

Article

The Relationship Between Probiotic Intake and Glycemic Profiles Among Metformin-Treated Type 2 Diabetes Patients

Article Info

Article history :

Received December 25, 2025

Revised February 15, 2026

Accepted February 23, 2026

Published February 28, 2026

Keywords :

Diabetes Mellitus,
Probiotik,
Metformin,
Blood Glucose,
Microbiome

Rahma Ayu Larasati¹, Silviah², Farabillah Afifah¹, Siti Hadzul Aniyah²

¹Department of Biomedicines, Faculty of Medicines and Health, Universitas Muhammadiyah Jakarta, Indonesia

²Medical student, Faculty of Medicines and Health, Universitas Muhammadiyah Jakarta, Indonesia

Abstract. The ideal management of Type 2 Diabetes Mellitus should evolve from mere glucose-lowering strategies to a more comprehensive framework encompassing personalized medicine, technological integration, and systemic organ protection. A significant number of patients with Diabetes Mellitus (DM) continue to suffer from mortality and serious complications despite being on pharmacological therapy. Although trillions of dollars are spent annually on its management, diabetes remains a leading cause of mortality, claiming millions of lives each year across the globe. Probiotics have been proposed as an adjunctive therapy due to their role in modulating gut microbiota and glucose metabolism. This study aimed to analyze the effect of probiotic supplementation on Fasting Blood Sugar (FBS) levels in T2DM patients receiving metformin monotherapy. This experimental study involved 32 respondents, divided into probiotic intervention and placebo groups. FBS levels were measured pre- and post-intervention. Statistical analysis using the Paired T-Test showed a significant reduction in FBS levels ($p=0.019$). Conclusion: Probiotic supplementation significantly reduced FBS levels in T2DM patients on metformin monotherapy. However, this reduction was not clinically significant, as the final FBS levels did not differ significantly between the probiotic and placebo groups.

This is an open access article under the [CC-BY](https://creativecommons.org/licenses/by/4.0/) license.



This is an open access article distributed under the Creative Commons 4.0 Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. ©2026 by author.

Corresponding Author :

Rahma Ayu Larasati

Department of Biomedicines, Faculty of Medicines and Health,
Universitas Muhammadiyah Jakarta, Indonesia

Email : rahmaayularasati@umj.ac.id

1. Introduction

Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disease characterized by hyperglycemia resulting from impaired insulin secretion, impaired insulin action, or both [1]. According to the International Diabetes Federation (IDF) 2024, the number of people with T2DM is estimated to be 589 million and is projected to increase to 853 million by 2050 [2]. This global epidemiological data highlights that T2DM has become a very serious health problem worldwide.

At the provincial level of West Nusa Tenggara (NTB), the NTB Provincial Health Office recorded a total of 64,544 T2DM patients by the end of 2023. Bima City itself had 3,609 T2DM cases at the end of 2023, of which 2,477 patients received health services according to standard protocols. This makes Bima City one of the areas with a significantly high incidence of T2DM in the province [3].

The problem with T2DM is not only limited to its high prevalence but also the treatment burden, which results in a high economic burden on the community. The Indonesian Society of Endocrinology (PERKENI) currently mandates T2DM treatment protocol using Oral Hypoglycemic Agents (OHAs) as the primary step and main therapy. However, the effectiveness of OHA is not the only factor which determine therapy goal. Numerous other factors hinder the achievement of therapeutic goals. These include patient concerns regarding potential adverse effects on the liver and kidneys. Other barriers to effective treatment encompass poor medication adherence, limited accessibility to healthcare facilities, inequitable drug distribution, and insufficient psychosocial support for patients with type 2 diabetes mellitus [4-5].

Poorly controlled T2DM leads to the emergence of various microvascular and macrovascular complications, increasing the economic and productivity burden on T2DM patients [6]. One proposed effort to enhance the effectiveness of OHAs is the use of adjunctive therapy, such as probiotics. Studies have reported that gut microbiota plays a role in glucose metabolism and insulin resistance [7-9].

