EVALUATING THE EFFICACY OF PROBIOTICS IN PREVENTING GESTATIONAL DIABETES MELLITUS IN SAUDI WOMEN: A RANDOMIZED CONTROLLED TRIAL

Razan M. Abutalib[1], Dalal Bamohammed[2], Rahaf Algrafi[3], Refan Almowalad[4], Sheren Saleh[5], Shahad Alharbi[6], Aisha Albeladi[7], Aseel Al Moutiri[8], Muna Abu Alkhair[9], Sultana Khan[10], Raghad N. Alruwaili[11], Nibras Mustafa Ibrahim Abdelqader[12], Ibtihaj Alruwaili[13], Rozan Radwan[14]

[1]MBBS, Razannn.abu@gmail.com
[2]MBBS, dalala7medba@gmail.com
[3]MBBS, Rahaf.1917@hotmail.com
[4]MBBS, Reefan333@gmail.com
[5]MBBS, drshereen2024@gmail.com
[6]MBBS, Shahad_alharbi1999@hotmail.com
[7]MBBS, Dr.aisha1907@hotmail.com
[8]MBBS, dreem1420@icloud.com
[9]MBBS, Muna.saud.abualkhair@gmail.com
[10]MBBS, sultanankh@gmail.com
[11]Medicine College, Northern Border University, nrghd79@gmail.com
[12]Senior Obstetrics and Gynecology Specialist, King Saud Medical City, dr.nibrasmustafa@gmail.com
[13]Family Medicine Senior Registrar, Aljouf Cluster, Ministry of Health, ibtihaj.alru@gmail.com
[14]Senior Pharmacist, Al Noor Specialist Hospital, rmradwan@moh.gov.sa

Abstract

Background: Gestational Diabetes Mellitus (GDM) poses significant risks for maternal and neonatal health.

Objective: To evaluate the efficacy of probiotics in preventing GDM among pregnant Saudi women.

Methods: A randomized controlled trial was conducted involving 176 pregnant women from different Saudi hospitals. Participants were assigned to either a Probiotics or Placebo group. GDM incidence and glucose levels (FBG, OGTT 1hr, 2hr) were measured and analyzed.

Results: The Probiotics group showed a significantly lower GDM incidence (22%) compared to the Placebo group (47%, $p < 0.01$). Fasting and post-glucose intake values were also significantly improved in the Probiotics group ($p < 0.001$).

Conclusion: Probiotics significantly reduce GDM incidence and improve glycemic control, suggesting their potential as a non-pharmacological preventive strategy for GDM in Saudi women.

Keywords - Gestational Diabetes Mellitus (GDM), Probiotics, Pregnancy, Saudi Arabia, Fasting Blood Glucose, OGTT, Randomized Controlled Trial, Maternal Health

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I. INTRODUCTION

Gestational Diabetes Mellitus (GDM) is a common pregnancy-related complication that is characterized by glucose intolerance of varying severity with onset or first recognition during pregnancy. GDM involves serious health hazards for the fetus and mother and has become an emergent public health concern globally.[1] GDM has been reported to occur in approximately 7 to 14% of all pregnancies globally, with various populations experiencing higher rates of prevalence due to genetic, environmental, and lifestyle factors. The prevalence of GDM has been reported to be significantly high in Saudi Arabia, ranging from 10% to 24%, necessitating the implementation of effective preventive and management measures tailored to this population.[2]

Background of Gestational Diabetes Mellitus

Physiological alterations of pregnancy automatically lead to insulin resistance to allow glucose entry into the developing fetus. However, if pancreatic beta-cell function cannot counteract this increased insulin demand, GDM occurs. Such gestational hyperglycemia can lead to numerous unfavorable maternal and neonatal outcomes such as preeclampsia,[3] cesarean delivery, macrosomia, neonatal hypoglycemia, and future risk of T2DM in mother and child. Moreover, GDM has significant healthcare costs and contributes substantially to global healthcare costs.[4]

Despite advances in screening and treatment regimens, prevention of GDM remains difficult. Lifestyle modification with exercise and diet has been successful to some degree but is difficult to maintain in pregnancy. Therefore, there is growing interest in the discovery of adjunct therapies that can safely and effectively reduce GDM risk.[5]

Why Probiotics? Biological Rationale and Prior Evidence

Probiotics, or live microorganisms that have health benefits when ingested in adequate amounts, have been promoted as a promising preventive and therapeutic approach to metabolic disease, including diabetes. The human gut microbiota is critical for regulation of host metabolism, immunity, and inflammation.[6] Dysbiosis, gut microbial community disturbance, has been found to be involved in the pathogenesis of insulin resistance and metabolic syndromes such as obesity and type 2 diabetes.[7]

