REVIEW

CYPRUS
JOURNAL OF MEDICAL SCIENCES

DOI: 10.4274/cjms.2023.2023-9
Cyprus J Med Sci 2023;8(4):241-249

A Review: Are Some Diet Models Beneficial or Harmful for Type II Diabetes Mellitus?

Taygun Dayı, Serpil Özsoy

Department of Nutrition and Dietetics, Near East University Faculty of Health Sciences, Nicosia, North Cyprus

Abstract

Diabetes mellitus (DM) is a chronic disease affecting millions worldwide. According to the current literature, type II DM is linked with some currently trending diet models such as high-protein, low-carbohydrate (CHO), ketogenic, gluten-free (GF), intermittent fasting (IF) nutrition models, the Mediterranean diet (MD), etc. The purpose of this review article was to shed light on the relationships between some currently trending diet models and type II DM, their potential effect mechanisms and any complications according to evidence from the current literature. High-protein, low-CHO, ketogenic, GF and IF nutrition models can potentially decrease inflammation and body weight, improve the lipid profile and gut microbiota, increase the secretion of incretin hormones and regulate immune responses and thus increase insulin sensitivity in tissues. However, these currently trending diet models may result in acute or chronic complications such as; hypoglycemia, fatigue, lethargy, nutrient deficiencies, acute abnormalities or other related chronic disorders. Some of these complications may be critical for life. Conversely, the MD has very important beneficial effects on the prevention of type II DM and there is no evidence in the literature which shows this diet model has any side effects. In conclusion, applying optimal nutritional principles is the most recommended nutritional approach in order to reduce risk and manage type II DM.

Keywords: Diabetes mellitus, high-protein/low-CHO diet, gluten-free diet, intermittent fasting, Mediterranean diet

INTRODUCTION

Diabetes mellitus (DM) is an endocrinopathy which is characterized by hyperglycemia which develops as a result of an insufficiency or lack of insulin production from the pancreas and peripheral insulin resistance (IR).[1] DM is a chronic disease with a rapidly increasing prevalence, and according to International Diabetes Federation's 2021 data, 537 million people between the ages of 20 and 79 have been diagnosed with type II DM. Approximately 10% of health expenditure is spent on the treatment of diabetes and diabetes-related diseases. Most countries try to control DM due to its socio-economic burden on both society and the population. Nutritional habits are a very important factor for both the prevention and management of DM.[2] Over the years, different nutritional models have been developed to prevent and manage chronic diseases such as obesity and DM, which have both reached epidemic proportions. It is possible to classify these different nutrition models under three basic groups: nutritional models with altered nutrient distribution [low-carbohydrate (CHO), fat, etc.], food or food group restriction [gluten-free (GF) diet, etc.] and altered meal timings [intermittent fasting (IF), etc.].[3] In the literature, there are some important comprehensive studies about these nutrition models with regards to DM (Table 2). The "A Secondary Analysis of the Dietary Intervention Randomized Controlled Trial" study aimed to examine the metabolic effects of three dietary patterns which they described as healthy: a low-fat diet model with restricted calories, a Mediterranean diet (MD) model with restricted calories and a low-CHO diet model with restricted calories. According to the results of that study, decreases in body weight (kg) and fasting plasma insulin levels (pmol/L) were observed after the first six months in all three dietary model intervention groups. However, the following 24-month results showed that there was an increase in both parameters but they did not go back to their initial values.[4]

To cite this article: Dayı T, Özsoy S. A Review: Are Some Diet Models Beneficial or Harmful for Type II Diabetes Mellitus?. Cyprus J Med Sci 2023;8(4):241-249

ORCID IDs of the authors: T.D. 0000-0003-2491-7609, S.Ö. 0000-0001-9518-5172.

