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Metabolic improvements associated with low-carbohydrate diet in overweight and obese adults: Contributions to public health nutrition

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Abstract

Background: Overweight (OW) and obesity (OB) are major public health challenges associated with metabolic disorders, chronic diseases, and rising healthcare costs. Low-carbohydrate diets (LCDs) have emerged as cost-effective strategies for prevention and treatment. **Objective:** The objective of the study is to evaluate the effects of an LCD (≤130 g/day) on anthropometric, metabolic, hepatic, and renal parameters in OW and obese adults over 12 months. **Methods:** This open-label, non-randomized, self-controlled clinical trial included 34 adults with body mass index (BMI) ≥ 25 kg/m^2 who received individualized nutritional counseling and followed an LCD for up to 12 months. Clinical and laboratory parameters were assessed at baseline and during follow-up (3–6 months and 7–12 months). Statistical analyses included generalized estimating equations and non-parametric tests with Bonferroni correction. **Results:** Participants achieved a mean weight loss of 10%, with reductions in BMI (–2.9 kg/m^2), waist circumference (–5.4 cm), and body fat percentage. Glycated hemoglobin decreased at 7–12 months ($p<0.05$), while insulin levels and insulin resistance declined at 3–6 months ($p=0.0497$ and $p=0.037$). Fasting glucose remained stable. Low-density lipoprotein cholesterol increased modestly at 7–12 months ($p=0.035$), whereas other lipid parameters showed no significant changes. Gamma-glutamyl transferase levels decreased ($p=0.0341$), with no adverse effects on renal or hepatic markers. **Conclusion:** An LCD was associated with improvements in glycemic control, body composition, insulin sensitivity, and liver enzymes without compromising renal function or lipid profiles, supporting its role in OB management and cardiometabolic risk reduction in primary care.

Keywords: Low-carbohydrate diet; Overweight; Obese; Metabolic health; Nutrition; Diet

1. Introduction

Obesity (OB) and overweight (OW) are global epidemics associated with adverse health outcomes and high healthcare costs.[1,2] According to the World Health Organization (WHO), more than 2.5 billion adults are OW, of whom 890 million are living with OB.[3] Approximately one in eight people globally has OB.[3] In the United States, the prevalence of OB is currently estimated at 41.9%,[4] and OB-related conditions have reached unprecedented levels. Nearly one in 10 Americans has type 2 diabetes (T2DM), and approximately 48.6% of adults live with some form of cardiovascular disease (CVD).[5] In Brazil, data from the Telephone-based Survey on Risk and Protective Factors for Chronic Diseases, coordinated by the Ministry of Health, revealed a striking 96% increase in OB prevalence over a 15-year period—from 11.8% in 2006 to 22.4% in 2021.[6]

This burden also extends to children and adolescents. In the Americas, the prevalence of OW and OB among this population is approximately 20–25%.[7] A survey by the Brazilian Institute of Geography and Statistics from 2008 to 2009 reported that the prevalence of OW and OB in the Brazilian population increased by about 50%.[8] In 2019, the Brazilian Ministry of Health reported that 55.4% of the population had excess weight and 20.3% were obese.[9] Globally, over 390 million children and adolescents aged 5–19 years were OW in 2022, including 160 million with OB, and in 2024, 35 million children under five were OW.[3] Moreover, the sustained prevalence of OB may reduce life expectancy in future generations.[10]

OB is a multifactorial condition influenced by biological, genetic, historical, economic, and sociocultural factors.[3] This epidemic represents one of the greatest public health challenges of the 21st century and is the fastest-growing nutritional problem globally.[11,12] It affects both developed and developing countries and contributes to the rise in non-communicable diseases (NCDs), increasing overall morbidity and mortality.[12,13] OW and OB are commonly classified using body mass index (BMI), which is applied to adults,[14] children and adolescents,[15] elderly individuals,[16] and pregnant women.[17] A high BMI is a well-established risk factor for NCDs, mental health disorders such as depression, and reduced quality of life. The global rise in OB is multifactorial, driven by a complex interplay of sociodemographic, economic, environmental, physiological, and psychosocial determinants. In Latin America, particularly in Brazil, these factors are compounded by rapid urbanization, increasing sedentary lifestyles, and shifts in dietary patterns toward greater consumption of ultra-processed foods. Such dynamics have significantly contributed to the acceleration of OB prevalence in recent decades.[1]

The major consequences of OB include a heightened risk of developing NCDs, many of which are directly associated with poor dietary habits. In Brazil, NCDs linked to inadequate nutrition have a substantial impact on mortality and morbidity, accounting for approximately 71% of all deaths. Among these, the four primary categories of nutrition-related NCDs were responsible for 55% of total deaths.[18] NCDs also remain the leading cause of premature mortality (ages 30–69), accounting for 37% of deaths in the 30–49 age group and 65% in individuals aged 50–69 years.[18] The main NCDs associated with OB and poor metabolic health include T2DM, non-alcoholic fatty liver disease (NAFLD), gout, obstructive sleep apnea, CVDs, musculoskeletal and orthopedic disorders, Alzheimer's disease, and various types of cancer.[19,20]

Between 2011 and 2022, Brazil implemented the National Plan for Tackling Non-Communicable Diseases, which established 12 strategic goals aimed at promoting the development and implementation of effective, integrated, and evidence-based public policies for the prevention and control of NCDs and their main risk factors, including OB. Building on this initiative, the current Plan for the Prevention and Control of Chronic Non-Communicable Diseases in Brazil (2021–2030) outlines 226 strategic actions to be implemented at the federal, state, and municipal levels. These actions include reducing alcohol and tobacco consumption, promoting healthy eating habits, and encouraging physical activity.[21] Given the substantial personal, social, and economic burden of NCDs, especially in low- and middle-income countries, prioritizing preventive measures is imperative. In Brazil, a country marked by pronounced regional and territorial inequalities, strengthening preventive strategies is not only a matter of public health efficiency but also a critical step toward reducing inequities in access to health services and opportunities for well-being. Investments in early intervention and health promotion are therefore essential to mitigate the growing impact of chronic diseases and to build more resilient and equitable health systems.

