DASH Diet Versus Intermittent Fasting on Insulin Resistance in NAFLD Patients

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KEYWORDS
DASH diet, fatty liver.

ABSTRACT
objectives: To compare between intermittent fasting and DASH diet on glycemic profile in non-alcoholic fatty liver patients. Methods:60 (men and women) prediabetic nonalcoholic fatty liver patients participated in this study; assigned randomly to three groups: Group (A): intermittent fasting time-restricted feeding (TRF) subjects consumed 100 % of their energy needs in an 8 hours period of time each day, with their caloric intake divided into three meals consumed at 1 p.m., 4 p.m., and 8 p.m. schedule (8-hr daily eating period, the remaining 16 hours per 24-hour period made up the fasting period). Group (B): the dietary approach to stop hypertension (DASH) subjects consumed 100 % of their energy needs divided into three meals consumed at 8 a.m., 1 p.m., and 8 p.m. (12-hr eating period). Group (C): control group; all subjects didn't follow any diet regimen or calorie deficit. all participants subjected to 30 minutes moderate aerobic exercise on treadmill. Subjects tested before and after 8 weeks of the study. Results: The nonalcoholic fatty liver patients in Group B received DASH diet program more improved fasting glucose reduction percentage (18.25%), followed by patients in Group A (14.79%) received intermittent fasting program, and then those in Group C (2.55%) control group & Group B received DASH diet program more improved HOMA IR reduction percentage (62.88%), followed by patients in Group A (45.23%) received intermittent fasting program, and then those in Group C (6.77%) received control group. Conclusion; both Dash & IF are effective therapeutic approach to control insulin resistance in NAFLD patients, prevention strategy for diabetes type 2.

1. Introduction

NAFLD

Type 2 diabetes mellitus (T2DM), obesity, insulin resistance, hypertension, hyperlipidemia, and metabolic syndrome are all linked to nonalcoholic fatty liver disease (NAFLD). Histologically classified as non-alcoholic steatohepatitis (NASH), this subtype of NAFLD can advance and eventually result in liver cirrhosis, hepatocellular carcinoma (HCC), liver transplantation, and liver fibrosis. Each of these NASH consequences has the potential to significantly impact individuals, their families, and society in terms of health, finances, and patient experience (1).

Risk factors for NAFLD

(A) obesity:

The risk of NAFLD is increased by obesity (2-12). The World Health Organization (WHO) defines obesity as having a body mass index (BMI) of 30 or higher, and overweight as having a BMI of 25 or higher. Because BMI is applicable to all adult populations, regardless of gender, it has shown to be the most valuable population-level indicator of overweight and obesity. However, the WHO has categorized the various BMI strata according to risk due to the diverse populations throughout Asia. Individuals with BMIs between 18.5 and 23 kg/m2 are thought to have a gradually increasing but manageable risk of obesity-related conditions; those with BMIs between 23 and 27.5 kg/m2 are more likely to develop obesity-related conditions; and those with BMIs of 27.5 kg/m2 or higher (2).

Since visceral obesity is a major risk factor for many metabolic syndrome issues, measuring waist circumference might be a more precise method of assessment. The benefits and drawbacks of using waist circumference measures in place of BMI are still up for discussion. In this situation, evaluating NAFLD risk and progression using both BMI and waist circumference may be the most appropriate course of action (13, 14).

According to World Health Organization (WHO) estimates from 2016, the number of overweight and obese adults (18 years of age and older) worldwide has nearly tripled since 1975, with 650 million of them being obese,

using these BMI boundaries. Worldwide, 39% of adults are estimated to be overweight, and 13% to be obese (3). It is important to keep in mind that adult obesity rates vary per country.

According to WHO data, China has 97,256,700 obese individuals, whereas the US has the highest number of obese adults (109,342,839). Adult obesity rates are lowest in Indonesia (Fig. 1). The Oceania islands (Cook Islands, Samoa, Tonga, Nauru, Palau, Niue, and the Marshall Islands) have the highest obesity prevalence in the world. With up to 75% of the population classified as obese or overweight, the Middle East (Qatar, United Arab Emirates, Saudi Arabia, Libya, Oman, Jordan, Egypt, and Kuwait) has the second highest prevalence. There are more fat or overweight persons in South America (Brazil, Mexico, Argentina, Peru, Chile) than anywhere else. (Figure 1) (4).

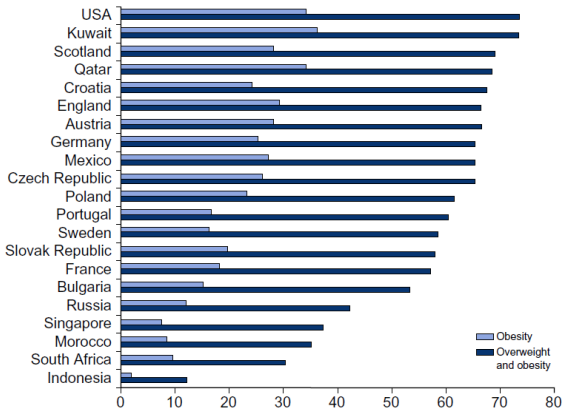

Fig. (1): Countries with the highest adult prevalence rate of overweight and obesity. (World Population: 7,505,257,673 and World Obesity Population: 774,000,000) (4-16).