Address for Correspondence: Serpil Özsoy
E-mail: serpil.ozsoy@neu.edu.tr
ORCID ID: orcid.org/0000-0001-9518-5172

Received: 25.01.2023
Accepted: 19.04.2023

In addition to diabetic risk factors, such as age, family, history and physical inactivity, the presence of obesity is another important risk factor which contributes to the development of diabetes (especially type II DM).[5] Therefore, while examining the effects of different nutritional models which are directly related to diabetes on metabolic parameters, their effects on body weight control should also be considered. Generally, knowledge in the current literature related to the effects of low-calorie diets (LCDs) on obesity and diabetes supports the idea that LCDs have beneficial effects on plasma glucose levels, HbA1c levels, Homeostatic Model Assessment for Insulin Resistance Index (HOMA-IR) measurements and body weight in diabetic and obese individuals. Evaluating the effectiveness of low-CHO nutrition models as a medical nutrition therapy for diabetes, obesity and cardiovascular diseases is a current research topic.[6] However, increasing the rate of energy from fat in low-CHO nutrition models also brings into question the applicability of these models. Although low-CHO/high-fat nutritional models, such as the Atkins diet, the Zone diet and the ketogenic diet (KD), have positive effects on insulin sensitivity and DM management in the short term, the long-term effects on health have not yet been fully demonstrated.[7] The literature emphasizes that low-CHO, low-glycemic index, low-energy and high-dietary fiber diet models are effective in providing ideal body weight and glycemic regulation. However, there is no single nutritional model which can be considered to be the best for the medical nutrition therapy of obesity and diabetes. Instead of a single general approach, individualized medical nutrition therapy with a patient-centered multidisciplinary approach is recommended.[8]

From this starting point, this current review aimed to examine the potential effects of some different nutrition models on body weight, certain blood parameters such as; HbA1c, fasting plasma glucose level, HOMA-IR, etc., and thus, to determine their effectiveness in both the prevention and management of type II DM.

Nutrition and Type II Diabetes Mellitus

According to the World Health Organization, nutrition has an important role in ensuring healthy growth and development, in prolonging life expectancy and in preventing non-communicable chronic diseases (NCDs), such as cardiovascular diseases, hypertension, diabetes, obesity, pulmonary diseases, cancer, etc., in every physiological process of life from the maternal period to old age.[9] Unhealthy eating habits are the most important modifiable risk factor contributing to the development of NCDs. The literature has drawn attention to the fact that there is an inverse relationship between the risk of NCDs and healthy eating models which contain high consumption rates of vegetables and fruits, whole grain products, legumes and nuts. On the other hand, high-fat foods, processed meats and meat products and the high consumption of saturated fat, salt and sugar (e.g., the Western diet) are associated with the risks of NCDs.[8] About 90% of all diabetes diagnoses are type II diabetes, which is a preventable type of DM because it has modifiable risk factors such as obesity, physical inactivity and unhealthy nutritional habits.[9] Studies showing the efficacy of lifestyle change in the prevention of diabetes are included in the Da Qing study, the Finnish Diabetes Prevention Study the Diabetes Prevention Program and the Malmö study. These studies showed that, for individuals with high type II DM risk, clinical type II DM development can be reduced by 58% as a result of increased physical activity, healthy eating habits, obesity management and behavior change interventions.[9-11]

The Nutrition Therapy Guidelines summarize the metabolic goals of individualized medical nutrition therapy (preferably applied by an experienced dietitian) in the treatment of type II diabetes as follows;

- HbA1c (glycated hemoglobin) <7%,
- Blood pressure (BP) <140/80 mmHg,
- Low-density lipoprotein-C <100 mg/dL,
- Triacylglycerol < (TAG) 150 mg/dL,
- High-density lipoprotein-C >40 mg/dL,
- Maintain/achieve ideal body weight,
- Delay/prevent diabetic complications.[12]

Although medical nutrition therapy is among the treatment components in the treatment of type II DM, there is no single nutritional model which is recommended. According to the American Diabetes Association's position statement, one of the following low-fat, low-CHO, vegetarian, Mediterranean or Dietary Approaches to Stop Hypertension diet models, which include cultural and individual preferences, can be applied.[13]

Diet Models and Type II Diabetes Mellitus

High-Protein and Low-Carbohydrate Diet Models

In the last decade, high-protein and low-CHO diet models have been more popular than low-fat diet models. In addition to the effects of high protein, a limited amount of CHO may increase the effects of these diet models on human health.[14] Although there are many studies in the literature about the effects of these diet models on weight loss,[15,16] it is also possible to find studies which aimed to determine the effects on DM, cardiovascular diseases, etc.[17,18] There are various types of high-protein diet models as well.[19] The most popular types and their contents are shown in Table 1.

