

Effects of probiotic supplements on insulin resistance in gestational diabetes mellitus: A double-blind randomized controlled trial

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Keywords

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ABSTRACT

Aims/Introduction: To evaluate the effect of probiotic supplements on insulin resistance in pregnant women with diet-controlled gestational diabetes mellitus.

Materials and Methods: A randomized, double-blind, placebo-controlled trial was carried out between June 2016 and February 2017. Pregnant women with diet-controlled gestational diabetes mellitus were enrolled in the study at 24–28 weeks-of-gestation and randomized to receive either probiotic supplements containing *Bifidobacterium* and *Lactobacillus* or a placebo daily for four consecutive weeks. Primary outcomes were mean differences in insulin resistance (homeostatic model assessment for insulin resistance), fasting insulin and fasting plasma glucose between the two groups. Secondary outcomes were changes in maternal weight after the intervention.

Results: Data from 28 patients in the probiotic group and 29 in the placebo group were analyzed. The changes in metabolic parameters after randomization showed significant improvement in glucose metabolism in the probiotic group compared with the placebo group, including fasting plasma glucose (0.68 ± 5.88 vs 4.620 ± 7.78 mg/dL, mean difference -3.94 mg/dL, 95% confidence interval $-7.62, -0.27$, $P = 0.034$), fasting plasma insulin (1.11 ± 1.71 vs 3.77 ± 1.70 mIU/L, mean difference -2.67 mIU/L, 95% confidence interval $-3.57, -1.76$, $P = 0.001$) and homeostatic model assessment for insulin resistance (0.25 ± 0.37 vs 0.89 ± 0.46 , mean difference -0.63 , 95% confidence interval $-0.86, -0.41$, $P = 0.001$). Weight gain during randomization was similar between the two groups.

Conclusions: Four weeks of probiotic supplements in women with diet-controlled gestational diabetes in the late second and early third trimester lowered fasting glucose and increased insulin sensitivity. Probiotic supplements may be considered as an adjunct treatment for glycemic control in these patients.

INTRODUCTION

Gestational diabetes mellitus (GDM) is a major medical complication during pregnancy, occurring in 9.3–25.5% of pregnant women¹. Increasing maternal insulin resistance, peaking at 24–28 weeks-of-gestation, in combination with inadequate β -cell function, results in glucose intolerance. High levels of maternal blood glucose can lead to adverse pregnancy outcomes, including pre-eclampsia², unplanned cesarean delivery³, macrosomia, birth trauma and neonatal hypoglycemia⁴. Based on previous

evidence, optimal glycemic control has been shown to reduce complications of mothers, fetuses and neonates^{5,6}. All pregnant women with GDM should be counseled regarding appropriate diet and exercise. However, approximately 11% of women with GDM fail to adequately control their glucose levels with diet and exercise alone, and require medication⁷.

Probiotics are defined as living microorganisms that, when consumed in adequate amounts, will provide health benefits to the host⁸. Most of them are prepared in the form of yogurt, fermented foods and capsule supplements. Ingestion of probiotics is generally considered safe in both pregnant women and their fetuses^{9,10}. The addition of these beneficial microorganisms

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help balance and increase the abundance of good microorganisms in the digestive tract. Indeed, the impact of probiotics on various outcomes has been shown, including dermatological diseases¹¹, gastrointestinal diseases^{12–14} and metabolic disorders^{15,16}. Recently, several studies from different countries (i.e., Iran, Ireland and Turkey) have shown the favorable effects of probiotic supplements with diverse compositions and durations of therapy on glycemic control in pregnant women with GDM^{17–23}. However, the impact of probiotics in South-East Asian populations has not been reported. Dietary traditions, geographic locations and human genetics can influence gut microbial composition among different ethnic groups^{24–26}. Furthermore, some studies have shown an abundance of *Bacteroides/Bifidobacterium* and *Prevotella* species in the digestive tracts of Asian populations²⁴. Thus, the effectiveness of probiotic supplements might differ based on the background microbiota compositions of the population and should be investigated in various geographic regions. Therefore, the purpose of the present study was to evaluate the effects of probiotic supplements on metabolic parameters, including fasting glucose and insulin resistance, in pregnant women with GDM in Thailand.

