DBT Embarks on Pre-term Birth Program

Preamble: Program on pre-term birth is the first inter-institutional program on maternal-infant health and spontaneous pre-term birth sciences in India funded by the Department under the Grand Challenge Program. The total cost of the project is Rs. 48.85crore for a period of 5 years. It envisages a multidisciplinary research effort to **predict & diagnose Preterm Birth** (PTB) by enhancing the knowledge of the underlying pathophysiological mechanisms. It is expected that the clinically relevant research outputs from the study will aid characterization of biological, clinical and epidemiological risk factors to achieve appropriate risk stratification of mothers who may deliver before term. These in turn would provide a basis for discovery of novel therapeutic agents & determine appropriate timing for their clinical application. Together, it would strengthen the commitment of the Department of Biotechnology to health equity, contributing significantly to reduction in infant and maternal mortality.

Importance: Globally PTB is the single largest cause of neonatal deaths. In India's 27 million birth cohort annually, born annually, 3.6 million are born preterm, and over 300,000 of them die each year. India, contributes the highest number of PT birth and deaths worldwide, specifically 25% of the overall global preterm related deaths. Despite substantial efforts to introduce new therapies for prevention, the problem persists and contributes significantly to neonatal and infant mortality and morbidity. Preterm birth has substantial long-term consequences for those affected, well in to late childhood and adult life.

Emphasis: The basic aim of the project is to understand the **epidemiology of PTB, its genetic and environmental interactions, and changes in vaginal microbial landscape**. The program highlights include development and evaluation of putative biomarkers, identification of simple microbiological tool based vaginal risk factors, modulation of vaginal microbiota for therapeutic purposes and evaluation of environmental modification chosen from SNP analysis. Some of the major public health concerns addressed by the program are biological risks and processes of fetal growth and PTB, clinical consequences of PTB and intra uterine growth retardation.

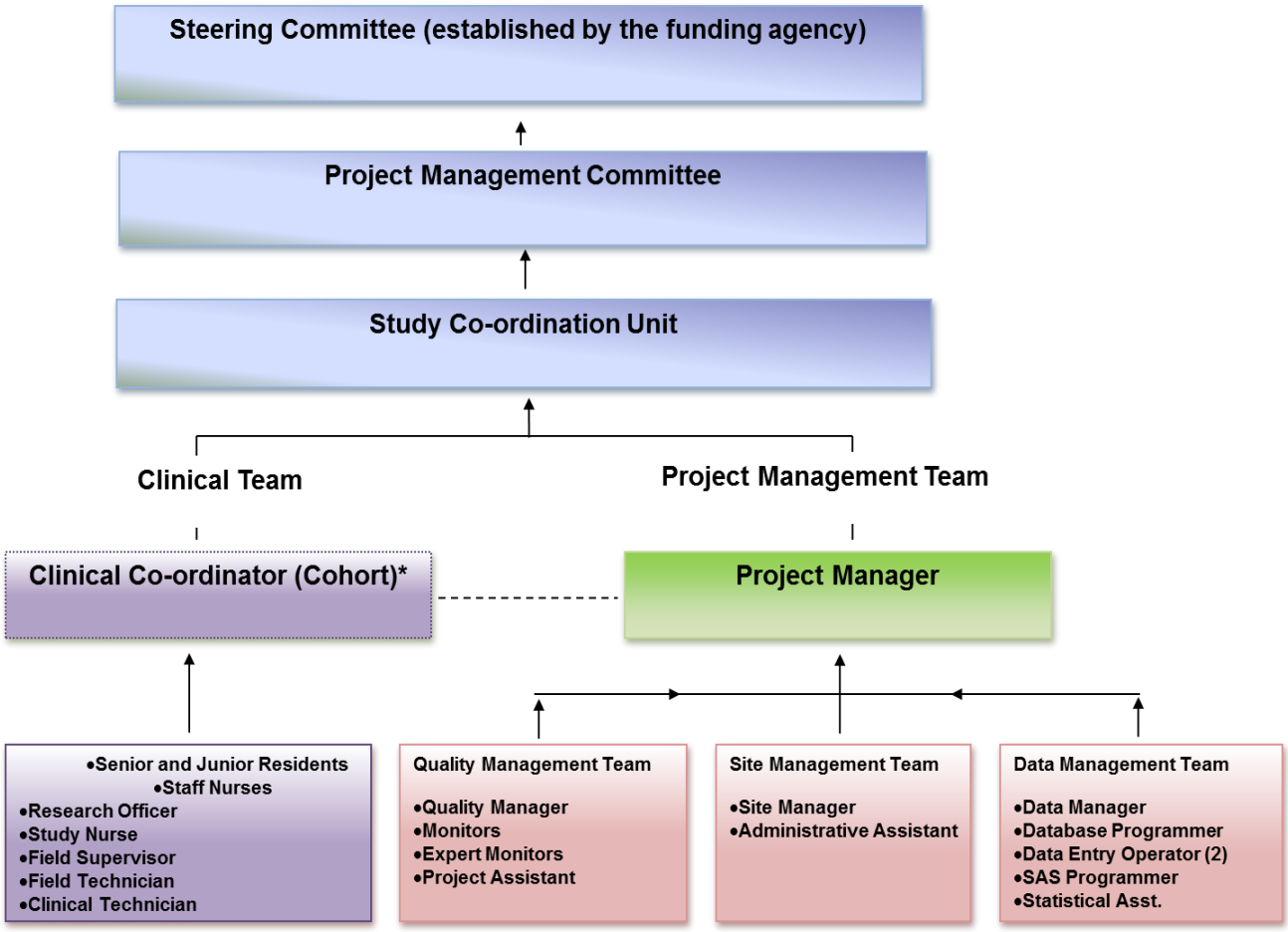
Strategic Plan and Future Perspectives: The initial step will be to establish a hospital-based cohort of pregnant women, starting from the first trimester, each of whom will be followed till delivery. Applying a cross-disciplinary approach, it is proposed to elucidate possible mechanisms and outline the etiology of PTB. **Whole-genome screens, study of genomics, epigenomics and proteomics** in different time frames, will be done to assess the biological risk factors and dynamic nature of PTB. A **metagenomic** approach for profiling of vaginal microbial flora would be taken up and this information will be correlated with PTB, and other dietary and epidemiological risk factors.