According to the literature, some potential mechanisms between high-protein and low-CHO diet models and type II DM have been put forward. As shown in Figure 1, low-CHO diets (providing <130 g CHO per day) may decrease plasma insulin levels and low plasma insulin helps weight loss and protects the body from issues with fatty liver. These potential effects may help reduce IR in human tissues.[24]

In addition, amino acids, especially branched-chain amino acids, produce some bioactive peptides (BPs) during their digestion.

Table 1. The most popular high-protein diet models and their contents

Diet model	CHO (%)	Protein (%)	Fat (%)	Reference
Zone	36	34	29	[20]
Atkins	6	35	59	[21]
Stillman	3	64	33	[22]
High-protein, optimal CHO	50	20	30	[23]

CHO: Carbohydrates.

These BPs are potential inhibitors of the incretin system.[25] BPs potentially inhibit dipeptidyl peptidase IV (DPP-IV), alpha-amylase and alpha-glucosidase enzymes, which have important roles in the development of type II DM. DPP-IV has a key role in releasing incretin gut hormones such as glucagon-like peptide I and glucose-dependent insulinotropic peptide. Alpha-glucosidase and alpha-amylase are enzymes which help the digestion of CHO in the human digestive system. When BPs inhibit these enzymes, they potentially help to decrease the plasma glucose and the glucose-dependent plasma insulin levels.[26] Because of these mechanisms, high-protein and low-CHO diet models have potentially positive effects on type II DM. There are some studies regarding this subject in the literature which report its effects on the both prevention and management of type II DM. According to the results of these human studies, this diet model can decrease HbA1c levels both for diabetic and non-diabetic obese patients. Furthermore, a high-protein/low-CHO diet can be beneficial in weight loss.[17,18,27] However, Larsen et al.[27] reported this nutritional model was not beneficial for type II DM in the long term. Although these potential effects exist, low-CHO diets with the use of some medical drugs such as insulin, oral anti-diabetics, etc. may cause hypoglycemia in the acute period[28] those wishing to decrease the risk of microvascular complications through glycemic control inevitably face an increased risk of hypoglycemia, often without warning symptoms and potentially with severe consequences. This is especially true for those with type I DM, but also for some with type II DM (Figure 1). Additionally, these diet models have negative effects on human health in the long term. It is possible to say these diet models may cause some complications such as atherosclerosis, endothelial dysfunction, ischemia-inducted arrhythmias, cardiac contractile function impairment, sudden death, osteoporosis, kidney damage, cancer, etc.[19,28]

Ketogenic Diet

The KD model is the most common treatment model for childhood epilepsy in the acute term (when patients have persistent symptoms). Additionally, it has started to be used as a therapeutic approach for obesity and type II DM.[29]

