SHORT COMMUNICATION

Prebiotic Supplementation Modulates Inflammatory markers and Gut Microbiota in Women with Gestational Diabetes Mellitus: A Randomized Controlled Trial

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Abstract

Introduction: Gestational diabetes mellitus (GDM) has become a major metabolic disorder of pregnancy associated with adverse maternal and neonatal outcomes. Emerging evidence suggests that prebiotics such as fructo-oligosaccharides (FOS) may improve glycemic control, reduce inflammation, and beneficially modulate gut microbiota. This study evaluated the effect of FOS supplementation on glycemic parameters, inflammatory markers, and gut microbiota in women with GDM. **Materials and Methods:** A total of 923 pregnant women attending a tertiary care hospital in rural Vadodara were screened using random blood sugar and oral glucose tolerance test, identifying 76 (8%) with GDM. A comparative assessment between 76 GDM and 76 non-GDM women evaluated socioeconomic, anthropometric, and dietary parameters. In a randomized controlled trial phase, 62 GDM women were allocated into control (n = 30) and experimental (n = 32) groups. The experimental group received 10 g/day FOS for 90 days. Glycemic indices (fasting blood sugar [FBS], glycated hemoglobin [HbA1c]), inflammatory markers (high-sensitivity C-reactive protein, interleukin-6 [IL-6]), and gut microbiota (*Bifidobacterium*, *Lactobacillus*, and *Escherichia coli*) were assessed pre- and post-intervention. **Results:** FOS supplementation significantly reduced FBS (2.8%) and HbA1c (4.3%). IL-6 levels decreased by 3%, with improved colonization of *Bifidobacterium* (15% increase) and reduced *E. coli* (22% decrease). Negative correlation was observed between IL-6 and *Bifidobacterium*, while HbA1c positively correlated with *E. coli*. **Discussion and Conclusion:** FOS supplementation improved glycemic control, reduced inflammation, and favorably modulated gut microbiota without affecting neonatal outcomes. FOS may serve as a beneficial adjunct in GDM management. Further large-scale studies are warranted.

Key words: Gestational diabetes mellitus, gut microbiota, inflammatory markers, prebiotics, pregnant women

INTRODUCTION

Globally, pregnancy is considered as an intricate process, which is influenced by several interconnected molecular along with cellular mechanisms, by people. Various changes take place, encompassing microbial, immunological, hormonal, and metabolic changes during pregnancy. However, enormous complications could take place if those physiological changes are disrupted,

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Received: 23-02-2026
Revised: 21-03-2026
Accepted: 28-03-2026

which might result in negative consequences for the mother as well as her baby.[1,2] Hence, gestational diabetes mellitus (GDM) is considered glucose intolerance, which develops as well as is detected as a collective metabolic disorder. Due to resistance or else minimized sensitivity to the insulin action, GDM develops as of carbohydrate intolerance, which results in maternal hyperglycemia.[3-5] Hence, the modulation and regulation of the fructo-oligosaccharides (FOS) of prebiotic supplementation have risen as auspicious methodologies to reduce or prevent, manage, or serve as an adjunct therapy in GDM. Bioactive agents, which extend potential welfare to the structure or else gastrointestinal flora's function, are termed prebiotics. A non-digestible food ingredient, which touches the host by exciting the growth or else activity of one or constrained bacteria in the colon, is termed a Prebiotic. Henceforth, host health is improved.[6,7] The interaction's schematic representation betwixt GDM as well as intestinal microbiota, inflammatory, along with oxidative stress processes is illustrated in Figure 1.

