Acta Scientific MEDICAL SCIENCES (ISSN: 2582-0931)

Volume 7 Issue 3 March 2023

Research Article

Probiotics in the Era of Diabetes, is it a Hope or a Hype; Narrative Review of Literature

Dakhel Fahad Almubarak[1], Alanoud Abdulaziz Alharkan[2] and Mostafa Kofi[3]*

[1]*Family Medicine Resident, Prince Sultan Military Medical City Riyadh, Saudi Arabia*

[2]*Medical Intern, College of Medicine, Princess Nourah Bint Abdulrahman University Riyadh, Saudi Arabia*

[3]*Consultant PSMMC, Saudi Arabia*

***Corresponding Author:** Mostafa Kofi, Consultant PSMMC, Saudi Arabia.

DOI: 10.31080/ASMS.2023.07.1476

Received: January 23, 2023

Published: February 10, 2023

Abstract

Diabetes is a metabolic disorder that is characterized by inadequate insulin secretion by pancreas or the lack in ability of the present insulin to function properly. Hence, diabetes forms a fertile media for several diseases and represents a greater risk on human-being health. Over decades, several strategies for management of diabetes have been tried by specialists, of which medical, herbal, and even live style modification has been tried.

Although diabetes mellitus represents a global growing epidemic disease, Till the moment there is no absolute solution at molecular level that targeting the disease. It's well known that commensal bacteria have an un-neglectable role in bode metabolism since infancy both in healthy and diseased patients. On a clinical base when we studied beneficial role of probiotics at cellular level in animals. It was proved in many studies the beneficial role of probiotic for people with DM; nevertheless, further prospective interventional research, mostly using human models, are required to fully understand the impact of probiotic use in diabetic patients.

Indeed, we need to test the probability of probiotics usage in the outpatient clinic. As Based on our reliable understanding the beneficial role of probiotics in patients with diabetes mellites specially at the level of cell, both in clinical trials and animal studies, in addition to their excellent tolerability. Also, probiotics have proved their ability to decrease insulin and fasting blood glucose level in diabetic patients in a preclinical setting and in human trials. Recently, probiotics are used in a multiple diseases like inflammation, allergic reactions, and autoimmune diseases. However, the heterogeneity in these studies is high. For example, species used, the dose of probiotic used, and the magnitude of efficacy.

In our review, we focused on reviewing the relation between probiotics and troubled metabolism of our body sugar.

Keywords: Probiotics; Diabetes; Type 2 DM; Inflammation

Introduction

Globally, the percentage of patients with diabetes mellitus (DM) type 2 now reached 90–95% of all those with diabetes. This percentage includes patients with insulin resistance and relative insulin deficiency [1]. The percentage of diabetic patients was found to be 8.3% of population all over the world [2]. In Saudi Arabia, IDF reports found that about 4.274. 1 million cases in Saudi Arabia, at which the population measure nearly 34.8 million, are diseased with DM [3].

As a result of (hyper-insulinemia, insulin resistance and deficiency, and obesity), DM is usually presents with other devastating illnesses like dyslipidemia, hypertension, and cardiovascular (CVD) consequences [4]. Also, the elevated lipid profiles among diabetic patients can lead to severe CVD disease and even can lead to death [5]. Also, hepatic and renal disease was recorded [6].

Management strategies are variable. It includes weight loss by lowering caloric intake and glycemic index in diet and increasing physical activity as the first line for patient with type 2 DM specifically [7].

Moreover, other policies for lowering lipid parameters in diabetic patients have been advocated. It includes using antioxidants, agents that lower the cholesterol, and mineral supplements [8]. In recent times, limited studies (mainly on animals) have also concluded that expenditure of probiotics can improve the metabolic profiles [9]. But these effects were noticed on animals and non-diabetic models.

Additionally, recorded data illustrating the effects of probiotics on serum lipid profiles are contradictory. Intake of a probiotics containing Lactobacillus acidophilus, fructo-oligosaccharide, inulin and mannitol for 8 weeks resulted in decreased serum triglycerides (TAG), total cholesterol (TC) and LDL-C levels as well as increased HDL-C concentrations in hypercholesterolemic pigs (10). In a study conducted on a healthy pregnant women showed decreased serum TAG and VLDL-C levels following consumption of probiotics food containing heat-resistant Lactobacillus sporogeneses and 0.04 g inulin as prebiotic per one g after nine weeks [11].

