

Effect of Probiotic Supplementation on Glycemic Control in Patients with Type 2 Diabetes Mellitus: An Evidence-Based Case Report

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ABSTRACT

Introduction: Type 2 diabetes mellitus (T2DM) remains a global health challenge with rising prevalence and significant long-term complications. Emerging evidence highlights the role of gut microbiota in glucose metabolism, with probiotics proposed as a potential adjunctive therapy to improve glycemic control. **Methods:** Literature searches were performed in PubMed, Cochrane, and Scopus for randomized controlled trials (RCTs) and meta-analyses published within the last five years. Studies were critically appraised using the Oxford Center for Evidence-Based Medicine (OCEBM) tools and outcomes for fasting blood glucose (FBG), glycated hemoglobin (HbA1c), and HOMA-IR were assessed. **Results:** Six studies met the inclusion criteria, including one network meta-analysis and five RCTs. Probiotic supplementation, particularly multi-strain formulations of *Lactobacillus* and *Bifidobacterium*, significantly improved FBG and HbA1c and enhanced β -cell function. However, heterogeneity in strains, dosage, and intervention duration limited definitive conclusions. Most studies reported that probiotic supplementation is well tolerated, with only mild and transient gastrointestinal side effects. **Conclusion:** Probiotic supplementation, especially a multi-strain combination of *Lactobacillus* and *Bifidobacterium*, may be a safe additional therapy to improve blood sugar control in people with type 2 diabetes. Larger clinical trials with stronger methodologies are still needed to determine the optimal dose, strain composition, and duration of supplementation.

Keywords: Glucose metabolism, glycemic control, gut microbiota, probiotics, type 2 diabetes mellitus.



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INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a major global health challenge, affecting 462 million people worldwide and projected to exceed 700 million cases by 2045.¹ In Indonesia, the prevalence of T2DM has also increased from 10.9% in 2018 to 11.7% in 2023.² Poorly controlled T2DM is associated with cardiovascular and neurodegenerative complications, leading to higher morbidity, mortality, and socioeconomic burden. This highlights the urgent need for more effective strategies to optimize glycemic control and prevent long-term complications.

The pathogenesis of T2DM is multifactorial, involving genetic predisposition, lifestyle, and adiposity, with emerging evidence pointing to the gut microbiota as a critical regulator of metabolic homeostasis.^{1,3} Dysbiosis has been shown to impair the production of microbial metabolites essential for insulin regulation

and glucose metabolism. Individuals with T2DM have higher levels of pathogenic bacteria such as *Enterobacteriaceae* and *Desulfovibrionaceae*, whereas butyrate-producing bacteria have been associated with improved insulin sensitivity and glycemic control. These findings suggest that restoring microbial balance may represent a novel therapeutic approach.^{1,4,5}

Probiotics have been proposed as an adjunct therapy to improve glycemic regulation by modulating the gut microbiota, reducing systemic inflammation, and enhancing insulin sensitivity.⁶ Evidence from clinical studies remains inconsistent: meta-analyses have reported significant reductions in inflammatory markers, fasting blood glucose (FBG), and glycated hemoglobin (HbA1c) following probiotic or synbiotic supplementation, while other trials found improvements limited to FBG without significant changes in HbA1c

or HOMA-IR.⁶⁻⁸ Given this heterogeneity, this evidence-based case report was conducted to further evaluate the potential of probiotics as an adjunctive therapy to optimize glycemic control in patients with T2DM.

CASE

A 56-year-old woman with a 5-year history of T2DM presented for routine follow-up. She has been receiving oral antidiabetic therapy with metformin 500 mg three times daily. Despite treatment, her dietary habits remain unfavorable, with frequent consumption of fast food and sugar-sweetened beverages. On examination, her body mass index was 27.8 kg/m². Laboratory investigations showed a fasting blood glucose of 130 mg/dL and an HbA1c of 7%. No clinical or laboratory evidence of microvascular or macrovascular complications was identified. Because glycemic control remains suboptimal under current management, the treating physician is

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considering probiotic supplementation as an adjunctive intervention to improve glycemic regulation.