METHODS

Study design

A double-blind, placebo-controlled, randomized clinical trial was carried out between June 2016 and February 2017 at the Antenatal Care Clinic, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand. This study was reviewed and approved by the Committee on Human Rights Related to Research Involving Human Subjects, Faculty of Medicine, Ramathibodi Hospital, and complied with the Declaration of Helsinki. Written informed consent was obtained from all participants. The study was registered at the Thai clinical trials registry, number 20170606002.

Participants

Newly diagnosed women with GDM between 24–28 weeks-of-gestation who attended the Antenatal Care Clinic and met the inclusion criteria were invited to participate in the study. GDM was diagnosed based on the International Association of Diabetes and Pregnancy Study Groups criteria²⁷ as follows: fasting plasma glucose ≥ 92 mg/dL at the first prenatal visit, or an abnormal glucose tolerance test at 24–28 weeks-of-gestation using a 75-g oral glucose load (defined as one or more of the following abnormal glucose values: fasting plasma glucose ≥ 92 mg/dL, 1-h ≥ 180 mg/dL, 2-h ≥ 153 mg/dL). Other inclusion criteria included: (i) singleton pregnancy; (ii) maternal age of 18–45 years; (iii) normal fetal structures or chromosomes based on ultrasound scanning during the second trimester and/or invasive prenatal diagnosis; and (iv) no history of chronic diseases, such as immunodeficiency, hypertension, pre-gestational diabetes, kidney disease or liver disease. Exclusion criteria included: (i) consuming probiotic food products, such as

yogurt, fermented foods and bean paste during the 2 weeks before enrollment; and (ii) exposure to antibiotics during the 4 weeks before enrollment.

Baseline characteristics

Age and pre-pregnancy weight (from chart review or patient interview) were obtained. Height was measured at first visit, and body mass index was calculated from the formula: weight (kg)/height² (m²). Additionally, educational level and family history of diabetes in first-degree relatives were obtained. Physical activity was evaluated using questionnaires. Participants were categorized into three groups based on their 3-day usual activity; that is, low, moderate and high physical activity. Low physical activity was defined as limited to chores, such as cooking, sewing and working on a computer. Moderate physical activity was defined as work requiring bodily movements, such as cleaning or taking care of children. High physical activity was defined as regular aerobic exercise, such as running, biking or swimming.

Randomization

A double-blind randomized controlled trial was carried out in which participants who agreed to participate in the study were randomly assigned to take one capsule containing either a probiotic or placebo. Random allocation sequence was carried out in blocks of four by the statistician. Researchers arranged the enrollment and intervention assignment of participants. The capsules and their packages were unidentified to participants, researchers and primary investigators.

Interventions

All participants were randomly allocated to take one capsule containing either a probiotic or placebo once daily after the morning meal for four consecutive weeks. The probiotic used in this study was Infloran[®] (Laboratorio Farmaceutico SIT, Mede, Italy, and imported by DKSH, Bangkok, Thailand). It is commercially available at Ramathibodi Hospital, where it has been used for the treatment of acute non-specific enterocolitis and chronic constipation. Each capsule contained 1,000 million CFU of *Lactobacillus acidophilus* and 1,000 million CFU of *Bifidobacterium bifidum*. This dose was similar to that utilized in previous studies^{18,20}. Each placebo capsule contained gelatin. Participants were counseled to avoid probiotic-containing foods and supplements throughout the study period to minimize the confounding from other probiotics.

Participants were given a 2-week package of either probiotic or placebo capsules and instructed to refrigerate them at 4°C. They were seen every 2 weeks at our antenatal care clinic for standard antenatal treatment, monitoring compliance with the treatment and monitoring for adverse effects from the interventions. Compliance monitoring was carried out by capsule count. Afterwards, a second 2-week package of either probiotic or placebo capsules was given to the patients. Additionally, weekly telephone follow-up calls were carried out to encourage

compliance with the assigned intervention and to monitor for any possible adverse events.

