

Nutritional Interventions for Improving Insulin Resistance in Type 2 Diabetes Mellitus: A Comprehensive Narrative Review

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ABSTRACT

Type 2 diabetes mellitus is a metabolic disorder characterized by persistent hyperglycemia due to impaired insulin secretion and insulin resistance. Indonesia ranks among countries with the highest diabetes burden. Insulin resistance worsens glycemic control and increases cardiometabolic complications, making nutritional interventions promising non-pharmacological strategies. This narrative review synthesized evidence from 2020 to 2025 on nutritional interventions for improving insulin resistance in type 2 diabetes mellitus. A literature search was conducted in three databases using keywords. Articles were selected using the PICO framework and synthesized narratively. Ketogenic and low-carbohydrate diets reduced glycated hemoglobin, fasting glucose, and homeostatic model assessment of insulin resistance. Dietary fiber improved insulin sensitivity through gut microbiota modulation and increased short-chain fatty acid production. Probiotics and prebiotics improved glycemic control and reduced inflammation. The Mediterranean diet improved insulin resistance and reduced cardiometabolic risk. Chrononutrition helped suppress postprandial glycemia and improve insulin sensitivity. Nutritional interventions play a role in type 2 diabetes mellitus management by targeting insulin resistance through gut microbiota modulation, reduced inflammation and oxidative stress, and improved lipid metabolism. Low-carbohydrate, high-fiber diets, probiotic and prebiotic supplementation, the Mediterranean diet, and chrononutrition are promising adjunctive strategies, but long-term randomized controlled trials are needed to establish sustainability and safety.

Keyword : Chrononutrition; dietary fiber; gut microbiota; insulin resistance; ketogenic diet; Mediterranean diet; nutritional intervention; type 2 diabetes mellitus.

Introduction

Type 2 diabetes mellitus is a chronic non-communicable disease that has reached epidemic proportions worldwide. According to the International Diabetes Federation, an estimated 589 million adults aged 20 to 79 years were living with diabetes in 2024, equivalent to 11.1 percent of the global adult population. This number is projected to rise to 852 million by 2050 ¹. The burden is disproportionately high in low- and middle-income countries, where access to diagnosis and treatment remains limited. Indonesia ranks fifth globally in terms of diabetes prevalence, with approximately 20.4 million people living with diabetes in 2024. This figure is expected to increase to 28.6 million by 2050 ¹. The Indonesian Endocrinology Association reports that the prevalence of diabetes among adults aged 15 years and older has reached 11.7 percent, meaning more than one in ten Indonesian adults is affected. Alarming, approximately 73.2 percent of diabetes cases in Indonesia remain undiagnosed ². This silent epidemic increases the risk of serious complications, reduces quality of life, and imposes a substantial burden on the national health system.

Type 2 diabetes mellitus is characterized by chronic hyperglycemia resulting from a combination of impaired insulin secretion by pancreatic beta cells and insulin resistance in target tissues, primarily skeletal muscle, liver, and adipose tissue. Insulin resistance is defined as a diminished biological response to physiological concentrations of insulin. It precedes the onset of hyperglycemia and is a key driver of disease progression. The mechanisms underlying insulin resistance are multifactorial and include ectopic fat accumulation, chronic low-grade inflammation, oxidative stress, gut microbiota dysbiosis, and circadian rhythm disruption. Excess lipid deposition in liver and skeletal muscle interferes with insulin signaling pathways, leading to impaired glucose uptake and increased hepatic glucose production. Adipose tissue secretes pro-inflammatory cytokines such as tumor necrosis factor-alpha, interleukin-6, and C-reactive protein, which impair insulin signaling. Increased reactive oxygen species damage cellular components and interfere with insulin receptor substrate signaling. Alterations in the composition and function of gut microbiota can increase intestinal permeability, leading to endotoxemia and systemic inflammation. Dysbiosis also reduces the production of beneficial short-chain fatty acids, particularly butyrate, which play a role in maintaining insulin sensitivity. Misalignment between eating patterns and the body's internal clock can impair glucose metabolism and worsen insulin resistance. Insulin resistance not only worsens glycemic control but also increases the risk of long-term cardiometabolic complications, including cardiovascular disease, neuropathy, and nephropathy ³. Therefore, strategies to improve insulin sensitivity

are a cornerstone of type 2 diabetes mellitus management.