The enzymatic deconjugation of bile acids [12], assimilation of cholesterol in the gastrointestinal tract, production of short chain fatty acids (SCFA), carbon disulfide, and methyl acetate, and conversion of cholesterol into coprostanol in the gut could all contribute to the positive effects of probiotics and probiotics on lipid profiles [13].

There are no obvious trials studying the effects of daily usage of probiotic on lipid profiles between diabetic patients. Although, some clinical trials on human samples using various probiotics have acquiesced a mixed result. Some of these studies found no effect [14], while other studies have found an obvious evidence of probiotics on lowering blood glucose [15].

We aim in current review to inspect the effects of regular expenditure of probiotics and their effect on lipid profiles in patients with T2DM.

Methods

We hold a thorough literature search till 2022 using PubMed dataset. We used the subheadings and the following keywords accordingly, “Probiotics; Bifidobacterium; bifidum, Fructo-oligosaccharide; Lactobacillus acidophilus; Microbiota; Diabetes; Glucose; Review

Pathophysiology

The effect of probiotics on glucose metabolism could be mediated by a variety of ways. According to several research, oxidative damage and antioxidative activity play an essential role in the etiology of diabetes [16,17]. The capability of probiotics has been established in earlier experiments [18]. In diabetic rats, Yadav et al. discovered that probiotics reduced oxidative damage by preventing lipid peroxidation and boosting the antioxidant content of glutathione, superoxide dismutase, catalase, and glutathione peroxidase [19]. Second, probiotics have been shown to have anti-diabetic effects against insulin resistance by boosting natural killer T (NKT) cells in the liver. By regulating TNF- expression and decreasing NF-B binding activity, probiotic therapy decreased insulin resistance and inflammation [20]. Furthermore, probiotics may improve glucose metabolism by boosting gliclazide bioavailability, blocking or delaying glucose absorption in the intestine, and altering autonomic nervous system activity [21,22].

Probiotics are live microorganisms that have a significant impact on healthy and diseased cases [23,24]. They were investigated for their potential health advantages in terms of immune system function and diarrhea prevention [25,26]. Probiotics have also been shown in animal models to lower blood glucose levels by improving inflammation and preventing -cell death [27].

Evidence of probiotic use for diabetic patients

We looked into ten papers with various methodology and comparison groups. The definitive proof is still uncertain and contentious. Most studies found no statistical difference in expected outcomes, and the majority of studies relied on animal models. However, due to differences in the groups studied in each trial, these findings cannot be considered strong proof for the positive function of probiotics in diabetes management. In a systematic review and meta-analysis study by Zheng 2019 [28] which investigated sixteen randomized control trial with a total of 1060 cases, it was found that probiotics and synbiotics have a positive effect on diabetic patients as all the inflammatory markers were reduced (hs-CRP and MDA with the P-value equal 0.000 for both) and the oxidative stress was increased as following (TAC

with the P-value equal 0.006, NO with the P-value equal 0.001, GSH with the P-value equal 0.000). these results were similar to that of Tabrizi., *et al*. 2019 [29].

In an update of Meta-Analysis by Liang., *et al*. 2021 [30] found that the usage of different types of probiotics has lowered FBS and increased insulin resistance. This study was conducted on 818 diabetic patients from 8 different countries and found that age, body mass index (BMI) and the duration of probiotic supplement intake are the backbone factors that demonstrate its efficacy. Jafarabadi., *et al*. 2021 shed light on HbA1c. It was found that probiotics has the ability to reduce HbA1c, FBG, and insulin concentration with P-value 0.01. Even with gestational diabetes mellites (GDM), RCT by Amirani., *et al*. 2022 conducted on 60 of cases comparing the effect of probiotic and selenium vs placebo found that, probiotics with selenium can reduce fasting blood sugar (FBS) and insulin concentration and resistance with P-value 0.004, 0.002, 0.001 respectively. while insulin sensitivity was significantly increased with P-value 0.002. Another SR and MA study by Pan., *et al*. [31] found that probiotics can reduce fasting serum insulin (P-value 0.00001) but, fasting plasma glucose wasn't reduced (p-value 0.09). other systematic reviews and meta-analysis [32-35] support the role of probiotics in patients with diabetes specially at cellular level. we summarized some of these studies in table 1.

