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Dietary pattern and gut microbiota in type 2 diabetes mellitus: A literature review

Pola makan dan mikrobiota usus pada diabetes mellitus tipe 2: Sebuah tinjauan pustaka

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Abstract

Nutrition has been identified as the primary modifiable factor, and the type of food, macronutrients, and micronutrient composition of the diet have distinct effects on gut microbiota and related metabolites. These effects significantly influence the mechanisms that regulate hyperglycemia and insulin resistance, influencing gut microbiota remodeling and the development of T2DM. This study aimed to gather information on changes in gut microbiota composition (Lactobacillus and Bifidobacterium) and describe the beneficial or detrimental effects, impacts, and outcomes of macronutrients (carbohydrate, protein, and fat) and fiber on gut microbiota composition in T2DM. Nine English articles were obtained from the literature review. Lactobacillus and Bifidobacterium can positively reduce the blood glucose levels. Changes in the gut microbiota and its metabolites, which are influenced by carbohydrate, protein, lipid, and fiber intake, can worsen or decrease biochemical parameters and improve T2DM complications. The conclusion of this literature review is that gut microbiota can be crucial in the future treatment of diabetes mellitus, especially in combination with other therapeutic options.

Keywords: Diabetes mellitus, dietary pattern, gut microbiota, lactobacillus, bifidobacterium

Abstrak

Zat gizi telah diidentifikasi sebagai faktor utama yang dapat dimodifikasi. Jenis makanan, komposisi makronutrien dan mikronutrien dari makanan memiliki efek yang berbeda pada mikrobiota usus dan metabolit terkait. Dampak ini secara signifikan memengaruhi mekanisme yang mengatur hiperglikemia dan resistensi insulin yang memengaruhi perubahan komposisi mikrobiota usus dan perkembangan T2DM. Studi ini bertujuan untuk mengumpulkan informasi tentang perubahan komposisi mikrobiota usus (*Lactobacillus* dan *Bifidobacterium*) dan mendeskripsikan efek menguntungkan atau merugikan, dampak, dan hasil makronutrien (karbohidrat, protein, dan lemak) dan serat terhadap komposisi mikrobiota usus di DMT2. Sebanyak 9 artikel berbahasa Inggris diperoleh dari hasil kajian pustaka. *Lactobacillus* dan *Bifidobacterium* secara positif dapat menurunkan kadar glukosa darah. Perubahan mikrobiota usus dan metabolitnya, yang dipengaruhi oleh asupan karbohidrat, protein, lipid, dan serat, dapat memperburuk atau menurunkan parameter biokimia dan memperbaiki komplikasi DMT2. Kesimpulan dari tinjauan pustaka ini adalah mikrobiota usus dapat berperan penting dalam pengobatan diabetes melitus di masa depan, terutama bila dikombinasikan dengan pilihan terapi lain.

Kata Kunci: Diabetes mellitus, mikrobiota usus, *Lactobacillus*, *Bifidobacterium*, pola makan

Introduction

Type 2 diabetes mellitus (T2DM) is the leading cause of death worldwide. The incidence of diabetes has increased rapidly in recent years. Currently, more than 400 million patients are diagnosed with diabetes and this number is expected to double by 2045 (Saeedi et al., 2019). T2DM is a metabolic disease characterized by hyperglycemia and lipid profile dysfunction (Sircana et al., 2018). The factors that can influence the occurrence of T2DM are genetic and environmental factors, such as diet and the structure of the intestinal microbiota (Sircana et al., 2018). Diet is an essential factor in determining the nature of the bacterial, viral, and fungal elements that comprise the intestinal microbiota (Ortega et al., 2020).

Interactions between diet and gut microbiota have been reported to influence obesity, insulin resistance, and chronic inflammatory responses (Ponzo et al., 2019). Food composition is essential for the development of diabetes mellitus (DM). A diet with high sugar, fat, and cholesterol levels increases the risk of diabetes (Lazar et al., 2019). This diet causes an imbalance in microbial homeostasis (gut dysbiosis) and damages the intestinal mucosal barrier, thereby facilitating the development of diabetes mellitus (Xi & Xu, 2021). Diet has a long-term influence on gut microbiota, which can be an appropriate strategy for managing diabetes mellitus.