Problem Formulation

The problem formulation is defined as follows:

- P (Population) : adults with type 2 diabetes mellitus (T2DM)
 I (Intervention) : probiotic supplementation
 C (Comparison) : placebo or without probiotic supplementation
 O (Outcome) : glycemic control

The clinical question is: "In adult patients with type 2 diabetes mellitus, what is the effect of probiotic supplementation on glycemic control?"

METHODS

Article searches were conducted across three electronic databases: PubMed, the Cochrane Library, and Scopus. An advanced search strategy was applied using a combination of MeSH terms and title/abstract/keyword fields derived from the PICO framework. We used the Boolean operator "OR" to increase sensitivity

and "AND" to increase specificity (**Table 1**). The search terms included probiotic, probiotics, glycemic control, glycemic index, type 2 diabetes mellitus, and T2DM. Filters restricted the search to randomized controlled trials (RCTs), systematic reviews, and meta-analyses.

Following the initial search, duplicate articles were removed using Mendeley Reference Manager. Titles and abstracts were then screened for relevance to the PICO framework, followed by full-text retrieval and assessment against the predefined eligibility criteria. Primary studies that were already included in systematic reviews or meta-analyses were excluded. The final selection of studies was critically appraised using the Oxford Center for Evidence-Based Medicine (OCEBM) appraisal tools, depending on study design. The level of evidence was subsequently determined based on the OCEBM Levels of Evidence guidelines.⁹

Inclusion criteria:

1. Studies including participants diagnosed with T2DM based on American Diabetes

Association (ADA) criteria:¹⁰ a fasting plasma glucose (FPG) of 126 mg/dL or higher, a 2-hour plasma glucose of 200 mg/dL or higher, or an HbA1c level of 6.5% or higher.

2. Participants aged ≥ 18 years.
3. Participants receiving antidiabetic medication.
4. Studies published within the last five years.
5. Studies providing probiotic supplementation as an intervention.
6. Outcome reporting glycemic control parameters, such as FBG, HbA1c, or postprandial blood glucose.
7. Study design limited to a systematic review/meta-analysis of randomized controlled trials or a randomized controlled trial.

Exclusion criteria:

1. Full-text articles are not available.
2. Animal studies.
3. Studies involving pregnant women.
4. Articles written in languages other than English and Indonesian.

RESULTS

Database searches (PubMed, Cochrane, Scopus) identified 1,024 records (**Table 1**). After removing 8 duplicates and excluding 1,000 records following title and abstract screening, 16 full-text articles were assessed for eligibility. Six studies met the inclusion criteria: one network meta-analysis (NMA) and five randomized controlled trials (RCTs), which we critically appraised using the validity, importance, and applicability (VIA) framework (**Figure 1**).

DISCUSSION

T2DM is a multifactorial disease shaped by genetic, lifestyle, and dietary influences, yet emerging evidence underscores the gut microbiota's critical role in its pathogenesis. Dysbiosis, characterized by reduced microbial diversity and compositional shifts, has been associated with impaired metabolite production, insulin resistance, and abnormal glucose regulation. Conversely, higher microbial diversity and the presence of butyrate-producing bacteria appear to exert protective effects, suggesting that the gut microbiota may serve as both an early biomarker and a potential therapeutic target. In this context, probiotics have emerged as

Table 1. Literature searching strategy.

Database	Searching Strategy	Hits (n)	Selected Articles (n)
PubMed	((((((((((probiotic[MeSH Terms]) OR (probiotic[Title/Abstract]) OR (probiotics[MeSH Terms]) OR (probiotics[Title/Abstract]) AND (glycemic control[MeSH Terms]) OR (glycemic control[Title/Abstract]) OR (glycemic index[MeSH Terms]) OR (glycemic index[Title/Abstract]) AND (type 2 diabetes mellitus[MeSH Terms]) OR (type 2 diabetes mellitus[Title/Abstract]) OR (T2DM[MeSH Terms] OR (T2DM[Title/Abstract]))))))))))	815	2
Cochrane	ID Search Hits #1 probiotic 8264 #2 probiotics 8986 #3 #1 OR #2 11626 #4 glycemic control 22418 #5 glycemic index 8107 #6 #4 OR #5 24673 #7 type 2 diabetes mellitus 76419 #8 T2DM 9674 #9 #7 OR #8 77157 #10 #3 AND #6 AND #9 131	131	5
Scopus	TITLE-ABS-KEY ("probiotic" OR "probiotics") AND TITLE-ABS-KEY ("glycemic control" OR "glycemic index") AND TITLE-ABS-KEY ("type 2 diabetes mellitus" OR "T2DM") AND PUBYEAR > 2020 AND PUBYEAR < 2026	78	3