ID	Disease	Number of patients treated	Design	Main outcomes	Main finding
Zheng 2019	Diabetic patients	1060 cases were randomly distributed into probiotic and/or synbiotic (n = 533) or into control (n = 527) groups.	systematic review and meta-analysis	Inflammatory markers in diabetic patients	Probiotic and synbiotic has a positive effect on serum hs-CRP and MDA levels, which was significantly decreased and increase oxidative factors like TAC, NO, and GSH.
Liang 2021	Cases with type 2dm	818 of cases from 8 countries	An update of MA	Glycemic, lipid, blood pressure and inflammatory biomarkers	Probiotics improve glycemic and inflammatory markers in diabetic patients specially those with age less than 50 and BMI less than 30
Jafarabadi 2021	Diabetic patients	--	Update of evidence	Glycemic control	HbA1c and insulin level could be decreased when using probiotics supplements rather than foods
Ding 2021	Patients with type 2DM	423 of diabetic patients	SR&MA	Inflammatory markers in diabetic patients	Probiotic can improve inflammatory biomarkers and glucose level in patients with T2DM. Probiotics could be used as adjuvant therapy for T2DM.
Pan 2017	Patients with GDM	830 Patients with GDM	SR&MA	Gestational DM	Probiotics could reduce serum insulin but not FBG
Amirani 2022	GDM	60 of cases with GDM divided into 30 in the intervention group and 30 in the control group	Randomized control trial	Glycemic control and lipid profile in patients with GDM	Probiotics and selenium can reduce both FBS and insulin. Also, can increase insulin sensitivity in patients with GD.

Table 1: GDM; Gestational Diabetes Mellites, T2DM; Type 2 Diabetes Mellites, CRP; C-Reactive Protein, NO; Nitric Oxide, FBG; Fasting Blood Glucose.

Limitations

The research featured used various approaches, which may have resulted in information biases. Some trials reviewed synbiotics instead of probiotics alone, and there was nonuniformity in the comparisons made across the investigations of the different groups. Furthermore, many routing factors, such as impaired nutritional condition [36] unquestionably affect outcomes and complications in diabetic patients. It is also difficult to establish clinical practice recommendations due to the wide diversity of probiotic strains, time spent using probiotics, and daily doses used in the studies [28].

Recommendations

So yet, no definite conceptual proof of the effect of probiotic therapy on diabetic patients has been properly demonstrated. The cause-effect association that may be created by the supplementations, as an example, was not visible in the most critical investigation till now. Furthermore, records that could explain the biological mechanics of such supplements are unavailable.

Due to the relatively recent approval of probiotics in clinical practise, the database, which includes biological agents with various action mechanisms, is still in its early years in worldwide literature. More clinical trials, as presented in this review, are needed to address concerns about probiotic bacterial species, treatment course, and daily dosage of therapy [37]. Neither the included studies nor the evaluation of the impact of active probiotics on the regulation of gut hormones profiled changes in gut microbiota [38]. Consuming live bacteria, particularly those present in fermented foods, may improve the harmony between intestinal permeability and barrier performance. A current focus of scientific and medical research is the microbiome [39]. A larger panel of stool and serum surrogate markers should be used in well-designed RCTs to uncover explanations and processes.

In order to design an effective study that will produce more meaningful results to resolve the controversy and aim for more reliable and high-quality evidence, we also advise prospective analysis and trials enroll a significant case sample with strict details and more comparison groups than are currently used.

Conclusion

Probiotic usage appears to be beneficial for people with DM; nevertheless, further prospective interventional research, mostly using human models, are required to fully understand the impact of probiotic use in diabetic patients. Even if the majority of the cited research demonstrated a statistically significant reduction in patients' levels of diabetes and improvement in other inflammatory outcomes, a conclusive connection from the available data is still debatable. Each case should receive a unique, interdisciplinary assessment, and decisions should be made while modifying the molecular and cellular mechanism of action in humans.

Bibliography

1. "Diagnosis and classification of diabetes mellitus". *Diabetes Care* 37.1 (2014): S81-90.

2. Catley D., *et al*. "Evaluation of an adapted version of the Diabetes Prevention Program for low- and middle-income countries: A cluster randomized trial to evaluate "Lifestyle Africa" in South Africa". *PLoS Medicine* 19.4 (2022): e1003964.