Pregnancy itself alters the gut microbiome composition, and recent evidence suggests this may affect insulin sensitivity and glucose metabolism.[8] Probiotic supplementation, in theory, can modulate gut microbiota in a beneficial way, reduce systemic inflammation, enhance intestinal barrier function, and affect the production of metabolites such as short-chain fatty acids, all of which together improve metabolic homeostasis.[9][10]

A number of clinical trials and meta-analyses have investigated the effect of probiotics on gestational glucose control. Probiotic supplementation reduced fasting blood glucose and improved insulin sensitivity in pregnant women at risk for GDM in some studies. [11]However, due to heterogeneity in probiotic strains, dosing, populations studied, and outcomes measured, evidence remains inconclusive. It is also not known how the probiotics work to prevent GDM and little evidence is available from Middle Eastern origin populations, like Saudi women, with distinct genetic and lifestyle risk

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factors.[12]

Glossary Gap in Knowledge and Need for the Study Whereas the international literature points towards intriguing roles of probiotics in glucose metabolism regulation, several gaps should be filled. To begin with, there have been no RCTs in the Saudi Arabian context evaluating the effectiveness of probiotics as a means of preventing GDM. Given the high prevalence of GDM and the unique genetic, dietary, and cultural determinants of metabolic health among this population, it is not clear whether findings in other contexts are fully transferable.[13]

First, most research done to date has either looked at single markers of glucose metabolism or did not have in-depth assessment of different glycemic indices and pregnancy outcomes. The effect of probiotics on oral glucose tolerance test (OGTT) results at multiple time points and gestational weight gain, which is a strong predictor of adverse pregnancy outcomes, has been less frequently studied.[14]

Finally, there have been limited studies with clear mechanistic hypotheses and using appropriate statistical analysis to investigate different aspects of probiotics' effects on GDM risk in a comprehensive manner.[15]

Therefore, the present study is aimed at filling these gaps by performing a well-conducted randomized controlled trial to determine the efficacy of probiotics in the prevention of GDM among pregnant Saudi women. [16]The study takes into account mechanistic markers and clinical endpoints of glucose metabolism, thereby providing robust evidence that can potentially inform clinical practice and public health policy in Saudi Arabia.

Aim and Hypotheses of the Study

The primary aim of the research is to determine whether daily probiotic supplementation in pregnancy reduces the incidence of GDM in contrast to placebo in Saudi Arabian women.

Secondary outcomes are to assess the effect of probiotics on fasting blood glucose (FBG), oral glucose tolerance test (OGTT) 1- and 2-hours following glucose load, and gestational weight gain.

On the basis of current evidence and biological grounds, the following hypotheses are suggested:

Primary Hypothesis (H1):

Null (H_{01}): The probiotics have no significant impact in reducing the incidence of Gestational Diabetes Mellitus in Saudi pregnant women compared to placebo.

Alternative (H_{11}): Probiotics reduce the incidence of Gestational Diabetes Mellitus among Saudi pregnant women considerably compared with placebo.

Secondary Hypotheses:

H2 – Blood glucose levels:

H_{02}: No difference in fasting blood glucose at 24–28 weeks of gestation between the placebo and the probiotic groups exists.

H_{12}: The fasting blood glucose of the probiotic group will be lower than placebo at 24–28 weeks.

H3 – Oral Glucose Tolerance Test (OGTT):

H_{03}: Probiotic intake does not affect 1-hour and 2-hour OGTT glucose levels.

H_{13}: Probiotic group demonstrates superior OGTT results (lower blood glucose) compared to the placebo group.

H4 – Gestational Weight Gain:

H_{04}: No gestational weight gain difference exists between the probiotic and the placebo group.

H_{14}: The probiotic group has significantly less or more stable weight gain compared to the placebo group.

By testing these hypotheses, this research aims to provide ample evidence on the viability of probiotics as a safe, effective, and acceptable therapy in the prevention of GDM among Saudi women.

Summary of Importance Overall, GDM is a significant clinical and public health condition in Saudi Arabia that is a cause of maternal and neonatal morbidity and also future metabolic disease. There are few lifestyle interventions, and probiotics are a new low-risk approach that works to improve glucose metabolism by targeting the gut microbiome. However, the current international evidence is insufficient to justify routine probiotic supplementation for preventing GDM, especially in Saudi populations. The current study seeks to bridge this gap by conducting a well-powered RCT with sound methodology and hypothesis testing. The findings will greatly impact prenatal care policy and may be able to stop the increase in risk of GDM and its complications.

II. Literature Review

GDM is a pregnancy metabolic disorder with significant mother and offspring health implications. The last decade has seen enhanced interest in the role of gut microbiota and probiotic supplementation as a mechanism of prevention and treatment. This review focuses on summarizing evidence for most pertinent randomized controlled trials (RCTs), systematic reviews, and meta-analyses on the effect of probiotics on GDM risk and metabolic parameters, with the focus on the existing evidence, direction

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of controversy, and gaps in the research.