The long-term goal envisages clinically relevant research outputs that would aim to (i) achieve appropriate risk stratification of women early in pregnancy (ii) identify simple and better prediction tools that will recognize the optimal time of prediction & clinical intervention, (iii) develop additional strategies to identify presence of unusual/novel microbes that could serve as biomarkers, (iv) identify focused remedies targeting one or more mechanistic pathways (e.g. infection, inflammation, hormonal), (v) apply currently available interventions based on better understanding of biological mechanisms.

The cohort and the biospecimens collected from enrolled women will serve as a resource for future studies and additional research questions from new investigators. Apart from addressing the basic biomedical research questions it would also help in training manpower, enhancing research capacity and formulation of viable policies.

***Approach*:** PTB program actively involves bridging expertise from disparate fields, such as, pediatrics, gynecology, infectious disease biology, epidemiology, microbiology, immunology, platform technologies, cellular & molecular biology, genetics, statistics and computational & systems biology. **The team also comprises of a clinical team and a project management team**. The clinical team will be stationed at Gurgaon General Hospital, which is the site of study, and comprises of the clinical coordinator, research physicians, nurses, attendants, field workers and field supervisors. The project management team comprises of specialized groups looking after quality management, site management team and the data management.

Flow chart of the study organization



* Radiology team will work with the Clinical Team

Management and Monitoring:

The Program will be monitored by a Steering Committee responsible for strategic guidance, review of study scientific data and advice on new directions for future research. The Steering Committee is represented by eminent national and international experts in the important domain areas. The Program Management Committee would address matters related to scientific, technical and financial aspects on regular basis and report to the Steering Committee. Further details are provided below:

The Team:

1. **Translational Health Science and Technology Institute (THSTI), Gurgaon**: An autonomous Institute of DBT and houses two more components involved in the PTB program, viz.:

(a) Pediatric Biology Centre (PBC): PBC will be the main coordinator of the program. It will be responsible for establishing and managing the cohort, for implementing the SOPs, and for conducting the epidemiological studies.

(b) Centre for Human Microbial Ecology (CHME): CHME will be responsible for **the microbiome analyses**. Phylotyping, abundance, functional prediction and significance of vaginal microbiome will be done jointly by **CHME and TCS** Innovation Labs.