In GDM, substantiation of the prebiotic effect on inflammatory biomarkers is constrained. Randomized clinical trial studies examining prebiotics effects taken before as well as after GDM diagnosis were exceptional, particularly those weighing the effect on inflammation in GDM women. On the relation of interleukin-6 (IL-6) along with high-sensitivity C-reactive protein (hs-CRP) with GDM, enormous studies were done. A few studies had depicted a key relation between high IL-6 levels along with GDM, but others didn't report such relations.[8-11] There is limited research deliberating the relationship amid inflammatory markers and GDM based on the existing studies. Thus, analyzing the prebiotic supplementation impact on inflammatory markers along with Gut Microbiota in women with GDM through a randomized controlled trial is the goal.

Primary objective

- To determine whether 90 days FOS) supplementation reduces inflammatory markers (hs-CRP and IL-6) and improve gut microbiota composition in women with GDM.

Secondary objectives

- To evaluate changes in glycemic parameters (fasting blood sugar [FBS], glycated hemoglobin [HbA1c]).
- To examine correlations between inflammatory markers, gut microbiota, and glycemic control.

MATERIALS AND METHODS

A randomized controlled trial was conducted to evaluate the effect of prebiotic supplementation on inflammatory markers and gut microbiota in women with GDM. A total of 723 pregnant women in their second trimester were screened for GDM, of whom 72 were diagnosed based on HbA1c levels >6.5%. Among these, 62 women met the inclusion criteria and provided informed consent for participation. Data were collected using a pretested structured questionnaire. Participants were randomly assigned into two groups: The control group (n = 30) and the experimental group (n = 32). The experimental group received 10 g of FOS powder daily for 3 months. The study assessed biochemical parameters including FBS, HbA1c, hs-CRP, and IL-6. Microbial analysis of gut flora specifically *Bifidobacterium*, lactic acid bacteria (LAB), and *Escherichia coli* were performed using culture techniques. Two participants from the experimental group withdrew during the study. Consequently, the final analysis included 30 participants in both the experimental and control groups.

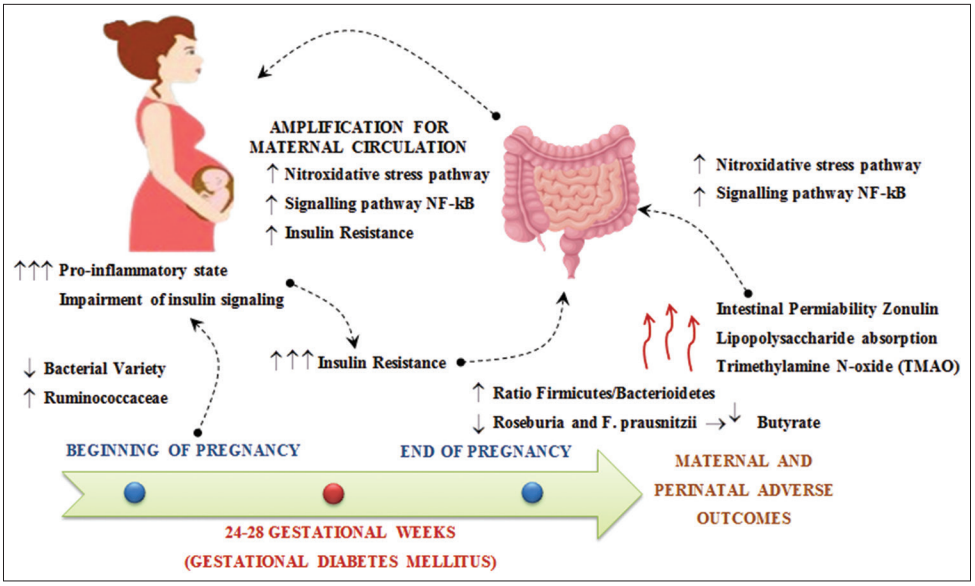

Figure 1: Activating inflammatory processes and autoimmune pathways[11]

Regarding the study, group mean ± standard deviation means for quantitative data, as well as frequency, along with % for qualitative data, were noted. The mean response scales were noted at a 6-week study period by using a mixed-effects model. The log transformation was considered tumor necrosis factor-α owing to the right skewness of the data. Furthermore, the $P < 0.05$ was regarded as important. Next, a meta-RA was performed to examine the source of heterogeneity and the influence.

