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Probiotic Consumption, Fatigue, and Glycemic Control in Patients with Type 2 Diabetes: A Cross-Sectional Study

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ABSTRACT

Introduction: Probiotics have recently been included in nutritional recommendations for achieving glycemic control in diabetic patients. Probiotic foods are not standardized, and their effectiveness can vary significantly between products and species. Therefore, the results of this study may not be generalizable to all probiotics consumed. This study aimed to determine the consumption of probiotics by type 2 diabetes patients and the relationship between probiotic consumption and their fatigue levels and glycemic control.

Methods: This study was conducted in a university hospital in the Central Anatolian Region of Turkey. A total of 235 diabetic patients were included in the cross-sectional study. Data were collected using a patient information form, a self-report probiotic consumption information form, and the Visual Analog Scale for Fatigue.

Results: The majority of the patients (83.4%) consumed probiotic products, and the most frequently consumed probiotic products by them were yogurt (80%), ayran (67.7%), and pickles (57.9%). The fatigue levels of probiotic-consuming and non-consuming patients were similar ($p > 0.05$), but the energy levels of probiotic-consuming patients were higher ($p<0.05$). The fasting blood glucose and HbA1c levels of the patients taking probiotics were low, but this difference was insignificant ($p>0.05$).

Conclusion: Since probiotics are beneficial to diabetes patients, it is essential to provide information about them and support the use of probiotics per expert recommendations.

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Introduction

The prevalence of type 2 diabetes is increasing worldwide, and it is a complex disease influenced by genetics and the environment (1). A lack of effective management of type 2 diabetes can lead to both short- and long-term complications (2). In recent years, the importance of gut microbiota has been examined to prevent the development of type 2 diabetes, and much attention has been drawn to the consumption of probiotics in maintaining a healthy state (3).

Probiotics contain living microorganisms called friendly or good bacteria that benefit health when taken in sufficient quantities (1,4). Probiotics have high numbers of microorganisms with no pathogenic or toxic properties. Probiotics are resistant to food additives and processing conditions, maintain their viability in foods during storage and usage, and keep their vitality in the intestines and metabolic activity in the body. In addition, probiotics can colonize the gastrointestinal tract by attaching to the intestinal epithelium and inhibit the attachment of pathogenic bacteria to the host by secreting antimicrobial substances (5). In addition to regulating intestinal flora (6, 7), they have many health benefits, including immune regulation and inflammatory functions and the production of short-chain fatty acids by the fermentation of dietary fiber. Probiotics regulate the secretion of glucose and fat metabolism, modulate intestinal permeability and intestinal hormones, increase absorption of minerals, and improve gastrointestinal functions (8,9). Additionally, probiotics can enhance the antioxidant defense, regulate blood glucose by improving insulin sensitivity and pancreatic β-cell processes, balance the blood lipid profile, and control weight, especially in diabetic patients (1,3). Meta-analyses have shown that probiotic consumption