3. Al-Quwaidhi AJ., *et al*. "Comparison of type 2 diabetes prevalence estimates in Saudi Arabia from a validated Markov model against the International Diabetes Federation and other modelling studies". *Diabetes Research and Clinical Practice* 103.3 (2014): 496-503.

4. Vaughan EM., *et al*. "Dual Therapy Appears Superior to Monotherapy for Low-Income Individuals With Newly Diagnosed Type 2 Diabetes". *Journal of Primary Care and Community Health* 8.4 (2017): 305-311.

5. Nille GC., *et al*. "Ethnopharmacological, Phytochemical, Pharmacological, and Toxicological Review on *Senna auriculata* (L.) Roxb.: A Special Insight to Antidiabetic Property". *Frontiers in Pharmacology* 12 (2021): 647887.

6. Yamashita T., *et al*. "Renal insufficiency without albuminuria is associated with peripheral artery atherosclerosis and lipid metabolism disorders in patients with type 2 diabetes". *Journal of Atherosclerosis and Thrombosis* 20.11 (2013): 790-797.

7. Ajala O., *et al*. "Systematic review and meta-analysis of different dietary approaches to the management of type 2 diabetes". *The American Journal of Clinical Nutrition* 97.3 (2013): 505-516.

8. Masana L. "Pitavastatin in cardiometabolic disease: therapeutic profile". *Cardiovascular Diabetology* 12 (2013): S2.

9. Davoodvandi A., *et al*. "An Update on the Effects of Probiotics on Gastrointestinal Cancers". *Frontiers in Pharmacology* 12 (2021): 680400.

10. Liong MT., *et al*. "Effects of a synbiotic containing Lactobacillus acidophilus ATCC 4962 on plasma lipid profiles and morphology of erythrocytes in hypercholesterolaemic pigs on high- and low-fat diets". *The British Journal of Nutrition* 98.4 (2007): 736-744.

11. Taghizadeh M., *et al*. "Synbiotic food consumption reduces levels of triacylglycerols and VLDL, but not cholesterol, LDL, or HDL in plasma from pregnant women". *Lipids* 49.2 (2014): 155-161.

12. Bustos AY., *et al*. "New insights into bacterial bile resistance mechanisms: the role of bile salt hydrolase and its impact on human health". *Food Research International (Ottawa, Ont).* 112 (2018): 250-162.

13. Ali SM., *et al*. "Hypolipidemic activity of lactic acid bacteria: Adjunct therapy for potential probiotics". *PLoS One* 17.6 (2022): e0269953.

14. Mazloom Z., *et al*. "Effect of probiotics on lipid profile, glycemic control, insulin action, oxidative stress, and inflammatory markers in patients with type 2 diabetes: a clinical trial". *Iranian Journal of Medical Sciences* 38.1 (2013): 38-43.

15. Obuchowska A., *et al*. "Effects of Probiotic Supplementation during Pregnancy on the Future Maternal Risk of Metabolic Syndrome". *International Journal of Molecular Sciences* 23.15 (2022).

16. Saxena N., *et al*. "Modulation of oxidative and antioxidative status in diabetes by asphaltum panjabinum". *Diabetes Care* 26.8 (2003): 2469-2470.

17. Friesen NT., *et al*. "Generation of hydrogen peroxide and failure of antioxidative responses in pancreatic islets of male C57BL/6 mice are associated with diabetes induced by multiple low doses of streptozotocin". *Diabetologia* 47.4 (2004): 676-685.

18. Willcox JK., *et al*. "Antioxidants and prevention of chronic disease". *Critical Reviews in Food Science and Nutrition* 44.4 (2004): 275-295.

19. Yadav H., *et al*. "Antidiabetic effect of probiotic dahi containing Lactobacillus acidophilus and Lactobacillus casei in high fructose fed rats". *Nutrition (Burbank, Los Angeles County, Calif)* 23.1 (2007): 62-68.

20. Ma X., *et al*. "Probiotics improve high fat diet-induced hepatic steatosis and insulin resistance by increasing hepatic NKT cells". *Journal of Hepatology* 49.5 (2008): 821-30.