Individuals with T2DM show varied gut microbiota results; these factors influence gut microbiota diversity, namely external complex factors (drugs), host genetic factors, and environmental factors (changes in eating habits) (Therdtatha et al., 2021). Complex carbohydrates in the intestine are digested by bacteria, producing short-chain fatty acids (SCFA) and their primary metabolites, such as lactate and succinate (Therdtatha et al., 2021). These products are directly or indirectly involved in metabolic and energy homeostasis (Fernández-Veledo and Vendrell, 2019). Biosynthesis dysfunction is believed to be related to metabolic diseases. Dysbiosis is characterized by an imbalance of microorganisms in the human digestive tract. Dysbiosis may contribute to the development of chronic diseases, such as T2DM.

Bifidobacterium belongs to the most abundant class of *Actinobacteria*, but its phylum is much smaller (Rinninella et al., 2023). *Bifidobacterium* plays an essential role in the biodegradation of resistant starch and in carbohydrate fermentation in the lower intestine (Ahmad et al., 2019). Consumption of various saccharides can result in a high proportion of *Bifidobacterium* (Kondo et al., 2021). *Bifidobacterium* has been shown to have the most consistent potential to protect against T2DM (Gao et al. 2018). *Lactobacillus* is a diverse genus containing the largest species in the human intestine among the classes of probiotic bacteria and belongs to the phylum *Firmicutes* (Al-Jameel, 2021). These bacteria have species-or strain-specific effects on individuals with T2DM.

Dysbiosis and increased intestinal permeability lead to lipopolysaccharide translocation, which can activate the innate immune system (Al-Ishaq et al., 2023). In patients with diabetes, plasma levels of lipopolysaccharide are higher than those in healthy participants, causing low-grade inflammation that may lead to insulin resistance (Al-Ishaq et al., 2023). The inflammatory response observed in patients with diabetes may be caused by dysbiosis of the gut microbiota and its primary metabolites, such as bile acids and SCFAs, which regulate glucose metabolism and insulin sensitivity (Al-Ishaq et al. 2023). This suggests that gut microbiota may be an essential driver of diabetes pathogenesis and could be used as a potential therapeutic target.

Nutrition has been identified as the primary modifiable factor influencing gut microbiota remodeling and the development of T2DM, with various diets, food groups, macronutrients, and micronutrients each having distinct effects on its composition ((Beam et al., 2021),Zmora et al., 2019)). The type of food and macronutrient and micronutrient composition of the diet have distinct effects on the gut microbiota and related metabolites. These effects significantly influence the mechanisms that regulate hyperglycemia and insulin resistance (Maestri et al., 2023).

This review highlights the crucial role of macronutrients at the intersection of gut microbial eubiosis and the development of T2DM. It examines the changes in gut microbiota composition, particularly focusing on *Lactobacillus* and *Bifidobacterium*, in individuals with T2DM. This review also explores how *Lactobacillus*, *Bifidobacterium*, and their related metabolites can either contribute to or protect against diabetes. Additionally, it discusses the

effects of different macronutrients on the microbiota and their relationship with T2DM.

This study aimed to gather information on changes in gut microbiota composition (*Lactobacillus* and *Bifidobacterium*) and describe the beneficial or detrimental effects, impacts, and outcomes of macronutrients (carbohydrate, protein, and fat) and fiber on gut microbiota composition in T2DM.

Methods

Data Sources and Collection

A literature review was conducted using the PubMed database. The search strategy is a combination of keywords, subject, and title words as follows, or the combination used is as follows: "diabetes mellitus," "gut microbiota," "*Lactobacillus*," "*Bifidobacterium*," and "diet." Articles published between January 1, 2018, and January 1, 2024, were included. The articles and abstracts were limited to studies written in English. The primary outcome of interest was the changes in the gut microbiota in terms of the levels of *Lactobacillus* and *Bifidobacterium*. Species-specific associations between fasting glucose and HbA1c levels can also be reported as a secondary outcome.

35 articles were obtained from the PubMed database, 1680 from the ScienceDirect database, and 31700 articles from the Google Scholar database (Figure 1).

Study selection

To continue the study, we selected 9 articles that were most relevant to the topic. Articles that met the inclusion criteria were selected for assessment. Eligibility criteria included studies that met the PICOS (Patients/participants, Intervention, Comparison/control Group, Outcomes and Study Design) where the study population consisted of 1) Individuals with diabetes mellitus, overweight, and/or obesity; 2) adults only (over 18 years); 3) minimum intervention duration of 1 month (4 weeks); 4) dietary intervention is carried out every day; and 5) the results reported are gut microbiota (levels *of Lactobacillus* and *Bifidobacterium*), fasting glucose, and HbA1c. 6) Consumption of diabetes mellitus medications. Exclusion criteria consisted of Individuals with hypertension, cardiometabolic disease, cardiovascular disease, metabolic syndrome, type 1 diabetes, gestational diabetes, NAFLD, cancer, gastrointestinal disease, end-stage renal disease, neurological disease, and research conducted in adolescents or middle age were excluded.