OB is characterized by chronic, low-grade inflammation of white adipose tissue (WAT), which plays a central role in the development of systemic metabolic dysfunctions (Figure 1). Excessive expansion of WAT leads to structural and functional alterations that compromise local oxygen supply. As adipocytes undergo hypertrophy, the decreased distance between cells and capillaries results in tissue hypoxia. This hypoxic microenvironment activates hypoxia-inducible factor 1-alpha, which promotes fibrotic remodeling and induces the expression of pro-inflammatory genes.[22,23] These processes facilitate the infiltration of immune cells, particularly macrophages,

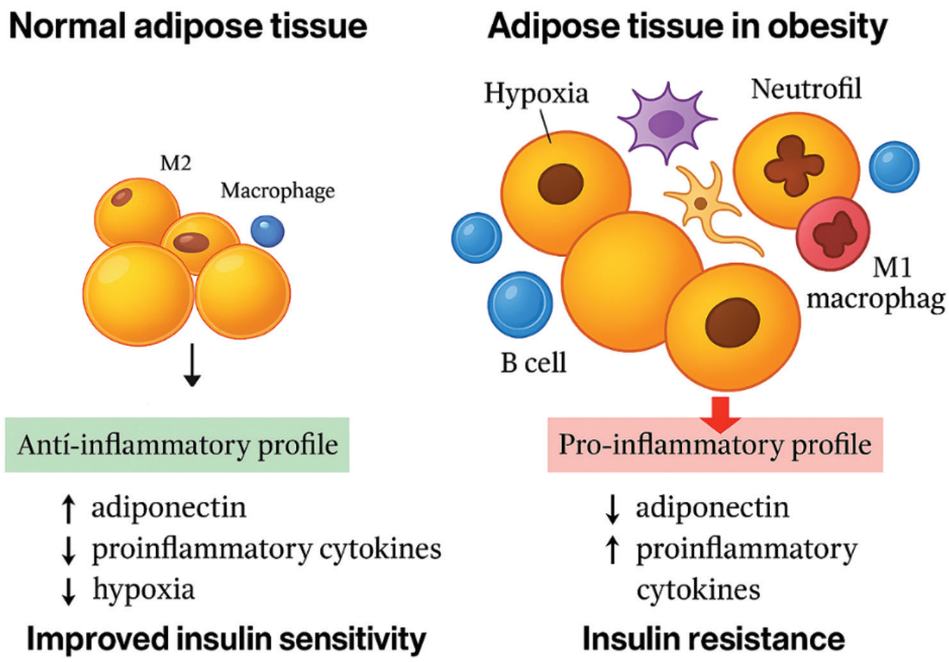

Figure 1. Comparison of normal and obese adipose tissue and their effects on insulin sensitivity. Left: Normal adipose tissue exhibits an anti-inflammatory profile characterized by the predominance of M2 macrophages, higher adiponectin levels, lower leptin levels, and minimal hypoxia, contributing to improved insulin sensitivity. Right: Obese adipose tissue is characterized by hypertrophied and necrotic adipocytes, infiltration of neutrophils and B cells, and a predominance of pro-inflammatory M1 macrophages. These alterations are associated with reduced adiponectin levels, increased hypoxia, chronic inflammation, and the development of systemic insulin resistance.

which shift from an anti-inflammatory M2 phenotype to a pro-inflammatory M1 profile, contributing to the sustained production of cytokines such as tumor necrosis factor-α, interleukin-6, and monocyte chemoattractant protein-1. This inflammatory response is further amplified by elevated levels of triglycerides (TG) and free fatty acids, which exacerbate cytokine expression and insulin resistance.[24-26] A hallmark of dysfunctional adipose tissue in OB is the increased rate of adipocyte death through multiple mechanisms, including apoptosis, necrosis, pyroptosis, and ferroptosis.[27] Dying adipocytes release damage-associated molecular patterns and lipids, which further stimulate immune cell recruitment. Macrophages surround these dead cells, forming crown-like structures, where they facilitate lipid clearance while amplifying local inflammation through the release of pro-inflammatory mediators. The resulting activation of innate immune pathways and sustained shift toward a pro-inflammatory cellular environment establishes a self-perpetuating inflammatory loop. This loop not only impairs adipose tissue homeostasis but also contributes to systemic insulin resistance, T2DM, and hepatic steatosis.[27]

Nutritional therapy remains the cornerstone of managing OW and OB, with the primary goals of preventing associated complications such as liver damage, chronic kidney disease, and cardiovascular events. Numerous dietary strategies have been explored, with particular focus on carbohydrate and fat restriction—approaches that have gained popularity over the past few decades for both disease management and weight control.[28,29] Low-carbohydrate diets (LCDs) have been studied since at least 1872, when limiting foods rich in starch and sugar was first recommended for individuals with OB.[30] In 1943, Cutting[31] demonstrated the effectiveness of restricting bread, potatoes, and sweets in promoting weight loss. The Atkins diet, which emphasizes carbohydrate restriction alongside increased protein and fat intake to stimulate fat mobilization, has been in use for more than 45 years.[32,33] Although dietary recommendations vary, multiple studies have consistently demonstrated the effectiveness of LCDs in promoting weight loss and improving glycemic control.[34-36] Recent consensus among nutrition and health experts highlights the growing body of evidence supporting LCD patterns as effective strategies for improving key risk factors associated with insulin resistance and CVD. Given the high prevalence of nutrition-related chronic conditions, particularly among adults, experts have proposed the inclusion of lower-carbohydrate approaches into official dietary recommendations as a means of broadening preventive strategies and promoting health equity at the population level.[37]

Currently, there is no universally accepted definition of a "low-carbohydrate" diet within the scientific community. While the Acceptable Macronutrient Distribution Range recommends that carbohydrates make up 45–65% of total daily energy intake,[38] and the Recommended Dietary Allowance establishes a reference intake of 130 g/day for all age and sex groups. This recommendation is primarily based on the estimated average glucose requirement of the brain. However, scientific evidence shows that the brain is metabolically adaptable and capable of utilizing alternative energy substrates, such as ketone bodies, and that glucose can be synthesized endogenously through gluconeogenesis.[34-36] These findings challenge the notion that dietary carbohydrate is essential in fixed amounts, and the absence of a standardized definition continues to hinder the development of consistent dietary recommendations for low-carbohydrate dietary patterns.

LCDs typically involve reducing carbohydrate intake and increasing protein and fat intake in appropriate proportions.[39,40] Such diet patterns have been associated with reductions in TG, abdominal fat, glycated hemoglobin (HbA1c), and circulating insulin levels, as well as increases in high-density lipoprotein (HDL) cholesterol levels.[41,42] Alterations in macronutrient distribution lead to lower serum insulin and higher serum glucagon levels.[43,44] This promotes gluconeogenesis[44] and mobilization of fatty acids from adipose tissue, with potential downstream effects on hepatic metabolism.[44] Overall, these metabolic adaptations favor reduced insulin secretion, enhanced fat oxidation, and the use of fat as a primary energy source while preserving lean body mass.[45] Although protein can also raise insulin levels, it concurrently increases glucagon levels, thereby supporting lipolysis.[46] This study aims to generate evidence on the practical implementation of LCDs in primary care settings, focusing on their medium-term effects (12 months) on metabolic health in the absence of pharmacological interference. Specifically, we evaluated the effects of an LCD (≤130 g/day) on anthropometric, metabolic, hepatic, and renal parameters in OW and OB adults over a 12-month intervention period.

2. Materials and methods

2.1. Study design and subjects

This study was designed as an open-label, non-randomized, self-controlled clinical trial, conducted according to a prespecified protocol between March 2019 and January 2021. Participants were recruited from a single integrated healthcare center located in Belo Horizonte, Brazil.

Inclusion criteria included men and women aged 18 years or older with a BMI classified as OW (25.0–29.9 kg/m^2) or obese (≥30.0 kg/m^2). To be eligible, participants were required to attend at least two of the three clinical visits and corresponding laboratory assessments scheduled throughout the study period.