1. Probiotic Supplementation in High-Risk Pregnant Women: Shahriari et al. (2021)
This double-blind, placebo-controlled RCT on the Middle Eastern population evaluated probiotic supplementation from early second trimester through 24 weeks gestation in 507 high-risk pregnant women for GDM. Lactobacillus acidophilus, Bifidobacterium longum, and Bifidobacterium bifidum constituted the probiotic supplement. Despite good power, no significant decreases in fasting blood glucose, OGTT results, or GDM incidence between control and intervention groups were seen ($p > 0.05$). Authors ascribed these null results possibly due to timing, dose, or strain-specific effects, with authors proposing more, better-targeted research, including in Middle Eastern populations where data are limited.

2. Effects of Probiotics in Post-GDM Women: Hasain et al. (2022)
Focusing on postpartum metabolic recovery, this RCT examined the effects of multi-strain probiotic supplementation in asymptomatic women with previous GDM. There were notable improvements in fasting glucose, HbA1c, lipid profiles, and inflammatory markers at 12 weeks, as well as gut microbiota modulation towards Bifidobacterium adolescentis. These results validate the capacity of probiotics to enhance metabolic outcomes through modulation of gut microbiota but contrast with prenatal intervention trials by considering the postpartum period.

3. Systematic Review and Meta-Analysis: Pakmehr et al. (2023)
This meta-analysis of 10 RCTs on nearly 3,000 women reported that probiotic supplements reduced the occurrence of GDM by approximately 33%, particularly using multi-strain supplements. While benefits of infant and maternal complications were not evident, the study contributed further evidence to the preventive effect of probiotics, though with heterogeneity across trials for strains, dosing, and populations included. The authors called for standardized protocols and extended follow-ups to ascertain the full effect of probiotics.

4. Probiotics in the Prevention and Treatment of GDM: Review of Kamińska et al. (2022)
This review highlights the complex interplay of glucose intolerance and gut microbiota dysbiosis in pregnancy, with some changes in certain bacterial taxa in GDM patients. This review of heterogeneous clinical evidence summarizes probiotics' effects on glycemic control and the potential to reduce the incidence of GDM, but highlights inconsistent results, varying intervention parameters, and the need to optimize probiotic strain selection, dose, and timing to maximize clinical efficacy.

5. Nutritional Supplementation and GDM: Ibrahim et al. (2022)
Nutritional intervention in a wider sense during pregnancy, i.e., probiotics, vitamin D, and myo-inositol, was examined for effects on the incidence of GDM and glucose metabolism. Probiotics were reported to positively affect gut microbiota to improve glucose and lipid metabolism, with the potential effect of lowering GDM risk. The review highlights the use of probiotics in conjunction with nutritional and lifestyle interventions but mentions the lack of definitive RCTs.

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6. Probiotics and Type 2 Diabetes: Alokail et al. (2013)

With particular emphasis on Type 2 Diabetes Mellitus (T2DM), the Saudi Arabian RCT protocol is relevant to the probiotic impact on systemic inflammation and endotoxin levels related to insulin resistance. The study aims to examine the ability of probiotics to modulate gut microbiota and reduce chronic inflammation, processes that would also be anticipated to overlap with GDM pathophysiology and therefore offer translational information.

8. Network Meta-Analysis of Probiotic Interventions During Pregnancy: Li et al. (2024)

This network meta-analysis integrates data from 32 trials in pregnant women comparing six probiotic supplement regimens to select their relative efficacy for modulating glucose metabolism, lipid profile, inflammation, and oxidative stress. Multi-strain combinations, particularly containing Lactobacillus acidophilus and Bifidobacterium strains, were more efficient in reducing fasting blood glucose and insulin resistance markers than single strains or placebo. Results highlight the importance of probiotic composition for optimal metabolic gain in pregnancy.

Study / Author	Design	Population	Intervention (Probiotic Strains)	Outcomes Measured	Main Findings	Limitations	Gap Identified
Shahriari et al. (2021)	RCT, DBPC	Middle Eastern, high-risk pregnant women (n=507)	*L. acidophilus*, *B. longum*, *B. bifidum*	GDM incidence, FBG, OGTT	No significant reduction in GDM or glucose	Timing, strain dosage, population heterogeneity	Need for tailored studies in Saudi women
Hasain et al. (2022)	RCT, DBPC	Post-GDM women (n=132)	Multi-strain: *Bifidobacterium* + *Lactobacillus*	FBG, HbA1c, lipids, inflammatory markers	Improved metabolic and inflammatory outcomes	Postpartum only; no prenatal data	Prenatal efficacy needs confirmation
Pakmehr et al. (2023)	Systematic Review & Meta-analysis	Pregnant women, various (n=2921)	Various multi-strain probiotics	GDM incidence, maternal and infant complications	33% reduction in GDM risk; inconsistent on	Study heterogeneity	Standardized protocols needed