Data Synthesis

The findings of the included studies will be presented as a narrative synthesis and illustrated in a table that contains the following information: author, year, subject characteristics, type of intervention, duration, primary outcome, and secondary outcomes. Subgroup analyses will be performed for different dietary intervention types, based on duration.

The data obtained were then studied by summarizing and analyzing it through narrative elaboration and determining the conclusions of the research results. Data analysis was performed by describing the relationship between macronutrient intake and gut microbiota in T2DM patients. Assessments related to the clinical parameters of diabetes mellitus were also performed.

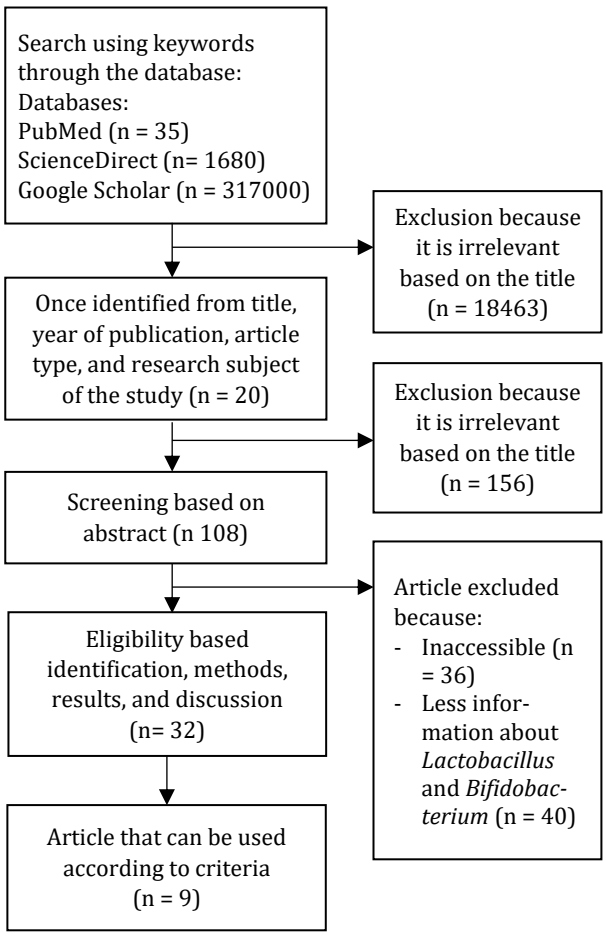

Figure 1. PRISMA diagram article selection scheme

Result and Discussion

Lactobacillus, *Bifidobacterium* and Diabetes Mellitus

The gut microbiota is a significant component of body health. The magnitude of the influence of gut bacteria on T2DM has been linked to changes in the taxonomy of the gut microbiota and differences in the production of gut metabolites, including SCFAs, amino acids, and bile acids. It has been shown to improve or worsen hyperglycemia and insulin resistance (Liu et al. 2022). *Lactobacillus* and *Bifidobacterium* participate in the deconjugation of conjugated bile acids via bile salt hydrolases (Jia et al., 2018).

Bifidobacterium and *Lactobacillus,* which are significant SCFA producers, are associated with reduced serum HbA1c levels (Hsieh et al., 2018). The results showed that *Bifidobacterium* and *Lactobacillus* were significantly and negatively correlated with HbA1c (Almugadam et al., 2020). Increased intestinal permeability causes changes in SCFAs and amino acid absorption in T2DM patients due to gut microbiota dysbiosis (L. Zhao et al., 2020).

Dysbiosis can significantly increase the glucose metabolism. Patients with T2DM experience changes in their gut microbiota, with a decreased ratio of *Bacteroidetes/Firmicutes* (F/B) and *Bifidobacterium* (Al-Jameel, 2021). The most abundant genus in the phylum *Actinobacteria* is *Bifidobacterium.* The most abundant genus in the *Actinobacteria* phylum is *Bifidobacterium*, which is negatively correlated with fasting blood glucose (GDP) because it is often associated with protective properties in T2DM (Gurung et al., 2020).

Metformin significantly improved *Bifidobacterium* and glucose tolerance (Gao et al., 2018). In addition, it plays an essential role in maintaining the permeability and integrity of the intestinal epithelium and produces anti-inflammatory metabolites (Stefani et al., 2018). *Bifidobacterium* is a group of bacteria that has beneficial effects on health, and a decrease in its composition has been associated with T2DM.

