in PCMC area to the DHO and Civil Surgeon of Pune District. The project team deliberated with the state and facilitated handing over these responsibilities to the Corporation for recruitment of staff and further management of these HWCs. World Health Day celebrations and several health awareness sessions were supported across all health centers. Efforts to strengthen the expanded range of service delivery are being initiated, with ongoing regular meetings with Zonal Medical Officers (ZMOs). The community level microplanning activity through Ward Action Plan Committee is ongoing.

Figure 1: Porta Cabin- Anandwan UHWC Sangvi Zone

Figure 2: Glimpses from the brainstorming meeting with State and PCMC officials on December 10, 2024 in YCM Hospital Pune

Table 1: Facility Assessment of 28 Urban Primary Health Centres (UPHCs) and 17 Health and Wellness Centres (HWCs)

Infrastructure	**UPHC**	**HWC**
Building in good condition	23 (82%)	17 (100%)
Electricity supply	25 (89%	10 (58.8%)
Potable Water supply 24X7	27 (96%)	8 (47%)
Availability of fans, clean drinking water in waiting space	26 (93%)	8 (47%)
Availability of Toilet facilities- separate for male and female	18 (64%)	11 (64.7%)
Availability of hand washing facility	27 (96%)	16 (94.1%)
Availability of colour coded bins	27 (96%)	6 (35.3%)
Facilities for people with disabilities	13 (46%)	7 (41.2%)
Space availability		
Dedicated space for patient examination with privacy	21 (75%)	12 (70.6%)
Dedicated waiting space for patient	27 (96%)	12 (70.6%)
Availability of adequate seating arrangements	21 (75%)	8 (47.1%)
Dedicated Space for laboratory/ diagnostics services	23 (82%	11 (64.7%)
Dedicated Space for pharmacy/ medicine dispensation	28 (100%)	13 (76.5%)
Dedicated Space/ room identified for Wellness activities including Yoga sessions	4 (14%)	7 (41.2%)
IT Infrastructure		
Availability of uninterrupted Internet connectivity	27 (96%)	9 (52.9%)
Availability of Tablet/laptop/desktop for reporting and tele-consultation	27 (96%)	3 (17.6%)
IT infrastructure availability for virtual training	14 (50%)	5 (29.4%)
Branding		
External branding	25 (89%)	10 (58.8%)
Clear display of signages for elderly, pregnant women, children, patients, disabled persons seats	3 (10%)	7 (41.1%)
Way finding signage displayed on the main and connecting roads to the facility	13 (46%)	5 (29.4%)
Patient charter displayed at the facility	22 (77%)	4 (23.5%)
Health promotion material displayed at the facility		
Care in pregnancy and childbirth	19 (68%)	6
Neonatal and infant health care	12 (43%)	0
Childhood and adolescent health care	12 (43%)	0
Family planning, Reproductive Health Care services	14 (50%)	0
Communicable diseases	8 (29%)	0
National Health Programmes	9 (32%)	0
NCD	22 (79%)	0
ENT Care	7 (25%)	0
Eye Care	7 (25%)	0
Oral Care	0	0
Elderly Care	1 (4%)	0
Palliative Care	0	0
Emergency Care	1 (4%)	0
Mental Neurological and Substance use Care	8 (29%)	3
Wellness(Eat Right, yoga, physical activity etc)	19 (68%)	3

Table 2: CPHC service availability at Centers:

Services availability at HWCs	UPHC		HWC	
	Completely available N=28 (%)	Partially available N=28 (%)	Completely available N=17 (%)	Partially available N=17 (%)
Outpatient care	28 (100%)	0		
Inpatient care	0	0	NA	NA
Care in pregnancy and childbirth	0	28 (100%)	0	12(70%)
Delivery services (child birth)	0	NA	NA	NA
Neonatal and infant health care	2 (6%)	25 (89%)	0	13(76.4%)
Childhood and adolescent health care	0	27 (96%)	1(6%)	14(82%)
Family planning, contraceptive services and other reproductive health care services	9 (32%)	19 (68%)	1(6%)	12(70%)
Communicable diseases including national health programmes	27 (96%)	1 (3%)	2(11.6%)	12(70%)
Treatment for common communicable diseases	27 (96%)	1 (3%)	11(64%)	5(29%)
Screening and management of diabetes and hypertension	24 (85%)	4 (14%)	5(29%)	6(35%)

8.5 Assessing Usage and Disposal Pattern of Menstrual Hygiene Products among Women in Rural and Urban India *(Funded by ICMR Extramural Grant)*

Principal Investigator	:	**Deepti Tandon**
Co-Principal Investigators	:	Ragini Kulkarni, Anushree Patil, Shahina Begum
Project Associates	:	Pratibha Kokate, M S Chalga
Collaborators	:	Vakdevi Validandi, ICMR-NIN Hyderabad S K Sharma, ICMR-RMRCNE Dibrugarh Umaer Alam, ICMR-RMRC Gorakhpur
Duration	:	2024-2025

This multi-centric study aims to assess the usage and disposal patterns of menstrual hygiene products among women in both rural and urban areas across India. The qualitative component of the study involves understanding the barriers and enablers faced by frontline health workers in providing menstrual hygiene products, particularly in underserved rural communities. It also seeks to explore the acceptance, preferences, and challenges related to current menstrual hygiene management (MHM) practices. The study is being conducted across four zones of the country: North, South, East/Northeast, and West. The participating study sites include ICMR-NIRRCH in Mumbai (West Zone), ICMR-NIN in Hyderabad (South Zone), ICMR-RMRC in Gorakhpur (North Zone), and ICMR-RMRCNE in Dibrugarh (East/Northeast Zone). Qualitative data collection and training for all sites was done at ICMR NIRRCH in Dec 2024. The training was given by qualitative experts like Dr Sanjay Juvekar, Dr Rutuja Patil and Dr Solomon Salve. The training was attended by participants from all four sites. The table 1 shows that sanitary napkins are the most widely used menstrual hygiene product across all surveyed regions, with the highest usage observed in rural (93.75%) and urban (91.25%) Hyderabad. Cloth continues to be used, particularly in rural Maharashtra (19%), indicating regional disparities in access or preference. Tampon usage is completely absent across all locations, while menstrual cups are used by a very small percentage, mostly in urban Maharashtra and rural Hyderabad. A minor proportion of respondents use a combination of products, such as cloth and sanitary napkins or sanitary pads with menstrual cups, suggesting a gradual shift in menstrual hygiene practices. For the quantitative component, data

collection have been completed at the Maharashtra and Telangana sites and is ongoing at Gorakhpur site and Dibrugarh site. On the qualitative front, in-depth interviews and focus group discussions have been completed at three of the four study sites—Maharashtra (ICMR-NIRRCH), Telangana (ICMR-NIN), and Gorakhpur (ICMR-RMRC). The project is ongoing.

Table 1: Distribution of types of menstrual hygiene products used across rural and urban areas in Maharashtra, Hyderabad, and Dibrugarh

Types of menstrual products	Maharashtra		Hyderabad		Dibrugarh
	Rural	Urban	Rural	Urban	Urban
Sanitary napkin	287 (71.75%)	336 (84.0%)	375 (93.75%)	365 (91.25%)	349 (87.25%)
Cloth	76 (19%)	30 (7.5%)	19 (4.75%)	23 (5.75%)	23 (5.75%)
Tampon	0	0	0	0	0
Menstrual cup	0	4 (1.0%)	2 (0.5%)	0	1 (0.25%)
Both cloth and sanitary napkin	37 (9.25%)	28 (7%)	4 (1%)	9 (2.25%)	29 (7.25%)
Both sanitary pad & menstrual cup	0	2 (0.5%)	0	1 (0.25%)	0
Others (cloth pads, period panties & sanitary napkin)	0	0	0	2 (0.5%)	0
Total	400	400	400	400	400

Figure 1: Two-days workshop on 'Basic workshop on Qualitative data analysis with focus on RAPID analysis for implementation Research' at ICMR-NIRRCH in December 2025

8.6 The Impact of Positive Aging Intervention on Flourishing of Elderly in India: A Pan-India Cluster Randomized Controlled Trial (*Funded by ICMR through Ramaiah University of Applied Sciences)*

Principal Investigator	:	**R K Prusty**
Project Associates	:	Sheetal Hiwarale, D Pawar, S Gaikwad, Ashwini Hirekar
Collaborator	:	Pratishtha Bhattacharyya, MS Ramaiah University of Applied Sciences, Bengaluru
Duration	:	2024-2026

This study explores the intersection of aging, well-being, mental health, and institutionalized elderly care in India—a domain where scientific research remains sparse. As India undergoes a demographic transition, the proportion of elderly individuals in the population is steadily rising. This demographic shift brings with it the inevitable challenges associated with aging, including a decline in physical and cognitive functioning. Consequently, it becomes imperative to identify and implement strategies that can help maintain or enhance the well-being of the elderly population. With this context in mind, the present study introduces an intervention module titled 'Swarna Mitra', which is specifically designed for elderly residents of old age homes. The intervention is grounded in the principles of positive psychology and aims to foster emotional, social, and psychological well-being—collectively referred to as flourishing. The Swarna Mitra module incorporates a series of evidence-based positive psychology interventions such as the cultivation of gratitude, optimism, compassion, forgiveness, altruism, resilience, savoring, character strength training, meaning in life, and hope. These components are designed to reinforce inner strengths and promote a sense of purpose, belonging, and contentment among participants. To rigorously assess the impact of this intervention, the study adopts a randomized controlled trial (RCT) design. Elderly participants residing in institutional care settings will be randomly assigned to intervention and control groups to ensure methodological rigor and unbiased evaluation of outcomes. The intervention is expected to enhance various dimensions of mental well-being and potentially reduce feelings of loneliness, depression, and anxiety, which are commonly observed in institutionalized elderly populations. By focusing on flourishing as a multifaceted concept that includes emotional stability, social integration, and psychological fulfilment, this study aims to broaden the scope of geriatric mental health research in India. The insights derived from the implementation and evaluation of the Swarna Mitra program can provide valuable evidence for developing comprehensive mental health strategies for the aging population. Furthermore, the findings have the potential to inform government policies on elderly care, not only in India but also in other countries facing similar demographic and societal transitions. In summary, this study seeks to contribute meaningfully to the emerging discourse on aging and mental health in India by presenting an innovative, culturally relevant, and empirically grounded intervention that promotes holistic well-being among the elderly. The study is initiated. Validation of scales and training for intervention is ongoing.

8.7 Feasibility, Acceptability and Costs of Providing Comprehensive Preconception Care services to Young Couples in Maharashtra *(Funded by Indian Council of Medical Research)*

Principal Investigator	:	**Beena Joshi**
Co-Principal Investigator	:	Ragini Kulkarni
Project Associates	:	Suchitra Surve, Deepti Tandon, S Pande, Bhavya MK
Collaborators	:	Thane District Health Officials, BMC Executive Health Officer, AHO
Duration	:	2023-2026

The study is in the second year undertaking activities to enroll newly married couples, screen them for identification of modifiable and non-modifiable risk factors, counsel and provide prophylactic iron folic acid treatment and refer for treatment or further management. Health system cost for providing PCC service is also being assessed. In urban area (with low enrolment), couples were identified through Eligible Couple Registers, incentivized-ASHA visits, marriage registration bureaus, and outreach camps. Data cross-linking from family folders and health registers and

private provider engagement supported identification. Health officials were engaged, and ASHAs, ANMs, and communities were sensitized through meetings and awareness sessions. A total of 966 newly married couples were enrolled in the reporting year, 300 each from tribal and rural areas, 208 from urban non-slum, and 158 from urban slum communities. Of the total, 634 couples (67%) intended to conceive within six months and received prophylactic folic acid, IFA, and deworming, while others were provided family planning support along with IFA and deworming. About 8% of the couples had consanguineous marriages, with the highest proportion (12%) in tribal areas. Modifiable risk factors were identified such as anemia, abnormal BMI, menstrual disorders, TORCH and other RTIs/STIs, and deranged metabolic profiles. Other risk factors included hemoglobinopathies, infertility and consanguinity. Those who wished to conceive were provided prophylactic Folic Acid. WIFS was initiated among non anemic and therapeutic iron dose was provided to anemic along with deworming. Referrals were made for other identified problems. Counselling including genetic testing and counselling was provided to identified couples. Among 193 women who conceived, 74.6% pregnancies were planned, and 36.8% had a history of infertility. Nutritional and metabolic risks persisted: 36.3% were underweight, 33.2% anemic, and 18.1% had high HbA1C. TORCH IgG positivity was 77.7%; genetic screening revealed thalassemia minor (3.1%) and sickle cell trait (1.0%). The average unit health system cost for PCC at the primary level was ₹6,777.28 (₹5,421.82–₹8,132.73). Preliminary rural and tribal costing will guide budgeting once urban data are available. Challenges are being documented and mitigation strategies are codeveloped to facilitate completing the target enrolment and screening. Enrollment is ongoing in urban areas. The study results are regularly updated with the key district and state health officials. IEC material has been developed and flip charts and posters have been disseminated and used in the project area. A number of key stakeholder meetings, ASHA sensitization meetings were held to engage the health system in this activity. The ICMR Task Force Committee has been regularly monitoring the progress of the study. In consultation with the committee the enrollment period for the urban area has been extended until August 2025.

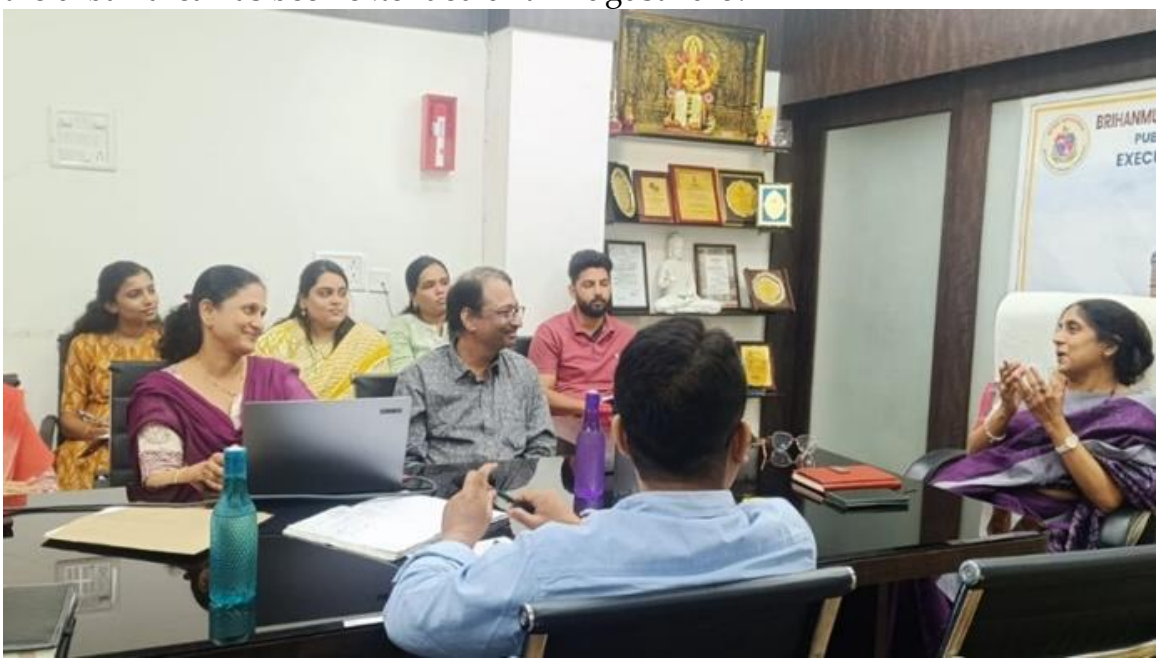

Figure 1: Meeting with EHO, AHO (F ward) along with Dr Aniruddha Deshpande, member of ICMR Ptoject Review Committee (Government of Maharashtra representative) on November 28, 2024)

Figure 2: Block level meetings at Shahpur and Ambernath to update the status of project and improve their involvement and conduct of community activities on September 29-30, 2024

Table 1: Risk Factors among the participants (N=943) and proportion of individuals with the risk factors (n, %)

Variables		Rural N=300 (%) n (%)	Tribal N=300(%) n (%)	Urban Slum N=139(%) n (%)	Urban Non-Slum N=204(%) n (%)	Total N=943(%) n (%)
Underage (<18 years)		03 (01)	26 (8.6)	0	0	29 (03)
Consanguinity (%)		10 (3.3)	36 (12)	17 (12.3)	12 (5.8)	75 (7.9)
BMI	Underweight	71 (24.6)	127 (44)	28 (20.4)	20 (10.2)	246 (27)
	Normal	143 (49.6)	136 (47.2)	60 (43.7)	90 (45.9)	429 (47.1)
	Overweight	67 (23.2)	21 (7.29)	37 (27)	66 (33.6)	191 (21)
	Obese	07 (2.6)	04 (1.51)	12 (8.9)	20 (10.3)	43 (4.9)
Infertility		121 (40.3)	84 (28)	78 (56.1)	81 (39.7)	364 (38.6)
Hypertension		01 (0.3)	01 (0.3)	03 (2.1)	04 (1.9)	09 (0.9)
Acanthosis Nigricans		0	07 (2.3)	08 (5.7)	09 ()	24 (2.5)
Haemoglobin	<7 gm/dl	02 (0.6)	03 (01)	01 (0.7)	0	06 (0.6)
	7-9.9 gm/dl	28 (9.3)	42 (14)	6 (4.3)	15 (7.3)	91 (9.6)
	10–11 gm/dl	44 (14.6)	61 (20.3)	21 (15.1)	27 (13.2)	153 (16.2)
HbA1C	5.7-6.4 mmol/L	31 (10.3)	80 (26.6)	13 (9.3)	27(13.2)	151 (16)
	>6.4 mmol/L	04 (1.3)	01 (.3)	03 (2.1)	05 (2.45)	13 (1.37)
TSH	<0.5 mIU/L	0	02 (0.6)	01 (0.7)	04 (1.9)	07 (0.7)
	>5 mIU/L	19 (6.3)	11 (3.6)	13 (9.3)	20 (9.8)	63 (6.6)
Deranged Lipid Profile (VLDL, LDL, triglyceride, cholesterol)		20 (6.6)	16 (5.3)	56 (40.2)	56 (27.4)	148 (15.6)

Table 2: Key risk factors and clinical findings among ANC participants (N=193)

Variables		Rural (n=68) n (%)	Tribal (n=78) n (%)	Slum (n=21) n (%)	Urban Non- Slum (n=26) n (%)	Total (n=193) n (%)
Planning for pregnancy		51 (75)	51 (65.3)	18 (85.7)	24 (92.3)	144 (74.6)
Underage (<18 years)		0	08 (10.2)	0	0	08 (4.1)
Consanguinity		01 (1.4)	11 (14.1)	03 (14.2)	01 (3.8)	16 (8.2)
Infertility (WHO definition)	Diagnosed	30 (44.1)	19 (24.3)	12 (57.1)	10 (38.4)	71 (36.7)
	Primary	24 (35.2)	15 (19.2)	11 (52.3)	09 (34.6)	59 (30.5)
	On Treatment	02 (2.9)	02 (2.5)	02 (9.5)	03 (11.5)	09 (4.6)
	Secondary	06 (8.8)	04 (5.1)	01 (4.7)	01 (3.8)	12 (6.2)
	On Treatment	02 (2.9)	0	0	0	02 (01)
Previous pregnancy losses	1	12 (17.6)	08 (10.2)	04 (19)	04 (15.3)	28 (14.5)
	≥02	0	0	0	01 (3.8)	01 (0.5)
Underweight		18 (26.4)	43 (55.1)	07 (33.3)	02 (7.6)	70 (36.2)
Haemoglobin	<7 gm%	01 (1.4)	01 (1.2)	01 (4.7)	0	03 (1.5)
	7 – 9.9 gm%	07 (10.2)	11 (14.1)	01 (4.7)	04 (15.3)	23 (11.9)
	10 – 11 gm%	11 (16.1)	15 (19.2)	04 (19)	08 (30.7)	38 (19.6)
HbA1C	5.7-6.5 mmol/L	04 (5.8)	24 (30.7)	01 (4.7)	03 (11.5)	32 (16.5)
	>6.5 mmol/L	03 (4.4)	0	0	0	03 (1.5)
TSH	<0.5 mIU/L	0	0	0	01 (3.8)	01 (0.5)
	>5 mIU/L	02 (2.9)	01 (1.2)	02 (9.5)	02 (7.6)	07 (3.6)
Deranged Lipid Profile		04 (5.8)	04 (5.1)	10 (47.6)	07 (26.9)	25 (12.9)
TORCH IgM		03 (4.4)	12 (15.3)	0	02 (7.6)	17 (08)
TORCH IgG		64 (94.1)	61 (78.2)	15 (71.4)	10 (38.4)	150 (77.7)
Sickle Cell Trait		02 (2.9)	0	0	0	02 (01)
Thalassemia Minor		03 (4.4)	03 (3.8)	0	0	06 (3.1)

8.8 A Systematic Review on Types of Preconception Care Interventions undertaken in South East Asia Region, their Impact on Awareness, Health Seeking Behaviour and Improvement in Preconception Health of Women, Maternal and Neonatal Outcomes and Cost Effectiveness of Interventions

Principal Investigator : **Beena Joshi**
Project Associates : Tejal Varekar, A Padhan
Duration : 2024-2024

In recent years, there has been increasing recognition that a woman's health status, lifestyle, and history prior to conception significantly influence pregnancy outcome. In many cases interventions become less effective once the women is already pregnant, especially in the early stage. For other cases, the effectiveness of the interventions declines as pregnancy progresses. Therefore, identifying and addressing the risk factors before conception increases the opportunity for timely and effective interventions. The World Health Organization (WHO) defines preconception care (PCC) as the provision of biomedical, behavioral and social health interventions to women and couples before conception occurs. PCC includes a range of services aimed at improving the health and well-being of women and couples while reducing adverse maternal and neonatal outcomes. Research has

shown that targeting the modifiable risk factors through preconception interventions can significantly reduce the incidence of various neonatal and birth disorders, thereby promoting healthier pregnancies and improved long-term health outcomes for children. Given the shared socio-cultural contexts and healthcare infrastructures among South-East Asian countries, this systematic review aims to provide a comprehensive overview of PCC interventions across the region. Specifically, it assessed their role in raising awareness among couples and healthcare workers, improving preconception health, enhancing maternal and neonatal outcomes, and contributing to cost efficiency in healthcare delivery. Systematic searches of published studies were done on PubMed, Cochrane and Web of Sciences. A synthesis of randomized controlled trials (RCTs), cohort studies, pre-post studies, and community-based implementation studies was conducted. Meta-analysis was performed for studies measuring low birth weight, preterm births, anemia among pregnant women, mean birth weight, mean birth length and maternal hemoglobin levels to quantify pooled effects of nutritional PCC interventions. This systematic review was registered with the Prospective International Register of Systematic Reviews (PROSPERO, number CRD42022362043) and was conducted following the guidelines for the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA).

Preconception care interventions were reported in only six of eleven South-East Asian countries with a total of 26 studies involving 1,15,209 participants. Twenty-five studies involved women of reproductive age, with four including husbands and one with mother in-laws. Interventions were primarily nutritional (15 studies), alongside socio-behavioural (11 studies) and health screening (7 studies) components. Nutritional interventions—especially food-based and micronutrient supplements initiated ≥90 days before conception—significantly improved foetal growth, reduced low birth weight, preterm birth, and small-for-gestational-age outcomes, and in some cases enhanced fetal survival and neurodevelopment. For mothers, pre-pregnancy nutrition reduced anemia and gestational diabetes, and improved vitamin B12 and folate levels. Socio-behavioral interventions, especially when integrated with medical strategies, reduced anemia, seizures in epileptic women, and improved therapy management. Furthermore, employing community-based socio-behavioural interventions with active stakeholder engagement significantly improves uptake of pre-conception care services such as contraception, family-planning, nutritional support, folic-acid usage and gender equity efforts. The higher uptake of these interventions were translated into better maternal and fetal outcomes, including improved fetal growth and birth weight.

One study highlighted that pre-conceptional screening plus amniocentesis for couples with previous child with structural chromosome abnormalities (SCA) compared to only amniocentesis for couples with previous child with SCA was identified to be cost-effective. Meta-analysis revealed that preconception nutrition significantly reduced low birth weight (OR=0.76; 95% CI: 0.67, 0.86) (Fig. 1), preterm births (OR=0.94; 95% CI: 0.79, 1.11) (Fig. 2), anemia among pregnant women (OR=0.53; 95% CI: 0.47, 0.60) (Fig.3), with modest, non-significant increases in mean birth weight (mean difference = 30.12 g; 95% CI: 1.91, 58.33), mean birth length (mean difference = 0.35 cm; 95% CI: 0.81, 0.52) and maternal haemoglobin (mean difference = 0.5; 95% CI: 0.43, 0.57); with minimal heterogeneity (I^2<5%). In conclusion the studies were limited in the spectrum of interventions that are expected to be delivered for preconception care. Among the various interventions, nutrition-based interventions during the preconception period significantly improved maternal and foetal health outcomes. Sociobehavioural and community interventions improved uptake and utilization of PCC services..

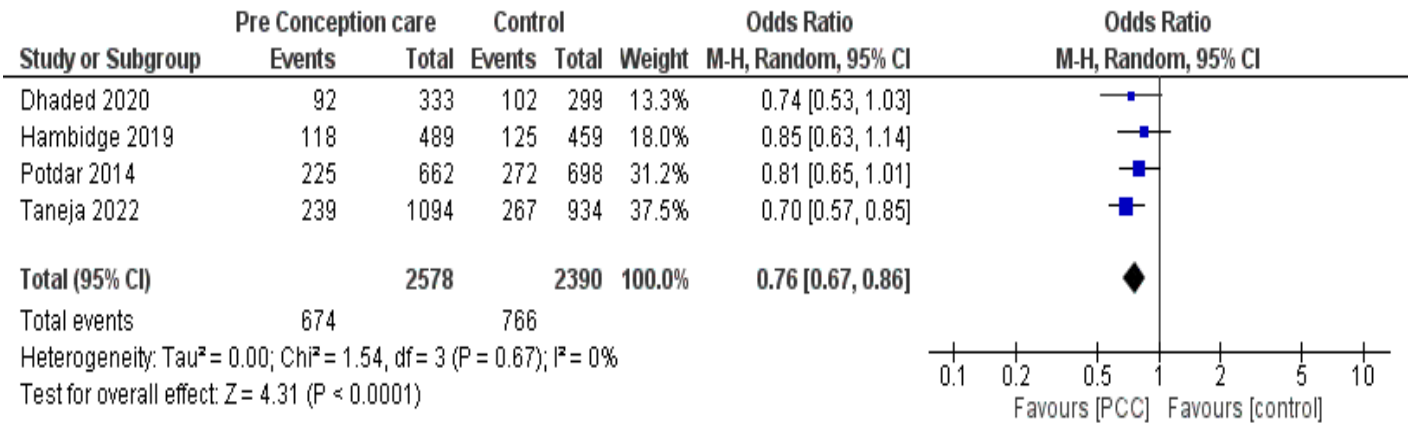

Figure 1: Pooled effect for Low Birth Weight

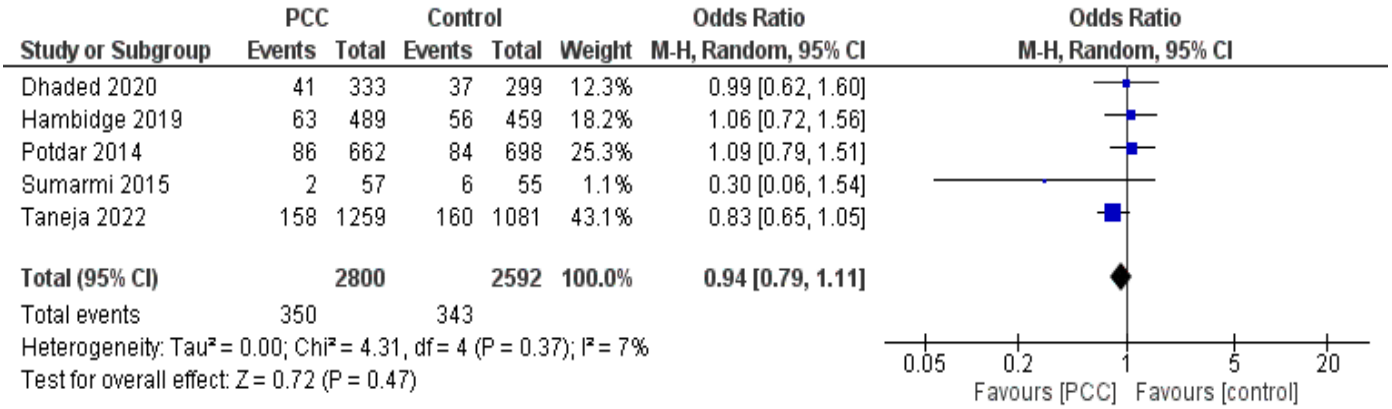

Figure 2: Pooled effect of Preterm Birth

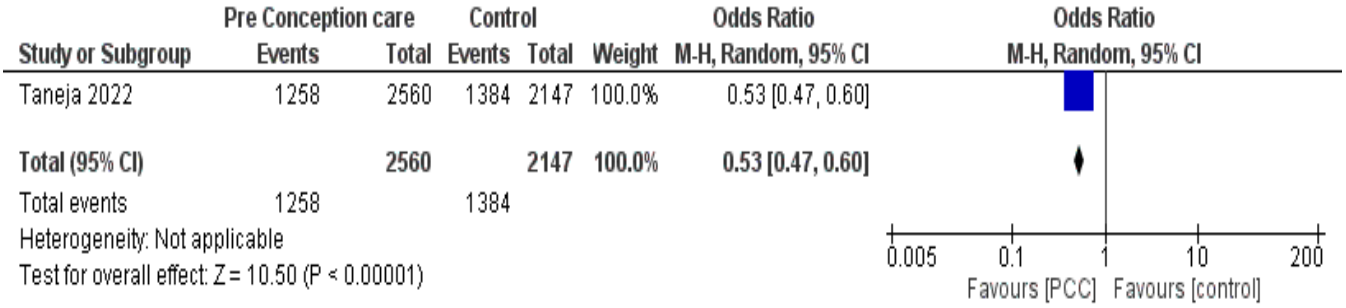

Figure 3: Pooled effect for Anemia among pregnant women

MODEL RURAL HEALTH RESEARCH UNITS (MRHRUS)

9. MODEL RURAL HEALTH RESEARCH UNITS (MRHRUs)

The Government of India in June 2013 approved the scheme for establishing Model Rural Health Research Units (MRHRUs) in the states during the 12th Plan period as a groundbreaking initiative to develop and strengthen the health research infrastructure in underserved areas for the benefit of rural and tribal communities. The scheme's objectives are to transfer technologies to rural areas to improve the quality of health services, to create an interface between researchers, health systems, and communities in rural areas, and to expand the geographical distribution of health research infrastructure across the country.