Three evaluation time points were defined for the assessment of clinical and laboratory parameters: Time 0 (baseline), Time 1 (3–6 months), and Time 2 (7–12 months). The first re-evaluation involved a comparison of data between baseline and time 1. The second re-evaluation included comparisons across all three time points (baseline, time 1, and time 2).

Exclusion criteria included individuals under 18 years of age, BMI < 25 kg/m^2, diagnosed with thalassemia or type 1 diabetes mellitus, current participation in other nutritional intervention programs, or prior adherence to a LCD (<130 g/day) before enrollment. In addition, participants who reported non-adherence to the dietary recommendations or who failed to complete the scheduled anthropometric and biochemical evaluations were also excluded. All physical examinations were conducted at the clinic located in Belo Horizonte. Blood samples were analyzed by certified laboratories within the same city, each operating under standardized quality protocols established by regulatory authorities.

All participants provided written informed consent before participation. The study was approved by the local research ethics committee and conducted in accordance with the Brazilian National Health Council guidelines under the CEP/CONEP system (approval number: 4.961.640; CAAE: 49593220.4.0000.5149). This study was registered at the Brazilian Registry of Clinical Trials (ReBEC) (registration no.: RBR-107jk4tn, UTN no.: U1111-1270-4313, registry link: https://ensaiosclinicos.gov.br/rg/RBR-107jk4tn) before participant enrollment.

2.2. Dietary interventions

A preliminary set of dietary education materials was collaboratively developed by the research physician and the registered dietitian involved in the study. These materials were designed to support participants in adopting an LCD pattern and included a structured meal planner, practical dietary recommendations, sample menus, nutritional information on commonly consumed foods, and specific guidance on foods to limit or avoid. During the baseline visit, each participant received individualized dietary counseling tailored to their specific needs, preferences, and metabolic profile. This counseling session served to clarify the objectives of the dietary intervention and to ensure understanding and adherence.

Given that the three macronutrients—carbohydrates (4 kcal/g), fat (9 kcal/g), and protein (4 kcal/g)—contribute differently to total energy intake, LCDs have been defined either by the percentage of total daily energy derived from carbohydrates or by absolute daily carbohydrate intake. Accordingly, they are commonly categorized as follows: Very LCDs (<10% of daily energy from carbohydrates or 20–50 g/day); LCDs (<26% of daily energy from carbohydrates or <130 g/day); moderate-carbohydrate diets (26–44% of daily energy from carbohydrates); and high-carbohydrate diets (≥45% of daily energy from carbohydrates) (Figure 2).

In this study, dietary guidance emphasized the inclusion of healthy, minimally processed fat sources as part of the low-carbohydrate approach. Participants were encouraged to consume olive oil, avocado, nuts, seeds, whole-fat dairy products such as yogurt, and naturally fatty fish as primary components of their meals, while limiting or avoiding industrial seed oils and ultra-processed fats. This strategy prioritized fat quality and natural origin of fats rather than restricting specific fat subtypes, with the aim of promoting satiety, metabolic flexibility, and long-term adherence to the dietary plan. Participants were instructed to maintain this dietary pattern throughout the study period and to report any difficulties or deviations during follow-up visits.

2.3. Biochemical parameters and anthropometric measurements

Biochemical and anthropometric data were collected at all three evaluation points: baseline (pre-intervention), Time 1 (3–6 months), and Time 2 (7–12 months). Biochemical analyses included fasting glucose, HbA1c, fasting insulin, total cholesterol (TC), low-density lipoprotein cholesterol (LDL cholesterol), HDL cholesterol, TG, creatinine, urea, gamma-glutamyl transferase (GGT), aspartate aminotransferase (AST), and alanine aminotransferase (ALT). Blood samples were obtained after an overnight fast and analyzed in certified laboratories using standard methods. Insulin resistance was estimated using the homeostatic model assessment of insulin resistance (HOMA-IR), calculated as follows:

$$\text{HOMA-IR} = (\text{fasting insulin } [\mu U/mL] \times \text{fasting glucose } [mg/dL])/405 \quad (1)$$

Anthropometric assessments included body weight, height, and waist circumference. BMI was calculated as weight in kilograms divided by height in meters squared (kg/m^2). All measurements were conducted by trained professionals using standardized procedures to ensure consistency and accuracy throughout the study period. Body fat percentage was assessed using bioelectrical impedance analysis with an InBody 270 body composition analyzer (InBody Asia, South Korea). Measurements were performed with participants standing upright and barefoot, according to the manufacturer's instructions. The resulting data were used to estimate body composition.

2.4. Risk evaluations

Risk assessments were performed to estimate potential comorbidities associated with OW and OB, with a particular focus on renal and CVD. Renal function was evaluated by estimating the glomerular filtration rate (eGFR), calculated using the Chronic Kidney Disease Epidemiology Collaboration formula, as implemented in

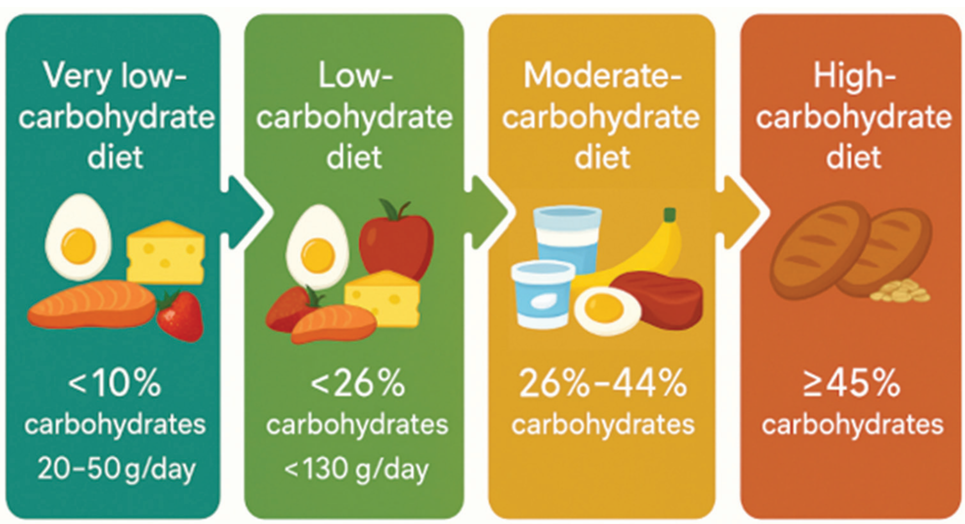

Figure 2. Classification of low-carbohydrate diets. A very low-carbohydrate diet provides <10% of daily energy or 20–50 g/day; a low-carbohydrate diet provides <26% of daily energy or <130 g/day; a moderate-carbohydrate diet provides 26–44% of daily energy; a high-carbohydrate diet provides ≥45% of daily energy, illustrated by the presence of large bread portions and grains. The progression visually demonstrates the increase in carbohydrate content and associated food choices across diet types.

the National Kidney Disease Education Program calculator (nkdep.nih.gov).