RESULTS AND DISCUSSION

In the present study, 62 pregnant women diagnosed with GDM who were assigned to either an experimental group ($n = 32$) or control group ($n = 30$) were encompassed.

Inflammatory markers (hs-CRP and IL-6)

Inflammatory markers are critical indicators of systemic inflammation as well as are particularly relevant in GDM, where inflammation plays a main role in the disease's pathophysiology. Hs-CRP and IL-6 are the two specific markers on which the study focused. These markers were measured before and after the intervention to evaluate the potential anti-inflammatory effects of FOS supplementation.

In the experimental group, the intervention with FOS led to a non-significant decrease in hs-CRP levels, from 1.0 mg/L to 0.9 mg/L. On the other hand, a significant decrease in IL-6 levels was observed in the experimental group, with levels dropping by 3% from 6.3 pg/mL to 6.1 pg/mL ($P < 0.01$). Proinflammatory cytokine related to GDM's insulin resistance, along with the pathogenesis is termed IL-6. Elevated IL-6 levels exacerbate insulin resistance, thereby worsening glucose intolerance. The noteworthy reduction in IL-6 levels in the experimental group indicates that FOS supplementation may help mitigate insulin resistance, improving overall glucose metabolism in these patients [Table 1].

Table 1: Inflammatory markers (Hs-CRP and IL-6) before and after intervention

Parameters	Control group (*n*=25)	Experimental group (*n*=25)	"*t*" test
Hs-CRP (mg/L)			
Pre	0.9±0.29	1.0±0.7	1.6^{NS}
Post	0.8±0.25	0.9±0.5	0.4^{NS}
Paired "*t*" test	0.9^{NS}	1.08^{NS}	
IL-6 pg/mL			
Pre	6.2±0.64	6.3±2.1	0.4^{NS}
Post	6.4±0.88	6.1±1.6	**3.4*** **
Paired "*t*" test	1.77^{NS}	**2.92****	

Hs-CRP: High-sensitivity C-reactive protein, IL-6: Interleukin-6. NS: not significant. level of significance: *P<0.05, ** P<0.01, *** P<0.001

Gut microbiota (GM) composition

The composition of GM is increasingly recognized as a key factor in metabolic health, particularly in conditions like GDM, where disruptions in the balance of gut bacteria can exacerbate inflammation and insulin resistance. Here, the effects of FOS supplementation on specific gut bacteria, including *E. coli*, *Bifidobacterium*, and LAB is assessed, by measuring their counts before and after the intervention. Post-intervention trial with FOS exhibited a significant reduction in *E. coli* from 4.65 ± 1.34 to 3.84 ± 1.53 in the experimental group. In contrast, the control group showed a non-significant increase in mean log values from 4.23 ± 1.47 to 4.70 ± 1.06. The experimental group showed a slight, non-significant increase from 6.20 ± 2.63 to 6.31 ± 1.37 in LAB count. However, a significant increase was found from 5.95 ± 1.67 to 6.83 ± 1.91 in the bifidobacteria count. These findings underscore the prebiotic effect of FOS, which promotes the growth of beneficial gut bacteria that are essential for maintaining a healthy microbial balance.

CONCLUSION

This study demonstrated that FOS supplementation may improve glucose metabolism in women with GDM, possibly by modulating gut microbiota and reducing inflammation, thereby enhancing insulin sensitivity. The significant increase in *Bifidobacterium* and LAB suggests a beneficial prebiotic effect, likely mediated through short-chain fatty acid production and improved gut barrier function. However, given the complex interactions between diet, microbiota, and metabolic health, larger studies across diverse populations are needed to validate these findings and better characterize gut microbiome profiles in normal and GDM pregnancies.

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Source of Support: Nil. **Conflicts of Interest:** None declared.