9.1 MODEL RURAL HEALTH RESEARCH UNIT, DAHANU, MAHARASHTRA

Nodal Officer : **Ragini Kulkarni**
Deputy Nodal Officer : **Kiran Munne**
Staff : S Kumar Mishra, K Thakur, G Dhodhade, S Bobbe, D Thakur, V Kudalkar, H Machhi, N Tamore, L Tandel, V Dubla

MRHRU Dahanu stands committed for improving the quality of life of the rural and tribal populations, transfer of technology and capacity building of the service providers in the district. Towards this, various research projects are being executed to address both local and national health priorities. These initiatives cover a wide range of critical health areas, from maternal and child nutrition to the prevention and control of infectious diseases, non-communicable diseases and common cancers. MRHRU Dahanu is one of the Regional Clinical Trial Units (RCTU) under Indian Clinical Trial & Education Network (INTENT). MRHRU Dahanu provides various diagnostic facilities such as dengue & chikungunya, leptospirosis, influenza [Influenza A (H3N2), A (H1N1) pdm09 and Influenza B (Yamagata and Victoria lineage)], COVID-19, Sickle cell disease and Thalassemia. During the reporting period, a total of 2748 serum samples were tested for anti-dengue IgM antibodies by ELISA, of which 462 (16.8%) were found positive. 13 samples were processed for dengue NS1 antigen, all were negative. For chikungunya, a total of 867 serum samples were tested by IgM capture ELISA, of which 184 (21.2%) were found positive (Figure 1). For Leptospira, 11 (7.9%) were found positive for Leptospira IgM out of 140 serum samples tested. Under the influenza diagnostic facility, three samples were processed with ICMR-NIV Multiplex Combo Kit for detection of Influenza & SARS-CoV2 and all samples were negative. Continued medical education programs for diagnosis and multidisciplinary management of PCOS have been conducted for the medical officers and other health workers in the district. Capacity building of linked medical college staff in grant writing and proposal development and qualitative research workshop was done. A basic workshop on qualitative data analysis with focus on RAPID analysis for Implementation research was conducted. Training of Health service providers on MPDSR conducted at Zilha parishad Palghar. Training to diagnose Dengue and Chikungunya by ELISA was imparted to lab technicians of Vasai-Virar Mahanagar Palika. Training of anganwadi workers of Ganjad on IYCF practices with hands on recipe demonstration was also done. Training on Gazelle Hb Variant point-of-care test and HPLC was given to project staff. ASHAs and ANMs at Ashagad PHC were trained in spacing contraception methods. We are also working on anemia among out of school adolescent girls and impact of capacity building of ASHAs and ANMs in couple counselling for improving the use of modern contraceptive methods among eligible couples. A total of 10 research articles and one policy brief were published through projects implemented at MRHRU Dahanu. Awareness on biomedical waste management, cleaning drive, IYCF hygiene practices and Walkathon conducted by MRHRU Dahanu under Swachhata Hi Seva campaign 4.0.

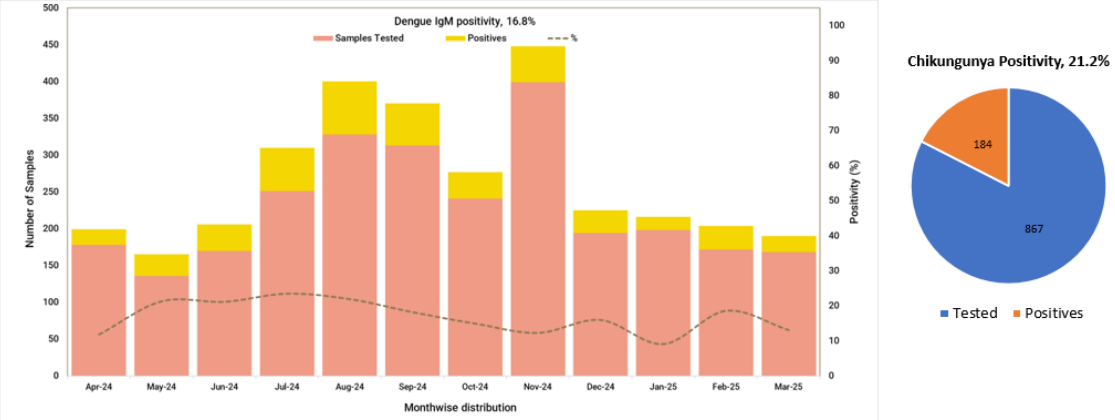

Figure 1: Month-wise distribution of the number of confirmed positive cases (IgM) of dengue virus infection from April 2024 to March 2025 in Palghar district. Total samples tested and positives identified for Chikungunya IgM shown in the pie chart

9.1.1 Validation of Novel Serum Biomarkers in Prediction of Early Onset Preeclampsia among the Pregnant Women and Correlation with Maternal and Neonatal Outcomes in a Tribal District of Palghar *[Partly Funded by ICMR (PM-ABHIM Scheme)]*

Principal Investigator	:	**Ragini Kulkarni**
Co-Principal Investigator	:	Taruna Madan Gupta
Co-Investigators	:	Shahina Begum, Anushree Patil, S K Mishra
Project Associates	:	S Gurav, Ashvani R Sutar, Sayali Mali, Snehal Davane, Samruddhi Araj
Collaborators	:	B Hengne, S Waghmare, B Mahale, Smita Bari, A Gadag, D Patil
Duration	:	2024-2026

The broad objective is to validate novel serum biomarkers in prediction of early onset of pre-eclampsia among pregnant women and correlation with maternal and neonatal outcome. The study is being conducted among pregnant women (10-16 weeks of pregnancy) above 18 years in Sub-District Hospital of Dahanu, Kasa and Jawhar and PHCs of Ganjad, Gholwad and Ashagad of Palghar district of Maharashtra. During the study, women with risk factors (n=224) and healthy controls (n=86) will be recruited to measure serum levels of SP-A, SP-D and P4/E2 ratio. Staff recruitment was completed in May 2024 and training of project staff was conducted at ICMR-NIRRCH on serological assays of biomarkers. All senior health officers in Palghar district were sensitized about the project staff on 4th May 2024. Health staff sensitization regarding study was undertaken at SDH Dahanu on 5th June 2024 and at SDH Kasa on 6th June 2024. Orientation about this project was given to community health officers, ASHA workers and ANMs of respective health facilities for smooth enrollment and follow-ups. During the reporting year, a total of 195 pregnant women were recruited (109 in study group and 86 in control group at their first antenatal care (ANC) visit during 10-16 weeks of gestation). These women are being followed up until 3-6 weeks post-delivery. Their clinical and socio-demographic parameters are being recorded in the case record form. Out of the total 195 pregnant women, 132 women have delivered (86 had a normal delivery and 46 had C-section delivery). There were eight abortions (three among control participants and five among study participants). One still birth was recorded. Blood samples were collected from all 195 participants, transported to laboratory at MRHRU Dahanu and stored for measurement of serum levels of SP-A, SP-D, P4/E2 ratio by ELISA. Four out of total 150 samples were processed in duplicate for serum SP-A; 165 for SP-D; 172 for progesterone and 170 for estradiol level measurement. Follow up of the enrolled participants is ongoing.

Figure 1: Health staff sensitization at sub-district hospital Dahanu

Figure 2: Training of ASHA workers on the objectives of the project in Dahanu

9.1.2 Strengthening Maternal and Perinatal Death Surveillance and Response (MPDSR) action in Tribal blocks of Palghar in Maharashtra *(Partly Funded by ICMR)*

Principal Investigator	:	**Ragini Kulkarni**
Co-Principal Investigators	:	S Chaudhari, District Health Officer R Marad, Civil Surgeon Suchitra Surve
Co-Investigators	:	Anushree Patil, Shahina Begum, S Patil
Project Associates	:	A Baruah, K Chaudhari, N Hase, Ashwini Padvale, Disha Patil
Duration	:	2024-2026

This is an implementation research study undertaken to develop a contextual model to strengthen the Maternal and Perinatal Death Surveillance and Response (MPDSR) in two blocks (Dahanu and Jawhar blocks) of Palghar district for completeness, accuracy and timeliness up to 80% in review of maternal and perinatal deaths and to enable district and block health system to identify most probable cause of death in at least 75% perinatal deaths and take appropriate actions. During the pre-implementation phase (April - October 2024) facility survey of 13 Primary Health Centres and 3 Sub District Hospitals in Dahanu and Jawhar blocks was carried out. Technical Support Unit (TSU) was constituted at state level to include state and district officials. The project staff participated in Maternal Death Review (MDR) and Child Death Review(CDR) meetings at district level during this phase. On the basis of gaps identified during the formative phase, sensitization and training of MOs, ANMs and ASHAs was done. It focused on accurate filling of forms, accurate ICD-10 coding for proper diagnosis, management of sickle cell anaemia in pregnancy and management of PPH. Training of the health staff (MOs, ANMs and ASHAs) for filling up the forms was conducted. Audit of all maternal and perinatal death forms was done (maternal death forms reviewed – 5, perinatal death forms reviewed – 10, stillbirth forms reviewed – 24). The following components of the model 0+ have been implemented from October 2024 – March 2025. (a) Regular participation of MDR and CDR meetings at district level by project staff (b) Follow up actions being taken based on recommendations during meetings • For Delay 1 – Ensuring awareness and health education by health staff of PHCs. IEC materials and videos along with a complete set of death review forms, were provided to the respective MOs in every PHC. In collaboration with Jhpiego monitoring and evaluation of recommendations, through MSV (Monitoring and Supportive Supervision) checklist for ANC clinic days was carried out. • For Delay 2 – Communication to state health officials regarding increase in number of ambulances. • For Delay 3 – Communication with state government for unavailability of blood bank facility in the district. Audit of all Maternal and Perinatal Death Forms in selected blocks – Dahanu and Jawhar, three months post-training of MOs and ANMs was done to assess compliance and data quality. Model +1 will be implemented from April 2025 – October 2025. This will include stillbirth review meetings which were not conducted previously and skilled based training of healthcare workers on leading causes of death. Depending on outcome indicators Model +2 will be implemented if needed. Post Implementation Phase will be conducted for 6 months from November 2025-April 2026. Data analysis and report writing will be done during this phase.

Figure 1: Training of Medical Officers, Taluka Health officers, Medical Superintendents of Dahanu block

Figure 2: Training of Medical Officers and ANMs of Jawhar block

9.1.3 Population-based Health Surveys at Model Rural Health Research Units (MRHRUs) in India-MRHRU Dahanu *(Partly Funded by DHR-ICMR)*

Principal Investigator	:	**Ragini Kulkarni**
Co-Principal Investigator	:	Kiran Munne
Co-Investigators	:	Geeta Pardeshi, R Gajbhiye, Suchitra Surve, Anushree Patil, Deepti Tandon, R K Prusty, H Munshi
Project Associates	:	S K Mishra, Kruti Thakur, Gulab Dhodhade, D Thakur, V Kudalkar, Henika Machhi, N Tamore, Prarthana Macchi, Mohini Avatar, Ankita Patil
Collaborators	:	S Chaudhari, R Marad
Duration	:	2024-2026

The aim of the project is to generate aggregate and local-level estimates of key indicators of common infectious diseases, non-communicable diseases and risk factors, and maternal & child health and nutrition in communities served by 34 MRHRUs across India. MRHRU Dahanu is one of the centers in Palghar. The total number of households in the specified area will serve as a sampling frame, from which at least 2000 households during each annual round of survey will be sampled. The activity was initiated on 7th October 2024. Field staff recruitment and approvals were obtained for data collection from Director Health Services, Govt. of Maharashtra on 28th October 2024. Permissions were taken from district health officer, civil surgeon Palghar, in-charge medical officers of respective PHC's (Ganjad & Chinchani) and Gram Panchayats in the selected villages (10) of the study. During the reporting period, a total of 2353 individuals were covered in this study. The survey for Module I -Household information (956); Module II - Children <5 years of age (136); Module III - Individuals (2353); Module IV - Diabetes & Hypertension (3); Module V - Biomarkers (1909); and Module VI - Women of reproductive age group (6) have been completed in 5 villages, Dhakti Dahanu, Badapokhran, Chandigaon, Chinchani 1 and Chanchani 2 of Dahanu block and

submitted to ODK tool. Blood and urine samples were collected from 2001 individuals (including 30 children) for various investigations such as hemoglobin (Hb), HbA1C, serum bilirubin, SGPT, serum creatinine, GFR, and urine albumin through HLL lab Ltd. For children (<5 years of age), only Hb was tested. Biochemical reports were given to the participants. A training was conducted on the use of Spirometer for project staff on 22nd January 2025 at MRHRU Dahanu. List of individuals with diabetes melitus, hypertention and women in reproductive age group and details of their infants were collected from the health facilities available in all 10 villages. All staff involved in population based survey attended ODK training conducted by DHR on 2nd December 2024. A review meeting was held on 16.12.2024 under the chairmanship of Secretory, DHR & DG-ICMR to review the progress of PBS study at MRHRU sites.

Figure 1: Field monitoring of the population based health survey in Dhakti Dahanu village

Figure 2: Field monitoring for the population based health survey in Badapokhran village

9.1.4 Assessing Feasibility of Point of Care Device in Community-Based Screening of Sickle Cell Disease and Thalassemia in Tribal District of Palghar, Maharashtra *(Partly Funded by ICMR)*

Principal Investigator	:	**Ragini Kulkarni, Suchitra Surve**
Co-Principal Investigators	:	Anita Nadkarni, Manisha Madkaikar
Co-Investigators	:	N Khargekar, Kiran Munne
Project Associates	:	Vanashree Malewar, Rita Wankhede, Saloni Sudhir Meher, M Lahu Khirari, Suvarna Kharpade, D Thakur
Collaborators	:	R Marad, S Chaudhari, S Patil
Duration	:	2024-2026

The study aims to assess feasibility of Gazelle (Point of Care test) for diagnosis of Sickle Cell Disease (SCD) and Thalassemia and to compare Gazelle results for diagnosis of SCD and Thalassemia (Disease and Trait) with HPLC. The study is being conducted in the Amgaon PHC of Talasari block in Palghar district through MRHRU, Dahanu. Approximately 5,541 children in the age group of 6 months to 6 years are expected to be enrolled during the study. During preparatory phase, sensitization meetings were conducted with district health officials and other stakeholders to provide an overview of project. The activities in the preparatory phase included procurement of Gazelle machine, training of project staff and community engagement activities. Qualitative data collection including 8 Focus Group Discussions (FGDs) with ASHA workers and 20 in-depth interviews (IDIs) with healthcare professionals - medical officers (MOs), lab technicians, and Auxiliary Nurse Midwives (ANMs) under Amgaon PHC were completed in the preparatory phase.

Figure 1: Focus group discussion with ASHAs at Kajli sub center under Amgaon PHC of Talasari block

Community activities were also conducted for gatekeepers and healthcare workers during pre-intervention to increase the awareness about SCD. The intervention phase was initiated in October 2024. Since then, 34 screening camps have been organized across various villages including Dongari, Kajali, Sambha, Anvir, to screen SCD and other hemoglobinopathies. A total of 1040 individuals

have been screened till date, identifying 117 individuals with SC trait, 27 with β-Thalassemia trait, 4 with SCD, 3 individuals with unknown haemoglobin variants, and 889 with normal haemoglobin profiles. In addition to screening the children, cascade screening for parents and siblings of individuals identified with either the trait or disease are also being done. The children diagnosed with SCD are being referred at the monthly hematology OPD conducted at Sub-District Hospital in Dahanu for further management. The feasibility of using Gazelle by healthcare providers will be assessed using a Likert scale during phase three, which will be followed by data analysis.

Figure 2: Counselling and written consent from the parents of children identified with hemoglobinopathies in a camp conducted at Dongari subcenter under Amgaon PHC

9.1.5 Infant and Young Child Feeding (IYCF) practices in Tribal block of Palghar District, Maharashtra through involvement of frontline workers *(Partly Funded by ICMR (PM-ABHIM Scheme))*

Principal Investigators	:	**Ragini Kulkarni, Suchitra Surve**
Co-Investigators	:	Shahina Begum, Bhavya MK Y Y Shivshankar, Purabi Mahajan, Tata Memorial Hospital, Mumbai
Project Associates	:	Shraddha Kyatam, N D Dhavare, Shweta Sarode, Arpita Kini, Kavita Agarkar, Tejal Machhi, Pranali Ambhire
Collaborators	:	S Chaudhari, S Patil, P Bhavsar, Bharati Kulkarni, S Prabhu
Duration	:	2024-2026

The study is being conducted at Ganjad Primary Health Centre (PHC), located in the tribal region of Palghar District, Maharashtra through MRHRU, Dahanu to improve Infant and Young Child Feeding (IYCF) practices. The study has four objectives: (1) To assess the knowledge, attitude, and practices (KAP) of healthcare workers and mothers regarding IYCF; (2) To develop and implement an intervention package; (3) To compare children's nutritional status and WHO-recommended IYCF indicators before and after intervention; and (4) To document the facilitating factors and challenges during implementation. The study will adopt quasi-experimental design comprising pre-intervention, intervention and post-intervention phases. Hence, an independent sample of 460

children will be selected for both the pre-intervention and post-intervention phases. During pre-intervention phase, the staff was recruited and training was provided. Sensitization meetings were conducted with district health officials and other stakeholders to provide an overview of the project. After the preparatory activities in Phase 1, in-depth interviews were conducted with key stakeholders along with baseline surveys involving 20 ASHAs, interviews with 414 mothers, to understand status, knowledge and perceptions of IYCF practices among caregivers and health care providers. Awareness activities were conducted during the World Breastfeeding Week and as a part of Swachhata Abhiyan. An intervention package was developed to enhance complementary feeding practices at Anganwadi Centers. New IEC materials in Marathi were created, including a flipchart, recipe book, month wise food brochure (6 to 12 months), health card and Nutritional Assessment Chart (Diet card). Educational videos on breastfeeding and feeding practices were selected for display. A detailed intervention plan was also prepared, outlining monthly activities like interactive sessions, recipe demos, nutritional assessments, and video screenings. Intervention phase i.e. Phase II of the IYCF project was initiated in October 2024 and currently ongoing, is focused on implementing a variety of educational and nutritional activities to promote appropriate IYCF practices. These include recipe demonstrations, video screenings, and role-plays aimed at educating mothers on timely complementary feeding and reducing the consumption of processed foods. The project team is actively monitoring child growth, identifying and referring cases of Severe Acute Malnutrition (SAM) and Moderate Acute Malnutrition (MAM), and distributing Vitamin D3 (Calshine P Drops) and Calcium supplements (Cipcal Syrup) to children over six months of age. Rations based on a structured weekly meal plan have been provided to Anganwadi Workers (AWWs), and prizes have been awarded to both AWWs and mothers who actively participated in the intervention. Nutritional indicators such as Minimum Dietary Diversity (MDD), Minimum Meal Frequency (MMF), and Minimum Acceptable Diet (MAD) are being closely tracked through regular follow-ups at Anganwadi Centers. The intervention also includes enhancing awareness regarding the optimal duration and practices of breastfeeding through educational displays with emphasis on hygiene practices. The intervention phase is being monitored through process indicators. The Post-Intervention phase will begin in October 2025 and will include follow-up surveys, followed by final report writing and stakeholder dissemination.

Figure 1: Training of anganwadi workers on Infant and Young Child Feeding (IYCF) practices

Figure 2: Breastfeeding and complementary feeding practices, recipe demonstrations using locally available ingredients

9.1.6 Developing & Implementing Effective Intervention Delivery Strategies of the Anemia Mukt Bharat Program 2.0 to Reduce Prevalence of Anemia amongst Vulnerable Populations in Selected Districts of India - An Implementation Research Study (PRAKASH) - Precision *(Partly Funded by ICMR)*

Principal Investigator	:	**Ragini Kulkarni**
Co-Principal Investigators	:	**N Ambadekar, Geeta Pardeshi, Kiran Munne**
Co-Investigators	:	R Waghmare, Pallavi Uplap
Project Associates	:	Samiksha Ingawale, Mansi Tamore, Krina Save, A Mahakal, Kaveri Kshirsagar, Mokshada Mahsalkar, Sujata Kambale, Pratima Ghoda, N Mahale, P Gharat
Collaborators	:	Puna Gandal, R Jagtap, R Marad, S Chaudhari, S Patil
Duration	:	2025-2028

Primary objective of the study is to co-design, optimize, implement and evaluate a model of implementation strategies to deliver the Anemia Mukt Bharat 2.0 interventions across target beneficiaries and reduce prevalence of anemia to ≤20% in among children 6-59 months and adolescent girls (10-19 years), Women of Reproductive Age (WRA) (20-49 years) and pregnant women in 2.5 years. The proposed implementation research (IR) will use a mixed-methods approach (qualitative and quantitative) for model optimization and interrupted time-series (ITS) measurements for the outcome evaluation. The study will be conducted across five sites in India. In Maharashtra it will be conducted in Palghar district through MRHRU Dahanu. The expected outcome of the study is that the prevalence of anemia in the selected four beneficiary groups will be reduced to ≤20%. An optimized model for implementation of strategies in the Anemia Mukt Bharat programme will be developed which can be scaled up in other districts of the country for reduction of anemia. During the reporting year, ethics committee approval and State Government approvals were obtained; recruitment of staff was initiated; attended virtual meetings conducted by ICMR Headquarters for finalization of tools; meeting with District health officials regarding project implementation was also held.

9.2 MODEL RURAL HEALTH RESEARCH UNIT, VANI, MAHARASHTRA

Nodal Officer	:	**R Gajbhiye**
Deputy Nodal Officer	:	H Munshi
Field Investigator	:	Anupriya Khedkar
Project Technical Support-III	:	Sakshi Gangurde
Assistant Multipurpose	:	N Dhivre
Field Worker	:	J Chaudhari
Field Worker	:	P Kale
Field Worker	:	Trunali Barde
Multi-Tasking Staff	:	A Bagul

9.2.1 D-SERPENT: Data-driven Approaches to Snakebite: Epidemiology, Reporting, Phenotypes, Environmental Factors, Inequalities, and Treatment Duration *(Partly Funded by Indian Council of Medical Research)*

Principal Investigator	:	**R Gajbhiye** *(Lead Principal Investigator, Maharashtra)*
Co-Principal Investigator	:	H Munshi, Sandhya Anand K Aher, Deputy Director Health Services, Nashik S More, District Health Officer, Nashik Sonali Gaidhani, Rural Hospital, Vani
Duration	:	2025-2027

This project addresses the persistent challenges of snakebite underreporting and inconsistent diagnosis in India, a country that bears nearly half of the global burden of snakebite deaths. Snakebite was first designated a Neglected Tropical Disease (NTD) by the WHO in 2009. This designation was removed in 2013, and reintroduced in 2017 due to data and definitional inconsistencies that hampered accurate disease burden estimation. The lack of standardized terminology and coding systems has made it difficult for clinicians, researchers, policymakers, and patients to manage and respond effectively to snakebite incidents. In India, snakebite cases are inconsistently recorded using terms like venomous bite, hemotoxic bite, neurotoxic bite, or unknown bite. These varied entries rarely make it into disease-specific registries, resulting in underreported national statistics. Currently, diagnosis and treatment of venomous snakebite in South Asia rely on a syndromic approach, where symptoms guide treatment: Hemotoxic symptoms suggest coagulopathy and neurotoxic symptoms indicate neuro-paralysis. However, this method lacks the standardization required for broad-scale data collection and research. This project proposes a menu-driven, geography-specific coding system for snakebite cases, modeled on international standards like ICD-11 and SNOMED-CT. By linking clinical syndromes to geographical data, this system aims to standardize how snakebites are recorded across facilities. This would enhance interoperability between datasets and allow for more accurate phenotyping, improved epidemiological models, and better-informed health interventions. This approach also supports the WHO's 2018 global strategy to halve snakebite-related deaths and disabilities by 2030 through improved data and care pathways.

The primary objective of the study is to develop, validate, and implement a standardized, geography-specific snakebite coding system based on syndromic diagnosis. Secondary objective is to evaluate how socioeconomic inequalities, environmental factors, and treatment delays influence snakebite outcomes across different Indian regions. A broader comparative analysis will involve one district each from four zones of India, enabling geographic representation. The effectiveness of

the coding system will be evaluated by comparing the proportion of coded snakebite cases to the total treated cases, assessing improvements in case documentation and epidemiological tracking. The study is observational in nature and will be carried out across all blocks in Nashik district. It includes both retrospective and prospective data collection phases. All snakebite cases from public and private healthcare facilities will be included. During the first reporting year (2024–25), the following preparatory activities were undertaken in Nashik:

- Document submission to the institutional ethics committee was completed.
- The study protocol, CRFs, and syndromic coding templates were finalized with Nashik-specific adaptations.
- Project staff underwent comprehensive training.

9.2.2 Strengthening Implementation of Antenatal Screening and Newborn Management for Sickle Cell Disease at Rural Hospital, Vani, in Tribal Block of Nashik, Maharashtra *(Partly Supported through MRHRU Vani Grant)*

Principal Investigators	:	**R Gajbhiye, Suchitra Surve**
Co-Principal Investigators	:	H Munshi, Sonali Gaidhani, Rural Hospital, Vani Kalpesh Chopade, Taluka Health Office, Panchayat Samiti Dindori, Nashik
Project Associates	:	N Wasekar, MRHRU Vani Sandhya Anand, S Pande P Kedar, ICMR-NIIH, Mumbai Sarika Patil, Nodal Officer, MRHRU Vani, Shri Bhausaheb Hire Medical College, Dhule
Duration	:	2025-2027

The study focuses on addressing the significant burden of haemoglobinopathies, particularly Sickle Cell Disease (SCD), among tribal populations of the Dindori block in Nashik, Maharashtra. This region, with limited health infrastructure, urgently needs enhanced antenatal and newborn screening programs for SCD. Current screening methods, primarily solubility tests, are inadequate due to their low accuracy and inability to identify various haemoglobin variants reported in SCD. To improve early detection and management, the study proposes the implementation of Gazelle, a low-cost, rapid, and highly accurate point-of-care (POC) diagnostic device capable of identifying haemoglobin variants, including HbA, HbS, and HbF (Figure 1). A recent study demonstrated Gazelle's accuracy at 99% when compared to high-performance liquid chromatography (HPLC) and haemoglobin electrophoresis, validating its feasibility for use in low-resource, high-prevalence settings like Dindori. The project is being conducted at Rural Hospital, Vani, through MRHRU Vani, and spans over three years, comprising a 6-month preparatory phase, a 26-month implementation period, and a 4-month data analysis phase. Training of the staff on using Gazelle has been completed at MRHRU, Vani. Approximately 650 pregnant women, their spouses, and around 550 newborns will be screened annually. A cascade screening strategy is being followed, which includes testing the parents and other siblings in the family, with support for follow-up visits or home-based collection if needed (Figure 2). The primary objectives of the study include: (i) assessing healthcare workers' knowledge of SCD and building their capacity; (ii) implementing and evaluating the feasibility of screening antenatal mothers and newborns for SCD using Gazelle; (iii) establishing a sustainable model for management and referral of affected mothers and newborns. To ensure comprehensive care, a monthly hematology outpatient clinic has been established at MRHRU, Vani

for follow-up and management of diagnosed cases. This study aims to generate scalable evidence for integrating Gazelle into national SCD screening protocols in underserved tribal areas.

