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Original Article

Role of Nutrients in Diabetes

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ABSTRACT

As a complicated metabolic disease, diabetes mellitus (DM) requires careful nutritional management to maximize glycemic control and minimize complications. With a focus on dietary fiber, gut microbiota, macronutrients, and micronutrients, this review article examines the critical role that nutrients play in the prevention and treatment of diabetes. Through a variety of processes, such as insulin sensitivity and glucose metabolism, macronutrients like proteins, carbs, and fats affect glycemic control. It is emphasized how crucial micronutrients—such as vitamins and trace minerals like copper, zinc, and manganese—are in regulating inflammatory and oxidative stress pathways. The review also covers how dietary fiber affects the composition of the gut microbiota and how it may help diabetes patients' metabolic health by increasing insulin secretion and short-chain fatty acid synthesis. Nutritional measures to avoid frailty and sarcopenia are the main focus of special considerations for older diabetic patients. In order to attain the best possible results for managing diabetes, the review also emphasizes the importance of customized dietary approaches that take individual metabolic objectives, cultural norms, and financial constraints into account.

Keywords: metabolic disease, diabetes mellitus, insulin sensitivity, glucose metabolism, macronutrients

INTRODUCTION

Nutritional interventions in the management of diabetes may involve reduction of calories in diets, the use of diets with low glycaemic index, and increasing the fibre content of diets. [1] The current editorial provides an overview of the articles published in the Special Issue on recent advances in nutrition and diabetes. It focuses on the role of diet in the pathophysiology and management of diabetes including its effect on gut microbiota in this regard, Ojo et al conducted a systematic review and meta-analysis of randomised controlled trials and sought to evaluate the role of dietary fibre in modulating gut microbiota dysbiosis in patients with type 2 diabetes. [2] The promotion of gut microbes which are SCFA producers in greater diversity and abundance by dietary fibre may be responsible for the improvement in glycated haemoglobin, which could be due in part to increased glucagon-like peptide-1 (GLP-1) production. There is evidence that Bifidobacterium lactis could increase glycogen synthesis, decrease expression of hepatic gluconeogenesis genes, improve translocation of glucose transport-4, and promote glucose uptake. Furthermore, the reduction in body weight of participants in the intervention group compared with control is another area of interest, as this may have contributed to the observed improvement in glycated haemoglobin Ojo et al. concluded that dietary fibre can significantly improve ($p < 0.05$) the relative abundance of Bifidobacterium, total SCFAs, and glycated haemoglobin. [3]

Dietary Nutrients for the Management of Patients DM:

The importance of nutrition in preventing DM individually is well established. Dietary management of these diseases has been focused on the study of macronutrients (carbohydrates, fats, proteins, macrominerals, and water), micronutrients (vitamins and other minerals), and other nutrients (fiber, food additives, and dietary supplements) to control the balance between energy expenditure and calorie intake. It is necessary to highlight the importance of food quality over food quantity by having dietary patterns rich in whole grains, fruit, vegetables, nuts, legumes, fish, or vegetable oils and poor in processed meats, refined grains, refined carbohydrates, and salt . In order to achieve these behavioral patterns, many recommendations and guidelines have been developed and implemented while also considering

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other points such as personal preferences (e.g., tradition, culture, religion, or economics) and metabolic goals. [4]

- **Macronutrients**

1)Proteins

A high-protein intake also remains inconclusive for DM patients since it has been associated with increased cardiometabolic disease risk, whereas a higher intake of plant protein is associated with a lower risk of DM. Protein intake can also be beneficial in improving glycemic control since proteins do not raise blood glucose levels, or their increment is relatively small]. On the other hand, protein intake should be decreased in the case of kidney disease, unless the patient is in dialysis. [5] A meta-analysis of human observational studies in non-diabetic people revealed higher all-cause mortality linked to a higher protein intake in exchange for carbs, and high protein diets decrease lifespan in several animal models. Although higher protein intakes were defined differently and compared between the populations' upper and lower quartiles or quintiles, they typically topped 20% of total calorie intake. Observational studies offer some limited data, however there are no randomized prospective intervention studies in individuals with diabetes mellitus. [6]