The T2DM group has a higher level of Bifidobacterium than the healthy, obese, and prediabetic groups (Düzgün et al., 2023). The results of this study are inconsistent with those of previous studies that found reduced numbers of *Bifidobacterium* in T2DM patients. *Bifidobacterium* may alter the function of dendritic cells to regulate intestinal immune homeostasis. This provides the body with excellent resistance to digestive disorders (Razmpoosh et al., 2019). Studies conducted in Japan have shown that subjects with T2DM have significantly higher levels of *Bifidobacterium spp*. than controls (Adachi et al., 2019). *Bifidobacterium spp.* and *Lactobacillales* are more abundant in T2DM patients because they use ∝-GI, which can affect the digestive system (Adachi et al., 2019).

Several studies have confirmed that the function and composition of the gut microbiota in T2DM patients are altered. Studies that have been conducted comparing healthy adults and T2DM patients showed a significant difference in the relative amount of *Lactobacillus* in the diabetes group compared to that in the control group (Bokhamada & Elmasli, 2021). The results of this study are related to research conducted in Egypt (Halawa et al., 2019). In this study, a low proportion of *Lactobacillus* in T2DM patients was needed to determine the correlation or cause and effect (Halawa et al., 2019).

Lactobacillus is positively correlated with fasting blood glucose and glycosylated hemoglobin (HbA1c) (Bokhamada & Elmasli, 2021). Probiotic bacteria, such as *Lactobacillus* and some other strains, can improve diabetes conditions by reducing GDP and HbA1c in T2DM patients (Bokhamada & Elmasli, 2021). This indicated that *Lactobacillus* has an inverse relationship with the amount of glucose in the blood.

Individuals with T2DM have significantly higher proportions of *Bifidobacterium* and *Lactobacillus* than do those with other types of diabetes (Kondo et al. 2021). Proportions of the *Bifidobacterium* and *Lactobacillus genera:* The high rate in T2DM patients in Japan was associated with α-glucosidase inhibitors (Gurung et al., 2020). Thus, α-glucosidase inhibitors may be closely related to T2DM-associated gut microbiota. *Lactobacillus plantarum* and *Bifidobacterium* in two groups (T2DM and non-T2DM) compared with healthy young subjects in Yogyakarta (Rustanti et al., 2023). In the T2DM group, *Lactobacillus plants* tended to be more common than in the non-T2DM group. *Lactobacillus plantarum* is the most common *Lactobacillus* species, and high levels have been detected in the intestine (Rustanti et al., 2023).

Patients with T2DM and obesity in Romania have significantly lower levels of *L. acidophilus*, *L. plantarum*, and *L. reuteri* than healthy individuals (Suceveanu et al., 2018). Gram-negative bacteria are often found in the feces of people with metabolic syndromes such as dyslipidemia, diabetes, and obesity (Suceveanu et al., 2018). Gram-negative bacteria can trigger subclinical pro-inflammatory processes typical of diabetes and obesity by releasing lipopolysaccharide (LPS). Clinical trials were conducted on humans using 12 species of *Lactobacillus* species, and adding other probiotics showed some protective effects ((Hsieh et al., 2018); Kobyliak et al., 2018)).

The critical role of *Actinobacteria* in biodegradation-resistant starch positively correlates with fasting blood glucose levels (Ahmad et al., 2019). *Firmicutes* can increase the absorption of monosaccharides from the host intestine by increasing hepatic triglyceride production, which can cause insulin resistance (Ahmad et al., 2019). These changes may positively contribute to low-grade inflammation, mainly through the activation of G-protein coupled receptors (GPCRs) associated with SCFAs, thereby causing metabolic disorders (Ahmad et al., 2019).

There was a progressive decrease in the abundance and diversity of gut microbiota with the duration of diabetes. This proves that some beneficial bacteria are negatively correlated with disease duration and changes in gut microbiota. This study is consistent with previous research on the relationship between dysbiosis and gut microbiota in T2DM (Zhang et al. 2019).

Table 1 summarizes the data available in the literature discussing the influence of *Bifidobacterium* and *Lactobacillus* species on diabetes mellitus, including the target pathways tested, route of administration, effects on diabetes, follow-up period, methods, and models used in each study.

Lactobacillus, *Bifidobacterium* and Diet

Increasing evidence suggests that the composition and metabolites of the gut microbiota can be influenced by dietary habits, thereby affecting human health and disease. Nutrition plays an essential role in changes in the pathophysiology and gut microbiota of T2DM, and is an essential factor in considering dietary interventions to reduce complications of hyperglycemia and insulin resistance (Hamamah et al., 2024).

