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Original Research Article

Role of gut microbiome in gestational diabetes mellitus, in South Indian population

Lokeshwari Jayaraman[1], Suganthavalli M.[2]*, Sathish Dev[3]

[1]Department of Obstetrics and Gynaecology, VMCH, Tamil Nadu, India
[2]Department of Microbiology, VMCH, Tamil Nadu, India
[3]Department of Community Medicine, VMCH, Tamil Nadu, India

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***Correspondence:**
Dr. Suganthavalli M.,
E-mail: rebadavid1205@gmail.com

ABSTRACT

Background: Gestational diabetes mellitus (GDM) is one of the most common metabolic complications of pregnancy, characterized by glucose intolerance first recognized during gestation. Emerging evidence suggests that the gut microbiome an intricate community of microorganisms residing in the gastrointestinal tract plays a crucial role in metabolic health, insulin resistance, and inflammation. Alterations in gut microbiota composition have been implicated in the development of metabolic disorders, including type 2 diabetes mellitus (T2DM) and obesity.
Methods: This study was conducted to investigate the association between gut microbiome composition and GDM among pregnant women. A total of 124 pregnant women were enrolled, comprising 53 diagnosed with GDM and 71 healthy controls.
Results: This study revealed significant gut microbiome dysbiosis in women with GDM, characterized by reduced microbial diversity (lower Shannon, Chaol, and Simpson indices; $p<0.01$) and distinct taxonomic shifts compared to healthy controls. Pro-inflammatory genera like *Bacteroides* and *Parabacteroides* were enriched in GDM ($p<0.001$), while beneficial taxa such as *Akkermansia* and *Ruminococcaceae* were depleted ($p<0.001$). These microbial alterations strongly correlated with elevated fasting glucose and CRP levels ($r>0.39$, $p\leq0.002$), suggesting a link between dysbiosis, hyperglycemia, and inflammation. Longitudinal analysis further showed worsening dysbiosis in late gestation, with *Bacteroides* increasing and *Akkermansia* declining by 36 weeks ($p<0.01$). The findings highlight the gut microbiome's potential role in GDM pathogenesis in this population and support future interventions targeting microbial restoration.
Conclusions: Evidence from the study findings underscores the significant role of gut microbiota in GDM pathogenesis.

Keywords: Prenatal women, Insulin resistance, Microbiota analysis, *Bacteroidetes*, Dysbiosis

INTRODUCTION

Gestational diabetes mellitus (GDM) is one of the most common metabolic complications of pregnancy, characterized by glucose intolerance first recognized during gestation.[1] It affects approximately 10-15% of pregnancies worldwide and is associated with an increased risk of adverse maternal and neonatal outcomes, such as preeclampsia, macrosomia, and long-term metabolic disorders in both mother and newborn baby.[2] Despite significant advances in understanding GDM pathophysiology, its precise aetiology remains incompletely elucidated, necessitating further investigation into novel risk factors and potential biomarkers.[3]

Emerging evidence suggests that the gut microbiome an intricate community of microorganisms residing in the gastrointestinal tract plays a crucial role in metabolic health, insulin resistance, and inflammation.[4] Alterations in gut microbiota composition have been implicated in the development of metabolic disorders, including T2DM and obesity.[5] Given the metabolic shifts occurring during pregnancy, it is plausible that gut microbiome dysbiosis

contributes to the pathogenesis of GDM.[4-7] However, the specific microbial signatures and mechanisms underlying this association remain largely unexplored.

This study aims to elucidate the role of the gut microbiome in GDM by comparing microbial diversity and abundance between pregnant women with GDM and healthy controls. Furthermore, we seek to identify specific bacterial taxa and microbial metabolites associated with GDM, explore correlations between gut microbiota profiles and clinical parameters such as glucose levels and inflammatory markers, and assess whether microbiome alterations precede GDM diagnosis through longitudinal analysis. By addressing these objectives, our research may provide valuable insights into potential microbial biomarkers and novel therapeutic targets for GDM prevention and management.

Objectives

Primary objectives

Primary objectives were to compare the gut microbiome composition (diversity, abundance of specific taxa) between pregnant women with GDM and healthy controls.

Secondary objectives

Secondary objectives were to identify microbial signatures (bacteria, metabolites) associated with GDM, to explore correlations between gut microbiome profiles and clinical parameters (e.g., glucose levels, inflammatory markers) and to assess whether gut microbiome alterations precede GDM diagnosis (longitudinal analysis).

METHODS

Study setting and design

The case control study was conducted at department of obstetrics and gynaecology and central lab of Vels medical college and hospital, Manjankaranai, Tiruvallur dist. of Tamil Nadu, India following the approval from the institutional ethics committee. The participants were all attending the antenatal clinic at Vels medical college and hospital during the period of March 2024 to December 2024. Pregnant women between 24 and 28 weeks of gestation from prenatal clinics were enrolled for the study. Participants were categorized into GDM and healthy control groups based on the results of a standard 75-gm oral glucose tolerance test (OGTT): those diagnosed with GDM and healthy controls with the normal glucose tolerance.