2) Carbohydrates

According to the American Diabetes Association (ADA), the functional definitions of carbs for Medical Nutritional Therapy (MNT) should be based on the classifications of sugars, starches, and fiber . Despite being widely used in the literature, words like simple sugars, complex carbs, and fast-acting carbohydrates are no longer advised for patient education and are discouraged from continued use. When it comes to carbohydrates, the main focus of MNT for DM is on the overall quantity of carbs consumed in relation to energy intake. The recommendations for MNT in DM explicitly emphasize the importance of choosing fruits, vegetables, and grains to ensure that the carbohydrates consumed contain sufficient levels of fiber and micronutrients. [7] The GI of meals is a topic of ongoing research and debate regarding the carbohydrate content of MNT for DM. The incremental increase in plasma glucose (above baseline) in comparison to that caused by a benchmark, typically 50 g glucose or a white bread challenge is known as the GI of a carbohydrate. A smaller rise in glucose is indicated by lower GI readings. The glycemic load, which is the quantity of carbohydrate multiplied by its GI, is another metric that is addressed in this context. While the GI considers various plasma glucose responses against a background of equivalent available carbohydrate challenges, the glycemic load can be influenced by the carbohydrate load. [8] The current editorial provides an overview of the articles published in the Special Issue on recent advances in nutrition and diabetes. It focuses on the role of diet in the pathophysiology and management of diabetes including its effect on gut microbiota in this regard, Ojo et al conducted a systematic review and meta-analysis of randomised controlled trials and sought to evaluate the role of dietary fibre in modulating gut microbiota dysbiosis in patients with type 2 diabetes. [9] The promotion of gut microbes which are SCFA producers in greater diversity and abundance by dietary fibre may be responsible for the improvement in glycated haemoglobin, which could be due in part to increased glucagon-like peptide-1 (GLP-1) production. There is evidence that Bifidobacterium lactis could increase glycogen synthesis, decrease expression of hepatic gluconeogenesis genes, improve translocation of glucose transport-4, and promote glucose uptake. Furthermore, the reduction in body weight of participants in the intervention group compared with control is another area of interest, as this may have contributed to the observed improvement in glycated haemoglobin Ojo et al. concluded that dietary fibre can significantly improve ($p < 0.05$) the relative abundance of Bifidobacterium, total SCFAs, and glycated haemoglobin. [10]

For four weeks, 25 healthy participants in a randomized controlled crossover research followed isocaloric diets that were all made in a metabolic kitchen [47]. Diets high in SFA, MUFA, or trans-fat did not affect insulin sensitivity; total fat was 28% E, while palmitic acid, oleic acid, and 18:1 trans-fat made up 9% E each. In contrast to MUFA, SFA decreased insulin sensitivity (by 24%) in the subgroup of overweight patients. However, because there were only seven patients in the subgroup, this decline was not statistically significant. The hypothesis needs additional research in larger trials, but this finding suggests that kind of fat may be more significant in patients with a "insulin resistant phenotype."[11]

- **Micronutrients**

1) Microminerals:

Microminerals (iron, copper, zinc, manganese, molybdenum, iodine, fluorine, cobalt, and selenium) are necessary for normal functioning of the body in low concentrations. They are found in a wide variety of foods of animal and plant origin, including meat, fish, dairy products, fruit, and vegetables. [12]

