Dean&Francis
ISSN 2959-409X

Effects of Low-Carbohydrate Diets on Overweight and Obesity in Patients with Type 2 Diabetes Mellitus

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Abstract:

Type 2 diabetes mellitus represents a major global health challenge, with over 90% of cases occurring in individuals who are overweight or obese. Lifestyle modification, particularly dietary intervention, is central to disease management. While several dietary patterns have demonstrated benefits, low-carbohydrate diets have drawn increasing attention due to their pronounced short-term effects on glycemic control and weight reduction. Current evidence indicates that low-carbohydrate diets can significantly lower glycated hemoglobin, fasting plasma glucose, and triglycerides, while promoting diabetes remission in the initial months of intervention. These improvements are largely attributable to reduced glycemic load, enhanced insulin sensitivity, and reductions in visceral adiposity. However, findings on long-term efficacy and safety remain inconsistent. Adherence commonly declines over time, benefits often diminish after 12 months, and concerns have been raised regarding potential elevations in low-density lipoprotein cholesterol and increased mortality risk when carbohydrates are replaced with animal-derived fat and protein. Compared with Mediterranean diets, low-carbohydrate diets may achieve greater metabolic improvements in short term, but lack robust evidence of long-term cardiovascular protection. Overall, low-carbohydrate diets can be considered an effective short-term strategy, but future research should prioritize long-term randomized trials, standardized definitions, and personalized approaches to clarify their sustainable role in type 2 diabetes mellitus management.

Keywords: Low-carbohydrate diets; type 2 diabetes mellitus; overweight and obesity; glycemic control; cardiovascular safety.

ISSN 2959-409X

1. Introduction

Type 2 diabetes mellitus is commonly defined as a metabolic disorder characterized by insulin resistance and relative insulin deficiency, particularly prevalent among individuals with overweight and obesity [1,2]. Clinically, overweight and obesity are defined as the presence of excessive or abnormal fat accumulation in the body [3]. In adults, overweight is defined as having a body mass index between 25.0 and 29.9, while obesity is defined as having a body mass index of 30 or higher [3]. By the end of 2024, approximately 589 million adults aged 20 to 79 were affected by diabetes worldwide, and this figure is projected to increase to 853 million by 2050, affecting one in eight adults [4]. Type 2 diabetes mellitus accounts for over 90-95% of all cases, and the majority of patients are concurrently affected by overweight and obesity [5]. This dual epidemic not only worsens glycemic control but also contributes to severe complications such as cardiovascular disease, diabetic kidney disease, retinopathy, and neuropathy, collectively imposing a profound burden on quality of life, disability, and health systems [2]. The International Diabetes Federation reported that global health-care expenditure attributable to diabetes exceeded 1.015 trillion United States dollars in 2024, and costs are expected to rise further in the coming decades [4].

Lifestyle modification is recognized as the primary treatment strategy for type 2 diabetes mellitus, with dietary intervention as its cornerstone [1,2]. Conventional dietary advice typically emphasizes low-fat intake and overall energy restriction, which can improve weight and metabolic outcomes but often suffers from poor long-term adherence and limited effectiveness [5,6]. In this situation, other dietary patterns have been explored, such as the Mediterranean diet, low-carbohydrate diets and low-fat diets. At present, a large number of studies have demonstrated that the Mediterranean diet provides protective effects on cardiovascular and metabolic health, while low-carbohydrate diets are especially noted for their rapid short-term effects on body weight and glycemic control [5,7]. A low-carbohydrate diet is typically defined as providing less than 26% of total energy or less than 130 grams of carbohydrates per day [5,6]. Recently, a meta-analysis of 23 randomized controlled trials has demonstrated that low-carbohydrate diets significantly increaed the short-term remission rates of type 2 diabetes, highlighting its potential as an effective dietary strategy [5]. However, the long-term effectiveness and safety of low-carbohydrate diets are still under debate because of the limitations imposed by inconsistent definitions, insufficient follow-up, poor compliance, and cardiovascular consequences [5,6,8]. With the worldwide epidemic of diabetes and obesity, and the substantial shortcomings of current dietary advice, it is timely and necessary to clarify the potential role of low-carbohydrate diets and apply them in clinical practice. This review aims to integrate the current evidence on the effectiveness and risks of low-carbohydrate diets in controlling overweight, obesity, and type 2 diabetes mellitus, highlight unresolved controversies, and suggest directions for future research and clinical practice.