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facilitates diabetes management and reduces glycosylated hemoglobin (HbA1c), fasting blood glucose (FBG), and insulin resistance (10-13).
Probiotics have been consumed for centuries in different cultures through different foods (14). A wide range of milk and products, including fermented milk, yogurt, and kefir, as well as capsules and powders, contain these nutrients (1). Additionally, some fermented herbal products, pickles, cabbage, turnip, boza, kumiss, fermented meat, soy-based products, cereals, nuts, fruits, legumes, and various non-dairy fruit juices are also among probiotic food items (15,16). Consumption of probiotics has recently gained significant attention because of reducing markers of oxidative stress, inflammatory factors, and metabolic parameters (17). Probiotics also have a variety of other benefits, such as increasing glutathione (GSH) levels, scavenging hydroxyl and superoxide radicals, and reducing interleukin-6 (IL6) production. There is little information about how probiotics affect metabolic control in individuals with diabetes. However, studies have mainly been conducted on animal models and non-diabetic patients (18). Yadav et al. showed that lactobacillus acidophilus and L. casei containing high fructose-fed rats reduced glucose intolerance, hyperglycemia, hyperinsulinemia, dyslipidemia, and oxidative oxidative stress (19). In another study, consumption of L. plantarum (299v) lowered systolic blood pressure, serum insulin levels, leptin, fibrinogen, F2-isoprostanes, and IL-6 (20).
There have been no studies showing a superiority between probiotics in different amounts and products, to our knowledge (21).
Fatigue is one of the most common symptoms that develop due to physiological and psychological causes in diabetic patients (22), which is a persistent and disturbing complaint in patients with type 2 diabetes. In addition, fatigue can adversely affect the well-being of patients with diabetes, their activities of daily living, family, work, and social lives (23). Physiopathological changes occur at the cellular level due to long-term hyperglycemia in diabetes caused by poor metabolic control. The first clinical sign of these changes is the emergence of fatigue symptoms with a severe decrease in patients' exercise capacity (20-24). Many causes of fatigue can be observed in patients with diabetes, including episodes of hypoglycemia, difficulties in self-care, complications of diabetes, endocrinopathy, and infection (25). Therefore, controlling hyperglycemia in diabetic patients can effectively alleviate fatigue (22). At the same time, it was emphasized that probiotics can be an alternative treatment for chronic fatigue (26).
Literature review showed that studies examine the relationship between probiotic consumption and glycemic indicators in type 2 diabetes patients (27-33), but the relationship between probiotic consumption and fatigue levels has not been examined. Probiotics, which support the immune system, may have fatigue-reducing properties. Probiotic use and fatigue may contribute to science by guiding healthcare professionals in dealing with fatigue, a common symptom of type 2 diabetes.

Methods

Objective and Design

This cross-sectional study was conducted to determine the consumption of probiotics by diabetic patients and the relationship between the probiotic consumption of these patients and their fatigue levels and glycemic control status.

Population and Sample

The study population consisted of 1220 individuals who presented to the endocrinology outpatient clinic of a university hospital between January and June 2022 and had been diagnosed with diabetes for at least one year. The minimum number of patients to be included in the sample was found to be 215 using the sampling formula for a known population (Nt^2pq / (d^2(N-1) + t^2pq)). In this context, 235 patients who met the inclusion criteria were included. The inclusion criteria were being literate, 18 years old and above, having type 2 diabetes, being independent in self-care, and agreeing to participate in the study. The exclusion criteria included having a verbal communication disorder, being diagnosed with an eating disorder, being pregnant, taking regular probiotic supplements, using insulin, cholesterol, or diuretic drugs, and having a gastrointestinal disease (such as Crohn's disease ulcerative colitis).

Data Collection Tools

The data were collected using a patient information form, a self-report probiotic consumption information form, and the Visual Analog Scale for Fatigue (VAS-F).
Patient Information Form: The form consisted of three parts with questions on the

sociodemographic characteristics of the patients (age, sex, marital status, education, employment), disease characteristics (e.g., duration of disease, type of treatment, regular use of drugs) in the second section, and metabolic parameters (e.g., FBG, HbA1C, blood pressure, total cholesterol, triglyceride).

Probiotic Consumption Information Form: The form was created to determine the probiotic consumption characteristics of the patients and contains questions on parameters such as whether the patients knew about probiotics, the types of probiotics they consumed, the frequency of their consumption, and the amount of their consumption. As a pilot implementation, the form was administered to 20 individuals with diabetes before starting the study and evaluated in terms of intelligibility.

Visual Analog Scale for Fatigue: VAS-F was developed by Lee et al. to measure fatigue and energy levels. The Turkish validity and reliability study of the scale was carried out by Yurtsever and Beduk (34,35). The fatigue and energy dimensions of this scale are composed of 18 items. VAS-F consists of 10 cm-long horizontal lines with positive statements at one end and negative statements at the other. Fatigue items progress from positive to negative, while energy items progress in the opposite direction. The lowest and highest scores in the fatigue dimension are 0 and 130. There is a 0 to 50 score range for the energy dimension. High scores in the fatigue dimension and low in the energy dimension indicate higher fatigue severity (31-35). In this study, Cronbach's alpha internal consistency coefficient of the scale was found to be 0.86 for the fatigue dimension and 0.93 for the energy dimension.