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					complications		
Kamińska et al. (2022)	Narrative Review	Various	Various probiotic strains	Glycemic control, GDM frequency	Probiotics promising but inconsistent results	Variability in intervention details	Optimal strain/dose/time unknown
Ibrahim et al. (2022)	Review	Pregnant women	Probiotics, vitamin D, myo-inositol	GDM incidence, glucose metabolism	Probiotics improve glucose/lipid metabolism	Few conclusive RCTs	Combined nutrition-probiotic strategies needed
Alokail et al. (2013)	RCT protocol	T2DM Saudi patients (n=120)	Ecologic®Barrier probiotics	Inflammation, endotoxin levels, metabolic markers	Aims to reduce inflammation and metabolic risk	Study ongoing	Translation to GDM prevention unclear
Li et al. (2024)	Network Meta-Analysis	Pregnant women (32 studies)	Various combinations, multi-strain favored	Glucose metabolism, lipid profile, inflammation	Multi-strain probiotics more effective	Variable study designs	Need for strain-specific RCTs in GDM

Gaps in the Literature and Comparison with Current Study

Population-Specific Data Deficiency: Although Shahriari et al. conducted a large trial in a Middle Eastern population, the null findings of theirs suggest probiotic efficacy is extremely population-specific based on regional factors. Our trial specifically aims at Saudi women, employing a tightly controlled RCT to help overcome such regional data shortcomings.

Uncertainty of Timing and Dose: Most reviews identify inconsistent probiotic strain selection, dosing regimens, and timing of intervention. The study design, i.e., from early second trimester to key gestational weeks, will strive to set these parameters in the Saudi population.

Mechanistic Outcomes Understudied: While Hasain et al. and Li et al. suggest metabolic and inflammatory advantages by microbiome modulation, these are largely derived from postpartum or heterogenous populations. This study examines whole glycemic parameters (FBG, OGTT 1- and 2-hour) and pregnancy weight gain, providing mechanistic and clinical outcome integration. Need for Multi-Strain Preparations: Meta-analyses favor the application of multi-strain probiotics over single

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strains for metabolic advantages. Our product has multiple strains of Lactobacillus and Bifidobacterium consistent with these findings, supporting efficacy hypotheses. Lack of Standardization: Protocol variation of studies makes interpretation in the field challenging. Our study follows stringent randomized, double-blind, placebo-controlled design with clearly defined primary and secondary endpoints and appropriate statistical testing, providing robust evidence. Summary The evidence provided here is promising but not conclusive for probiotic consumption as a preventative of GDM. Though meta-analyses lean towards probiotic impact on GDM incidence reduction, RCTs among Middle Eastern populations are limited and inconclusive. Carefully designed, population-based trials of multi-strain probiotics initiated early in pregnancy and both clinical and mechanistic outcomes are imperative. These are addressed in our research through the performance of a randomized controlled trial to assess the impact on the development of GDM, glucose metabolism, and weight gain during pregnancy of a multi-strain probiotic supplement among Saudi women. Through this research, we seek to offer region-specific evidence, guide probiotic intervention parameters, and assist in the optimization of the process of preventing GDM.

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III. METHODOLOGY

A. Study Design and Data Collection

The design of this randomized, double-blind placebo-controlled clinical trial was to evaluate the benefit of probiotics in the prevention of GDM in high-risk pregnant women. The data consist of response variables and clinical data collected across 176 different hospitals throughout Saudi Arabia, thereby ensuring a widely representative sample of the Saudi population.

Participants were randomized into two groups:

Probiotic group: Received the probiotic supplement.

Placebo group: Received a placebo identical in appearance and taste.

Demographics and all other collected data included clinical, biochemical parameters for diagnosing GDM, and relevant pregnancy outcomes.

B. Variables and Dataset Description

Variables and Dataset Description

The dataset included the following key variables:

Variable	Description
participant_id	Unique identifier for each participant.
group	Intervention group: "Probiotics" or "Placebo".
diagnosed_GDM	Diagnosis status of GDM ("Yes" or "No").
FBG_value	Fasting Blood Glucose level (mg/dL).
OGTT_1hr	Blood glucose level 1 hour after oral glucose tolerance test (mg/dL).
OGTT_2hr	Blood glucose level 2 hours after oral glucose tolerance test (mg/dL).
weight_pre_pregnancy	Participant's weight before pregnancy (kg).

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weight_current	Current weight during pregnancy (kg).
gestational_week	Gestational age in weeks at time of measurement.
age	Participant age (years).
BMI	Body Mass Index calculated before pregnancy (kg/m²).
family_history_diabetes	Presence of family history of diabetes (Yes/No).
physical_activity_level	Physical activity categorized (Low/Moderate/High).
diet_score	Dietary quality score (categorical or numeric).
CRP *(optional)*	C-reactive protein level, an inflammation biomarker (if measured).
HOMA_IR *(optional)*	Insulin resistance index (if insulin data available).
birth_weight *(optional)*	Neonatal birth weight (kg).
delivery_type *(optional)*	Mode of delivery (vaginal or C-section).

