BMC Endocrine Disorders

RESEARCH

Open Access

The effect of probiotics on gestational diabetes mellitus: an umbrella meta-analysis

Guixia Sun[1*], Hongli Hou[1] and Shanshan Yang[1]

Abstract

Background Prior studies indicated the positive effects of probiotics on glycemic regulation in patients with gestational diabetes mellitus (GDM). Nonetheless, the results remain inconclusive. To address this, we conducted an umbrella meta-analysis to evaluate the impact of probiotics on glycemic indicators in GDM.

Methods A comprehensive search was conducted on the PubMed and Scopus databases to identify all relevant meta-analyses of randomized clinical trials published until July 2024. The outcomes included serum hemoglobin A1C (HbA1c), fasting blood insulin (FBI), fasting blood sugar (FBS), homeostatic model assessment for insulin resistance (HOMA-IR), quantitative insulin sensitivity check index (QUICKI), homeostatic model assessment of beta cell function (HOMA-B), C-peptide, and oral glucose tolerance test (OGTT). Standardized mean difference (SMD) was used to test the effects.

Results In total, 27 studies, comprising 33,378 participants, were included in the analysis. Probiotics resulted in a significant decrease in FBS (SMD: -0.39, 95% CI: -0.56 to -0.23), especially when administered for ≤ 7 weeks. Significant reductions were also observed in FBI (SMD: -1.99, 95% CI: -2.41 to -1.58), HOMA-IR (SMD: -0.61, 95% CI: -0.72 to -0.50), and HOMA-B (SMD: -24.58, 95% CI: -30.59 to -18.56). Moreover, supplementation with probiotics significantly improved QUICKI (SMD: 0.007, 95% CI: 0.004 to 0.01). There was significant evidence of heterogeneity and publication bias. No significant effects were observed on 1-h OGTT, 2-h OGTT, HbA1c, and C-peptide. No dose-specific effect was observed.

Conclusions Supplementation with probiotics could improve glycemic control in women with GDM. The effects of probiotics on HOMA-IR, HOMA-B, and fasting insulin were clinically important, while, their effect on FBS was not clinically important.

Keywords Gestational diabetes, Probiotics, Glycemic control, Umbrella meta-analysis

*Correspondence:
Guixia Sun
sgx8647@126.com
[1]Department of Gynecology and Obstetrics, Shanxi Provincial Children's Hospital (Shanxi Provincial Maternal and Child Health Hospital), No.13 Xinmin North Street, Taiyuan, Shanxi 030001, China

Background

Gestational diabetes mellitus (GDM), distinguished by glucose intolerance, is among the prevalent pregnancy complications typically emerging in the second or third trimester of pregnancy, affecting approximately 5–20% of pregnant mothers [1]. The pathogenesis of GDM is multifaceted, encompassing genetic and environmental factors, such as obesity, maternal age, multiple pregnancies, and a history of diabetes [2]. This condition is linked to unfavorable consequences for both mothers and newborns, including preeclampsia, miscarriage, and an elevated risk of type 2 diabetes (T2DM) in mothers after childbirth [3]. Additionally, infants may face respiratory problems, birth defects, and excessive birth weight [4]. To minimize the likelihood of these health consequences, the optimal management for GDM is suggested to be adherence to a healthy diet, physical activity and pharmacological interventions like insulin, as the first line, as well as metformin and sulfonylureas [5, 6]. Sulfonylureas and metformin are discouraged since they can cross the placenta [6]. Although medications have some advantages, they can lead to remarkable side effects, including birth-related complications, neonatal hypoglycemia, and large-for-gestational-age infants [5]. Pregnant mothers may also encounter various challenges after the consumption of antidiabetic drugs, including hypoglycemia, dizziness, abdominal discomfort, and diarrhea [7]. Given the limitations of lifestyle changes and pharmaceutical treatments in managing GDM effectively, it is essential to explore alternative approaches to improve insulin resistance and hyperglycemia.

Dysregulation of gut microbiota has been associated with insulin resistance and metabolic disorders in pregnancy [4, 8]. Women with GDM exhibit decreased alpha diversity compared to non-GDM individuals during mid- and late gestation [9]. In pregnancy, there is an increase in Actinobacteria and Proteobacteria phyla and a decline in beneficial strains like Faecalibacterium prausnitzii and Roseburia intestinalis [4]. Furthermore, in GDM, the Firmicutes/Bacteroidetes ratio elevates towards late pregnancy [9]. These alterations in gut microbiota composition align with the accumulation of fat mass, elevated blood glucose levels, and insulin resistance [10]. Accordingly, the manipulation of the gut flora through the use of probiotics is emerging as an encouraging therapeutic approach for managing GDM. Despite the growing body of evidence, the results of randomized clinical trials (RCTs) [11, 12] on the efficacy of probiotics in managing GDM have been inconsistent, with remarkable differences in treatment duration, probiotic strains used, dose of treatment, and participant characteristics. The meta-analyses of RCTs have also revealed contradictory findings. While some meta-analyses have suggested an improvement in FBS [3, 13], other studies failed to identify any effect on FBS [4, 14–19]. This heterogeneity has led to uncertainty regarding the overall effectiveness of probiotics as a therapeutic approach for GDM. An umbrella meta-analysis, which synthesizes findings from multiple meta-analyses, can provide a comprehensive overview of the current evidence, clarify the potential benefits of probiotics, and identify gaps in the literature that require further investigation. This umbrella meta-analysis was conducted to evaluate the effect of probiotics on glycemic parameters in pregnant women with GDM by analyzing existing literature.

Methods

This umbrella meta-analysis was conducted according to the guidelines outlined in the PRISMA statement [20].

Search strategy

Two researchers carried out a literature search on PubMed and Scopus databases to obtain all relevant studies published in English up to July 2024. The search was limited to English-language publications. The search strategy included both text terms and medical subject headings (MeSH). The search strategy included the following terms: ("probiotic" OR "prebiotic" OR "synbiotic" OR "probiotics" OR "prebiotics" OR "synbiotics") AND ("gestational diabetes" OR "GDM") AND ("meta-analysis" OR "meta analysis"). A supplementary hand search of references within pertinent studies was also conducted to include missing studies.

Inclusion criteria

Two authors assessed the eligibility of publications separately, and any discrepancies were resolved through a group discussion. The calculated kappa for the inter-rater reliability between the two authors was 0.81 for the data screening and selection process. The inclusion criteria were as follows: (1) Participants: pregnant women with GDM, (2) Intervention: supplementation with probiotics alone or in combination with prebiotics (synbiotics), (3) Comparator: placebo, (4) Outcomes: the outcomes were HbA1c, FBI, FBS, HOMA-IR, QUICKI, HOMA-B, 1-h OGTT, 2-h OGTT, and C-peptide, and (5) Study type: meta-analyses of RCTs. Exclusion criteria included review articles, letters, editorials, protocols, and studies with irrelevant interventions or outcomes.

Data extraction and quality assessment

Two investigators independently conducted data extraction, and any differences were resolved through discussion. The following data were extracted from the studies: the first author's name, country, sample size, risk of bias (RoB) assessment, year of publication, number of studies, dose and duration of supplementation, and effect sizes. When necessary, the corresponding authors were

contacted to obtain any necessary information that was not reported in the studies. The methodological quality of the included studies was measured using A Measurement Tool to Assess Systematic Reviews-2 (AMSTAR-2) criteria [21]. This tool provides a structured approach to assess the critical domains of systematic reviews by considering factors like the appropriateness of the research question, the comprehensiveness of the search strategy, the study selection process, data extraction methods, and the assessment of bias in the included studies.

Data synthesis

The Stata software (version 17) was used to analyze the data. The results were pooled using the standardized mean difference (SMD) and a 95% confidence interval (CI) as the effect size. Q-statistic test and the I^2 test were applied to investigate heterogeneity, where a value of $I^2 \geq 50\%$ or $p < 0.10$ indicated significant heterogeneity [22, 23]. Given the expected heterogeneity among the studies, the data were pooled with the use of a random effects model. In addition, we performed subgroup analysis to investigate the sources of heterogeneity, such as the dose of probiotics, duration of supplementation, type of intervention, study quality, and sample size. Sensitivity analysis was also carried out to measure the impact of each study on the pooled results by systematically excluding one study at a time. To investigate publication bias, the funnel plot and the Egger's test were employed [24]. In cases where the p-values from the Egger's tests were less than 0.05, the trim-and-fill analyses [25] were additionally carried out to address potential publication biases. Meta-regression analysis was done to evaluate the influence of publication year, sample size, dosage and duration of supplementation, and the proportion of high-quality RCTs in each meta-analysis on the pooled estimates.