All participants received counseling regarding diet control and lifestyle modification from nutrition counselors and nurses as per the standard of care at Ramathibodi Hospital. Additionally, a 24-h dietary recall questionnaire for three consecutive days was completed after 2 weeks of intervention and used as the participant's representative diet during the study period. Daily caloric intake, along with carbohydrates, fat, protein and fiber consumption, were analyzed using the Thai nutritional database developed by the Institute of Nutrition, Mahidol University, Thailand (INMUCAL software).

Participants were discontinued from the study if one of the following occurred: (i) use of antibiotics or immunosuppressive drugs during the intervention; (ii) serious adverse effects from probiotics, such as diarrhea, nausea/vomiting or sepsis; and (iii) need for insulin.

Outcome measures

Primary outcomes of the present study were mean differences in the changes of metabolic parameters between the two groups during the intervention, including fasting plasma glucose, insulin and insulin resistance index. At baseline and 4 weeks after randomization, blood samples were obtained after an overnight fast. Fasting plasma glucose and fasting plasma insulin were measured (see below). Homeostatic model assessment for insulin resistance (HOMA-IR), an index of fasting insulin resistance, was calculated from the formula: fasting plasma insulin (U/mL) \times fasting plasma glucose (mmol/L)/22.5^{28,29}. For the present study, plasma glucose was measured by hexokinase/glucose-6-phosphate dehydrogenase (Architect c Systems; Abbott Core Laboratories, Abbott Park, IL, USA), and fasting plasma insulin was measured immunometrically using chemiluminescence detection (Immulite 2000; Siemens, Erlangen, Germany; coefficients of variance <5%).

The mean difference in maternal weight gain across the study period was a secondary outcome. Although not a pre-specified planned outcome of the study, pregnancy outcomes were collected from medical records. These included total gestational weight gain, birth weight and rates of neonatal hypoglycemia.

Sample size

Based on similar randomized clinical trials in which HOMA-IR was used as an outcome measure¹⁸, assuming types I and II error rates of 5% ($\alpha = 0.05$) and 20% ($\beta = 0.2$; power = 80%), respectively, the sample size for each group was calculated at 30 women.

Statistical analysis

Data were analyzed using the SPSS statistical software package version 22 IBM (International Business Machines Corp.), Armonk, New York, USA. The variables were expressed as means (standard deviation) and n (%). After testing data for

normality, two-sample t -tests or Mann–Whitney tests were used to compare continuous variables between the two groups at baseline as appropriate. The χ^2 -test and Fisher's exact tests were used to compare categorical data. Mean differences in the changes in metabolic parameters during the intervention period between the two groups were compared by independent t -tests. P -values <0.05 were considered statistically significant.

RESULTS

A total of 122 potential participants were screened. Of these, 40 did not meet the inclusion criteria, and 22 declined to participate. This resulted in 60 newly diagnosed GDM pregnant women enrolled in the trial and randomized into either the probiotic or placebo group (Figure 1). Two pregnant women were discontinued from the probiotic group; one due to a subsequent diagnosis of systemic lupus erythematosus requiring steroid treatment, and the other due to antibiotic use during the study period. One woman discontinued from the placebo group due to a subsequent diagnosis of systemic lupus erythematosus requiring steroid treatment. As a result, data from the 28 patients in the probiotic group and 29 in the placebo group were analyzed at study completion. The CONSORT diagram of the study is shown in Figure 1.

Baseline characteristics of participants in each group are shown in Table 1. The mean age, gestational age, pre-pregnancy body mass index, body weight at enrollment and baseline physical activity levels were not significantly different between the probiotic and placebo groups. There were no statistically significant differences between the two groups in fasting plasma glucose, fasting plasma insulin and HOMA-IR at baseline.