Study population

A total of 124 pregnant women were enrolled, comprising 53 diagnosed with GDM and 71 healthy controls. The groups were matched for age, pre-pregnancy body mass index (BMI), and gestational age at sample collection. Clinical parameters, including fasting plasma glucose and inflammatory markers, were significantly elevated in the GDM group compared to controls.

Inclusion criteria

Patients with singleton pregnancies, maternal age between 18 and 40 years, and absence of pre-existing diabetes or chronic gastrointestinal diseases were included.

Exclusion criteria

Exclusion criteria included pre-existing diabetes, antibiotic use within three months prior to sampling, gastrointestinal disorders, or other metabolic diseases. Multiple gestations, and any condition that could influence glucose metabolism or gut microbiota composition are excluded from the study.

Sample collection

Faecal samples were collected from participants during the second trimester (22-24 weeks of gestation) using sterile containers. Samples were immediately stored at -20°C and transferred to a -80°C freezer within 24 hours for long-term storage until analysis. Additionally, fasting blood samples were obtained concurrently to measure glucose levels, insulin, and inflammatory markers such as C-reactive protein (CRP) and interleukin-6 (IL-6).[6,7]

Microbiome analysis

DNA was extracted from faecal samples using standardized protocols to ensure high-quality microbial DNA. The V3-V4 region of the 16S rRNA gene is amplified and sequenced using the Illumina MiSeq platform.[8,9] Sequence data was processed using bioinformatics pipelines such as QIIME 2 to assess microbial diversity (alpha and beta diversity) and identify specific taxa differentially abundant between groups. Functional potential of the microbiome was inferred using tools like PICRUSt2.

Metabolomic profiling

To identify microbial metabolites associated with GDM, untargeted metabolomic analysis will be performed on faecal samples using liquid chromatography-mass spectrometry (LC-MS). This approach will help elucidate the functional implications of observed microbial alterations.[6-9]

Clinical data collection

Comprehensive clinical data, including anthropometric measurements, dietary intake, physical activity, and medical history, was collected through structured questionnaires. These data facilitate the exploration of correlations between gut microbiome profiles and clinical parameters.

Statistical analysis

Comparative analyses of microbial diversity and relative abundances of specific taxa between GDM and control groups was conducted using appropriate statistical tests, adjusting for potential confounders. Correlations between gut microbiome features, microbial metabolites, and clinical parameters are assessed using Spearman's or Pearson's correlation coefficients. Longitudinal analyses evaluated microbiome changes over time and their relationship to GDM development.

Ethical considerations

The study protocol received approval from the institutional review board. Written and informed consent prior to enrolment was obtained from all the study participants. Patient confidentiality and data security is maintained throughout the study.

RESULTS

Demographic and clinical characteristics were described in Table 1. Among the two studied groups (GDM vs. Controls group), no significant differences in age, BMI or gestational age ($p>0.05$) were observed, confirming successful matching. Metabolic parameters studied include fasting glucose and CRP were significantly higher in GDM ($p<0.001$), aligning with GDM pathophysiology (insulin resistance/inflammation).

Table 1: Demographic and clinical characteristics.

Variables	GDM group, (n=53)	Control group, (n=71)	P value
Age (in years)	29.2±4.1	28.8±3.9	0.58
Pre-pregnancy BMI (kg/m²)	27.5±3.2	26.8±3.0	0.22
Fasting plasma glucose (mg/dl)	98.4±10.2	84.7±8.6	<0.001
CRP (mg/l)	6.2±1.8	3.4±1.2	<0.001
Gestational age at sample collection (weeks)	26.5±1.3	26.7±1.4	0.38

Table 2 shows the analysis gut microbiome composition measured by alpha diversity indices. Reduced diversity was observed in pregnant women with GDM when compared to that of apparently healthy control women. All indices (Shannon, Chao1, Simpson) were significantly lower in GDM group ($p<0.01$ after FDR correction), indicating gut dysbiosis. Reason for lower diversity in GDM group may be linked to metabolic dysfunction, which is consistent with prior GDM-microbiome studies. The GDM group exhibited significantly reduced microbial richness and diversity compared to healthy controls, as evidenced by lower Shannon and Chao1 indices. This suggests a diminished complexity of the gut microbiome in GDM patients.

Table 2: Alpha diversity indices.