The KD is characterized by high fat, moderate protein and low CHO intake. It contains 55-60% of energy in the form of fats, 30-35% in protein and 5-10% in CHO.[30] In addition, KD has some potentially beneficial effects on cardiovascular diseases, the gastrointestinal system and cancer.[31] KD causes ketosis, which is related to increased ketone bodies, in the human body and shows some potentially beneficial effects on health via them.[32] However, these ketone bodies are related to many complications which may even cause death.[33] According to the current literature on the potential effects of KD on type II DM, it may positively affect intestinal microbiota, decrease inflammation in the pancreas and liver and thus increase insulin sensitivity on the related cells and improve mitochondrial impairment which is very important in decreasing IR. In addition, KD potentially benefits weight loss. Due to these potential effects, KD is a potentially effective nutrition model which decreases plasma glucose and HbA1c levels and increases insulin sensitivity.[29,31] These mechanisms are shown in Figure 1. The meta-analysis results showed that KD was an effective diet model for the reduction of HbA1c, TAG and body weight in diabetic patients.[34-36] Choi et al.[34] observed that the KD was more beneficial for diabetic patients than for non-diabetics. The detailed methods and results of these studies are shown in Table 2. However, in addition to these beneficial effects, "keto-flu" with fatigue, lethargy and headache are the most common complications of KD at the beginning. Furthermore, constipation, low-grade acidosis, hypoglycemia, dehydration, dyselectrolytemia and dyslipidemia may occur in the short term. Growth retardation for children, hyperuricemia, kidney damage, osteoporosis, sudden death etc. are the long-term critical complications of KD.[28,33,37-39]

Gluten-Free Diet

Another popular nutrition model nowadays is the GF diet. The GF diet is necessary for some diseases, such as celiac disease, wheat allergy and non-celiac gluten sensitivity.[40] Gluten is a protein found primarily in grains.[41]

All natural cereal products, except corn, rice, buckwheat, etc., include gluten.[40] Some GF products are available in supermarkets for people who cannot or do not want to consume gluten.[42] In addition to disorders of the lower gastrointestinal system, the GF diet may be effective in treating metabolic syndrome, obesity, cardiovascular health and type II DM.[43-45] On the other hand, there are some negative effects of GF diets on overall health. GF diets may cause obesity, dysbiosis of the gut microbiota, dyslipidemia, non-insulin-dependent DM, etc.[46] The GF diet has some potential effects on type II DM (Figure 1). The GF diet may improve gut microbiota and provide biosis so it can decrease glucose absorption via the strengthening of tight junctions and regulate the immune system.[47] It may also reduce pro-inflammatory cytokines, such as TNF-α and adipokines in our bodies. Thus, it may decrease the stress levels of pancreatic beta cells and IR on muscle cells.[45] These potential effects are related to the absence of gluten proteins. On the other hand, the GF diet is mainly related to limited cereal or simple CHO intake, which is an important approach for type II DM prevention and management.[48] Table 2 shows relevant current studies about this subject. Zong et al.[48] found that higher gluten intake with dietary fiber consumption was not a risk factor for type II DM in healthy people. On the other hand, some studies observed that gluten-related increased type II DM risk. Furthermore, these studies showed that there is a bidirectional relationship between the GF diet and obesity. Ehteshami et al.[44] observed a decrease in waist circumference while Tortora et al.[49] observed an increase in this anthropometric measurement. Although there are some beneficial effects of the GF diet, this diet model has some complication risks. It is possible to classify these complications into two groups, namely nutrient deficiencies and chronic diseases. Dietary fiber, protein, essential amino acids, vitamins A, D, E, K and the B group of vitamins, calcium, iron, magnesium and zinc deficiencies may be observed.

In addition, obesity, dysbiosis of gut microbiota, dyslipidemia and non-insulin-dependent DM are some of the GF diet-related chronic diseases in the long term.[46,50-52]

Intermittent Fasting

IF is one of the effective nutritional models in the treatment of obesity and obesity-related metabolic disorders. It is thought that this nutrition model, which is based on energy restriction at certain time intervals, can yield more successful results when the circadian rhythm hypothesis is taken into account[53] which may present independent health benefits. However, the number of diet books advising how fasting can be incorporated into our daily lives is several orders of magnitude greater than the number of trials examining whether fasting should be encouraged at all. This review will consider the state of current understanding regarding various forms of intermittent fasting (e.g. 5:2, time-restricted feeding and alternate-day fasting. The circadian rhythm theory argues that a well-adjusted IF model will optimize the physiological processes occurring in the peripheral, fat,

muscle and skeletal tissues and may be effective in preventing obesity and cardiometabolic disorders. It is thought that IF approaches which restrict food intake, especially late in the evening, may have positive effects on IR and glycemic regulation.[18,54] The following are the four most common types of IF models;