Nutritional interventions are fundamental to type 2 diabetes mellitus management. Unlike pharmacological therapies, which primarily target glycemic control, nutritional interventions can address the underlying mechanisms of insulin resistance, including inflammation, oxidative stress, and gut microbiota dysbiosis. Various dietary patterns have been studied for their potential to improve insulin sensitivity, including ketogenic diets, low-carbohydrate diets, high-fiber diets, probiotic and prebiotic supplementation, the Mediterranean diet, and chrononutrition. This review aims to provide a comprehensive synthesis of recent evidence from 2020 to 2025 on the effects of nutritional interventions on insulin resistance in type 2 diabetes mellitus, with a focus on underlying mechanisms and clinical implications.

Material and Methods

This study employed a comprehensive narrative review design. A narrative review was chosen to allow for a broad synthesis of diverse study designs, including randomized controlled trials, systematic reviews, meta-analyses, and observational studies, which collectively provide a holistic understanding of the topic. A systematic literature search was conducted in PubMed, ScienceDirect, and Google Scholar. The search was performed using keywords and Boolean operators related to the population, intervention, and outcome. The population terms included type 2 diabetes mellitus, T2DM, and diabetes mellitus type 2. The intervention terms included nutritional intervention, diet therapy, ketogenic diet, low-carbohydrate diet, dietary fiber, probiotics, prebiotics, Mediterranean diet, and chrononutrition. The outcome terms included insulin resistance, HOMA-IR, glycemic control, and glycated hemoglobin. The search was limited to articles published from 2020 to 2025, available as open-access full texts in English or Indonesian.

The PICO framework was used to guide article selection. The population was adults with type 2 diabetes mellitus. The intervention was nutritional interventions, including dietary patterns, specific nutrients, and supplements. The comparison was standard care, other dietary interventions, or placebo. The outcome was insulin resistance, measured for example by homeostatic model assessment of insulin resistance, or glycemic control, measured for example by glycated hemoglobin and fasting glucose. Inclusion criteria were original research articles or reviews discussing nutritional interventions in relation to insulin resistance in type 2 diabetes mellitus, published in accredited or indexed national or international journals, available in full text, and conducted in human populations. Exclusion criteria were conference proceedings, theses, dissertations, editorials, articles not available

in full text, and articles that discussed type 2 diabetes mellitus generally without addressing nutritional interventions and insulin resistance. Data were extracted from each included article, including author, year, study design, population, intervention, duration, outcomes, and key findings. Due to the heterogeneity of study designs and outcome measures, a narrative synthesis was performed. Findings were grouped by type of nutritional intervention. As this was a narrative review, no formal risk-of-bias assessment was performed, although the methodological quality of included studies was considered when interpreting the findings. Systematic reviews and meta-analyses were prioritized for evidence synthesis.

Results

The initial search yielded [isi jumlah] records. After removal of duplicates and screening of titles and abstracts, [isi jumlah] full-text articles were assessed for eligibility. Of these, 16 publications met the inclusion criteria and were included in the final synthesis. The key studies are summarized in **Table 1**.

Table 1. Characteristics of key studies on nutritional interventions and insulin resistance in T2DM

Author (Year)	Study Design	Population	Intervention	Duration	Outcomes	Key Findings
Yuan et al. (2020) ³	Systematic review & meta-analysis	Adults with T2DM	Ketogenic diet	4–24 weeks	HbA1c, fasting glucose, HOMA-IR, lipid profile	Significant reductions in HbA1c and HOMA-IR; increased HDL
Putri Herada et al. (2022) ⁴	Scoping review	Adults with T2DM	Low-carbohydrate ketogenic diet	8–24 weeks	Blood glucose, body weight, insulin sensitivity	glucose and body weight; improved insulin sensitivity
Ojo et al. (2020) ⁵	Systematic review & meta-analysis	Adults with T2DM	High fiber/soluble fiber	4–12 weeks	HOMA-IR, gut microbiota, butyrate	Reduced insulin resistance; increased SCFA/butyrate
Wang et al. (2023) ⁶	Review	Adults with T2DM	Probiotics and prebiotics	6–12 weeks	HbA1c, fasting glucose,	Significant reductions in HbA1c and

Pavlidou et al. (2024) ⁷	Review	Adults with T2DM obesity	with and Mediterranean diet	≥12 weeks	HOMA-IR	HOMA-IR
					Body weight, HOMA-IR, lipid profile	Improved insulin sensitivity and weight loss
Papakonstantinou et al. (2022) ⁸	Review	Adults with T2DM	Diet, lifestyle, chrononutrition	4–16 weeks	Postprandial glycemia, HOMA-IR	Meal timing reduced postprandial glycemia and insulin resistance
Angga (2022) ⁹	Literature review	Adults with T2DM	Dietary management and nutrition education	Not specified	Glycemic control, nutritional fulfillment	Dietary management is a key pillar in T2DM care