The fact that 41 million children under the age of five and over 340 million children and adolescents aged 5 to 19 were overweight or obese in 2016 is even more concerning. The majority of people on the planet reside in nations where being overweight or obese causes more deaths than being underweight. A study sponsored by Imperial College London and the WHO predicts that by 2022, more children and adolescents would be fat than moderately or severely underweight if current trends continue (3). Moldova has the lowest percentage of obese boys and girls among all the countries with varying prevalence values for overweight and obese children for both boys and girls. However, India continued to hold the title of being the country with the highest number of children.

The WHO has classified obesity as one of the nine noncommunicable illnesses that need to be treated globally due to the exponential rise in obesity prevalence. In order to reduce relative obesity-related mortality by 25%, the World Health Assembly called on all stakeholders to act at the global, regional, and local levels to improve dietary and physical activity patterns as well as to identify and treat obesogenic variables at the population level (10). These statistics on the obesity pandemic around the world are contributing to a number of obesity-related problems, such as NAFLD (1). As a matter of fact, the incidence of NAFLD increases in direct proportion to rising BMI (1). In this particular setting, the general population has a prevalence of roughly 25% of NAFLD, however for extremely obese people having weight reduction operations and surgeries, the prevalence rises to over 90% (1). This problem emphasizes how crucial it is to incorporate weight control into any plan aimed at combating the NAFLD epidemic.

(B) T2DM:

In tandem with the growing rate of obesity, type 2 diabetes is becoming more commonplace globally. Another significant risk factor for NAFLD and NASH is T2DM. As of 2015, the International Diabetes Federation estimates that over 400 million individuals worldwide had diabetes (5). According to WHO estimates, T2DM accounts for 90% of all diabetes cases globally (6). An estimated 1.5 million deaths were attributed to diabetes in 2012; about 80% of these deaths occurred in low- and middle-income countries. Over half of diabetes patients in underdeveloped countries remain undiagnosed. According to WHO estimates, diabetes-related fatalities will quadruple globally by 2030. According to age, diabetes affects 0.26 percent of children (19 years of age and under), 12.3% of all adults (20 years of age and older), and 25.9% of people (65 years of age and above). However, the age group with the highest incidence of diabetes globally is people 40 to 59 years old; by 2030,

this is predicted to change to persons 60 to 79 years old (5, 6).

It is estimated that 29.1 million people in the US have type 2 diabetes, of which 8.1 million are undiagnosed and ignorant of their illness. Furthermore, over 10% of persons aged 20 and above have diabetes, with 1.4 million new cases of the disease identified in the US each year. Seniors (those 65 and older) make up 25% of the population; in 2012, healthcare resources were projected to have cost $245 billion, and these figures are still rising (5). In comparison to non-Hispanic whites, some ethnic groups in the US have a higher risk of type 2 diabetes: The risk of diabetes is higher among Asian Americans (9% higher), Non-Hispanic Blacks (13.2% higher), and Hispanics (12.8% higher). The prevalence of type 2 diabetes in Hispanics varies by country of origin; among these individuals, 8.5% are from Central and South America, 9.3% are from Cuba, 13.9% are Mexican Americans, and 14.8% are Puerto Ricans. However, with 33% of adults having diabetes, native American adults in southern Arizona have the highest rate of T2DM worldwide.

All racial and cultural origins have a low incidence of type 2 diabetes, but some minority groups—particularly Asian Pacific Islanders (ages 10–19) had a greater incidence than Caucasians. Children are more likely to develop type 2 diabetes as they get older, particularly as they hit puberty (5, 6). In fact, the incidence of type 2 diabetes starts to rise in all ethnic groups around adolescence, particularly among overweight youngsters. The US Centers for Disease Control report that in 2008–2009, the incidence of new cases among children aged 10 and under was 0.8 per 100,000, while the rate for children aged 10 - 19 was 11 per 100,000 (7).

Despite having a strong relationship with obesity, T2DM has two distinct roles in NAFLD. First, more than 60% of T2DM patients have NAFLD and NASH (1 – 11,12). Second, having T2DM appears to hasten the progression of NAFLD and is associated with an increased risk of advanced fibrosis and death (12). In this context, comprehensive evaluation of T2DM in NASH patients offers possible treatment alternatives in addition to prognostic implications.

Insulin resistance across NAFLD

Insulin resistance (IR) is defined as a reduced response to insulin action from target tissues and is associated with an increased risk of developing type 2 diabetes mellitus (T2DM). Different degrees of glucose and lipid metabolism are hampered by insulin resistance (IR). Insulin resistance (IR) is a metabolic abnormality commonly observed in patients with nonalcoholic fatty liver disease (NAFLD) and is thought to have a major role in the pathogenesis of nonalcoholic steatohepatitis (NASH) and the progression of liver disease. The main sites involved in IR are skeletal muscle, the liver, and adipose tissue; the development of NAFLD and NASH is likely to be significantly influenced by the active crosstalk between these organs. (17)

Dietary Approaches to Stop Hypertension (DASH) diet

In 1997, the DASH diet was first suggested as a way to lower blood pressure (18). The diet was low in total fat (25·6% of energy) and saturated fat (7% of energy) and high in fruits (5·2 servings/d), vegetables (4·4 servings/d), and low-fat dairy products (2 servings/d). Additionally, the diet included fewer servings of red meat (0·5 servings/d), sweets, and beverages sweetened with sugar (0·7 servings/d), and more nuts, seeds, and legumes (0·7 servings/d), whole grains (3·8 servings/d), and fish (0·5 servings/d). On the whole, Na was unrestricted. The original DASH diet included about 3 g/d of sodium (about 8 g of salt each day). Nevertheless, complementary studies showed that limiting dietary Na to fewer than 6 g/d improves the blood pressure-lowering effects of DASH (19). Owing to the consumption of particular foods, the DASH diet offers restricted amounts of total fat, saturated fat, cholesterol, and Na and high amounts of fiber, K, Ca, Mg, and antioxidants (Fig. 2) (20). It has been shown that consuming all of the good dietary components and minimizing the intake of all of the unfavorable ones is beneficial for preventing hypertension (21). Nonetheless, combining these dietary elements into a pattern offers more significant advantages (22).