The Food and Agriculture Organization (FAO) defines probiotics as live microorganisms that, when administered in adequate amounts, confer a health benefit on the host [10-11]. Probiotics are supplements that can modulate the composition of the gut microbiota, particularly beneficial bacteria, with the potential to support T2DM management by increasing insulin sensitivity and reducing systemic inflammation frequently observed in T2DM patients. Several studies have shown that probiotic consumption can yield positive results in blood sugar control [12-13].

While the potential of probiotics in improving glycemic profiles has been extensively discussed globally, clinical research and its implementation in Indonesia remain markedly limited. Most Indonesian studies on probiotics have primarily focused on their correlation with gastrointestinal disorders, such as diarrhea or inflammatory bowel disease (IBD) [14-15]. Consequently, current literature is predominantly shaped by international studies with demographic characteristics and dietary patterns that differ significantly from the local population, particularly in Bima, West Nusa Tenggara. Therefore, this study aims to evaluate the effect of probiotic administration on Fasting Blood Sugar (FBS) levels in T2DM patients in Bima City, West Nusa Tenggara (NTB) Province.

2. Experimental Section

The study employed an experimental design utilizing a single-blinded randomization process. The research was conducted in December 2024. This study was approved by the Health Research Ethics Committee of the Faculty of Medicine and Health, Universitas Muhammadiyah Jakarta. The target population consisted of all Type 2 Diabetes Mellitus (T2DM) patients undergoing metformin monotherapy at the Jatibaru Primary Health Center (Puskesmas) in Bima, West Nusa Tenggara (NTB).

A total of 32 respondents were included based on the sample size calculation using the Frederer formula. Participants were divided into two groups: the intervention group and the control group. The inclusion criteria for participation were [16-17] subjects diagnosed with T2DM, subjects currently receiving metformin monotherapy, subjects willing to undergo Fasting Blood Sugar (FBS) level

checks, subjects free from T2DM complications (macrovascular or microvascular), and subjects who consented in writing, were willing to participate, and agreed to complete the entire study protocol.

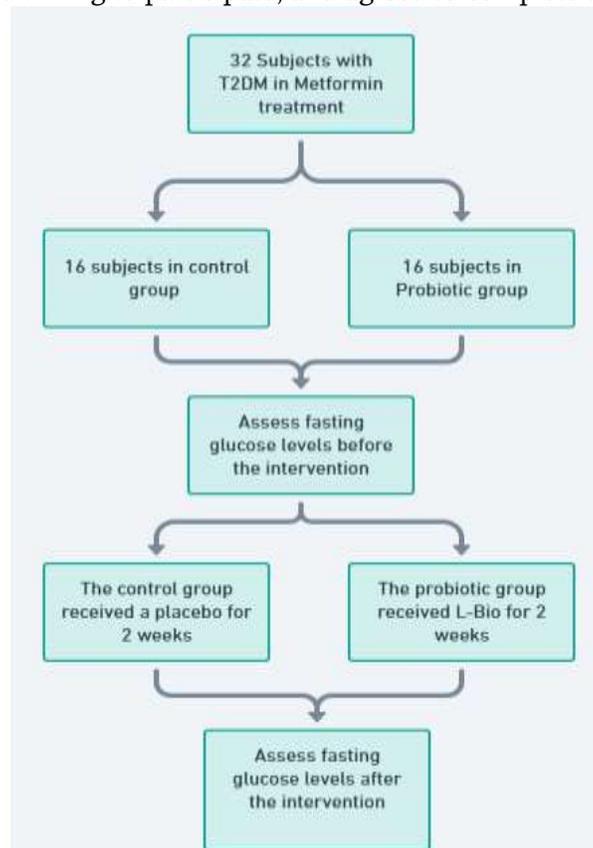


Figure 1. Flowchart of Research

The researcher provided the probiotic product to the intervention group, specifically using the L-Bio Cap brand. The dosage administered was 1 capsule per day (1x1 daily), with each capsule containing 440 mg. The L-Bio Cap probiotic product has a concentration of 1×10^9 Colony-Forming Units (CFU)/gram and contains the following strains: *Lactobacillus acidophilus W55*, *Lactobacillus Casei W56*, *Lactobacillus Salivarius W57*, *Lactobacillus Lactis W52*, and *Lactobacillus Lactis W58*, along with Maltodextrin and Rice Starch as excipients [18-20].

