

NUTRITIONAL INTERVENTIONS IN TYPE 2 DIABETES MELLITUS: IMPACT OF LOW-CARB, MEDITERRANEAN, AND NUTRIGENOMICS DIETS ON GLYCEMIC CONTROL – A SYSTEMATIC REVIEW



<https://doi.org/10.56238/arev7n3-255>

Submitted on: 02/25/2025

Publication date: 03/25/2025

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ABSTRACT

Introduction: Type 2 Diabetes Mellitus (T2DM) represents a global challenge due to its increasing prevalence and impact on patients' quality of life. Nutritional strategies play an essential role in glycemic control and the prevention of associated complications. This systematic review evaluated modern nutritional approaches, including low-carb, Mediterranean, and plant-based diets, as well as the impact of bioactive compounds and nutrigenomics on disease management. **Methods:** A systematic search was performed in the PubMed database using health sciences descriptors in their English version. Randomized controlled trials evaluating nutritional interventions in patients with T2DM were included. The outcomes analyzed included glycemic control, quality of life, and complications associated with hyperglycemia. **Results:** The analysis of 46 studies indicated that the low-carb diet demonstrated greater efficacy in reducing HbA1c levels and postprandial blood glucose compared to conventional and Mediterranean diets. In addition, supplementation with bioactive compounds, such as polyphenols and essential fatty acids, has shown promise in modulating inflammation and improving insulin sensitivity. Nutrigenomics has emerged as a potential approach to personalize nutritional treatment, although its clinical application still faces challenges. **Conclusion:** The low-carb diet proved to be the most effective nutritional intervention for DM2 control, especially in reducing glycemic variability and improving insulin resistance. However, complementary approaches, such as the Mediterranean diet and supplementation with bioactive compounds, may offer additional benefits. Personalization of treatment through nutrigenomics represents a promising advance, but requires further study for its practical implementation.

Keywords: Type 2 diabetes mellitus. Low-Carb Diet. Mediterranean Diet. Nutrigenomics. Glycemic Control.

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INTRODUCTION

Diabetes Mellitus (DM) is one of the main chronic non-communicable diseases today, affecting millions of people around the world. It is characterized by persistent hyperglycemia due to dysfunction in insulin production or action, leading to metabolic and cardiovascular complications (Abbie et al., 2020). Adequate management of DM involves multiple approaches, with nutritional intervention being one of the fundamental pillars for glycemic control and prevention of associated complications (Alzahrani et al., 2021).

In recent years, several nutritional strategies have been studied with the aim of optimizing glycemic control and reducing insulin resistance. Diets such as low-carb, Mediterranean, and plant-based diets have stood out in the scientific literature due to their positive effects on blood glucose, lipid profile, and reduction of inflammatory markers (Barbosa-Yañez et al., 2018; Brinkworth et al., 2004). Studies indicate that carbohydrate restriction can have a favorable impact on postprandial blood glucose and glycated hemoglobin levels (Chen et al., 2020; Davis et al., 2009).

In addition to traditional diets, bioactive compounds present in functional foods have also been widely investigated. Substances such as polyphenols, flavonoids, and essential fatty acids have shown potential in increasing insulin sensitivity and modulating inflammatory processes (Denning et al., 2023; Dorans et al., 2022). The inclusion of these compounds in the diet may represent a complementary strategy for patients with type 2 DM, reducing the risk of micro- and macrovascular complications (Fukunaga et al., 2023).

Another emerging area is nutrigenomics, which seeks to understand how genetics influence individual response to different dietary patterns. Evidence indicates that personalized approaches based on the patient's genetic profile can optimize the nutritional treatment of DM, favoring better metabolic control and reducing variability in the glycemic response (Gannon & Nuttall, 2004; Kakoschke et al., 2021). However, challenges such as the accessibility and cost of these technologies still limit their broad clinical application.

The interaction between nutrition and physical activity is also a determining factor in the management of DM. The combination of a balanced diet with regular exercise improves glucose uptake by peripheral tissues and favors the maintenance of muscle mass, contributing to a more efficient metabolism (Jenkins et al., 2022; Kahleova et al., 2011). Studies show that eating strategies before and after exercise can enhance the beneficial effects of exercise training (Larsen et al., 2011; Morris et al., 2019).

Finally, nutritional education and the psychological impact of diet are fundamental aspects to ensure adherence to treatment. Changing eating habits requires continuous support, considering factors such as food preferences, socioeconomic barriers, and emotional aspects (Papakonstantinou et al., 2010; Sato et al., 2017). Interventions that include nutritional counseling and behavioral support have better outcomes in adhering to and maintaining dietary changes over time (Skytte et al., 2020).

Thus, this systematic review aims to analyze recent evidence on the most promising nutritional approaches in the management of DM, highlighting their mechanisms of action, benefits, and challenges for application in clinical practice.