2. Mechanism of Action and Dual Nature of Low-Carbohydrate Diets

2.1 Reduction of Glucose Intake

Glucose is the primary energy source for human metabolism and is mainly derived from carbohydrates in the diet. The fundamental mechanism of a low-carbohydrate diet is to reduce the amount of carbohydrate consumed, which in turn reduces the total glycemic load of the diet [5,6,9]. Since glucose absorbed into the bloodstream raises postprandial blood glucose levels, a lower glycemic load can slow the rate and reduce the magnitude of this increase, consequently minimizing blood glucose fluctuations and limiting peak concentrations [5,6]. These attenuated postprandial blood glucose responses reduce the demand for insulin secretion, reducing the burden on pancreatic β-cells and limiting the development of hyperinsulinemia and glucotoxicity [9]. These improvements, in turn, contribute to enhanced insulin sensitivity and more stable long-term glycemic control [5,6].

2.2 Improvement of Insulin Sensitivity

Insulin, produced by pancreatic β-cells, is the principal hormone maintaining glucose homeostasis by promoting glucose uptake in peripheral tissues and limiting hepatic glucose production. In healthy individuals, insulin binding initiates receptor autophosphorylation and recruits insulin receptor substrates, which activate the phosphoinositide 3-kinase–Akt pathway [9]. This cascade drives glucose transporter 4 translocation to the plasma membrane, leading to increased glucose uptake [9]. In patients with type 2 diabetes mellitus, insulin resistance manifests as reduced sensitivity of peripheral tissues—particularly skeletal muscle and adipose tissue—to insulin signaling [2,9]. Chronic exposure to elevated insulin, or hyperinsulinemia, further disrupts signaling by inducing abnormal serine/threonine phosphorylation of insulin receptor substrates proteins and reducing downstream phosphoinositide 3-kinase–Akt signaling pathway activity [9]. As a result, glucose transporter 4 translocation is impaired, exacerbating glucose intolerance and metabolic dysfunction [9].

Sustained carbohydrate restriction reduces the demand for insulin secretion, thereby alleviating chronic hyperinsulinemia [5,6]. Since prolonged hyperinsulinemia is a major driver of defective insulin signaling, its reduction helps slow the progression of insulin resistance [9]. Consequently, peripheral tissue sensitivity to insulin is improved, leading to more efficient glucose uptake and utilization, with significant improvements in glycated hemoglobin and fasting plasma glucose [5,6]. In addition, low-carbohydrate diets usually result in marked weight loss, especially reductions in visceral adipose tissue [5,6]. The decline in visceral adiposity lowers the secretion of pro-inflammatory adipokines and alleviates low-grade chronic inflammation, further enhancing insulin sensitivity [2,9].

2.3 Endocrine Regulation

In addition to their direct effects on glucose and insulin, low-carbohydrate diets achieve metabolic benefits by modulating key endocrine pathways [7]. Under conditions of carbohydrate restriction, glucagon secretion rises, stimulating gluconeogenesis and fatty acid oxidation to maintain glucose homeostasis [1,7]. At the same time, the reductions in adiposity lead to a decline in circulating leptin levels and an enhancement in leptin sensitivity, thereby restoring energy balance regulation [9]. Some evidence also suggests that low-carbohydrate diets inhibit postprandial ghrelin secretion, enhance satiety, and reduce overall energy intake [7]. Importantly, adiponectin levels tend to rise after weight and fat mass are reduced, which not only enhances insulin sensitivity but also exerts anti-inflammatory effects [9]. Overall, these hormonal changes show that the benefits of low-carbohydrate diets are not limited to glucose and insulin but also involve broader hormonal adjustments that improve metabolic health [2].