The researchers also provided a placebo product to the control group. The placebo was administered at a dosage of 1 capsule per day (1x1 daily) for a period of two weeks, with each capsule containing 440 mg. To maintain blinding, both the probiotic and placebo products were repackaged into identical containers [21].

3. Results and Discussion

The majority of the study subjects were concentrated in the age group ranging from late adulthood to pre-elderly (28.1%). Most participants had been living with T2DM for a duration of 1 to 5 years (71.9%). The most prevalent occupation among the respondents was private employees or traders (38.7%). Although more than half of the respondents presented with a normal nutritional status (or normal Body Mass Index/BMI), the proportion of subjects classified as obese remained considerably high, reaching 34.38%.

Table. 1 Characteristics of Participants

	Characteristics	N	%
Gender	Male	4	12.5
	Female	28	87.5
Usia	Adult(35-44 yo.)	10	31.2
	Pre-elderly (45-54 yo)	9	28.1
	Elderly (55-64 yo.)	9	28.1
	Oldest old (>65 yo. tahun)	4	12.5
Job	Unemployed	11	35.5
	Courier	2	6.5
	Trader	12	38.7
	Civil Servant	6	19.4
Duration of T2DM	< 1 Tahun	5	15.6
	1-5 Tahun	23	71.9
	5-10 Tahun	4	12.5
BMI	Normal	17	53.1
	<i>Overweight</i>	4	12.5
	Obesitas I	8	25
	Obesitas II	3	9.38

The results of the inter-group analysis showed that the average fasting blood glucose levels after the intervention were lower in all groups (Table 2).

Table 2. Fasting Blood Sugar Levels in Two Groups

Parameter	Mean ± SD			
	Placebo		Probiotics	
	Before	After	Before	After
FBS (mg/dL)	179.1 ± 30.3	171.9 ± 26.5	18.4 ± 29.8	174.6 ± 26.7

The Shapiro-Wilk test indicated that the data were normally distributed in the experimental group (both pre- and post-treatment) and in the control group at baseline ($p= 0.960; 0.730; 0.290$). In the control group post-treatment, the normality test yielded a p -value of 0.010, indicating that the data were not normally distributed. The results of the inter-group analysis showed that FBS levels after the intervention were not significantly different between the probiotic and placebo groups. The statistical analysis of fasting blood glucose levels indicates no significant difference across the observed periods. The p -values for both 'before' (0.650) and 'after' (0.777) are well above the standard significance threshold of 0.05.

Using Paired T- test analysis The study evaluate the effectiveness of an intervention, treatment, or program by comparing the mean scores of the same group under two different conditions or at two different time points. The Sig. (2-tailed) value is $0.019 < 0.05$. Therefore, it can be concluded that there is a significant decrease in GDP levels before and after probiotic administration. Despite the observed differences between groups, the L-Bio intervention exhibited a low effect magnitude, falling into the small effect size category (cohen's $d = 0.3$).

This study demonstrated that probiotic supplementation significantly reduced Fasting Blood Glucose levels in Type 2 Diabetes Mellitus patients undergoing Metformin monotherapy over a two-week period. These findings suggest that probiotics can be a beneficial adjunctive therapy for enhancing glycemic control in this specific patient population, warranting further investigation with larger sample sizes and longer intervention durations.

Based on the results, a significant reduction in Fasting Blood Sugar (FBS) levels was observed in the probiotic group when comparing pre- and post-intervention measurements. Although the effect size was relatively small (Cohen's $d = 0.3$), the reduction in blood glucose achieved within only 2 weeks at the minimum dosage should be viewed positively (Δ FBS = 9.4 mg/dl). Future studies are expected to extend the intervention duration and increase the sample size to further evaluate the full extent of probiotic effectiveness in patients with Type 2 Diabetes Mellitus.