The role of iron remains controversial in DM and CVD. By analyzing diverse ethnic and geographic populations, epidemiologic studies provided strong evidence that iron intake contributes to oxidative damage as well as ID and IR, which is associated with DM, and to the development of atherosclerotic plaques, which increases the risk of CVD In addition, The Cohort on Diabetes and Atherosclerosis Maastricht study observed associations between iron metabolism (ferritin, transferrin, serum iron, and non-transferrin-bound iron) with adipocyte IR and T2DM .[13] The roles of zinc and copper also remain controversial, possibly due to micromineral disturbances. Zinc is a trace element with a potent immunoregulatory role and has shown insulin-like action both in vitro and in vivo experiments]. A meta-analysis suggested that higher levels of copper were present in DM patients compared with healthy individuals, while both in vitro and in vivo studies showed that zinc had beneficial effects in the disease In CHD, one study showed mortality to be positively associated with copper intake in women and men, and inversely correlated with zinc intake in men but not in women]. Other studies concluded that zinc intake could reduce the risk of T2DM by 13%, whereas elevated serum or plasma zinc levels were associated with a 64% increased risk of T2DM, It has also been suggested that zinc deficiency is negatively correlated with IL-6, promoting inflammation, T2DM, and atherosclerosis.Manganese intake seems beneficial. A strong inverse relationship between its intake and the risk of T2DM has been reported in women but not men which could be mediated by inflammatory biomarkers in postmenopausal women]. Urinary manganese has also been inversely correlated with systolic and diastolic blood pressure, thus protecting against hypertension. [14]

2) Vitamins:

Vitamins are another essential part of nutrition and are also required in low concentrations. They are found in a large variety of foods, including meat, fish, fruit, vegetables, dairy products, and cereals. The role of vitamins in patients with both DM and CVD has been little investigated. For example, in this type of patient, vitamin E intake proved to play a cardioprotective role, since it lowers the risk of cardiovascular complications, morbidity and mortality, which may be mediated by an improvement in HDL functionality. In addition, vitamin E could improve the outcome of cardiovascular events in patients with CVD or diabetes. Vitamin C intake improved endothelial function in patients with T2DM and coronary artery disease. However, other studies suggested there was no relationship between vitamin C supplementation and improved CVD risk factor status in diabetic individuals, which could lead to increased mortality from CVD in postmenopausal women with DM. iduals], which could lead to increased mortality from CVD in postmenopausal women with DM [15] Other types of vitamins have been individually studied in DM and CVD. In this respect, the maintenance of serum vitamin D levels may be beneficial in both diabetic and cardiovascular conditions, since high vitamin D levels have been shown to be inversely correlated with CVD and its deficiency has been associated with vascular dysfunction, hypertension, hyperlipidemia, and T2DM. This can be explained because vitamin D regulates a variety of genes involved in important cardiovascular processes, such as cell proliferation, apoptosis, or oxidative stress, and its receptors have been found in cardiomyocytes, arterial wall cells, and immune cells]. By contrast, vitamin D supplementation did not produce clear improvements in blood pressure and insulin sensitivity in CVD patients, thus suggesting that the role of vitamin D in CVD, diabetes, or other cardiometabolic diseases could be inconclusive [16] The role of vitamin B is quite promising in both DM and CVD. There are several types of vitamin B, although folate or folic acid (vitamin B9), vitamin B6, and vitamin B12 have been the most studied. In this respect, folate and vitamin B12 levels were not associated with the risk of cardiovascular disorders, including stroke, coronary artery disease, myocardial infarction, or peripheral arterial disease. Folate intake has also been inversely associated with DM, being even more beneficial than both vitamins B6 and B12. Furthermore, high-dose vitamin B supplementation (which included folic acid, vitamin B6, and vitamin B12) significantly slowed the progression of early-stage subclinical atherosclerosis. It is important to

note that low folate and B12 levels, especially in DM taking metformin, raise homocysteine levels, and this is a cardiovascular risk factor. The determination of folate and B12 is recommended in DM patients. [17]