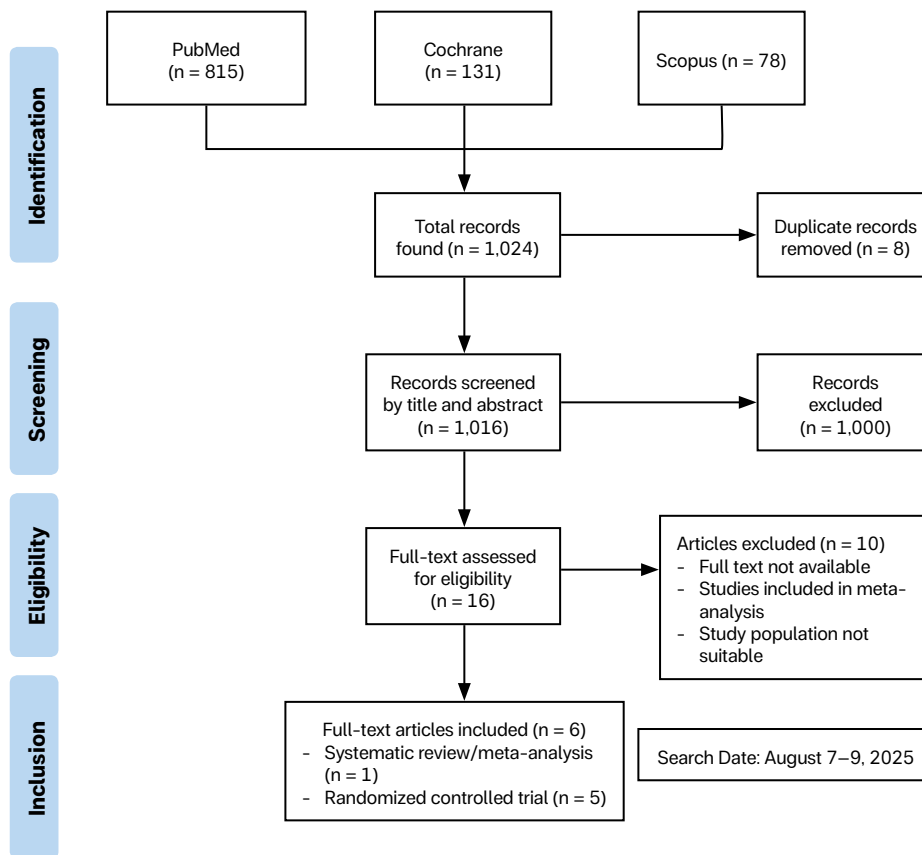


Figure 1. PRISMA flow chart.

a promising strategy to restore microbial balance and improve glycemic control in T2DM. Nevertheless, current American Diabetes Association guidelines have not yet established recommendations for the routine use of probiotics in patients with T2DM.^{4,7,9,11}

This review identified six studies that met the eligibility criteria: one NMA and five RCTs. The NMA by Allam, *et al.*, which included 60 studies conducted in multiple countries, evaluated the efficacy of various probiotic interventions in T2DM management (**Table 2**). The analysis demonstrated that combinations of *Bifidobacterium* and *Lactobacillus* probiotic strains significantly reduced FBG [MD = -73.50, 95% CI (-113.13, -33.86)]. Furthermore, yogurt containing these strains was associated with significant reductions in FBG [MD = -73.32, 95% CI (-110.14, -36.5)] and HbA1c [MD = -1.59, 95% CI (-3.07, -0.12)] compared with other probiotic formulations. Yogurt containing *Bifidobacterium animalis* alone also significantly lowered HbA1c [MD = -1.44, 95% CI (-2.67, -0.21)], while *Lactobacillus*

casei supplementation significantly improved insulin resistance as measured by HOMA-IR [MD = -7.56, 95% CI (-11.78, -3.34)].¹²

This meta-analysis demonstrated overall good validity (**Table 3**). The risk of bias across the included studies was generally low to moderate, although 14 trials were assessed as having a high risk of bias. Intervention durations ranged from 4 to 24 weeks. The analysis indicated that probiotic supplementation improved glycemic control in patients with T2DM, particularly with multi-strain combinations of *Lactobacillus* and *Bifidobacterium* or probiotic-enriched yogurt containing these strains. However, substantial variability in probiotic dosage, formulation, and intervention duration across studies remains a limitation, preventing the establishment of an optimal regimen for effective glucose management in T2DM.