Results

Study characteristics

In total, 119 studies were identified by the search strategy. Finally, 27 meta-analyses [3–6, 8, 9, 14–19, 26–40], with a total sample size of 33,378 participants, were included. The flow diagram of study selection is reported in Fig. 1. In all studies, the intervention was multistrain probiotics. The sample size ranged from 225 to 9,443 subjects. The dose of probiotics varied from 0.5×10^9 to 823×10^9 colony-forming units (CFU). The duration of supplementation was between 6 and 14 weeks. Data was reported for FBS in 25 studies [3–6, 8, 9, 14–19, 26–31, 33–37, 39, 40], FBI in 20 studies [3, 5, 6, 9, 14–16, 19, 26–34,

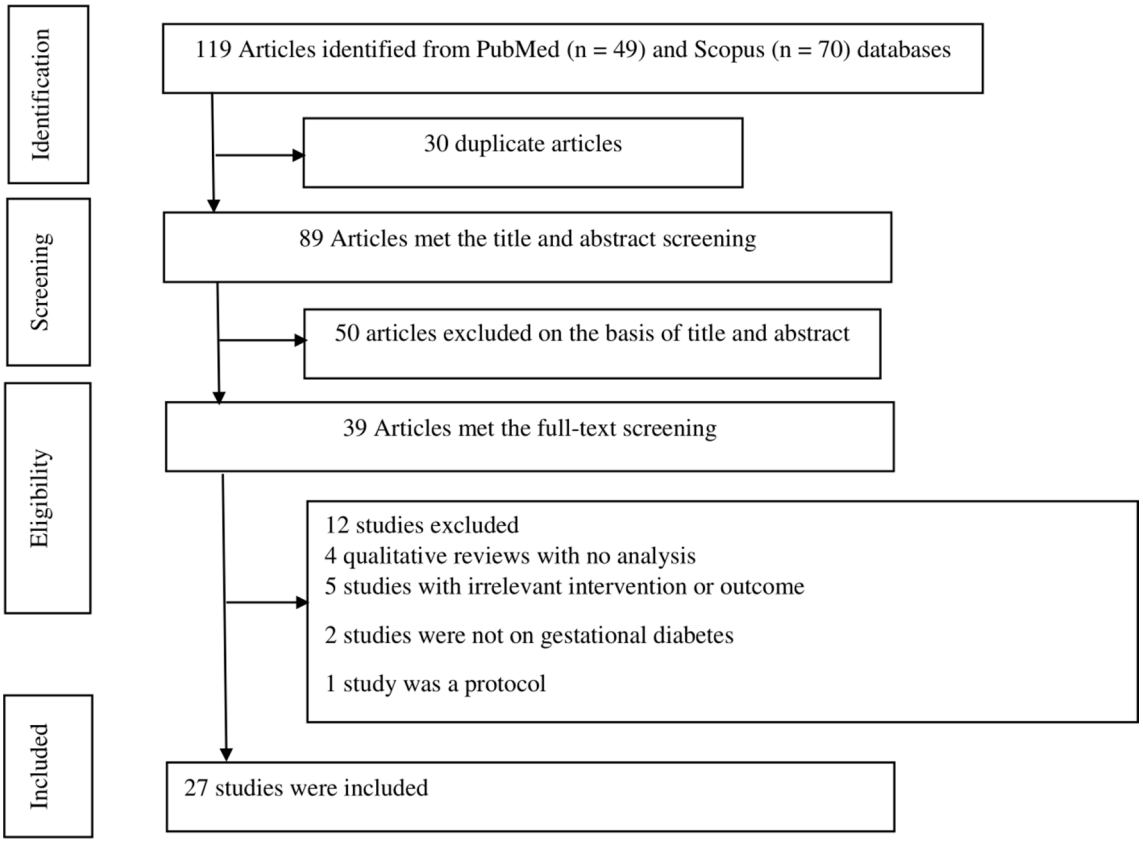

Fig. 1 Flow diagram of the study

38–40], HOMA-IR in 21 studies [3–6, 9, 14, 16, 18, 19, 26–31, 33, 34, 37–40], HOMA-B in 5 studies [5, 6, 14, 30, 33], QUICKI in 12 studies [5, 9, 14, 26, 27, 30, 31, 33, 34, 38–40], 1-h OGTT in 2 studies [15, 30], 2-h OGTT in 3 studies [15, 30, 35], HbA1c in 2 studies [33, 34], and C-peptide in 2 studies [14, 33]. The characteristics of the included studies are presented in Table 1.

Quality assessment

According to the AMSTAR-2 criteria, 16 studies were rated as moderate quality and 11 studies were rated as high quality (Table S1).

Results of the umbrella meta-analysis

The meta-analysis found that probiotics significantly reduced FBS (SMD: -0.39, 95% CI: -0.56 to -0.23). A significant heterogeneity was observed (I^2=76.1%, P=0.0001) (Fig. 2). In the subgroup analysis, the favorable impact of probiotics on FBS was found across different subgroups. The beneficial effect of probiotics was solely evident when the supplementation period was <7 weeks (Table 2). A significant reduction in FBI was also found (SMD: -1.99, 95% CI: -2.41 to -1.58), with considerable heterogeneity (I^2=82.9%, P=0.0001). However, no significant effects were observed on 1-h OGTT, 2-h OGTT, HbA1c, and C-peptide (Fig. 2; Table 2). Moreover, supplementation with probiotics significantly improved QUICKI (SMD: 0.007, 95% CI: 0.004 to 0.01) and reduced HOMA-IR (SMD: -0.61, 95% CI: -0.72 to -0.50) and HOMA-B (SMD: -24.58, 95% CI: -30.59 to -18.56) (Fig. 3).

Sensitivity and meta-regression analysis

In the sensitivity analysis, no study significantly impacted the pooled effect sizes, indicating the reliability of the results (Fig. S1 to Fig. S5). Additionally, in the meta-regression analysis, the pooled effect sizes were not affected by publication year, the proportion of high-quality studies in each meta-analysis, sample size, and the dose and duration of treatment (Table S2).

Publication bias

Although a significant publication bias was identified for the majority of outcomes (Fig. 4), the trim-and-fill analysis did not alter the pooled estimates. This indicates the minimal impact of publication bias on the results.

Grade assessment

Based on the GRADE criteria, the quality of evidence was moderate for HOMA-B and low for the other outcomes (Table S3).

Discussion

This analysis indicated that probiotics improved glycemic indices in GDM patients. The results revealed that probiotics reduce serum FBS, FBI, HOMA-B, and HOMA-IR index, but increase QUICKI. However, no significant effects were observed on 1-h OGTT, 2-h OGTT, HbA1c, and C-peptide. The positive effect of probiotics on FBS was evident when probiotics were given for a short term (≤7 weeks). Other indices of glycemic control were not affected by the treatment duration and intervention dosage. The effects of probiotics on HOMA-IR, HOMA-B, and fasting insulin were clinically important, while, their effect on FBS was not clinically important.

GDM can result in various adverse outcomes if not adequately managed, emphasizing the necessity for safe and efficient therapies. Studies have observed shifts in gut microbiota composition in pregnant women, showing a reduction in favorable bacteria regulating metabolism and an elevation in bacteria with detrimental metabolic impacts. These alterations can disrupt host energy metabolism [4, 8]. Introducing exogenous probiotics to reshape gut microbiota represents a novel approach to GDM management. In this study, the concurrent reduction in FBS and FBI levels, alongside improvements in HOMA-IR and QUICKI, suggests an enhancement in insulin sensitivity rather than insulin secretion. This is in agreement with previous findings in GDM [41, 42], T2DM [43], and metabolic syndrome [44]. However, our analysis did not reveal a significant impact of probiotics on 1-hour OGTT, 2-hour OGTT, HbA1c, and C-peptide. These results should be interpreted with caution due to the heterogeneity and limited number of studies analyzed for the outcomes. The findings from the present meta-analysis have several clinical utilities. Probiotics may provide a safe and effective non-pharmacological adjunct for managing GDM, potentially reducing the need for insulin or other medications that may have side effects. Effective management of GDM through probiotics may also lower the possibility of future metabolic diseases in both mothers and infants, promoting better long-term health outcomes.