Data Collection

The researchers obtained the data by interviewing patients in an allocated interview room. Researchers informed the patients verbally about the study and administered the data collection forms to those who consented verbally and in writing. Approximately 20 minutes were spent applying the data collection forms to each patient. Additionally, the metabolic parameters of the patients, including routine follow-up results, were obtained from their laboratory result papers after the physician ordered the measurements at the time of their visit to the outpatient clinic.

Table 1. Disease-Related Characteristics of Patients

Characteristics	n	%
Disease duration (years) (Mean±SD)	8.06±5.52	
Form of treatment		
Oral antidiabetic therapy	148	63.0
Insulin therapy	48	20.4
Oral antidiabetic and insulin therapy	39	16.6
Treatment is administered regularly		
Yes	141	60.0
Sometimes	66	28.1
No	28	11.9
Does regular exercise (at least three times a week and for at least 20 minutes)		
Yes	201	89.3
No	24	10.7
Has received education about the disease from a doctor or nurse		
Yes	140	59.6
No	95	40.4
Has other chronic diseases		
Yes	113	48.1
No	122	51.9
Has diabetes-related complications		
Yes	53	22.6
No	182	77.4
Frequency of hospitalization due to diabetes or complications in the past year		
Once	146	62.1
Twice	59	25.1
Three or more times	30	12.8
General health assessment		
Good	65	27.7
Medium	152	64.7
Bad	18	7.6

Data Analyses

The data were analyzed using SPSS software version 22.0. Students' t-tests were used in the analysis of the data in addition to descriptive statistical methods to determine the relationship between probiotic consumption, metabolic control, and fatigue levels. Furthermore, multiple linear regression analysis was used to determine the explanatory effect of some variables for fatigue. Statistical significance was evaluated at a threshold of $p<0.05$.

Ethical Aspects of the Study

Before starting the study, written permission was obtained from the Sivas Cumhuriyet University Non-Invasive Clinical Research Ethics Committee (Decision No: 2020-02/10) and the institution where the study was conducted. Additionally, the purpose of the study was explained to diabetic patients, and written and verbal consent was obtained from the patients who agreed to participate. The patients were informed that the data they would provide would only be used within the scope of the study, and their confidentiality would be ensured.

Table 2. Distribution of Metabolic Parameters of Patients

Characteristics	Mean ± SD	n	%
Fasting blood glucose (mg/dl)	168.90 ± 98.50		
<100		21	8.9
≥100		214	91.1
HbA1C (%)	7.35 ± 1.51		
<7.0		119	50.6
≥7.0		116	49.4
Systolic blood pressure (mmHg)	127.18 ± 17.92		
≤140		214	91.1
>140		21	8.9
Diastolic blood pressure (mmHg)	75.91 ± 10.14		
≤80		206	87.7
>80		29	12.3
Total cholesterol (mg/dl)	216.71 ± 59.14		
<200		72	30.6
≥200		163	69.4
Low-density lipoprotein (mg/dl)	188.36 ± 102.68		
<100		168	71.5
≥100		67	28.5
High-density lipoprotein (mg/dl)	56.71 ± 22.09		
>40 in men, >50 in women		24	1.7
<40 in men, <50 in women		231	98.3
Triglyceride (mg/dl)	199.85 ± 78.42		
<150		64	27.2
≥150		171	72.8

Results

The mean age of the diabetes patients participating in the study was 52.87±11.85 years, and 84.7% of them were under 65 years of age. While 53.2% of the patients were male, 80% were married, 33.6% were primary school graduates, 62.6% did not work in any job, and 8.9% lived alone. Only 10.7% of the patients exercised regularly. About 27.2% of the patients were current smokers, and 5.1% consumed alcoholic beverages. Moreover, 42.1% of the patients were overweight, and 37.4% were obese. Table 1 shows the disease-related characteristics of the patients.

The metabolic parameters of the patients are shown in Table 2, and it was determined that 37.9% of them had glycemic control above the target value.

