Swapnil K., Snehal M.

THE ROLE OF THE MATERNAL GUT MICROBIOME IN PREGNANCY OUTCOMES

Tutor: assistant professor Pavlukova S.
Department of Obstetrics and Gynecology
Belarusian State Medical University, Minsk

As traditional prenatal care fails to address the high incidence rates of gestational disorders, the modifiable nature of the gut microbiome is increasingly defining global maternal health. Gestational diabetes mellitus (GDM) affects approximately 14% to 15% of pregnancies worldwide, while hypertensive disorders such as preeclampsia (PE) affect 5% to 8% of gestations, accounting for 16% of global maternal deaths–approximately 42,000 per year. Preterm birth (PTB) continues to be the leading cause of death for children under five, taking almost one million lives annually. The "Developmental Origins of Health and Disease" (DOHaD) framework recognizes the maternal microbiome as a crucial, early-window target for intervention because 50% to 60% of neonatal gut bacteria are maternally derived.

This report details the microbial-metabolic mechanisms through which the maternal gut microbiome controls pregnancy outcomes and fetal neurodevelopment.

This synthesis integrates data from human cohorts and gnotobiotic models (C57BL/6J and SD rats). Human studies utilized 16S rRNA gene sequencing (V3-V4) and metagenomic shotgun sequencing to identify taxonomic markers. Predictive logic was tested using Random Forest models and Latent Profile Analysis (LPA), with performance measured by Area Under the Curve (AUC) and ROC values. Statistical significance was confirmed using two-sided Mann-Whitney tests and Unpaired t-tests.

Technical analysis confirms that healthy pregnancies exhibit higher diversity, whereas pathological states show an over-proliferation of Proteobacteria. In GDM studies, a prospective cohort of 33 individuals (15 GDM, 18 NGT) identified *Streptococcus infantis* as a primary risk marker, with levels positively correlated to blood glucose even after BMI adjustment. Advanced machine-learning models predicted GDM in the first trimester with an AUC of 0.83, while pre-pregnancy signatures of ten bacteria and ten metabolites achieved a ROC of 0.712. For Preeclampsia (PE), groundbreaking evidence demonstrates that dysbiosis causes a significant increase in fetal resorption at 12.5 ($p=0.0259$) and 14.5 ($p=0.0003$) embryonic days, often leaving only placental remnants. Placental efficiency was significantly reduced ($p=0.0115$), alongside a reduction in the labyrinth area ($p=0.0052$) and upregulated Hif-1α ($p=0.0194$). This was driven by a lower placental glycolytic rate impairing the uNK cell-IFN-β axis ($p=0.0022$), which was successfully reversed with oral glucose supplementation. Regarding PTB, a Ugandan cohort ($n=258$) found that elevated anti-LPS IgG was significantly associated with shorter gestation ($\beta= -1.01$ weeks, $p=0.019$) and reduced birth length ($p=0.039$). A Chinese cohort ($n=63$) confirmed reduced proportions of beneficial *Lactobacillus* in the preterm group ($p < 0.05$). Finally, landmark Nature (2020) research proved that maternal microbial IPA is required for fetal thalamocortical axonogenesis, with adults from GF dams showing altered tactile sensitivity.

The maternal gut microbiome functions as a high-output biological factory whose chemical signals are essential for placental development and the architecture of the fetal brain. The discovery that dysbiosis-induced placental failure and impaired axonogenesis can be reversed in preclinical models using glucose or specific metabolites (IPA, TMAO) offers a new frontier for preventive medicine.