Original Article

Effect of Low-Carbohydrate Diet on Non-Alcoholic Fatty Liver Disease

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Submission: November 13, 2025 Accepted: December 20, 2025 Published: December 31, 2025

Abstract

Background: Non-alcoholic fatty liver disease has become a common cause of chronic liver disease, and is commonly associated with metabolic comorbidities. **Objectives:** Due to the potential for progression to fibrosis and hepatocellular carcinoma, non-alcoholic fatty liver disease is managed through several different aspects, and there is a growing need to assess the effect of dietary interventions on the disease. **Materials and Methods:** This single-arm study was conducted in Sulaymaniyah in between 2023-2024 among patients visiting an obesity clinic who met our inclusion criteria. Each participant was put on a low-carbohydrate diet and measures of weight, body mass index, and visceral fat area were taken before and after the intervention and compared, dietary compliance was assessed verbally. After data collection it was entered into a Google Sheets sheet and data analysis was done using Google Sheets and R (v4.4.0), the statistical significance of our results were measured using a 2-tailed paired t-test, 2-tailed independent t-test, Wilcoxon Signed Rank test, Mann-Whitney test as well as a chi-square test. Comparison of interest in this study was the mean and median change in weight, BMI, and visceral fat area, overall and among genders. **Results:** Majority (52%) of our participants were female, Arabs constituted the majority ethnicity (68%). 44% of participants reported a good dietary adherence. changes were: median change in weight: -6.6 kg ± 6.55, mean change in body mass index: -3 ± 2.5, mean change in visceral fat area -21 ± 23.8, p-value for these changes were < 0.05. **Conclusion:** This study shows that a low-carbohydrate diet may have beneficial effects on non-alcoholic fatty liver disease. On average, participants experienced significant reductions in weight, BMI, and visceral fat. No statistically significant difference was seen in changes of body metrics and visceral fat between genders. The diet may also have beneficial effects in other chronic conditions, as majority of subjects reported discontinuing their medications whilst on the diet.

Keyword: NAFLD, Low-carbohydrate diet, Obesity, BMI, Visceral fat area, Dietary intervention.

Introduction

In the past 2 decades non-alcoholic fatty liver disease (NAFLD) has become the commonest form of chronic liver disease, closely associated with the increase incidence rates of type 2 diabetes and obesity [1,2]. NAFLD encompasses a range of liver abnormalities characterized by fat deposition in hepatocytes that is not related with alcohol consumption, with simple steatosis and non-alcoholic steatohepatitis on the disease spectrum and the potential to advance to cirrhosis and hepatocellular carcinoma [3-5]. Commonly recognized as the liver manifestation of metabolic syndrome, new evidence shows that NAFLD may be the primary contributor to metabolic syndrome [6]. Therefore NAFLD is also shown to be associated with the presence of insulin resistance, dyslipidemia, hypertension, and obesity as influential elements [1]. Lines of management of NAFLD consists of many aspect among these weight loss through dietary programs or intervention remains the cornerstone therapeutic strategy. Among abundant dietary strategies, Low-carbohydrate diets have shown their significant potential to lower intrahepatic lipid content and ameliorate metabolic comorbidities [5,7]. Studies have demonstrated that a low-carbohydrate diet is capable of substantial lowering hepatic fat content and weight loss, even regardless of a caloric restriction program [8,9]. Associations have also been made between low-carbohydrate diet program and improvements in insulin sensitivity and lipid profiles [10]. In addition, intrahepatic triglyceride reduction is where low-carbohydrate ketogenic diets particularly effective [9]. Despite these findings however, the necessity to assess carbohydrate-restricted dietary program in its aspects of long-term sustainability and safety still stands [11,12]. Considering the heterogenic patterns of NAFLD in terms of presentations and associated metabolic disorders, individualized planning is crucial. Low-carbohydrate diets are an essential part of a multifaceted approach under a more comprehensive and broader strategy to manage NAFLD, in particular in individuals with type 2 diabetes and hyperinsulinemia, focusing attention on the need for an individualized nutritional planning to address both intrahepatic and extrahepatic manifestations of the disease [6,13]. Overall, despite the positive results of a low-carbohydrate diet as a management for NAFLD, further studies and clinical trials are necessary in order to better understand role of the diet program in the broad context of NAFLD treatment patterns and to make the individualization of a low-carbohydrate dietary program for NAFLD to individual patients.