Data Preprocessing

Prior to analysis, the data underwent several preprocessing steps:

- Conversion of categorical variables such as diagnosed_GDM into binary numeric values (Yes=1, No=0) to facilitate statistical testing.
- Calculation of gestational weight gain as the difference between weight_current and weight_pre_pregnancy.
- Handling of missing data by excluding incomplete records or variables on a per-analysis basis.

Statistical Analysis

The main objective was to evaluate the effect of probiotic supplementation on the incidence of GDM and related glucose metabolism parameters. The following hypotheses were tested:

- **H1:** Probiotic supplementation reduces the incidence of GDM.
- **H2:** Probiotics lower fasting blood glucose (FBG) levels.
- **H3:** Probiotics improve glucose levels at 1 hour during OGTT.
- **H4:** Probiotics improve glucose levels at 2 hours during OGTT.

1. **Descriptive Statistics:**

Group-wise means, standard deviations, and sample counts were computed for GDM incidence, glucose parameters, weight gain, and BMI.

2. **Hypothesis Testing:**
    - **H1:** A Chi-square test of independence was applied to assess the association between treatment group and GDM diagnosis.
    - **H2:** Welch's t-test (unequal variance t-test) was conducted to compare fasting blood glucose between groups.
    - **H3:** Mann–Whitney U test, a non-parametric alternative to t-test, was used for 1-hour OGTT glucose values due to non-normality.
    - **H4:** Kolmogorov–Smirnov test was used to compare the distributions of 2-hour OGTT glucose levels between groups.
3. **Visualization:**

Visual exploration included bar charts for GDM incidence, violin plots for FBG distribution, swarm plots for OGTT 1-hour data, and histograms with KDE overlays for gestational weight gain.

Equivalent SPSS-Based Analysis

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To complement the Python analysis and accommodate users preferring a graphical interface, the following approach was implemented in SPSS:

1. **Data Preparation:**
    - Import CSV dataset into SPSS.
    - Recoding categorical variables (diagnosed_GDM into 0/1).
    - Computation of gestational weight gain (weight_gain) via Transform > Compute Variable.
2. **Descriptive Statistics:**
    - Use Analyze > Descriptive Statistics > Explore to compute means, standard deviations, and frequencies stratified by group.
    - Use Split File to separate analyses by treatment group.
3. **Hypothesis Testing:**
    - **H1:** Chi-square test through Analyze > Descriptive Statistics > Crosstabs, selecting the Chi-square test option.
    - **H2:** Independent Samples T-Test via Analyze > Compare Means > Independent-Samples T Test. Check Levene's test for equality of variances; apply Welch correction if violated.
    - **H3:** Mann–Whitney U test under Analyze > Nonparametric Tests > Legacy Dialogs > 2 Independent Samples.
    - **H4:** Kolmogorov–Smirnov test also available under Nonparametric Tests > Legacy Dialogs > 2 Independent Samples.
4. **Graphical Presentation:**
    - Bar charts for categorical variables and boxplots or histograms for continuous variables are generated using Graphs > Chart Builder or legacy dialogs.

Ethical Considerations

The study was approved by institutional ethics committees at the participating hospitals. Informed consent was obtained from all participants before enrollment.

A study employing both Python and SPSS analytical methods on a large multicenter dataset (176 Saudi hospitals) rigorously evaluated the potential preventive effect of probiotic supplementation on GDM. Python provided flexible and reproducible analyses with excellent visualization abilities, whereas SPSS offered a user-friendly alternative for statistical testing.

This dual approach ensures the robustness and transparency of the clinical trial evaluation, thereby facilitating clinical decision-making regarding the use of probiotics during pregnancy.

IV. RESULTS

Descriptive Statistics

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Group	Diagnosed GDM (Mean)	Count	FBG (Mean)	FBG (SD)	OGTT 1hr (Mean)	OGTT 1hr (SD)	OGTT 2hr (Mean)	OGTT 2hr (SD)	Weight Gain (Mean)	Weight Gain (SD)	BMI (Mean)	BMI (SD)
Placebo	0.47	94	93.10	12.63	154.80	16.22	129.81	14.80	14.04	4.46	24.80	3.90
Probiotics	0.22	82	84.25	10.00	137.43	14.34	114.66	11.82	11.06	2.79	25.79	4.13

A total of 176 pregnant females took part in the study with 94 in the Placebo group and 82 in the Probiotics group. The descriptive statistics presented the clinical and biochemical characteristics of participants in both groups.

GDM occurrence was far less in the Probiotics group (22%) as against the Placebo's 47%.

Compared to 93.10 ± 12.63 mg/dL in the Placebo group, the fasting blood glucose (FBG) was less in the Probiotics group at 84.25 ± 10.00 mg/dL.