According to self-reports, 19.6% of the patients had two meals per day, and 35.3% had four or more meals per day. Additionally, 28.9% said they skipped meals often, while 54.5% said they occasionally. Further, 70.9% of the patients mostly skipped lunch. Nutritional supplements other than drugs were used by 6.4% of the patients to treat diabetes. The frequently stated supplements included vitamin D, vitamin B12, and vitamin C supplements. Furthermore, 18.7% of the patients reported consuming less than one liter of fluids per day, and 50.6% stated that they consumed one or two liters of fluids. Table 3 shows some information on the probiotic consumption characteristics of the patients.

Table 3. Probiotic Consumption Characteristics of Patients

Characteristics	n	%
Knows about probiotics		
Yes	109	46.4
No	126	53.6
Consumes probiotics		
Yes	196	83.4
No	39	16.6
Type of probiotic food consumed *		
Yogurt	188	80.0
Ayran	159	67.7
Pickles	136	57.9
Olives	78	33.2
Kefir	52	22.1
Other fermented dairy products	43	18.3
Turnip	36	15.3
Tarhana	35	14.9
Goat cheese	23	9.8
Boza	3	1.3
Probiotic consumption frequency		
Once a day	117	49.8
Two to three times a day	63	26.8
Once a week	51	21.7
Rarely	4	1.7
Quantity of probiotics consumed at one time		
Half a bowl	57	24.3
A bowl	178	75.7
Feels benefit in diabetes-related symptoms related to probiotic consumption		
Yes	97	41.3
No	138	58.7
Feels benefits of probiotic in health conditions such as…		
Constipation	119	50.6
Diarrhea	21	8.8
Inflammatory bowel disease	16	6.8
Hyperlipidemia	16	6.8

* Multiple choices were allowed.

The patients' mean VAS-F fatigue dimension score was 65.16±17.37, while their mean VAS-F energy dimension score was 25.71±10.74. According to these scores, the patients had moderate levels of overall fatigue.

There was no significant difference between the fatigue levels of patients who consumed probiotics and those who did not consume probiotics ($p>0.05$), but there was a statistically significant difference between energy levels ($p<0.05$). Accordingly, A higher energy level was observed in patients who consumed probiotics.

The fasting blood glucose and HbA1c levels of the patients who were taking probiotics were low. Still, the difference between the HbA1c values of patients who consumed probiotics and those who did not was insignificant. Similarly, the metabolic indicators of the patients in these two groups did not differ significantly ($p>0.05$) (Table 4).

The multiple regression analysis determined that HbA1c was a determinant of the patient's fatigue levels, and age was a determinant of their energy levels ($p<0.05$). However, probiotic consumption status and the frequency of probiotic consumption were not variables that were significantly associated with fatigue or energy levels (p>0.05) (Table 5).

Table 4. Comparison of Fatigue Levels and Metabolic Parameters of Patients Taking and Not Taking Probiotics

	Using probiotics (n=196; %83.4)	Don't using probiotics (n=39; %16.6)	Test
	Mean ± SD	Mean ± SD	
Visual Analogue Scale for Fatigue			
Fatigue	64.85 ± 17.24	66.71 ± 18.15	t = -0.612 *P*= .541
Energy	26.41 ± 10.83	22.23±9.66	t = 2.239 *P* = .026*
Metabolic parameters			
Fasting blood glucose (mg/dl)	160.92 ± 77.26	209.00 ± 164.76	t = -2.824 *P* = .005**
HbA1C (%)	7.30 ± 1.43	7.59 ± 1.86	t = -1.104 *P* = .271
Systolic blood pressure (mmHg)	127.32 ± 18.12	126.46 ± 17.10	t = 0.275 *P* = .784
Diastolic blood pressure (mmHg)	76.32 ± 9.91	73.84 ± 11.14	t = 1.397 *P* = .164
Total cholesterol (mg/dl)	214.90 ± 60.82	225.84 ± 49.53	t = -1.055 *P* = .292
Low-density lipoprotein (mg/dl)	56.84 ± 23.74	56.07 ± 10.55	t = 0.198 *P* = .843
High-density lipoprotein (mg/dl)	187.70 ± 104.17	191.66 ± 96.09	t = -0.219 *P* = .827
Triglyceride (mg/dl)	202.35 ± 79.97	187.30 ± 69.68	t = 1.095 *P* = .275