Nutrients shape the gut microbiota and contribute to over 20% of the variability in human interindividual microbiota (Rothschild et al., 2018). Therefore, identifying various dietary patterns, macronutrients, micronutrients, and other food groups may influence gut microbiota. This is an essential approach to the prevention and control of diabetes. The effects of interactions between dietary components and T2DM are still not fully understood. However, high-fruit and vegetable diets benefit glucose metabolism (Hamamah et al., 2024).

The low intake of fermented foods and beverages in T2DM in Japan shows that the proportion of *Bifidobacterium* and *Lactobacillus* genera is significantly higher than that in individuals without diabetes mellitus (Kondo et al., 2021). In addition, the high proportions of *Bifidobacterium* and *Lactobacillus* in T2DM patients were associated with the use of α-glucosidase inhibitors (Gurung et al., 2020). The use of α-glucosidase inhibitors may affect the gut microbiota of T2DM patients.

The high proportion of *Bifidobacterium* is caused by traditional and unique Japanese foods that contain various types of saccharides. Therefore, the gut microbiota composition of Japanese people is unique compared that with of other ethnicities (Kondo et al., 2021). The proportion of *Lactobacillus spp*. in the intestine decreases when consuming foods that are high in salt (Hashimoto et al. 2020). Moreover, the typical Japanese diet has become Westernized (high in fat and low in fiber) (Murakami et al., 2018). Changes in eating habits that cause gut dysbiosis may increase the incidence of T2DM (Adachi et al., 2019).

A study conducted by Hur et al. (2022) showed an increase in *Bifidobacterium longum* in obese women who followed a low-glycemic diet. Additionally, individuals who followed a control diet had lower serum butyric acid levels than those who followed a low-glycemic diet (Hur et al., 2022). A long-term diet causes the formation of the main enterotypes, *Prevotella*, *Bacteroides*, and *Ruminococcus* (Hur, Yang, et al., 2022). *Bifidobacterium spp.* and *Lactobacillus spp*. are some of the bacteria influenced by diet, so it can be said that diet is the primary

modulator of the gut microbiota (Hur, Wu, et al., 2022); Hur, Yang, et al., 2022).

Carbohydrate

Many studies have highlighted the strong association between high sugar intake and the development of T2DM (Lazar et al., 2019). Carbohydrates are divided into two categories based on their enzymatic degradation ability in the small intestine: digestible carbohydrates (starch and sugar, including glucose, lactose, fructose, and sucrose) and indigestible carbohydrates (resistant starch and fiber). After degradation, digestible carbohydrates release glucose into the bloodstream and induce insulin response. In contrast, bacteria are also present in the digestive tract (Lazar et al., 2019). Absorption of high amounts of carbohydrates can cause the microbiota to be enriched with *Bifidobacterium* (Lazar et al., 2019).

An increase in the genus *Bifidobacterium* was the main change in T2DM patients in Japanese (Adachi et al., 2019). Sucrose intake, a characteristic of a westernized diet, correlates with these changes (Adachi et al., 2019). Sucrose intake is associated with *Bifidobacterium* (Sikalidis & Maykish, 2020). Not all sucrose can be absorbed in the small intestine; however, some can reach the large intestine (Jang et al., 2018). Whether the relative abundance of Bifidobacterium in T2DM increases or decreases is still debated (Adachi et al., 2019). Research on T2DM patients in Japan has shown an increase *in Bifidobacterium* in patients taking α-glucosidase inhibitors (Adachi et al., 2019).

Bifidobacterium strains are important probiotics because they aid in carbohydrate fermentation via the fructose-6-phosphate phosphoketolase pathway (Takahashi, 2019). Several *Bifidobacterium* species have high levels of fructose transporters and acetic acid production (Hashimoto et al., 2020). *Bifidobacterium* have a *bifid shunt* that can efficiently produce adenosine triphosphate from glucose. The unique pathway for *Bifidobacterium* to degrade hexose sugars, glucose, and fructose is called the "bifid shunt" (Devika & Raman, 2019).

Increased *Bifidobacterium* levels lead to increased insulin signaling, decreased inflammation in adipose tissue, insulin-stimulated glucose uptake, and increased glucose transporter-4 translocation. This finding indicates that dietary sucrose intake is associated with insulin sensitivity (Hashimoto et al. 2020). Glycolysis, or gluconeogenesis, is related to carbohydrate metabolism, in which carbohydrates are converted into short-chain fatty acids. This phenomenon is often observed in T2DM patients (Hashimoto et al., 2020).