The primary outcomes, which were mean differences in the changes of fasting plasma glucose, fasting plasma insulin and HOMA-IR, after the intervention between the two groups, are provided in Table 2. The changes in metabolic parameters after randomization showed significantly improved glucose metabolism in the probiotic group compared with the placebo group, including fasting plasma glucose (0.68 ± 5.88 vs 4.620 ± 7.78 mg/dL, mean difference (MD) -3.94 mg/dL, 95% confidence interval [CI] $-7.62, -0.27$), $P = 0.034$), fasting plasma insulin (1.11 ± 1.71 vs 3.77 ± 1.70 mIU/L, MD -2.67 mIU/L, 95% CI $-3.57, -1.76$, $P = 0.001$) and HOMA-IR (0.25 ± 0.37 vs 0.89 ± 0.46 , MD -0.63 , 95% CI $-0.86, -0.41$, $P = 0.001$).

After 4 weeks of intervention, weight gain between the participants in the probiotic and placebo group was not significantly different (1.69 ± 0.64 vs 1.76 ± 0.78 kg, MD -0.06 kg, 95% CI $-0.51, 0.39$, $P = 0.781$). In addition, dietary intake obtained from 3-day food record at 2 weeks after treatment initiation, including the amount of carbohydrates, fat, protein and fiber intake, was not different between the two groups.

Participant compliance in each group was analyzed and did not differ significantly (probiotic 96.42% vs placebo 93.10%, $P = 0.65$). Furthermore, there were no any adverse effects, such as diarrhea, nausea/vomiting or sepsis in each group.

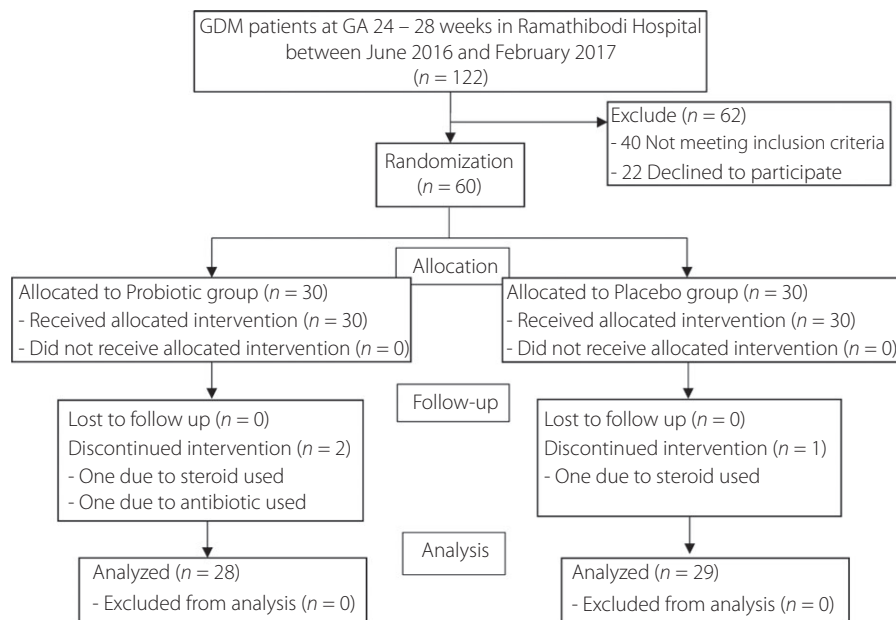


Figure 1 | CONSORT 2010 flow diagram for 'Effects of probiotic supplements on insulin resistance in gestational diabetes mellitus: A double-blind randomized controlled trial.'