- 5:2 Fasting model: two days fasting, five days libitum,

- Alternate-day fasting model: fasting days alternated with libitum eating,

- Time-restricted fasting model: <8 h/day fasting model,

- Religious fasting model (Ramadan): 12-16 h/day fasting during the Ramadan month.[4,55]

IR is a pathological disorder which contributes to the development of type II diabetes. A time-restricted IF model has been reported to cause an increase in adiponectin levels. Increased adiponectin levels stimulate the AMP-activated protein kinase (AMPK) signaling pathway. Thus, it contributes to the regulation of the glucose metabolism, lipolysis and insulin sensitivity.[56]

In addition to IF's direct effects on glucose and the insulin metabolism, it is thought to be effective in the prevention of type II DM by suppressing pro-inflammatory cytokines and peptides such as interleukin-6, C-reactive protein and homocysteine[57] (Figure 1). According to Table 3, a study on lean healthy men reported that Ramadan IF decreased HbA1c levels and proinflammatory mediators.[58] Another study showed IF (fasting 18-20 hours/day) had positive effects on both IR and body weight in diabetic patients.[55] In addition, a positive relation was determined between 18 hours of fasting and IR in overweight, prediabetic men.[59] These beneficial effects are noted in the "Nutrition Therapy for Adults with Diabetes or Prediabetes: A Consensus report- 2019" which lists IF models among the different diets. However, the report emphasizes that the evidence is insufficient to recommend an IF diet as one of the nutritional therapy methods for diabetes or pre-diabetes.[13] Furthermore, these diet models may cause side effects of hypoglycemia, ketonemia, dizziness and fatigue.[60,61]

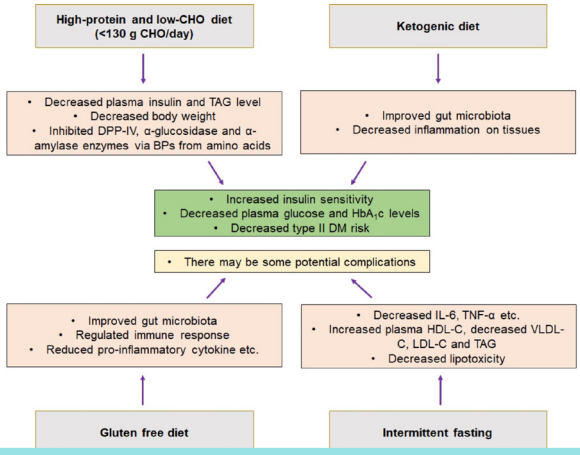

Figure 1. Potential effects of some diet models on type II DM.[24-26,31,45,47,62-64]

DM: Diabetes mellitus, CHO: Carbohydrates, TAG: Triacylglycerol, DPP-IV: Dipeptidyl peptidase IV, BP: Blood pressure, IL-6: Interleukin-6, TNF-α: Tumor necrosis factor-alpha, HDL-C: High-density lipoprotein, VLDL-C: Very low-density lipoproteins, LDL-C: Low-density lipoprotein, TAG: Triacylglycerol.

The MD was developed by Ancel Keys in the 1960s. This is a dietary model which is characterized by plant-based nutritional habits.[65] The MD includes low saturated fatty acids, high monounsaturated fatty acids-MUFA (from olive oil), dietary fiber, complex CHOs, etc. Bach-Faig et al.[66] developed a pyramid which shows MD-specific nutritional habits and this pyramid was later revised by Serra-Majem et al.[67] This diet model is related to a high consumption of olive oil, whole grains, legumes, seeds, nuts, vegetables and fruits, a moderate consumption of fish, red wine and dairy products and a limited consumption of poultry, red meat and processed red meat products.[65,66] As shown in Figure 2, the MD has some potentially positive effects on human health as a result of the beneficial nutrients and nutritional substances it includes.[68]