Consumption of a low-carbohydrate diet (LCD) for three months is known to increases GLP. One secretion reduces the HbA1c levels and increases the abundance of SCFA-producing species (Ren et al. 2020). The free fatty acid receptors, FFAR2 (GPR43) and FFAR3 (GPR41), assist in the fermentation of carbohydrates in the intestine to produce SCFA. This causes the mitogen-activated protein kinase (MAPK)/extracellular protein kinase (ERK) pathway to stimulate the release of GLP-1. Administration of *Bifidobacterium* and *Lactobacillus spp*. can increase the secretion of GLP-1 and butyrate by two-fold (Hernández et al., 2019). Metabolic signaling pathways generated by gut microbiota play an essential role in the response to carbohydrate intake. High carbohydrate intake can cause metabolic endotoxemia, insulin resistance, and hyperglycemia, leading to changes in the composition of gut microbiota.

Protein

Proteases and peptidases hydrolyze food proteins to produce amino acids, peptides, and tripeptides. With the help of the gut microbiota, these products are absorbed into enterocytes in the small intestine (J. Zhao et al., 2018). Gut microbiota is essential for recycling dietary proteins and nitrogen in the small intestine. Ammonia, SCFA, hydrogen, and sulfate are the end products of the metabolism of undigested amino acid-fermenting bacteria (J. Zhao et al., 2018). Plant-based proteins increase insulin sensitivity and improve glycemic control in T2DM patients with. Additionally, increasing plant-based protein intake is associated with lower odds of T2DM and lower odds of T2DM and its comorbidities (Gutierrez-Mariscal et al., 2023).

Plant-based proteins increase insulin sensitivity and improve glycemic control in T2DM patients with. Additionally, increasing plant- based protein intake is associated with lower odds of T2DM and lower odds of T2DM and its comorbidities (Gutierrez-Mariscal et al., 2023). Plant-based proteins have beneficial effects, whereas animal proteins, such as red meat and processed meat, have the opposite

effects on gut microbiota and T2DM (Hamamah et al., 2024). Compared with animal proteins, vegetable proteins can increase the abundance of *Bifidobacterium* and *Lactobacillus* (Rinninella et al., 2019).

Fat

Similar to protein, a high intake of animal fats has detrimental effects on vegetable fats. High intake of vegetable fat is associated with a significantly reduced risk of developing T2DM (Hamamah et al., 2024). A meta-analysis reported a high intake of vegetable fats, especially α-linolenic acid from plants and polyunsaturated fatty acids, which is inversely correlated with the incidence of T2DM (Neuenschwander et al., 2020). Intervention with dairy products or yogurt for three weeks can increase the growth of *Lactobacillus* and *Bifidobacterium* (Aslam et al., 2020). The four-week intervention of yogurt-based drinks, such as kefir, can increase the abundance of *Lactobacillus* ((Yilmaz et al., 2020); Butler et al., 2020)).

Consumption of milk and its derivative products can trigger significant changes in the composition of the gut microbiota, thereby reducing the adverse effects of T2DM. Omega-3 polyunsaturated fatty acids (omega-3 PUFAs) obtained from the diet are partially metabolized by anaerobic bacteria such as *Bifidobacteri*a and *Lactobacilli* (Fu et al., 2021). Omega-3 PUFAs supplementation (4 g daily) in healthy middle-aged volunteers increased the abundance of *Bifidobacterium* and *Lactobacillus.* However, it did not affect gut microbiota diversity, and there were no changes in taxa at the phylum level (Watson et al., 2018).

Fiber

SCFA-producing bacteria can increase owing to high fiber intake, which can significantly increase butyric acid levels, such that GLP-1 increases, HbA1c decreases, and glucose homeostasis increases. Changes in the gut microbiota in T2DM can improve glucose homeostasis through the intervention of a high-fiber diet (L. Zhao et al., 2018). Low dietary fiber intake is associated with dysbiosis (Kondo et al., 2021). A high intake of dietary fiber and omega-3 PUFAs may improve the composition of the gut microbiota and reduce the risk of hyperglycemia (Riccio & Rossano, 2018).

High-fiber diets such as the Mediterranean diet (MD) are known to cause an increase in the relative abundance of *Lactobacillus* and *Bifidobacterium* as the main SCFA-producing genera, which plays an essential role in glucose homeostasis (Meslier et al., 2020). Low-fiber diets have the opposite effects, such as decreased gut microbiota diversity, decreased butyrate production, worsened insulin resistance, and increased susceptibility to infection (Leshem et al., 2020). Dietary fiber can increase *Bifidobacterium spp*., and other SCFA-related genera can increase GLP-1 secretion, reduce HbA1c levels, and reduce harmful bacterial metabolites such as indole and hydrogen sulfide (Riccio & Rossano, 2018).