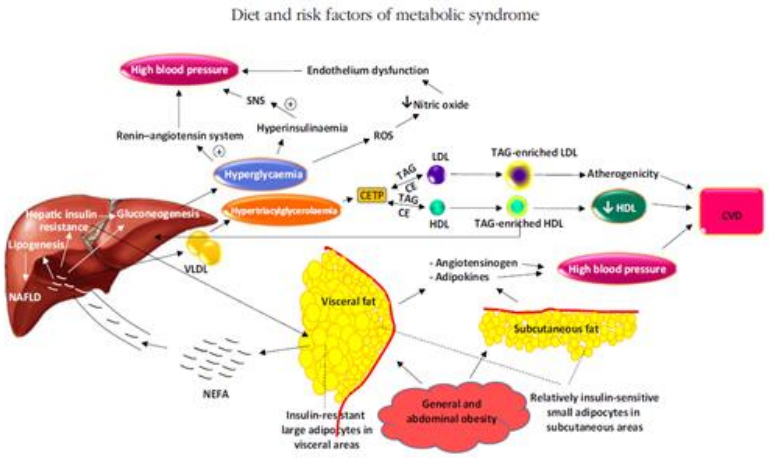

Fig. 2. An overview of the pathogenic processes that eventually result in the metabolic syndrome's constituent parts. The acronyms for the following terms are: NAFLD, non-alcoholic fatty liver disease; CETP, cholesteryl ester transfer protein; and CE, cholesteryl esters(20).

While the DASH diet was first created to manage or control hypertension, there are other metabolic benefits to following this diet. For example, DASH has been demonstrated to help the metabolic syndrome in epidemiological research. The highest proportion of people with the metabolic syndrome were found in the DASH first quartile, which had the highest consumption of fat and Na and the lowest consumption of protein, fiber, calcium, and potassium, according to a large-scale cross-sectional study conducted in Korea (23). Additionally, the odds ratio (OR) for developing metabolic syndrome in the highest quartile of DASH score compared to the lowest was 0·36 (24) in a 3·6-year cohort study involving children and adolescents. Together with increased adherence to the DASH diet, the incidence of elevated fasting glucose, hypertension, and abdominal obesity declined (24).

Adherence to the DASH diet was also linked to a decreased risk of CHD and stroke, according to a 24-year prospective cohort research (25). RCTs have validated observational study results. For example, 8 weeks of DASH consumption reduced body weight, serum TAG, VLDL cholesterol, total to HDL cholesterol ratio, insulin levels, and insulin resistance, and raised the insulin sensitivity index in overweight and obese people (26). Similarly, DASH decreased body weight, waist circumference, fasting blood glucose levels, and Systolic and diastolic blood pressure, LDL cholesterol, HbA1c, and inversely elevated HDL cholesterol (65). Additionally, the DASH diet decreased predicted 10-year CHD risk by 18 and 11%, respectively, in a large-scale 8-week experiment when compared to regular and diets high in fruits and vegetables (27). A meta-analysis predicting a 13% drop in the 10-year Framingham CVD risk score with DASH drinking was in accord (28). DASH lowered total and LDL cholesterol, as well as systolic and diastolic blood pressure, but it had no effect on HDL or TAG levels (28).

Intermittent fasting:

1) Definition

The term "intermittent fasting" has been used to describe several approaches to calorie restriction for health or weight loss. when a patient restricts their caloric intake for several hours at a time (usually 16 hours, with the remaining 8 hours requiring full energy intake). While other techniques allow for the consumption of protein but not carbohydrates, they are nonetheless classified as intermittent fasting (31). Because it is low in calories yet nevertheless encourages ketosis, some refer to this diet as a mimicking fasting diet, while others permit carbohydrates or macro/micronutrients up to a particular amount (32). The fact that non-caloric fluid consumption is always permitted sets this apart from religious fasting in several important ways. This significantly reduces the risk of hypotension and dehydration, which are serious concerns during religious fasting.

2) Benefits

It has long been known that calorie restriction improves insulin resistance, the main characteristic of type 2

diabetes (36). Insulin sensitivity increases and insulin levels decrease following a fasting period (34, 35). Postprandial glucose levels and fasting are enhanced as a result of this. Additionally, there is a decreased risk of weight gain and possibly even weight loss because insulin promotes the formation of adipose tissue. Thus, it makes sense that intermittent fasting might have an impact on weight loss, particularly if it is practiced regularly. It was first proposed that fasting could help to mitigate some of the main negative effects of weight reduction programs in the research on the health effects of fasting (33). But recent small-scale, short-term experiments have shown that intermittent fasting can aid in weight loss just as much as consistent calorie restriction (31, 30). Consequently, when done frequently enough, fasting can be a healthy weight loss method; nonetheless, the best available research indicates that fasting is not a better weight loss technique (31, 33). Atherosclerosis, the onset of coronary artery disease, decreased adiponectin, decreased low-density lipoprotein (LDL) particle size, and other metabolic variables are associated with or contribute to these processes (37). An elevated inflammatory state is also linked to insulin resistance.