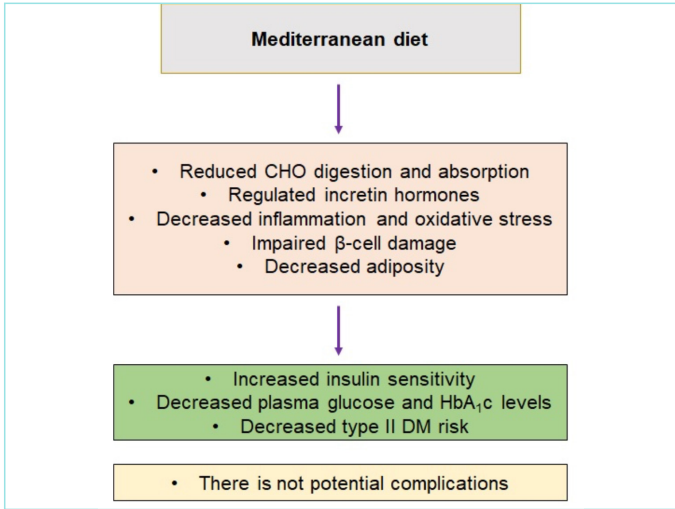

Figure 2. Potential effects of the Mediterranean diet on type II DM.[69-71]

DM: Diabetes mellitus, CHO: Carbohydrates, HbA1c: Hemoglobin A1c.

Mediterranean Diet

The MD includes a lower amount of CHO than other diet models and complex CHOs. Thus, the MD may reduce the digestion and absorption of CHOs, increase glucose uptake into cells and regulate incretin hormones. Additionally, the MUFA and polyunsaturated fatty acids-PUFA in the MD have anti-inflammatory roles. Thus, they may increase insulin sensitivity in tissues.[31] Some micronutrients and phytochemicals in the MD have antioxidant and anti-inflammatory effects. Also, they may impair β-cell damage and increase insulin secretion. At the same time, the MD provides an adequate amount of energy and may decrease the prevalence of obesity, which is a risk factor for DM.[32] Dietary fiber is high in the MD and can delay gastric emptying and decrease the absorption of glucose. Thus, it can regulate plasma glucose levels.[69] The MD is characterized by moderate red wine consumption. Red wine includes resveratrol, which is a polyphenol. It has anti-inflammatory and anti-oxidant roles and thus may help decrease IR in tissues.[71] Studies on healthy people showed that there is an inverse relationship between the MD and type 2 DM risk. Higher adherence to the MD could decrease type 2 DM risk.[72,73] In line with this, Esposito et al.[74] noted the importance of the MD to delay the need for DM medications in type II diabetic obese patients. Detailed information about these studies is

shown in Table 2. When the literature was researched by the authors, no study was found which showed any side effects of the MD.

"High protein, low-CHO diets", "KD", "GF diet", "IF", "MD" and "type II DM" were used as keywords to search the PubMed and ScienceDirect databases. Only diabetic and non-diabetic human studies (including case-controlled, epidemiological and meta-analyses) were included and the results of some current studies are shown in Table 2 for each trending diet model separately.

CONCLUSION

This review found some trending diet models to have potentially beneficial effects. Although the results of some original articles support the idea that high-protein, low-CHO, ketogenic, GF, and IF nutrition models have beneficial effects on the prevention and management of type II DM, neither the side effects nor the long-term negative effects of these should be disregarded. Additionally, it can be said that the MD includes nutrients and nutritional substances which may have potentially positive effects on type II DM development. According to the current literature, the MD nutrition model does not have any side effects. Thus, the adaption of the principles of the MD can be recommended in order to prevent the development type II DM and other NCDs.

MAIN POINTS

- Nutritional habits are a modifiable risk factor in the etiopathogenesis of chronic non-communicable diseases.
- Different dietary patterns may affect the metabolic parameters associated with type II diabetes.
- Although some of the trending nutrition models have positive effects on the metabolic parameters associated with type II diabetes, the effects of long-term practices on health need to be examined in more detail.