Previous studies have reported that gut microbiota plays a pivotal role in glucose metabolism and insulin resistance. Probiotics function by fermenting carbohydrates to produce metabolites such as short-chain fatty acids (SCFAs) and antibacterial bacteriocins, which assist in modulating the immune response. SCFAs, the primary byproducts of non-digestible carbohydrate fermentation in the colon, are highly dependent on the gut microbiota composition. These fatty acids regulate inflammatory responses and stimulate cytokine production essential for maintaining and repairing epithelial integrity [12],[22-23].

SCFAs modulate inflammatory pathways through the activation of G-protein-coupled receptors (GPCRs), specifically FFAR2 and FFAR3. The activation of these receptors enhances the production of Interleukin-10 (IL-10), an anti-inflammatory cytokine that suppresses systemic inflammation. Furthermore, SCFAs inhibit histone deacetylase (HDAC) activity, which regulates the expression of inflammatory genes. HDAC inhibition attenuates the activation of the Nuclear Factor-kappa B (NF- κ B) pathway, a key transcription factor that induces pro-inflammatory gene expression, including Tumor Necrosis Factor-alpha (TNF- α), Interleukin-1 β (IL-1 β), and inducible Nitric Oxide Synthase (iNOS) [22],[24-25].

Probiotics are known to enhance insulin sensitivity and reduce insulin resistance, both of which are critical factors in the management and control of Type 2 Diabetes Mellitus (T2DM). The underlying mechanism involves the stimulation of short-chain fatty acid (SCFA) production, which subsequently promotes the growth of beneficial gut microbiota. Within the intestinal lumen, SCFAs trigger the release of Glucagon-Like Peptide-1 (GLP-1), an incretin hormone that augments insulin secretion and inhibits glucagon release, thereby maintaining glycemic stability. Furthermore, SCFAs stimulate the secretion of Peptide YY (PYY), which acts on the appetite control centers in the brain to induce satiety and regulate caloric intake, ultimately contributing to the modulation of blood glucose levels [26-27].

Numerous studies have demonstrated the potential of probiotics in glycemic control. One study reported that the administration of probiotic preparations containing *Lactobacillus casei* Shirota for four weeks maintained glycemic control and fasting insulin levels (28). Another trial involving the administration of two probiotic strains, *Lactobacillus reuteri* ADR-1 and ADR-3, to T2DM patients yielded significant improvements in glycemic control and blood pressure. Furthermore, a study involving patients with metabolic syndrome found that the consumption of yogurt fortified with *Lactobacillus acidophilus* La5 and *Bifidobacterium lactis* Bb12 for two months resulted in a significant reduction in blood glucose levels and favorable changes in insulin resistance, as measured by HOMA-IR [29-30].

In our study, the analysis of fasting blood glucose levels between the placebo and probiotic groups showed no statistically significant difference in reduction. This outcome may be attributed to several limitations inherent in our study. Firstly, the duration of the intervention administration significantly influences the final research results. The intervention period in this study was 14 working days; thus,

the results are short-term, which may be insufficient to demonstrate the expected effects, especially in the treatment of chronic diseases.

Furthermore, we did not take into account the duration of medication adherence and the severity of the disease. Research subjects demonstrating strict medication adherence would naturally exhibit better-controlled blood glucose levels. Moreover, several confounding factors were not assessed in this study, including stress levels, dietary habit, physical activity and smoking habits. These factors could potentially influence the efficacy of the probiotic mechanism in the gut.

4. Conclusion

The analysis revealed a statistically significant reduction in fasting blood Sugar (FBS) levels within the intervention group following probiotic administration. However, despite this intra-group improvement, the findings were not clinically significant. This lack of clinical relevance is attributed to the fact that post-intervention FBS levels did not differ significantly when compared to the placebo group ($p > 0.05$).