- **Other Nutrients:**

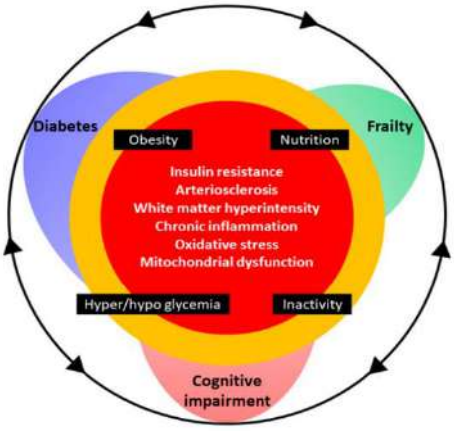
Dietary fibers (e.g., arabinoxylan, β-glucan, pectin, bran, and resistant starches) are non-digestible carbohydrates owing to lack of the required digestive enzymes. Fiber intake has been shown to play an important role in human health, including lowering the risk of many types of cancer, precancer lesions, and cardiometabolic diseases such as CVD, CVD mortality, obesity, and DM. However, only cereal fibers appear to improve IR and protect against T2DM compared with other types of dietary fibers such as fruit fibers . The mechanisms remain unclear, but could be attributed to processes such as increased antioxidants, vitamins, minerals, short-chain fatty acid production, reduced calorie intake, prevention of dietary protein absorption, and modulation of the amino acid metabolic signature.Dietary supplements, whose industry has benefits over $100 billion globally, are believed by consumers to be necessary for a healthy diet or disease treatment. Some supplements such as fiber, selenium, and zinc represent an improvement in T2DM by most studies. [18]

- **Microbiota:**

The gut microbiota is an important regulator of the host metabolism. Recent studies have suggested that gut bacteria play a fundamental role in diseases such as obesity, diabetes, and CVD. Data are accumulating in both animal models and humans, suggesting that obesity and T2DM are associated with profound dysbiosis. [19] Gut microbiota-produced metabolites, such as short-chain fatty acids, amino acid derivatives, and secondary bile acids, participate in glucose homeostasis. A healthy gut microbiota plays a role in health, but imbalances can become pathological, increasing inflammation, and contributing to metabolic dysfunction. Diet plays a significant role in shaping the composition and function of the microbiota. Eating patterns high in fruits, vegetables, whole grains, and legumes promote the abundance of healthier bacteria that produce short-chain fatty acids and other health-promoting metabolites. Jardine (2016) reviewed the functions of the microbiota, how it is formed, and nutritional strategies to improve gut health. [20]

Role of nutrients in elderly diabetic patients:

An important social cost is the rising number of older persons with diabetes. With age, the effect of nutrients varies, therefore, it may be essential to adjust dietary therapy approaches from addressing obesity/metabolic syndrome to preventing frailty in diabetic patients over 75 years old who exhibit frailty or sarcopenia and suffer from malnutrition. Treatment of diabetes in elderly patients should include awareness about glycemic index, in order to aim at enhancing healthy life expectancy via healthy nutritional diet and exercise. [21]



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1) Proteins

Adequate protein consumption is crucial for decreasing the risk of frailty and mortality among older adults. In studies conducted, it has been observed that higher intake of proteins results in lower incidence of frailty. In an interventional study involving prefrail and frail patients, increased protein intake was associated with improvements in muscle mass and physical performance. In a 3-year follow-up study of older persons with diabetes, those getting ≥ 1.0 g/kg body weight/day protein showed less

decrease in knee extension power and physical function than those receiving lower protein. [22]

2) Vitamin D

Randomised studies have been carried out but the results were found to be conflicting. Although, studies still suggest that vitamin D improves the metabolic parameters (lipids, insulin resistance, glucose) and also reduces the complications of T2DM in elderly patients affected by diabetes. It has been found that many elderlies were also deficient in vitamin D and VD supplementation in their diet was needed to be done [23].

Goals of medical nutrition therapy that apply to specific situations include the following:

1. For youth with type 1 diabetes, to provide adequate energy to ensure normal growth and development, integrate insulin regimens into usual eating and physical activity habits.
2. For youth with type 2 diabetes, to facilitate changes in eating and physical activity habits that reduce insulin resistance and improve metabolic status.
3. For pregnant and lactating women, to provide adequate energy and nutrients needed for optimal outcomes.
4. For older adults, to provide for the nutritional and psychosocial needs of an aging individual.
5. For individuals treated with insulin or insulin secretagogues, to provide self-management education for treatment (and prevention) of hypoglycemia, acute illnesses, and exercise-related blood glucose problems.
6. For individuals at risk for diabetes, to decrease risk by encouraging physical activity and promoting food choices that facilitate moderate weight loss or at least prevent weight gain. [24]