Other studies have also shown that probiotics could improve various metabolic parameters. An umbrella meta-analysis by Zarezadeh et al. [45] revealed that probiotics have beneficial effects on FBS, HbA1c, HOMA-IR, and insulin levels. A period of less than 8 weeks of probiotic supplementation at moderate dosages (10^8 or 10^9 CFU) was an effective approach for improving glycemic parameters. Another umbrella review suggested that probiotics could be used as a complementary therapy for controlling high blood pressure [46]. Additionally, an umbrella meta-analysis indicated that synbiotic supplementation can slightly improve lipid profiles and anthropometric indices and might be a therapeutic option for

Table 1 Characteristics of studies included in umbrella meta-analysis

Reference	Country	Year	No of studies	Sample size	Intervention	Outcomes	Bias tool, high quality/total studies	Percentage of high quality studies	Follow-up duration, week	Dose of probiotics (CFU)	Quality
Wang	China	2022	7	1149	Mixed probiotics	FBS, HOMA-IR	Cochrane, 4/7	57	7	122×10^9	High
Suastika	Indonesia	2024	13	896	Mixed probiotics and symbiotic	FBS, HOMA-IR, FBI	Cochrane, 13/13	100	6	249×10^9	Moderate
Okesene-Gafa	New Zealand	2020	9	695	Mixed probiotics	FBS, HOMA-IR, HOMA-B, FBI, QUICKI, C-peptide	Cochrane, 9/9	100	6	235×10^9	High
Chan	China	2021	15	9443	Mixed probiotics	FBS, HOMA-IR, HOMA-B, FBI, 1-h OGTT, 2-h OGTT, QUICKI	Cochrane, 12/15	80	NR	NR	Moderate
Chen	China	2020	7	462	Mixed probiotics	FBS	Jadad,7/7	100	6	139×10^9	Moderate
Davidson	Australia	2021	6	1440	Mixed probiotics	FBS, FBI, 1-h OGTT, 2-h OGTT	Cochrane, 6/6	100	14	21×10^9	High
Han	China	2019	13	1139	Mixed probiotics	FBS, HOMA-IR, FBI, QUICKI	Cochrane, 13/13	100	8	55×10^9	High
Pan	china	2021	10	740	Mixed probiotics and symbiotic	FBS, HOMA-IR, HOMA-B, FBI, QUICKI	Cochrane,8/10	80	6	257×10^9	High
Hasain	Malaysia	2021	9	594	Mixed probiotics	FBS, HOMA-IR, FBI, QUICKI	Cochrane,9/9	100	6	147×10^9	High
Jin	China	2020	4	225	Mixed probiotics	FBS, HOMA-IR, FBI	Cochrane, NR	NR	6	24×10^9	Moderate
Lagowska	Poland	2019	11	560	Mixed probiotics and symbiotic	FBS, HOMA-IR, FBI	Cochrane,11/11	100	6	238×10^9	High
Lan	China	2023	11	713	Mixed probiotics and symbiotic	FBS, HOMA-IR, FBI, QUICKI	NR	NR	NR	6×10^9	Moderate
Masulli	Italy	2020	7	1966	Mixed probiotics	FBS	Cochrane, 7/7	100	10	84.5×10^9	High
Mu	China	2023	11	779	Mixed probiotics and symbiotic	FBS, HOMA-IR, FBI, QUICKI	Cochrane,12/13	92	6	227×10^9	Moderate
Pan	China	2017	6	830	Mixed probiotics	FBS, HOMA-IR, FBI	Jadad,6/6	100	8	130×10^9	Moderate
Peng	Taiwan	2018	6	438	Mixed probiotics and symbiotic	FBS, HOMA-IR	Cochrane,6/6	100	7	101×10^9	Moderate
Ramanathan	India	2020	5	409	Mixed probiotics	FBI	Cochrane, 5/5	100	7	NR	High
Wu	Germany	2023	15	1006	Mixed probiotics	FBS, HOMA-IR, FBI, QUICKI	Cochrane,13/15	86	6	261×10^9	Moderate
Hao	China	2021	12	894	Mixed probiotics and symbiotic	FBS, HOMA-IR, HOMA-B, FBI	Cochrane/, 12/12	100	7	250×10^9	Moderate
Ozdemir	Turkey	2022	6	391	Mixed probiotics	FBS, HbA1c, HOMA-IR, FBI, QUICKI	Cochrane,6/6	100	6	134×10^9	Moderate
Tabatabaeizadeh	Iran	2023	4	533	Mixed probiotics	FBS	Cochrane,3/4	75	NR	0.5*10^9	Moderate
Taylor	Australia	2017	4	288	Mixed probiotics	FBS, HOMA-IR	Cochrane,4/4	100	7	26×10^9	Moderate
Yefet	Israel	2023	14	854	Mixed probiotics	HOMA-IR, FBI, QUICKI	CONSORT checklist, 14/14	100	6	277×10^9	Moderate
Zhang	China	2019	11	719	Mixed probiotics and symbiotic	FBS, HOMA-IR, FBI, QUICKI	Cochrane,10/11	91	6	154×10^9	High
Zheng	China	2018	4	1428	Mixed probiotics	FBS, HOMA-IR, FBI	Cochrane,4/4	100	7	119×10^9	High
Chen	China	2023	6	NR	Mixed probiotics	FBS, 2-h OGTT	NR	NR	NR	NR	Moderate
Mahdizade Ari	Iran	2022	26	4787	Mixed probiotics and symbiotic	FBS, HbA1c, HOMA-IR, HOMA-B, FBI, QUICKI, C-peptide	JBI, 26/26	100	11	823×10^9	Moderate

NR: Not reported, FBS: fasting blood sugar, HOMA-IR: homeostatic model assessment for insulin resistance, HOMA-B: homeostatic model assessment of beta cell function, FBI: fasting blood insulin, OGTT: oral glucose tolerance test, QUICKI: quantitative insulin sensitivity check index, HbA1c: glycated hemoglobin, JBI: the Joanna Briggs Institute