Moreover, insulin has been demonstrated to be an atherogenic agent as well as to raise the risk of fluid retention and congestive heart failure (38,39). Therefore, reducing insulin levels with intermittent fasting may reduce major adverse cardiovascular events. Such a decrease in insulin might be possible. According to Furmli et al. (29), three patients were able to stop receiving insulin five to eighteen days after they started intermittent fasting, which involved skipping breakfast and lunch three days a week or on alternate days. If this finding can be safely and reliably replicated in large groups, it might be a game-changer. However, more research in larger populations is required to fully explore this possibility.

Research has shown that calorie restriction and intermittent fasting improve a variety of metabolic and inflammatory processes. Among them are increased heat shock protein, cellular autophagy promotion, lowered inflammatory cytokines, decreased advanced glycation end products, and enhanced adiponectin (40). Since fewer vascular dysfunction is the outcome of each of these impacts, it stands to reason that cardiovascular risk and/or mortality would improve. It is yet to be determined if the modifications brought about by fasting are substantial and long-lasting enough to do this.

Even though there are no prospective clinical trials examining the benefits of intermittent fasting on major adverse cardiovascular events, observational population studies have demonstrated the benefits of intermittent fasting on metabolism and cardiovascular health, including a decreased risk of diabetes and coronary artery disease, from as little as one day of energy restriction per month (performed over several decades) (41). A recent prospective clinical trial did report on the impact of intermittent fasting on hemoglobin A1c management (31). In a sample of 97 individuals with type 2 diabetes mellitus, intermittent fasting was found to be non-inferior to continuous energy restriction in terms of reducing hemoglobin A1c (40 out of 137 included in the trial withdrew early) (31). Regretfully, there was no difference in weight reduction between the fasting and calorie-restricted groups in that trial, nor in other metabolic metrics (31). Overall, studies of the evidence indicate that there is currently not enough human data to support the use of low-calorie diets or intermittent fasting to prevent diabetes or, in the case of those who already have it, to prevent its sequelae (42, 43).

2. Materials and Methods

Study design

A randomized, controlled, pre-post measurement double-blinded trial.

Setting

This study was carried-out in the nutrition outpatient clinic of Suez Canal Authority Hospital in Ismailia, Egypt from january 2022 to November 2022.

Sample size estimation

G*Power (version 3.0.10) was used for calculating the sample size. The F-test MANOVA was

chosen for the analysis of variance, both within and between interactions. With a power of 0.80, an α level of 0.05 (2-tailed), as well as an effect size of 0.39, along with two groups as well as two measurements, a minimum of 54 people was needed for the sample, with an additional 6 subjects (10%) dropped out, resulting in a total of 60 subjects randomly assigned.

Participants

60 (men and women) prediabetic nonalcoholic fatty liver patients participated in this study. They selected from nutrition-outpatient clinic of Suez Canal Authority Hospital; their ages ranged from 30 to 40 years old. They assigned randomly to three groups:

Group (A): intermittent fasting time-restricted feeding (TRF) subjects consumed 100 % of their energy needs in an 8 hours period of time each day, with their caloric intake divided into three meals consumed at 1 p.m., 4 p.m., and 8 p.m. schedule (8-hr daily eating period, the remaining 16 hours per 24-hour period made up the fasting period) (69), all participants subjected to 30 minutes moderate aerobic exercise on treadmill.

Group (B): the dietary approach to stop hypertension (DASH) subjects consumed 100 % of their energy needs divided into three meals consumed at 8 a.m., 1 p.m., and 8 p.m. (12-hr eating period), all participants subjected to 30 minutes moderate aerobic exercise on treadmill.

Group (C): control group; all subjects didn't follow any diet regimen or calorie deficit but all participants subjected to 30 minutes moderate aerobic exercise on treadmill.

Subjects tested before and after 8 weeks of the study. The Harris Benedict Equation is a formula that uses basal metabolic requirements (BMR) and then applies an activity factor to determine the total daily energy expenditure. Macronutrients distributed as 30% fat, 50% carbohydrate, and 20% protein the number of calories consumed was adjusted for each participant's specific energy needs. Both groups will be on moderate aerobic exercise (40- 60 % THR) on treadmill estimated individually by The Karvonen Formula which is a mathematical formula that helps to determine target heart rate (HR) training zone. Target Heart Rate = [(max HR − resting HR) × %Intensity] + resting HR

Data collection

Data were tested for homogeneity of variance and the normalcy assumption test. Normality test of data using Shapiro-Wilk test was used, that reflect the data was normally distributed ($P>0.05$) after removal outliers that detected by box and whiskers plots. Additionally, Levene's test for testing the homogeneity of variance revealed that there was no significant difference ($P>0.05$). So, the data are normally distributed and parametric analysis is done.

Statistical analysis

The statistical SPSS Package application version 25 for Windows was used to do the statistical analysis (SPSS, Inc., Chicago, IL). Numerical data are expressed as mean and standard deviation for patient's anthropometric data, HbA1c, HOMA IR, fasting insulin, and fasting glucose variables. Categorical data are expressed as frequency (percentage) for gender variable and compared among groups by chi square test. One-way analysis of variance (ANOVA-test) used to compare among Group A, Group B, and Group C for patient's anthropometric data variables. Multivariate analysis of variance (MANOVA) used to compare the tested major variables of interest (HbA1c, HOMA IR, fasting insulin, and fasting glucose) at different tested groups (Group A, Group B, and Group C) and measuring periods (pre- and post-treatment). Bonferroni was used to compare between pairwise within and between groups of the tested variables which correction test P-value was significant from MANOVA test. All statistical analyses were significant at probability ($P \leq 0.05$).