Materials and Methods

Study design

Single-arm prospective study design.

Setting and population

This study was conducted in Sulaymaniyah, a city in the Kurdistan region of Iraq, at an obesity clinic. The population of this study consisted of individuals who visited the clinic and met our inclusion criteria from the age of 16-70. Data was collected from the 13th of November 2023 until 10th of April 2024.

Sampling and sample technique

The sample of this study was collected using the “purposive sampling” method. The following were the criteria for inclusion in the research: Visceral fat area $\geq$ 200 cm^2 and BMI $\geq$ 30 kg/m^2**.** Any subject with a visceral fat area $\geq$ 200cm^2 from their Body Composition Analysis results were assumed to have Non-Alcoholic Fatty Liver Disease (NAFLD), as studies have shown a significant relationship between Visceral Fat Area and NAFLD [14–17]. Increases in visceral fat area were regarded as worsening of NAFLD, and decreases were regarded as an improvement of the condition. Exclusion criteria were the following: Alcohol intake, use of medication associated with steatosis or steatohepatitis, histologic diagnosis of cirrhosis, other causes of chronic liver disease, and pregnancy.

Initial meeting and follow-up

Subjects eligible for inclusion were met at the clinic every 1-2 months, and followed up for a duration of minimum 3 months period. Duration of each visit was about 25-40 minutes.

Diet

Subjects were assigned a low carbohydrate diet, in which carbohydrate intake would be a third of total daily intake. The diet consisted of unlimited amounts of salads and vegetables, 1-2 bowl(s) of soup (any soup), and 150-200 grams of meat (all kinds of meat), every day. There was no determined limit on the amount of daily caloric intake and subjects were instructed to eat until they felt satiated. Supplements were not part of the diet. Exercise was not part of the intervention nor was it suggested, so that results were purely from the diet. Subjects with chronic conditions on regular medication were instructed to gradually lower their medication dosage.

Dietary Compliance

Dietary compliance was assessed verbally, at the end of the course, on the following scale: 0 (no adherence), 1 (poor), 2 (fair), 3 (good), 4 (very good).

Measures

Body Composition

For all subjects, total body composition was ordered using a bioelectric impedance scale (InBody Company, South Korea) for analysis of total body weight (TBW) and visceral fat area (VFA), and Body Mass Index (BMI). Bioelectric impedance scale has been shown to be an accurate method for determining VFA [18-23]. Manual measurements of weight and height were also done.

Serum Tests

For all subjects with and without medical conditions (diabetes, hypertension, etc.), fasting serum samples were instructed to be taken for analysis of fasting glucose, fasting insulin, Hemoglobin A_{1C}, C-peptide, lipid profile, and liver function tests. These tests were to be done on each visit for follow-up. However, no subject did these tests adequately, due to the fact that the cost of these tests was borne on the subjects, therefore pre-intervention to post-intervention comparisons could not be made.

Data Collection

Data was collected on ground, at the obesity clinic, at the initial meeting and each follow-up, the results of their body composition analysis was collected from the clinic. In total 110 subjects were identified, but due to lack of adequate follow-up, only 25 were included in this study.

Statistical analysis

After collection of the data, it was entered into a Google Sheets sheet. Mean, standard deviation, median and interquartile range were derived for the quantitative variables. Descriptive statistics (frequency, percentage) were performed for the qualitative variables. The data was demonstrated using tables and figures. Comparison of interest in this study design was the mean and median change from baseline to 16 weeks overall, and among genders. Using the Jarque-Bera test, we found that the post-intervention measures of weight, and BMI, as well as the change in weight were not normally distributed. Therefore, for normally distributed variables, mean and average were used for central tendency, 2-tailed paired t-test was used to find association between pre-post intervention changes, and 2-tailed independent t-test was used to compare changes between genders. For non-normally distributed variables, median and interquartile range were used for central tendency, Wilcoxon Signed Rank test was used to find association between pre-post intervention changes, and Mann-Whitney test was used to compare changes between genders. The chi-square test was used to find association between categorical variables (gender, adherence), 2-tailed paired t-test was used to find association between pre-post intervention changes. $P<.05$ was used for statistical significance.