Medical Nutrition Therapy for Type 1 And Type 2 Diabetes:

- **Carbohydrate and diabetes**

When referring to common food carbohydrates, the following terms are preferred: sugars, starch, and fiber. Terms such as simple sugars, complex carbohydrates, and fast-acting carbohydrates are not well defined and should be avoided. Studies in healthy subjects and those at risk for type 2 diabetes support the importance of including foods containing carbohydrate, particularly from whole grains, fruits, vegetables, and low-fat milk in the diet of people with diabetes. [25] A number of factors influence glycemic responses to foods, including the amount of carbohydrate, type of sugar (glucose, fructose, sucrose, lactose), nature of the starch (amylose, amylopectin, resistant starch), cooking and food processing (degree of starch gelatinization, particle size, cellular form), and food form, as well(1) as other food components (fat and natural substances that slow digestion—lectins, phytates, tannins, and starch-protein and starch-lipid combinations). Fasting and preprandial glucose concentrations, the severity of glucose intolerance, and the second meal or lente effect of carbohydrate are other factors affecting the glycemic response to foods. However, in persons with type 1 or type 2 diabetes, ingestion of a variety of starches or sucrose, both acutely and for up to 6 weeks, produced no significant differences in glycemic response if the amount of carbohydrate was similar. Studies in controlled settings and studies in free-living subjects produced similar results. Therefore, the total amount of carbohydrate in meals and snacks will be more important than the source or the type. [26] Studies in subjects with type 1 diabetes show a strong relationship between the premeal insulin dose and the postprandial response to the total carbohydrate content of the meal. Therefore, the premeal insulin doses should be adjusted for the carbohydrate content of the meal. For individuals receiving fixed doses of insulin, day-to-day consistency in the amount of carbohydrate is important. [27] In persons with type 2 diabetes, on weight maintenance diets, replacing carbohydrate with monounsaturated fat reduces postprandial glycemia and triglyceridemia. However, there is concern that increased fat intake in ad libitum diets may promote weight gain. Therefore, the contributions of carbohydrate and monounsaturated fat to energy intake should be individualized based on nutrition assessment, metabolic profiles, and treatment goals. [28]

- **Glycemic index:**

Although low glycemic index diets may reduce postprandial glycemia, the ability of individuals to maintain these diets long-term (and therefore achieve glycemic benefit) has not been established. The available studies in persons with type 1 diabetes in which low glycemic index diets were compared with high glycemic index diets (study length from 12 days to 6 weeks) do not provide convincing evidence of benefit. In subjects with type 2 diabetes, studies of 2–

12 weeks duration comparing low glycemic index and high glycemic index diets report no consistent improvements in HbA_{1c}, fructosamine, or insulin levels. The effects on lipids from low glycemic index diets compared with high glycemic index diets are mixed. [29] Although it is clear that carbohydrates do have differing glycemic responses, the data reveal no clear trend in outcome benefits. If there are long-term effects on glycemia and lipids, these effects appear to be modest. Moreover, the number of studies is limited, and the design and implementation of several of these studies are subject to criticism. [30]

- **Fiber.**

As for the general population, people with diabetes are encouraged to choose a variety of fiber-containing foods, such as whole grains, fruits, and vegetables, because they provide vitamins, minerals, fiber, and other substances important for good health. Early short-term studies using large amounts of fiber in small numbers of subjects with type 1 diabetes suggested a positive effect on glycemia. Recent studies have reported mixed effects on glycemia and lipids. In subjects with type 2 diabetes, it appears that ingestion of very large amounts of fiber are necessary to confer metabolic benefits on glycemic control, hyperinsulinemia, and plasma lipids. It is not clear whether the palatability and the gastro-intestinal side effects of fiber in this amount would be acceptable to most people. [31]

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