3. Results

Descriptive statistics and statistical analysis (Table 1) for main variable outcomes (HbA1c, HOMA IR, fasting insulin, and fasting glucose) within each group revealed that there were significantly ($P<0.05$) decreased in HbA1c, HOMA IR, fasting insulin, and fasting glucose at post-treatment compared to pre-treatment within Group A ($P=0.031$, $P=0.001$, $P=0.019$, $P=0.0001$, respectively) and Group B ($P=0.002$, $P=0.0001$, $P=0.001$, and $P=0.0001$, respectively). But, there were insignificantly ($P>0.05$) decreased in HbA1c ($P=0.923$), HOMA IR ($P=0.854$), fasting insulin ($P=0.983$), and fasting glucose ($P=0.396$) within Group C. These significant differences in main variable outcomes are favorable of pre-diabetic nonalcoholic fatty liver patients who received the DASH diet program (Group B), followed by patients received the intermittent fasting program (Group A), and then those received control diet (Group C). Moreover, pre-diabetic nonalcoholic fatty liver patients in Group B improved more HbA1c (33.38%), HOMA IR (62.88), fasting insulin (18.12%), and fasting glucose (18.25%) followed by patients in group A (25.70, 45.23, 12.78, and 14.79 %, respectively), and then patients in Group C (2.87, 6.77, 2.34, and 2.55%, respectively).

Descriptive statistics and statistical analysis (Table 2) for main variable outcomes among groups A, B, and C revealed that no significant differences (P>0.05) at pre-treatment among groups A, B, and C in HbA1c (P=0.720), HOMA IR (P=0.753), fasting insulin (P=0.692), and fasting glucose (P=0.164). In contrast, there were significant differences (P<0.05) at post-treatment among groups A, B, and C in HbA1c (P=0.013), HOMA IR (P=0.027), fasting insulin (P=0.033), and fasting glucose (P=0.001)

Table1. Within and between group comparison for main variable outcomes

Variables	Items	Groups (Mean ±SD)			P-value[2]
		Group A (n=20)	Group B (n=20)	Group C (n=15)	
HbA1c	Pre-treatment	7.55 ±0.24	7.52 ±0.49	7.67 ±2.18	0.720
	Post-treatment	5.61 ±0.47	5.01 ±0.29	7.45 ±2.14	0.013*
	MD (Change)	1.94	2.51	0.22	
	95% CI	3.00 – 6.88	1.13 – 6.15	-1.09 – 1.53	
	Change %	25.70%	33.38%	2.87%	
	P-value[1]	0.031*	0.002*	0.923	
HOMA IR	Pre-treatment	6.19 ±1.59	6.60 ±2.86	6.65 ±1.16	0.753
	Post-treatment	3.39 ±1.06	2.45 ±1.64	6.20 ±1.73	0.027*
	MD (Change)	2.80	4.15	0.45	
	95% CI	1.58 – 7.18	0.87 – 9.17	-0.86 – 1.76	
	Change %	45.23%	62.88%	6.77%	
	P-value[1]	0.001*	0.0001*	0.854	
Fasting insulin	Pre-treatment	16.74 ±8.52	16.83 ±10.53	16.64 ±4.32	0.692
	Post-treatment	14.60 ±6.76	13.78 ±6.41	16.25 ±7.33	0.033*
	MD (Change)	2.14	3.05	0.39	
	95% CI	4.45 – 8.73	6.71 – 12.81	-0.19 – 0.97	
	Change %	12.78%	18.12%	2.34%	
	P-value[1]	0.019*	0.001*	0.983	
Fasting glucose	Pre-treatment	96.70 ±13.76	97.25 ±15.58	93.00 ±14.72	0.164
	Post-treatment	82.40 ±21.68	79.50 ±12.73	95.37 ±21.52	0.001*
	MD (Change)	14.30	17.75	2.37	
	95% CI	2.53 – 26.07	8.90 – 26.60	-21.69 – 26.43	
	Change %	14.79%	18.25%	2.55%	
	P-value[1]	0.0001*	0.0001*	0.396	

Group A: intermittent fasting group; Group B: DASH diet group; Group C: control group

Data are expressed as mean ±standard deviation and compared statistically by MANOVA test

HBA1c: Glycated hemoglobin; HOMA IR: homeostatic model assessment for insulin resistance

MD: Mean difference CI: confidence interval P-value: probability value * Significant (P<0.05)

P-value[1]: Probability value within each group; P-value[2]: Probability value within among groups

Post-hoc test between each pairwise group comparisons at post-treatment main variable outcomes is presented in Table (2). No significant differences (P>0.05) between pairwise of Group A versus Group B in HbA1c (MD=0.60; P=0.305), HOMA IR (MD=0.94; P=0.229), fasting insulin (MD=0.82; P=0.249), and fasting blood glucose (MD=2.90; P=0.980). There were significant differences (P<0.05) between pairwise of Group A versus Group C in HbA1c (MD=0.181; P=0.039), HOMA IR (MD=0.281; P=0.001), fasting insulin (MD=1.65; P=0.025), and fasting blood glucose (MD=12.97; P=0.0001). Moreover, there were significant differences (P<0.05) between pairwise of Group B versus Group C in HbA1c (MD=2.44; P=0.005), HOMA IR (MD=3.75; P=0.001), fasting insulin (MD=2.47; P=0.001), and fasting blood glucose (MD=15.87; P=0.0001). The post-hoc test and mean differences between pairwise groups showed that the intermittent fasting program (Group A) and DASH diet program (Group B) gave the best HbA1c, HOMA IR, fasting insulin, and fasting glucose values.