Peng, *et al.*, investigated the effects of a *Lactobacillus* probiotic beverage administered at $> 10^8$ CFU/mL, four times daily, in patients with T2DM (**Table 2**). The study

demonstrated strong methodological rigor, incorporating appropriate randomization, allocation concealment, double blinding, and an intention-to-treat (ITT) analysis, with a relatively long follow-up duration of 16 weeks. Overall, the trial had a low risk of bias. Results showed a reduction in HbA1c (-0.44; 95% CI -0.66 to -0.22) and FBG (-0.97; 95% CI -1.49 to -0.46) in the probiotic group, compared with HbA1c (-0.33; 95% CI -0.52 to -0.15) and FBG (-0.90; 95% CI -1.32 to -0.47) in the placebo group.¹³

However, these findings were not statistically significant in either the intention-to-treat or per-protocol analyses. Several factors may explain this outcome. First, the liquid form of the probiotic used in this study may have been more susceptible to environmental influences such as temperature and light exposure, potentially reducing bacterial viability. Second, the study tested only a single probiotic strain, whereas multi-strain formulations have shown greater efficacy in lowering glycemic indices in other trials. Finally, a placebo effect may have contributed, as the placebo matched the probiotic in taste and odor, potentially leading participants to perceive clinical improvement independent of biological activity.¹³

Chaithanya, *et al.*, investigated the effects of multi-strain probiotic supplementation on glycemic control in patients with T2DM (**Table 2**).¹⁴ Critical appraisal revealed methodological limitations, as the study lacked double blinding, provided incomplete details regarding interventions in the probiotic group, and did not apply an ITT analysis, thereby increasing the risk of attrition bias. Notably, the trial achieved a six-month follow-up with a dropout rate below 20%, demonstrating robust participant retention and enhancing the reliability of the findings.

The findings showed no statistically significant differences between groups in FBG or 2-hour postprandial blood glucose (PPBG). However, the probiotic group showed a significant reduction in HbA1c (-0.44 ± 1.17) compared with the control group (-0.05 ± 0.92 ; $p = 0.004$). Despite methodological shortcomings, this study highlights the potential of multi-strain probiotics to reduce HbA1c, suggesting their role as a promising adjunctive therapy for managing T2DM.¹⁴

EVIDENCE-BASED CASE REPORT

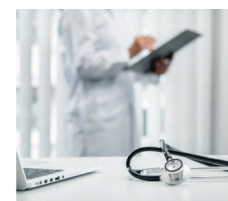
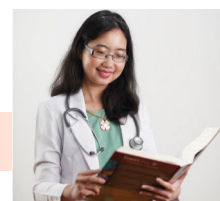


Table 2. Characteristics of included studies.

Author	Year	Country	Studi Design	Total (n)	Population	Intervention	Comparison	Outcome
Allam, <i>et al.</i> ¹²	2025	Egypt	Network meta-analysis	60 studies	Type 2 diabetes mellitus	Probiotics (dose varies, strain varies) for 4–24 weeks	Placebo	FBG, HbA1c, HOMA-IR
Peng, <i>et al.</i> ¹³	2024	China	Double-blind, randomized controlled trial	490	Type 2 diabetes mellitus	<i>Lactobacillus</i> 10 ⁸ CFU/mL four times daily for 16 weeks	Placebo	FBG, HbA1c, HOMA-IR
Chaithanya, <i>et al.</i> ¹⁴	2024	India	Randomized controlled trial	130	Type 2 diabetes mellitus	Multispecies probiotic supplements capsules twice daily for 24 weeks	Placebo	FBG, PPBG
Zikou, <i>et al.</i> ¹⁵	2023	Greece	Double-blind, randomized controlled trial	91	Type 2 diabetes mellitus	Multi-strain probiotic supplement for 6 months	Placebo	FBG, HbA1c
Mirjalili, <i>et al.</i> ¹⁶	2023	Iran	Randomized controlled trial	72	Type 2 diabetes mellitus	Probiotic yoghurt containing 4,65 x 10 ⁶ CFU/g <i>Lactobacillus acidophilus</i> and <i>Bifidobacterium lactis</i> for 12 weeks	Placebo	FPG, HbA1c
Savytska, <i>et al.</i> ¹⁷	2023	Ukraine	Double-blind, randomized controlled trial	68	Type 2 diabetes mellitus s	Live multi-strain probiotics for 8 weeks	Placebo	C-peptide, HOMA-β, FBG, HbA1c