Software

Google sheets was utilized for entry of data as well as analysis, such as deriving mean, standard deviation, median, and interquartile range for quantitative measures. It was also utilized for deriving the p-value using 2-tailed paired t-test, 2-tailed independent t-test and chi-square test for statistical significance of outcomes. R (v4.4.0) was used for performance of Wilcoxon Signed Rank test, and the Mann-Whitney test.

Ethics approval and consent to participate

Approval (Number 197) was granted from the ethical committee of the College of Medicine/University of Sulaimani, Iraq. The work was implemented in accordance with international guidelines and 2008 Declaration of Helsinki. Verbal consent for participation in this study, ensuring the preservation of subject confidentiality, was taken from the initial meeting with the subjects.

Results

In total, data from 25 participants were used, the mean age of participants was 46 years ± 12 (range, 16-67 years), and the mean height was 165.2 cm ± 9.2 (range, 149 – 179 cm). Table 1 shows demographic characteristics of participants.

Table 1: Demographic characteristics of participants

Variable		Frequency	Percentage
Gender	Male	12	48 %
	Female	13	52 %
Ethnicity	Kurd	8	32 %
	Arab	17	68 %
Gender-Ethnicity Distribution	Arabic Males	11	44 %
	Arabic Females	6	24 %
	Kurdish Males	1	4 %
	Kurdish Females	7	28 %
Total		25	100 %

The majority of participants were Female (52%): Arab (68%): Arabic males (44%). Kurdish males represented the minority of participants (4%). There was no significant difference in age between males and females, but there was a significant difference in height between males and females, as shown in Table 2.

Table 2: Age and height difference between genders

Variable	Gender		P value
	Male	Female	
Mean Age ± SD (years)	42.8 ± 12	48.9 ± 12.8	0.23
Mean Height ± SD (cm)	171.7 ± 5.8	159.2 ± 7.5	< 0.01

14 out of our 25 participants (56%) had associated chronic conditions; 2 participants had diabetes mellitus (8%); 3 had hypertension (12%); 6 had diabetes mellitus and hypertension (24%); 2 had hypothyroidism (8%); 1 participant had asthma (4%). At baseline, the mean weight was 114.7 kg ± 21.1 (range, 78.2 – 167.3 kg), mean BMI was 41.8 kg/m^2 ± 5.2 (range, 35.2 – 53.4 kg/m^2), and mean visceral fat area was 243.2 cm^2 ± 26.3 (range, 207 – 308.5 cm^2). There was a significant difference in weight between males and females, but no significant difference in BMI, and visceral fat area as shown in Table 3.

Table 3: Difference in body metrics and visceral fat among genders at baseline

Variable	Gender		P value
	Male	Female	
Mean Weight ± SD (kg)	123.5 ± 18.3	106.6 ± 20.8	0.04
Mean BMI ± SD (kg/m^2)	41.8 ± 4.9	41.8 ± 5.6	0.997
Mean VFA ± SD (cm^2)	243.2 ± 26.1	243.1 ± 27.6	0.996

Compliance to the diet program were as follows; 9 subjects reported a “very good” adherence (36%); 11 subjects reported a “good” adherence (44%); 3 subjects reported a “fair” adherence (12%); 2 subjects reported a “poor” adherence. Figure 1 shows adherence rates among genders.