Figure 1: Gazelle: A POC device for identification of haemoglobin variants in Sickle Cell disease patients

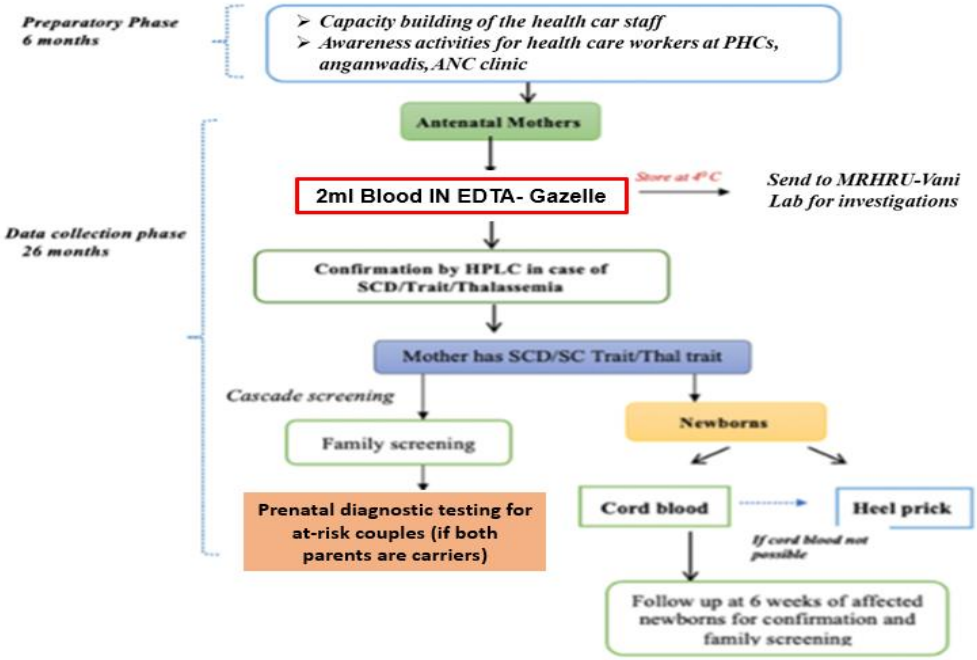

Figure 2: Flowchart of methodology to be adopted in the study

9.2.3 A Situational Analysis of the Disease Burden in the North Maharashtra Region *(Partly Supported though MRHRU Vani Grant)*

Principal Investigator	:	**R Gajbhiye**
Co-Principal Investigator	:	H Munshi K Aher, Deputy Director Health Services, Nashik & Nodal Officer, MRHRU Vani Sarika Patil, Government Medical College, Dhule & Nodal Officer, MRHRU Vani

Collaborators	:	C Shinde, Civil Surgeon Nashik, S More, District Health Officer, Nashik, Sonali Gaidhani, Rural Hospital, Vani, K Chopade, Taluka Health Officer, Dindori, Suchitra Surve, Sandhya Annad
Duration	:	2024-2026

This project aims to conduct a situational analysis of disease burden in the North Maharashtra region, MRHRU Vani is aligned with the national objective of promoting basic, applied, and clinical research in rural areas. To guide evidence-based research planning, it is crucial to understand patterns in health service utilization (both outpatient and inpatient) across public health facilities. This data-driven insight will help shape community-need-based research priorities and enable monitoring of the impact of research interventions over time. The study focuses on Nashik and the adjoining tribal-dominated districts of Dhule, Jalgaon, and Nandurbar, as well as the Dindori, Peth, and Surgana blocks in Nashik district. These three blocks have a very high tribal population: 55.8% in Dindori, 96.4% in Peth, and 96.5% in Surgana. By comparing health-seeking patterns across these areas, the project aims to identify inequities in access to healthcare and inform research planning in these socio-economically challenged tribal regions. Primary objectives of the study are to (i) record outpatient visits and inpatient admissions at public health facilities in North Maharashtra from 2017 to 2022; (ii) document causes of death, including maternal mortality, in the same timeframe and region; (iii) estimate disparities in healthcare utilization between North Maharashtra, Nashik district, and the tribal blocks (Dindori, Peth, Surgana). The study uses anonymized retrospective data from the public health sector, supported by the health authorities in each district. Data have been collected from the Health Management Information System (HMIS) and duty registers maintained at healthcare facilities for a wide range of diseases i.e. communicable and non-communicable diseases, maternal and child health issues, trauma, accidents, and tropical illnesses. Where data gaps were identified, follow-ups were made with specific facilities to retrieve missing information. Only anonymized data was used to ensure patient confidentiality. Maternal and child health indicators demonstrate consistent antenatal care (ANC) registration and institutional delivery rates across the districts; however, variations in obstetric complications and caesarean section rates indicate the need for continued strengthening of maternal healthcare services and referral mechanisms. A progressive increase in cases is observed in all districts of North Maharashtra - Dhule, Jalgaon, Nandurbar, and Nashik from 2018–19 to 2022–23, with Nashik consistently reporting the highest numbers, followed by Jalgaon and Nandurbar. The rising trend may reflect both an actual increase in incidence and improved case reporting through public health facilities. The data highlight snakebite as a continuing public health concern in rural and tribal areas of the region, emphasizing the need for strengthened surveillance, timely availability of anti-snake venom, and community awareness programs to reduce related morbidity and mortality (Fig. 2). Snakebites and leprosy also persist as serious health concerns, especially in tribal areas like Dindori. Findings will support evidence-based health planning by highlighting critical gaps in service delivery and access. Maternal deaths and mortality patterns may prompt targeted improvements in emergency care. Disparities in utilization suggest a need for interventions such as mobile clinics, community outreach, and transport schemes in tribal areas. The study also provides baseline data for monitoring future health programs and improving resource allocation across the region.

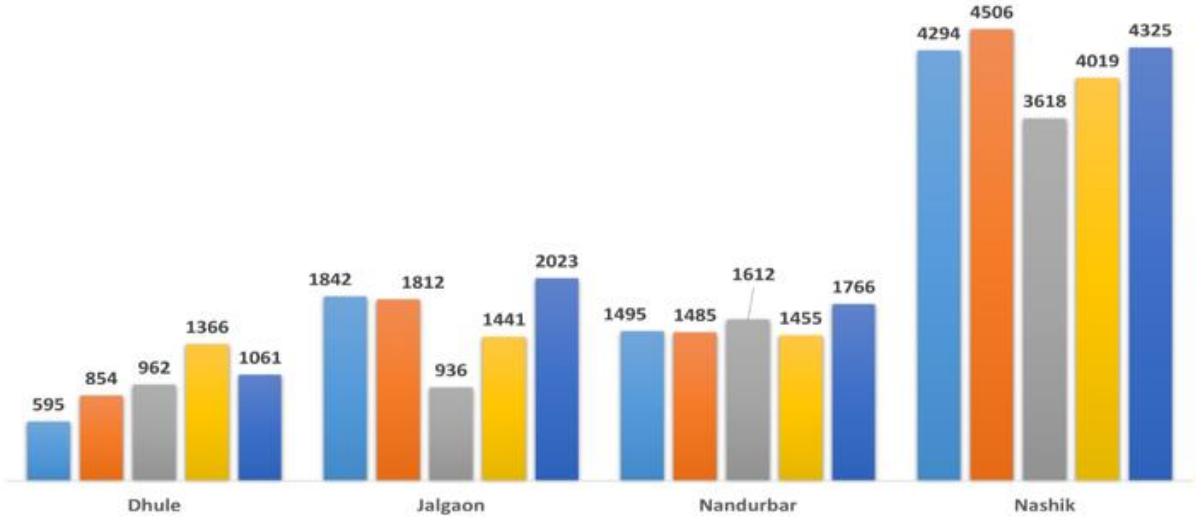

Figure 2: Year-wise distribution of snakebite cases across four districts of North Maharashtra Dhule, Jalgaon, Nandurbar, and Nashik from 2018–19 to 2022–23

9.2.4 Retrospective Study on the Utilization and Adverse Reactions of Snake Antivenom Administration at a Rural Hospital in Vani, District Nashik, Maharashtra *(Partly Supported though MRHRU Vani Grant)*

Principal Investigators : **S Jadhav, MUHS, Nashik**
R Gajbhiye
Project Associates : H Munshi, Sandhya Anand
Sonali Gaidhani, Rural Hospital, Vani
Duration : March 2025 - July 2025

Snakebite envenoming (SBE) remains a major public health threat in many tropical countries, with India accounting for an estimated 58,000 deaths annually. Maharashtra is one of the high-burden states, and within Maharashtra, Nashik district reports some of the highest incidences of snakebite cases. Anti-snake venom (ASV) derived from horses and targeted against the "big four" venomous snakes (Russell's viper, saw-scaled viper, common krait, and Indian cobra) is the only treatment currently available for snakebite. However, in rural healthcare settings, particularly at First Referral Units such as the Rural Hospital (RH), Vani, there is a significant lack of standardized information regarding ASV usage patterns, dosage variability, and the incidence and management of adverse drug reactions (ADRs). Recognizing and addressing these gaps are required for improving the quality of care, ensuring patient safety, and informing state-level health logistics. The present study has been conceptualized to address these gaps. This retrospective study is being conducted at RH Vani, involving a review of case records for all snakebite admissions from January to December 2023. The data will enable the calculation of monthly trends in ASV supply and utilization, as well as the identification of average dosages administered for different types of envenoming. In addition, the types, frequency, and severity of ADRs such as allergic reactions or systemic responses are being documented, along with their clinical management practices. This study will generate critical insights into current ASV utilization patterns in rural settings, help to identify inconsistencies and potential risks. Emerging findings on dosing variability and ADRs profiles will support the development of evidence-based protocols for reducing overuse or misuse of ASV. The documentation of real-world ADR management is guiding the design of targeted training programs for healthcare providers to ensure prompt and effective responses. The outcomes from this ongoing study are expected to

contribute to optimizing ASV supply chains and inventory management at RH Vani and potentially serve as a foundation for improving regional and national snakebite management strategies. By addressing critical knowledge gaps, the project supports broader public health objectives to enhance the safety, efficiency, and effectiveness of snakebite treatment across India's rural healthcare system.

9.2.5 ICMR National Snakebite Project (INSP) on Capacity Building of Health System on Prevention and Management of Snakebite Envenomation including its Complications *(Funded by ICMR National Task Force for Snakebite Research in India)*

Principal Investigator	:	**R Gajbhiye**
Co-Principal Investigator	:	H Bawaskar, Dr Bawaskar Hospital and Research Centre, District Raigad
Project Associate	:	H Munshi
Collaborators	:	A Yadav, Former Assistant Director of Health Services, Directorate of Health Services, Government of Maharashtra M V Bansode, Former Medical Superintendent, Sub District Hospital, Shahapur, Government of Maharashtra
Duration	:	2021-2024

Snakebite envenomation is a significant public health challenge in India, especially in rural and tribal regions. Recognizing its urgency, the Indian Council of Medical Research (ICMR) identified it as a priority research area under the Hon'ble Prime Minister's Vision for New India 2022. In response, Phase I of the ICMR-funded National Snakebite Project on capacity building of health systems on prevention and management of snakebite envenomation including its complications was launched. The project was implemented in four high-burden blocks: Shahapur (Thane) and Aheri (Gadchiroli) in Maharashtra, and Khordha (Khordha) and Kasipur (Rayagada) in Odisha. The objectives were to strengthen the health system's response, empower communities with knowledge on prevention and early care-seeking, assess healthcare providers' knowledge and practices, and reduce mortality and morbidity through the implementation of Government of India's Standard Treatment Guidelines (STG). A Technical Advisory Committee (TAC), comprising national experts, guided the project by reviewing study tools, training content, and IEC materials, and supported the training of master trainers. Retrospective data on 1,415 snakebite cases from 2020–2021 highlighted that 65% of victims were male and 25.4% were aged 30–40 years. Bites primarily affected lower limbs (88.2%), and only 27% of victims reached a health facility within one hour of the bite. Key gaps in timely treatment and documentation were identified. To address these, extensive capacity-building initiatives were undertaken. Medical and community health officers (n=248) received training, which included practical sessions on life-saving skills such as CPR, Ambu bag use, and endotracheal intubation. Additionally, 24 master trainers were developed across the four blocks. A total of 338 healthcare workers were interviewed, and 34 public health facilities were assessed for snakebite preparedness. Community engagement included 28 focus group discussions to explore perceptions and practices, and regionally adapted IEC materials in English, Hindi, Marathi, and Odia were developed and disseminated. Following these interventions, prospective data from 760 snakebite cases showed marked improvement in several indicators. Documentation of bite sites increased to 70%, and timely hospitalization within one hour increased significantly from 25.3% to 39.2%, reflecting a 54.9% absolute increase. The proportion of victims receiving first aid doubled (from 20.3% to 41.1%), while the administration of unnecessary ASV test doses dropped by 34.2%. The most impactful outcome was a 30.8% reduction in the case fatality rate. These results affirm that targeted interventions including community education, health worker training, and strengthened protocols can significantly

enhance outcomes in snakebite envenomation management. The project generated critical evidence on burden, behaviors, and system gaps in the four high-risk regions and demonstrated a scalable model for other endemic areas. The findings will directly inform the implementation of the upcoming National Action Plan for Prevention and Control of Snakebite Envenoming (NAP-SE), helping shape a coordinated national response to reduce the impact of snakebite across India.

9.2.6 Nationwide Study to Estimate Incidence Mortality, Morbidity, and Economic Burden Due to Snakebites in India *(Funded by ICMR National Task Force for Snakebite Research in India)*

Principal Investigator : **R Gajbhiye**
Project Associates : Smita Mahale, H S Bawaskar, D Punde, S Raut, B Shinde, N I Bhosikar, B Pawar, S More, S Mane, H Munshi
Collaborators : S N Rathod, A S Deshmukh, Government Medical College Nanded
P V Salve, V S Dange, Pimpri Chinchwad Municipal Corporation, Pune
Duration : 2022-2024

Snakebite remains a significant public health concern in India, disproportionately affecting rural agrarian communities with limited access to timely medical care. Due to poor record-keeping and underreporting the true scale of the problem is underestimated. To address this, the present study, the first large-scale, prospective, community-based survey on snakebite burden in India, covering 13 states across five geographical zones, was undertaken. It includes data from 1-4 districts per state, gathered not only from health facilities but also from affected communities. The study's objectives were to: (a) determine the incidence of snakebites, (b) understand the pattern of injuries, morbidity, and mortality, (c) assess treatment-seeking behavior, and (d) estimate the economic burden posed by snakebite. In Maharashtra, data were collected from Raigad, Pune, and Nanded districts with a combined population of over 17 million. Training of Accredited Social Health Activists (ASHAs) was central to the study`s implementation. Of 6,862 ASHAs, 5,414 (78.9%) participated in training, with the highest attendance in Raigad (80.6%). Evaluation compliance was strong (80.3%), especially in Raigad (97.9%) and Nanded (96.8%). Snakebite incidence was highest in Raigad (34.1 per 100,000), followed by Nanded (22.6 per 100,000), and lowest in Pune (2.3 per 100,000). However, the case fatality rate (CFR) painted a different picture: Pune reported the highest CFR (5.4%), despite low incidence, compared to Nanded (3.4%) and Raigad (1.6%), highlighting the need for region-specific interventions. Venomous bites were primarily attributed to the "Big Four" snake species, responsible for nearly 90% of cases. About 90% of victims sought hospital treatment, with 80% admitted to government facilities. Despite this, the economic impact remained significant. The average snakebite victim incurred an economic burden of ₹13,899 comprising ₹2,637 in wage loss and ₹11,262 as out-of-pocket medical expenses. For low-income rural families, such costs are catastrophic. The implications of this study extend well beyond data collection. The high ASHA participation and evaluation compliance show that grassroots-level training programs are both feasible and impactful. Scaling up such training could improve early recognition, first aid, and referral practices, ultimately reducing mortality. Furthermore, these findings provide robust, community-based evidence to guide national policy. Health systems must focus on strengthening emergency response capacity, particularly in high-CFR regions, while also integrating economic support measures into public health programs. The study advocates for investigating the underlying causes of high CFRs in certain regions, evaluating the long-term impact of ASHA training, and assessing the effectiveness of financial aid programs in reducing post-bite distress. By combining epidemiological insights and socioeconomic

data, the study provides a comprehensive foundation to reshape India's response to snakebite, from reactive treatment to proactive, community-based prevention and support.

9.2.7 Utilizing the Model Rural Health Research Units to Improve Snakebite Management through Rationalized Antivenom Distribution Models in India: An Implementation Research Project *(Funded by Department of Health Research)*

Principal Investigator	:	**R Gajbhiye**
Co-Principal Investigator	:	H Munshi
Project Associates	:	Y Kalkonde, Sangwari, Ambikapur H Bawaskar, Bawaskar Hospital and Research Center, Mahad S Raut, Vighnahar Nursing Home, Pune D Punde, Dr Punde's Clinic, Nanded
Duration	:	2024-2026

This multicenter collaborative implementation research project aims to improve Snakebite Envenoming (SBE) management and reduce bite-to-needle time, ultimately enhancing clinical outcomes in high-burden rural regions of Maharashtra, Karnataka, and Odisha. The study is being conducted through established Model Rural Health Research Units (MRHRUs) located in high-burden regions across Maharashtra, Karnataka, and Odisha. The key objectives are: (i) To develop rationalized antivenom distribution models, optimized by the geographic location of SBE and primary healthcare facilities in high burden regions in Maharashtra, Odisha and Karnataka; (ii) To conduct an economic evaluation of various models of optimized, rationalized antivenom delivery in Maharashtra, Odisha and Karnataka; and (iii) To conduct a formative evaluation of a culturally relevant SBE care package. The research will use advanced analytics to map the spatial distribution of snakebite cases and public health infrastructure, enabling customized intervention models. The project will also estimate Disability Adjusted Life Years (DALYs) and conduct economic assessments to evaluate impact. By the end of the study, a context-specific, multimodal intervention for optimized antivenom delivery will be developed and piloted. This scalable model will strengthen India's capacity in SBE response and may serve as a blueprint for improving access to treatment for other critical conditions in resource-limited settings. This study has the potential to transform antivenom delivery by providing evidence-based distribution models that improve access in high-risk areas. Economic findings will support policy-level decisions for cost-effective antivenom logistics. The culturally adapted care package will enhance community engagement, reduce treatment delays, and improve outcomes. Collectively, the outcomes can guide national protocols and be scaled to other SBE-endemic regions in India, contributing to WHO's goal of halving snakebite deaths and disabilities by 2030. In the reporting year: (i) ethical approval has been obtained; (ii) research staff has been recruited and training has been completed; and (iii) data collection tools have been drafted.

9.2.8 Population-based Health Surveys at Model Rural Health Research Units in India, MRHRU, Vani *(Supported through MRHRU Vani Grant and PM-ABHIM)*

Principal Investigator	:	**R Gajbhiye**
Co-Principal Investigators	:	H Munshi, Sandhya Anand
Project Associates	:	K Aher, Deputy Director Health Services, Nashik & Nodal Officer, MRHRU Vani C Shinde, Civil Surgeon Nashik

S More, District Health Officer, Nashik
Sonali Gaidhani, Rural Hospital, Vani
K Chopade, Taluka Health Officer, Dindori Block, Nashik
Anupriya Khedkar, Sakshi Gangurde, J Chaudhari, Trunali Barde, P Kale

Duration : 2024-2026

Monitoring trends in health indicators is essential for designing responsive public health interventions. India faces a dual burden of communicable and non-communicable diseases (NCDs), along with persistent challenges in maternal and child health (MCH) and nutrition. However, national-level estimates often mask local disparities. Model Rural Health Research Units (MRHRUs), functioning as decentralized research platforms in 34 locations across India, offer an opportunity to bridge this gap by generating reliable, district-level estimates of key health indicators and their changes over time. This evidence is critical to support targeted, data-driven health policy and resource planning. Major objectives of the study are: (i) to generate aggregate and local-level estimates of key indicators of common infectious diseases, non-communicable diseases & risk factors, maternal & child health and nutrition in communities served by 34 MRHRUs across India; (ii) to estimate the annual rate of change in the above-mentioned key indicators in communities served by 34 MRHRUs across India. The study is generating both aggregate and community-level estimates for a wide range of indicators, including the prevalence of common infectious diseases, mental health disorders, geriatric health, hypertension and diabetes, nutritional status of children, and women's health. Estimations of annual rate of change in these indicators will help to identify districts that are improving versus those lagging behind. 10 villages in Dindori block of Nashik district have been selected for the survey (Figure 1). In the reporting year, the household health survey covered 1,251 households, assessing a total of 4,294 individuals aged 10 years and above. Additionally, 279 children aged between 6 to 59 months were included in the study. As part of the health assessments, 2,776 blood samples and 2,349 urine samples were collected from participants. This extensive data collection supports comprehensive health analysis across age groups and will contribute to a deeper understanding of health trends and risks within the surveyed population (Fig. 2). The findings will support more granular, localized public health planning and highlight regions requiring intensified interventions. Annual change estimates enable policymakers to assess program impact and course-correct in real time. The MRHRU-based data system may serve as a model for scalable rural health surveillance, facilitating evidence-based allocation of health resources and improving equity in health outcomes across India.

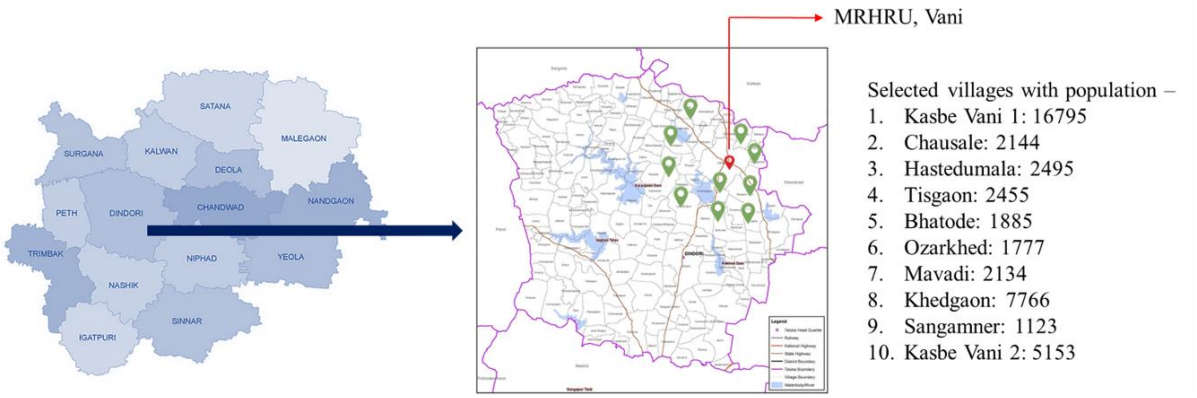

Figure 1: Selected study sites for population based health surveys

Figure 2: MRHRU, Vani team conducting the survey

9.2.9 Healthcare Journeys of Snakebite Victims Admitted at Rural Hospital, Vani *(Partly Supported through MRHRU Vani Grant)*

Principal Investigators	:	**V Aher, Maharashtra University of Health Sciences, Nashik** **H Munshi**
Project Associates	:	R Gajbhiye, Sandhya Anand Sonali Gaidhani, Rural Hospital, Vani
Duration	:	2025-2026

Snakebite is a life-threatening public health emergency in India, with an estimated 58,000 deaths annually. The lifetime risk of dying from snakebite for an average Indian is approximately 1 in 250. The burden is disproportionately high in rural regions like Nashik district in Maharashtra, where healthcare infrastructure, access, and awareness are often limited. Traditional first-aid practices and reliance on informal care pathways still dominate in many areas. Victims often face multiple barriers before reaching appropriate treatment facilities such as misidentification of the snake, lack of ambulance services, delay in symptom recognition, and referrals across multiple healthcare providers. These delays directly affect the time taken to administer Anti-Snake Venom (ASV), the only specific and effective treatment for snakebite envenoming. Despite the critical nature of snakebite treatment, the journeys of patients from the moment of envenoming to receiving care are poorly documented in India. This study addresses that gap by examining the treatment pathways and the challenges faced by snakebite victims admitted at the Rural Hospital in Vani, a high-burden region. Primary objective of the study is to document the treatment journeys of snakebite victims admitted at RH Vani. Secondary objectives are to identify factors influencing the treatment of snakebite; and to explore the challenges faced by snakebite victims from bite to outcome. This exploratory longitudinal study is scheduled from March to June 2025. The project has been initiated. A sample size of 50 patients is being recruited, based on seasonal trends in case load. Data is being collected using structured case record forms (CRFs), focusing on demographics, timelines, treatment steps, and outcomes. Quantitative analysis will be conducted using descriptive statistics,

T-tests for continuous variables, and Chi-square tests for categorical data. The study is expected to reveal critical points of delay in the care-seeking journey, such as traditional healer visits, poor transportation access, or lack of early symptom recognition. Documenting treatment journeys can guide improvements in emergency response systems, ASV accessibility, and community education. The findings can also be used to strengthen referral linkages and healthcare worker training, especially in high-risk rural areas. Ultimately, the study has the potential to reduce snakebite-related mortality and morbidity through evidence-based policy and practice.

9.2.10 Retrospective Study to Understand Drug Prescription Patterns at Rural Hospital, Vani, District Nashik, Maharashtra *(Partly Supported through MRHRU Vani Grant)*

Principal Investigators	:	**S Jadhav, Maharashtra University of Health Sciences, Nashik** **Sandhya Anand**
Project Associates	:	R Gajbhiye, H Munshi Sonali Gaidhani, Rural Hospital, Vani
Duration	:	March 2025 - July 2025

Understanding drug prescription patterns is a vital component of rational pharmacotherapy and public health planning. In India, rural healthcare settings face unique challenges, including limited access to specialists, inconsistent availability of medications, and a higher prevalence of self-medication and polypharmacy. Maharashtra, particularly in semi-urban and rural areas like Vani in Nashik district, reflects this disparity. Urban centers often benefit from more modern therapeutic options, while rural hospitals rely heavily on subsidized essential medicines. Despite this, there is limited published data on prescribing trends in such regions. Misuse of antibiotics, inappropriate polypharmacy, and seasonal prescribing shifts remain underexplored areas, especially in relation to the burden of infectious and non-communicable diseases. Objectives of this study are to determine the drug prescription patterns among general OPD patients visiting RH Vani over the past year; and to analyse these patterns by age, gender, drug type, and seasonal variation to identify influencing trends and prescribing practices. This retrospective observational study has been initiated at Rural Hospital, Vani, using medical records from January 2024 to December 2024. All eligible general OPD case records with valid prescriptions have been included. Data are being manually extracted using screening forms capturing demographics, diagnosis, drug details, and comorbidities. Descriptive statistics such as frequency, mean, and standard deviation will be used to summarize drug use by patient characteristics. Seasonal trends in prescribing such as increased antibiotics during monsoons or antipyretics during summer will also be analyzed. The study is expected to provide insights into prescribing habits and reveal patterns such as overuse of antibiotics, gender-based preferences, or polypharmacy in elderly patients. It may uncover whether prescribing aligns with diagnosis and standard treatment guidelines, or if irrational or habitual prescribing dominates. Findings from this study will help improve rational drug use, identify training needs for prescribers, and shape policies for essential drug stocking in rural hospitals. Seasonal variation analysis can inform targeted inventory management and better preparedness for disease surges. The research also addresses gaps in regional data critical for antimicrobial resistance (AMR) control strategies. Ultimately, this evidence will contribute to more efficient, safe, and cost-effective prescribing practices at the grassroots level.