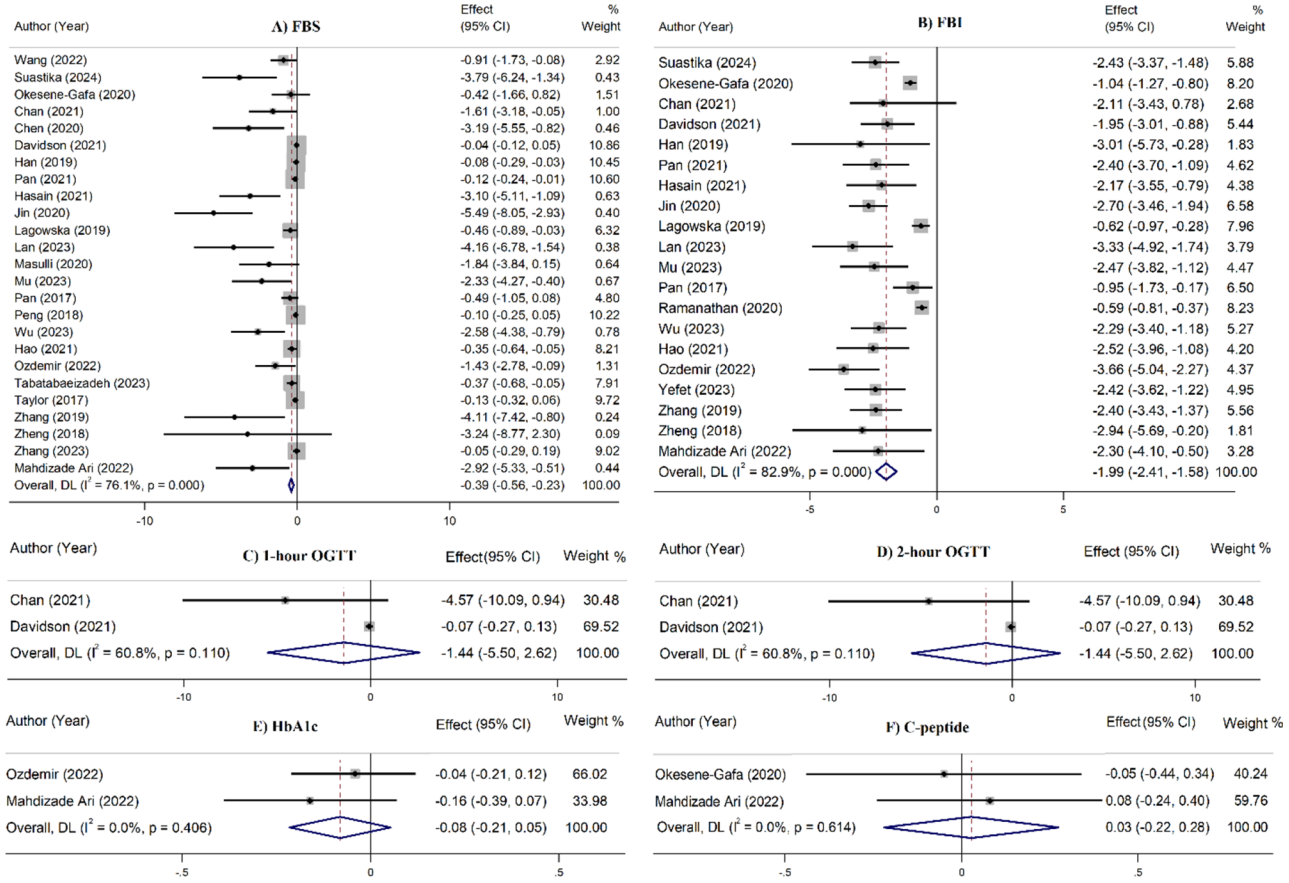

Fig. 2 Pooled analysis for the effect of probiotics on (**A**) FBS (fasting blood sugar, (**B**) FBI (fasting blood insulin), (**C**) 1-hour OGTT (oral glucose tolerance test), (**D**) 2-hour OGTT, (**E**) HbA1c (glycated hemoglobin), and (**F**) C-peptide

obesity and its related disorders [47]. Probiotics have also been shown to reduce inflammatory biomarkers [48] and biomarkers of oxidative stress [49].

The Minimal Clinically Important Difference (MCID) is a critical concept in clinical research that quantifies the smallest change in a patient-reported outcome that is perceived as beneficial by the patient and would necessitate a change in their management. Initially defined by Jaeschke et al. in 1989 [50], the MCID serves to bridge the gap between statistical significance and clinical relevance, emphasizing the importance of patient perspectives in evaluating treatment efficacy. It reflects the threshold at which changes in health status are meaningful enough to impact clinical decisions, thus guiding healthcare providers in assessing the effectiveness of interventions. The MCID for FBS, HOMA-IR, HOMA-B, and fasting insulin is reported to be 1.6 mmol/L, 0.05 units, 5 units, and 1.5 IU/mL, respectively [51]. In our study, the pooled effect size for FBS, HOMA-IR, HOMA-B, and fasting insulin was −0.35, -0.61, -24.58, and −1.99, respectively. Therefore, the effects of probiotics on HOMA-IR, HOMA-B, and fasting insulin were clinically important, while, their effect on FBS was not clinically important. The positive impact of probiotics intake on glycemic indices in GDM is mediated through various mechanisms, comprising modulation of gut microbiota, improvement of insulin sensitivity, reduction of inflammation, increased production of short-chain fatty acids (SCFAs), and reduction of oxidative stress [52, 53]. Probiotics, such as Lactobacillus casei, Bifidobacterium bifidum, and Lactobacillus acidophilus can alter the gut microbial composition and promote the growth of advantageous bacteria. This shift in the gut flora could result in improved glucose metabolism [54]. Probiotics can decrease inflammation by affecting the immune system and decreasing the production of inflammatory cytokines, such as tumor necrosis factor-a (TNF-a) and interleukin-6 (IL-6) [19]. Chronic inflammation is a well-identified contributor to insulin resistance, and its reduction can improve glycemic control [55]. Probiotics can stimulate the production of SCFAs, such as acetate, propionate, and butyrate, by fermenting dietary fiber [56]. SCFAs can improve insulin sensitivity, suppress gluconeogenesis, and reduce glucose levels [31]. Probiotics enhance glucagon-like peptide-1 (GLP-1) secretion, subsequently reducing glucose levels via the following mechanisms: (a) enhancing insulin release and

Table 2 Overall and subgroup analyses for the effect of probiotics on glycemic indices in women with gestational diabetes

			Test of effect	Test of heterogeneity		
Outcomes	**Subgroups**	**Studies**	**SMD (95%CI)**	**I^2 (%)**	***P***	**Publication bias**
FBS	Overall	25	-0.35 (-0.56, -0.23)	76.1	0.001	0.001
Sample size	≥ 800 participants	11	-0.44 (-0.71, -0.17)	74.6	0.001	
	< 800 participants	13	-0.53 (-0.82, -0.25)	79.6	0.001	
	NR	1	-0.05 (-0.29, 0.19)	-	-	
Type of intervention	Probiotics	16	-0.10 (-0.16, -0.04)	75.7	0.001	
	Probiotics and synbiotics	9	-0.17 (-0.25, -0.08)	78.5	0.001	
Dose of probiotics	≥ 125×10^9 CFU	13	-1.01 (-1.44, -0.57)	77.1	0.001	
	< 125×10^9 CFU	9	-0.19 (-0.38, -0.01)	77.2	0.001	
	NR	1	-1.63 (-3.17, -0.05)	-	-	
Duration of supplementation	≥ 7 weeks	7	-0.12 (-0.27, 0.02)	52.6	0.04	
	< 7 weeks	14	-0.81 (-1.16, -0.47)	80.8	0.001	
	NR	4	-0.57 (-1.19, 0.05)	79.3	0.002	
Quality (AMSTAR-2)	Moderate	15	-0.69 (-1.00, -0.38)	79.7	0.001	
	High	10	-0.21 (-0.38, -0.03)	66.7	0.001	
Serum insulin	Overall	20	-1.99 (-2.41 to -1.58)	82.9	0.001	0.003
Sample size	≥ 800 participants	10	-2.02 (-2.45, -1.59)	10.7	0.34	
	< 800 participants	10	-1.87 (-2.40, -1.34)	88.5	0.001	
Type of intervention	Probiotics	12	-1.02 (-1.16, -0.87)	83.9	0.001	
	Probiotics and synbiotics	8	-1.27 (-1.55, -0.99)	82.7	0.001	
Dose of probiotics	≥ 125×10^9 CFU	5	-2.60 (-3.15, -2.04)	0.0	0.65	
	< 125×10^9 CFU	13	-1.96 (-2.46, -1.47)	79.2	0.001	
	NR	2	-0.97 (-2.27, 0.32)	49.5	0.15	
Duration of supplementation	≥ 7 weeks	6	-1.44 (-2.20, -0.68)	66.6	0.01	
	< 7 weeks	12	-2.15 (-2.70, -1.59)	84.3	0.001	
	NR	2	-2.89 (-4.16, -1.62)	0.0	0.36	
Quality (AMSTAR-2)	Moderate	11	-2.39 (-2.88, -1.90)	45	0.05	
	High	9	-1.34 (-1.78, -0.91)	77.7	0.001	
HOMA-IR	Overall	21	-0.61 (-0.72, -0.50)	68.8	0.001	0.01
Sample size	≥ 800 participants	10	-0.62 (-0.73, -0.50)	0.0	0.87	
	< 800 participants	11	-0.59 (-0.74, -0.44)	78	0.001	
Type of intervention	Probiotics	12	-0.37 (-0.41, -0.32)	73.0	0.001	
	Probiotics and synbiotics	9	-0.63 (-0.74, -0.53)	0.0	0.95	
Dose of probiotics	≥ 125×10^9 CFU	13	-0.58 (-0.71, -0.45)	71	0.001	
	< 125×10^9 CFU	7	-0.69 (-0.82, -0.56)	0.0	0.91	
	NR	1	-0.52 (-0.88, -0.16)	-	_	
Duration of supplementation	≥ 7 weeks	5	-0.67 (-0.91, -0.44)	0.0	0.90	
	< 7 weeks	14	-0.59 (-0.72, -0.46)	75.1	0.001	
	NR	2	-0.64 (-0.85, -0.43)	0.0	0.39	
Quality (AMSTAR-2)	Moderate	13	-0.63 (-0.72, -0.55)	0.0	0.93	
	High	8	-0.58 (-0.77, -0.39)	71.9	0.001	
HOMA-B	Overall	5	-24.58 (-30.59, -18.56)	0.0	0.98	0.03
Sample size	≥ 800 participants	3	-24.07 (-31.87, -16.27)	0.0	0.86	
	< 800 participants	2	-25.32 (-34.75, -15.88)	0.0	0.98	
Type of intervention	Probiotics	2	-25.38 (-34.53, -16.23)	0.0	0.99	
	Probiotics and synbiotics	3	-23.97 (-31.94, -15.99)	0.0	0.87	
Dose of probiotics	≥ 125×10^9 CFU	4	-24.36 (-31.15, -17.57)	0.0	0.95	
	< 125×10^9 CFU	1	-25.38 (-38.32, -12.44)	-	_	
Duration of supplementation	≥ 7 weeks	1	-20.58 (-35,52, -5.64)	-	_	
	< 7 weeks	3	-25.34 (-32.96, -17.72)	0.0	1.000	
	NR	1	-25.38 (-38.32, -12.44)	-	_	
Quality (AMSTAR-2)	Moderate	3	-24.07 (-31,87, -16.27)	0.0	0.86	