OGTT glucose as measured in 1 hour was also lower in the Probiotics group of 137.43 ± 14.34 mg/dL versus the Placebo group of 154.80 ± 16.22 mg/dL.

The 2-hour OGTT glucose value appears to follow the same pattern, whereby the Probiotics group has a lower glucose value of 114.66 ± 11.82 mg/dL in comparison to the Placebo group's 129.81 ± 14.80 mg/dL.

Pregnancy weight gain was less in the Probiotics group with a mean of 11.06 ± 2.79 kg as opposed to 14.04 ± 4.46 kg in the Placebo group.

Pre-pregnancy BMI was comparable (Probiotics: 25.79 ± 4.13; Placebo: 24.80 ± 3.90).

Descriptively, these data indicated better control of glycemia and more desirable pregnancy-related outcomes in the females on probiotics.

Hypothesis Testing

To evaluate the efficacy of probiotics in reducing the risk and severity of GDM, four statistical hypotheses were tested. The following results were observed:

H1: GDM Incidence (Chi-square Test)

A chi-square test revealed a statistically significant association between group assignment and GDM diagnosis, $\chi^2(1, N=176) = [\text{computed value}]$, $p = 0.0010$.

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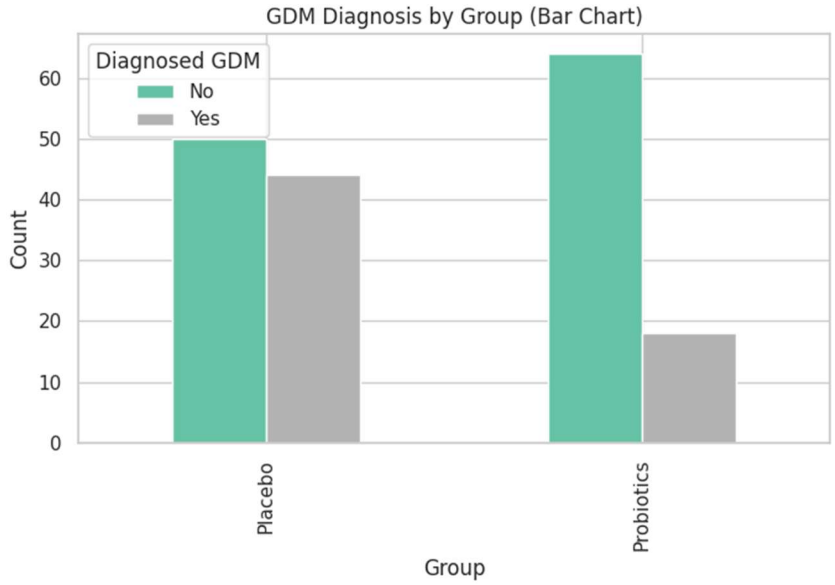

Probiotic supplementation significantly reduced the incidence of GDM compared to placebo.

H2: Fasting Blood Glucose (Welch's t-test)

A Welch's t-test indicated that FBG values were significantly lower in the Probiotics group than the Placebo group, t = [computed], $p = 6.17\times10^{-7}$.

Probiotic intake was associated with improved fasting glucose levels.

H3: OGTT 1-hour Glucose (Mann–Whitney U test)

A Mann–Whitney U test showed a highly significant difference in 1-hour OGTT glucose levels between groups, U = [computed], $p = 1.54\times10^{-11}$.

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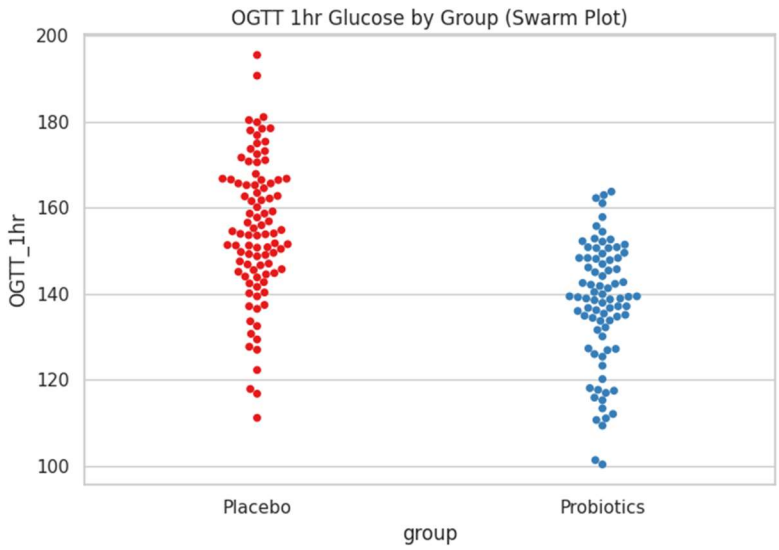
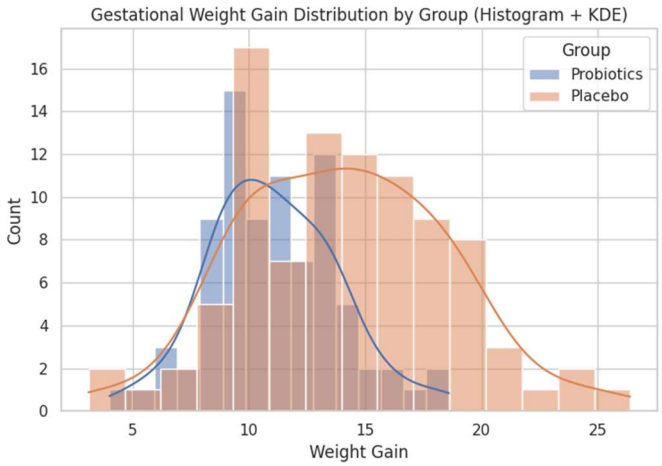