9.2.11 Exploring Factors Influencing Treatment Adherence among Leprosy Patients in a Rural Hospital Setting: A Mixed-Methods Study in Dindori, Maharashtra *(Partly Supported through MRHRU Vani Grant)*

Principal Investigators	:	**P Shivgunde, Maharashtra University of Health Sciences, Nashik** **Kiran Munne**
Project Associates	:	R Gajbhiye, H Munshi, Sandhya Anand
Duration	:	March 2025 - July 2025

According to recent World Health Organization (WHO) data, more than 200,000 new leprosy cases are reported globally each year. India alone accounts for a large portion of the global burden. Despite national-level efforts, rural areas continue to struggle with persistent prevalence due to gaps in access, stigma, and adherence to treatment. Maharashtra, with a prevalence of 1.16 per 10,000 (2023–24), reflects this ongoing challenge, particularly in tribal and underserved areas like Dindori. Although multidrug therapy (MDT) is freely available, many patients fail to complete the full treatment regimen, resulting in relapses, disability, and continued transmission. Factors such as social discrimination, misinformation, stigma, and weak follow-up systems are known to impact treatment adherence. However, few studies have explored these issues holistically using both patient and healthcare provider perspectives, especially in rural settings. Objectives of this study are (i) to study the patient-intrinsic and extrinsic factors influencing treatment adherence among leprosy patients attending the outpatient department at Rural Hospital (RH), Dindori; (ii) to understand the healthcare provider`s perspective on factors contributing to treatment adherence; and (iii) to identify patterns of non-adherence (missed doses, incomplete cycles) among patients at RH Dindori. This cross-sectional mixed-methods study is based at RH Dindori. Data collection has started. Through semi-structured interviews with newly diagnosed patients and focus group discussions (FGDs) with patients undergoing ongoing treatment. Healthcare providers including a medical officer, leprosy technician, and pharmacist are being interviewed to gain system-level insights. Quantitative data has been statistically analyzed using SPSS, while qualitative data is undergoing thematic analysis. The study is expected to reveal a range of patient-related and systemic barriers such as fear of stigma, poor awareness, side effects of treatment, economic burden, and lack of transport or follow-up support. It will also highlight enablers such as good provider communication, peer support, and targeted counseling. By integrating perspectives from both patients and providers, the research will offer a comprehensive understanding of adherence behavior in rural Maharashtra. Findings from this study will help inform local and state-level strategies for improving treatment adherence in leprosy. Recommendations include enhanced patient education, community sensitization programs, improved follow-up, and resource allocation for rural outreach.

RESEARCH SUPPORT FACILITIES

10. RESEARCH SUPPORT FACILITIES

10.1 Family Welfare Clinics

The Family Welfare Clinics of ICMR NIRRCH provide family planning services and also services for other aspects of reproductive health. Services include information, education and counseling on various contraceptives and motivation to accept a reliable method, screening and treatment of Reproductive Tract Infections (RTIs), screening for cervical cancers and pelvic ultrasonography for women. Women attending these clinics are then enrolled for clinical and basic research studies approved by the institutional ethics committee. The institute has two Family Welfare Clinics – one at Wadia Hospital and another at Abhyudaya Nagar.

10.1.1 Family Welfare Services at Wadia Clinic

In-Charges : **Anushree Patil, Deepti Tandon**

Staff : Sunita Kale, Sunita Kharat, Halima Khan, Sunita Kendre

10.1.2 Family Welfare Services at Abhyuday Nagar Clinic

In- Charges: **Suchitra Surve, Kiran Munne**
Staff: Rachna Dalvi, Sharmila Kamat, Sarita Bhange

Details of the services provided by two family welfare clinics during year 2024-2025 are as given in Table 1 below:

Table 1: Clinical services provided by two Family Welfare Clinics

Clinical Services	Wadia Family Welfare Clinic	Abhyuday Nagar Family Welfare Clinic
Women who attended the clinic	1571	693
Women counselled for contraception	490	85
Women who accepted CuT-380	9	-
Women who accepted Oral Contraceptive Pills (OCPs)	10	16
Condoms distributed	3590	1125
Women who accepted Injectable Contraception	7	6
Women tested for RTI/STI	133	155
Women who were tested by Papanicolaou test	78	74
Women treated for Anemia	51	138
Collaborative research projects from infertility clinic	16	
Participants recruited for various collaborative research studies	171	74
Copper T follow up	-	33
Treated for Vit D deficiency	-	21
Treated for Calcium deficiency	-	181
Treated for UTI	-	54
Referred to Infertility and PCOS clinic at NIRRCH	-	23
Referral to other Hospitals	-	82

10.2 Infertility and Reproductive Endocrinology Clinic

In-Charges : **Anushree Patil, Deepti Tandon**

Staff : Vineeta Murtadak, Pratibha Kokate, Shobha Banage, Anamika Akula, A Hussain, Akshaya Rathod, Shalini Lambade

During the reporting year, clinical services were provided to infertile couples through the Infertility clinic and infertile males availed the services of visiting andrologist to the department. The results obtained helped in management and prognosis of the infertile couples. Telephonic consultations were offered to infertile couples. Pre-conception and pre-natal diagnostic techniques (PCPNDT) report were compiled and sent to Municipal Corporation of Greater Mumbai on monthly basis. Details are shown in table 01.

Table 1: Infertility and Reproductive Endocrinology Clinic (2024-2025)

Clinical Services	**Numbers**
Infertility couple registered and consultation provided	229
Telephonic consultation	215
New infertile couples	229
Old/follow up infertile couples	1944
Follow up patient for diagnosis, counseling and management	1695
New andrology cases detected	88
Ultrasound for serial follicular monitoring	221
Hysterosalpingography (HSG) repots obtained and evaluated	158
Pregnancies reported	26
Couples referred for IUI	28
Couples referred for IVF at Wadia Hospital	39
Couples counseled for Adoption	19
Women diagnosed and treated for RTI/STI	112
Women who were tested by Papanicolaou test	241
Women diagnosed and treated for Anemia	35
Couples referred for Genetic evaluation	64
Women referred to Preventive Oncology department (TATA Hospital) for evaluation	43
Collaborator research projects ongoing from infertility clinic	15
Participants recruited for collaborative research studies at NIRRCH	356

10.3 Child Health Clinic

In-Charge : **Suchitra Surve**

Staff : Kiran Munne, Rachana Dalvi, Sharmila Kamat, Sarita Bhange

At ICMR-NIRRCH, our commitment towards better child health extends from comprehensive research programs encompassing newborn screening to pubertal disorders. Our initiatives address a wide spectrum of child health concerns, ranging from nutrition, latent TB infection, vitamin D deficiency, genetic disorders, and precocious puberty in children. Moreover, our collaborative approach fosters partnerships with neighboring pediatric hospitals and health systems, amplifying

the impact of our work. Since 2015, our Child Health Clinic has been a beacon of support for the community, offering vital services such as growth monitoring, nutritional guidance, disease and deficiency screening, child development and mental health support, as well as health education and counseling on nutrition and puberty. With an annual attendance of approximately 800 individuals, the clinic serves as a cornerstone of community health, providing essential care to families in need. Child Health Clinic serves as a hub for the development of new research projects in the community. Through various outreach activities, including initiatives focused on Poshan Abhiyaan, Health and Hygiene, and Swachh Bharat Abhiyaan, we actively engage with Anganwadi centers and schools in the surrounding areas, amplifying our impact and reaching those most in need.

Table 1: Child Health Clinic Data (April 2024 – March 2025)

Child Health Services	**Number**
Total number of children attending the clinic	691
Total number of new children attending the clinic	209
Total follow ups	479
Children treated for deworming	270
Children treated for anemia	264
Dietary counseling of children	512
Children treated with calcium and Vitamin D supplementation	431
Puberty counseling	8
Children recruited in research studies	33
Children attending paediatric endocrinology clinic	10
Children attending nutrition OPD	13
Children referred from schools (growth + puberty)	199
Monthly yoga session for children	27

10.4 Multidisciplinary PCOS Clinic

In-Charges : **Anushree Patil, Deepti Tandon**

Staff : Pratibha Kokate, Shobha Banage, Anamika Akula, Akshaya Rathod, Shalini Lambade

ICMR-NIRRCH has a multidisciplinary team conducting research in clinical, epidemiological, genetic and bio-informatics aspects of PCOS.Women with PCOS are managed on a regular basis and once in a month, an integrated multidisciplinary PCOS clinic is conducted. A multidisciplinary team of specialty doctors like infertility specialist, dermatologist, psychiatrist, nutritionist and Yoga expert provides holistic management to women with PCOS. This is a unique model in India in a government health research institute for holistic management and research in PCOS.

Women diagnosed with PCOS using Rotterdam criteria were screened for metabolic co-morbidities with anthropometry, hormonal tests biochemical tests ultrasound and also for psychological health. Personal and medical history was noted in the designed case record form.

An electronic database is created of physical, hormonal, biochemical, ultrasound and emotional health parameters of the women with PCOS. Cohorts of adolescent and infertile women with PCOS are studied and followed at the clinic.

Table 1: Multidisciplinary PCOS Clinic details (April2024 to March 2025)

Clinical services provided	Number
PCOS cases detected	57
Registration of married women	35
Registration of unmarried girls	22
PCOs conducted at the clinic	12
PCOs blood test referred	60
Clients attending the PCOS clinic	119
Ongoing collaborator research projects	5
Participants recruited for collaborative research studies at NIRRCH	88

10.5 Multidisciplinary Clinic for Premature Ovarian Insufficiency

In-Charges : **Deepti Tandon, Anushree Patil**

Staff : Vineeta Murtadak, Pratibha Kokate, Shobha Banage, Anamika Akula, Akshaya Rathod, Shalini Lambade

The Premature Ovarian Insufficiency clinic which was initiated in 2022 continued in the reporting year. This clinic was held once in three months with the aim aim to evaluate the clinical spectrum, common autoimmune disorders, genetic factors and quality of life of women diagnosed with Spontaneous Premature Ovarian Insufficiency (POI). An additional objective of following up the cohort of women diagnosed with POI with yearly evaluation of metabolic, autoimmune parameters was taken from Ethics in the reporting year. Details of the clinical services provided are given below.

Table 1: Clinical services provided in Multidisciplinary Clinic for Premature Ovarian Insufficiency

Clinical services provided	Number
Number of POI cases detected	6
POI conducted at the clinic	3
POI blood test referred	25
Clients attending the POI clinic	24

10.6 Andrology Clinic

In-Charges : **R Gajbhiye and Priyank Kothari, Andrologist (Consultant)**

Staff : Anushree Patil, Deepti Tandon, Shobha Banage, Anamika Akula, Pratibha Kokate, Akshaya Rathod, Shalini Lambade

The services include clinical examinations, Scrotal Doppler, semen analysis, diagnosis, treatment, and counseling for infertile couples. During the reporting year, there were 30 new male infertility patients, 215 follow-up patients, and a total of 245 patients who used the clinic's services. Study participants were recruited for the research projects at NIRRCH. Thirty new male infertility patients attending the clinic. Total number of old male infertility patients for follow up was 215. Total number of patients availed services at clinic were 245.

10.7 Bone Health Clinic, Reproductive and Bone Health Unit, Naigaon

In-Charge : **Lalita Savardekar**

Staff : Neera Mehta, K Chavan, Swaroopa Khedekar, V Prashant

The community based Bone Health Clinic is a unique model to address osteoporosis while attending to knee/ spine problem and improvement in physical activity / quality of life by Yoga and stretching exercises. This multidisciplinary and comprehensive health care management may help in compliance of treatment for osteoporosis. In the reporting year, DXA was done in 44 new registered and 60 old registered clienteles repeat scans done (total 104 scans). Total clinic attendees for the current year was 1919 attendees and were given various referrals as required for cardiac opinion, urology, physiotherapy, diabetologist and follow up for hypertensive treatment with physician. All clienteles given monthly stock of routine calcium supplements, multivitamins, vitamin C and vitamin D. Regular follow ups were taken for all the registered clients via telephonic calls (2888 calls) regarding intake of medicines. Conduct of spine OPD (clinic consultation) with 17 OPD's for the year with attendance of 176 clienteles. Endocrine OPD for non communicable diseases (diabetes mellitus type II, hypertension, thyroid disorders) with total 12 OPD's and 85 attendees in the current year

10.8 Woman's Health Clinic, Reproductive and Bone Health Unit, Naigaon

In-Charge : **Lalita Savardekar**

Staff : Neera Mehta, K Chavan, Swaroopa Khedekar, V Prashant

The Woman's Health Clinic, a community-based service-cum-research clinic located at BDD Chawl offers services for minor ailments, gynaecological complaints, family planning needs etc. Routine health services include clinical examination, breast examination, cytology screening and contraception services. During the current year, gynaecology consultation was done at clinic for 106 women. Cervical cancer screening was done for 38 women. Services included Copper-T 380A insertions, condoms distribution and any gynaecological complaints. These consultations included women who came with menorrhagia, incomplete abortion, PCOS, irregular menstruation, post-menopausal bleeding, urinary tract infections, Copper- T users etc.

10.9 Genetic Research Centre

In-Charge : **Shailesh Pande**

Staff : Shiny Babu, H Gawde, D S Naik, Neha Minde

The Genetic Research Center provided testing and counseling services for couples presenting with infertility, recurrent pregnancy loss, IVF failures, women with conditions like bad obstetric history, primary ovarian insufficiency, pediatric/adult-onset genetic conditions. Pre-test and Post-test genetic counseling was done for 700 cases, karyotyping was carried out for 350 cases, FISH was carried out for 120 cases and molecular genetic testing was done in 250 cases.

10.10 National Center for Preclinical Reproductive and Genetic Toxicology

In-Charge : **V D Dighe**

Staff : S V Jadhav, Shilpa C Kerkar, Y N Kamble, P S Salunkhe, N B Shelar

The National Center for Pre-Clinical Reproductive and Genetic Toxicity has a mandate of research, services and capacity building. Services to various academic bodies and industries are being undertaken following Organization for Economic Co-operation and Development (OECD) guidelines and Good Laboratory Practices (GLP). Following research projects were undertaken in collaboration with academic institutions during 2024-2025:

1. Acute and subacute Toxicity of organo-selenium compound 3-# Diselenodipropionic acid (3-3 DSEPA) (*Funded by ACTREC, Mumbai)*
2. Evaluation of immunomodulatory and anti-cancer properties of Hydroxychavicol, a major constituent of Piper betel *(Funded by Institute of Chemical Technology, Mumbai)*
3. Preclinical study on efficacy, safety and toxicity and Swarna Prashan regimen as adjunct therapy in pediatric acute lymphoblastic leukemia *(Funded by the RARP-CCRAS, Mumbai)*
4. Developmental and Reproductive toxicity studies and 28-day repeated dose oral toxicity studies for Cap. PCOSnil in Rats. *(Funded by Acuere Biosciences Pvt. Ltd., Pune)*
5. Genotoxicity studies for Cap.PCOSNIL in rats *(Funded by Acuere Biosciences Pvt. Ltd., Pune)*

10.11 Hematology and Nutrition Outpatient Department

In-Charges : **R Gajbhiye, H Munshi, Suchitra Surve, N Wasekar (Hematology), M Bhadane (Nutrition)**

Staff : Anupriya Khedkar, Sakshi Gangurde, Trunali Barde, J Chaudhari, P Kale

Model Rural Health Research Unit (MRHRU), Vani, located in Dindori block of Nashik district, is actively contributing to rural public health through focused outpatient services. It serves as vital support system for tribal and rural population in and around Dindori block by offering free, specialized outpatient departments (OPDs), especially in the areas of haematology and nutrition. The Haematology Clinic at MRHRU Vani provides free consultation, diagnosis, and follow-up care for individuals suffering from blood-related disorders such as anaemia, sickle cell disease, and other haematological conditions. These disorders are common in tribal communities, often leading to chronic illnesses due to delayed diagnosis and limited treatment options. The clinic ensures that the patients receive accessible, quality care without financial burden. By offering regular services and disease monitoring, it helps in reducing complications and improving long-term health outcomes. Alongside, Nutrition Outpatient Department addresses the persistent issue of malnutrition among children in the region. It conducts growth assessments, nutrition counselling, and clinical evaluation of children, with a special focus on those identified as moderately or severely undernourished. Significantly, the program includes capacity-building of Anganwadi workers, who are trained in accurate anthropometric measurement techniques (such as height, weight, MUAC). This ensures timely identification of malnourished children within the community and referral to MRHRU Vani for further care. Both OPDs function with community-oriented approach, providing ongoing healthcare support to patients from remote and underserved rural areas. Services offered not only fill major gaps in rural health infrastructure but also align with broader public health goals by

promoting early diagnosis, prevention, and awareness. In reporting year, 105 patients sought care at these OPDs.

10.12 Health Technology Assessment Resource Hub

In-Charge : **Beena Joshi**

Staff : Pooja Gund, A Padhan, Tejal Varekar, Nikita Phadtare, N Mungekar

HTA Resource Hub has been established with support from HTAIn DHR since 2018. Its main objectives are to conduct HTA studies, sensitize state and municipal stakeholders on HTA and facilitate its institutionalization. The HTA Resource Hub oversees 3 states namely Maharashtra, Goa and Madhya Pradesh and 1 union territory i.e. Dadra Nagar Haveli. It has a role in capacity building and dissemination of HTA results for suitable adaptation by the states.

10.13 Experimental Animal Facility

In-Charge : **D K Das**

Staff : S M Metkari, P R Chavan, G C Patil, R S Sandis, S B Bavdane, M V Mali, S S Chavan, S Kadam, KV Kadam, P K Shingare, R G Rane, M S Qureshi, R S Marchande, A Anglekar, B K Koli, Y B Shinde, S Gode, S Ram, S Krishnan, R Kumar, A Musale, P Adepu, S S Mane, A Kumar

The Institute has well maintained animal facility distributed over three floors and houses different species of laboratory animals viz mice, rats, rabbits, bonnet monkeys and marmosets. The animals are maintained and well taken care of by qualified and trained staff everyday including weekends and holidays. The details of animals bred and supplied during the year are given in Table 1.

Table 1: Animals bred and supplied after due approval of IAEC during April 2024 - March 2025.

Species	**Animal Bred**	**Animals Supplied**
Swiss Mice	796	203
Balb/c Mice	1004	512
C57BL/6	1049	448
DBA2/J	233	NIL
FVB-NJ	785	61
GFP- BL/6	248	NIL
GFP- FVB	588	NIL
Transgenic Mice WB/Rej/Kit	538	NIL
Transgenic Mice C57BL/6/ Kit/J	456	NIL
Transgenic Mice Mgat1 -/-	37	NIL
Transgenic C57BL/6-Tg (TRAMP)	260	80
Transgenic Mice B6:CBA Tg- Oct4	691	90
Wistar rats	1534	1145
Rabbits	NIL	NIL
Bonnet Monkeys 7 (In house)	NIL	NIL
Marmosets	10	20

10.14 Institutional Animal Ethics Committee

In-Charge : **S M Metkari** *(Member Secretary)*

Staff : S Petkar

The Institute is registered for breeding and experimentation on laboratory rodents including non-human-primates with Committee for the Control and Supervision of Experiments on Animals (CCSEA), Department of Animal Husbandry and Dairying; Ministry of Fisheries, Animal Husbandry and Dairying, Government of India (vide Registration No. 78/GO/ReBi/SL/99/CPCSEA dated 11th March 1999) and this registration is renewed periodically. The Institutional Animal Ethics Committee (IAEC) members including CPCSEA Nominees critically review, approve and monitor research protocols on the laboratory animals. The IAEC also conducts inspection of animal house facility periodically to ensure animal welfare activities being stringently followed before, during and after animal experimentation. The institute upholds the principals of 3R's - Reduction, Refinement and Replacement principal for humane use of experimental animals in the scientific research. During the year 2024-25, two IAEC meetings were convened on 5th July 2024 and 11th February 2025 respectively. Total 24 animal study protocols were reviewed and approved by the IAEC.

10.15 NIRRCH Ethics Committee for Clinical Studies (2024-2025)

In-Charge : **V Bhor** *(Member Secretary)*

Staff : Zakia Ansari, A Hankare, S Toshatwad

The ICMR-NIRRCH Ethics Committee for Clinical Studies or Institutional Ethics Committee (IEC), comprises of a total of four affiliated and ten non-affiliated members with Prof. Shubhada Chiplunkar as the chairperson, Dr. Vikrant M. Bhor as Member Secretary and Dr. Bhakti Pathak as Joint Member Secretary. During the reporting period, Dr. Sumitra Venkatesh (Paediatrician, B J Wadia Hospital for Children), Dr. Smitha Nair (Social Scientist, Tata Institute of Social Sciences), Mrs. Reema Dikshit (community representative member) committee as non-affiliated members while Dr. Vainav Patel joined as an affiliated member, on account of the completion of the tenure of a few previous members. The IEC secretariat was staffed by Mrs. Zakia Ansari, Mr. Ananda Hankare and Mr. Shivraj Toshatwad. The IEC held six full board meetings and reviewed various projects throughout the reporting year. A total of 26 new proposals, 18 amendments to the proposals, 4 revisions, 79 continuing review reports and 19 completion reports underwent full board evaluation. One project was deemed to be exempt from the review process and 3 new projects underwent expedited review. Additionally, 20 revised proposals and 4 amendments were reviewed through circulation among the IEC members. Overall, the IEC approved 39 new proposals and 33 amendments during the reporting period. Furthermore, a revised version of the IEC Standard Operating Procedures (SOP) Version 7.0, dated November 8, 2024, was formulated after extensive review of the existing SOPs to ensure that it is comprehensive, effective, and aligned with the ICMR bioethics guidelines. In addition to the above, as part of its mandate for continued training of its members, the IEC also conducted a Good Clinical Practices (GCP) workshop on March 27, 2025.

10.16 Biosafety Committee

In-Charge : **D K Das** *(Member Secretary)*

Staff : Kiran Munne, Antara Banerjee, S Pande, P Kuppusamy, Shaini Joseph

The research activities using genetically engineered (GE) organisms, hazardous microorganisms, or cells and their products are governed by the rules, established under the Environment (Protection) Act, 1986 by the Ministry of Environment, Forest and Climate Change, Government of India. This rule mandates institutions in handling such activities to establish an Institutional Biosafety Committee (IBSC) that serves as a nodal point for implementing the biosafety regulatory framework within the Institution. In compliance with this rules, ICMR-NIRRCH has established an Institutional Biosafety Committee (IBSC) to oversee all research activities involving use of genetically engineered (GE) organisms, hazardous microorganisms, or cells within the Institute.

10.17 Dr GM Phadke Memorial Library and Information Centre

In-Charge : **Prabhjeet Kaur**

Staff : Simmy Saji, Priya Menon, V Shinde, A Gode

Dr GM Phadke Memorial Library and Information Centre is a specialized resource hub dedicated to reproductive health care and allied biomedical sciences. It houses an exclusive collection of books, manuals, journals, and reports covering diverse subjects such as molecular biology, immunology, and cell biology. To support the research needs of the Institute's staff and students, the library subscribes to 37 online journals focused on reproductive and child health, accessible through the institutional intranet. Beyond serving internal users, the library also extends its services to researchers and visitors from other institutions. It plays a vital role in compiling monthly, quarterly, and annual reports that highlight the Institute's significant achievements and publications. The library staff actively contributes to the digital presence of the Institute by updating its website and managing social media platforms including Twitter, Facebook, LinkedIn, Instagram, and YouTube. Additionally, the library coordinates educational visits for students and staff from external institutions interested in learning about the Institute's research and facilities. To further support users, the library offers photocopying and printing services, having provided 26,236 photocopies during the reporting year.

10.18 Communication Cell

In-Charges : **Susan Thomas, Prabhjeet Kaur**

Staff : Kumari Nishi, R K Prusty, H Munshi, Antara Banerjee, Bhavya M K, Neha Minde, Priya Menon

The Communication Cell actively promoted the Institute's health research initiatives through targeted communication campaigns across its social media platforms. During the reporting year, the Cell facilitated the dissemination of key research highlights—including findings on declining male reproductive health and institutional support for children with atypical genitalia and disorders of sex development (DSD)—in leading newspapers and popular dailies. The institute staff and students were encouraged to participate in health observance days through interactive

activities such as skits, reel competitions, and invited talks. To further broaden outreach, the Cell regularly created and shared infographics on platforms including Twitter, Instagram, Facebook and LinkedIn as part of various health awareness campaigns. The Cell also enhanced the visibility of government campaigns on public health initiatives through the dissemination and amplification of official messages via retweets and reposts across social media platforms. Activities conducted at the Institute were regularly featured on social media to spread awareness among the research community.

10.19 Core Facilities

10.19.1 Flow Cytometer and DNA Sequencing

In-Charge : **Srabani Mukherjee**

Staff : Sushma Khavale, Gayatri Shinde, Nanda Joshi

These facilities provide services for institutional projects an d inter-institutional projects. During the reporting year, 1200 samples were processed for flow cytometry (BD FACS Aria SORP, Cytek Aurora) and DNA sequencing was performed for 5319 samples.

10.19.2 Confocal Microscopy Facility

In-Charge : **Dipty Singh**

Staff : Shobha Sonawane, Reshma Gaonkar

The facility is equipped with Olympus FV3000 confocal microscope and provides support to staff and students of the Institute and outside institution for colocalization, 3D imaging tiling and stitching, FRET on LASER confocal system. During the reporting period, 52 users, 1050 LASER hours, both from the Institute and outside Institutes used the facility.

10.19.3 Histology Work Station

In-Charge : **V D Dighe**

Staff : Pravin Salunke, Manish Ghosalkar

The histology workstation in the National Center for Preclinical Reproductive and Genetic Toxicology is a state of art facility equipped with an automatic tissue processor, automatic slide stainer, tissue embedder, microtome, and automatic cover slipper. This central facility is utilized by researchers in the institute as well as other academic and private institutions. During the reporting year, 1085 tissue samples were processed, embedded and paraffin blocks were prepared. 5228 tissue blocks were sectioned, and 1259 slides were stained using Haematoxylin and eosin stating.

10.19.4 Infectious FACS Core

In-Charge : **V Patel**

Staff : Tejaswini Pandey, Sapna Yadav

The facility consisting of two analyzers and one sorter have been integrated into the IRISE portal and over the last year, this facility has helped researchers as the institute and other organizations resulting in seven PubMed indexed research articles.

PUBLICATIONS

11. PUBLICATIONS

11.1 Peer Reviewed Publications

1. Agrawal S, Kasarpalkar N, Ghosh S, Paradkar G, Daund V, Bhowmick S, Chitalia V, Rao P, Sankpal A, Kalsurkar V, Shah K, Khan S, Patil A, Jagtap D, Khandkar O, Kaneria M, Mahale SD, Sachdeva G, Bhor VM, Shastri J, Patel V. Integrated viral and immune monitoring in a prospective COVID-19 cohort from India. ***J Leukoc Biol***. 2024 Sep 2:qiae187. doi: 10.1093/jleuko/qiae187. Epub ahead of print. PMID: 39219468. **[IF: 3.6]**

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11.2 Papers / Posters Presented at Conference / Symposia

11.2.1 International

1. **International Papillomavirus Conference (IPVC), Edinburgh, UK, December 11, 2024**
   - **Munne K**. Implementation of cervical cancer screening during covid-19 pandemic in urban and tribal areas of Maharashtra, India: Challenges encountered and solutions implemented.

11.2.2 National

1. **SBC (I) Mumbai Chapter and GATC Lite Western Region Meeting, ICMR-NIRRCH, Mumbai, October 2, 2024**
   - **Batgire J**. Gut microbiota derived metabolites from pregnant women with bad obstetric history exhibit altered macrophage polarization.
   - **Chandel N**. Changes in gut microbiome composition indicates susceptibility to bloodstream infection in a child with acute lymphoblastic leukemia: A case report.

- **Devadiga P**. Dysbiotic gut microbiome is associated with altered gut homing of T lymphocyte subsets in people living with HIV.
- **Pawar R**. Immunogenic potential of *Gardnerella vaginalis* membrane vesicle proteins predicted by computational analysis.

2. **The Cytometry Society of India, 16th Annual Meeting & Workshops, ACTREC, Navi Mumbai, October 17-20, 2024**
   - **Batgire J**. Association between Innate Immune Modulation and Gut Microbiome Dynamics in Early Pregnancy
   - **Bhowmick S**. Modulation of HIV-1 pathogenesis by latent TB infection: Immunological correlates.
   - **Devadiga P**. Altered gut microbiome composition correlates with reduced frequency of integrin α4ß7+ B cells and increased immune activation in HIV+ individuals
   - **Kaginkar S**. In depth immunological and viral analysis of HIV-1C putative reservoirs in an Indian cohort.
   - **Mohite N**. Immune monitoring in survivors of the 2023 Nipah outbreak in Kerala, India
   - **Palav H**. Systemic and HCMV specific cellular immune signatures associated with pregnancy outcomes and congenital transmission: a prospective cohort study

3. **22nd Annual meeting of the AE-PCOS society, Queenstown, New Zealand, November 7-9, 2024**
   - **Naigaonkar A**. Metabolic coupling between oocyte and granulosa cells: nexus unravelled in women with PCOS.

4. **International Conference on Progress in Mitochondrial Research and Therapy, and 10th Annual Conference of The Society for Mitochondria Research (SMRM), SDM University, Dharwad, November 11-12, 2024**
   - Shukla P. New insights into the role of mitochondria in the pathophysiology of PCOS

5. **International Conference on Reproductive Sciences and Molecular Medicine: Innovations in Therapeutics and Technologies (ICRSMM-2024) 41st Annual Meet of Society for Reproductive Biology and Comparative Endocrinology (SRBCE), Delhi, November 15-17, 2024**
   - **Bhingardeve S**. Epigenetic regulation of miRNA by DNA methylation alters Actin Cytoskeleton pathway in PCOS.
   - **D'souza S**. Investigating the role of endocannabinoid system in placental development: preliminary findings.
   - **Gaonkar R**. Investigating the effect of L-NAME induced hypertension on male fertility.
   - **Khade K**. Elucidating role of gut microbiota composition in pathophysiology of polycystic ovary syndrome.
   - **Kuppusamy P**. Testicular volume and clinical correlates of hypothalamic–pituitary–gonadal functions in Idiopathic infertile men: A cohort study.