3. Clinical Efficacy and Key Controversies

3.1 Short-Term Efficacy

Systematic literature reviews and meta-analytic studies consistently demonstrate that low-carbohydrate diets produce significant short-term benefits for populations affected by overweight and obesity in the context of type 2 diabetes mellitus [5-7]. Within a six-month period, low-carbohydrate diets have been shown to produce meaningful improvements in glycated hemoglobin, fasting plasma glucose, body weight, and lipid metabolism, particularly through reductions in triglycerides and increases in high-density lipoprotein cholesterol, without a notable rise in adverse events [5].

Despite these shared conclusions, important differences exist between studies. A systematic review and meta-analysis of 23 randomized controlled trials demonstrated that low-carbohydrate diets achieved an absolute 32% higher remission rate of type 2 diabetes mellitus at six months compared with control diets, in addition to improvements in weight and lipid profiles [5]. Another meta-analysis of 17 randomized controlled trials examined metabolic parameters and confirmed significant improvements in glycated hemoglobin, fasting plasma glucose, triglycerides, and high-density lipoprotein cholesterol, but did not assess remission outcomes [6].

Taken together, these findings demonstrate that low-carbohydrate diets provide robust short-term efficacy in improving glycemic control, weight, and lipid metabolism, and in some cases may enable clinically meaningful type 2 diabetes mellitus remission, although the durability of these effects beyond six months remains uncertain [5,6].

3.2 Long-Term Efficacy and Comparative Controversies

The primary academic debate centers on the efficacy of low-carbohydrate diets and their long-term sustainability. The metabolic benefits observed at 6 months often diminish gradually by 12 months [5,6]. A systematic review and meta-analysis of 23 randomized controlled trials demonstrated that the increase in remission rates with low-carbohydrate diets declined from about 32 percentage points at six months to a nonsignificant 5 percentage points at twelve months [5]. Recently, another systematic review and meta-analysis of 17 randomized controlled trials confirmed that although low-carbohydrate diets result in greater short-term weight loss reduction, the effect diminishes at 12 months, when changes in body weight, body mass index, and waist circumference are no longer significantly different from those observed with control diets [6]. This diminished effect is primarily attributed to insufficient long-term adherence. The highly restrictive nature of low-carbohydrate diets easily triggers “diet fatigue” [6]. Without sustained professional support and motivation, patients often have difficulty adhering to carbohydrate restrictions in the long term [6].

3.3 Potential Risks and Adverse Effects

Despite the clear benefits of low-carbohydrate diets, they also have important potential risks. Hypoglycemia is one of the most immediate problems, especially in patients treated with sulfonylureas or insulin [6]. A sudden reduction reductions in carbohydrates without appropriate adjustment of medication may trigger a severe hypogly-

ISSN 2959-409X

cemic episode [6]. In addition, the effect on blood lipids is of concern. Although consistent evidence shows reductions in triglycerides and increases in high-density lipoprotein cholesterol, the impact on low-density lipoprotein cholesterol remains controversial [5]. A systematic review and meta-analysis of 23 randomized controlled trials have reported clinically significant low-density lipoprotein cholesterol elevations after 12 months, raising concerns about long-term cardiovascular safety [5]. Highly restrictive low-carbohydrate diets such as the ketogenic diet may induce early adverse effects characterized by headaches and nausea, which are referred to as "ketogenic flu" [7]. In addition, poorly planned diets increase the risk of nutritional deficiencies, particularly micronutrients and dietary fiber [6,7]. All these potential adverse effects emphasize the need of individualized clinical monitoring and balanced dietary planning when implementing low-carbohydrate strategies.