Table 1 | Baseline characteristics of the participants

Demographic data	Probiotic group (n = 28)	Placebo group (n = 29)	P-value
Maternal age (years)	32.50 ± 5.02	30.72 ± 5.05	0.19
Gestational age at study (weeks)	27.29 ± 2.42	27.97 ± 2.54	0.31
Pre-pregnancy BMI (kg/m ²)	22.74 ± 3.73	22.04 ± 3.12	0.45
Body weight at study (kg)	63.49 ± 10.75	62.88 ± 9.33	0.82
Physical activity, n (%)			
Low	22 (78.6)	24 (82.8)	0.69
Moderate	6 (21.4)	5 (17.2)	
High	0 (0)	0 (0)	
Gestation, n (%)			
Primigravida	10 (35.7)	13 (44.8)	0.25
Multiparity	18 (64.3)	16 (55.2)	
History of diabetes in first-degree relatives, n (%)	6 (21.4)	7 (24.1)	0.36
Physical activity, n (%)			
Low	22 (78.6)	24 (82.8)	0.69
Moderate	6 (21.4)	5 (17.2)	
High	0 (0)	0 (0)	
Education, n (%)			
Less than college degree	5 (17.9)	2 (6.9)	0.69
College degree or higher	23 (82.1)	27 (93.1)	

BMI, body mass index.

Pregnancy outcomes are shown in Table 3. Total pregnancy weight gain was comparable in both groups. Neonatal birth-weight and rates of neonatal hypoglycemia were not significantly different between the probiotic group and placebo group.

DISCUSSION

In the present study of pregnant women with GDM in Thailand, probiotic supplementation for 4 weeks during the late second to early third trimester resulted in favorable metabolic

Table 2 | Changes in glucose metabolism indices, weight gain and caloric intake of the participants

Results	Probiotic group (n = 28)	Placebo group (n = 29)	Mean difference (95% CI)	P-value
Fasting plasma glucose (mg/dL)				
Pre-intervention	82.96 ± 6.70	83.68 ± 8.30	-0.72 (-4.74, 3.29)	
Post-intervention	83.92 ± 6.48	88.31 ± 8.74	-4.39 (-8.48, -0.28)	
Mean change	0.68 ± 5.88	4.62 ± 7.78	-3.94 (-7.62, -0.27)	0.03
Fasting insulin (mIU/mL)				
Pre-intervention	8.77 ± 4.56	6.76 ± 3.98	2.01 (-0.26, 4.28)	
Post-intervention	9.88 ± 4.15	10.53 ± 5.33	-0.65 (-3.20, 1.89)	
Mean change	1.11 ± 1.71	3.77 ± 1.70	-2.67 (-3.57, -1.76)	0.01
HOMA-IR				
Pre-intervention	1.82 ± 0.99	1.44 ± 0.94	0.38 (-0.14, 0.90)	
Post-intervention	2.07 ± 0.94	2.34 ± 1.30	-0.27 (-0.88, 0.34)	
Mean change	0.25 ± 0.37	0.89 ± 0.46	-0.63 (-0.86, -0.41)	0.01
Weight (kg)				
Pre-intervention	63.49 ± 10.75	62.88 ± 9.33	0.61 (-4.72, 5.95)	
Post-intervention	65.18 ± 11.42	64.64 ± 10.11	0.54 (-4.11, 6.08)	
Mean change	1.69 ± 0.64	1.76 ± 0.78	-0.06 (-0.51, 0.39)	0.78
Caloric intake (kcal)	2,167.38 ± 253.99	2,175.40 ± 243.84	-8.02 (-140.17, 124.12)	0.90
Carbohydrate (g)	277.42 ± 32.59	275.60 ± 29.83	1.82 (-14.75, 18.40)	0.78
Fat (g)	80.59 ± 14.12	81.57 ± 14.81	-0.98 (-8.66, 6.70)	0.79
Protein (g)	83.32 ± 13.97	84.81 ± 12.90	-1.49 (-8.62, 5.64)	0.83
Dietary fiber (g)	11.50 ± 3.59	12.93 ± 6.83	-1.43 (-4.34, 1.48)	0.20
Distribution of carbohydrate (%)	51.27 ± 3.89	50.80 ± 3.46	0.47 (-1.48, 2.43)	0.27
Distribution of fat (%)	33.39 ± 3.71	33.59 ± 3.28	-0.19 (-2.05, 1.67)	0.54
Distribution of protein (%)	15.35 ± 1.47	15.60 ± 1.65	-0.25 (-1.08, 0.59)	0.33

CI, confidence interval; HOMA-IR, homeostatic model assessment for insulin resistance.