Cardiovascular risk was assessed using lipid profile-derived ratios, including the TC to HDL cholesterol ratio (TC/HDL) and the TG to HDL cholesterol ratio (TG/HDL), which serve as surrogate markers of atherogenic risk. In addition, the risk of atherosclerotic CVD (ASCVD) was estimated using the ASCVD Risk Estimator Plus, developed by the American College of Cardiology (available at www.acc.org). For participants younger than 40 years, the tool provided an estimate of lifetime ASCVD risk, while for those aged 40 years or older, the estimate reflected the 10-year ASCVD risk. Together, these tools allowed for a comprehensive evaluation of cardiometabolic health and long-term disease risk within the study population.

2.5. Statistical analysis

Data were analyzed using Python version 3.11 with the SciPy and Matplotlib libraries. The normality of continuous variables was assessed using the Shapiro–Wilk test. As most variables did not follow a normal distribution, non-parametric tests were applied. Comparisons across the three time points—Time 0 (baseline), Time 1 (3–6 months), and Time 2 (7–12 months)—were performed using the Friedman test for repeated measures. Although the timing of Time 1 assessments varied slightly among participants, with most evaluations occurring at months 5 or 6 and a small number at month 3, this variability was addressed using statistical methods robust to within-subject timing differences. When overall statistical significance was observed ($p<0.05$), *post hoc* pairwise comparisons were conducted using the Wilcoxon signed-rank test with Bonferroni correction. Generalized estimating equations were also used to support longitudinal analyses. Results are presented as mean ± standard deviation, and statistical significance was defined as $p<0.05$. Graphical representations were generated as box plots displaying individual data points, mean lines, and significance bars marked with asterisks, where applicable.

3. Results

The baseline characteristics of the enrolled participants are presented in Table 1. 203 individuals were excluded based on the predefined inclusion and exclusion criteria, and a total of 34 participants (10 men and 24 women), with a mean age of 44.8 ± 10.5 years, were included in the study. By the second follow-up, 15 participants were unable to complete the protocol within the defined schedule. Endocrinology clinic follow-up visits occurred, on average, at approximately 5 and 12 months after baseline.

Data are presented as mean ± standard deviation and median. A total of 34 participants (10 men and 24 women) were included after applying the inclusion and exclusion criteria. The mean age of the cohort was 44.8 ± 10.5 years. Fifteen participants did not complete the second follow-up within the defined study period.

Table 1. Baseline biochemical and anthropometric characteristics of study participants

Biochemical and anthropometric characteristics	Results	
	$\bar{x}$ ±SD	Median
Fasting glucose (mg/dL)	88.3±8.7	88.7
HbA1c (%)	5.3±0.3	5.3
Serum insulin (µU/mL)	9.9±4.6	8.8
HOMA-IR	2.1±0.9	2.1
TC (mg/dL)	215.0±53.0	221.0
LDL (mg/dL)	133.7±33.8	134.0
HDL (mg/dL)	58.8±17.2	54.0
TG (mg/dL)	106.9±73.5	82.0
TC/HDL	3.8±0.9	3.8
TG/HDL	2.0±1.4	1.6
Creatinine (mg/dL)	0.8±0.1	0.8
Urea (mg/dL)	34.6±8.2	34.5
GGT (U/L)	30.8±30.7	16.5
AST (U/L)	23.5±9.7	20.0
ALT (U/L)	25.2±12.9	21.5
BMI (kg/m^2)	30.6±4.6	28.8
Weight (kg)	84.9±15.8	81.1
WC (cm)	98.2±13.2	94.5

Abbreviations: ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; BMI: Body mass index; GGT: Gamma-glutamyl transferase; HbA1c: Glycated hemoglobin; HDL: High-density lipoprotein; HOMA-IR: Homeostatic model assessment of insulin resistance; LDL: Low-density lipoprotein; TC: Total cholesterol; TG: Triglycerides; WC: Waist circumference; $\bar{x}$±SD: Mean±standard deviation.

Throughout the 12-month follow-up period, a consistent and statistically significant reduction in body weight (Figure 3A) was observed across all time points. Median body weight decreased progressively from baseline to Time 1 (3–6 months), and further to Time 2 (7–12 months), with statistically significant differences between each consecutive time point ($p<0.05$) for all comparisons. Similarly, body fat percentage also showed a sustained decline over time, with significant reductions from baseline to both Time 1 and Time 2. Notably, a statistically significant difference was also observed between Time 1 and Time 2 ($p=0.0421$), indicating continued improvement beyond the initial 6 months. BMI decreased by an average of 2.9 points, corresponding to an average weight loss of 8.24 kg (Figure 3B). By the end of the

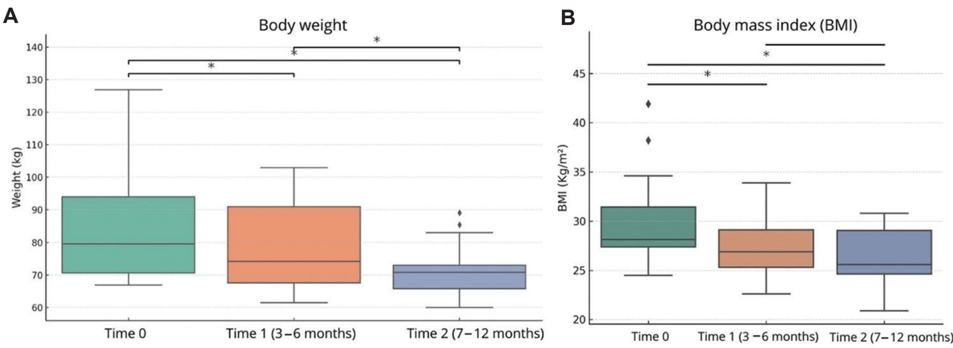

Figure 3. Anthropometric outcomes at three time points: Time 0 (baseline), Time 1 (3–6 months), and Time 2 (7–12 months). (A) Body weight: Significant reduction was observed between Time 0 and Time 1 (p=0.0004), Time 0 and Time 2 (p<0.0001), and Time 1 and Time 2 (p=0.0022). (B) Body mass index: Significant reduction was observed between Time 0 and Time 1 (p=0.0156), Time 0 and Time 2 (p=0.0022), and Time 1 and Time 2 (p=0.0421).
Notes: Statistical analysis was performed using the Friedman test followed by pairwise comparisons with Bonferroni correction. ♦ indicates the outliers. * denotes statistically significant at p<0.05.

study, participants achieved an average weight loss of 10% compared with baseline. At baseline, 29.2% of participants were classified as OB and 70.8% as OW. After 12 months, only 4.2% remained OB, 58.3% were OW, and 37.5% had reached a normal (eutrophic) weight range.

Fasting glucose levels remained relatively stable throughout the study period, with no statistically significant differences among the three time points (p=0.139) (Figure 4A). In contrast, HbA1c levels showed a statistically significant reduction between Time 0 and Time 2 (p=0.042), indicating improved long-term glycemic control (Figure 4B). Serum insulin levels also decreased significantly between Time 0 and Time 2 (p=0.0497), suggesting enhanced insulin sensitivity (Figure 4C). Notably, HOMA-IR, a surrogate marker for insulin resistance, exhibited a significant decline as early as between Time 0 and Time 1 (p=0.037), with a trend toward further improvement by time 2 (p=0.053) (Figure 4D). Collectively, these findings suggest that the intervention exerted a favorable effect on metabolic markers related to glycemic regulation and insulin resistance.