Abbreviations: FBG: Fasting blood glucose; HbA1c: Glycated hemoglobin HOMA-IR: Homeostasis model assessment of insulin resistance.

Table 3. Internal validity of included systematic review and meta-analysis (SR-MA) study.

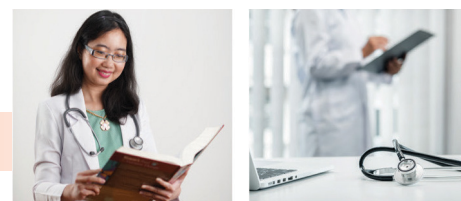
Author	Year	PICO Question Addressed Clearly	No Relevant Studies Missed	Appropriate Eligibility Criteria	Validity of Included Studies	Similar Results Across Studies
Allam, <i>et al.</i> ¹²	2025	+	+	+	+	+

Table 4. Internal validity of included RCT studies.

Author	Year	Randomization	Similar Characteristics Between Groups	Equall Treatment on Both Groups	All Patients Accounted For	Double-Blinded Objective Measurement
Peng, <i>et al.</i> ¹³	2024	+	+	+	+	+
Chaithanya, <i>et al.</i> ¹⁴	2024	+	+	-	-	-
Zikou, <i>et al.</i> ¹⁵	2023	+	+	+	-	+
Mirjalili, <i>et al.</i> ¹⁶	2023	+	+	+	+	+
Savytska, <i>et al.</i> ¹⁷	2023	+	+	+	+	+

Table 5. Importance and applicability of included studies.

Author	Year	Importance		Applicability			Level of Evidence
		Large Treatment Effect, Not Coincidence	Precisely Estimated Treatment Effect, Clinically Significant	Similarity to My Patients and Applicability of Results	Treatment Feasibility in My Setting	Potential Benefits Outweigh the Harms of Treatment for My Patient	
Allam, <i>et al.</i> ¹²	2025	+	+	+	+	+	1a
Peng, <i>et al.</i> ¹³	2024	-	-	+	+	+	2
Chaithanya, <i>et al.</i> ¹⁴	2024	+	+	+	+	+	2
Zikou, <i>et al.</i> ¹⁵	2023	+	+	+	+	+	2
Mirjalili, <i>et al.</i> ¹⁶	2023	+	+	+	+	+	2
Savytska, <i>et al.</i> ¹⁷	2023	+	+	+	+	+	2



Zikou, *et al.*, evaluated daily multi-strain probiotic capsule supplementation in patients with T2DM. The study demonstrated reasonable validity, with a six-month follow-up and a low attrition rate (4%), although it did not perform an ITT analysis (**Table 4**). Results showed significant improvements in glycemic control, with greater reductions in HbA1c at six months in the probiotic group than in placebo (-0.73 ± 0.42 vs. -0.14 ± 0.46 , $p < 0.001$). FBG also declined significantly in the probiotic group (-1.39 ± 1.08 mmol/L) relative to placebo (-0.28 ± 0.96 mmol/L, $p < 0.001$).¹⁵

Mirjalili, *et al.*, investigated probiotic-enriched yogurt (200 g/day containing 4.65×10^6 CFU/g *Lactobacillus acidophilus* and *Bifidobacterium lactis*) in T2DM patients. This trial was methodologically robust, incorporating randomization, allocation concealment, adequate double blinding, and ITT analysis (**Table 4**). While crude results showed no significant changes in FBG or HbA1c between groups, adjusted analyses revealed a significant reduction in HbA1c in the probiotic group compared with control (-0.76 ± 1.3 vs. -0.15 ± 1.3 , $p < 0.01$).¹⁶