Table 2 (continued)

			Test of effect	Test of heterogeneity		
Outcomes	**Subgroups**	**Studies**	**SMD (95%CI)**	**I^2 (%)**	***P***	**Publication bias**
	High	2	-25.32 (-34.75, -15.88)	0.0	0.98	
QUICKI	Overall	12	0.01 (0.00, 0.01)	61.5	0.003	0.43
Sample size	≥ 800 participants	6	0.01 (0.01, 0.01)	0.0	0.97	
	< 800 participants	6	0.00 (0.00, 0.01)	74.7	0.001	
Type of intervention	Probiotics		0.01 (0.00, 0.01)	69.6	0.003	
	Probiotics and synbiotics		0.00 (0.00, 0.01)	53.6	0.04	
Dose of probiotics	≥ 125 × 10^9 CFU	8	0.01 (0.00, 0.01)	67.6	0.003	
	< 125 × 10^9 CFU	3	0.01 (0.01, 0.01)	0.0	1.00	
	NR	1	0.01 (0.01, 0.01)	-	_	
Duration of supplementation	≥ 7 weeks	3	0.01 (0.00, 0.02)	0.0	1.00	
	< 7 weeks	7	0.00 (0.00, 0.01)	70.8	0.02	
	NR	2	0.01 (0.01, 0.01)	0.0	1.00	
Quality (AMSTAR-2)	Moderate	7	0.01 (0.00, 0.01)	68.6	0.004	
	High	5	0.01 (0.00, 0.01)	57.8	0.05	
1 h OGGT	Overall	2	-1.44 (-5.50, 2.62)	60.8	0.11	-
2 h OGGT	Overall	3	-0.02 (-0.17, 0.13)	16.6	0.30	-
Serum C-peptide	Overall	2	0.03 (-0.22, 0.28)	0.0	0.61	-
Serum HbA1C	Overall	2	-0.08 (-0.21, 0.05)	0.0	0.40	-

NR: Not reported, FBS: fasting blood sugar, HOMA-IR: homeostatic model assessment for insulin resistance, HOMA-B: homeostatic model assessment of beta cell function, OGTT: oral glucose tolerance test, QUICKI: quantitative insulin sensitivity check index

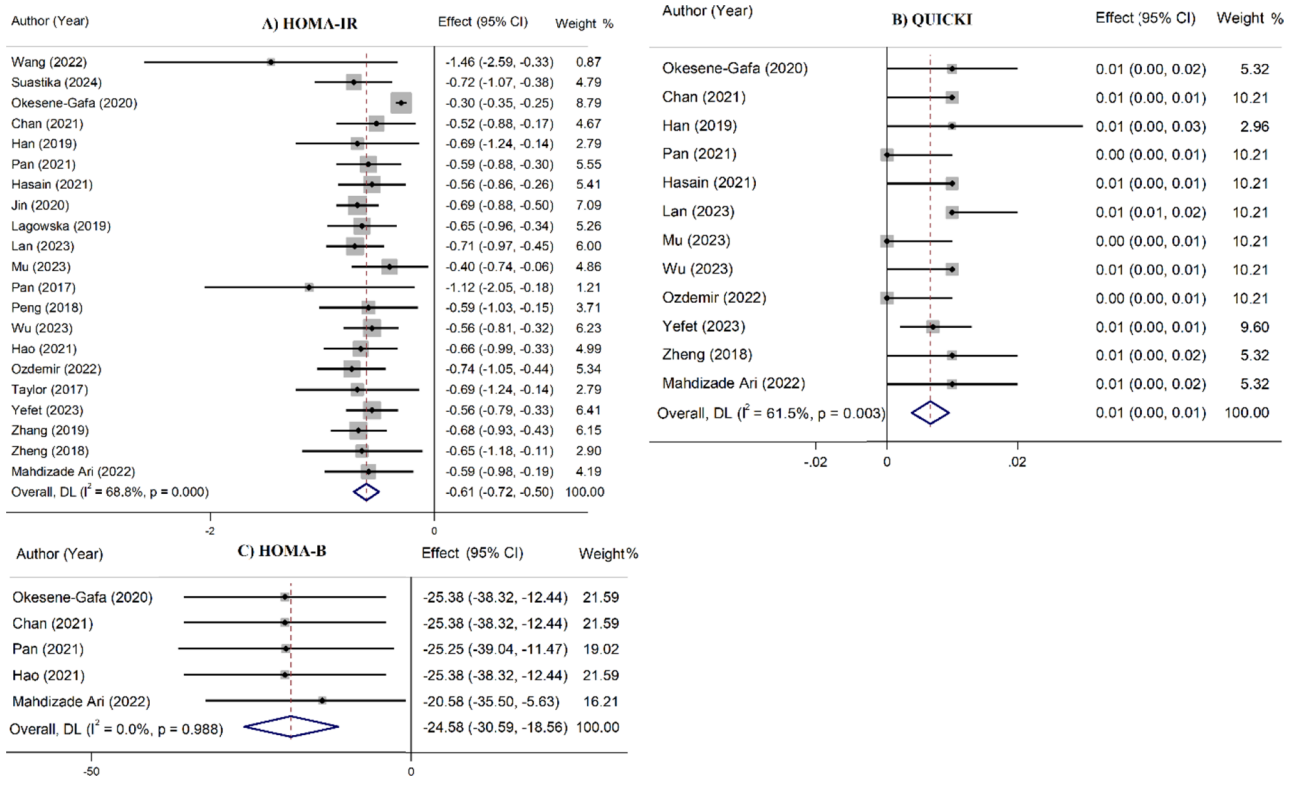

Fig. 3 Pooled analysis for the effect of probiotics on (**A**) HOMA-IR (homeostatic model assessment for insulin resistance, (**B**) QUICKI (quantitative insulin sensitivity check index), and (**C**) HOMA-B (homeostatic model assessment of beta cell function)