The lipid profile analysis is summarized in Figure 5. No statistically significant changes were observed in TC, HDL cholesterol, or TG levels throughout the study period (Figure 5A, B, and D), suggesting that the intervention did not adversely affect these major lipid parameters. However, a modest but statistically significant increase in LDL cholesterol level was detected between Time 0 and Time 2 (7–12 months; p=0.035), as shown in Figure 5C. Importantly, lipid ratios, including TC/HDL cholesterol and TG/HDL cholesterol, which are often considered stronger predictors of cardiovascular risk than individual lipid parameters, did not differ significantly across the time points (Figure 5E and F). Overall, these findings indicate a relatively stable lipid profile and suggest that, despite the observed increase in LDL cholesterol, the dietary or therapeutic intervention did not negatively impact cardiovascular lipid risk markers.

Renal and hepatic function markers are presented in Figure 6. No statistically significant changes were observed in serum creatinine (p=0.626; Figure 6A) or urea levels (p=0.517; Figure 6B) across the three time points, as determined by the Friedman test followed by Bonferroni-corrected pairwise comparisons. These findings suggest that the dietary intervention did not adversely affect renal function. Regarding hepatic biomarkers, GGT levels showed a statistically significant reduction from baseline to 12 months (p=0.0341; Figure 6C), which may indicate a reduction in hepatic metabolic stress. In contrast, no significant changes were observed in AST or ALT levels (p=0.958 and p=0.9854, respectively; Figure 6D and E), suggesting preservation of hepatocellular integrity throughout the intervention period.

Finally, at Time 1 (3–6 months), the proportion of patients using antihypertensive medications decreased from 20.6% to 11.8%. This reduction suggests a potential improvement in blood pressure control, possibly related to lifestyle modifications or metabolic benefits associated with the intervention. Although blood pressure measurements were not the primary endpoint of the study, the reduced reliance on pharmacological treatment may reflect a clinically meaningful response. This observation is particularly relevant in the context of OB-related hypertension, which is commonly associated with insulin resistance, chronic low-grade inflammation, and endothelial dysfunction. Improvements in dietary habits, weight loss, and reductions in visceral adiposity may have contributed to enhancing vascular function and blood pressure regulation, thereby reducing the need for antihypertensive agents in a subset of participants.

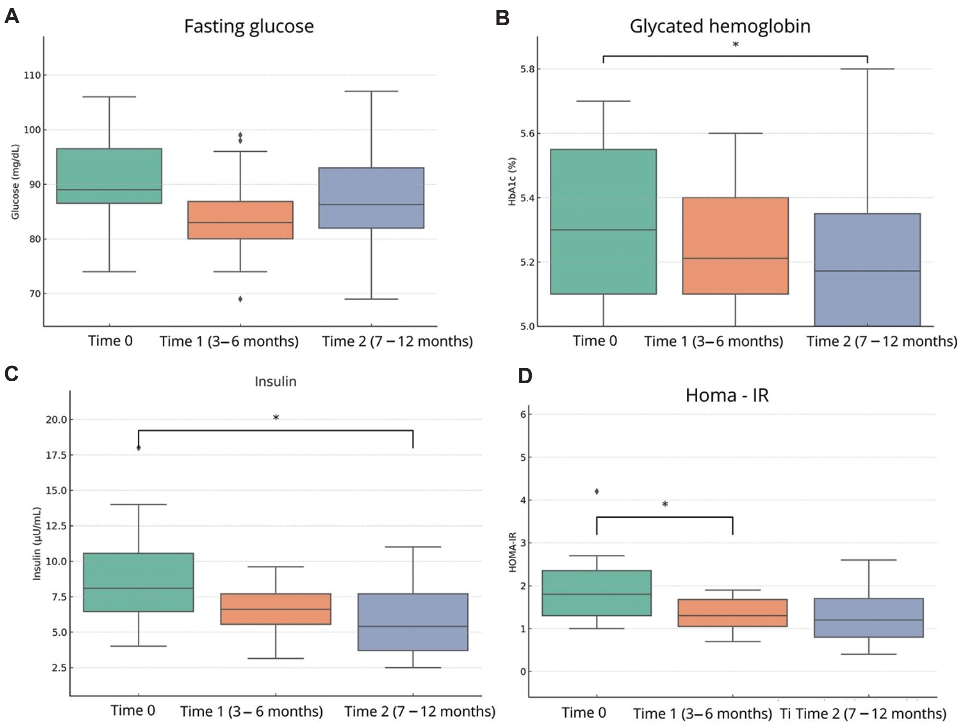

Figure 4. Variations in fasting glucose, glycated hemoglobin (HbA1c), insulin, and homeostatic model assessment of insulin resistance (HOMA-IR) levels in obese patients. Analyses were conducted on fasting samples obtained from participants at three time points: Time 0 (pre-intervention), Time 1 (3–6 months after intervention), and Time 2 (7–12 months after intervention). (A) Fasting glucose: Fasting glucose levels remained stable throughout the study period. (B) HbA1c: HbA1c levels showed a statistically significant reduction between Time 0 and Time 2 (p<0.05; Friedman test followed by pairwise comparisons with Bonferroni correction). (C) Insulin: A significant reduction in insulin levels was observed between Time 0 and Time 2 (p=0.0497; Wilcoxon test with Bonferroni correction). (D) HOMA-IR: A statistically significant reduction in HOMA-IR was observed between Time 0 and Time 1 (p=0.037; Wilcoxon test with Bonferroni correction). No other comparisons reached statistical significance, although a trend toward reduction was observed between Time 0 and Time 2 (p=0.053).

Notes: ♦ denotes the outliers. * denotes statistically significant at p<0.05.

Collectively, these findings reinforce the potential role of non-pharmacological strategies in the management of cardiometabolic risk factors. CVD risk was assessed using the TC/HDL cholesterol and TG/HDL cholesterol ratios, with no significant differences observed over the study period. ASCVD risk was also estimated based on age: A 10-year CVD risk for individuals over 40 years old and a lifetime CVD risk for those under 40 years. No statistically significant changes in ASCVD risk were detected in either group over the study period.

4. Discussion

Given its increasing prevalence and its strong association with elevated morbidity and mortality, OB represents one of the most critical public health challenges of the 21st century. Beyond its detrimental effect on individual health and well-being, OB contributes to social vulnerability and imposes a substantial burden on healthcare systems. These burdens encompass not only direct medical and non-medical expenses but also indirect costs, such as loss of productivity, and intangible consequences, including diminished quality of life.[47] In Brazil, direct costs attributable to OB within the Unified Health System (SUS) were estimated at approximately BRL 378 million (USD 75 million) in 2018. When OB is considered as a contributing factor to other chronic conditions, such as hypertension and diabetes mellitus, the economic impact becomes even more significant, reaching an estimated BRL 1.39 billion (USD 278 million).[48] This scenario highlights the urgent need to strengthen cross-sectoral coordination and promote integrated policy planning. Alignment between economic strategies and health initiatives is essential to build a coherent budgetary framework that supports food and nutrition security and enables effective nationwide prevention and control of OB.