* *P* < .05; ** *P* < .01

Table 5. Stepwise Multiple Regression Analysis of Predictors of Fatigue and Energy Levels

Variables	Fatigue					Energy				
	B	SE	ß	t	*P*	B	SE	ß	t	*P*
Year	0.098	0.103	0.067	0.949	.344	-0.186	0.063	-0.205	-2.979	.003**
Disease duration	0.078	0.217	0.025	0.361	.718	0.039	0.131	0.020	0.297	.766
HbA1C	1.641	0.753	0.143	2.179	.030*	-0.439	0.457	-0.062	-0.962	.337
Using probiotics	0.488	3.245	0.010	0.150	.881	-2.226	1.968	-0.077	-1.131	.259
Frequency of using probiotics	0.230	1.307	0.012	0.176	.861	-0.780	0.793	-0.066	-0.984	.326
	R = 0.164, R^2 = 0.027, F = 1.259, *P* = .283					R = 0.253, R^2 = 0.064, F = 3.124, *P* = .010*				

* *P* < .05; ** *P* < .01

Discussion

Today, the consumption of nutritional supplements has increased in parallel with the awareness of healthy nutrition (15). Probiotics have a significant role in the general health of individuals and can be used as anti-diabetic agents (30). In this study, the consumption of probiotics in patients with type 2 diabetes was examined, and its effects on the fatigue levels and glycemic control statuses of these patients were evaluated.

Considering the beneficial effects of probiotics on health, individuals need to know about probiotics and their consumption (15). In this study, only about half of the patients knew about probiotics. In other studies conducted on adults in Turkey, the rates of participants who knew about probiotics varied between 46.8 and 66.5% (36-38). The low level of knowledge about probiotics and the lack of necessary guidance by doctors and/or dietitians can be cited as the reasons for the low consumption of probiotics and probiotic-added food/food supplements among the patients participating in this study (16). In a study conducted with hospitalized patients in the US, 43% of the participants stated that they knew the term probiotic (39). The result of this study, which was similar to those in the relevant literature, showed that patients with type 2 diabetes do not have sufficient knowledge about the use of probiotics. In this context, it may be useful to inform patients with type 2 diabetes about including probiotics in their diet.

Diabetics should include whole grain products and legumes since they are low in glycemic index and regulate blood glucose more effectively than yogurt and milk (40). These foods with probiotic properties increase satiety and reduce hunger (41). The results of this study demonstrated that the majority of the patients consumed probiotics, and they mostly consumed yogurt, ayran, and pickles. Another study on diabetic patients showed that the most frequently consumed probiotic foods were yogurt, olives, and ayran. Moreover, the same study revealed that goat cheese, kefir, boza, tarhana, and pickles were the least frequently consumed probiotic foods (16). An analysis of hospitalized patients found that yogurt and cereals were the most commonly consumed probiotic products (39). Food consumption in Turkey varies according to geographical and cultural characteristics. The fact that this study was conducted in the Central Anatolian Region of Turkey may have influenced the patients' food preferences. It may be essential to create a nutrition program to support the desirable use of probiotic products in individuals with type 2 diabetes and teach this program to patients.

This study determined that the fasting blood glucose and HbA1c levels of the patients who were consuming probiotics were low. However, the HbA1c levels of the patients who consumed probiotics and those who did not were not significantly different. The literature shows that the FBG and HbA1c values of groups taking probiotics are reduced considerably compared to the control groups in randomized controlled studies (27-33). According to a meta-analysis, probiotics reduced FBG to a greater extent in the placebo/no intervention group, with a mean difference of 12.99 mg/dl in the short term and 2.99 mg/dl in the long term (13). Another meta-analysis study showed that the consumption of probiotics can reduce HbA1c, FBG, and insulin resistance in patients with type 2 diabetes (12). Similar to the findings of this study, no significant relationship was found between the consumption of probiotic foods and HbA1c in diabetic patients in a study conducted in Turkey (16). This finding, inconsistent with the literature, may have resulted from the number of different probiotics consumed by the patients and the frequency of their consumption. Probiotics may significantly impact glucose regulation when studies are conducted based on the amount of probiotics consumed.