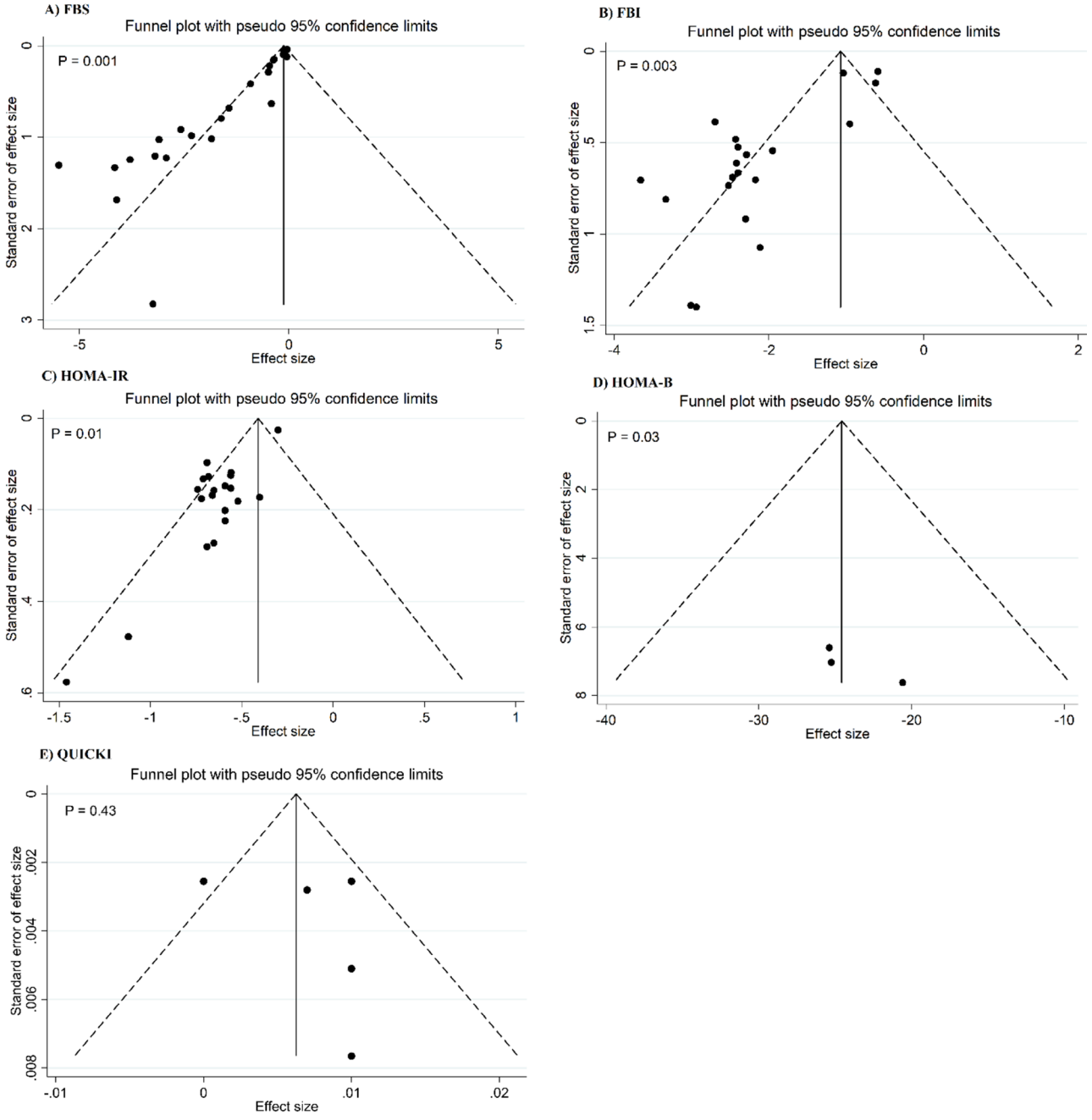

Fig. 4 Funnel plots for publication bias for outcomes

slowing gastric emptying [57], (b) modification of gene expression of proteins associated with glucose metabolism, including PPAR-gamma, glucose transporter type 4, ghrelin, leptin, and glucose-6-phosphatase [58], and (c) decreasing toll-like receptor activity, thereby increasing insulin sensitivity in muscle. This can result in lower FBS and FBI levels, as well as improved HOMA-IR and QUICKI [59]. Probiotics also reduce oxidative stress by elevating the antioxidant enzyme activities, resulting in a reduction in the production of reactive oxygen species [60]. Oxidative stress is known to be related to insulin resistance and impaired glucose tolerance [61].

To our knowledge, this umbrella meta-analysis represents the first investigation assessing the impact of probiotics on glycemic parameters in GDM. The strength of our umbrella meta-analysis is inclusion of a high number of studies and a thorough evaluation of diverse metabolic factors associated with glycemic regulation. The results were obtained from meta-analyses with moderate to high quality, increasing the reliability of the findings. Moreover, the sources of heterogeneity were examined using

subgroup and meta-regression analyses by considering various factors, especially dose and duration of intervention. Several limitations should be acknowledged in this study. First, significant heterogeneity was found among the included studies, reducing the generalizability of the results. Random effects models were employed to minimize the influence of heterogeneity on the combined estimates. In the subgroup analysis, differences in sample sizes, supplementation dose, duration of treatment, and study quality were recognized as the origins of the heterogeneity. Second, a significant publication bias was detected. The search strategy was limited to publications in the English language, which may have resulted in the omission of some smaller studies. Nevertheless, using the trim-and-fill analysis, we revealed that the influence of publication bias on the pooled estimates is insignificant. Third, studies have highlighted that different probiotic strains may have diverse metabolic impacts [62]. While all studies in this analysis administered multistrain probiotics, information regarding the impact of different strains on outcomes was scarce. Nevertheless, research indicates that utilizing a combination of various probiotic strains offers greater efficacy compared to single-strain probiotics, as the synergistic interaction among multiple strains may enhance their overall effects [33]. Additionally, the timing of intervention might influence the results [63], a factor that was not investigated in the included studies. Consequently, subgroup analysis considering intervention timing and probiotic strains could not be conducted. These factors likely contributed to increased heterogeneity among the studies, emphasizing the need for their consideration in the future studies. Another limitation of this study is that no dose-specific effects were observed in the analysis, thus, the optimal dosage of probiotics for improving glycemic parameters in GDM remain unclear. Moreover, while some glycemic indicators showed significant improvements, other important measures such as HbA1c, C-peptide, and OGTT did not demonstrate significant changes. This inconsistency in outcomes may limit the overall conclusions about the effectiveness of probiotics.

Conclusion

In conclusion, this analysis indicated that probiotics could offer beneficial effects on the indices of glucose metabolism in patients with GDM. Yet, to generalize these findings effectively, more clinical trials with larger sample sizes are essential, given the heterogeneity observed across current studies. Moreover, further research is necessary to explore the impact of various probiotic strains and their optimal timing of intervention on individuals with GDM.

Abbreviations

GDM	Diabetes mellitus
HbA1c	hemoglobin A1C
FBI	fasting blood insulin
FBS	fasting blood sugar
HOMA-IR	homeostatic model assessment for insulin resistance
QUIKI	quantitative insulin sensitivity check index
HOMA-B	homeostatic model assessment of beta cell function
OGTT	C-peptide, oral glucose tolerance test
SMD	standardized mean difference
T2DM	type 2 diabetes
RCTs	randomized clinical trials
MeSH	medical subject headings
RoB	risk of bias
AMSTAR-2	A Measurement Tool to Assess systematic Reviews-2
CI	confidence interval
CFU	colony-forming units
JBI	Joanna Briggs Institute scale
SCFAs	short-chain fatty acids
TNF-a	tumor necrosis factor-a
IL-6	interleukin-6
GLP-1	glucagon-like peptide-1

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12902-024-01751-w.

Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

Supplementary Material 4

Acknowledgements
Not applicable.

Author contributions
GS performed data collection, data analysis, article preparation, supervision, and re-writing of the manuscript. HH and SY performed the analysis, writing the draft of the manuscript, methodology, investigation, and collation of the literature. GS and SY conceived of the study idea and article review. All authors read and approved the final manuscript.

Funding
No funding was received.