Similarly, Savytska, *et al.*, examined the effects of multi-strain probiotic supplementation in sachet formulation. The study demonstrated strong validity with appropriate randomization, allocation concealment, double blinding, and ITT analysis (**Table 4**). Compared with placebo, FBG (42.56 ± 64.29 vs. 5.08 ± 43.46 mg/dL, $p = 0.006$) and HbA1c (8.86 ± 1.28 vs. 8.48 ± 1.22 , $p = 0.043$) improved significantly. Notably, probiotic supplementation also enhanced pancreatic β -cell function, as indicated by an increase in HOMA-IR (32.48 ± 13.12 vs. 45.71 ± 25.18 , $p = 0.03$) after eight weeks, a benefit not observed in the placebo group.¹⁷

From one NMA and five RCTs critically appraised in this review, probiotic

supplementation, particularly with *Bifidobacterium* and *Lactobacillus* strains, appears to improve glycemic control in patients with T2DM. One RCT reported nonsignificant findings, which may be explained by reliance on a single probiotic strain and potential placebo effects. Overall, the reviewed studies demonstrated acceptable methodological validity, and the study populations were comparable to patients in clinical practice, supporting external applicability (**Table 5**).

Regarding safety, probiotic supplementation was generally well tolerated, with no reports of serious adverse events. Across trials, participants receiving probiotics exhibited good compliance and tolerability. The most frequently reported adverse effects were mild and transient gastrointestinal complaints such as abdominal discomfort, bloating, and diarrhea, observed in the studies by Savytska, *et al.* and Zikou, *et al.*, which were not severe enough to warrant treatment discontinuation.^{13,15–17}

Taken together, these findings suggest that probiotics may represent a promising and safe adjunctive therapy in T2DM, complementing standard lifestyle and pharmacological management. Nevertheless, heterogeneity in strain selection, dosage, formulation, and treatment duration limits definitive recommendations regarding the optimal regimen. Future large-scale, high-quality RCTs are required to establish standardized protocols.

CONCLUSION

Probiotic supplementation, particularly multi-strain formulations containing *Bifidobacterium* and *Lactobacillus*, may serve as a beneficial adjunctive therapy for improving glycemic control in patients with T2DM, especially those with suboptimal glycemic control (baseline HbA1c > 8%) and overweight or obesity (BMI approximately 28–30 kg/

m²). Multi-strain probiotic formulations administered for approximately 8–12 weeks appear to demonstrate the most consistent improvements in HbA1c and metabolic parameters. Probiotics are generally safe and well tolerated, with no reported serious adverse events. Nevertheless, probiotics should be considered only as an adjunctive nutritional intervention. They cannot replace the established role of standard antidiabetic therapy, including metformin and other glucose-lowering agents, in managing T2DM. Further well-designed clinical trials are needed to determine the optimal strain composition, dosage, target population, and duration of supplementation better to define the long-term role of probiotics in T2DM management.

DECLARATIONS

Consent for Publication

Written informed consent for publication of the clinical information presented in this case report was obtained from the patient.

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Author Contributions

GRA contributed to the conception and design of the study, collected the data, and wrote the first draft of the manuscript. DS reviewed and edited the manuscript. All authors reviewed and approved the final manuscript.

Conflict of Interest

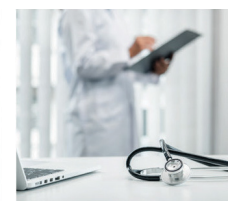
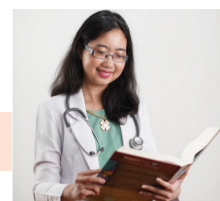
The authors declare that there is no conflict of interest.

Declaration on the Use of Artificial Intelligence (AI)

The authors declare that no artificial intelligence was used for the study design, data collection, or data analysis of this manuscript. All authors reviewed, verified, and approved the entire content of the manuscript and accept full responsibility for its accuracy and integrity.

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