Most studies have shown that components in cereals can reduce the risk of disease ((Li et al., 2023); Iversen et al., 2022)). Individuals who consume high amounts of whole-grain cereals, barley, oats, and rye, and limit their intake of refined grains or cereals with refined sugar and artificial sweeteners show increased blood glucose levels and insulin sensitivity (Iversen et al., 2022).

Individuals with a high intake of tree nuts and almonds show increased HbA1 levels, which are markers of inflammation and blood glucose (Hou et al., 2018). However, the impact of almonds on HbA1c levels requires further investigation. Increases in *Faecalibacterium*, *Clostridium*, *Dialister*, and *Roseburia* and decreases in *Ruminococcus*, *wanted*, *Oscillopira*, and *Bifidobacterium* have been found in individuals with a high intake of nuts (Holscher et al., 2018).

Table 1. Representative bacterial species and their underlying anti-diabetic effects.

Bacterial Genus/Species	Subjects	Methods	Drugs	Mode of Administration	Number of Strain Tested/Concentration/Genes	Results	References
Lactobacillus reuteri	86 individu with T2DM	Double-blinded, randomized for 9 months	Individuals taking anti-diabetic drugs, and antibiotics,	Orally (prebiotic supplements)	ADR-1 dan ADR-3 (4×10^9 CFU of ADR-1 or 2×10^{10} cells of ADR-3 every day)	- Significant reductions HbA1c in participants in the live ADR-1 consumption group. - There was no significant difference in the HbA1c serum level among participants who	(Hsieh et al., 2018)

Bacterial Genus/Species	Subjects	Methods	Drugs	Mode of Administration	Number of Strain Tested/Concentration/Genes	Results	References
			or other probiotic products for >4 weeks			consumed heat-killed ADR-3. *L. reuteri* or *Bifidobacterium spp*. were significantly increased in the ADR-1 and ADR-3 consumption groups, after 6 months of intake. - A significant reduction in HbA1c was observed in the ADR-1 and ADR-3 consumption participants who displayed at least an 8-fold increase in fecal *L. reuteri*. - A significantly positive correlation between *Bifidobacterium spp*. and *Lactobacillus spp*. in participants with increased levels of fecal *L. reuteri*. - *Lactobacillus spp*. level displayed a positive correlation with *Bifidobacterium spp*.	
Bifidobacterium, *Lactobacillus*, *Lactococcus*, *Propionibacterium*, *Acetobacter*	53 patients with T2DM	Single-center double blind, randomized clinical trial (8 weeks)	Metformin, insulin on a stabilized dose for at least 3 months	Orally (prebiotic supplements)	*Lactobacillus* + *Lactococcus* (6 x 10^{10} CFU/g), *Bifidobacterium* (1 x 10^{10} CFU/g), *Propionibacterium* (3 x 10^{10} CFU/g), *Acetobacter* (1 x 10^{6} CFU/g)	- HbA1c insignificant decreased in placebo and probiotics groups. - In probiotics responders after supplementation a siginificant reduction in HbA1c.	(Kobyliak et al., 2018)
Lactobacillus, *Bifidobacterium* and *Streptococcus*	68 patients with T2DM	The randomized double blind clinical trial (6 weeks)	Drugs prescribed by doctors	Orally (prebiotic supplements)	*Lactobacillus acidophilus* (2 x 10^{9} CFU), *Lactobacillus casei* (7 x 10^{9} CFU), *Lactobacillus rhamnosus* (1,5 x 10^{9} CFU), *Lactobacillus bulgaricus* (2 x 10^{8} CFU), *Bifidobacterium breve* (3 x 10^{10} CFU), *Bifidobacterium longum* (7 x 10^{9} CFU), *Streptococcus thermophilus* (1,5 x 10^{9} CFU)	- Significant decrease and increase in the level of fasting plasma blood in probiotic group. - No significant alterations were observed for within and between group comparasons in the level of insulin and insulin resistance.	(Razmpoosh et al., 2019)
Lactobacillus plantarum, Bifidobacterium, *Prevotella*	11 non-T2D women and 11 women with T2D	Cohort study	Metformin, glimepiride, and nontherapeutic	NA	The 16S rRNA gene	- Fasting blood sugar and HbA1c were positively associated with age, duration of T2DM. - Fasting blood sugar was also slightly negatively associated with *Prevotella*, meanwhile HbA1c with *Bifidobacterium*.	(Rustanti et al., 2023)