Since probiotics interact with intestinal bacteria when digested, they positively affect physical and psychological health. Probiotics reduce cortisol, also known as the stress hormone, and increase the secretion of oxytocin, which is closely related to positive physical and psychological effects in humans (42). Fatigue levels of the patients who were consuming probiotics and those who were not did not differ significantly. On the other hand, the energy levels of patients consuming probiotics were higher. However, the consumption of probiotics and frequency did not significantly affect fatigue and energy levels. There are no similar studies conducted with diabetic patients in the literature. The information in the literature highlights that the consumption of probiotics positively affects chronic fatigue patients (43). A systematic review of probiotic consumption in athletes emphasized that probiotics improved the immune system and exercise performance, regulated immunomodulation, and reduced fatigue (14). A randomized controlled study on the effects of probiotics on mood found a significant decrease in the dimensions of unhappiness, irritability, and fatigue in the intervention group (44). This study showed that consuming probiotics helped type 2 diabetes patients feel energetic. In this context, probiotic products can be added to the diet programs of patients with type 2 diabetes, in line with the recommendations of dieticians.

Limitations

This is the only study examining the relationships between probiotic consumption in type 2 diabetes patients in Turkey and the fatigue levels and glycemic control statuses of these patients. Additionally, the results offer a different perspective on ensuring glycemic control in parallel with the increasing incidence of diabetes. However, this study had some limitations. The most important limitation of the study was that it was conducted with diabetic patients who presented to one institution at a particular time. Therefore, the findings cannot be generalized. The second limitation of the study was that the information collected on probiotic consumption and fatigue levels was based on the self-reports of the patients who took part in the study. Another limitation of the study was that the relationship between the variables of probiotic consumption fatigue and glycemic control was only examined due to its cross-sectional design. Additionally, evaluations were made based on the amounts of the probiotic products consumed by the patients based on their self-reports, and the exact quantities of the products they consumed were not evaluated within the scope of the study. Longitudinal studies can provide more information on statistical relationships among these variables.

Conclusion

Based on the results, the majority of patients with diabetes consumed probiotic products. Although the energy levels of the patients taking probiotics were higher, glycemic control status and fatigue levels did not differ between the patients' consuming probiotics and those not consuming probiotics. There was no statistically significant difference in fatigue severity levels between the probiotic-consuming and non-consuming patients, but the finding that probiotic consumption was associated with lower fatigue severity levels suggests that probiotics may have benefits. As part of nutrition education, probiotics can be discussed with patients, and their consumption can be encouraged under expert recommendations. Furthermore, long-term case-control studies examining the impact of probiotics on fatigue levels in diabetic patients will shed light on the literature and diabetes management.