4. Core Challenges in Current Research

The existing evidence of low-carbohydrate diets faces multiple challenges in terms of reliability and generalizability. First, the lack of a standardized definition of "low-carbohydrate diets" affects comparability across studies [7,10]. Current trials employ widely varying thresholds, ranging from very low-carbohydrate ketogenic diets providing less than 10% of daily energy from carbohydrates to milder forms allowing up to 26% of total energy [5]. Such heterogeneity makes it difficult to pool data, integrate findings, and establish consistent clinical guidelines. For example, the metabolic effects of a 50-gram daily carbohydrate intake may differ substantially from those of a 120-gram intake [6]. Without a unified definition, cross-study synthesis remains problematic and weakens the reliability of evidence.

Second, the accurate assessment and long-term maintenance of dietary adherence remain major obstacles. Most studies rely on self-reported food records or recall questionnaires, which are prone to recall bias and measurement error [7,10]. Poor adherence not only affects outcome assessment but also contributes to the gradual waning of benefits over time. Since the efficacy of low-carbohydrate diets mainly depends on continued restriction, metabolic improvements tend to diminish once participants have difficulty adhering to them [5]. This complicates the interpretation of long-term trials: it is difficult to determine whether the diminished effects observed at 12–24 months reflect inherent dietary limitations or are primarily the result of declining adherence.

Third, the evidence regarding long-term safety and cardiovascular outcomes of low-carbohydrate diets remains highly inconsistent [7]. For instance, while some studies have reported no significant changes in low-density lipoprotein cholesterol, others have observed clinically meaningful elevations after 12 months of intervention [5]. Moreover, a meta-analysis and large prospective cohort study suggested that long-term adherence to low-carbohydrate diets might be linked to a rise risk of all-cause mortality, raising substantial safety concerns [8]. Importantly, this excess risk appeared to depend on the source of replacement for carbohydrates: mortality risk increased when they were replaced with animal-based protein and fat, but not when replaced with plant-based sources [8]. These discrepancies highlight the uncertainty of the long-term health consequences of low-carbohydrate diets. Critically, the lack of high-quality randomized controlled trials with follow-up durations beyond two years further limits the potential to yield conclusive findings [7]. Therefore, the overall certainty of the evidence remains low, which hinders the development of clear and evidence-based long-term clinical recommendations [7].

5. Conclusion

In conclusion, the existing evidence supports low-carbohydrate diets as an effective tool for the short-term management of overweight and obesity patients with type 2 diabetes mellitus. This dietary partten able to help patients lose weight, improve glycemic control blood, lipid profiles, and reduce the remission rate of diabetes by lowering the glycemic load. However, its long-term efficacy and safety are limited by multiple factors: the lack of a clear definition of "low-carbohydrate", poor long-term compliance, and significant differences among studies. These factors have collectively reduced the reliability and generalizability of current research results. In addition, there is considerable heterogeneity in terms of cardiovascular safety, especially the potential adverse effects on lipid profiles and all-cause mortality, which require more rigorous investigations.

Future research should focus on well-designed, long-term randomized controlled trials, using standardized "low-carbohydrate" definitions and objective methods to monitor compliance. Moreover, the development of personalized nutritional strategies that take into account patients' metabolic characteristics, cultural backgrounds and dietary preferences may help to enhance the benefits of short-term efficacy and long-term sustainability. This may provide insights into how low-carbohydrate diets can be safely and effectively integrated into clinical practice and long-term management of type 2 diabetes.

This review has several limitations. First, this analysis is based on a limited number of published trials, which may not reflect ongoing or unpublished trials, and thus is prone to publication bias. Most of the available evidence comes from adults, and is scarce among adolescents and Asians. Furthermore, as it was a secondary review, this analysis could not control for changes in the study design, dietary composition, or cultural acceptability. These limitations indicate that this review provides a useful overview of the currentevidence base, but its conclusions should be interpreted with caution and updated as stronger evidence becomes available.

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