Dietary interventions have long been recognized as effective tools for the management of chronic diseases, with historical records of their application dating back nearly 200 years. LCDs, including ketogenic approaches, were initially established for the treatment of epilepsy

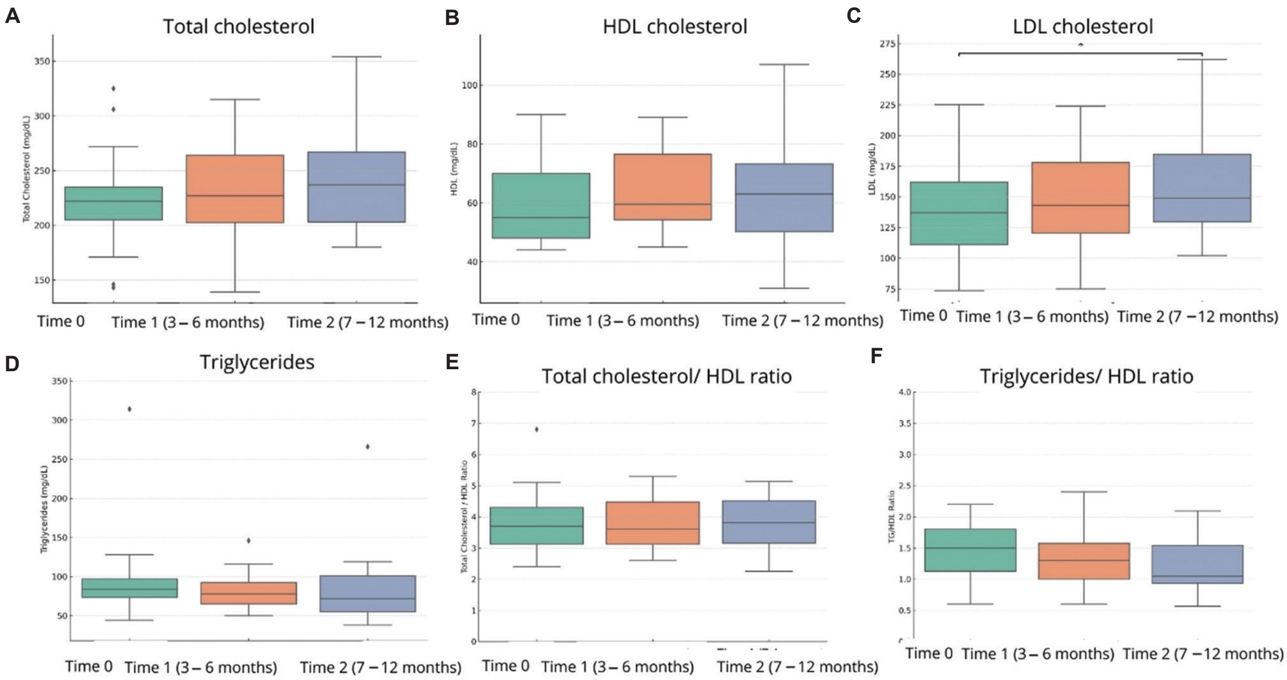

Figure 5. Lipid profile of obese patients evaluated at three different time points: Time 0 (pre-intervention), Time 1 (between 3 and 6 months), and Time 2 (between 7 and 12 months). (A) Total cholesterol: No statistically significant differences were observed between time points (p=0.141; Friedman test). (B) High-density lipoprotein (HDL) cholesterol: No statistically significant differences were observed between time points, according to the Friedman test (p=0.676) and pairwise comparisons after Bonferroni correction (p>0.05 for all pairs). (C) Low-density lipoprotein (LDL) cholesterol: A statistically significant increase in LDL levels was observed between Time 0 and Time 2 (p=0.035; Wilcoxon test with Bonferroni correction). (D) Triglycerides: No statistically significant differences were observed across time points, according to the Friedman test (p=0.692) and pairwise comparisons after Bonferroni correction (p>0.05 for all pairs). (E) Total cholesterol/HDL cholesterol ratio: No statistically significant differences were observed across time points, according to the Friedman test (p=0.759) and pairwise comparisons after Bonferroni correction (p>0.05 for all pairs). (F) Triglycerides/HDL cholesterol ratio: No statistically significant differences were observed across time points, according to the Friedman test (p=0.200) and pairwise comparisons after Bonferroni correction (p>0.05 for all pairs).

Notes: ♦ denotes the outliers. * denotes statistically significant at p<0.05.

but have since been extensively investigated in a wide range of metabolic and neurological conditions such as glucose transporter type-1 deficiency syndrome, pyruvate dehydrogenase deficiency, migraine, Alzheimer's disease, multiple myeloma, amyotrophic lateral sclerosis, NAFLD, non-alcoholic steatohepatitis, Parkinson's disease, and certain cancers.[49] More recently, LCDs have gained prominence as a promising public health strategy to address the growing burden of OB and its associated cardiometabolic consequences. Diets providing <130 g of carbohydrates per day have demonstrated superior outcomes in average weight loss and improvements in selected cardiovascular risk markers compared with traditional low-fat diets.[50,51] A systematic review and meta-analysis of 38 clinical trials involving 6,499 adults showed that LCDs were more effective in promoting weight loss and enhancing HDL cholesterol and triglyceride levels over 6–12 months.[50] In addition, a meta-analysis of long-term randomized controlled trials (lasting from 8 weeks to 24 months) in individuals with OW and OB found that LCDs led to significantly greater reductions in body weight and estimated ASCVD risk, based on pooled cohort equations developed by the National Heart, Lung, and Blood Institute.[51]

In the present cohort of OW and OB adults, the LCD resulted in significantly improvements in anthropometric and metabolic indicators, including insulin sensitivity, HOMA-IR, HbA1c, and pancreatic insulin regulation.[42,52] Reduced circulating insulin level facilitates lipolysis, fat oxidation, and glycogenolysis in muscle and liver, key metabolic mechanisms underlying effective OB intervention. By restricting carbohydrate intake and leveraging fat and protein for energy, LCDs may also support beta (β)-cell preservation and lean body mass retention.[53] In addition, these diets promote greater satiety and reduced caloric intake, bolstering weight loss.[42]

Avoidance of hyperglycemia is crucial to prevent the activation of reactive oxygen species (ROS), T cells, inflammatory cytokines, and lipid peroxidation pathways.[53] OB is associated with chronic low-grade inflammation,