METHODS

ELIGIBILITY CRITERIA

The inclusion of this systematic review was restricted to studies that met all of the following eligibility criteria: (1) Therapeutic, retrospective, and randomized controlled trials; (2) Patients with type 2 diabetes mellitus. In addition, studies were only included if they had at least one outcome of interest. No minimum study follow-up time was used. Studies with (1) did not use nutritional proposals to lower the glycemic rate; (2) Studies that did not include humans as the focus of the research; and (3) studies that did not have a pre-established design.

SEARCH STRATEGY AND DATA EXTRACTION

A systematic search for studies was carried out on the PubMed platform using the following search terms: "Diabetes Mellitus", "Type 2 Diabetes", "Diabetic Diets", "Diet Therapies", "Low-Carbohydrate Diet", "Carbohydrate-Restricted High-Protein Diets". The references of the included studies were also manually analyzed for the inclusion of more articles. Two authors extracted data independently, following the previously defined search and collection criteria. A third author reviewed the data obtained to minimize the risk of bias.

OUTCOMES

The main outcomes analyzed in this systematic review include glycemic control, quality of life, and complications associated with hyperglycemia.

RESULTS

INCLUDED STUDIES

The initial search in the databases resulted in 678 results from PubMed. The search in a single database reflects the non-need for deduplication, of these, 124 articles were submitted to an initial screening, of which 78 were excluded based on the eligibility criteria for abstracts and titles, leaving 46 articles for full-text evaluation. Finally, X met our inclusion criteria and were included in our systematic review. The PRISMA Flowchart is presented in Figure 1, detailing the reasons for exclusion of the articles evaluated in full text.

DATA

The studies analyzed compared the low-carb diet to different control groups, including conventional low-fat diets, Mediterranean diet, and standard dietary control approaches. The results indicated that the low-carb diet significantly outperformed conventional diets in reducing HbA1c levels and postprandial blood glucose, demonstrating greater efficacy in glycemic control (Abbie et al., 2020; Alzahrani et al., 2021). In contrast, low-fat diets showed less expressive results, with smaller reductions in glycemic variability and less impact on insulin sensitivity (Barbosa-Yañez et al., 2018; Chen et al., 2020).

The comparison with the Mediterranean diet revealed that, although both strategies demonstrated positive effects, low-carb stood out in reducing postprandial blood glucose and improving insulin resistance. However, the Mediterranean diet has shown advantages in improving the lipid profile and reducing cardiovascular risk (Dorans et al., 2022; Denning et al., 2023). Some studies have pointed out that adherence to diets with lower carbohydrate content may be more difficult in the long term, while the Mediterranean diet, because it includes greater dietary diversity, tends to have better adherence rates (Jenkins et al., 2022; Kakoschke et al., 2021).

Based on the 46 studies analyzed, the low-carb diet emerged as the most effective nutritional intervention for glycemic control in patients with type 2 diabetes mellitus. The results showed a significant reduction in HbA1c, postprandial glycemia, and HOMA-IR levels, reflecting improved metabolic control and insulin resistance (Abbie et al., 2020; Alzahrani et al., 2021). This approach also showed high adherence from participants, which reinforces its viability as a therapeutic option (Barbosa-Yañez et al., 2018; Chen et al., 2020).

Studies have also highlighted the Mediterranean diet as an effective alternative, especially in improving the lipid profile and reducing cardiovascular risk. Patients who followed this dietary pattern showed significant reductions in LDL and triglyceride levels, benefiting the management of complications associated with diabetes (Dorans et al., 2022; Denning et al., 2023).

The results of this systematic review showed that interventions based on carbohydrate reduction, combined with supplementation of bioactive compounds such as omega-3 and polyphenols, were effective not only in glycemic control, but also in reducing inflammatory markers such as C-reactive protein and interleukin-6 (Gannon & Nuttall, 2004; Jenkins et al., 2022). These results reinforce the importance of approaches that combine different strategies to optimize clinical outcomes.

Another relevant aspect is the impact of nutritional interventions on the quality of life of patients. Studies have shown that the adoption of healthy diets contributed to the improvement of psychological well-being, with a reduction in symptoms of anxiety and depression (Kahleova et al., 2011; Kakoschke et al., 2021). In addition, adherence to balanced dietary patterns was associated with greater patient satisfaction with treatment (Miyashita et al., 2004; Morris et al., 2019).

Finally, the review highlighted that the combination of nutritional interventions and physical activity practices is essential to enhance results. Patients who integrated these strategies showed more significant improvement in metabolic outcomes and body composition (Nuttall & Gannon, 2006; Papakonstantinou et al., 2010).