The ketogenic diet, characterized by very low carbohydrate intake (<50 g/day) and high fat intake, has gained attention for its potential to improve glycemic control. A systematic review and meta-analysis by Yuan et al. (2020) reported that ketogenic diets significantly reduced HbA1c, fasting glucose, and HOMA-IR in patients with T2DM ³. These effects were accompanied by improvements in lipid profiles, including increased HDL cholesterol. A scoping review by Putri Herada et al. (2022) supported these findings but noted heterogeneity in study designs and relatively short intervention durations ⁴. The proposed mechanisms include reduced hepatic glucose production, increased insulin sensitivity in skeletal muscle, and weight loss.

Dietary fiber, particularly soluble fiber, has been shown to improve insulin sensitivity. A systematic review and meta-analysis by Ojo et al. (2020) found that fiber intake significantly reduced HOMA-IR in patients with T2DM ⁵. The mechanisms involve modulation of gut microbiota, increased production of SCFAs (especially butyrate), and reduced systemic inflammation. Butyrate serves as an energy source for colonocytes, enhances intestinal barrier function, and reduces translocation of lipopolysaccharides (LPS), thereby decreasing inflammation and improving insulin signaling.

Probiotics (live beneficial bacteria) and prebiotics (non-digestible fibers that feed beneficial bacteria) have emerged as potential adjunctive therapies for T2DM. A review by Wang et al. (2023) reported that supplementation with probiotics and prebiotics significantly reduced HbA1c and HOMA-IR in patients with T2DM ⁶. These effects are mediated through modulation of gut microbiota composition, increased SCFA production, and reduced

inflammation. Synbiotics, which combine probiotics and prebiotics, may offer synergistic benefits.

The Mediterranean diet is characterized by high intake of olive oil, fruits, vegetables, whole grains, legumes, nuts, and fish, with moderate consumption of dairy and red wine. It is rich in MUFA, PUFA, fiber, and polyphenols. A review by Pavlidou et al. (2024) found that the Mediterranean diet consistently improved insulin sensitivity and reduced body weight in patients with T2DM and obesity ⁷. The mechanisms include anti-inflammatory effects, reduced oxidative stress, and improved lipid profiles. Polyphenols, such as oleuropein in olive oil and resveratrol in red grapes, have been shown to activate AMP-activated protein kinase (AMPK) and improve glucose uptake.

Chrononutrition refers to the alignment of eating patterns with circadian rhythms. A review by Papakonstantinou et al. (2022) reported that meal timing interventions, such as consuming the largest meal earlier in the day and avoiding late-night eating, reduced postprandial glycemia and insulin resistance in patients with T2DM ⁸. The mechanisms involve improved synchronization of peripheral clocks in metabolic tissues, enhanced insulin secretion, and better glucose tolerance. **Table 2** show the effect of nutritional interventions in insulin resistance on human body.

Table 2. Summary of effects of nutritional interventions on insulin resistance markers

Intervention	HbA1c	Fasting Glucose	HOMA-IR	Other Benefits
Ketogenic diet	↓↓	↓↓	↓↓	↑ HDL, weight loss
Low-carbohydrate diet	↓	↓	↓	Weight loss
Dietary fiber	↓	↓	↓	↑ SCFA, improved gut microbiota
Probiotics/prebiotics	↓	↓	↓	Reduced inflammation
Mediterranean diet	↓	↓	↓↓	Weight loss, improved lipids
Chrononutrition	↔/↓	↓	↓	Reduced postprandial glycemia

Legend: ↓ = decrease; ↓↓ = significant decrease; ↔ = no significant change.

Nutrition education and behavioral interventions are essential for translating dietary recommendations into practice. A literature review by Kusuma (2022) emphasized that dietary management remains a key pillar of T2DM care in Indonesia ⁹. Behavioral interventions, such as self-management education, have been shown to improve adherence and glycemic control ¹⁰. Folic acid supplementation has also been reported to support glycemic control, although its direct effect on insulin resistance remains limited ^{11,12}.

Discussion

The beneficial effects of nutritional interventions on insulin resistance are mediated through several interconnected mechanisms. The gut microbiota plays a critical role in host metabolism. In type 2 diabetes mellitus, dysbiosis is characterized by reduced diversity and an altered ratio of Bacteroidetes to Firmicutes. Dietary fiber, probiotics, and prebiotics can restore microbial balance, leading to increased production of short-chain fatty acids, particularly butyrate, propionate, and acetate. Butyrate enhances insulin sensitivity by activating G-protein-coupled receptors that stimulate glucagon-like peptide-1 secretion, inhibiting histone deacetylases leading to anti-inflammatory effects, and strengthening intestinal barrier function, thereby reducing endotoxemia ¹³.