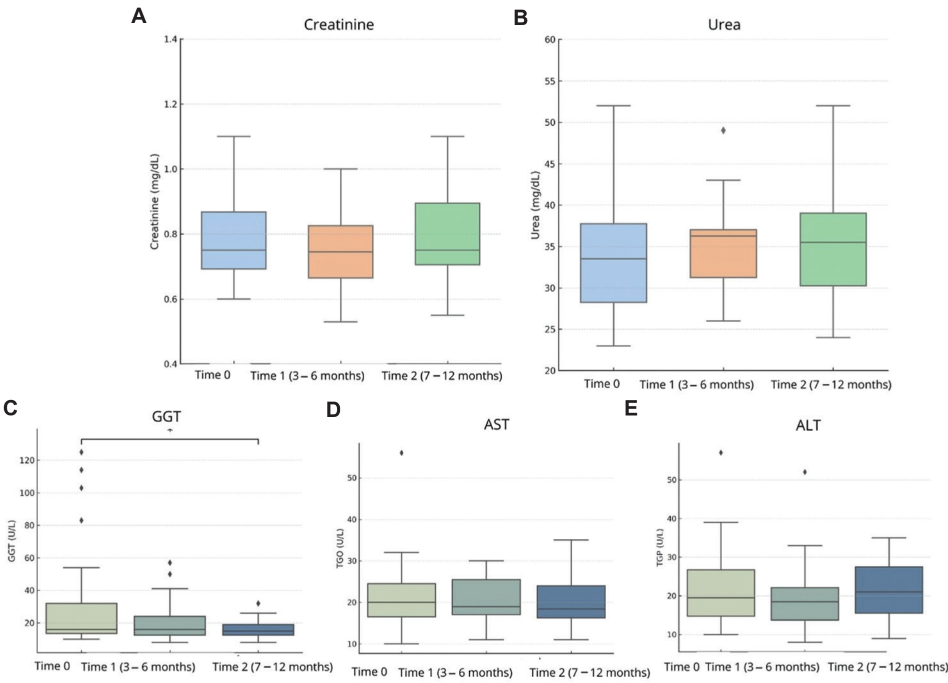

Figure 6. Evaluation of renal (panels A and B) and hepatic function (panels C-E) in obese patients at three time points: Time 0 (pre-intervention), Time 1 (3–6 months after intervention), and Time 2 (7–12 months after intervention). (A) Creatinine: Serum creatinine levels did not differ significantly across time points (Friedman test, p=0.626), and all pairwise comparisons were non-significant after Bonferroni correction (p>0.05). (B) Urea: No statistically significant differences were observed across the three time points (p=0.517; Friedman test), confirmed by pairwise comparisons with Bonferroni correction (p>0.05 for all pairs). (C) Gamma-glutamyl transferase (GGT): A statistically significant reduction was observed between Time 0 and Time 2 (p=0.0341; Wilcoxon test with Bonferroni correction). (D) Aspartate aminotransferase (AST): AST levels remained stable over time, with no statistically significant changes (global p=0.958; Friedman test). (E) Alanine aminotransferase (ALT): No statistically significant variations were observed in ALT levels across time points (global p=0.9854; Friedman test).
Notes: ♦ indicates the outliers. * denotes statistically significant at p<0.05.

which, when coupled with hyperglycemia, may induce oxidative stress, leading to vascular damage.[54] The significant reduction in anthropometric measures observed in the present study demonstrates the effectiveness of LCDs in achieving weight loss, a cornerstone of OB management. Weight loss is fundamental to the prevention of severe complications.[55,56] A 10% decrease in body weight has been linked to an approximate 20% reduction in CVD risk.[57]

In patients with OW and OB, weight loss is an effective strategy for reducing the risk of T2DM. A study by Hamman *et al.*[58] found a 16% reduction in diabetes risk per kilogram of weight lost, suggesting that a 5–7% reduction in body weight could translate into a diabetes risk reduction exceeding 90%. Beyond BMI reduction, additional anthropometric measures should be considered. Ross *et al.*[59] highlighted waist circumference as a key clinical sign associated with increased cardiometabolic risks and mortality with the risk of death increasing by 13–17% for every 5 cm increase in waist circumference. In addition, data from the Framingham Study showed that weight loss of 6.8 kg or more was associated with a 21–29% reduction in the long-term hypertension risk.[55]

The assumption that high-fat diets negatively impact cardiovascular health is largely based on the notion of a linear association between fat intake and increased cardiovascular events. However, a large-scale study by Dehghan *et al.*[60] found a significant association between high carbohydrate consumption and increased mortality risk, while no significant association was observed between total fat intake and adverse cardiovascular outcomes. In fact, isocaloric substitution of carbohydrates with fats was associated with an 11% reduction in mortality risk. Rather than focusing solely on total LDL cholesterol, emerging evidence emphasizes the importance of assessing the presence of small dense LDL particles (sdLDL), which are considered the most atherogenic subclass of LDL and are associated with phenotype B. This lipid profile is typically linked to elevated TG, reduced HDL cholesterol, metabolic disorders, OB, T2DM, and increased coronary risk.[60,61] Lipid ratios such as TC/HDL and TG/HDL are increasingly recognized as robust predictors of CVD, with values below 4 mg/dL generally considered desirable due to their inverse association with sdLDL levels.[62,63]

One randomized, parallel-group trial that compared a very-LCD (<40 g/d) with a low-fat diet (<30% fat;

<7% saturated fat) reported significant reductions in the estimated 10-year Framingham risk score in the very-low-carbohydrate group at both 6 and 12 months, whereas no significant changes were observed in the low-fat group.[64] This risk score integrates multiple cardiovascular risk factors, such as TC and HDL cholesterol and systolic blood pressure, thereby providing a more comprehensive assessment of coronary heart disease risk than reliance on a single biomarker such as LDL cholesterol, to determine the risk. The results of these studies indicate that lower-carbohydrate dietary patterns result in significant reductions in weight and improvements in risk markers for CVD. In the present study, both the TC/HDL and TG/HDL ratios, commonly regarded as more reliable predictors of cardiovascular risk than isolated lipid values, remained stable over time. These findings suggest that, despite the observed increase in LDL levels, the dietary intervention did not adversely affect overall lipid-related cardiovascular risk markers. TG levels reflect both hepatic production and intestinal absorption, although current laboratory methods cannot distinguish between these sources. Evidence suggests that TG can accumulate in the arterial wall, and lower levels are associated with a reduced risk of cardiovascular events. In addition to pharmacological interventions, such as statin use, which remain central to CVD prevention, dietary strategies are also well-established as effective interventions for reducing CVD risk and related comorbidities.[65] Moreover, TGs are capable of crossing the blood-brain barrier and can induce leptin and insulin resistance, potentially affecting cognition and appetite regulation. Hypertriglyceridemia is commonly observed in individuals with OB and T2DM; thus, reducing TG levels represents a key therapeutic target in weight management and cardiometabolic risk reduction.[66]

A protein intake considered “higher” relative to conventional dietary guidelines has been associated with multiple metabolic benefits, including reduced insulin demand, enhanced fat oxidation, improved satiety, and preservation of lean body mass.[56] It is important to note that these intake levels do not represent excess protein consumption, but rather an adjustment toward physiologically appropriate amounts, particularly for individuals with OW or OB. Despite longstanding concerns regarding the potential impact of higher protein consumption on kidney function, especially in relation to glomerular filtration rate (GFR), current scientific evidence does not support a detrimental effect. Studies comparing diets with varying protein contents have found no significant differences in GFR, a finding that is consistent with the results observed in the present study. Moreover, physiological adaptations such as the 65% increase in GFR observed during pregnancy occur without elevating the risk of kidney damage, suggesting that moderate elevations in protein intake are well tolerated by the kidneys.[67] Additional support for the renal safety of higher-protein, low-carbohydrate dietary patterns comes from the 2-year Dietary Intervention Randomized Controlled Trial, which demonstrated comparable improvements in eGFR among participants adhering to low-fat, Mediterranean, and LCDs. These findings indicate that a properly formulated low-carbohydrate dietary pattern, often accompanied by adequate protein intake, is not only safe but may also be effective in maintaining or enhancing kidney function in individuals with OB, irrespective of the presence of TD2M.[68] Collectively, these results reinforce the renal safety and clinical viability of LCDs that incorporate physiologically appropriate protein levels, particularly when guided by healthcare professionals.