21. Al-Salami H., *et al*. "Probiotic Pre-treatment Reduces Gliclazide Permeation (*ex vivo*) in Healthy Rats but Increases It in Diabetic Rats to the Level Seen in Untreated Healthy Rats". *Archives of Drug Information* 1.1 (2008): 35-41.

22. Yamano T., *et al*. "Effects of the probiotic strain Lactobacillus johnsonii strain La1 on autonomic nerves and blood glucose in rats". *Life Sciences* 79.20 (2006): 1963-1967.

23. Zok C. "[The importance of the human intestinal microbiota]". *Deutsche medizinische Wochenschrift (1946)* 139.24 (2014): 1282-1283.

24. Morelli L. "Yogurt, living cultures, and gut health". *The American Journal of Clinical Nutrition* 99 (2014): 1248s-1250s.

25. Iebba V., *et al*. "Gut microbiota and the immune system: an intimate partnership in health and disease". *International Journal of Immunopathology and Pharmacology* 25.4 (2012): 823-833.

26. Guandalini S. "Probiotics for prevention and treatment of diarrhea". *Journal of Clinical Gastroenterology* 45 (2011): S149-153.

27. Al-Salami H., *et al*. "Probiotic treatment reduces blood glucose levels and increases systemic absorption of gliclazide in diabetic rats". *European Journal of Drug Metabolism and Pharmacokinetics* 33.2 (2008): 101-106.

28. Zheng HJ., *et al*. "The effect of probiotic and synbiotic supplementation on biomarkers of inflammation and oxidative stress in diabetic patients: A systematic review and meta-analysis of randomized controlled trials". *Pharmacological Research* 142 (2019): 303-313.

29. Tabrizi R., *et al*. "The effects of probiotic and synbiotic supplementation on inflammatory markers among patients with diabetes: A systematic review and meta-analysis of randomized controlled trials". *European Journal of Pharmacology* 852 (2019): 254-264.

30. Liang T., *et al*. "Probiotics supplementation improves hyperglycemia, hypercholesterolemia, and hypertension in type 2 diabetes mellitus: An update of meta-analysis". *Critical Reviews in Food Science and Nutrition* 61.10 (2021): 1670-1688.

31. Pan J., *et al*. "Efficacy of probiotic supplement for gestational diabetes mellitus: a systematic review and meta-analysis". *The Journal of Maternal-Fetal and Neonatal Medicine* 32.2 (2019): 317-323.

32. Tabrizi R., *et al*. "The Effects of Synbiotic Supplementation on Glucose Metabolism and Lipid Profiles in Patients with Diabetes: a Systematic Review and Meta-Analysis of Randomized Controlled Trials". *Probiotics and Antimicrobial Proteins* 10.2 (2018): 329-342.

33. Li C., *et al*. "Effect of probiotics on metabolic profiles in type 2 diabetes mellitus: A meta-analysis of randomized, controlled trials". *Medicine (Baltimore)* 95.26 (2016): e4088.

34. Zhang C., *et al*. "Meta-analysis of randomized controlled trials of the effects of probiotics on type 2 diabetes in adults". *Clinical Nutrition (Edinburgh, Scotland)* 41.2 (2022): 365-373.

35. Zhang Q., *et al*. "Effect of probiotics on glucose metabolism in patients with type 2 diabetes mellitus: A meta-analysis of randomized controlled trials". *Medicina (Kaunas, Lithuania)* 52.1 (2016): 28-34.

36. Nabhani Z., *et al*. "The effect of synbiotic supplementation on atherogenic indices, hs-CRP, and malondialdehyde, as major CVD-related parameters, in women with gestational diabetes mellitus: a secondary data-analysis of a randomized double-blind, placebo-controlled study". *Diabetology and Metabolic Syndrome* 14.1 (2022): 87.

37. Suez J., *et al*. "Post-Antibiotic Gut Mucosal Microbiome Reconstitution Is Impaired by Probiotics and Improved by Autologous FMT". *Cell* 174.6 (2018): 1406-1423.e16.

38. Freedman SB., *et al*. "Multicenter Trial of a Combination Probiotic for Children with Gastroenteritis". *The New England Journal of Medicine* 379.21 (2018): 2015-2026.

39. Sun Z., *et al*. "Using probiotics for type 2 diabetes mellitus intervention: Advances, questions, and potential". *Critical Reviews in Food Science and Nutrition* 60.4 (2020): 670-683.