Bacterial Genus/Species	Subjects	Methods	Drugs	Mode of Administration	Number of Strain Tested/Concentration/Genes	Results	References
Firmicutes, *Bacteroides*, and *Bifidobacterium*	15 individu with T2DM, 15 individu with prediabetes, 15 individu with obese dan 15 individu lean	A cross-sectional study	NA	NA	The 16S rRNA gene	- The levels of Bifidobacterium in fecal microbiota were significantly higher in T2DM compared with lean, prediabetic, and obese. - The levels of Bifidobacterium in urinary microbiota were decreased in obese, prediabetic, and T2DM subjects as controls.	(Düzgün et al., 2023)
Bifidobacterium spp., Order *Lactobacillales, Bacteroides spp.„ Prevotella spp.*	59 patients with T2DM	A cross-sectional study	Stable doses of medication for at least 1 month	NA	The 16S rDNA	- The level of bacteria of the order *Lactobacillales* was significantly higher in the patients with T2DM than that in the control subjects. - The level of *Bifidobacterium spp*. was significantly higher in the patients with T2DM than that in the control subjects - The patients with T2DM had significantly lower levels of *Bacteroides spp.* than those in the control subjects.	(Adachi et al., 2019)
B. vulgatus, *B. rodentium*, *P. copri*, *E. coli*, *S. aureus*, *B. subtilis*, *Lactobacillus acidophilus*	20 diabetic patients	A cross-sectional study	Treatment with insulin or oral hypoglycemic agents	NA	The blood agar, the nutrient agar and the bacterial agar diffusion	- The relative abundance of *Lactobacillus acidophilus* decreased significantly in patients with T2DM. - The relative abundance of *Lactobacillus acidophilus* was positively correlated with fasting blood sugar and HbA1c level.	(Bokhamada & Elmasli, 2021)
Bifidobacterium, *Lactobacillus*, *Blautia*, *Phascolarctobacterium*	114 without diabetes, 17 with type 1 diabetes, 383 with T2DM, and 8 with other types of diabetes	A cross-sectional study	The medications used for diabetes (α-glucosidase inhibitors and glinide medications)	NA	The 16S rRNA gene	- T2DM had higher percentages of the *Bifidobacterium* and *Lactobacillus* genera and lower percentages of the *Blautia* and *Phascolarctobacterium* genera. - Higher proportions of patients with T2DM in the red group used *α-glucosidase* inhibitors and glinide medications.	(Kondo et al., 2021)
Lactobacillus acidophilus, Lactobacillus reuteri, Lactobacillus fermentum, Lactobacillus plantarum,	100 patients with T2DM	Experimental study	NA	NA	The standard pour plate method	- The bacterial counts of the *L. acidophilus*, *L plantarum* and *L. reuteri* subgroups of *Lactobacillus sp* were significantly lower among patients with T2DM and obesity than in controls.	(Suceveanu et al., 2018)

Bacterial Genus/Species	Subjects	Methods	Drugs	Mode of Administration	Number of Strain Tested/Concentration/Genes	Results	References
Lactobacillus salivaricus and Lactobacillus johnsonii Bifidobacterium longum, Bifidobacterium adolescentis, Bifidobacterium bifidum, Bifidobacterium infantis, Bifidobacterium breve and Bifidobacterium choerinum						- The counting of *Bifidobacterium spp.* revealed a higher presence of *B. bifidum* in controls than in obese or T2DM. - Low counts of *L. acidophilus* and *L. reuteri* were positively correlated with the increased levels of HbA1c no matter of diet, age, ethnicity or metabolic disorders history.	

Conclusion

Gut microbiota has recently been frequently used in diabetes mellitus research because of its essential role in the pathophysiology of T2DM. There is a lack of data in the literature discussing the correlation between *Lactobacillus* and *Bifidobacterium* and diabetes mellitus in humans. To improve complications and reduce biochemical parameters in T2DM, *Lactobacillus* and *Bifidobacterium* require more research regarding standardization in protocols followed, models used, and interpretation of results.

Nutrients in food majorly affect host physiology through the mediation of the gut microbiota and metabolism. These interactions involve the intestinal and immune systems. Various descriptive relationships have been found between nutrients and gut microbes. However, their relevance must be further explored through mechanistic studies that can encompass the complexity of the subject and translate results from animal models to humans. Given the enormous variability of gut microbiota among individuals, it is necessary to gradually move beyond standard dietary approaches to personalized nutrient intake tailored to the host microbiota system.

Research to explore and understand the interaction between diet and gut microbiota in T2DM patients is still limited. Therefore, it is recommended to conduct further research on the development of strategies and identification of effective dietary intervention targets that can improve the function of gut microbiota to prevent and control T2DM.

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