Table 3 | Pregnancy outcomes of the participants

Pregnancy outcomes	Probiotic group (n = 28)	Placebo group (n = 29)	P-value
Total weight gain (kg)	10.72 ± 4.00	11.82 ± 4.80	0.35
Birth weight (g)	3,120.36 ± 411.09	3,123.45 ± 369.81	0.98
Neonatal hypoglycemia, n (%)	5 (17.86)	7 (24.13)	0.35

changes on fasting plasma glucose, fasting plasma insulin and HOMA-IR, compared with placebo. These effects occurred without significant differences in caloric intake, dietary macronutrient composition, fiber intake or weight gain between the placebo and probiotic groups. In addition, probiotic supplementation was shown to be well tolerated and safe in the participants. These results support the beneficial effects of probiotics on glucose metabolism in women with GDM.

In pregnancy, insulin resistance increases, especially around the late second trimester and beyond. The present data are in agreement with this, as fasting glucose, insulin and HOMA-IR increased during the 4-week period in the placebo group. Probiotic supplementation in the current study resulted in significantly less increase in insulin resistance, and more favorable fasting glucose and insulin levels, compared with placebo. A few previous studies have also shown a favorable effect on

fasting glucose levels. Dolatkhah *et al.*¹⁸ studied 64 pregnant women with newly diagnosed GDM who were randomized to daily probiotic supplements (4-strain bacteria: *L. acidophilus*, *Bifidobacterium*, *Streptococcus thermophilus* and *Lactobacillus delbrueckii bulgaricus*) or placebo for 8 weeks. Fasting glucose levels showed a greater decline in the intervention group compared with the control group. In another study of 60 pregnant women in Iran, probiotic treatment for 6 weeks also resulted in significant decreases in fasting plasma glucose compared with placebo (-9.2 mg/dL vs +1.1 mg/dL, $P < 0.001$)²⁰. However, not all studies have found effects on fasting glucose levels. For example, one of the largest studies was carried out by Lindsay *et al.*¹⁹ in 149 pregnant women with GDM who were randomized to either a daily probiotic (*Lactobacillus salivarius*) or placebo capsule for 4–6 weeks. There were no significant differences in fasting glucose levels between the two groups

after the intervention. Consequently, it is not surprising that a recent meta-analysis including four randomized controlled studies (288 women) did not find significant effects of probiotics on fasting glucose levels³⁰. It is possible that the lack of positive effects in fasting glucose levels seen in some studies could be due to a relatively mild degree of hyperglycemia in these women with diet-controlled GDM, and probiotics could not further lower glucose levels, as some of them might have been in the normal range at baseline. More consistent findings, however, were shown for HOMA-IR, a marker of insulin resistance^{18–21}. The meta-analysis of these studies found a significant reduction in HOMA-IR as a result of probiotic supplementation, compared with placebo, with a mean difference of -0.69^{30} . This effect size was remarkably similar to the findings in the present study. Thus, the present data are in agreement with these previous studies and collectively further support the role of probiotics for improving glucose metabolism in GDM.