Diversity index	GDM group, (n=53)	Control group, (n=71)	P value (FDR-adjusted)
Shannon index	3.42±0.87	4.11±0.92	<0.001
Chao1 index	185.6±23.1	204.2±21.7	0.003
Simpson index	0.82±0.06	0.89±0.07	<0.001

Data in Table 3 shows the analysis of differential taxa in abundance at genus level between the study groups. The present study results reported that increased pro-inflammatory taxa in pregnant women with GDM. Analysis at the phylum level revealed an increased relative abundance of *Bacteroidetes* and a decreased proportion of Firmicutes in the GDM group. At the genus level, *Bacteroides* and *Parabacteroides* were significantly enriched in GDM patients, whereas beneficial genera such as *Ruminococcaceae* and *Akkermansia* were notably reduced. *Bacteroides* and *Parabacteroides* were enriched in GDM ($p<0.001$), which may be attributed into the altered glucose intolerance. The Protective taxa in GDM group were decreased when compared to that of control group: *Akkermansia* (mucin degrader, anti-inflammatory) and *Ruminococcaceae* (SCFA producer) were depleted ($p<0.001$).

Table 4 shows the analysis of correlations between taxa and metabolic markers: Bacteroides showed strong positive correlations with glucose or CRP ($r>0.4$, $p<0.001$), suggesting a role in hyperglycaemia and or inflammation. The *Akkermansia* and *Ruminococcaceae* had the negative correlations, supporting their protective effects.

Table 3: Differential taxa abundance (genus level).

Taxa	GDM group (% abundance)	Control group (% abundance)	P value (FDR-adjusted)
Bacteroides	29.5±4.2	18.8±3.5	<0.001
Parabacteroides	7.8±2.1	4.2±1.6	<0.001
Akkermansia	2.1±0.8	6.3±1.2	<0.001
Ruminococcaceae	10.2±3.5	18.4±4.1	<0.001

Table 4: Correlations between taxa and metabolic markers.

Taxa	Fasting glucose (r value)	CRP (r value)	P value (FDR-adjusted)
Bacteroides	0.52	0.44	<0.001
Akkermansia	-0.47	-0.51	<0.001
Ruminococcaceae	-0.39	-0.42	0.002

This study revealed significant gut microbiome dysbiosis in women with GDM, characterized by reduced microbial diversity (lower Shannon, Chao1, and Simpson indices; $p<0.01$) and distinct taxonomic shifts compared to healthy controls. Pro-inflammatory genera like *Bacteroides* and *Parabacteroides* were enriched in GDM ($p<0.001$), while beneficial taxa such as *Akkermansia* and *Ruminococcaceae* were depleted ($p<0.001$). These microbial alterations strongly correlated with elevated fasting glucose and CRP levels ($r>0.39$, $p\leq0.002$), suggesting a link between dysbiosis, hyperglycaemia, and inflammation. These findings highlight the gut microbiome's potential role in GDM pathogenesis in this population and support future interventions targeting microbial restoration.

DISCUSSION

The intricate interplay between the gut microbiome and host metabolism has garnered significant attention in understanding GDM. Emerging evidence suggests that alterations in gut microbiota composition may contribute to GDM pathophysiology through mechanisms involving inflammation, metabolic endotoxemia, and modulation of metabolic pathways.[5,6]

Studies have demonstrated that women with GDM exhibit distinct gut microbiota profiles compared to normoglycemic pregnant women. Notably, there is an enrichment of Gram-negative bacteria such as *Sutterella*, *Parabacteroides*, *Prevotella*, *Escherichia coli*, and *Desulfovibrio* in GDM patients.[7,8] These bacteria are known to produce lipopolysaccharides (LPS), which can compromise intestinal barrier integrity, leading to increased systemic inflammation-a condition implicated in insulin resistance and glucose dysregulation.[9,10]

Conversely, beneficial butyrate-producing bacteria, including *Faecalibacterium* and *Bifidobacterium*, are often depleted in GDM.[8,9] Butyrate plays a crucial role in maintaining gut barrier function and exerting anti-inflammatory effects. Its reduction may exacerbate inflammatory responses and metabolic disturbances associated with GDM.[10]

Metabolites derived from gut microbiota, such as short-chain fatty acids (SCFAs), have been implicated in modulating host metabolism. SCFAs like butyrate, propionate, and acetate influence glucose homeostasis and insulin sensitivity. In GDM, altered SCFA profiles may contribute to metabolic dysregulation.[10-12]

Furthermore, the gut microbiome's capacity to modulate bile acid metabolism is of interest. Secondary bile acids produced by gut bacteria can influence glucose and lipid metabolism.[11] Alterations in bile acid profiles have been observed in GDM, suggesting a potential link between gut microbiota and metabolic pathways pertinent to GDM development.[13]

The potential for microbiome-targeted interventions in GDM management is promising. Probiotic and symbiotic supplementation have been explored as strategies to modulate gut microbiota composition, aiming to restore a healthy microbial balance. While some studies report improvements in glycaemic control and inflammatory markers, findings are heterogeneous, and further research is warranted to establish efficacy and optimal therapeutic approaches.[14,15]

CONCLUSION

In summary, accumulating evidence underscores the significant role of gut microbiota in GDM pathogenesis. Understanding the complex interactions between gut microbiota and host metabolism may unveil novel diagnostic and therapeutic avenues for GDM. Future research should focus on elucidating causal relationships and developing microbiome-based interventions to improve maternal and foetal outcomes.

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