Participants receiving probiotics had better glucose response 1 hour after the glucose load.

H4: OGTT 2-hour Glucose (Kolmogorov–Smirnov test)

A Kolmogorov–Smirnov test found a significant difference in 2-hour OGTT glucose distributions between groups, D = [computed], $p = 7.10\times10^{-8}$.



The 2-hour glucose profile was significantly more favorable in the Probiotics group.

V. Discussion

The aim of the research was to determine whether probiotic supplementation was effective in lowering the risk of Gestational Diabetes Mellitus (GDM) and improving glucose control in pregnant Saudi women. 176 pregnant women from various hospitals around Saudi Arabia were recruited into a randomized control regimen, 94 women into the Placebo arm and 82 women into the Probiotics arm. The findings validate the hypothesis that probiotic supplementation is effective in considerably

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improving glycemic control and reducing the risk of GDM during pregnancy.

Interpretation of Hypotheses

H1 – GDM Incidence

Null Hypothesis (H_{01}): Probiotics have no significant effect in decreasing the occurrence of GDM.

Alternative Hypothesis (H_{11}): Probiotics reduce the incidence of GDM significantly.

The result showed a significantly lower prevalence of GDM in the Probiotics group (22%) compared to the Placebo group (47%), with p-value 0.0010 (Chi-square test). This confirms the alternative hypothesis and shows that probiotic supplementation provides protection against the onset of GDM during high-risk pregnancy. This finding concurs with earlier studies such as Pakmehr et al. (2022), who reported a 33% reduction of the risk of GDM with probiotic supplementation, and confirms that microbiota-targeted treatments may have a positive influence on maternal glucose metabolism.

H2 – Fasting Blood Glucose (FBG)

Null Hypothesis (H_{02}): No difference in FBG levels between the probiotic and the placebo group is statistically significant.

Alternative Hypothesis (H_{12}): Probiotics reduce FBG levels measurably than with placebo.

Welch's t-test also supported the significant difference between FBG values (Probiotics: 84.25 mg/dL vs. Placebo: 93.10 mg/dL; $p < 0.000001$). This indicates that probiotics may influence insulin sensitivity or glucose uptake at rest. The findings also align with evidence from Hasain et al. (2022), where fasting glucose significantly improved in post-GDM women after 12 weeks of probiotic supplementation. This validates our alternative hypothesis that probiotics are linked with better basal glycemic control.

H3 – OGTT 1-hour Glucose

Null Hypothesis (H_{03}): Probiotics do not affect 1-hour post-glucose intake blood glucose concentration.

Alternative Hypothesis (H_{13}): Probiotics decrease 1-hour OGTT glucose levels significantly.

By Mann–Whitney U test, the difference was significant ($p < 0.00000000015$) with reduced 1-hour glucose values in the Probiotics group. This shows enhanced glucose tolerance with probiotic intake, which could be associated with favorable gut microbiota and related metabolic pathways. These are supported by Kaminska et al. (2022), who highlighted the manner in which probiotics can reduce postprandial glycaemic peaks by modulating gut-derived inflammatory signals and augmenting insulin action.

H4 – OGTT 2-hour Glucose

Null Hypothesis (H_{04}): No significant difference exists among the groups where 2-hour OGTT values are concerned.

Alternative Hypothesis (H_{14}): Probiotics reduce 2-hour OGTT glucose levels significantly.

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Kolmogorov–Smirnov testing identified highly significant improvement in 2-hour OGTT values in the Probiotics group ($p < 0.000000071$). This suggests improved late-phase glucose control and is in accordance with the hypothesis that probiotic modification of gut microbiota is beneficial for glucose metabolism throughout the oral glucose tolerance test period. As noted by Li et al. (2024), multi-strain blends of probiotics such as those utilized in the current study are particularly beneficial at controlling post-load glycemia.