References

1. Celebi F, Sanlier N. Probiotics, prebiotics and diabetes mellitus. Clinical Medicine Journal of Family Medicine. 2019; 11(2):63-70.
2. Clinical Practice Guideline for Diagnosis, Treatment and Follow-up of Diabetes Mellitus and Its Complications. The Socıety of Endocrınology and Metabolism of Turkey (SEMT) English Version of the 12th Edition, Ankara. 2019.
3. Altun HK, Yıldız EA. Relationship between prebiotics-probiotics and diabetes mellitus. Turkish Journal of Life Sciences. 2017; 2(1):149-56.
4. Hill C, Guarner F, Reid G, Gibson GR, Merenstein DJ, Pot B, Morelli L, Canani RB, Flint HJ, Salminen S, Calder PC, Sanders ME. Expert consensus document. The International Scientific Association for probiotics and prebiotics consensus statement on the scope and appropriate use of the term probiotic. Nat Rev Gastroenterol Hepatol. 2014; 11(8):506-14.
5. Kamarli H. Pre- probiotics and diabetes. Bes Diy Derg. 2019; 47(Special Issue):92-101.
6. Panwar H, Rashmi HM, Batish VK, Grover S. Probiotics as potential biotherapeutics in the management of type 2 diabetes - prospects and perspectives. Diabetes Metab Res Rev. 2013; 29(2):103-12.
7. Idzior-Waluś B, Waluś-Miarka, M. Is now the time for probiotics in diabetes management?. Polskie Archiwum Medycyny Wewnetrznej. 2015; 125.
8. Kellow NJ, Coughlan MT, Reid CM. Metabolic benefits of dietary prebiotics in human subjects: a systematic review of randomised controlled trials. Br J Nutr. 2014;111(7):1147-61.
9. Rabiee MR, Babajafari S. Probiotics and diabetes: A review. Int J Nutr Sci. 2018; 3(2):73-81.
10. Wang X, Juan QF, He YW, Zhuang L, Fang YY, Wang YH. Multiple effects of probiotics on different types of diabetes: A systematic review and meta-analysis of randomized, placebo controlled trials. J Pediatr Endocrinol Metab. 2017; 30:611-22.
11. Sun J, Buys NJ. Glucose- and glycaemic factor-lowering effects of probiotics on diabetes: A meta-analysis of randomised placebo-controlled trials. Br J Nutr. 2016; 115:1167-77.
12. Tao YW, Gu YL, Mao XQ, Zhang L, Pei YF. Effects of probiotics on type II diabetes mellitus: a meta-analysis. J Transl Med. 2020; 18(1):30.
13. Rittiphairoj T, Pongpirul K, Janchot K, Mueller NT, Li T. Probiotics contribute to glycemic control in patients with type 2 diabetes mellitus: A systematic review and meta-analysis. Adv Nutr. 2021;12(3):722-34.
14. Imamlı H, Akca, F. Effects of probiotics supplementation on health and exercise performance. SPORMETRE Journal of Physical Education and Sports Sciences. 2018;16(2):196-208.
15. Ozgül AA, Bozat C, Seziş M, Badur Y, Özcan ÖÖ, Sarıyer ET, Çevik E, Çolak H, Karahan M. Determination of knowledge level and consumption status of individuals in working life about probiotic foods. Istanbul Gelisim University Journal of Health Sciences. 2020;12: 365-78.
16. Karahasan Mercan S. Relationship between frequency of urinary tract infection and probiotic product use in diabetics mellitus patients. 19 Mayis University, (Master Thesis), Samsun. 2019.
17. Ejtahed HS, Mohtadi-Nia J, Homayouni-Rad A, Niafar M, Asghari-Jafarabadi M, Mofid V. Probiotic yogurt improves antioxidant status in type 2 diabetic patients. Nutrition. 2012; 28: 539–43.
18. Asemi Z, Zare Z, Shakeri H, Sabihi SS, Esmaillzadeh A. Effect of multispecies probiotic supplements on metabolic profiles, hs-CRP, and oxidative stress in patients with type 2 diabetes. Ann Nutr Metab. 2013; 63(1-2):1-9.
19. Yadav H, Jain S, Sinha PR: Antidiabetic effect of probiotic dahi containing Lactobacillus acidophilus and Lactobacillus casei in high fructose fed rats. Nutrition. 2007; 23: 62–8.