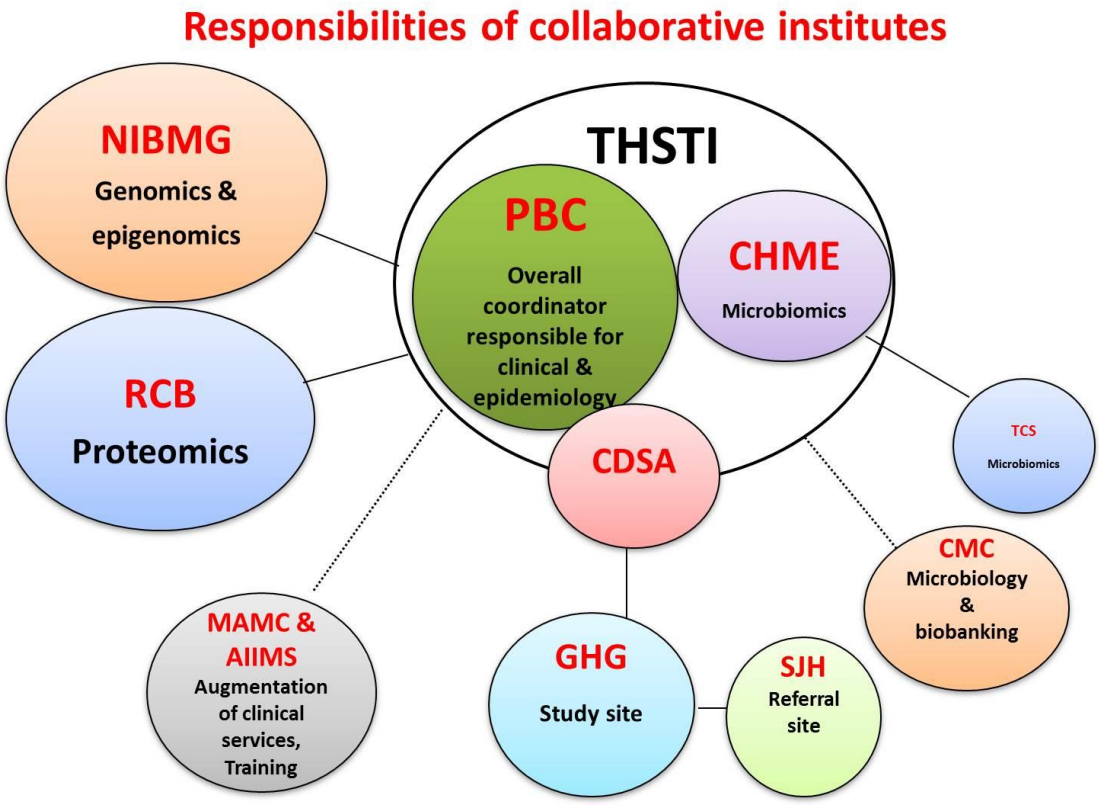
2. **General Hospital Gurgaon (GHG)**: This is the main study site where the cohort will be established.

3. **Regional Centre for Biotechnology (RCB), Gurgaon**: It is a category-II institution under the auspices of UNESCO, established by the Department. It will be responsible for proteomic analysis.

4. **National Institute of Biomedical Genomics (NIBMG), Kalyani, West Bengal**: An autonomous institute of DBT which would be responsible for genomic and epigenomic assays.

NIBMG and RCB will exchange information on an ongoing basis, as a part of designing new experiments or for validating inferences drawn by each other. **THSTI and NIBMG** will also exchange information on micronutrient intakes and epigenomics. **THSTI and RCB** will be constantly engaged with each other because the microbiome ecology and levels of various proteins change in a dynamic manner and their changes are expected to be correlated. **NIBMG**, with a major arm that specializes in biostatistics and statistical genomics, will provide help to the other institutions in respect of epidemiological and other statistical analyses, as required.

5. **CDSA**: This is an extramural unit of THSTI and would be involved in implementation and quality management of the study.



In addition to the aforesaid institutes, other institutes/organizations involved are Maulana Azad Medical College (MAMC), All India Institute of Medical Sciences (AIIMS), Safdarjung Hospital (SJH) New Delhi, Christian Medical College (CMC), Vellore, Tata Consultancy Services (TCS), The Department of Health Research (DHR) & Indian Council of Medical Research (ICMR) and National Rural Health Mission (NRHM).

***Note*:**

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