As dietary intake, including calories, macronutrients and fiber consumption, and weight gain were comparable between the two groups, the improvement in metabolic parameters likely involved other mechanistic pathways. Potential mechanisms by which probiotics improve glucose metabolism include reduction in oxidative stress and inflammation, reduction in intestinal permeability, and increased secretion of incretins^{31–34}. In a study of 60 GDM women, 6 weeks of probiotic supplementation led to a significant reduction in serum high-sensitivity C-reactive protein and a significant increase in total anti-oxidant capacity levels, along with reduction in fasting glucose levels²³. Probiotics have also been shown to increase the expression of adhesion proteins within the intestinal epithelium and to reduce intestinal permeability, leading to less systemic inflammation that might contribute to less insulin resistance³⁵. In addition, production of short-chain fatty acids, propionate and butyrate were facilitated by probiotics, leading to enhanced glucagon-like peptide-1 (GLP-1) secretion³². GLP-1 is one of the incretin hormones that stimulates insulin secretion and delays gastric emptying, leading to improved glucose levels; indeed, GLP-1 receptor agonists are widely used as antidiabetic medications³⁶. Other mechanisms involved could be downregulation of fasting-induced adipose factor, leading to increased triglyceride deposition in adipocytes³⁷, suppression of the release of adenosine monophosphate-activated protein kinase, which leads to increased glucose uptake and insulin secretion^{38,39}, and the ability to convert choline to trimethylamine, which indirectly affects the storage of triglycerides in the liver⁴⁰. Collectively, these data help explain how probiotics might exert beneficial effects on glucose metabolism.

In the present study, the participants had diet-controlled GDM; hence, their fasting glucose values were relatively close to the normal range. However, a mean difference in fasting glucose levels of 3.9 mg/dL between the probiotic and placebo groups could still be clinically meaningful. According to the Hyperglycemia and Adverse Pregnancy Outcome study⁴¹, every

4-mg/dL increase in fasting glucose levels >75 mg/dL was associated with an incremental risk of macrosomia and primary cesarean section. It is possible that probiotics might be beneficial in women with more severe degrees of hyperglycemia, such as those requiring insulin, but this remains to be investigated. In addition, probiotic supplementation has been shown in some studies to provide benefits beyond the pregnancy period. In a study by Laitinen *et al.*¹⁷, probiotic supplementation coupled with dietary counseling in the first trimester exerted positive effects on glucose and insulin levels, as well as HOMA-IR, that persisted over the 12-month postpartum period. Furthermore, probiotic supplementation was also shown to be associated with favorable changes in breast milk composition⁴², and moderated excessive weight gain in the offspring from the fetal period until 24–48 months-of-age⁴³. Finally, favorable effects of probiotics on lipid profiles of pregnant women with GDM have also been shown²⁰. As the intrauterine environment can affect the long-term metabolic health of the offspring, future research should explore longitudinal effects of probiotics use during pregnancy in both mothers and their children.

Although this study had the strength of being a double-blind randomized controlled study, there were some limitations. We did not have data on the gut microbiota composition of the participants at baseline or after the intervention to evaluate the impact of the intervention on the intestinal microbial community and relate them to changes in metabolic parameters. In addition, we did not have information on changes in GLP-1 or short-chain fatty acids levels, which could help elucidate the mechanisms linking probiotic use and improved insulin resistance. This should be explored in future research. Although some studies used longer treatment periods^{18–21,23}, the intervention period in the present was just 4 weeks, and we used two-strain probiotics, whereas some investigators used probiotics with four strains¹⁸. The decision to use the two-strain probiotic was driven by their availability and approval at our institution for treatment of other conditions. Therefore, the optimum duration to achieve maximum metabolic effects without adverse outcomes, along with the most suitable probiotic compositions, should be explored in the future. As the present study only enrolled diet-controlled women with GDM, the results might not be generalized to other groups of patients, such as those with more severe hyperglycemia requiring insulin. In addition, we did not observe any effects on pregnancy outcomes, as the study was not powered to capture these. Whether improved maternal metabolic parameters associated with probiotics use will result in favorable pregnancy outcomes should be further investigated.

In summary, the present study showed that two-strain probiotic supplements for 4 weeks in diet-controlled Thai women with GDM in the late second to early third trimester exerted beneficial effects on fasting glucose levels and markers of insulin resistance without any adverse effects. As GDM is a global problem with maternal and offspring consequences, the data of the present study should be replicated in various populations,

with optimization of strains and duration of probiotic use. The present results suggest that probiotic supplements may be considered as an adjunctive treatment for glycemic control in women with GDM.

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DISCLOSURE

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