6. **16th Annual Meeting of Proteomics Society of India and International Conference on OMICS in Decoding Biological Research, 2024, NCL, Pune, November 21-23, 2024**
   - **Panchal D**. Decoding metabolic shifts from pre-ovulation to ovulation: insights from a rat model.

7. **20th National Research Scholars Meet, Advance Center for Treatment, Research, and Education in Cancer (ACTREC), Navi Mumbai, ACTREC, Navi Mumbai, December 11-12, 2024**
   - **Panchal D**. Understanding sperm chemotaxis with a novel microfluidics device.

8. **35th Annual Meeting of the Indian Society for Indian Society for the Study of Reproduction and Fertility (ISSRF-2025) and International Conference on Reproductive Biomedicine: Integrating Basic Biological and Applied Research into Clinical Practice for Human Welfare, Jaipur, Rajasthan, February 14-16, 2025**
   - **Bhonde G**. Gut Microbiome composition is associated with fecal Short-Chain Fatty Acid profiles of CMV PCR-Positive and Negative Pregnant Women with Bad Obstetric History.
   - **Samant M**. Exploring genetic variants in PCOS: whole exome sequencing analysis.
   - **Nishi K**. Investigating the effects of L-NAME induced hypertension on the reproductive system of male rats
   - **Panchal D**. Decoding metabolomic shifts from pre-ovulation to ovulation.

9. **34th Annual Meeting of Indian Society for the Study of Reproduction and Fertility (ISSRF), Indian Institute of Chemical Technology (IICT), Hyderabad, India, February 23, 2024**
   - **Tharayil SP**. Mitochondrial oxidative stress, dysfunction, and rare mitochondrial DNA variants: novel contributors in the pathophysiology of PCOS.

10. **International Symposium on Health Technology Assessment (ISHTA) 2025, New Delhi, March 8-9, 2025**
    - **Joshi B**. OOPE incurred by couples seeking infertility services at tertiary level facilities in India.
    - **Joshi B**. Out-of-pocket expenditure experience by couples seeking IVF services at tertiary care facilities in India.
    - **Joshi B**. Health system costing of invitro-fertilisation (IVF) services in India.

11. **69th National Annual Conference of Indian Public Health Association IPHCON, 2025, Jawaharlal Nehru Medical College (KAHER), Belagavi, March 21, 2025**
    - **Joshi B**. Health Technology Assessment for evidence based decision making.

12. **Indian Society for Extracellular Vesicles (InSEV) Annual Meet, AIIMS New Delhi, March 24-26, 2025**
    - **Pawar R**. *Gardnerella vaginalis* membrane vesicles disrupt biofilm formation by *Lactobacillus gasseri*.

11.3 Newsletter:

Role of Health Technology Assessment to aid Evidence Based Decision Making for procurement of New Technologies in Public Health System published in Indian Public Health Maharashtra Association- July-Sept 2024 Issue.

CAPACITY BUILDING

12. CAPACITY BUILDING

12.1 Workshop / Training Program Organized

- **Bhavya M K**. Training Sessions for Medical Officers and Community Health Officers (CHOs) on TB Management, Dadra Nagar Haveli, October 5, 2024
- **Bhavya M K**. Launch of IEC Material & TB Day Celebration at CHC Rakholi, Dadra Nagar Haveli March 24, 2025
- **Bhor VM, Modi D**. SBC (I) Mumbai Chapter and GATC West Lite Meeting on the Theme Genes, Genetics and Genomics, ICMR-NIRRCH, October 2, 2024
- **Bhor VM**. Good Clinical Practices Workshop for Institutional Ethics Committee Members at ICMR-NIRRCH, March 27, 2025
- **Joshi B, NIRRCH HTA Team**. Sensitization Workshop, Grant Medical College, Mumbai, May 22, 2024
- **Joshi B, Gurav Y, NIRRCH HTA Team**. Sensitization Meeting-Brainstorming on Indigenous HPV Vaccine Program Introduction Strategy in Maharashtra and Identifying New Topics for HTA at State Health Society Resource Centre (SHSRC), Pune, June 6, 2024
- **Joshi B, NIRRCH HTA Team**. Workshop on Health System Costing, Grant Medical College, Mumbai, September 3-4, 2024
- **Joshi B, NIRRCH HTA Team**. Sensitization Meeting on Health Technology Assessment for Evidence Based Decision Making in India at CHC Moti Daman, Dadra & Nagar Haveli and Daman Diu, October 4, 2024
- **Joshi B, NIRRCH HTA Team**. Sensitization Meeting on Health Technology Assessment & Workshop on RMNCH+A Planning and Management for District RCH Officers, Govt of Maharashtra at State Public Health Training Institute, Nagpur, October 8, 2024
- **Joshi B, Patil A, Tandon D, Kokate P, Banage S, Akula A, Kendre S, Rathod A, Lambade S**. XXXIIIrd P.K. Devi Oration by Prof. Dr. Vidita Vaidya on Imprints of Early Adversity: How the Brain and Body Keep Score Jointly Organized by ICMR-NIRRCH, Mumbai and Kasturba Health Society -Medical Research Centre, Mumbai, November 11, 2024
- **Joshi B, NIRRCH HTA Team**. Sensitization Meeting on Health Technology Assessment for Evidence Based Decision Making in India at Directorate Health Services and Goa Medical College, Campal, Panaji Goa, January 17, 2025
- **Kulkarni R, Mishra SK**. Sensitization of Health Service Providers as a Part of Preeclampsia Project at SDH Dahanu at Sub District Hospital Dahanu, June 5, 2024
- **Kulkarni R, Mishra SK**. Sensitization of Health Service Providers as a Part of Preeclampsia Project at SDH Kasa at Sub District Hospital Kasa, June 6, 2024
- **Kulkarni R, Surve S**. Training of Health Service Providers (MOs, THOs & MS) on Maternal and Perinatal Death Surveillance Response and Action, Zilla Parishad Palghar, September 13, 2024
- **Kulkarni R, Surve S**. Training of Anganwadi Workers of Ganjad on Infant and Young Child Feeding (IYCF) Practices, Sub District Hospital, Dahanu, September 14, 2024
- **Kulkarni R, Munne K**. Workshop on Grant Writing and Proposal Development, Grant Medical College & JJ Hospital, November 22, 2024
- **Kulkarni R, Munne K**. Training on Spirometer for Population Based Health Survey at MRHRU Dahanu, January 22, 2025.

- **Mukherjee S, Patel V, Bhor V**. Workshop on High Dimensional Data Driven Discovery by TCS (The Cytometry Society of India) at ICMR-NIRRCH, Mumbai, October 17-18, 2024
- **Munne K, Mishra SK**. ELISA Training on Chikungunya for Vasai-Virar Mahanagarpalika Hospital's Lab Technicians at MRHRU Dahanu, August 19, 2024
- **Munne K**. Postgraduates and Interns Exposure Visit from Pt. JNM Medical College Raipur Chhattisgarh at NIRRCH, Mumbai, February 10, 2025
- **Pande S**. Application of Medical Genetics in Reproductive and Child Health, ICMR-NIRRCH, Mumbai, June 3-28, 2024
- **Pande S**. CME on Haemoglobinopathies at ICMR-NIRRCH, Mumbai, June 22-23, 2024
- **Patel V**. On-Site Training of Lab Personnel at ICMR-NIRRCH, Mumbai for Operationalization of COBAS 6800 to Perform HIV-1 Viral Load Testing Under NACP at ICMR-NIRRCH, Mumbai, May 8-10, 2024
- **Patel V, Sakpal G**. Training Program for CMI Sites as a Part of Hands-on Laboratory Training for Phase III Clinical Trial of Dengiall Vaccine for Trial Site Laboratories, NIV, Pune, August 1, 2024
- **Patel V, Bhor VM, Mukherjee S, Tembhare P**. 16th Annual Meeting and Workshop of the Cytometry Society, India, ICMR-NIRRCH, October 17-18, 2024
- **Patil A, Tandon D, Limaye M, Murtadak V, Kokate P, Banage S, Akula A, Rathod A, Lambade S, Kerkar A, Walmiki R**. Continuous Medical Education (CME) and Stakeholder Consultation of Recommendations for the Diagnosis and Multidisciplinary Management of Polycystic Ovary Syndrome (PCOS) in the Indian Healthcare System, Gowardhan Ecovillage Wada, Palghar, June 21, 2024.
- **Patil A, Tandon D, Murtadik V, Kokate P, Kale S, Banage S, Akula A, Kharat S, Hussain A, Kendre S, Rathod A, Lambade S**. Orientation Programme for 4th year Basic BSc 28 Nursing Students from P. D. Hinduja National Hospital and Medical Research Centre, College of Nursing, ICMR-NIRRCH, November 26, 2024
- **Sachdeva G, Mukherjee S, Modi D, Banerjee A**. Opening Gates: Conception Foundations and Exploring Contraceptive Innovations, Society for the Study of Reproduction / Bill and Melinda Gates Foundation (SSR/BMGF), ICMR-NIRRCH, Mumbai, December 2-6, 2024
- **Singh D**. Histopathology & Immunofluorescence Technique & Confocal Microscopy SERB Scientific Social Responsibility (SSR), ICMR-NIRRCH, August 29, 2024
- **Tandon D, Khan S, Baing G, Kokate P, Akula A, Rathod A, Lambade S**. Training on the Concepts of Qualitative Data Collection for Menstrual Hygiene Project at ICMR-NIRRCH, November 21, 2024
- **Tandon D, Kokate P, Khan H, Banage S, Akula A, Kendre S, Rathod A, Lambade S**. Lecture on Adoption: Understanding the Process at Bala Asha Trust, a CARA-Recognized Adoption Centre, ICMR-NIRRCH, November 29, 2024
- **Tandon D, Kulkarni R, Kokate P, Banage S, Akula A, Hussain A, Kendre S, Rathod A, Lambade S**. Basic Workshop on Qualitative Data Analysis with Focus on RAPID Analysis for Implementation Research for Menstrual Hygiene Project, ICMR-NIRRCH, December 12-13, 2024.
- **Thomas S, Pathak B**. DHR Sponsored Training Course entitled 'Human Disease Models: Approaches, Advances and Applications', ICMR-NIRRCH, May 6-31, 2024
- **Thomas S**. ICMR-DHR Funded Workshop Entitled Application of AI/ML in Disease Informatics, ICMR-NIRRCH, June 4-7, 2024

12.2 Community Outreach Activities

- **Bhavya M K**. Awareness Session on TB in Tighra Ram Mandir, April 1, 2024
- **Bhavya M K**. Awareness Session on TB in Mahendra Bhai Ki Chawl Naroli, Dadra Nagar Haveli, April 10, 2024
- **Bhavya M K**. TB Awareness Session and Screening Camps at Filatex Ltd, Dadra, Dadra Nagar Haveli, July 6, 2024
- **Bhavya M K**. TB Awareness and Screening Camps at Sub Jail, Silvassa, August 23, 2024
- **Bhavya M K**. TB Awareness and Screening Camps at Sub Jail, Silvassa, February 15, 2025
- **Bhavya M K**. TB Awareness and Screening Camps in Neelkamal Industries, Dadra Nagar Haveli, March 25, 2025
- **Bhavya M K**. TB Awareness and Screening Camps, Govt High School Dapada, Dadra Nagar Haveli, March 26, 2025
- **Bhavya M K**. TB Awareness and Screening Camps, Jenstar, Rudana, Dadra Nagar Haveli, March 31, 2025
- **Gajbhiye R**. World Thalassemia Day Celebration at PHC Borgaon, Nashik, May 8, 2024
- **Gajbhiye R**. World Sickle Cell Anaemia Day: Awareness and Screening Camp in Ahivantwadi, Nashik, June 9, 2024
- **Gajbhiye R**. Awareness Session on Biosafety and Waste Segregation for Health Workers, MTS, Lab Technicians and Research Fellows, September 20, 2024
- **Gajbhiye R**. MPOX Awareness Session at Ashram School Paregaon, Dindori, Nashik, September 20, 2024
- **Gajbhiye R**. MPOX Awareness Session for ASHAs and Health Workers at Model Rural Health Research Unit, Vani, Nashik, September 30, 2024
- **Gajbhiye R**. MRHRU Vani Team provided 200 Snake Anti-Venom Vials to Rural Hospital Vani, Maharashtra, to Support Enhanced Snakebite Management and Treatment, January 28, 2025
- **Joseph SM**. Awareness Session for Students from PD Hinduja College of Nursing, October 29, 2024
- **Joseph SM**. Awareness Session on Genetic Diseases at KMS Dr. Shirodkar Special School, Mumbai, December 9, 2024
- **Joseph SM**. Ummeed Child Development Center, Lower Parel, July 23 and December 17, 2024
- **Joseph SM**. Awareness Session at Rugna Mitra Sneh Sanwad, January 19, 2025
- **Joseph SM**. Awareness Session for M.Sc. Nursing students from the Institute of Nursing Education, JJ Hospital, March 25, 2025
- **Kulkarni R**. Pediatric Screening Camps Targeting Children Aged 6 months to 6 years Undertaken at Anganwadi Centers under Amgaon PHC in Talasari Block, Dahanu (Palghar), June 13, 2024
- **Kulkarni R**. IAP Palghar Organized Free Anemia OPD for Sickle Cell and Thalassemia Patients at Sub-District Hospital, Dahanu, July 28, 2024
- **Kulkarni R**. An Outreach Camp under Phase II of the IYCF project, initiated in October 2024 and Currently Ongoing was Conducted to Promote Appropriate Infant and Young Child Feeding (IYCF) Practices, September 14, 2024
- **Kumari N**. Arranged a Visit to ICMR-NIRRCH for 75 students of Ahilya Vidya Mandir, Secondary School, Abhyuday Nagar, Mumbai, on the Occasion of National Science Day, February 24, 2025
- **Kumari N**. National Science Day, March 7, 2025

- **Munne K**. Child Health Clinic Team Celebrated International Day of Yoga with 300 students and Teachers at Shivaji Vidyalay, Kalachowki with "Yog Asana" Session to Promote Physical and Mental Well-Being and Health & Hygiene Practices Awareness Essential for Monsoon, June 21, 2024
- **Munne K**. Child Health Clinic Team Conducted an Awareness Talk at Shivaji Sangh Anganwadi, Kalachowki. They Demonstrated Breastfeeding Techniques, and Spoke About Its Importance and Dietary Intake During Breastfeeding, August 2, 2024
- **Savardekar L**. IDY Celebrations by Reproductive and Bone Health Unit, ICMR-NIRRCH at Padmashaali Yuwak Sangh Hall, Naigaon on "Integrated Approach for a Better Musculoskeletal Health: Preventive strategies" with 49 Attendees, June 18, 2024
- **Savardekar L**. IDY Celebrations Organized by Reproductive and Bone Health Unit, ICMR-NIRRCH at Padmashaali Yuwak Sangh Hall, Naigaon on "Addressing Nutrition Needs Beyond 50s" with 55 Attendees, June 19, 2024
- **Savardekar L**. World Breastfeeding Week Celebrations, August 1-7, 2024, Three Focus Group Discussions Were Organized as part of CCRAS-ICMR Project at Thane, August 1, 2024
- **Savardekar L**. World Breastfeeding Week Celebrations, August 1-7, 2024 One Focus Group Discussion Was Organised as Part of CCRAS-ICMR project at Kalyan, August 3, 2024
- **Savardekar L**. World Breastfeeding Week Was Celebrated at Naigaon Maternity Home with 30 Women Attendees with Lectures on Galactagogues, its Ayurvedic Perspectives, Guidance on Breast Feeding Positions, Impact of Lactation on Bone Health, August 6, 2024
- **Savardekar L**. 'Obesity in Adolescent Programme' at Prabhavati Kulkarni High School, 100 Children from Secondary School Attended. Staff took Height Weight and `Plotting Your BMI on Indian Standards Chart` Was A Home Activity for All Children, August 14, 2024
- **Savardekar L**. Bone Health Clinic Celebrated World Osteoporosis Day 2024 at Naigaon & Prabhadevi Maternity Homes, USG Calcaneum Done in 80 pregnant Women and Also Given Counselling On Diet and Bone Building Measures, October 29, 2024

12.3 Meetings / Conferences / Seminars / Workshops Attended

- **Banerjee A**. Invited Scientific Expert by the Department of Life Sciences, Sophia College for review of dissertation thesis of MSc students, Khandala, August 2-3, 2024
- **Banerjee A**. Invited Judge for Poster Presentation for National Conference 'A blueprint for planetary sustainability at 2040', Jai Hind College, Mumbai, March 1, 2025
- **Banerjee A**. Invited Member of Board of Studies, St Xavier`s College, Mumbai, March 24, 2025
- **Bhavya MK**. Artificial Intelligence in Public Health, School of Health System, Tata Institute of Social Sciences, Mumbai, April 22-23, 2024
- **Bhavya MK**. Strategic Communication for Public Health in the 21st century, Harvard T.H. Chan School of Public Health, India Researcher Centre, Mumbai, June 6-7, 2024
- **Bhavya MK**. ICMR Scientists' Observership, St.John's Medical College, Bengaluru, July 8-21, 2024
- **Bhavya MK**. Young Scientist Induction Program, IIM Vishakapatanam, September 30, 2024 to October 26, 2024
- **Bhavya MK**. India Innovation Summit -Pioneering Solutions to End TB, New Delhi, March 18-19, 2025
- **Bhavya MK**. Accomplishing the Child Survival Agenda in India, Harvard T.H. Chan School of Public Health -India Research Center, Mumbai, March 20, 2025

- **Bhor V**. FERCAP-FERCI Workshop on Ethics Committee Management; Current Advances, Online Workshop, July 20, 2024
- **Bhor V**. Satellite Meeting of the Genomics Analysis and Technology Conference (GATC, 2024) for the Eastern Region, Kolkata, August 24-25, 2024
- **D'Souza S**. International Conference on Reproductive Sciences and Molecular Medicine: Innovations in Therapeutics and Technologies (ICRSMM-2024), 41st Annual Meet of Society for Reproductive Biology and Comparative Endocrinology (SRBCE), Delhi, November 15-17, 2024
- **Das DK**. International Conference on Progress in Mitochondrial Research and Therapy (Annual Conference of Society of Mitochondrial Research and Medicine), SDM University, Dharwad, November 11-12, 2024
- **Das DK**. 49th Annual Meeting of Indian Society of Human Genetics and International Conclave on Neurogenetics, NIMHANS, Bengaluru, January 20-22, 2025
- **Itta KC**. 50th American Society for Histocompatibility and Immunogenetics, Annual Meeting, Anaheim, California, USA, October 21-25, 2024
- **Gajbhiye RK**. MRHRU Conclave, New Delhi, April 16, 2024
- **Gajbhiye RK**. Future Directions in Endometriosis and Adenomyosis Research Organized by the Endometriosis and Adenomyosis Association of Sri Lanka, Colombo, Sri Lanka, July 29-30, 2024
- **Gajbhiye RK**. Expert Group Meeting to Review the Draft Proposal for Standing Finance Committee (SFC) for National Programme for Prevention & Control of Snakebite Envenoming in India (NPSE), NCDC New Delhi, August 2, 2024
- **Gajbhiye RK**. DHR ICMR Health Summit, New Delhi, November 14, 2024
- **Gaonkar R**. International Conference on Reproductive Sciences and Molecular Medicine: Innovations in Therapeutics and Technologies (ICRSMM-2024), 41st Annual Meet of Society for Reproductive Biology and Comparative Endocrinology (SRBCE), Delhi, November 15 -17, 2024
- **Jagtap D**. Pioneering the Future of Healthcare and Diagnostics Using 4D Omics, Department of Bioscience and Bioengineering, IIT-Bombay, November 12-13, 2024
- **Jagtap D**. International Conference on Metabolomics and Lipidomics, Department of Chemical Engineering, IIT Bombay, February 24-25, 2025
- **Joshi B, NIRRCH HTA Team**. Economic Evaluation of Health Care Programs, IIPH, Delhi, November 17-22, 2024
- **Joshi B, NIRRCH HTA Team**. Health Technology Assessment in India Conclave, India Habitat Centre, Delhi, December 23, 2024
- **Joshi B, NIRRCH HTA Team**. State Sensitization Workshop on Health Technology Assessment, AIIMS Bhopal, January 13, 2025
- **Joshi B, NIRRCH HTA Team**. Workshop on Health Technology Assessment for Evidence-Based Decision-Making in India, TMH, Pune, February 14-15, 2025
- **Joshi B, NIRRCH HTA Team**. Workshop on Modelling in HTA, ICMR-NIV Pune, February 17-21, 2025
- **Joshi B, NIRRCH HTA Team**. International Symposium on Health Technology Assessment (ISHTA) 2025, Bharat Mandapam, Delhi, March 8-9, 2025
- **Joshi B, NIRRCH HTA Team.** NIRRCH. IPHCON, 2025, Jawaharlal Nehru Medical College (KAHER), Belagavi, March 21-23, 2025
- **Khade K**. SERB High-End Workshop Karyashala National Workshop on Human Metagenomic Sequencing Data Analysis: Emphasis on Health and Disease, BRIC-National Institute of Biomedical Genomics, Kalyani, West Bengal, India, July 22-29, 2024

- **Khambata K**. Genomics Analytics and Technologies (GATC) and Meeting of Society of Biological Chemists, Mumbai, October 2, 2024
- **Khambata K**. 41st Annual Meeting of SRBCE and International Conference on Reproductive Sciences and Molecular Medicine, New Delhi, November 15-17, 2024
- **Kokate P**. 5th Anniversary Celebration of Science and Heritage Research Initiative (SHRI), Prithvi Bhavan, New Delhi, December 16, 2024
- **Kulkarni R**. MRHRU Conclave, Vanijya Bhavan, New Delhi, April 16, 2024
- **Kulkarni R**. Continuing Medical Education Event for Consensus Opinion on the "PCOS" Project, Wada, Palghar, June 21, 2024
- **Kulkarni R**. Research Meeting with Nodal Officer & Staff of Community Medicine Department of Grant Government Medical College, Mumbai, July 5, 2024
- **Kulkarni R**. Meeting with District Health Officials for in Depth Discussion on Implementation Research Proposal on Anemia, Zilha Parishad Palghar, August 8, 2024
- **Kulkarni R**. Dissemination Meeting of ICMR Funded New Born Screening Project and Release of IEC Materials for Sickle Cell Disease, Dahanu, August 23, 2024
- **Kulkarni R**. Meeting on Population-based Health Survey Project Development, Online, September 9, 2024
- **Kulkarni R**. Meeting with District Health Officials on Formation of Technical Support Unit (TSU) under the Maternal and Perinatal Death Surveillance and Response (MPDSR) project, Online, November 7, 2024
- **Kulkarni R**. DHR-ICMR Health Research Excellence Summit 2024, Delhi, November 14, 2024
- **Kulkarni R**. Training on ODK App for Population-Based Survey by DHR, Online, December 2, 2024
- **Kulkarni R**. Workshop on Anemia Project Tool Development, New Delhi, December 3-4, 2024
- **Kulkarni R**. Review Meeting under the Chairmanship of Secretory, DHR & DG-ICMR on Progress of Population Based Survey Study with MRHRU Sites, Online, December 16, 2024
- **Kulkarni R**. Routine Meeting with Nodal Officers and Scientists for Population Based Survey by DHR, Online, December 30, 2024
- **Kulkarni R**. Meeting on Maternal and Perinatal Death Surveillance and Response (MPDSR), Online, January 20, 2025
- **Kulkarni R**. Maternal and Perinatal Death Surveillance and Response Project Discussion Meeting held with District Health Officials, Online, February 6, 2025
- **Kulkarni R**. Eighth L-RAC Meeting of MRHRU Dahanu, February 28, 2025
- **Kulkarni R**. Project Review Committee Meeting of Preeclampsia Project under PM-ABHIM Scheme, Online, March 6, 2025
- **Kulkarni R**. Workshop to Develop Costing Component of ICMR National Health Research Priority Projects, Online, March 14-15, 2024
- **Kulkarni R**. Project Review Committee Meeting of Maternal and Perinatal Death Surveillance and Response Project, Online, March 21, 2025
- **Kumari M**. Workshop on Metabolomics, Center for Systems Biology and Molecular Medicine, Yenepoya Research Centre, Yenepoya, Mangalore, September 3-5, 2024
- **Kumari M**. National Symposium on Mass Spectrometry Based Lipidomics, BRIC-RGCB, Thiruvanathapuram, Kerala, India, February 20-22, 2025
- **Kumari N**. Work and Industry Neutral Growth Skills, a Capacity-Building Workshop Women in Scientific Domain (WisDom)-Flagship Program organized by Indian National Young Academy of Science, Mumbai, August 8-10, 2024

- **Kuppusamy P**. Persons with Disabilities and their Rights by Dr Hemlata, National Centre for Disability Studies, ICMR, New Delhi, Online, July 3, 2024
- **Kuppusamy P**. Workshop on Gyan Daan on Systematic Review as Part of The TERIIP Project Team, ICMR Headquarters, New Delhi, July 24-26, 2024
- **Kuppusamy P**. Lecture Cum Sensitization Session on Accessibility and Inclusion: Need of the Hour, Dr Navjit Gaurav, Assistant Professor, Architecture and Planning, IIT Roorkee (online), Online Conducted by ICMR Headquarter, New Delhi, October 4, 2024
- **Kuppusamy P**. Workshop on How to Conduct Qualitative Systematic Review (online), Online Conducted by Cochrane Affiliate Centre, ICMR, New Delhi, January 21, 2025
- **Mehta N**. Two-Day Workshop on 'Artificial Intelligence in Public Health', TISS Main Campus in Mumbai, April 22-23, 2024
- **Mehta N, Khedekar S, Chavan K**. Talk by Dr. Bhavuk Garg, AIIMS, Delhi, on Backpain-Prevention to Cure, ICMR, Delhi, Online, July 3, 2024
- **Mehta N, Khedekar S, Chavan K**. Persons with Disabilities and their Rights by Dr. Hemlata, Additional Director National Centre for Disability Studies (NCDS), Indira Gandhi National Open University, Online, July 3, 2024
- **Mehta N**. Strengthening ICMR's Intramural Research Programme Organized by Division of Reproductive, Maternal, Child Health and Nutrition, ICMR-HQ, Online, July 4, 2024
- **Mehta N**. Factorial Trials by Clinical Trial Service Unit and Epidemiological Studies Unit, University of Oxford, UK, online, July 6-7, 2024
- **Mehta N**. Mastering Biomedical Systematic Literature Reviews: Methodologies, Challenges, and Tools, Elsevier, online, July 18, 2024
- **Mehta N**. National Workshop on Systematic Reviews & Meta -Analysis Organized by Resilient Foundation for Academic Innovation & Scientific Research, New Delhi in collaboration with Biostatistics Consortium, INDIA, Online, August 22-28, 2024
- **Mehta N**. One Week Online International Workshop on Biostatistics, Resilient Foundation for Academic Innovation & Scientific Research, New Delhi in collaboration with Biostatistics Consortium, India, Online, October 18-20, 2024
- **Mukherjee S**. Recent Advances in Flow Cytometry (Spectral flow cytometer), ICMR-NIRRCH, Mumbai, July 2, 2024
- **Mukherjee S**. Antimicrobial Resistance (AMR), AMR in India, Challenges and Way Forward by Dr Jyoti Iravane, Professor Head, Microbiology, Government Medical College, Chhatrapati Sambhajinagar, Webinar, July 3, 2024
- **Mukherjee S**. Strengthening ICMR's Intramural Research Programme, Division of Reproductive, Maternal, Child Health and Nutrition, ICMR-HQ, Webinar, July 4, 2024
- **Mukherjee S.** Biomarker Development and Commercialization by Dr. Steven Piccoli, Sun Pharma Advanced Research, USA in Webinar on Biomarker Development and Utilization in Drug Development for Pat, Webinar, July 12, 2024
- **Munne K**. Dissemination Meeting for ICMR Funded Project on New Born Screening for Sickle Cell Anemia at MRHRU Dahanu, Govardhan Eco Village, Wada, Palghar, August 23, 2024
- **Munne K**. 36th International Papillomavirus Conference, Edinburgh, UK, November 12-15, 2024
- **Munne K**. Basic Workshop on Qualitative Data Analysis with Focus on RAPID analysis, ICMR NIRRCH, Mumbai, December 12-13, 2024
- **Munne K**. India TB Innovation Summit – Pioneering Solutions to End TB, Bharat Mandapam Convention Centre, New Delhi, March 18-19, 2025