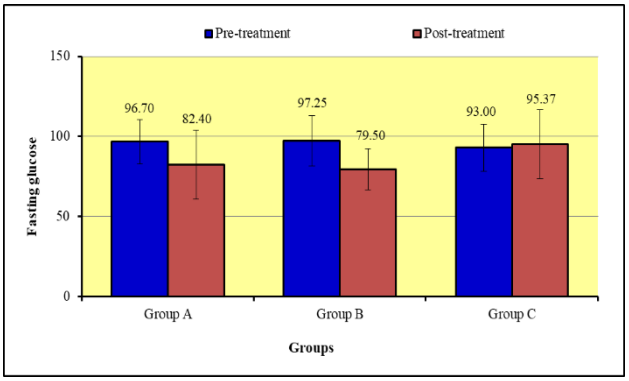

Figure (21): Mean values of pre- and post-treatment fasting glucose within each group.

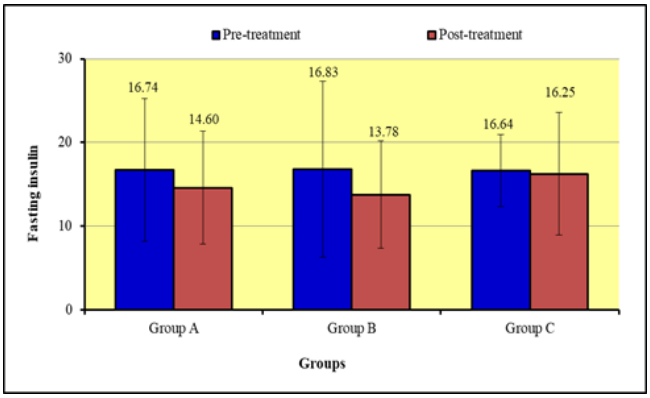

Figure (23): Mean values of pre- and post-treatment fasting insulin within each group.

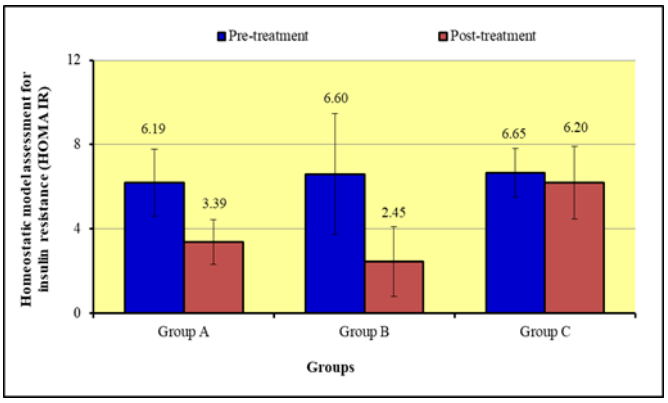

Figure (25): Mean values of pre- and post-treatment HOMA IR within each group.

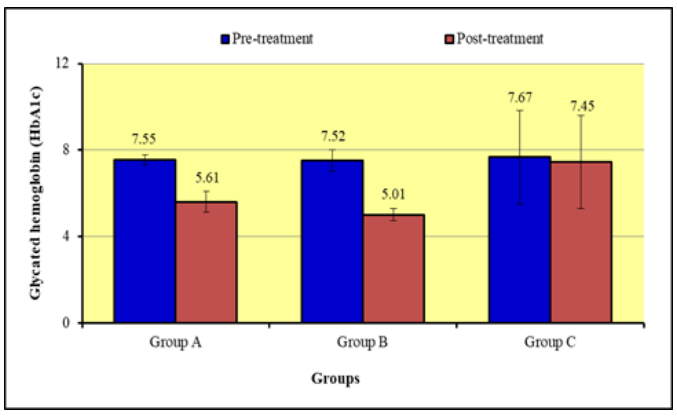

Figure (27): Mean values of pre- and post-treatment HbA1c within each group.

Table 2. Pairwise comparison (Post-hoc test) between groups for main variable outcomes at post-treatment

Variables	Items	Post-hoc test (post-treatment)		
		Group A vs. Group B	Group A vs. Group C	Group B vs. Group C
HbA1c	MD (95% CI)	0.60 (-3.21 – 4.41)	1.81 (2.98 – 6.60)	2.44 (3.20 – 8.08)
	P-value	0.305	0.039*	0.005*
HOMA IR	MD (95% CI)	0.94 (-1.64 – 3.52)	2.81 (1.50 – 7.12)	3.75 (1.02 – 8.52)
	P-value	0.229	0.001*	0.001*
Fasting insulin	MD (95% CI)	0.82 (-1.45 – 3.09)	1.65 (2.39 – 5.69)	2.47 (4.80 – 9.74)
	P-value	0.249	0.025*	0.001*
Fasting blood glucose	MD (95% CI)	2.90 (-28.14 – 33.94)	12.97 (9.64 – 16.30)	15.87 (12.88 – 18.86)
	P-value	0.980	0.0001*	0.0001*

Group A: intermittent fasting group; Group B: DASH diet group; Group C: control group

Data are expressed as mean difference and compared statistically by Bonferroni correction test.