Table 2. Some literature examples about the effects of these diet models on type II DM

	Authors	Year	Sample of features	Methods	Results
High-protein low-CHO diets	Larsen et al.[27]	2011	**Sample size** 99 type II DM-diagnosed patients **Backgrounds of participants** Age: 30-75 years BMI: 27-40 kg/m^2 HbA1c: 6.5-10.0% If they had another significant disease, they were excluded.	**There were two study groups** (HP & high CHOs-HC) HP (n=53): 30% of energy from fats, 30% protein, 40% CHOs HC (n=46): 30% fats, 15% protein, 55% CHOs Time: 12 months (data was collected in the first three months and then at the end of the research)	1. HbA1c levels decreased in both groups with no statistical significance. 2. There was no highly beneficial effect of the HP diets on type II DM in the long term. 3. Body weight and plasma TAG levels decreased in both groups but there was no statistical significance.
	Evangelista et al.[17]	2021	**Sample size** 76 overweight and obese patients **Backgrounds of participants** Age: 57.7±9.7 years old BMI: 36.2±7.1 kg/m^2 HbA1c: 7.2±1.3%	**There were two study groups** (HP & SP) HP (n=33): 30% of energy from fats, 30% protein, 40% CHOs SP (n=43): 30% fats, 15% protein, 55% CHOs Each group consumed >25 g of dietary fiber per day Time: Three months (data was collected at the end of the research)	1. HP decreased plasma HbA1c and TAG levels statistically significantly more than SP. 2. Both diet models were effective for weight loss.
	Dong et al.[18]	2020	**Meta-analysis** Nine different types of research There were 418 type II DM-diagnosed patients	**There were nine different types of research papers** Time of the studies: Four-24 weeks Protein contents of diet: 25-32% of energy for SG and 15-20% for CG	1. HP diets decreased plasma HbA1c levels with a statistical significance. 2. They did not affect plasma fasting glucose levels significantly. 3. There was no difference between lipid levels.
Ketogenic diet	Choi et al.[34]	2020	**Meta-analysis** 14 different research studies	**There were 14 different research papers** No age restriction There were diabetic and non-diabetic patients in the studies. The studies included compared the effects of KD on glycemic regulation according to CG (low-fat diets).	1. KD had greater effects on the HbA1c levels of diabetic participants than low-fat diets. 2. According to the comparison of diabetic and non-diabetic participants, KD was more effective for diabetic patients. 3. KD showed significant beneficial effects on the diabetic participant's plasma TAG level and body weight.
	Yuan et al.[35]	2020	**Meta-analysis** 13 different research studies There were 567 type II DM-diagnosed patients	**There were 14 different research studies** Included studies compared the before-after effects of KD.	1. Plasma fasting glucose and HbA1c levels decreased after the KD intervention. 2. KD improved plasma lipid profile and provided weight loss.
	Alarim et al.[36]	2020	**Meta-analysis** Six different research studies	**There were six different research papers** There were type II DM-diagnosed participants for each study. The studies included had to have a control group.	1. KD had statistically significant effects on plasma fasting glucose and HbA1c levels. 2. Effects of the KD on the HbA1c levels were greater than for the plasma fasting glucose.