Data availability
All data generated or analyzed during this study are included in this published article. The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 12 August 2024 / Accepted: 10 October 2024
Published online: 25 November 2024

References

1. Modzelewski R, Stefanowicz-Rutkowska MM, Matuszewski W, Bandurska-Stankiewicz EM. Gestational diabetes mellitus—recent literature review. J Clin Med. 2022;11(19):5736.
2. Cho AR, Kyeung KS, Park MA, Lee YM, Jeong EH. Risk factors of gestational diabetes mellitus. Korean J Perinatol. 2007:329–37.
3. Suastika AV, Widiana IGR, Fatmawati NND, Suastika K, Paulus IB, Sujaya IN. The role of probiotics and synbiotics on treatment of gestational diabetes: systematic review and meta-analysis. AJOG Global Rep. 2024;4(1):100285.
4. Taylor BL, Woodfall GE, Sheedy KE, O'Riley ML, Rainbow KA, Bramwell EL, et al. Effect of probiotics on metabolic outcomes in pregnant women with gestational diabetes: a systematic review and meta-analysis of randomized controlled trials. Nutrients. 2017;9(5):461.
5. Pan Y-Q, Zheng Q-X, Jiang X-M, Chen X-Q, Zhang X-Y, Wu J-L. Probiotic supplements improve blood glucose and insulin Resistance/Sensitivity among healthy and GDM pregnant women: a systematic review and Meta-analysis of Randomized controlled trials. Evidence-Based Complement Altern Med. 2021;2021(1):9830200.
6. Hao Y, Zhou L, Ding C, Wu J, Chen X, Ng DM, et al. Probiotics and synbiotics show clinical efficacy in treating gestational diabetes mellitus: a meta-analysis. Prim Care Diabetes. 2021;15(6):937–47.
7. Carpio GRA, Fonseca VA. Update on safety issues related to antihyperglycemic therapy. Diabetes Spectrum: Publication Am Diabetes Association. 2014;27(2):92.
8. Chen Y, Yue R, Zhang B, Li Z, Shui J, Huang X. Effects of probiotics on blood glucose, biomarkers of inflammation and oxidative stress in pregnant women with gestational diabetes mellitus: a meta-analysis of randomized controlled trials. Med Clínica (English Edition). 2020;154(6):199–206.
9. Mu J, Guo X, Zhou Y, Cao G. The effects of probiotics/synbiotics on glucose and lipid metabolism in women with gestational diabetes mellitus: a meta-analysis of randomized controlled trials. Nutrients. 2023;15(6):1375.
10. Liu H, Pan L-L, Lv S, Yang Q, Zhang H, Chen W, et al. Alterations of gut microbiota and blood lipidome in gestational diabetes mellitus with hyperlipidemia. Front Physiol. 2019;10:1015.
11. Karamali M, Dadkhah F, Sadrkhanlou M, Jamilian M, Ahmadi S, Tajabadi-Ebrahimi M, et al. Effects of probiotic supplementation on glycaemic control and lipid profiles in gestational diabetes: a randomized, double-blind, placebo-controlled trial. Diabetes Metab. 2016;42(4):234–41.
12. Nachum Z, Perlitz Y, Shavit LY, Magril G, Vitner D, Zipori Y, et al. The effect of oral probiotics on glycemic control of women with gestational diabetes mellitus—a multicenter, randomized, double-blind, placebo-controlled trial. Am J Obstet Gynecol MFM. 2024;6(1):101224.
13. Wang Z, Li W, Lyu Z, Yang L, Wang S, Wang P, et al. Effects of probiotic/prebiotic/synbiotic supplementation on blood glucose profiles: a systematic review and meta-analysis of randomized controlled trials. Public Health. 2022;210:149–59.
14. Okesene-Gafa KA, Moore AE, Jordan V, McCowan L, Crowther CA. Probiotic treatment for women with gestational diabetes to improve maternal and infant health and well-being. Cochrane Database Syst Reviews. 2020(6).
15. Davidson SJ, Barrett HL, Price SA, Callaway LK, Nitert MD. Probiotics for preventing gestational diabetes. Cochrane Database Syst Reviews. 2021(4).
16. Pan J, Pan Q, Chen Y, Zhang H, Zheng X. Efficacy of probiotic supplement for gestational diabetes mellitus: a systematic review and meta-analysis. J Maternal-Fetal Neonatal Med. 2019;32(2):317–23.
17. Masulli M, Vitacolonna E, Fraticelli F, Della Pepa G, Mannucci E, Monami M. Effects of probiotic supplementation during pregnancy on metabolic outcomes: a systematic review and meta-analysis of randomized controlled trials. Diabetes Res Clin Pract. 2020;162:108111.
18. Peng T-R, Wu T-W, Chao Y-C. Effect of probiotics on the glucose levels of pregnant women: a meta-analysis of randomized controlled trials. Medicina. 2018;54(5):77.
19. Zheng J, Feng Q, Zheng S, Xiao X. The effects of probiotics supplementation on metabolic health in pregnant women: an evidence based meta-analysis. PLoS ONE. 2018;13(5):e0197771.
20. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372.
21. Bojcic R, Todoric M, Puljak L, Adopting. AMSTAR 2 critical appraisal tool for systematic reviews: speed of the tool uptake and barriers for its adoption. BMC Med Res Methodol. 2022;22(1):104.
22. Rashidi K, Razi B, Darand M, Dehghani A, Janmohammadi P, Alizadeh S. Effect of probiotic fermented dairy products on incidence of respiratory tract infections: a systematic review and meta-analysis of randomized clinical trials. Nutr J. 2021;20:1–12.
23. Rashidi K, Darand M, Garousi N, Dehghani A, Alizadeh S. Effect of infant formula supplemented with prebiotics and probiotics on incidence of respiratory tract infections: a systematic review and meta-analysis of randomized clinical trials. Complement Ther Med. 2021;63:102795.
24. Taheri A, Raeisi T, Darand M, Jafari A, Janmohammadi P, Razi B, et al. Effects of pre/probiotic supplementation on breast milk levels of TGF-b1, TGF-b2, and IgA: a systematic review and meta-analysis of randomized-controlled trial. Breastfeed Med. 2022;17(1):22–32.
25. Duval S, Tweedie R. Trim and fill: a simple funnel-plot–based method of testing and adjusting for publication bias in meta-analysis. Biometrics. 2000;56(2):455–63.
26. Han M-M, Sun J-F, Su X-H, Peng Y-F, Goyal H, Wu C-H et al. Probiotics improve glucose and lipid metabolism in pregnant women: a meta-analysis. Annals Translational Med. 2019;7(5).
27. Zhang J, Ma S, Wu S, Guo C, Long S, Tan H. Effects of Probiotic supplement in pregnant women with gestational diabetes Mellitus: a systematic review and Meta-analysis of Randomized controlled trials. J Diabetes Res. 2019;2019(1):5364730.
28. Jin S, Sha L, Dong J, Yi J, Liu Y, Guo Z, et al. Effects of nutritional strategies on glucose homeostasis in gestational diabetes mellitus: a systematic review and network meta-analysis. J Diabetes Res. 2020;2020(1):6062478.
29. Łagowska K, Malinowska AM, Zawieja B, Zawieja E. Improvement of glucose metabolism in pregnant women through probiotic supplementation depends on gestational diabetes status: meta-analysis. Sci Rep. 2020;10(1):17796.
30. Chan KY, Wong MMH, Pang SSH, Lo KKH. Dietary supplementation for gestational diabetes prevention and management: a meta-analysis of randomized controlled trials. Arch Gynecol Obstet. 2021;303:1381–91.
31. Hasain Z, Che Roos NA, Rahmat F, Mustapa M, Raja Ali RA, Mokhtar NM. Diet and pre-intervention washout modifies the effects of probiotics on gestational diabetes mellitus: a comprehensive systematic review and meta-analysis of randomized controlled trials. Nutrients. 2021;13(9):3045.
32. Ramanathan K, Jagadeesh NS, Vishwanath U, Dayal C, Chandrababu R, Hayter M. Efficacy of supplementation of probiotics on maternal glycaemic control–A systematic review and meta-analysis of randomized controlled trials. Clin Epidemiol Global Health. 2021;10:100674.
33. Mahdizade Ari M, Teymouri S, Fazlalian T, Asadollahi P, Afifirad R, Sabaghan M, et al. The effect of probiotics on gestational diabetes and its complications in pregnant mother and newborn: a systematic review and meta-analysis during 2010–2020. J Clin Lab Anal. 2022;36(4):e24326.
34. Özdemir SÇ, Paşa BK, Metin T, Dinçer B, Sert H. The effect of probiotic and synbiotic use on glycemic control in women with gestational diabetes: a systematic review and meta-analysis. Diabetes Res Clin Pract. 2022;194:110162.
35. Chen X, Pan L, Zhang Z, Niu R, Zhang H, Ma T. Probiotic supplement for the prevention of gestational diabetes: a meta-analysis of randomized controlled trials. Z für Geburtshilfe Und Neonatologie. 2023;227(01):24–30.
36. Tabatabaeizadeh S-A, Tafazoli N. Effect of probiotic yogurt on gestational diabetes mellitus: a systematic review and meta-analysis. Diabetes Metabolic Syndrome: Clin Res Reviews. 2023;17(4):102758.
37. Wang J, Zhang Y, Wang Y. Effects of Probiotic supplementation on inflammation and oxidative stress for gestational diabetes: a Meta-analysis study. Z für Geburtshilfe Und Neonatologie. 2023;227(02):106–11.
38. Yefet E, Bar L, Izhaki I, Iskander R, Massalha M, Younis JS, et al. Effects of probiotics on glycemic control and metabolic parameters in gestational diabetes mellitus: systematic review and meta-analysis. Nutrients. 2023;15(7):1633.
39. Lan X, Li B, Zhao J, Stanton C, Ross RP, Chen W, et al. Probiotic intervention improves metabolic outcomes in gestational diabetes mellitus: a meta-analysis of randomized controlled trials. Clin Nutr. 2024;43(7):1683–95.
40. Wu R, Luan J, Hu J, Li Z. Effect of probiotics on pregnancy outcomes in gestational diabetes: systematic review and meta-analysis. Arch Gynecol Obstet. 2024:1–13.
41. Laitinen K, Poussa T, Isolauri E. Probiotics and dietary counselling contribute to glucose regulation during and after pregnancy: a randomised controlled trial. Br J Nutr. 2008;101(11):1679–87.
42. Mantaring J, Benyacoub J, Destura R, Pecquet S, Vidal K, Volger S, et al. Effect of maternal supplement beverage with and without probiotics during pregnancy and lactation on maternal and infant health: a randomized controlled trial in the Philippines. BMC Pregnancy Childbirth. 2018;18:1–12.
43. Alihosseini N, Moahboob S, Farrin N, Mobasseri M, Taghizadeh A, Ostadrahimi A. Effect of probiotic fermented milk (kefir) on serum level of insulin