P-value[3]: probability value between pairwise groups (post-hoc test) MD: Mean difference * Significant (P<0.05)

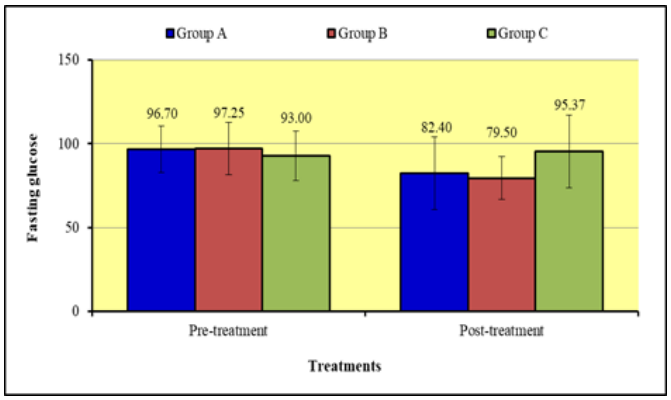

Figure (22): Mean values of fasting glucose at pre- and post-treatment among groups

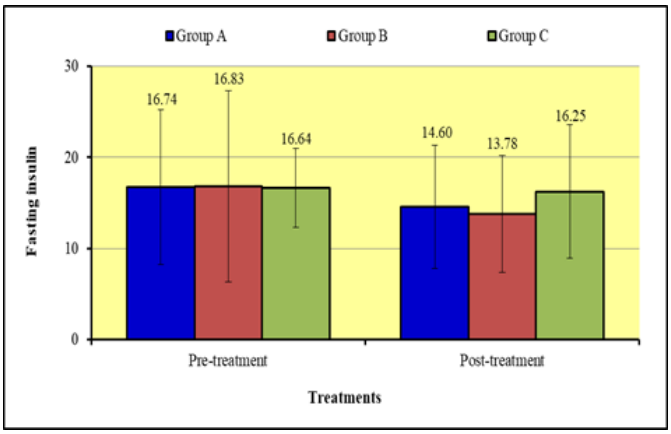

Figure (24): Mean values of fasting insulin at pre- and post-treatment among groups.

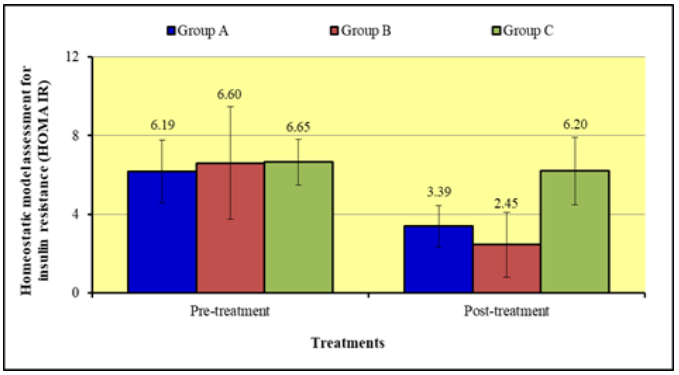

Figure (26): Mean values of HOMA IR at pre- and post-treatment among groups

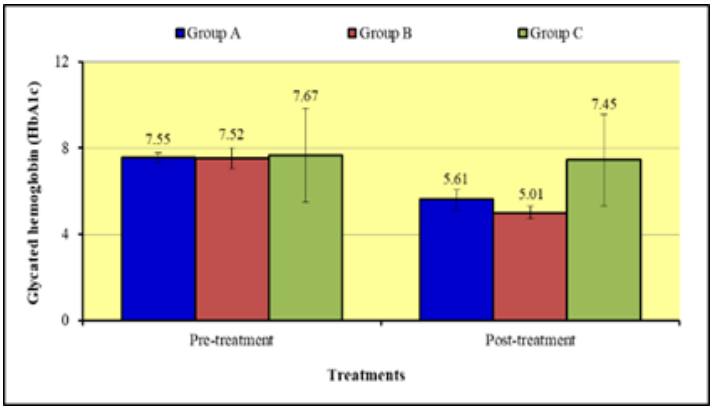

Figure (28): Mean values of HbA1c at pre- and post-treatment among groups.

4. Discussion

Dash diet

Due to its link to a lower risk of cardiovascular disease, the dietary approach to halt hypertension (DASH) is a low-glycemic index and low energy-dense diet that was initially recommended to individuals with hypertension. This diet is characterized by a high intake of fruits, vegetables, whole grains, and low-fat foods. It contains less added sugar, sugar-sweetened drinks, and processed and red meats. Therefore, this diet lowers the risk of cardiovascular disease, improves glycemic and lipid metabolism, and aids in weight loss. The primary objectives of treating NAFLD patients are all these consequences, which is why experts who treat NAFLD patients are becoming more interested in this diet (44).

In an RCT, 60 overweight or obese adults, ages 25 to 75, with elevated serum ALT levels and US-proven non-alcoholic fatty liver disease were randomized to either a control diet or the DASH diet for a period of eight weeks. The BMI and degree of steatosis were significantly lower in the DASH group, while aminotransferases and metabolic markers such insulin levels, the HOMA (homeostatic model assessment) index, serum triglycerides, and the ratio of total to HDL cholesterol were improved. A case-control research that looked at the relationship between following the DASH diet and the chance of developing NAFLD in 102 patients with recently diagnosed NAFLD and 204 controls produced different findings. The DASH-style diet was found to have an inverse connection with the risk of non-alcoholic fatty liver disease (NAFLD): participants in the top quartile of the DASH diet score—a score that is derived from the foods and nutrients that are either emphasized or minimized in the DASH diet—were 30% less likely to develop NAFLD (OR: 0.70; 95% CI: 0.61, 0.80). Nevertheless, after accounting for BMI and dyslipidemia, the correlation was not statistically significant (OR: 0.92; 95% CI: 0.73, 1.12) (44).