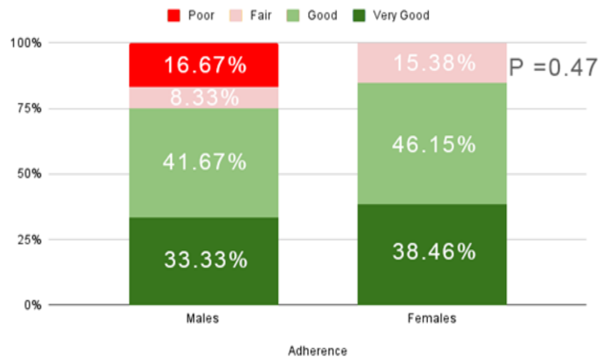

Figure 1: Adherence rates among genders

In both males and females, majority reported a “good” adherence to the dietary program; no females reported a “poor” adherence, whilst 2 males reported a “poor” adherence. There was no significant difference in adherence between males and females.

The median change in weight was -6.6 kg ± 6.55 (range, -29.2 to 3.1 kg; P = <0.001), the mean change in BMI was -3 kg/m^2 ± 2.5 (range, -9.5 to 1 kg/m^2; P = <0.001), the mean change in visceral fat area was -21 cm^2 ± 23.8 (range, -80.8 to 17.4; P = <0.001). Figure 2 correlates the changes perceived in weight, BMI, and visceral fat area with dietary compliance, as shown in Table 4 and Figure 2.

Table 4: Changes in body metrics and visceral fat among genders

Variable	Gender		P value
	Male	Female	
Median change in weight ± IQR (kg)	-8.9 ± 5.3	-6.5 ± 8.95	0.9
Mean change in BMI ± SD (kg/m^2)	-2.7 ± 1.99	-3.2 ± 2.9	0.7
Mean change in visceral fat area ± SD (cm^2)	-28.6 ± 26.5	-13.9 ± 19.4	0.13

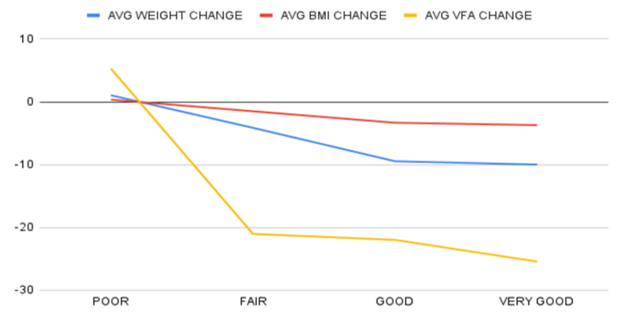

Figure 2: Dietary adherence and changes in body metrics and visceral fat

There was no statistically significant difference between males and females in the changes perceived. Out of 14 participants with chronic conditions, majority (85.7%) reported completely discontinuing the use of medications for their chronic conditions whilst on the diet, and only 2 subjects (14.3%) reported continuing the use of their medications, at lowered doses.

Discussion

This study investigated the effect of a low carbohydrate diet on NAFLD, our study included 25 participants, which is a larger sample size compared to a study conducted in Israel by O. Benjaminov et al, [24], the reason for the difference may be due to differences in inclusion criteria, whereas we included subjects with or without comorbidities (provided they met the BMI and visceral fat criteria), they included only subjects whose BMI > 35 kg/m^2 and had associated comorbidities, unless they had a BMI exceeding 40 kg/m^2. Our criteria for BMI were lower than theirs as well (30kg/m^2). Out of our 25 participants, majority (52%) were female, this is similar to a study conducted in Italy by