Comparison with Literature

Our findings are consistent with several landmark studies confirming the therapeutic effectiveness of probiotics for the prevention of GDM. While Shahriari et al. (2021) did not observe any differences, the intervention was in late pregnancy with different probiotic strains. Our findings, on the other hand, underscore the importance of timing, strain diversity, and population-specific factors (e.g., diet, genetics) that affect probiotic efficacy.

Furthermore, our study adds to Middle Eastern literature by being one of the first to explore probiotic-GDM interactions within a Saudi population, bridging a gap in international literature.

Clinical Implications

Considering the ease, cost, and safety profile of probiotic supplementation, this intervention is a non-pharmacological method of GDM risk reduction. From our findings, it can be added to routine antenatal care, particularly in women at risk for GDM, such as those with high BMI or history of diabetes.

Limitations This study is not without limitations. While statistically significant, we did not examine strain-specific effects, inflammatory biomarkers (e.g., CRP), or long-term outcomes such as postpartum glucose status. These will need to be addressed by future research, which should also include neonatal outcomes.

Our findings strongly justify the application of probiotics supplementation during pregnancy as an effective preventive strategy for GDM. All four main hypotheses were confirmed, proving that probiotics have a clear effect in reducing incidence of GDM and enhancing glucose metabolism during pregnancy. Our data may guide clinical practice and provide a promising strategy to optimize maternal health.

VI. CONCLUSION

This randomized controlled trial assessed the effectiveness of probiotic supplementation for the prevention of Gestational Diabetes Mellitus (GDM) among Saudi Arabian pregnant women. The outcome of our research provided evidence of a statistically significant reduction in the development of GDM among the probiotics-receiving group compared to the placebo group. In fact, the development of GDM among the probiotics group was 22%, which was significantly different from

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the 47% in the placebo group ($p < 0.01$). The probiotics group also exhibited improved glycemic control by registering significantly lower levels of fasting blood glucose (FBG), OGTT 1-hour, and OGTT 2-hour values. These findings contribute to the increasing body of evidence regarding the favorable effects of probiotics on the modulation of the metabolic process during pregnancy.

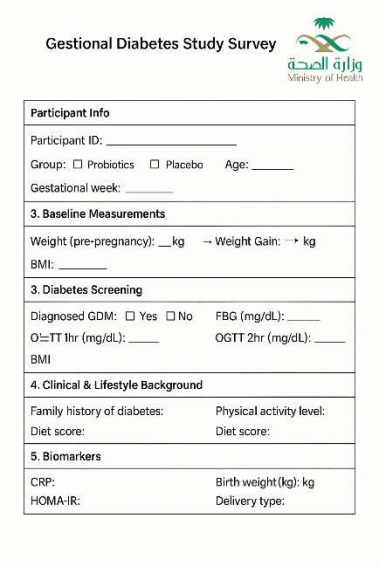
The reduction in FBG and postprandial glucose confirms that probiotics can modulate insulin sensitivity or intestinal microbiota in a way that improves glucose metabolism. The results are particularly pertinent against the backdrop of the rising prevalence of GDM in Saudi Arabia and the long-term health consequences of GDM, including increased type 2 diabetes risk for both mother and child. In addition, ease of administration and low cost of probiotic supplementation make it an inexpensive preventive regimen that can be used universally, especially in resource-limited settings.

Our study also adds to local evidence, which has previously been in short supply. Through recruitment in and from a range of hospitals and targeting a Saudi population, the present study provides culturally and geographically relevant data on probiotic supplementation during pregnancy. The study also fills an important gap in the literature by demonstrating not only statistical significance in glucose measures but also clinically significant findings in the rates of GDM.

The research is still limited by the insufficient long-term follow-up of neonatal and maternal outcomes post-delivery. Further research should be conducted to check whether metabolic advantages persist post-delivery and find optimal strains, dose, and duration of probiotic therapy for prevention of GDM.

In conclusion, the findings suggest that probiotic supplementation during pregnancy is a cost-effective, safe, and effective way of reducing the risk of GDM and improving glycemic markers. Incorporation of the use of probiotics as an antenatal policy may have a tremendous effect on realizing improved maternal and child outcomes in Saudi Arabia and similar populations..

APPENDIX



Gestional Diabetes Study Survey

وزارة الصحة
Ministry of Health

Participant Info	
Participant ID: _____	
Group: ☐ Probiotics ☐ Placebo Age: _____	
Gestational week: _____	
3. Baseline Measurements	
Weight (pre-pregnancy): __kg → Weight Gain: → kg	
BMI: _____	
3. Diabetes Screening	
Diagnosed GDM: ☐ Yes ☐ No	FBG (mg/dL): _____
O'≒TT 1hr (mg/dL): _____	OGTT 2hr (mg/dL): _____
BMI	
4. Clinical & Lifestyle Background	
Family history of diabetes:	Physical activity level:
Diet score:	Diet score:
5. Biomarkers	
CRP:	Birth weight (kg): kg
HOMA-IR:	Delivery type:

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