Also in our study, the glycemic profile in The nonalcoholic fatty liver patients in Group B received DASH diet program more improved fasting glucose reduction percentage (18.25%) which is significant decreases in mean values of fasting glucose at post-treatment is favorable of Group B (79.50 ±12.73), improved fasting insulin reduction percentage (18.25%) which is significant decreases in mean values of fasting insulin at post-treatment is favorable of Group B (13.78 ±6.41), improved HOMA IR reduction percentage (62.88%) which is significant decreases in mean values of HOMA IR at post-treatment is favorable of Group B (2.45 ±1.64), improved HbA1c reduction percentage (33.38%) which is significant decreases in mean values of HbA1c at post-treatment is favorable of Group B (5.01 ±0.29).

Time-restricted feeding and intermittent fasting

Time-restricted feeding (TRF) and intermittent fasting (IF) have gained popularity in recent years. Dietary programs that require varying durations of fasting—usually one or two days per week to up to 21 days—are referred to as intermittent fasting. On the other hand, eating habits known as time-restricted feeding (TRIF) restrict food intake to a window of eight hours or less per day, for variable amounts of time. These dietary interventions have shown several beneficial metabolic effects in overweight and obese individuals, including those with diabetes. The cornerstone of all these regimens is the "metabolic switch," which specifies the body's preferred transition from glucose utilization from glycogenolysis to fatty acids and fatty acid-derived ketones (45).

FBG was examined as an outcome of interest in six RCT arms (a total of 454 individuals; intervention ¼ 279, control ¼ 175). When comparing IF to control, there was no discernible change in FBG readings (WMD: -1.35 mg/dl, 95% CI: -5.61 to 2.91, p ¼ 0.534). There was significant inter-RCT heterogeneity (I 2 ¼ 90%, p < 0.001) (46).

In addition to improving the fasting insulin reduction percentage by 14.79% with substantial drops in the mean fasting insulin values at post-treatment (14.60 ±6.76), FBG also enhanced the reduction by 14.79% with significant declines in the mean fasting glucose values (82.40 ±21.68).

Insulin was examined as an outcome of interest in three RCT arms (124 individuals total; intervention ¼ 61, control ¼ 63). Comparing IF to control, there was no discernible change in insulin concentrations. Table 1: Qualities of research that qualify. (p ¼ 0.069; WMD: -4.79 mI U/mL, 95% CI: -9.95 to 0.37). There was significant inter-RCT heterogeneity (I2 ¼ 97%, p < 0.001) (47).

HbA1c was examined as an outcome of interest in three RCT arms (129 individuals; intervention ¼ 65, control ¼ 64). IF significantly decreased HbA1c concentrations in comparison to the control group (WMD: -0.14%, 95% CI: -0.20 to 0.08, p < 0.001). Inter-RCT heterogeneity was present to some extent (I2 ¼ 72%, p ¼ 0.026) (47).

HOMA-IR (129 individuals; intervention ¼ 65, control ¼ 64) was examined as an outcome of interest in four RCT arms. When comparing IF to control, HOMA-IR readings were significantly lower (WMD: -1.21, 95% CI: -2.08 to 0.34, p ¼ 0.006). Inter-RCT heterogeneity was present to some extent (I2 ¼ 93%, p ¼ 0.026) (47).

We found also improved HOMA IR reduction percentage by (45.23%) with significant decreases in mean values of HOMA IR at post-treatment (3.39 ±1.06), improved HbA1c reduction percentage by (25.70%) with significant decreases in mean values of HbA1c at post-treatment (5.61 ±0.47).

FBG and insulin levels were similar in all groups, despite the fact that multiple studies have demonstrated that IF regimens activate AMPK, improving glucose uptake and insulin sensitivity. Conversely, when compared to control groups, IF regimens decreased HbA1c and HOMA-IR. In fact, the idea that IF regimens prescribed for NAFLD patients can improve glycemic indices is supported by the pathophysiological and clinical link between NAFLD and pre-diabetes or diabetes (47).

Moon et al. showed that TRF raises fasting blood glucose levels in a meta-analysis. A meta-analysis by Faris et al. suggests that observing Ramadan can benefit insulin, glucose, and HOMA-IR readings. A meta-analysis of studies on individuals without chronic metabolic disease also shown that intermittent fasting significantly improves insulin resistance and glycemic management. Another meta-analysis found that intermittent fasting was associated with improved glycemic control in obese individuals with type 2 diabetes (47).

Statistically significant increases were observed in the fasting blood glucose levels (85.5 mg/dL vs. 133.6 mg/dL, p < 0.001 in men; 100 mg/dL vs. 120.2 mg/dL, p < 0.001 in women) in the meta-analysis research. Furthermore, insulin levels were examined and it was shown that there was a change in the female group of 15.9 ± 7.1 mg/dL vs. 12.7 ± 4.6 mg/dL, p = 0.01: 15.1 ± 2.8 IU/mL vs. 15.3 ± 2.8 IU/mL, p < 0.001. When HOMA-IR was additionally considered, slight decreases that were not statistically significant were noticed (46).

5. Conclusion

both Dash & IF are effective therapeutic approach to control insulin resistance in NAFLD patients, prevention strategy for diabetes type 2.

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