- **Munshi H**. Functional and Behavioral Skills Training ICMR Young Scientist Induction Program, Indian Institute of Management, Visakhapatnam, August 19 - September 14, 2024
- **Munshi H, Anand S**. MRHRU Workshop, New Delhi, November 18-19, 2024
- **Panchal D**. 16th Annual Meeting of Proteomics Society of India and International Conference on OMICS in Decoding Biological Research, NCL, Pune, November 21-23, 2024
- **Panchal D**. 20th National Research Scholars Meet, Advance Center for Treatment, Research, and Education in Cancer (ACTREC), Navi Mumbai, December 11-12, 2024
- **Patel V**. DengiAll Vaccine Trial Investigators Meeting, ICMR, New Delhi, June 10-11, 2024
- **Patel V**. Meeting on HIV-1 Drug Resistance Equipment Technical Specifications, New Delhi, March 25, 2025
- **Savardekar S.** Two-day Workshop on 'Artificial Intelligence in Public Health', TISS Main Campus in Mumbai, April 22-23, 2024
- **Savardekar S**. Factorial Trials by Clinical Trial Service Unit and Epidemiological Studies Unit, University of Oxford, UK, Online, June 7, 2024
- **Savardekar S**. Intrauterine Contraceptive Devices: Adverse Events Management in Clinical Practices, Online, June 21-23, 2024
- **Savardekar S**. Lancet Series on Sustainable Access to Antibiotics with topic "The Scope of Antimicrobial Resistance Challenge, ICMR, online, July 18, 2024
- **Savardekar S**. Mastering Biomedical Systematic Literature Reviews: Methodologies, Challenges, and Tools, Elsevier, Online, July 18, 2024
- **Savardekar S**. Ethics Committee Management: Current Advances, Online, July 20, 2024
- **Savardekar S**. Ultrasound by Society of Fetal Medicines, NMOGS, Online, July 24-October 2, 2024
- **Shukla P**. Biostatistics: A User's Perspective Workshop, IISER, Pune, July 13-21, 2024
- **Shukla P**. International Conference on Progress in Mitochondrial Research and Therapy, and 10th Annual Conference of the Society for Mitochondria Research (SMRM), SDM University, Dharwad, November 11-12, 2024
- **Thomas S**. Evidence and Gap Map, ICMR-Cochrane Affiliate Center, Online, August 27, 2024
- **Thomas S**. ICMR Nodal Communications Officers Meeting, Online, ICMR, February 15, 2025

12.4 Invited Lectures

- **Banerjee A**. Kisspeptins: Diagnostic and Therapeutic Potential in Human Reproduction, International Conference on Reproductive Sciences and Molecular Medicine: Innovations in Therapeutics and Technologies, Society for Reproductive Biology and Comparative Endocrinology, University of Delhi, November 15-17, 2025
- **Banerjee A**. Puberty and Pubertal Disorders, Inter-Collegiate Research Fest Primers 2025, Elphinstone College, Mumbai, January 23, 2025
- **Bhavya M K**. Unpaid Work is Work: Recognizing the Women's Contribution Beyond the Workplace, International Women's Day, Online, March 7, 2025
- **Bhor V**. Gut Microbiome Signatures of HIV-TB Coinfection, 5th Genomic Analysis and Technology Conference, GATC 2024, ICGEB, New Delhi, April 12-14, 2024
- **Bhor V**. Harnessing the Microbiome: A New Frontier in the Battle against Multidrug Resistance, Indian Woman Scientists Association (IWSA)-BRNS Popular Science Lecture, K C College, Mumbai, July 16, 2024

- **Bhor V**. Delineating the Role of Integrin α4β7 and MAdCAM-1 in HIV Pathogenesis: Implications for Monitoring COVID19 Disease Progression, Molecular Immunology Forum Meeting 2024, IISER Bhopal, September 26-28, 2024
- **Bhor V**. ROS Exacerbate HCMV Infection Associated Gut Microbiota Metabolite Mediated Intestinal Epithelial Barrier Dysfunction Ex Vivo, International Conference on Developments in the Science of OxidatiVE Stress and Redox Medicine (SFRR-India-DISCOVER-2024) & 18th Meeting of The Society for Free Radical Research India (SFRR-India), DAE Convention Center, Anushakti Nagar, Mumbai, November 6-9, 2024
- **Bhor V**. Role of Microbiome in Shaping Child Growth, 2nd International Conference of Manashakti Research Center, Manashakti Research Centre, Lonavla, January 17-19, 2025
- **Bhor V**. Microbiome Mediated Immune Modulation Influencing the Course of HCMV Infection During Pregnancy, 35th Annual Meeting of the ISSRF, Rajasthan International Center, Jaipur, February 14-16, 2025
- **Gajbhiye RK**. Gaps in Recognition and Management of Rural Health Issues: Morbidity-Mortality Related to Snakebites, 3rd Meeting on Dynamic Historiography, Kasturba Health Society-Medical Research Center, Mumbai, September 24, 2024
- **Gajbhiye RK**. Reproductive Health in India: A Public Health Perspective, MPH Students Course Work, Center for Cancer Epidemiology, ACTREC-Tata Memorial Center, Navi Mumbai, November 25, 2024
- **Joshi B**. Understand Leaders' Dilemma-Stakeholder Engagement in HTA, International Technical and Economic Cooperation (ITEC) Course on Strategizing Approaches for Health Technology Assessment, IIPH Gandhinagar, December 2, 2024 to February 15, 2025
- **Joshi B**. Economic Modelling for HTA, HTA Workshop, AFMC Pune, December 5, 2024
- **Joshi B**. Role of HTA in Decision Making, Health Technology Assessment for Evidence Based Decision Making in India, TMH, Parel, Mumbai, February 14-15, 2025
- **Joshi B**. Introduction to Economic Modelling, ICMR NIV Pune, February 17-21, 2025
- **Khambata K**. Estrogen Receptors: Regulators of Sperm Epigenome and Male Fertility, Genomics Analytics and Technology (GATC) and Meeting for Society of Biological Chemist, Mumbai, October 2, 2024
- **Khambata K, Sanketa Raut, Parte P, Balasinor NH**. Estrogen Receptors: Epigenetic Regulators of Spermatogenesis and Male Fertility, International Conference on Reproductive Sciences and Molecular Medicine and Annual Meeting of SRBCE, New Delhi, November 15-17, 2024
- **Mukherjee S**. Understanding Pathophysiology of Polycystic Ovary Syndrome, DBT-Star College Program, Ravenshaw University, Cuttack, September 11, 2024
- **Mukherjee S**. Altered Angiogenesis Underlying Follicular Defect in Women with Polycystic Ovary Syndrome, International Webinar on Recent Advances & Innovations in Reproductive Health (RAIRH), Department of Zoology, Banaras Hindu University, September 20, 2024
- **Mukherjee S**. Demystifying the Mechanism of Follicular Defect in Women with Polycystic Ovary Syndrome, B B Kaliwal Gold Medal Oration Award talk, International Conference on Reproductive Sciences and Molecular Medicine: Innovations in Therapeutics and Technologies (ICRSMM-2024) and the 41st Annual Meet of Society for Reproductive Biology and Comparative Endocrinology (SRBCE), November 15, 2024
- **Mukherjee S**. Unraveling Pathophysiology of Polycystic Ovary Syndrome by Multifaceted Approach, Dr. T. C. Anand Kumar Memorial Oration Talk at International Conference on Reproductive Biomedicine: Integrating Basic Biological and Applied Research into Clinical Practice for Human Welfare and 35th Annual Meeting of the Indian Society for the Study of Reproduction and Fertility, Jaipur, February 14, 2025

- **Mukherjee S**. Pathophysiology of Polycystic Ovary Syndrome – A Multifaceted Approach, International Conference on Psychosocial Challenges Among Women with PCOS Psychophysiology Laboratory Department of Humanities and Social Sciences, Institute of Technology Bombay, Mumbai, February 26, 2025
- **Munshi H**. Research Methodology for Medicos, LTMMC Research Society, Indian Medical Association Hall, Mumbai, May 27, 2024
- **Pande S**. Recurrent Pregnancy Loss and Abnormal Pregnancy Outcomes, National Conference: The Pathology Association, Thane, Maharashtra, June 22-23, 2024
- **Pande S**. Genetics of Rare Diseases, Organization for Rare Diseases India, January 19, 2025
- **Pande S**. Genetic Diagnosis and Prevention of Haemoglobinopathies, Navi Mumbai Obstetrics & Gynecology Society, February 16, 2025
- **Pande S**. Role of Genetic Counselors in Social Outreach Activities, National Genetic Counselling Symposium, Centre for DNA Fingerprinting and Diagnostics, Hyderabad, March 8, 2025
- **Patel V**. Host-Pathogen Interplay at the Pathogenic and Transmission Interface: Insights from HIV-1C Cohorts in India, American Society for Reproductive Immunology Meeting, Houston, Texas, USA, May 18-22, 2024
- **Patel V**. Frontline Immune Monitoring using Flow Cytometry, Flow cytometry Workshop organized by Zoology Dept., GN Khalsa College and The Cytometry Society of -India, Mumbai, Maharashtra, September 21, 2024
- **Patel V**. Maternal Screening of HCMV Infection in India: Why Aren't We Doing It? Molecular Immunology Forum 2024, IISER Bhopal, Madhya Pradesh, September 26-28, 2024
- **Patel V**. Invited Panelist: Translation Track – Beyond CAR-T, 4th SACT event, Series on Advancements in Cell Therapy, ACTREC, Navi Mumbai, March 6-9, 2025
- **Prusty RK**. Data Management and Statistical Analysis Using SPSS, Workshop on Data Management, IIHMR Bengaluru-Virtual, March 26-28, 2025
- **Sachdeva G.** Endometriosis, International Conference on Reproductive Sciences and Molecular Medicine: Innovations in Therapeutics and Technologies (ICRSMM-2024), 41st Annual Meet of Society for Reproductive Biology and Comparative Endocrinology, November 15-17, 2024
- **Savardekar S**. EC Structure and Responsibilities, S Nijalingappa Medical College, Bagalkote, Karnataka-Online, September 23, 2024
- **Savardekar S**. Consideration of Ethical issues: Special reference to Integrative Health Research, 1st ICMR-NITM-KAHER Joint Workshop on Clinical Research in Integrative Medicine, Belgaum, November 18, 2024
- **Savardekar S**. Ethics Committee functioning as part of GCP training, GCP training at Ummeed Foundation, Mumbai, December 7, 2024
- **Shukla P**. Mitochondria in Health and Diseases, PhD Coursework 2024, ICMR-NIIH, Mumbai, August 13, 2024
- **Singh D**. Idiopathic Recurrent Pregnancy Loss: Possible Association with Paternal Exposure to Endocrine Disruptors and Epigenetic Modifications in Sperm, International Conference on Reproductive Sciences and Molecular Medicine: Innovations in Therapeutics and Technologies (ICRSMM-2024), 41st Annual Meet of Society for Reproductive Biology and Comparative Endocrinology (SRBCE), University of Delhi, November 15-17, 2024
- **Singh D**. Epigenetics: The Case for a Greater Focus on Sperm, Indo-German workshop on Translational Research in Andrology, Kasturba Medical College, L Manipal Academy of Higher Education, February 28, 2025 -March 1, 2025

- **Sudhakar DVS**. Genetics of Male infertility, ReproMed Update on Male Infertility-2024, AIIMS, Jodhpur, May 11-12, 2024
- **Sudhakar DVS**. Genetic Basis of Ciliopathies, Cilia Meeting: Centrosomes, Cilia and Ciliopathies, Indian Institute of Technology, Mumbai, November 27-28, 2024
- **Sudhakar DVS**. Monogenic Causes of Human Sperm Flagellar Defects, PCD meeting-2025, Mumbai Chapter, UM-DAE, Centre for Excellence in Biosciences, University of Mumbai, March 29, 2025
- **Tandon D**. Evaluation of The Infertile Couple, Certificate Course of General Practitioners, Nowrosjee Wadia Maternity Hospital, December 3, 2025
- **Thomas S**. Hands on Bioinformatics: Coding Workshop, Hands on Bioinformatics: Coding Workshop, Armed Forces Medical College (AFMC), Pune, June 19, 2024
- **Thomas S**. In Silico Approaches for Drug Target Discovery: Insights from a Study on Candidiasis, National Symposium on Emerging Trends in Computational Biology, S K Somaiya College, Vidyavihar, June 28, 2024
- **Thomas S**. Orientation on Bioinformatics, Expert Lecture Series at Seth GS Medical College, July 11, 2024

12.5 Inter-Institutional Collaborations

12.5.1 National Collaborations

- Amrita Institute of Medical Sciences, Kochi
- Apollo Hospital, Hyderabad
- Apollo Hospitals, Navi Mumbai
- Arihant Hospital, Nagpur
- ART Fertility Clinic, Mumbai
- Assam Medical College, Dibrugarh
- Bai Jerbai Wadia Hospital for Children, Mumbai
- Centre for Research, Management and Control of Hemoglobinopathies, ICMR-NIIH, Chandrapur
- Christian Medical College, Vellore
- Director Health services and Executive Director SHSRC, Govt of Maharashtra
- District Health Officer, Palghar District
- District Health Officer, Thane District
- Dr Bhubaneswar Borooah Cancer Institute, Guwahati
- Fertility Clinic & IVF Center, Mumbai
- Gleneagle HealthCity, Chennai
- Institute of Chemical Technology, Mumbai
- Indian Institute of Technology Bombay, Mumbai
- Indian Institute of Technology, Madras
- IVF Spring Fertility Center Mumbai
- Kamala Polyclinic & Nursing Home, Grant Road, Mumbai
- Kasturba Hospital, Mumbai
- King George's Medical College, Lucknow
- Lokmanya Tilak Municipal General Hospital and Medical College, Mumbai
- Medanta Hospital, Gurugram
- Mumbai Oncocare Hospital, Mumbai

- Municipal Corporation of Greater Mumbai, Mumbai
- National Institute of Mental Health and Neuro Sciences, Bengaluru
- Nowrosjee Wadia Maternity Hospital, Mumbai
- Topiwala National Medical College and BYL Nair Charitable Hospital, Mumbai
- ICMR -National Institute of Immunohaematology, India
- Icmr -Regional Medical Research Centre, Sri Vijaya Puram
- Maharashtra University of Health Sciences Regional Centre, Mumbai
- MS Ramaiah University of Applied Sciences, Bengaluru
- Medanta Hospital, Gurugram
- Pimpri Chinchwad Municipal Corporation Medical Department, Pune
- Saifee Hospital, Mumbai
- Seth Gordhandas Sunderdas Medical College and King Edward Memorial Hospital, Mumbai
- Specialty Surgical Oncology Hospital, Mumbai
- SVKM's Dr. Bhanuben Nanavati College of Pharmacy, Mumbai
- St. John's National Academy of Health Sciences, Bengaluru
- SRL Avinash Phadke Labs, Mumbai
- Tata Institute of Fundamental Research, Mumbai
- Tata Memorial Hospital, Mumbai
- Translational Health Science and Technology Institute, Faridabad

12.5.2 International Collaborations

- Advanced Organ Bioengineering, and Therapeutics, University of Twente, The Netherlands
- Department of Obstetrics, Gynecology, and Reproductive Sciences, Division of Complex Family Planning, University of California, San Diego, La Jolla, CA, USA
- Center on Gender Equity and Health, Department of Medicine, Division of Infectious Disease and Global Public Health, University of California, San Diego, La Jolla, CA, USA
- College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, CO, USA

12.6 Trainees

Twenty one summer, nineteen winter trainees and three NASI/INSA fellows were inducted in various departments namely Molecular Endocrinology, Gamete Immunobiology, Genetic Research Centre, Cell Physiology and Pathology, Molecular and Cellular Biology, Infectious Diseases Biology, Cellular and Structural Biology, Bioinformatics, Neuroendocrinology, Molecular Immunology and Microbiology, Innate Immunity, National Center For Preclinical Reproductive and Genetic Toxicology, Biochemistry, Infectious Diseases Biology, Clinical Research Laboratory. These trainees were introduced to technological innovations in different fields and were trained in various scientific processes in ongoing projects.

HONORS AND AWARDS

13. HONORS AND AWARDS

13.1 Awards

- **Anand S.** ICMR-DHR International Fellowship Award for Young Indian Biomedical Scientists 2024-2025.
- **Arya D.** Appreciation for the best PhD paper, ICMR-NIRRCH, Mumbai, February 21, 2025
- **Bal M.** Best Oral Presenter Award 2025 at the Indian Society for the Study of Reproduction and Fertility (ISSRF), Indian Society for the Study of Reproduction and Fertility (ISSRF), 35th Annual meeting of the ISSRF, Rajasthan International Center, Jaipur, February 14-16, 2025.
- **Batgire J.** Best Poster Award at the 16th Annual Conference the Cytometry Society-2024, ACTREC, Tata Memorial Centre, Navi Mumbai, October 20, 2024.
- **Bhavya MK.** Certificate of Appreciation by ICMR and IIM Visakhapatnam, IIM Visakhapatnam, October 26, 2024
- **Bhide A.** Best Poster Award at Joint Annual Meeting of the SBC (I) Mumbai Chapter and GATC-LITE, WEST, October 2, 2024
- **Bhide A.** Best Poster and Best Innovation Award at 4th Asian Congress for Alternatives to Animal Experiments, Jamia Hamdard University, New Delhi, December 12-14, 2024
- **Bhor VM.** Prof. N. R Moudgal Memorial Oration Award, Indian Society for the Study of Reproduction and Fertility (ISSRF), Indian Society for the Study of Reproduction and Fertility (ISSRF), 35th Annual meeting of the ISSRF, Rajasthan International Center, Jaipur, February 14-16, 2025.
- **Bhowmick S.** Second Prize for Oral Presentation at TCS 16th Annual Conference & Workshops, ACTREC, Mumbai, October 17-18, 2024.
- **Chaaithanya K.** ICMR-DHR International Fellowship Award for Young Indian Biomedical Scientists 2023-2024, University of California San Francisco, California, USA, July 2024 - December 2025
- **D'souza J.** Second Prize for Oral Presentation at the 5th Student Research Congress, SVKM's Dr Bhanuben Nanavati College of Pharmacy, Mumbai, December 20-21, 2024.
- **Devadiga P.** Best Poster Award at the Joint Annual Meeting of SBC(I) Mumbai Chapter and GATC Lite, West, ICMR-NIRRCH, October 2, 2024.
- **Gajbhiye R.** World's Top 2% Scientists, as per global ranking by Stanford University and Elsevier (2024).
- **Gajbhiye R.** Elected as a Fellow of the National Academy of Sciences, India (FNASc) in 2024.
- **Irani D.** Dr. (Mrs.) Mridula Kamboj Young Scientist Award by the Indian Society for the Study of Reproduction and Fertility (ISSRF), 35th Annual meeting of the ISSRF, Rajasthan International Center, Jaipur, February 14-16, 2025.
- **Joshi B.** Recognition of Excellence for the Best HTAIn Centre at the DHR- ICMR Health Research Excellence Summit 2024, Sushma Swaraj Bhawan, Delhi, November 14, 2024.
- **Kaginkar S**. Best Oral Presentation at the Cytometry Society of India, TCS 16th Annual Conference & Workshops, ACTREC, Mumbai, October 17 - 18, 2024.
- **Kamble P:** Best PhD student award at the DHR-ICMR Health Research Excellence Summit 2024, November 15, 2024

- **Modi DN:** World's Top 2% Scientists, as per global ranking by Stanford University and Elsevier (2024).
- **Modi DN:** KC Krishna Murti award from Society of Biological chemists India SBC(I)
- **Mohite N.** 5th Prize for Oral Presentation at TCS 16th Annual Conference & Workshops, ACTREC, Mumbai, October 17 - 18, 2024.
- **Mukherjee S**. B B Kaliwal Gold Medal Oration Award, Society for Reproductive Biology and Comparative Endocrinology (SRBCE), SRBCE - Reproductive Sciences and Molecular Medicine: Innovations in Therapeutics and Technologies, November 17, 2024.
- **Mukherjee S.** Dr. T. C. Anand Kumar Memorial Oration award, Indian Society for the Study of Reproduction and Fertility, Jaipur, February 14-16, 2025.
- **Mukherjee N**. DHR International fellowship for Young Biomedical Scientists 2024, University of Twente, The Netherlands, May 6, 2024 to April 30, 2025
- **Naigaonkar AA.** Travel Grant for the Oral Presentation at 22nd Annual Meeting of the AE-PCOS Society, at Queenstown, New Zealand, 22nd Annual Meeting of the AE-PCOS Society, Queenstown, New Zealand, November 7-9, 2024.
- **Negi B:** Best PhD Oral Presentation at the 5th Student Research Congress, SVKM's Dr Bhanuben Nanavati College of Pharmacy, Mumbai, December 20-21, 2024.
- **Negi B:** Best Oral Presentation Award in Immunocon-2024 conference, IISc, Bengaluru, October 17-20, 2024.
- **Palav H.** Third Prize for Oral Presentation at TCS 16th Annual Conference & Workshops, ACTREC, Mumbai, October 17-18, 2024.
- **Panchal D.** Best Poster Award at the Proteomics Society of India, CSIR - NCL, Pune, November 23, 2024
- **Panchal D.** Second Best Oral Presentation Award at the 20th National Research Scholars Meet, Advance Center for Treatment, Research, and Education in Cancer, Navi Mumbai, December 12, 2024
- **Panchal D.** V. P. Kamboj Young Scientist Award at the Indian Society for the Study of Reproduction and Fertility (ISSRF), Indian Society for the Study of Reproduction and Fertility (ISSRF), 35th Annual meeting of the ISSRF, Rajasthan International Center, Jaipur, February 14-16, 2025.
- **Pawar R.** Best Poster Award, EVOLVE 2025 conference, Indian Society for Extracellular Vesicles (InSEV), All India Institute of Medical Sciences, Delhi, March 27, 2025
- **Saha D.** Travel Grant from DST-SERB Programme to present her work at the Annual meeting of American Society of Human Genetics (ASHG 2024), Denver, Colorado, November 5-9, 2024
- **Sharma K.** Women Scientist Award at the Indian Society for the Study of Reproduction and Fertility (ISSRF), Indian Society for the Study of Reproduction and Fertility (ISSRF), 35th Annual meeting of the ISSRF, Rajasthan International Center, Jaipur, February 14-16, 2025.

13.2 Patents Filed:

- **Thomas S**. Development of less virulent strain of Candida albicans SC5314 by knockout of novel target gene encoding alanine transaminase protein and uses thereof with Application No. 202411050602 on July 2, 2024

13.3 PhD Degrees Awarded

1. **Mr Aniket Patankar**
   Thesis title: Functional significance of Testis-specific Histone H2B variant (TH2B) in spermatozoa
   Research Guide: Dr Priyanka Parte

2. **Ms Kashmira A. Bane**
   Thesis title: Pathways to Oncogenesis in the Pathophysiology of Endometriosis
   Research Guide: Dr Geetanjali Sachdeva

3. **Ms Kasturi Ganguly**
   Thesis title: Deciphering the Mechanisms of Innate Immune Surveillance in Prostate Cancer for Immunotherapy
   Research Guide: Dr Taruna Madan

4. **Ms Pradnya Kamble**
   Thesis title: Trop2 in Ovarian Cancer: Investigating its Therapeutic Potential
   Research Guide: Dr Bhakti Pathak

5. **Ms Sandhya Nair**
   Thesis title: Osteoprotegerin and Receptor Activator of Nuclear Factor κ-B Ligand: Exploring their Potential as Biomarkers for Assessing Bone Health
   Research Guide: Dr Nafisa H Balasinor

6. **Ms Sanketa Raut**
   Thesis title: Molecular Mechanisms involved in Prolactin and Dopamine Signaling in Male Reproduction
   Research Guide: Dr Nafisa H Balasinor

7. **Ms Shuvechha Chakraborty**
   Thesis title: Identification and Validation of Novel Drugs and Targets of Candida Species
   Research Guide: Dr Susan Thomas

8. **Ms Sushama Gadkar**
   Thesis title: Identification of Cell Surface Estrogen Binding Protein(s) and its Functional Significance in the Pathogenesis of Prostate Cancer
   Research Guide: Dr Geetanjali Sachdeva

ADVISORY COMMITTEES

14. ADVISORY COMMITTEES

14.1 Scientific Advisory Committee

Dr Neerja Bhatla (*Chairperson*)
Former Head, Department of Obstetrics and Gynaecology,
All India Institute of Medical Sciences, Ansari Nagar, New Delhi

Dr Bharati Kulkarni (*ICMR representative*)
Scientist 'G' and Head, Division of RBMCH & Nutrition
Indian Council of Medical Research, V Ramalingaswami Bhawan, Ansari Nagar, New Delhi

Dr Ashutosh Halder
Professor & Head, Reproductive Genetics
All India Institute of Medical Sciences, Ansari Nagar, New Delhi

Dr Vishwajeet Kumar
Founder, Community Empowerment Lab,
Shivgarh Main Rd, Shivgarh, Uttar Pradesh

Dr Sanjay Mehendale
Director Research, PD Hinduja Hospital and Medical Research Center
8-12, SVS Rd, Mahim West, Mahim, Mumbai

Dr Kumaraswamy Thangaraj
Former Director, Centre for DNA Fingerprinting & Diagnostics,
Inner Ring Road, Uppal, Hyderabad

Prof Sidharth Ramji
Former Dean and Director, Maulana Azad Medical College, New Delhi

Dr Manisha Madkaikar (*Special Invitee*)
Director, ICMR - National Institute of Immunohaematology
13th floor, New Multistoreyed Building, KEM Hospital Campus, Parel, Mumbai

Dr Pawan Kumar
Advisor, (Family Planning/Maternal Health & Immunization),
Ministry of Health and Family Welfare, Room No. 522 A, Nirman Bhawan, New Delhi

Dr Zoya Ali Rizvi
Deputy Commissioner (Child Health Nutrition),
Ministry of Health and Family Welfare, Room No. 207-D, Nirman Bhawan, New Delhi

Dr Sunita Taneja
Deputy Director, Centre for Health Research and Development
Society for Applied Studies, 45, Kalu Sarai, New Delhi

Dr Sanjeev Galande
Dean, School of Natural Sciences, Shiv Nadar University,
Gautam Buddha Nagar, Uttar Pradesh

Dr Smita Mahale (*Special Invitee*)
Former Director, ICMR-NIRRCH
A-503, Devdeveshwar CHS, Telly Galli Cross Lane, Andheri (East), Mumbai

Dr Vaishali Chandanshive
Medical Officer, Municipal Corporation Greater Mumbai, Mumbai
3rd Floor, F/S Ward Office Building, Dr B Ambedkar Marg
Parel, Mumbai - 400012

Dr Rajendra Singh
Central Drug Research Institute,
Sitapur Rd, Sector 10, Jankipuram Extension, Lucknow, Uttar Pradesh

Dr Geetanjali Sachdeva (*Member Secretary*)
Director, ICMR-NIRRCH, Parel, Mumbai

14.2 Members of ICMR-NIRRCH Ethics Committee for Human Studies

Prof Shubhada Chiplunkar *(Chairperson)*
Former Director ACTREC-TMC, Principal Investigator, Chiplunkar Lab,
Tata Memorial Centre, Kharghar, Navi Mumbai

Dr Yogeshwar S. Nandanwar
Professor, Obstetrics and Gynaecology, DY Patil Medical College, Nerul, Navi Mumbai

Dr Sandeep Bavdekar
Ex-Professor & Head, Paediatrics Department,
BYL Nair Charitable Hospital & TN Medical College, Mumbai

Dr Sivakami Muthusamy
Professor, Tata Institute of Social Sciences, Deonar, Mumbai

Dr Rakhi Tripathi
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Dr Ketki Kulkarni
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Dr Bipin Kulkarni
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Mrs Sudha Sathaye
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Dr Smita Nair
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RTO Colony, Mumbai Central, Mumbai

Dr Bhakti Pathak *(Joint Member Secretary)*
Scientist-F, ICMR-NIRRCH, Parel, Mumbai

Dr Vikrant Bhor *(Member Secretary)*
Scientist-E, ICMR-NIRRCH, Parel, Mumbai

14.3 Members of Institutional Animal Ethics Committee

Dr Geetanjali Sachdeva
Director, ICMR-NIRRCH, Parel, Mumbai

Dr K Pani Prasad
Principal Scientist, ICAR-Central Institute of Fisheries Education,
Yari Road, Panch Marg, Varsova, Mumbai

Dr Prabhakar Ukale
Veterinarian, Animal House Facility, Institute of Chemical Technology, Matunga (E), Mumbai

Dr Eshita Kishor Waghela
Veterinarian, Mumbai Veterinary College, Parel Village, Sindhu Nagar, Parel, Mumbai

Dr Sangram Shankarrao Chavan
Central Laboratory Animal House, Department of Pharmacology& Toxicology,
Bombay Veterinary College, Parel, Mumbai

Dr Padma Devrajan
Dean Research & Innovation, Professor in Pharmacy and former Head,
Department of Pharmaceutical Sciences and Technology,
Institute of Chemical Technology, Matunga, Mumbai

Dr Vikas Dighe
Scientist-F, ICMR-NIRRCH, Parel, Mumbai

Dr Dhanjit Das
Scientist-E, ICMR-NIRRCH, Parel, Mumbai

Dr SM Metkari
In-Charge, Animal House Department, ICMR-NIRRCH, Parel, Mumbai

14.4 Members of the Local Research Advisory Committee of MRHRU, Dahanu

Dr Sanghamitra Pati
Director & Scientist-G, ICMR-RMRC Bhubaneswar, Odisha

Dr Vishwajeet Kumar
Founder & Principal Scientist, Community Empowerment Lab, Gomti Nagar, Lucknow