Hepatic health is another important concern due to risk factors such as NAFLD, hepatic steatosis, and cirrhosis. Elevated levels of GGT and ALT may be linked to impaired insulin response and an increased risk of T2DM, particularly among individuals with a BMI above 27 kg/m^2. Previous studies have associated these enzymes with a higher incidence of T2DM over follow-up periods of up to 9 years. GGT, in particular, has been implicated in the development of β-cell dysfunction and is considered an indirect marker of elevated hepatic insulin resistance and impaired insulin secretion. Mechanistically, GGT plays a role in ROS production and the maintenance of intracellular glutathione levels.[69,70] Although GGT is also related to biliary tract function, AST and ALT are considered more specific indicators of hepatocellular health, with ALT being primarily elevated in liver damage. Despite differing degrees of hepatic association, all three enzymes are linked to excessive fat accumulation in the liver.[69] In the present study, GGT levels showed a significant reduction, suggesting a potential decrease in hepatic metabolic stress. In contrast, AST and ALT levels remained stable, indicating preservation of hepatocellular integrity throughout the intervention period. Beyond liver enzyme monitoring, dietary interventions have gained prominence in the context of metabolic dysfunction–associated fatty liver disease (MAFLD). A recent international expert consensus emphasized the central role of nutritional strategies in the prevention and management of MAFLD, particularly in individuals with OB or metabolic syndrome.[71] These recommendations emphasize low-glycemic, nutrient-rich diets and the avoidance of ultra-processed foods, added sugars, and alcohol. Although hepatic imaging and fibrosis markers were not assessed in the present study, the observed improvements in metabolic parameters—including reduced waist circumference, HOMA-IR, and GGT—highlight the potential translational relevance of carbohydrate-restricted diets for improving hepatic health. Additional reductions in alcohol intake may further enhance these benefits, especially in high-risk populations.

The perception that LCDs are financially inaccessible has often been cited as a barrier to their widespread adoption, particularly when considering health equity. While the cost of lower-carbohydrate dietary patterns can vary substantially depending on food choices and preferences, emerging evidence suggests that these diets can be both affordable and nutritionally adequate when properly planned. A study by Zinn *et al.*[72] challenges the assumption of high cost by demonstrating that a low-carbohydrate and healthy-fat diet had only a modest cost difference compared with New Zealand's national dietary guidelines (NZ$ 51.67 vs. NZ$ 43.42/day for a family of four), representing an additional expense of just NZ$ 2.06/person/day. Zinn *et al.*[72] emphasize that this gap can be further minimized through practical substitutions, such as using sardines instead of salmon, without compromising nutritional quality. Staples like eggs, meats with natural fat, frozen vegetables, and nuts can be incorporated economically into an LCD when consumed in appropriate portions.

Moreover, recent assessments indicate that well-formulated LCDs can be compatible with budget-conscious dietary frameworks. These insights support the notion that cost should not be viewed as an intrinsic barrier to the implementation of low-carbohydrate strategies, particularly given their potential to improve metabolic health and reduce long-term healthcare expenditures. Nonetheless, more detailed analyses are needed to assess affordability and accessibility across diverse socioeconomic groups, ensuring that such dietary approaches are equitably available within public health systems.

In light of the growing body of scientific evidence, current dietary guidelines, which continue to prioritize calorie restriction as the central strategy for weight management, should be critically reassessed.[60,73] Interventions based on LCDs have demonstrated significant benefits for individuals with OB, including improvements in weight, metabolic markers, and cardiovascular risk, often surpassing the outcomes observed with conventional low-fat or calorie-restricted approaches. An important limitation of this study is the reduced number of participants who completed all follow-up assessments. Although 34 individuals were initially enrolled and evaluated at baseline, only 19 completed the full protocol through the second follow-up. This loss to follow-up, while anticipated in real-world outpatient settings, limits statistical power and generalizability of our findings. Nevertheless, as a self-controlled pilot trial, the study was designed to explore feasibility and generate preliminary effect estimates, rather than to provide definitive conclusions. These initial findings reinforce the need for future randomized controlled trials with larger and more diverse populations to validate and expand upon these results.

5. Conclusion

Addressing the global epidemic of OW and OB remains a critical public health priority, as emphasized by the WHO. In Brazil, the high and rising prevalence of OB highlights the urgent need for comprehensive, sustained, and culturally relevant strategies. Nutritional interventions that are accessible, evidence-based, and behaviorally sustainable represent non-invasive and cost-effective approaches for reducing the burden of NCDs. In the present study, implementation of an LCD resulted in clinically meaningful improvements in metabolic and anthropometric parameters, including reductions in HbA1c, waist circumference, and body weight. These improvements were accompanied by favorable shifts in BMI classification, with several participants transitioning from OB to OW or normal weight. Such changes have important implications for reducing chronic disease risk at the population level.

From a public health perspective, LCDs may offer a scalable and adaptable tool for the prevention and management of NCDs, especially when implemented with professional guidance and aligned with local dietary practices. Their relative simplicity, affordability, and potential for integration into primary care and community-based health promotion support their viability for large-scale adoption. Moreover, to strengthen the impact of nutritional strategies, Brazil should also advance regulatory policies—such as controlling the marketing of ultra-processed foods, expanding access to fresh and healthy food, and implementing fiscal measures like taxation on unhealthy products—drawing on successful examples from other countries. In contexts marked by limited resources and territorial inequalities, structured and culturally sensitive dietary interventions, such as LCDs, can support the reorientation of health systems toward prevention, equity, and the promotion of long-term well-being. Future research should further investigate their long-term safety, sustainability, and equity in access, particularly within the framework of Brazil's SUS and national food and nutrition policies. It is important to note that this was a pilot study with a limited sample size. Although the findings are promising, they should be interpreted with caution and considered exploratory. Larger studies involving more diverse populations are necessary to confirm and expand these results.

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Conflict of interest

The authors declare that they have no competing interests.

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Ethics approval and consent to participate

The study was approved by the local Research Ethics Committee and conducted in accordance with the Brazilian National Health Council's guidelines under the CEP/CONEP system (approval number: 4.961.640; CAAE: 49593220.4.0000.5149). This study was registered at the Brazilian Registry of Clinical Trials (ReBEC) (registration no.: RBR-107jk4tn, UTN no.: U1111-1270-4313, registry link: https://ensaiosclinicos.gov.br/rg/RBR-107jk4tn) before participant enrollment. All participants provided written informed consent before undergoing any study-related procedures.

Consent for publication

All participants provided written informed consent for the publication of anonymized data and results.

Availability of data

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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