Chronic low-grade inflammation is a hallmark of type 2 diabetes mellitus. Nutritional interventions can reduce inflammation by decreasing pro-inflammatory cytokines such as tumor necrosis factor-alpha, interleukin-6, and C-reactive protein, increasing anti-inflammatory cytokines such as interleukin-10, and providing antioxidants such as polyphenols and vitamins that neutralize reactive oxygen species and reduce oxidative damage. The Mediterranean diet is particularly rich in polyphenols and antioxidants, which may explain its consistent benefits for insulin resistance ¹³.

Excess ectopic fat in liver and skeletal muscle contributes to insulin resistance. Weight loss induced by ketogenic and low-carbohydrate diets reduces ectopic fat, improves hepatic insulin sensitivity, and enhances muscle glucose uptake. The Mediterranean diet also promotes weight loss and improves lipid profiles. Circadian clocks regulate glucose metabolism, insulin secretion, and insulin sensitivity. Misalignment, such as eating late at night, can impair these processes. Chrononutrition interventions, such as time-restricted eating and front-loading calories, help synchronize peripheral clocks and improve glycemic control ¹⁴.

While all reviewed interventions showed some benefit, the magnitude of effect varied. Ketogenic and low-carbohydrate diets produced the most rapid and pronounced reductions in glycated hemoglobin and homeostatic model assessment of insulin resistance, but concerns remain about long-term adherence and safety. The Mediterranean diet offers a more sustainable approach with comprehensive cardiometabolic benefits. Dietary fiber, probiotics, and prebiotics are safe, well-tolerated, and can be easily incorporated into existing diets. Chrononutrition is a promising adjunct but requires further research ¹⁵.

Based on the evidence, practical recommendations can be made for patients with type 2 diabetes mellitus. Reducing refined carbohydrate intake and considering a low-

carbohydrate or ketogenic diet under medical supervision may be beneficial. Increasing dietary fiber intake to twenty-five to thirty-five grams per day, with an emphasis on soluble fiber from oats, barley, legumes, and fruits, is recommended. Including probiotic-rich foods such as yogurt, kefir, and fermented vegetables, as well as prebiotic foods such as garlic, onions, bananas, and whole grains, may support gut health. Adopting a Mediterranean-style diet rich in olive oil, nuts, fish, fruits, and vegetables is advisable. Practicing chrononutrition by consuming the largest meal earlier in the day and avoiding late-night eating may help. Participating in nutrition education and behavioral support programs can enhance adherence¹⁶.

This review has several limitations. As a narrative review, it lacks the methodological rigor of a systematic review, including formal risk-of-bias assessment and meta-analysis. The included studies were heterogeneous in design, population, intervention duration, and outcome measures, limiting comparability. Most studies had short follow-up periods, so long-term sustainability and safety are unknown. Publication bias may have influenced the findings, as positive results are more likely to be published. The review focused primarily on English and Indonesian literature, potentially missing relevant studies in other languages.

Future research should conduct long-term randomized controlled trials lasting at least twelve months to evaluate sustainability and safety. Standardized outcome measures, including homeostatic model assessment of insulin resistance, glycated hemoglobin, and inflammatory markers, should be used. The synergistic effects of combining multiple interventions, such as diet with probiotics and chrononutrition, should be investigated. The role of personalized nutrition based on gut microbiota profiling should be explored. Culturally tailored interventions for specific populations, such as Indonesia, should be developed.

Conclusion

Nutritional interventions play a crucial role in the management of type 2 diabetes mellitus by improving insulin resistance and metabolic control. Effective strategies include low-carbohydrate, high-fiber diets, probiotic and prebiotic supplementation, the Mediterranean diet, and chrononutrition. These interventions work through multiple mechanisms, including modulation of gut microbiota, reduction of inflammation and oxidative stress, and improvement of lipid metabolism. Nutrition education and behavioral support are essential for successful implementation. Although current evidence is promising, long-term studies are needed to assess sustainability and safety. Nutritional interventions should complement pharmacotherapy within an integrated, culturally appropriate approach.

Declaration of Generative AI in Scientific Writing

The authors affirm that the usage of generative artificial intelligence tools, including Open AI (Chat GPT), is intended solely for improvement and refinement the manuscript. These tools were not used for generating content, data analysis, or interpretation. The authors are fully responsible for the accuracy and integrity of the content as well as the conclusions presented in this study

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