Dr Rajesh Karyakarte
Head, Department of Microbiology, BJ Government Medical College & Sassoon Hospitals, Pune

Dr Manisha Madkaikar
Director, ICMR-NIIH, Parel, Mumbai

Dr Mamta Manglani,
Director, Comprehensive Thalassemia Care & BMT Centre, Mumbai

Dr Anuradha Khadilkar
Deputy Director, Hirabai Cowasji Jehangir Medical Research Institute (HCJMRI)

Dr Reena Wani
Head, Dept. Obstetrics & Gynecology, HBTMC - Dr Rustom Narsi Cooper Municipal General Hospital, Mumbai

Dr Pallavi Saple
Dean, JJ Group of Hospitals, Mumbai

Dr Dilip Mhaisekar
Director, Directorate of Medical Education and Research (DMER), Mumbai

Dr Nitin Ambadekar
Additional Director of Health Services, Executive Director, SHSRC, Maharashtra

Dr Geetanjali Sachdeva
Director, ICMR-NIRRCH, Parel, Mumbai

Dr Ragini Kulkarni
Scientist F, ICMR-NIRRCH, Parel, Mumbai

Dr Geeta Pardeshi
Head, Dept of Community Medicine
Nodal Officer, Grant Medical College and Sir JJ group of Hospitals, Mumbai

Dr Aparna Mukherjee
Scientist F, Development Research, ICMR, New Delhi

Dr Tanu Anand
Scientist E, Development Research, ICMR, New Delhi

Dr Kiran Munne
Scientist C, ICMR-NIRRCH, Parel, Mumbai

14.5 Members of the Local Research Advisory Committee of MRHRU, Vani

Dr Manisha Madkaikar (Chairperson)
Director, ICMR-NIIH, Parel, Mumbai

Dr Yogesh Kalkonde (Co-chair)
Public Health Researcher, Sangwari, Chhattisgarh

Dr Smita Mahale *(Special Invitee)*
Former Director, ICMR-NIRRCH, Parel, Mumbai

Dr Himmatrao Bawaskar
Director, Bawaskar Hospital and Research Center, Mahad, District Raigad, Maharashtra

Dr Satish Pawar
Former Director of Health Services, Maharashtra

Dr Archana Patil
Former Director of Health Services, Maharashtra

Dr Kapil Aher *(Nodal Officer, State Health Department)*
Deputy Director Health Services, Nashik Division
Public Health Department, Government of Maharashtra
Executive Director, State Health Systems Resource Center, Maharashtra

Dr Sadanand Raut
Director, Vighanhar Nursing Home,Narayangaon, District Pune, Maharashtra

Dr Shubhra Sengupta
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Dr Niraj Mahajan
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Topiwala National Medical College and BYL Nair Hospital, Mumbai

Dr Sanjay Prabhu
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Dr Sarika Patil *(Nodal Officer, MRHRU Vani - Linked Medical College)*
Professor and Head, Department of Community Medicine, Government Medical College, Dhule
Medical Superintendent, Rural Hospital Vani, Nashik

Dr Geetanjali Sachdeva
Director, ICMR- NIRRCH, Parel, Mumbai

Dr Rahul Gajbhiye *(Nodal Officer, ICMR Mentor Institute)*
Scientist E, ICMR-NIRRCH, Mumbai

Dr Taruna Madan *(DHR representative)*
Head, Development Research, ICMR, New Delhi

Dr Rajesh Dikshit
Director, Centre for Cancer Epidemiology, Tata Memorial Centre, Mumbai

Dr Charudatta Shinde
Civil Surgeon, Nashik

Dr Sudhkar More
District Health Officer, Nashik
Taluka Health Officer, Dindori

Dr Tanu Anand *(DHR representative)*
Scientist E, Department of Health Research, New Delhi

Dr Venkat Gite
Dean, MPGIMER, Nashik
Dean, Shri Bhausaheb Hire, Government Medical College, Dhule

Dr Milind Bhadane *(Special Invitee)*
Pediatrician, Civil Hospital, Nashik

Dr Geetanjali Sachdeva
Director, ICMR- NIRRCH, Mumbai

Dr Rahul Gajbhiye *(Nodal Officer, MRHRU Vani - ICMR Mentor Institute)*
Scientist E, ICMR-NIRRCH, Mumbai

Dr Swati Jadhav *(Special Invitee)*
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Dr Akhilesh Thakur *(DHR Representative)*
Scientist C, Department of Health Research, New Delhi

EXTRAMURALLY FUNDED PROJECTS

15. EXTRAMURALLY FUNDED PROJECTS

S No	Name of PI	Title	Start year	End year	Funded by
1.	Antara Banerjee	Delineation of the role of isoforms of kisspeptin in mammalian reproduction	2022	2024	SERB Start up grant
2.	Antara Banerjee	Study of kisspeptin receptor oligomerization and its functional significance	2023	2026	BRNS-DAE
3.	Anushree Patil	Centre for Product Development	2019	2024	ICMR
4.	Anushree Patil	Prospective evaluation of etiological factors, trajectory of co morbidities and, efficacy and safety of various therapeutic agents among Indian women with Polycystic ovary syndrome (PCOS): A multicentric ICMR-PCOS cohort study phase II	2023	2028	ICMR
5.	Anushree Patil	Validation study of indigenous HPV tests for cervical cancer screening (i-HPV)	2023	2025	BIRAC
6.	Beena Joshi	Assessment of RMNCAH+N service delivery costs, work patterns and efficiency of primary healthcare teams at Ayushman Bharat- Health and Wellness Centres	2024	2025	UNICEF through PGIMER
7.	Beena Joshi	Equitable, quality universal health coverage implementation research project for optimizing comprehensive primary health care through Health and Wellness Centers in Pimpri Chinchwad Municipal Corporation, Pune district, Maharashtra	2024	2027	ICMR
8.	Beena Joshi	Feasibility, acceptability and costs of providing comprehensive pre-conception care services to young couples in Maharashtra	2024	2025	ICMR
9.	Beena Joshi	Health technology assessment of point of care test kit for hemophilia and von-Willebrand Disease (vWD) screening developed at ICMR-NIIH	2024	2025	DHR HTAIn
10.	Beena Joshi	Health technology assessment to determine cost-effectiveness of hydroxyurea oral suspension as prophylaxis for management of Sickle cell anemia in children	2024	2025	DHR HTAIn
11.	Beena Joshi	Understanding availability of essential diagnostics in health care systems: identifying barriers and facilitators	2023	2024	ICMR
12.	Bhakti Pathak	Evaluating the role and proteolytic processing of Trop1 and Trop2 in normal placentation and placental pathologies	2021	2026	DBT
13.	Bhavya MK	Accelerating efforts to END TB in India	2023	2025	ICMR

14.	Dhanjit Das	Human endometrial stem cells and their possible role in the etiology of endometriosis	2023	2026	DBT
15.	Deepak Modi	Deciphering the immunomodulatory roles of Homeobox A10 in the endometrium during embryo implantation	2020	2025	DBT
16.	Deepak Modi	Elucidate the endometrial mesenchymal stem cells role in mediating early pregnancy: Function of reversible mesenchymal epitheial transition	2023	2026	Wellcome Trust India Alliance
17.	Deepak Modi	Identification of HOXA10-driven genetic networks in the endometrium	2024	2027	DBT
18.	Deepak Modi	Integrative transcriptomics approach for predicting endometrial receptivity using liquid biopsy	2024	2027	DBT-BioCARe
19.	Deepti Tandon	Evaluating the inflammatory, microbiome profile and co-infections in women diagnosed with treatment failure, relapse or recurrent bacterial vaginosis: Prospective analytic study	2023	2026	ICMR
20.	Deepti Tandon, Ragini Kulkarni	Assessing usage and disposal pattern of menstrual hygiene products among women in rural and urban India	2024	2026	ICMR
21.	Dhanashree Jagtap	Delineating the role of human β-microseminoprotein in male reproduction	2023	2025	ICMR
22.	Dipty Singh	Blood and urine levels of phthalates and VOCs and their association with the use of menstrual hygiene products	2024	2026	ICMR
23.	Dipty Singh	Clinical relevance of differentially methylated sperm lncRNA genes in male partners of couples experiencing idiopathic recurrent pregnancy loss	2024	2027	ANRF (SERB)
24.	Dipty Singh	*In vitro* studies to investigate the permeability and effects of phthalates and VOCs on vaginal epithelium	2024	2026	ICMR
25.	Dipty Singh	Therapeutic potential of Epigallocatechin-3-gallate (EGCG) for improving sperm quality, fertility and pregnancy outcomes in a murine model of endocrine disruption	2023	2026	ICMR
26.	Dipty Singh	Validation of sperm DNA Epimutations as diagnostic biomarker for idiopathic recurrent pregnancy loss	2023	2026	DHR
27.	Geetanjali Sachdeva	Eutopic endometrial cell repertoire in women presenting different subtypes of endometriosis and its association with endometrial receptivity	2023	2026	ICMR
28.	Krishna C Itta	Evaluation of micronutrient status following nutritional intervention among under 5 children with severe and moderate acute malnutrition in a tribal block of Jawhar, Palghar district	2024	2026	ICMR

29.	Krishna C Itta	Molecular analysis of HLA-G in pregnant tribal women and its role in infectious etiologies modulating intrauterine inflammation - A prospective cohort study	2023	2026	ICMR
30.	Kumari Nishi	Investigating the role of endocannabinoid system in first trimester chorionic villi of women experiencing recurrent spontaneous abortions	2023	2026	ANRF
31.	Kushaan Khambata	Investigating sperm 5hmC landscape in male infertility and recurrent pregnancy loss	2024	2027	DBT
32.	Lalita Savardekar	Impact of Mukta Shukti Bhasma and Saubhagya Shunti in reversal of bone mineral density among lactating women consuming traditional diet foods in Maharashtra: A randomized controlled preliminary clinical study	2023	2026	CCRAS
33.	Madhu Mohanty, Vikrant Bhor	Study of immune response in patients with long COVID	2023	2026	ICMR
34.	Nupur Mukherjee	Develop multicellular 3D tumor model of metastatic breast cancer as a platform to test novel therapeutic drugs	2024	2025	DHR International Fellowship for Young Biomedical Scientists 2024
35.	Nupur Mukerjee	Immune and microbiome correlates of TB reactivation in PLHIV and a NHP model	2020	2024	Indo-US Joint Program on HIV/AIDS and STI Prevention Research
36.	Nupur Mukherjee	Role of Wnt /β-Catenin signaling pathway in placenta mediated breast carcinogenesis during pregnancy	2023	2026	DST-SERB
37.	Pallavi Shukla	Delineating pathogenesis of obese and lean PCOS phenotype using integrated transcriptomics and proteomics approach	2023	2026	DHR
38.	Pallavi Shukla	Study of maternally inherited mitochondrial DNA variants in women with polycystic ovarian syndrome	2021	2027	ICMR
39.	Periyasamy Kuppusamy	Taskforce on Establishment of Reference Intervals in Indian Population (TERIIP): A multi-centric observational cross-sectional study	2025	2028	ICMR

40.	Prashant Shivgunde, Kiran Munne	Exploring factors influencing treatment adherence among leprosy patients in a rural hospital setting: A mixed-methods study in Dindori, Maharashtra	2025	2025	MRHRU Vani Grant
41.	Ragini Kulkarni	Developing & implementing effective intervention delivery strategies of the Anemia Mukt Bharat Program 2.0 to reduce prevalence of anemia amongst vulnerable populations in selected districts of India- An implementation research study (PRAKASH) – Precision Driven Response for Anemia Control and Sustainable Health	2025	2028	ICMR
42.	Ragini Kulkarni	Immune status against SARS-CoV-2 among COVID-19 vaccinated adults in India: A health facility-based multicentric serial cross-sectional survey	2023	2024	ICMR
43.	Ragini Kulkarni	Integrated Palliative Elderly and Mental Health Care (I-PEM) under for establishment of MRHRU under umbrella scheme of development of infrastructure for promotion of health research	2023	2026	DHR
44.	Ragini Kulkarni	Population-based health surveys at Model Rural Health Research Units in India-MRHRU Dahanu	2024	2025	DHR-ICMR
45.	Ragini Kulkarni	Strengthening Maternal and Perinatal Death Surveillance and Response (MPDSR) action in tribal blocks of Palghar district in Maharashtra-Implementation phase	2024	2026	ICMR
46.	Ragini Kulkarni	Validation of novel serum biomarkers in prediction of early onset preeclampsia among pregnant women and correlation with maternal and neonatal outcomes in a tribal district of Palghar Maharashtra	2024	2026	ICMR
47.	Rahul Gajbhiye	Clinical phenotypes and genetic regulation of endometriosis in Indian women (ECGRI study)	2019	2025	DBT Wellcome India Alliance
48.	Rahul Gajbhiye	A situational analysis of the disease burden in the North Maharashtra region	2024	2026	MRHRU Vani Grant
49.	Rahul Gajbhiye	D-SERPENT: Data-driven approaches to Snakebite: Epidemiology, Reporting, Phenotypes, Environmental factors, Inequalities, and Treatment duration	2025	2027	ICMR
50.	Rahul Gajbhiye	Identification of new male infertility genes in obstructive azoospermic men with congenital bilateral absence of vas deferens	2019	2023	DBT

51.	Rahul Gajbhiye	ICMR National Snakebite Project (INSP) on capacity building of health system on prevention and management of snakebite envenomation including its complications	2021	2024	ICMR National Task Force for Snakebite Research in India
52.	Rahul Gajbhiye	Nationwide study to estimate incidence mortality, morbidity, and economic burden due to snakebites in India	2022	2024	ICMR National Task Force for Snakebite Research in India
53.	Rahul Gajbhiye	Population-based health surveys at Model Rural Health Research Units in India, MRHRU, Vani	2024	2026	MRHRU grant and PM-ABHIM
54.	Rahul Gajbhiye	Strengthening implementation of antenatal screening and newborn management for Sickle cell disease at Rural Hospital, Vani, in tribal block of Nashik, Maharashtra	2025	2027	MRHRU Vani Grant
55.	Rahul Gajbhiye	Utilizing the Model Rural Health Research Units to improve snakebite management through rationalized antivenom distribution models in India: An implementation research project	2024	2026	DHR
56.	Ranjan Kumar Prusty	The impact of positive aging intervention on flourishing of elderly in India: A pan-India cluster randomized controlled trial	2024	2026	ICMR
57.	Shahina Begum	Pragmatic stepped wedge cluster randomization trial to evaluate the screening of clinical breast examination through health education interventions in rural Maharashtra	2023	2026	DHR
58.	Shailesh Pande	Comprehensive genetic evaluation of fetus in antenatally-detected abnormal pregnancies with fetal-malformations	2021	2025	ICMR
59.	Shailesh Pande	Establishment of Centre for Maternal and Child Health Genetics	2024	2027	DBT
60.	Shailesh Pande	Mission program on paediatric rare genetic disorders	2022	2027	DBT
61.	Shailesh Pande	Support to Indian institutes for imparting training	2021	2025	DHR
62.	Srabani Mukherjee	Integrated analysis of gut microbiome and metabolome in women with Polycystic Ovary Syndrome	2023	2027	DBT
63.	Srabani Mukherjee	Unravelling the metabolic nexus in the granulosa cells of women with PCOS	2023	2026	DHR

64.	Suchitra Surve	Exploring clinical and therapeutic relevance of novel biomarkers among the children presenting with idiopathic and incomplete precocious pu berty at Tertiary Hospital, Mumbai	2021	2024	ICMR
65.	Suchitra Surve, Ragini Kulkarni	Assessing feasibility of point of care device in community based screening of Sickle cell disease and Thalassemia in tribal district of Palghar, Maharashtra	2024	2026	ICMR
66.	Suchitra Surve, Ragini Kulkarni	Assessment of neonatal screening approaches for Sickle cell disease in tribal populations	2019	2024	ICMR
67.	Suchitra Surve, Ragini Kulkarni	Improving Infant and Young Child Feeding (IYCF) practices in tribal block of Palghar district Maharashtra through involvement of frontline workers	2024	2026	ICMR
68.	Susan Thomas	Establishment of Bioinformatics and Computational Biology Centre (Centre for advanced research in bioinformatics and computational biology for woman and child health)	2021	2026	DBT
69.	Susan Thomas	Integrated analyses of genomic scale metabolic models and omics profiles to capture the host-pathogen-environment interplay of Candida sp	2021	2024	SERB
70.	Susan Thomas	National Network Project of ICMR-National Institute for Research in Reproductive and Child Health, Mumbai	2023	2028	DBT
71.	Susan Thomas	Machine learning algorithms for voice-based detection of psychological stress and post-partum depression	2023	2025	ICMR - AI Cell
72.	Swati Jadhav, Rahul Gajbhiye	Retrospective study on the utilization and adverse reactions of snake antivenom administration at a Rural Hospital in Vani, District Nashik, Maharashtra	2025	2025	MRHRU Vani Grant
73.	Swati Jadhav, Sandhya Anand	Retrospective study to understand drug prescription patterns at Rural Hospital, Vani, district Nashik, Maharashtra	2025	2025	MRHRU Vani Grant
74.	Uddhav Chaudhari	To investigate role of HMGB1-RAGE axis in regulation of immune cells repertoire during endometrial breakdown and repair	2024	2027	SERB
75.	Vaibhav Aher, Hrishikesh Munshi	Healthcare journeys of snakebite victims admitted at Rural Hospital, Vani	2025	2026	MRHRU Vani Grant

76.	Vainav Patel	An integrated approach towards characterizing the Treg reservoir in HIV-1 infection	2023	2026	ANRF
77.	Vainav Patel	Developing broadly neutralizing monoclonal antibody mediated prevention and treatment strategies by assessing their effectiveness in neutralizing HIV-1 subtype C circulating in India across different regions and distinct risk groups	2020	2026	DBT Wellcome India Alliance
78.	Vainav Patel	Laboratory strengthening for conducting dengue vaccine trials in India	2023	2026	ICMR
79.	Vikas Dighe	Exploring the therapeutic potential of peptides targeting lysophosphatidic acid receptors in ovarian cancer	2022	2025	DBT
80.	Vikas Dighe	Preclinical study on efficacy, safety, and toxicity of Swarna Prashan regimen as adjunct therapy in pediatric acute lymphoblastic leukemia	2023	2026	CCRAS
81.	Vikas Dighe	Identification and characterization of Sertoli and Leydig cell homing peptides	2021	2024	ICMR-DHR
82.	Vikas Dighe	Evaluation of immunomodulatory and anti-cancer properties of hydroxychavicol, a major constituent of piper betel	2024	2027	ICMR-DHR
83.	Vikas Dighe	Evaluation of synergistic impact of nano-curcumin and alpha-linolenic acid on pathophysiology of pre-eclampsia	2022	2025	ICMR
84.	Vikas Dighe	Pre-clinical efficacy, safety and toxicity of colostrum whey protein derived formulations ('Propep') in animal model	2024	2026	ICMR-DHR
85.	Vikas Dighe	Development of a probiotic formulation containing Lactiplantibacillus plantarum Lp91 (MTCC 5690) and its pre-clinical safety and efficacy study for human use	2024	2026	ICMR-DHR
86.	Vikrant Bhor	Development of a sustainable network of laboratories in India for identification, monitoring and research on viruses and bacteria causing acute encephalitis syndrome and other novel pathogens through capacity building in advanced biomedical technologies	2023	2025	ICMR
87.	Vikrant Bhor	Evaluating the inflammatory, microbiome profile coinfections in women diagnosed with treatment failure, relapse and recurrent BV-Prospective analytic study	2023	2026	ICMR
88.	Vikrant Bhor	Evaluation of the immunogenic potential of membrane vesicles from clinical isolates of *Gardnerella vaginalis* in a murine model of bacterial vaginosis	2024	2027	ANRF (SERB-CRG)
89.	Vikrant Bhor	High-performance computing Next Generation Sequencing (NGS) Hub	2024	2027	ICMR

90.	Vikrant Bhor	Longitudinal cohort study of lactating women to assess the impact of SARS-CoV- 2 exposure and vaccination on systemic and vertically transferred SARS-CoV-2 specific immunity in the mother-infant dyad	2023	2025	ICMR

ANRF *Anusandhan National Research Foundation*
BioCARe *Biotechnology Career Advancement and Re-orientation*
BIRAC *Biotechnology Industry Research Assistance Council*
BRNS *Board of Research in Nuclear Sciences*
CCRAS *Central Council for Research in Ayurvedic Sciences*
CRG *Core Research Grant*
DAE *Department of Atomic Energy*
DBT *Department of Biotechnology*
DHR *Department of Health Research*
DST *Department of Science and Technology*
HTAIn *Health Technology Assessment in India*
MRHRU *Model Rural Health Research Unit*
ICMR *Indian Council of Medical Research*
PGIMER *Postgraduate Institute of Medical Education and Research, Chandigarh*
PM-ABHIM *Prime Minister - Ayushman Bharat Health Infrastructure Mission*
SERB *Science and Engineering Research Board*
UNICEF *United Nations International Children's Emergency Fund*

INTRAMURALLY FUNDED PROJECTS

16. INTRAMURALLY FUNDED PROJECTS

16.1 ICMR Intramural Research Grant

S. No	Name of PI	Title	Start year	End year
1.	Bhakti Pathak	Urinary PLGF as a predictive marker for preterm delivery with SGA infant: Evaluating the efficacy and attempting development of point-of-care device	2025	2028
2.	Dhanashree Jagtap, Geetanjali Sachdeva, Smita Mahale	Utility of estimating serum PSP94 levels in management of patients with raised PSA in clinical setting: A multicentric study	2024	2027
3.	Pallavi Shukla	Investigating the clinical relevance of environmental chemicals and exosomal miRNA biomarkers in the pathophysiology of Polycystic Ovary Syndrome	2024	2027

16.2 ICMR-NIRRCH Institutional Grant

S. No	Name of PI	Title	Start year	End year
1.	Antara Banerjee	Development and validation of indigenous diagnostics for evaluating the plasma levels of kisspeptin among Indian girls with central precocious puberty	2025	2028
2.	Antara Banerjee	Investigating the factors contributing to the metabolic regulation of onset of puberty	2024	2027
3.	Anushree Patil	Implementation of Multidisciplinary Intervention Model (MDIM) to improve reproductive and health outcomes in women with Polycystic Ovary Syndrome (PCOS)	2023	2024
4.	Bhakti Pathak	Analysis of molecular cargo and paracrine effects of extracellular vesicles secreted by ovarian cancer cells	2021	2026
5.	Deepak Modi	Determining the role of HOXA10 in the pathogenesis of endometriosis	2023	2025
6.	Deepak Modi	Development of a microfluidic-based tool for assessing placental functions and evaluating its potential application in pregnancy-related disorders	2023	2027
7.	Deepak Modi	Investigating the role of epithelial to mesenchymal transition in the process of embryo implantation	2023	2026
8.	Deepak Modi	Study on placenta of women with coronavirus disease 2019 (COVID-19) and its correlation with pregnancy and neonatal outcomes	2023	2025

9.	Deepti Tandon	Comprehensive assessment of women diagnosed with Spontaneous Premature ovarian insufficiency	2023	2026
10.	Dhanjit K Das	Genetic aberrations and their functional analysis in patients with intellectual disability: Implications of genetic defect in iPSCs derived neurons	2024	2029
11.	Dipty Singh	Effect of maternal gestational micronutrient deficiency on offspring's fertility and its underlying epigenetic mechanisms in germline	2019	2024
12.	Dipty Singh	Idiopathic recurrent pregnancy loss: Possible association with paternal exposure to endocrine disruptors and epigenetic modifications in sperm	2021	2026
13.	Dipty Singh	Unravelling the sperm epigenetic landscape in infertile men with clinical varicocele	2020	2025
14.	DVS Sudhakar	Identification and characterization of genetic factors associated with multiple morphological abnormalities of sperm flagella (MMAF)	2022	2025
15.	Geetanjali Sachdeva	Investigating the contribution of DNA damage, repair and demethylation in the pathogenesis of endometriosis	2023	2026
16.	Geetanjali Sachdeva	Investigating the key elements in estrogen signalling in the context of prostate cancer	2021	2027
17.	Geetanjali Sachdeva	Uterine alarmins and their relevance in implantation	2019	2025
18.	Kiran Munne	Evaluating utility of molecular workflow for establishing microbial profile and antimicrobial resistance for neonatal sepsis in a tertiary care NICU, Mumbai	2023	ongoing
19.	Kiran Munne	Exploring the association of cervicovaginal microbiome with transient and persistent high-risk HPV infection and cervical precancerous lesions	2023	ongoing
20.	Kumari Nishi	Development of a point of care electrochemical biosensor for the estimation of autoantibodies for obstetric antiphospholipid syndrome - A proof of concept study	2024	2029
21.	Kumari Nishi	Transgenerational effects of paternal hypertension on fertility and pregnancy outcome: An epigenetic approach	2021	2025
22.	Kushaan Khambata	Unravelling sperm epigenetic landscape regulated by estrogen receptors in adult male rats	2021	ongoing
23.	Mahadev Bhise	Trends, patterns and determinants of sex-selective abortions in India using nationally representative survey data	2023	ongoing
24.	Nupur Mukherjee	Deciphering the trophoblast-breast epithelial cell cross talk in pregnancy associated breast cancer (PABC)	2021	2024
25.	Nupur Mukherjee	Role of Toll-like receptors and TLR agonists in modulating response to chemotherapy in TNBC patients	2019	2026
26.	Pallavi Shukla	Analysis of mitochondrial DNA sequence variants in polycystic ovarian syndrome women with insulin resistance	2018	2024

27.	Pallavi Shukla	Study of epigenetic factors involved in mitochondrial dysfunction in PCOS women	2019	2027
28.	Periyasamy Kuppusamy	Identification of steroid metabolites as prognostic markers for spontaneous preterm delivery: A prospective cohort study	2025	2028
29.	Periyasamy Kuppusamy	Implications of gonadotropin and their receptor gene variants in male infertility	2022	2026
30.	Priyanka Parte	Investigation of potential chemotactic metabolites in the follicular fluid	2020	2024
31.	Ragini Kulkarni	Epidemiological and clinical features of Leptospirosis cases reported at Model Rural Health Research Unit Dahanu Maharashtra 2021-2022: A Retrospective study	2023	2024
32.	Ragini Kulkarni	Retrospective analysis of data from Dengue and Chikungunya testing facility at MRHRU Dahanu	2025	2026
33.	Sadhana Gupta	Deciphering gut microbial signatures in breast cancer and impact of their modulation on immune response following therapy	2023	2026
34.	Susan Thomas	Establishment of Bioinformatics and Computational Biology Centre (Centre for advanced research in bioinformatics and computational biology for woman and child health)	2021	2026
35.	Shaini Joseph	Deciphering the functional significance of candidate genes associated with polycystic ovary syndrome identified from network analysis	2021	2024
36.	Shaini Joseph	Establishing a predictive algorithm for fetal growth restriction in Indian population: a prospective cohort and a nested case-control study	2025	2028
37.	Shaini Joseph	Exploring the genetic factors influencing poor ovarian response associated with IVF failures	2025	2028
38.	Srabani Mukherjee	Assessment of coagulation and fibrinolytic factors as contributors of thrombotic state in PCOS	2021	ongoing
39.	Srabani Mukherjee	DNA methylation and histone modifications in dehydroepiandrosterone induced cystic ovarian murine model	2023	ongoing
40.	Srabani Mukherjee	Epigenetic alterations regulating miRNA expression in women with PCOS	2021	ongoing
41.	Srabani Mukherjee	PON1 expression, activity and its relationship with oocyte and embryo quality in women with PCOS undergoing assisted reproductive technique	2014	2026
42.	Srabani Mukherjee	Unravelling Pathogenetic Mechanisms of Polycystic Ovary Syndrome by Whole Exome Sequencing	2017	2026
43.	Uddhav Chaudhari	Heterogeneity of gestational diabetes mellitus based on insulin resistance	2022	2025

44.	Uddhav Chaudhari	Role of HMGB1 and RAGE in endometrial repair	2023	2026
45.	Vainav Patel	Studies on HIV latency and reactivation in cellular reservoirs	2020	2025
46.	Vainav Patel	Host pathogen signatures associated with congenital transmission and pathogenesis of human cytomegalovirus Part A: Immune correlates and viral signatures associated with congenital transmission and pathogenesis of human cytomegalovirus	2020	2025
47.	Vikrant Bhor	Characterization of the human gut microbiome-immune axis in pregnancy and functional assessment in an animal model	2022	2027
48.	Vikrant Bhor	Host-Pathogen signatures associated with congenital transmission and pathogenesis of human cytomegalovirus Part B: Exploring the gut and breast milk microbiome associated with congenital transmission and pathogenesis of human cytomegalovirus	2021	2026
49.	Vikrant Bhor	Microbiome correlates of TB reactivation in people living with HIV	2021	2026
50.	Vikas Dighe	Deciphering the molecular mechanism of effects of triclosan on hypothalamus pituitary gonadal axis	2018	2025
51.	Vikas Dighe	Evaluation of apocynin efficacy in bisphenol-A induced reproductive toxicity	2025	2028
52.	Vikas Dighe	MicroRNA regulation in prostate and ovary upon exposure to endocrine disruptors	2019	2025
53.	Vikas Dighe	Understanding the role of antioxidants in endocrine disrupters-induced Polycystic Ovary Syndrome (PCOS) like condition	2024	2027

