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The Effect of Weight Reduction on Metabolic, Ultrasound and Anthropometric Parameters among Patients with Obesity with NAFLD and NAFPD

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Abstract— Background: Nonalcoholic fatty liver disease (NAFLD) and nonalcoholic fatty pancreatic disease (NAFPD) are expected to increase because of the rising prevalence of central obesity. Aim: to study weight reduction effects on metabolic, anthropometric, and ultrasound parameters in non-diabetic, overweight, and obese people with NAFLD and NAFPD. Subjects and methods: 133 adults aged 35-65 who were obese or overweight and had no diabetes participated in this study for six months. Participants underwent an individualized, intensive lifestyle program that included dietary changes. The diet recommendation was a low-fat hypocaloric meal. All subjects underwent ultrasound (US) examinations before the program, at 3rd month as well as at 6 months. We assessed the effects of weight loss on NAFPD (at baseline, 3 months, and 6 months) by linear mixed components. Result: Triglycerides and transaminases, two laboratory parameters, were significantly reduced by the ending of the study. The ultrasound outcomes revealed that in non-diabetic people who are overweight or obese, losing weight significantly lowers NAFLD while leaving NAFPD unaffected. No association was found between NAFPD and anthropometric parameters, blood pressure assessments, or blood indicators at rho > 0.4. Conclusion: weight reduction leads to a substantial drop in NAFLD in overweight and obese non-diabetics. Losing weight, on the other hand, seems not to affect the NAFPD.

Keywords: Weight reduction, Metabolic, anthropometric.

Introduction

Non-alcoholic fatty liver disorder (NAFLD) and non-alcoholic fatty pancreatic disease (NAFPD) are expected to increase as a result of the rising prevalence of central obesity across all age groups. Some research has found a bond among nonalcoholic fatty liver disease (NAFLD) and obesity [1–3]. Abdominal imaging studies confirm NAFPD in about 50%–80% of patients with non-alcoholic staetoheptitis [4,5]. These findings indicated that NAFLD status might be associated with NAFPD risk. NAFPD is seen in over 70% of NAFLD patients and has been connected to numerous of the disease's famous risk factors, comprising insulin resistance (IR), diabetes mellitus (DM), hyperlipidemia, metabolic syndrome, visceral fat, and obesity [6]. As a result, individuals with MS should be screened for both NAFLD and NAFPD; nevertheless, further epidemiological research is necessary to clarify NAFPD. [7].

Adipose tissue is considered as an endocrine organ since it can interact with other organs. When the storage capacity of adipose tissue exceeds the limit, fat is redistributed from adipose to non-adipose tissues as skeletal muscle, the pancreas, and the liver during weight gain [8]. Clinical conditions like insulin resistance, b-cell dysfunction, and type 2 diabetes can all be related back to the pancreatic fatty infiltration, which promotes the hyperplasia and hypertrophy of pancreatic cells. [9,10].

Since NAFPD is linked to inflammatory conditions like acute pancreatitis and pancreatic cancer, it is likely that it is a condition of chronic glucogenic and lipogenic inflammation. This inflammation is most likely triggered by elevated oxidative stress generated by the metabolism of free fatty acids (FFA) and the stimulation of pro-inflammatory cascades by FFA (e.g., nuclear factor kappa beta [NF-kB], interleukin 1β, tumour necrosis factor α [TNFα]), could lead to progressive acinar cell death, neoplasia, and/or acute pancreatitis [11–15].

Weight loss is a crucial part of treating patients who are overweight and have metabolic syndrome [16,17]. All national and international guidelines recommend weight loss as the most beneficial NAFLD therapy at present. Losing weight, either through meal and lifestyle programs, pharmacotherapy, or bariatric surgery, has been shown to improve indicators of NAFLD, stop its progression, and even reverse fibrosis in some people [18].

There have been a number of studies looking at how losing weight affects pancreatic fat content (PFC). According to ***Tene et al***. [19] and ***Gaborit et al.***,[20] the PFC reduces following bariatric surgery or exercise-induced weight loss. However, neither surgical nor calorie restriction-induced weight loss resulted in a decrease in PFC, as found by ***Steven et al.*** [21] and ***Vogt et al.*** [22]. There is still a need for more research to be done to fully understand the impact of losing weight on the associated features of NAFPD.