D'Abbondanza et al [25], in which females constituted 60% of the subjects. One way of explaining this similarity could be that the setting of the studies, which were set in clinics, have a higher prevalence of obesity, which is often more common in females, who might be more likely to seek medical attention for weight loss, since in a lot of societies there is a greater focus on women's body image. At baseline, there was a significant difference between males and females in weight, however both BMI and visceral fat area among genders were similar indicating that despite the difference in weight, the body composition and fat deposition are equal. The same was observed in the study conducted in Italy [25]. In this study we noticed a general trend towards improved health markers (Weight, BMI), as well as reduced visceral fat area. Subjects on average had a mean change in weight of (-8.2 kg), This is a smaller reduction than a similar study conducted in the United States by Tendler et al, [8]**,** which had a mean reduction of -12.8 kg and this could be due to the larger sample size of our study, where ours was 25 and theirs was 5, or due to the shorter period of follow up, where ours was 3 months and theirs was 6 months. In this study we used visceral fat area as an assessment of the condition of NAFLD, on average the change in visceral fat area was -28.6 $cm^2 \pm 26.5$, this indicates that a low-carbohydrate diet can improve the NAFLD condition, though we could not find similar studies, as other studies, like the one conducted in the United States by Tendler et al, utilize liver histology, whilst we relied on visceral fat. However, similar improvements of NAFLD were still demonstrated in the study [8]. As illustrated by Figure 2, the better the dietary compliance, the greater the reductions in body metrics and visceral fat area. However, in our study, notable variations in results were observed. Some subjects who reported a "good" compliance exhibited minuscule changes in health markers, sometimes less than subjects who reported "fair" dietary compliance. This suggests that there may be wide individual variations in response to the diet, but it may have also been due to the method of assessing dietary compliance, which was a self-reported verbal response, which is liable to many forms of bias, such as recall bias, social desirability bias, and response bias, among others. We couldn't find a study with similar results, and we think the reason for that is our study assessed dietary compliance with patient reports, whilst others use urinary ketones for assessment of dietary compliance [8, 25]. In this study, out of 14 participants with chronic conditions, majority (85.7%) reported completely eliminating the use of drugs for control of their chronic conditions while on the diet, and those that continued to do so did at a lowered dose. This suggests that a low-carbohydrate diet may have a beneficial effect in the control of chronic conditions. Due to the lack of a comparison treatment in this study, we cannot attribute whether the observed effects were due to a low-carbohydrate diet or to weight loss. But a decreased carbohydrate intake can still be beneficial for NAFLD [26]. Excessive intake of monosaccharides, such as fructose, can lead to hepatic lipogenesis, which can advance the pathogenesis of NAFLD [27, 28].

Strength and limitations

We believe that our study strength is that this is the first study conducted in Iraq on the effects of low-carbohydrate diet on non-alcoholic fatty liver disease, to the best of our knowledge. However, limitations include the lack of a control group, to determine whether the effects perceived in the study were due to the diet or not. Secondly, the use of verbal self-reported responses for adherence is another limitation as it is susceptible to many forms of bias. The relatively short follow-up period is another limitation as the long-term effects of the diet could not be assessed. One other limitation was that our participants did not perform the serum tests as they were instructed to.

Conclusion

This study evaluated the effects of a low-carbohydrate diet on non-alcoholic fatty liver disease and shows that a low-carbohydrate diet can have a beneficial effect on NAFLD. Whilst there was a significant weight difference in males and females, the BMI, and visceral fat area were similar, meaning despite the weight differences, body composition and fat deposition were similar. Significant reductions in weight, BMI and visceral fat area were observed over a period of 3 months. Overall, subjects who reported better dietary compliance exhibited better reductions in weight, BMI, and visceral fat area, which suggest a link between the observed changes and the diet. No statistically significant difference in weight, BMI, and visceral fat area reduction between males and female were observed. Majority of subjects reported discontinuing the use of medications for their chronic conditions, which suggests that the diet may play a beneficial role in the control of chronic conditions as diabetes mellitus and hypertension.

Consent for publication

Not applicable.

Availability of data and materials

The datasets supporting the conclusions of this article are included within the article and its additional files.

Competing interests

The authors declare that they have no competing interests.

Funding

There is no funding in this work to be reported.

Acknowledgments

We would like to express our most sincere gratitude to the following individuals, their support and co-operation have been fundamental for the completion of this research, without them and their help this paper would have not been possible. We would like to thank our Supervisor Dr. Sirwan A. Ali, for his guidance, continuous motivation, and his expertise in shaping up this research. His insights and feedback have been crucial for the direction and scope of this study. We would also like to thank the kind staff at the obesity clinic, for their continuous aid with the collection of data, without them sufficient data for this research would have not been possible. We would also like to thank Dr. Saman Mohammed and Dr. Shahow Ezzadin, for taking their time to review this paper and give their valuable feedback and advice for improving the paper’s writing and its accuracy.

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