and homocysteine in type 2 diabetes patients. Acta Endocrinol (Bucharest). 2017;13(4):431.
44. Rezazadeh L, Gargari BP, Jafarabadi MA, Alipour B. Effects of probiotic yogurt on glycemic indexes and endothelial dysfunction markers in patients with metabolic syndrome. Nutrition. 2019;62:162–8.
45. Zarezadeh M, Musazadeh V, Faghfouri AH, Sarmadi B, Jamilian P, Jamilian P, et al. Probiotic therapy, a novel and efficient adjuvant approach to improve glycemic status: an umbrella meta-analysis. Pharmacol Res. 2022;183:106397.
46. Zarezadeh M, Musazadeh V, Ghalichi F, Kavyani Z, Nasernia R, Parang M, et al. Effects of probiotics supplementation on blood pressure: an umbrella meta-analysis of randomized controlled trials. Nutr Metabolism Cardiovasc Dis. 2023;33(2):275–86.
47. Musazadeh V, Mohammadi Anilou M, Vajdi M, Karimi A, Sedgh Ahrabi S, Dehghan P. Effects of synbiotics supplementation on anthropometric and lipid profile parameters: finding from an umbrella meta-analysis. Front Nutr. 2023;10:1121541.
48. Faghfouri AH, Afrakoti LGMP, Kavyani Z, Nogourani ZS, Musazadeh V, Jafarlou M, et al. The role of probiotic supplementation in inflammatory biomarkers in adults: an umbrella meta-analysis of randomized controlled trials. Inflammopharmacology. 2023;31(5):2253–68.
49. Musazadeh V, Faghfouri AH, Zarezadeh M, Pakmehr A, Moghaddam PT, Hamedi-Kalajahi F, et al. Remarkable impacts of probiotics supplementation in enhancing of the antioxidant status: results of an umbrella meta-analysis. Front Nutr. 2023;10:1117387.
50. Jaeschke R, Singer J, Guyatt GH. Measurement of health status: ascertaining the minimal clinically important difference. Control Clin Trials. 1989;10(4):407–15.
51. Goldenberg JZ, Day A, Brinkworth GD, Sato J, Yamada S, Jönsson T et al. Efficacy and safety of low and very low carbohydrate diets for type 2 diabetes remission: systematic review and meta-analysis of published and unpublished randomized trial data. BMJ. 2021;372.
52. Homayouni A, Bagheri N, Mohammad-Alizadeh-Charandabi S, Kashani N, Mobaraki-Asl N, Mirghafurvand M, et al. Prevention of gestational diabetes mellitus (GDM) and probiotics: mechanism of action: a review. Curr Diabetes Rev. 2020;16(6):538–45.
53. Kamińska K, Stenclik D, Błażejewska W, Bogdański P, Moszak M. Probiotics in the prevention and treatment of gestational diabetes mellitus (gdm): a review. Nutrients. 2022;14(20):4303.
54. Santacruz A, Collado MC, Garcia-Valdes L, Segura M, Martín-Lagos J, Anjos T, et al. Gut microbiota composition is associated with body weight, weight gain and biochemical parameters in pregnant women. Br J Nutr. 2010;104(1):83–92.
55. Barbour LA, McCurdy CE, Hernandez TL, Kirwan JP, Catalano PM, Friedman JE. Cellular mechanisms for insulin resistance in normal pregnancy and gestational diabetes. Diabetes Care. 2007;30.
56. Hasain Z, Mokhtar NM, Kamaruddin NA, Mohamed Ismail NA, Razalli NH, Gnanou JV, et al. Gut microbiota and gestational diabetes mellitus: a review of host-gut microbiota interactions and their therapeutic potential. Front Cell Infect Microbiol. 2020;10:188.
57. McNabney SM, Henagan TM. Short chain fatty acids in the colon and peripheral tissues: a focus on butyrate, colon cancer, obesity and insulin resistance. Nutrients. 2017;9(12):1348.
58. Miraghajani M, Dehsoukhteh SS, Rafie N, Hamedani SG, Sabihi S, Ghiasvand R. Potential mechanisms linking probiotics to diabetes: a narrative review of the literature. Sao Paulo Med J. 2017;135(02):169–78.
59. Hommelberg PP, Langen RC, Schols AM, Mensink RP, Plat J. Inflammatory signaling in skeletal muscle insulin resistance: green signal for nutritional intervention? Current opinion in Clinical Nutrition & Metabolic Care. 2010;13(6):647–55.
60. Hajifaraji M, Jahanjou F, Abbasalizadeh F, Aghamohammadzadeh N, Abbasi MM, Dolatkhah N. Effect of probiotic supplements in women with gestational diabetes mellitus on inflammation and oxidative stress biomarkers: a randomized clinical trial. Asia Pac J Clin Nutr. 2018;27(3):581–91.
61. Lappas M, Hiden U, Desoye G, Froehlich J, Mouzon SH-d, Jawerbaum A. The role of oxidative stress in the pathophysiology of gestational diabetes mellitus. Antioxid Redox Signal. 2011;15(12):3061–100.
62. Kobyliak N, Falalyeyeva T, Tsyryuk O, Eslami M, Kyriienko D, Beregova T, et al. New insights on strain-specific impacts of probiotics on insulin resistance: evidence from animal study. J Diabetes Metabolic Disorders. 2020;19:289–96.
63. Nordqvist M, Jacobsson B, Brantsæter A-L, Myhre R, Nilsson S, Sengpiel V. Timing of probiotic milk consumption during pregnancy and effects on the incidence of preeclampsia and preterm delivery: a prospective observational cohort study in Norway. BMJ open. 2018;8(1):e018021.

Publisher's note