STAFF AND STUDENTS

17. STAFF AND STUDENTS

DIRECTOR'S OFFICE

Dr. Geetanjali Sachdeva, *Director*
Mr. Mahesh P. Chabukswar, *Personal Assistant*
Mr. Kishor N. Kadam, *Laboratory Assistant*

BIOMEDICAL INFORMATICS CENTRE

Dr. Susan Thomas, *Scientist 'F'*
Ms. Sailee D. Shahane, *Technical Assistant (Bioinformatics)*
Mr. Sachin Bhajeekhaye, *Technical Assistant (Computer Science)*
Mr. Saravanan P, *Technician - 1 (Laboratory)*
Ms. Aboli S. Kadam, *Technician - 1 (Information Technology)* ** Joined on 10.04.2024*
Mr. Siddhesh Dattatray Shinde, *Technician - 1 (Information Technology)*
Mr. Nilkanth B. Shelar, *Laboratory Assistant*
Ms. Indra Kundu, *Ph. D. Scholar*
Ms. Kshitija S. Rahate, *Ph. D. Scholar*
Ms. Karishma Desai, *Ph. D. Scholar*
Ms. Ulka Gawde, *Ph. D. Scholar*
Ms Amisha Dalvi, *Ph. D. Scholar*

BIOSTATISTICS DEPARTMENT

Dr. Shahina Begum, *Scientist 'F'*
Dr. Ranjan Kumar Prusty, *Scientist 'C'*
Mr. Mahadev Bhise, *Scientist 'C'*
Mrs. Madhuri Kumre, *Laboratory Assistant*

CELL PHYSIOLOGY AND PATHOLOGY LABORATORY

Dr. Geetanjali Sachdeva, *Scientist 'G' and Director*
Dr. Uddhav K. Chaudhari, *Scientist 'E'*
Dr. Nupur Mukherjee, Scientist C
Ms. Sushma Gadkar, *Sr. Technical Officer-2 & Ph. D. Scholar*
Mr. Balaji G. Jamdare, *Technical Assistant (Life Sciences)*
Ms. Rupal Shah, *Technical Assistant (Dietician)* ** Joined on 29.04.2024*
Mr. Balvant P. Mayekar, *Laboratory Assistant*
Mr. Mahesh Sakharam Dhuri, *Lab. Attendant - 1*
Ms. Rithika Rajendran, *Ph. D. Scholar*
Ms. Junita Desouza, *Ph. D. Scholar*
Ms. Itti Munshi, *Ph. D. Scholar*
Mr. M. I. F. J. Shaikh, *Ph. D. Scholar*
Mr. Aditya Khandvilkar, *Ph. D. Scholar*
Mr. Golden R. Paswan, *Ph. D. Scholar*
Ms. Nikita Sharma, *Ph. D. Scholar*
Ms. Nisha Bilkhiwal, *Ph. D. Scholar*
Ms. Rishigandha Salunkhe, *Ph. D. Scholar*

CELLULAR AND STRUCTURAL BIOLOGY LABORATORY

Dr. Bhakti Pathak, *Scientist 'F'*
Dr. Dhanashree Jagtap, *Scientist 'E'*
Dr. Antara Banerjee, *Scientist 'C'*
Ms. Ananya Breed, *Technical Officer -C*
Mr. Bhalchandra J. Kulkarni, *Technical Officer –B*
Mr. Jesing M. Rabhadiya, *Laboratory Assistant*
Mr. Vasudev V. Pawar, *Laboratory Assistant*
Ms. Vaidehi Miya, *Ph. D. Scholar*
Ms. Apoorva Pawar, *Ph. D. Scholar*
Ms. Meghali Borkotoky, *Ph. D. Scholar*
Ms. Pradnya Mohite, *Ph. D. Scholar*

CHILD HEALTH RESEARCH DEPARTMENT

Dr. Suchitra Surve, *Scientist 'D'*
Dr. Kiran Munne, *Scientist 'C'*
Ms. Leena V. Tendulkar, *Sr. Technical Officer - 2*
Ms. Rachana R. Dalvi, *Sr. Technical Officer - 2*
Ms. Shilpa C. Kerkar, *Technical Officer -C*
Ms. Sharmila S. Kamat, *Technician -2*
Ms. Sarita Bhange, *Attendant (Services)*
Ms. Guguloth Saritha, *Lab. Attendant – 1* ** Resigned on 18.10.2024*
Ms. Sonali Kamble, *Technician – 1* ** Resigned on 20.09.2024*
Mr. Mansingh Balmiki, *Lab. Attendant – 1* ** Joined on 26.09.2024*

CLINICAL RESEARCH LABORATORY

Dr. Rahul Gajbhiye, *Scientist 'E'*
Dr. Periyasamy Kuppusamy, *Scientist 'C'*
Dr. Hrishikesh Munshi, *Scientist 'C'* ** Transferred from ICMR Hqrs on 29.04.2024*
Dr. Sandhya Anand, *Technical Officer-C*
Mr. Krishna R. Naik, *Laboratory Assistant*
Ms. Vaishali Chalke, *Labortory Assistant*

GAMETE IMMUNOBIOLOGY LABORATORY

Dr. Priyanka Parte, *Scientist 'F'* ** Retired on 30.10.2024*
Dr. Kushaan Khambata, *Scientist 'C'*
Dr. Shagufta Khan, Sr. *Technical Officer - 2*
Mrs. Smita V. Yevate, *Technical Officer-B*
Mr. Madhukar More, *Laboratory Assistant*
Mr. Devidas Gaikwad, *Laboratory Assistant*
Ms. Durva Panchal, *Ph. D. Scholar*

GENETIC RESEARCH CENTER

Dr. Shailesh Pande, *Scientist 'E'*
Dr. Shaini Marina Joseph, *Scientist 'D'*
Dr. D. V. S. Sudhakar, *Scientist 'D'*
Dr. Venkanna Bhanothu, *Scientist 'C'* ** Transferred to ICMR-NIN on 04.04.2024*

Ms. Neha Minde, *Sr. Technical Officer-2*
Mr. Harshvardhan Gawde, *Sr. Technical Officer-2*
Ms. Shiny Babu, *Sr. Technical Officer-2*
Mr. Desavath C. Naik, *Technical Assistant (Life Sciences)*
Ms. Rushali Jadhav, *Technician – 1*
Mr. Kisan Mali, *Laboratory Assistant*

INFECTIOUS DISEASES BIOLOGY LABORATORY
Dr. Sadhana Gupta, *Scientist 'D'*
Ms. Mohini Barku Vishve, *Technician - 1 (Laboratory)* ** Resigned on 30.09.2024*
Mr. Anil S. Hatle, *Laboratory Assistant*
Mr. Alok K. Tembhurne, *Ph. D. Scholar*
Ms. Samruddhi Ranmale, *Ph. D. Scholar*
Ms. Puja Kumari, *Ph. D. Scholar*

INNATE IMMUNITY LABORATORY
Dr. Susan Thomas, *Scientist F*
Ms. Aishwarya Rao, *Ph. D. Scholar*
Ms. Hajra Gupta, *Ph. D. Scholar*
Ms. Rutwija Athalye, *Ph. D. Scholar*

MOLECULAR AND CELLULAR BIOLOGY LABORATORY
Dr. Deepak N. Modi, *Scientist 'G'*
Ms. Sarika Ahire, *Technical Officer*
Mr. Sanjay G. Sakpal, *Laboratory Assistant*
Mr. Ramesh D. Shinde, *Laboratory Assistant*
Ms. Nancy S. Achary, *Ph. D. Scholar*
Ms. Richa R. Sharma, *Ph. D. Scholar*
Mr. Anshul Bhide, *Ph. D. Scholar*
Ms. Babita Negi, *Ph. D. Scholar*
Mr. Pratik Rasal, *Ph. D. Scholar*
Mr. Ponsankaran R *Ph. D. Scholar*

MOLECULAR ENDOCRINOLOGY LABORATORY
Dr. Srabani Mukherjee, *Scientist 'G'*
Dr. Pallavi Shukla, *Scientist 'D'*
Ms. Sushma Khavle, *Technical Officer-C*
Ms. Gayatri Shinde, *Technical Officer-C*
Ms. Nanda Joshi, *Technical Officer-B*
Mr. Pradip More, *Technician 'C'*
Mr. Vijay M. Khedekar, *Laboratory Assistant*
Mr. Aalaap Naigaonkar, *Ph. D. Scholar*
Ms. Snehal Bhingardeve, *Ph. D. Scholar*
Ms. Komal Khade, *Ph. D. Scholar*
Ms. Medini Samant, *Ph. D. Scholar*
Ms. Manisha Kumari, *Ph. D. Scholar*
Ms. Jyotsna Khitani, *Ph. D. Scholar*

MOLECULAR IMMUNOLOGY AND MICROBIOLOGY

Dr. Vikrant Bhor, *Scientist 'E'*
Dr. Itta Krishna Chaaithanya, *Scientist 'C'*
Ms. Gauri Bhonde, *Technical Officer-C*
Mr. Omkar Shiraskar, *Technical Assistant (Life Sciences)*
Mr. Sunil D'Souza, *Laboratory Assistant*
Ms. Kalyani A. Karandikar, *Ph. D. Scholar*
Mr. Pratik Devadiga, *Ph. D. Scholar*
Ms. Jyoti S. Batgire, *Ph. D. Scholar*
Mr. Rohan Pawar, *Ph. D. Scholar*
Ms. Niteeka Chandel, *Ph. D. Scholar*
Ms. Shreya Pravinkumar Peddakolmi, *Ph. D. Scholar*

NEUROENDOCRINOLOGY LABORATORY

Dr. Dipty Singh, *Scientist 'E'*
Dr. Kumari Nishi, *Scientist 'C'*
Ms. Shobha Sonawane, *Technical Officer - C*
Ms. Reshma Gaonkar, *Technical Officer - B*
Ms. Vaishali H. Nakhawa, *Sr. Technical Officer- 2*
Mr. Mahadev G. Pawar, *Technician 'C'* ** Retired on 30.09.2024*
Mr. Suryakant Mandavkar, *Technician 'C'* ** Retired on 31.05.2024*
Mr. Deepak B. Shelar, *Technician 'C'*
Mr. Praveen Kumar Verma, *Technician - 1 (Laboratory)*
Mr. Prasad G. Tawade, *Lab Assistant*
Ms. Sweta Mohan, *Ph. D. Scholar*
Ms. Mamata V. Datar, *Ph. D. Scholar*
Ms. Delna Irani, *Ph. D. Scholar*
Ms. Deepashika Arya, *Ph. D student*
Ms. Anushruti Singh, *Ph. D student*
Ms. Nayanika Roy, *Ph. D student*
Mr. Aman Chaurasia, *Ph. D student*

OPERATIONAL AND IMPLEMENTATION RESEARCH DEPARTMENT

Dr. Beena Joshi, *Scientist 'G*
Dr. Ragini Kulkarni, *Scientist 'F'*
Ms. Bhavya M K, *Scientist 'B'*
Mr. Srinivas Gurav, *Scientist B (Non Medical)*
Mrs. Kimthianhoih, *Technical Assistant (Social Worker)*
Mr. Iranna S. Mashal, *Technician - 2*
Mr. Pravin S. Sanap, *Technician - 2*
Ms. Devyani Dhiraj Rathod, *Lab. Attendant - 2*
Mr. J. Jayanth, *Lab. Attendant – 1*

PRECLINICAL REPRODUCTIVE AND GENETIC TOXICOLOGY CENTRE

Dr. Vikas D. Dighe, *Scientist 'F'*
Mr. Sudhir V. Jadhav, *Sr. Technical Officer-2*
Mr. Manish Ghosalkar, *Sr. Technical Officer-2*
Mr. Yash N. Kamble, *Technical Assistant (Life Sciences)*
Mr. Pravin S. Salunkhe, *Sr. Technician-2*
Ms. Bhavana Bhat, *Ph. D. Scholar*
Mr. Aniruddh Tiwari, *Ph. D. Scholar*
Mr. Bipradip Saha, *Ph. D. Scholar*
Ms. Shilpa Kerkar, *Ph. D. Scholar*
Ms. Shruti Atmaram Desai, *Ph. D. Scholar*

REPRODUCTIVE AND BONE HEALTH DEPARTMENT

Dr. Lalita Savardekar, *Scientist 'F'*
Ms. Neera Mehta, *Technical Officer 'C'*
Mr. Kiran Y. Chavan, *Laboratory Assistant*
Ms. Swarupa R. Khedekar, *Technician - 1 (Laboratory)*
Mr. V. Prashanth, Lab. Attendant – 1
Mrs. Pradhnya Nikam, *Technician - 1 (Laboratory)* ** Joined on 04.02.2025*

REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY DEPARTMENT

Dr. Anushree Patil, *Scientist 'F'*
Dr. Deepti Tandon, *Scientist 'C'*
Mrs. Varsha H. Tryambake, *Principal Technical Officer* ** V.R.S. on 08.07.2024*
Ms. Pratibha Kokate, *Sr. Technical Officer*
Ms. Shobha Banage, *Sr. Technical Officer-2*
Ms. Sunita Kale, *Sr. Technical Officer-2*
Ms. Anamika Akula, *Sr. Technician -2*
Ms. Sunita Kharat, *Sr. Technician-2*
Ms. Sunita Kendre, *Laboratory Assistant*
Ms. Akshaya A. Rathod, *Lab. Attendant – 2*
Ms. Shalini S. Lambade, *Lab. Attendant – 2*
Mr. Ameer Hussain, *Technician - 1 (Laboratory)*

STEM CELL BIOLOGY LABORATORY

Dr. Dhanjit K. Das, *Scientist 'E'*
Dr. Shyla Ravindran, *Technical Officer -C* ** Retired on 30.11.2024*
Mrs. Vaishali N. Bhogate, *Technical Officer-C*
Ms. Jidnyasa Rajendra Kore, *Technical Assistant (Life Sciences)*
Mr. Sandip C. Gondhalekar, *Sr. Technician - 2*
Mr. Shivaji Gondhali, *Laboratory Assistant*
Mr. Sanjay Ghadigaokar, *Laboratory Assistant*
Mr. Bipin R. Shekhar, *Ph. D. Scholar*
Ms. Debolina Saha, *Ph. D. Scholar*
Ms. Mousumi Bal, *Ph. D. Scholar*
Mr. Aliyah Mohammed Husain Sayyed, *Ph. D. Scholar*

VIRAL IMMUNOPATHOGENESIS LABORATORY

Dr. Vainav Patel, *Scientist F*
Ms. Varsha Padwal, *Sr. Technical Officer-3* ** Retired on 30.09.2024*
Ms. Shilpa M. Velhal, *Sr. Technical Officer-2*
Mr. Sharad T. Bhagat, *Technical Officer –C*
Mr. Ganesh A. Shinde, *Laboratory Assistant*
Mr. Satyajit Sunil Musale, *Laboratory Attendant-1*
Ms. Snehal Kaginkar, *Ph. D. Scholar*
Ms. Harsha Palav, *Ph. D. Scholar*
Ms. Shilpa Bhowmick, *Ph. D. Scholar*
Mr. Nandan Mohite, *Ph. D. Scholar*
Ms. Sapna Yadav, *Ph. D. Scholar*
Mr. Sharad Tejrao Bhagat, *Ph. D. Scholar*

EXPERIMENTAL ANIMAL FACILITY

Dr. Dhanjit K. Das, *Scientist 'E'*
Dr. Siddhanath.M. Metkari, *Principal Technical Officer*
Mr. Ravindra G. Rane, *Laboratory Assistant*
Mr. Prakash R. Chavan, *Laboratory Assistant*
Mr. Ganesh C. Patil, *Laboratory Assistant*
Mr. Ratilal S. Sandis, *Laboratory Assistant*
Mr. Subhash B. Bavdane, *Laboratory Assistant*
Mr. Maruti V. Mali, *Lab. Attendant – 2*
Mr. Shankar S. Chavan, *Lab. Attendant – 2*
Mr. Kiran V. Kadam, *Lab. Attendant – 2*
Mr. Subhash S. Kadam, *Lab. Attendant – 2*
Mr. Prakash K. Shingare, *Lab. Attendant – 2*
Mr. Mohmmed Subhan Mohammed Saheb Qureshi, *Lab. Attendant - 2*
Mr. Rajendra S. Marchande, *Lab. Attendant - 2*
Mr. Bhupendra K. Koli, *Lab. Attendant - 2*
Mr. Yogesh B. Shinde, *Lab. Attendant - 2*
Mr. Amol V. Anglekar, *Lab. Attendant - 2*
Mr. Shree Ram, *Lab. Attendant - 1 (Welder)*
Mr. Roushan Kumar, *Lab. Attendant - 1*
Mr. Musale Akshay Sunil, *Lab. Attendant - 1*
Mr. Adepu Prashanth, *Lab. Attendant - 1*
Mr. Sujendra, *Lab. Attendant - 1*
Mr. Arvind Kumar, *Lab. Attendant - 1*
Mr. Sarang Suresh Mane, *Lab. Attendant - 1*
Mr. Annat Kumar, *Lab. Attendant - 1*
Mr. Mohammad Faizan Shah, *Lab. Attendant - 1* ** Joined on 01.04.2024*
Mr. Nagothu Shivakrishna, *Lab. Attendant - 1* ** Joined on 04.04.2024*
Mr. Sarvesh Gode, *Lab. Attendant - 1* ** Joined on 22.07.2024*

CONFOCAL FACILITY
Dr. Dipty Singh, *Scientist 'E'*
Ms. Shobha Sonawane, *Technical Officer- C*
Ms. Reshma Gaonkar, *Technical Officer- B*

DNA SEQUENCING FACILITY
Dr. Srabani Mukherjee, *Scientist 'G'*
Ms. Nanda Joshi, *Technical Officer- B*

ELECTRON MICROSCOPY FACILITY
Dr. Dipty Singh, *Scientist 'E'*
Dr. Kumari Nishi, *Scientist 'C'*
Ms Vaishali Nakhwa, *Sr. Technical Officer-2*
Mr. Mahadev G. Pawar, *Technician 'C'*

FLOW CYTOMETRY FACILITY
Dr. Srabani Mukherjee, *Scientist 'F'*
Ms. Sushma Khavale, *Technical Officer-C*
Ms. Gayatri Shinde, *Technical Officer- C*

ETHICS SECRETARIAT
Dr. Vikrant Bhor, *Scientist 'E'*
Ms. Zakiya Ansari, *Technical Assistant*
Mr. Anand H. Hankare, *Laboratory Assistant*
Mr. Shivraj Toshatwad, *Lab. Attendant - 1* ** Joined on 22.07.2024*

ACCOUNTS
Mr. Waman Narkar, *Accounts Officer (Additional Charge)*
Mr. Vishnukant M. Satav, *Section Officer*
Mr. Sandip Gaikwad, *Assistant*
Ms. Swara M. Zagde, *UDC*
Mr. Mandar Shinde, *UDC*
Mr. Motiram Gavit, *UDC*
Mr. Sunil T. Chorage, *UDC*

ADMINISTRATION
Ms. Swati Gaikwad, *Sr. Administrative Officer*
Mrs. Seema Deshmukh, *Administrative Officer* ** Retired on 30.07.2024*
Mr. Prasanna K. Chavan, *Section Officer*
Mr. Aditya Sarnaik, *Assistant*
Mr. Kunal Pawar, *UDC*
Ms. Meghana Nikam, *LDC* ** Joined on 18.07.2024*
Mr. Kumar Keni, *Laboratory Assistant*
Mr. Mangesh Yadav, *Lab. Attendant - 1* ** Joined on 29.04.2024*
Mr. Kamlesh Kumhar, *Lab. Attendant - 1* ** Joined on 02.08.2024*

GENERAL ADMINISTRATION
Mrs. Akanksha A. Dalvi, *Section Officer*
Mr. Prabhat Chauhan, *Technician - 1 (Civil)* ** Joined on 03.04.2024*

PROJECT CELL
Mr. Vinod M. Guram, *Technical Officer-B*
Mr. K.R. Sukumar, *Technical Assistant*
Ms. Ruchita Veerkar, *UDC*

PAY BILL SECTION
Mr. Haresh V. Jadhav, *Section Officer*
Mr. Shailendrakumar A. Sangelkar, *Assistant*
Mr. Sameer S. Petkar, *UDC*
Mr. Harshal D. Raut, *UDC*

STORES (NIRRH Budget)
Ms. Supriya Lad, *Section Officer*
Mr. Gurunath M. Darpe, *Assistant*
Mr. Sajith V, *Office Assistant*
Mr. Chetan G. Nakade, *Technical Assistant (Mechanical)*
Mr. Shivaji S. Sawant, *UDC*
Mr. Nilesh P. Bavdane, *Laboratory Assistant*
Mr. Yogesh C. Joshi, *Lab. Attendant - 2*

STORES (Extramural Budget)
Mr. Vinod Guram, *Technical Officer-B*
Mr. Aditya Dinkar Ghodke, *Assistant*
Ms. Mamta T. Jadhav, *UDC*

ESTABLISHMENT
Mrs. Akansha A. Dalvi, *Section Officer*
Mr. Khimji T. Solanki, *Section Officer* ** Retired on 30.06.2024*
Ms. Kranti S. Patankar, *Personal Assistant*
Ms. Harsha Kurup, *UDC*
Mr. Rakesh K. Parab, *Laboratory Attendant – 1*

ICMR INTERNATIONAL HOSTEL AND STAFF QUARTERS
Dr. Shahina Begum, *Scientist F*
Mr. Nitesh Rathor, *Technical Assistant (Mechanical)* ** Joined on 04.04.2024*

INSTRUMENTATION RESEARCH & MAINTENANCE/WORKSHOP
Mr. Vinay D. Koli, *Sr. Technical Officer*
Mr. Jagdish S. Patharwat, *Technical Officer-C*
Mr. Joseph D. Lobo, *Sr. Technician - 3*
Mr. Vinod G. Rane, *Sr. Technician – 3*
Mr. Gopu Shivakrushna, *Technical Assistant (Civil)*
Mr. Sudip Maity, *Technical Assistant (Electrical)* ** Joined on 06.08.2024*

Mr. Kaustubh Ghaywat, *Technical Assistant (Electronics & Instrumentation)* * *Joined on 01.08.2024*
Mr. Devesh Prajapati, *Technical Assistant (Mechanical)* * *Resigned on 11.10.2024*
Mr. Somesh Manohar Mahadik, *Technician - 1 (Electrical)*
Mr. Vishal Subhash Jadhav, *Technician - 1 (Mechnical)*
Mr. Sudhansh Sanjay Kamble, *Technician -1 (Electronics/ Instrumentation)*
Mr. Ajit D. Bhandwalkar, *Laboratory Assistant*
Mr. Mohan Singh, *Lab. Attendant - 1 (Refrigeration & Air Conditioning)*
Mr. Sachin Dilip Salok, *Lab. Attendant - 1 (Refrigeration & Air Conditioning)* * *Joined on 04.04.2024*
Mr. Dhanna Ram, *Lab. Attendant - 1 (Carpenter)*
Mr. Indrraj, *Lab. Attendant - 1 (Plumber)* * *Resigned on 13.03.2025*
Mr. Rajendra Kumar Meena, *Lab. Attendant - 1 (Electrician)*
Mr. Vivek Kumar Nayak, *Lab. Attendant - 1 (Mason)*

INSTRUMENTATION & MAINTENANCE, NCPBR
Dr. Vikas D. Dighe, *Scientist F*
Mr. Pankaj Meena, *Technical Assistant (Civil)*
Mr. Abhishek Singh, *Technical Assistant (Civil)* * *Joined on 14.08.2024*
Mr. Amit Kumar, *Technician - 1 (Mechanical)* * *Resigned on 24.01.2025*
Mr. Sonu Meena, *Lab. Attendant - 1 (Electrician)*

LIBRARY AND INFORMATION CENTER
Dr. Prabhjeet Kaur, Library and Information Officer
Ms. Simmy Saji, *Technical Officer-C*
Ms. Priya Menon, *Technical Officer-C*
Mr. Vaibhav L. Shinde, *Technician- 2*
Mr. Amar Gode, *Laboratory Assistant*

SECURITY AND MAINTENANCE
Mr. Joseph D. Lobo, *Sr. Technician - 3*
Ms. Swaruparani Karunakaran, *Office Assistant* * *Retired on 31.05.2024*
Mr. Shirin F. Cardoza, *Laboratory Assistant*
Mr. Manoj S. Palande, *Laboratory Assistant*
Mr. Satyawan Y. Urankar, *Lab. Attendant - 2*
Mr. Narendra S. Bhilare, *Sr. Technician - 2*
Mr. Ganesh P. Narayan, *Sr. Technician - 2*
Mr. Sundarraj S. Subramanian, *Technician - 2*
Mr. Sunil K. Jadhav, *Technician - 2*
Mr. A. Y. Lokhande, *Laboratory Assistant* * *Retired on 30.04.2024*
Mr. Rajan Naik, *Laboratory Assistant*
Mr. Sanjay Misal, *Laboratory Assistant*

ACTIVITIES DURING 2024-2025

18. ACITIVITIES DURING THE YEAR 2024-2025

DHR sponsored course on 'Human Disease Models: Approaches, Advances and Applications' was organized during May 6-31, 2024

DHR sponsored course on 'Application of Medical Genetics in Reproductive and Child Health' was organized during June 3-28, 2024

ICMR-DHR sponsored workshop on 'Applications of Artificial Intelligence and Machine Learning in Disease Informatics' was organized during June 4-7, 2024.

An awareness cum screening program was organized by MRHRU Vani and Public Health Department, Maharashtra at Janata Vidyalaya, Ahivantwadi Village, Dindori Block Nashik for high school students, ASHA workers & ANC mothers to celebrate World Sickle Cell Day on June 19, 2024

International Day of Yoga was celebrated by Child Health Clinic team with 300 students at Shivaji Vidyalay, Kalachowki on June 21, 2024

Awareness program was conducted by MRHRU Dahanu in tribal area of Ganjad village for pregnant / lactating / newly married women and Anganwadi workers to mark the World Breastfeeding Week on August 8, 2024

Staff and students of ICMR-NIRRCH celebrated the 78th Independence Day on August 15, 2024

An interactive program on obesity in adolescents was organized by Reproductive and Bone Health Clinic team for 100 students at Prabhavati Kulkarni High School on August 16, 2024

Birth anniversary of Hockey Legend Major Dhyan Chand was commemorated by organizing events for National Sports Day on August 29, 2024

A preventive health checkup was organized for sanitation workers and animal house staff as part of 'Swacchata Hi Seva' campaign on September 24, 2024

Mpox awareness campaign was organized for 150+ students by MRHRU Vani staff under 'Swacchata Hi Seva' campaign on September 26, 2024

A walkathon was organized by MRHRU Dahanu staff to spread awareness about 'Swacchata Hi Seva' campaign on September 30, 2024

MRHRU Vani organized an awareness session on Mpox for ASHAs, ANMs and MPWs from PHCs Pandane and Khedgaon, Dindori Block, Nasik, Maharashtra on September 30, 2024

MRHRU Dahanu team conducted screening of children for Sickle Cell disease at Anganwadi, Kajali Subcentre, Talasari, Palghar district on October 24, 2024

Children's Day was celebrated by Child Health Clinic for 110 pre-primary school children at Ahilya Vidyamandir, Kalachowki on November 14, 2024

A skit competition and cultural program were organized for staff and students to celebrate International Men's Day on November 21, 2024

Workshop 'Opening Gates: Conception Foundations and Exploring Contraceptive Innovations' was organized during December 2-6, 2024

A structured module on Yoga in PCOS developed in collaboration with Kaivalyadham Institute of Yoga and funded by DST was launched at 5th Anniversary Celebration of Science and Heritage Research Initiative (SHRI) on December 16, 2024

Scientific Advisory Committee was held during December 19-20, 2024

Satya Narayan puja was organized to mark the Foundation Day of ICMR-NIRRCH on February 21, 2025

A painting competition was organized for students of Ahilya Vidya Mandir, Secondary School, Abhyudaya Nagar to celebrate National Science Day on February 28, 2025

Local Research Advisory Committee meeting was organized along with GGMC & JJ Hospital and Public Health Department, Government of Maharashtra at MRHRU, Dahanu on February 28, 2025

DBT-NIDAN Kendra was inaugurated by Dr Mohan Joshi at ICMR-NIRRCH on March 19, 2025

A session on the role of genetics in nursing practice was organized for MSc Nursing students from the Institute of Nursing Education, JJ Hospital on March 25, 2025