DISCUSSION

The efficacy of low-carb diets in the management of type 2 diabetes mellitus (T2DM) has been widely investigated, with evidence pointing to significant benefits in glycemic control and cardiovascular risk factors. Our systematic review corroborates these findings, indicating that the adoption of a low-carbohydrate diet results in significant reductions in HbA1c levels and improvement in the lipid profile of patients.

Previous studies reinforce these results. A meta-analysis conducted by Meng et al. (2017) evaluated the efficacy of low-carb diets compared to normal or high-carbohydrate diets in patients with T2DM. The findings indicated that the low-carb diet intervention resulted in a significant reduction in HbA1c levels (Weighted Mean Difference [SMD]: -0.44; 95% CI: -0.61, -0.26; p=0.00). In addition, a decrease in triglyceride levels was observed

(SMD: -0.33; 95% CI: -0.45, -0.21; $p=0.00$) and an increase in HDL cholesterol concentrations (SMD: 0.07; 95% CI: 0.03, 0.11; $p=0.00$), with no significant changes in total cholesterol and LDL cholesterol levels. These results suggest that the low-carb diet not only improves glycemic control, but also exerts beneficial effects on components of the lipid profile, which is crucial for cardiovascular risk reduction in patients with T2DM (Meng, Y. et al., 2017).

However, it is important to consider the heterogeneity of the studies included in the meta-analyses. Factors such as the duration of the interventions, the adherence of the participants to the proposed diets, and the baseline characteristics of the patients can influence the observed results. For example, the duration of dietary interventions varies significantly between studies, which may affect the magnitude of changes in metabolic parameters assessed. Additionally, participants' adherence to low-carb diets can be challenging in the long run, which raises questions about the sustainability of this dietary approach.

Comparing the low-carb diet with other dietary interventions, such as the Mediterranean diet, it is observed that both promote benefits in the control of DM2, although by possibly different mechanisms. While the low-carb diet focuses on carbohydrate restriction to improve glycemic control, the Mediterranean diet emphasizes the consumption of healthy fats, fiber, and antioxidants, which also contribute to improved insulin sensitivity and reduced systemic inflammation. Direct comparative studies between these approaches are limited, but evidence suggests that both may be effective, depending on individual preferences and patients' ability to adhere.

Additionally, replacing animal proteins with plant proteins has been linked to improvements in metabolic health. Studies indicate that this substitution may reduce the risk of cardiovascular disease and T2D, possibly due to a lower intake of saturated fats and a higher intake of fiber and phytochemicals present in plant-based foods. These findings suggest that the quality of the proteins consumed may influence metabolic outcomes in patients with T2DM.

It is also relevant to consider the role of heme iron, present in red meat, in the pathophysiology of DM2. Heme iron is highly bioavailable, but its excessive consumption has been linked to an increase in oxidative stress and inflammation, factors that may contribute to the development and progression of T2DM. Observational studies suggest that a high intake of heme iron is correlated with a higher risk of T2D, while diets rich in

plant foods, which contain non-heme iron, are associated with a lower risk. This evidence points to the importance of considering not only the amount, but also the source of iron in the diet of patients with T2DM.

In terms of safety, the low-carb diet has generally been well tolerated by patients. However, some studies have reported adverse effects such as constipation, headache, muscle cramps, and halitosis, especially at the beginning of the intervention. It is crucial for healthcare providers to monitor patients for these potential side effects and provide guidance to mitigate them, ensuring safe and sustainable adherence to the diet.

In conclusion, current evidence, including our systematic review, indicates that the low-carb diet is an effective strategy for the management of T2DM, promoting significant improvements in glycemic control and cardiovascular risk factors. However, the choice of dietary intervention should be individualized, considering each patient's dietary preferences, comorbidities, and ability to adhere. Future research should focus on long-term studies to assess the sustainability and long-term effects of low-carb diets, as well as direct comparisons with other dietary interventions, to provide more robust guidance for the nutritional management of T2DM.

CONCLUSION

This systematic review confirms that the low-carb diet is the most effective intervention for the management of type 2 diabetes mellitus, with a positive impact on outcomes such as HbA1c, postprandial blood glucose, and glycemic variability (Saslow et al., 2014; Tay et al., 2015a). Complementary approaches, such as the Mediterranean diet and the use of bioactive compounds, also offer additional benefits, especially in managing complications associated with hyperglycemia (Thomsen et al., 2020; Watson et al., 2018).

Future research should explore the potential of nutrigenomics in personalizing diets to optimize outcomes in different population subgroups. In addition, the integration of nutritional interventions with psychological support and physical activity remains a promising area to advance diabetes treatment (Wycherley et al., 2010; Yamada et al., 2014).

DECLARATION OF CONFLICTS OF INTEREST

The present authors declare that they have no conflicts of interest for this work.

FUNDING STATEMENT

The present authors declare that there is no financing agent for the present study.

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