References

- [1] Purnamasari D. (2014). Buku Ajar Ilmu Penyakit Dalam. VI. Vol. 2. *Interna Publishing*.
- [2] International Diabetes Federation. <https://idf.org/about-diabetes/diabetes-facts-figures/>. 2025. Diabetes Facts and Figures.
- [3] Dinas Kesehatan Provinsi NTB. Cakupan Pelayanan Kesehatan Penderita Diabetes Melitus Provinsi NTB. <https://data.ntbprov.go.id/dataset/pelayanan-kesehatan-penderita-diabetes-melitus-dm-di-provinsi-ntb/resource/bdba586e-5698-2023>
- [4] Abhilash, P., Dsouza, D. J., Sradha, S., Nandakumar, U. P., Ahmed, S., Kolar, R., & Chand, S. (2023). Factors influencing adherence towards oral hypoglycaemic agents-A cross-sectional study among patients with Type II Diabetes Mellitus. *Diabetes Epidemiology and Management*, 12, 100163.
- [5] Elmuzghi, R. F. (2023). Assessing the influential factors associated with medication non-adherence and self-care practices among type 2 diabetes mellitus patients in Tripoli, Libya. *Sciences of Pharmacy*, 2(2), 104-116.
- [6] Indonesia, P. E. (2015). Pengelolaan dan pencegahan diabetes melitus tipe 2 di Indonesia. *Pb Perkeni*, 6.
- [7] Dewvi, P. A. S., Aryaweda, M. D. W., Mahayana, N. P. K., Devi, N. P., Yadmika, N. P. W. P., & Sumartini, N. K. (2025). The effects of probiotic or synbiotic supplementation on glycemic control and lipid profile for type 2 diabetic patients. *Intisari Sains Medis*, 16(2), 695-701.
- [8] Ayesha, I. E., Monson, N. R., Klair, N., Patel, U., Saxena, A., Patel, D., ... & Ayesha, I. E. (2023). Probiotics and their role in the management of type 2 diabetes mellitus (Short-term versus long-term effect): A systematic review and meta-analysis. *Cureus*, 15(10).
- [9] AkbariRad, M., Shariatmaghani, S. S., Razavi, B. M., Majd, H. M., Shakhsemampour, Z., Sarabi, M., ... & Khorasani, Z. M. (2023). Probiotics for glycemic and lipid profile control of the pre-diabetic patients: a randomized, double-blinded, placebo-controlled clinical trial study. *Diabetology & Metabolic Syndrome*, 15(1), 71.
- [10] FAO, W. (2006). Probiotics in food: Health and nutritional properties and guidelines for evaluation. 2006. *FAO Food and Nutritional Paper*, 85.
- [11] Latif, A., Shehzad, A., Niazi, S., Zahid, A., Ashraf, W., Iqbal, M. W., ... & Korma, S. A. (2023). Probiotics: mechanism of action, health benefits and their application in food industries. *Frontiers in microbiology*, 14, 1216674.
- [12] He, J., Zhang, P., Shen, L., Niu, L., Tan, Y., Chen, L., ... & Zhu, L. (2020). Short-chain fatty acids and their association with signalling pathways in inflammation, glucose and lipid metabolism. *International journal of molecular sciences*, 21(17), 6356.