Table 2. Continued

	Authors	Year	Sample of features	Methods	Results
Gluten-free diet	Zong et al.[48]	2018	**Sample size** 202,114 participants **Backgrounds of participants** Age: 24-75 years	Time: At least 22 years (It was a cohort study) Researchers aimed to determine the relationship between gluten intake and type II DM. Physicians screened participants to diagnose type 2 DM, nutritionists determined their gluten intake with a food frequency questionnaire-FFQ every 2-4 years.	1. Higher gluten intake was related to higher starch and cereal dietary fiber intake. 2. Higher Gluten intake with dietary fiber sources did not show any harmful effects on the development of type II DM. 3. Simple CHOs sources were related to the development of type II DM. 4. Researchers found that gluten intake did not increase the risk of type II DM in this study.
	Ehteshami et al.[44]	2018	**Sample size** 45 metabolic syndrome-diagnosed patients **Backgrounds of participants** Age: 25-70 years BMI: 25-35 kg/m^2	**There were two study groups** (GF diet & RD) GF: <2 g/day gluten RD: Participants' nutritional habits	1. There were statistically positive differences between the groups for waist circumference, plasma fasting glucose, and TAG levels. 2. There was no statistical difference for the HOMA-IR index.
	Tortora et al.[49]	2015	**Sample size** 98 coeliac-diagnosed patients	Time: 12 months Data was collected at the beginning and end of the study (after one year).	1. GF diet had increased patients' plasma fasting glucose and TAG levels significantly at the end of the year. 2. BMI and waist circumference increased after one-year of GF diet intervention.

DM: Diabetes mellitus, CHO: Carbohydrates, BMI: Body mass index HbA1c: Hemoglobin A1c, HP: High protein, TAG: Triacylglycerol, SP: Standard protein, SG: Study groups, CG: Control group, KD: Ketogenic diet, FFQ: Food frequency questionnaire, GF: Gluten-free, RD: Regular diet, HOMA-IR: Homeostatic Model Assessment for Insulin Resistance Index.

Table 3. A study on lean healthy men reported

	Authors	Year	Sample of features	Methods	Results
Inter-mitten diets	Harder-Lauridsen et al.[58]	2017	**Sample size** Ten lean healthy men	28 days Ramadan IF	1. Ramadan IF decreased HbA1c. 2. Decreased TNF-α, IL-6, and IL-10 were found to be related to Ramadan IF
	Antoni et al.[55]	2017	**Sample size** 20 type II DM-diagnosed people **Backgrounds of participants** Age: 18-65 years	2-week standard diet model 2-week IF model (fasting 18-20 hours/day) 2-weeks follow up	1. Researchers reported decreased CRP, HOMA-IR, and waist circumference
	Sutton et al.[59]	2018	**Sample size** Eight overweight men diagnosed with prediabetes	18 hours of fasting for five weeks	IF was found to be related with: 1. Increased insulin sensitivity, 2. Increased insulinogenic index, 3. Decreased insulin resistance
Mediterranean diet	Esposito et al.[74]	2014	**Sample size** 215 newly diagnosed type II DM overweight patients	**There were two study groups** (Low CHO MD-LCMD & Low-fat diet) Time: Four years	1. LCMD was more effective at decreasing patients' HbA1c levels. 2. It helped in further delaying the need for DM medications
	Ahmad et al.[72]	2020	**Sample size** 25,317 healthy women	Time: 20 years Adherence to the MD is determined by a special questionnaire. Physicians screened them for type 2 DM regularly	1. High adherence to the MD reduced by 30% the risk of type II DM such as insulin resistance, adiposity, and inflammation
	Khalili-Moghadam et al.[73]	2019	**Sample size** 2,139 healthy adults	168-item FFQ was used to determine the participant's nutritional habits. Traditional MD scores were used to evaluate their adaptation status to this diet	1. Recommended consumption of MD patterns such as fish, legumes, nuts, and olive oil can decrease the risk of type II DM. 2. An inverse relationship between the MD and the risk of type II DM was found in this study

LCMD: Low carbohydrate Mediterranean diet, DM: Diabetes mellitus, IF: Intermittent fasting, IL: Interleukin, TNF: Tumor necrosis factor, MD: Mediterranean diet, CHO: Carbohydrates, FFQ: Food frequency questionnaire, HbA1c: Hemoglobin A1c, CRP: C-reactive protein, HOMA-IR: Homeostatic Model Assessment for Insulin Resistance Index.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: T.D.; Design: T.D., S.Ö.; Data Collection and/or Processing: T.D., S.Ö.; Analysis and/or Interpretation: T.D., S.Ö.; Literature Search: T.D., S.Ö.; Writing: T.D., S.Ö.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study had received no financial support.

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