20. Naruszewicz M, Johansson ML, ZapolskaDownar D, Bukowska H: Effect of Lactobacillus plantarum 299v on cardiovascular disease risk factors in smokers. Am J Clin Nutr. 2002; 76:1249–55
21. Shane-McWhorter L. Dietary supplements and probiotics for diabetes. Am J Nurs. 2012;112(7):47-53.
22. Kalra S, Sahay R. Diabetes fatigue syndrome. Diabetes Ther. 2018;9(4):1421-9.
23. Singh R, Teel C, Sabus C, McGinnis P, Kluding P. Fatigue in type 2 diabetes: Impact on quality of life and predictors. PLoS ONE. 2016; 11(11):e0165652.
24. Bayram D, Demir Y. Effect of fatigue and sleep quality on the quality of life in patient with type 2 diabetes. Turkiye Klinikleri J Nurs Sci. 2016; 8(2):131-9.
25. Hillson R. Fatigue and tiredness in diabetes. Practical Diabetes. 2020; 37(2):45-6.
26. Saglam A. Probiotics are a cure for many diseases. Journal of Food and Nutrition. 18(2): 36-9.
27. Ejtahed HS, Mohtadi-Nia J, Homayouni-Rad A, Niafar M, Asghari-Jafarabadi M, Mofid V. Probiotic yogurt improves antioxidant status in type 2 diabetic patients. Nutrition. 2012; 28(5):539-43.
28. Asemi Z, Zare Z, Shakeri H, Sabihi SS, Esmaillzadeh A. Effect of multispecies probiotic supplements on metabolic profiles, hs-CRP, and oxidative stress in patients with type 2 diabetes. Ann Nutr Metab. 2013; 63(1-2):1-9.
29. Mohamadshahi M, Veissi M, Haidari F, Shahbazian H, Kaydani GA, Mohammadi F. Effects of probiotic yogurt consumption on inflammatory biomarkers in patients with type 2 diabetes. Bioimpacts. 2014; 4(2):83-8.
30. Mahboobi S, Rahimi F, Jafarnejad S. Effects of prebiotic and synbiotic supplementation on glycaemia and lipid profile in type 2 diabetes: A meta-analysis of randomized controlled trials. Adv Pharm Bull. 2018; 8(4):565-74.
31. Sabico S, Al-Mashharawi A, Al-Daghri NM, Wani K, Amer OE, Hussain DS, Ahmed Ansari MG, Masoud MS, Alokail MS, McTernan PG. Effects of a 6-month multi-strain probiotics supplementation in endotoxemic, inflammatory and cardiometabolic status of T2DM patients: A randomized, double-blind, placebo-controlled trial. Clin Nutr. 2019;38(4):1561-9.
32. Kijmanawat A, Panburana P, Reutrakul S, Tangshewinsirikul C. Effects of probiotic supplements on insulin resistance in gestational diabetes mellitus: A double-blind randomized controlled trial. J Diabetes Investig. 2019;10(1):163-70.
33. Jiang H, Zhang Y, Xu D, Wang Q. Probiotics ameliorates glycemic control of patients with diabetic nephropathy: A randomized clinical study. J Clin Lab Anal. 2021;35(4):e23650.
34. Lee KA, Hicks G, Nino-Murcia G. Validity and reliability of a scale to assess fatigue. Psychiatry Res. 1991; 36(3):291-8.
35. Yurtsever S, Bedük T. Evaluation of fatigue on hemodialysis patients. Journal of Research and Development in Nursing. 2003; 2: 3-12
36. Aslan S, Kara R, Yaman H. Determining the Consumption Habits Related to Probiotic Products. Turk J Agric Food Sci Technol. 2019; 7(6):861-5.
37. Kağan DA, Özlü T, Yurttaş H. A research on the knowledge and consumption of probiotic foods in adults. Eur J Lipid Sci Technol. 2019; 17:556-63.
38. Pehlivan B. Evaluation frequency of adults probiotic food consumption and levels of knowledge. Scientific Journal of Complementary Medicine, Regulation and Neural Therapy .2020; 14(3):75-85.
39. Betz M, Uzueta A, Rasmussen H, Gregoire M, Vandrwall C, Witowich G. Knowledge, use and perceptions of probiotics and prebiotics in hospitalized patients. Nutrition and Health Sciences. 2015; 72: 261-6.
40. Mirmiran P, Bahadoran Z, Azizi F. Functional foods-based diet as a novel dietary approach for management of type 2 diabetes and its complications: A review. World J Diabetes. 2014;5:267-81.
41. Manzoor MS, Mustafa ZU. Prebiotics and their activity for the handling of diabetes: Literature review. J Food Sci Nutr The. 2019;5(1):7-10.
42. Cheng LH, Liu YW, Wu CC, Wang S, Tsai YC. Psychobiotics in mental health, neurodegenerative and neurodevelopmental disorders. J Food Drug Anal. 2019; 27(3):632-48.
43. Sharma A, Wakode S, Sharma S, Fayaz F. Role of Gut Microbiota and Probiotic in Chronic Fatigue Syndrome. Probiotic Research in Therapeutics. 2022;4: 211-36.
44. Marotta A, Sarno E, Del Casale A, Pane M, Mogna L, Amoruso A, Felis GE, Fiorio M. Effects of probiotics on cognitive reactivity, mood, and sleep quality. Front Psychiatry. 2019;10:164.