- [13] Rittiphairoj, T., Pongpirul, K., Janchot, K., Mueller, N. T., & Li, T. (2021). Probiotics contribute to glycemic control in patients with type 2 diabetes mellitus: a systematic review and meta-analysis. *Advances in nutrition*, 12(3), 722-734.
- [14] Vallejos, O. P., Bueno, S. M., & Kalergis, A. M. (2025). Probiotics in inflammatory bowel disease: microbial modulation and therapeutic prospects. *Trends in molecular medicine*, 31(8), 731-742.
- [15] Samsudin, D. D., Firmansyah, A., Hidayati, E. L., Yuniar, I., Karyanti, M. R., & Roeslani, R. D. (2020). Effects of probiotic on gut microbiota in children with acute diarrhea: a pilot study. *Paediatrica Indonesiana*, 60(2), 83-90.
- [16] Mafi, A., Namazi, G., Soleimani, A., Bahmani, F., Aghadavod, E., & Asemi, Z. (2018). Metabolic and genetic response to probiotics supplementation in patients with diabetic nephropathy: a randomized, double-blind, placebo-controlled trial. *Food & function*, 9(9), 4763-4770.
- [17] Madempudi, R. S., Ahire, J. J., Neelamraju, J., Tripathi, A., & Nanal, S. (2019). Efficacy of UB0316, a multi-strain probiotic formulation in patients with type 2 diabetes mellitus: a double blind, randomized, placebo controlled study. *PloS one*, 14(11), e0225168.
- [18] BPOM (OTSKK). (2024). Daftar Strain Probiotik yang telah diizinkan. <https://standar-otskk.pom.go.id/otskk-db/kategori/daftar-strain-probiotik-yang-telah-diizinkan>.
- [19] MIMS. <https://www.mims.com/indonesia/drug/info/1-bio?type=brief&lang=id>. 2026. L - Bio.
- [20] Speich, B., Logullo, P., Deuster, S., Marian, I. R., Moschandreas, J., Heravi, A. T., ... & MAKing Randomized Trials Affordable (MARTA) Group. (2021). A meta-research study revealed several challenges in obtaining placebos for investigator-initiated drug trials. *Journal of clinical epidemiology*, 131, 70-78.
- [21] Wulandari, L. S., Kusumastuty, I., Cempaka, A. R., & Nugroho, F. A. (2023). Effect of Buffalo Curd Milk-Edamame Pudding Snack Consumption on Fasting Blood Glucose Levels and Lipid Profile in Diabetes Mellitus Patients. *Amerta Nutrition*, 7(4).
- [22] Fusco, W., Lorenzo, M. B., Cintoni, M., Porcari, S., Rinninella, E., Kaitsas, F., ... & Ianiro, G. (2023). Short-chain fatty-acid-producing bacteria: key components of the human gut microbiota. *Nutrients*, 15(9), 2211.
- [23] Viana, M. D. M., Santos, S. S., Cruz, A. B. O., de Jesus, M. V. A. C., Lauria, P. S. S., Lins, M. P., & Villarreal, C. F. (2025). Probiotics as antioxidant strategy for managing diabetes mellitus and its complications. *Antioxidants*, 14(7), 767.
- [24] Watt, R., Parkin, K., & Martino, D. (2020). The potential effects of short-chain fatty acids on the epigenetic regulation of innate immune memory. *Challenges*, 11(2), 25.
- [25] Feng, C., Jin, C., Liu, K., & Yang, Z. (2023). Microbiota-derived short chain fatty acids: Their role and mechanisms in viral infections. *Biomedicine & Pharmacotherapy*, 160, 114414.
- [26] Zheng, J., An, Y., Du, Y., Song, Y., Zhao, Q., & Lu, Y. (2024). Effects of short-chain fatty acids on blood glucose and lipid levels in mouse models of diabetes mellitus: A systematic review and network meta-analysis. *Pharmacological Research*, 199, 107041.
- [27] Pham, N. H., Joglekar, M. V., Wong, W. K., Nassif, N. T., Simpson, A. M., & Hardikar, A. A. (2024). Short-chain fatty acids and insulin sensitivity: a systematic review and meta-analysis. *Nutrition Reviews*, 82(2), 193-209.
- [28] Hulston, C. J., Churnside, A. A., & Venables, M. C. (2015). Probiotic supplementation prevents high-fat, overfeeding-induced insulin resistance in human subjects. *British Journal of Nutrition*, 113(4), 596-602.

-
- [29] Rezazadeh, L., Alipour, B., Jafarabadi, M. A., Behrooz, M., & Gargari, B. P. (2021). Daily consumption effects of probiotic yogurt containing *Lactobacillus acidophilus* La5 and *Bifidobacterium lactis* Bb12 on oxidative stress in metabolic syndrome patients. *Clinical nutrition ESPEN*, *41*, 136-142.
- [30] Hsieh, M. C., Tsai, W. H., Jheng, Y. P., Su, S. L., Wang, S. Y., Lin, C. C., ... & Chang, W. W. (2018). The beneficial effects of *Lactobacillus reuteri* ADR-1 or ADR-3 consumption on type 2 diabetes mellitus: a randomized, double-blinded, placebo-controlled trial. *Scientific reports*, *8*(1), 16791.