The main objective of this study was to assess and compare the efficacy of a calorie restriction-weight reduction program on ultrasonography, anthropometric, and metabolic parameters in obese and non-diabetic overweight people with both NAFPD and NAFLD. We also investigated if alterations to NAFPD during weight loss were associated with a specific pattern of circulating indicators of glucose metabolism, lipid metabolism, and anthropometric measures.

Patients and methods

This six-month prospective study was carried out at Tropical Medicine and Internal Medicine Departments of Minia University Hospital. Participants who had both NAFPD and NAFLD recognized via abdominal US (ultrasonography) during examination as a part of the health checkup were potentially eligible. The research was accepted by the Institute Ethics Committee. All participants provided informed consent.

Study subjects:

The investigation involved 160 non-diabetic, overweight, or obese non-smokers aged 35–65 years. Patients' exclusion criteria were men and women ingesting >30 g or >20 g daily of alcohol, respectively, lactating or pregnant females; cases identified with thyroid abnormalities or Cushing's syndrome; HbA1c scores ≥6.5% and/or fasting plasma glucose concentrations >126 mg/dL; and patients with severe chronic disorders (hepatic or renal dysfunction; massive cardiovascular abnormalities; cancer history). Long-term steroid users, as well as individuals suffering from various secondary manifestations of fatty liver, those with eating disorders, those currently enrolled in a formal dietary program for weight loss, and those who had dropped 5% or more of their total body size through dietary and exercise changes in the preceding 3 months were not included in the study. Due to these exclusions, the study population was limited to obese or overweight adults having no diabetes.

Only 43 people, or 32.3% of the study population, met the modified WHO specifications for metabolic syndrome [23]: high insulin levels (the upper 4th of non-diabetic subjects' fasting insulin level) or high blood sugar levels (fasting glucose 110 mg/dl) plus a minimum of two of the following factors: waist circumference 94 cm, dyslipidemia (triglycerides 150 mg/dl or HDL cholesterol 40 mg/dl), or blood pressure 140/90 mmHg or taking blood pressure medication.

Participants in the study underwent a scientifically developed, individualized, intensive lifestyle program that focused on dietary changes. A low-fat hypocaloric diet was suggested, with an energy deficit of 750 kcal/d relative to their estimated basal metabolic frequency using the Mifflin St. Jeor equation [24]. Carbohydrates made up 64% of the diet, fat 22% (with less than 10% of overall calories coming from saturated fatty acids), and protein 14%. Food diaries were given to participants so they could track what they ate and drank each day and see how closely they were meeting their macronutrient and energy goals. Six months of monthly patient monitoring were performed. All individuals received monthly visits to the clinic during the six months to detect any adverse impacts and track self-reported compliance. The current research's analytical group comprised 133 of the 160 initial trial participants (4 unknown reasons, 3 personal/stress, 1 pregnancy, and 19 who did not achieve the desired weight reduction percentage of 10%). These 19 individuals reported minor physical signs, involving dizziness, fatigue, lack of concentration, and cold sensation, and they stopped the dietary weight reduction program.

Subject assessment and ongoing observation:

Height and weight were estimated via standard procedures. The WC (waist circumference) was calculated by measuring the distance across the lower rib border and the superior iliac spine. The BMI (body mass index) was described as body weight divided by body height squared. Liver enzymes, HbA1c, fasting glucose, Serum alanine aminotransferase (ALT), and aspartate aminotransferase (AST) were acquired. The insulin resistance index (HOMA-IR) was calculated. Lipids were gathered in the morning following a fast of more than eight hours. All of the participants in the trial had abdominal US examinations with high-resolution US utilizing a 3.5

MHz linear transducer and regular approach, and the data were analyzed by a single expert radiologist.

NAFPD was diagnosed when the pancreatic body's echogenicity was higher than that of the renal cortex. All of the subjects were divided into three groups: Grade I NAFPD: the pancreatic parenchyma appears more echogenic compared to the kidney. Grade II NAFPD: The pancreatic parenchyma has a higher echogenicity than that of the kidney but a lower echogenicity than that of the retroperitoneal fat. Grade III NAFPD: Pancreatic parenchyma has a higher echogenicity than that of the retroperitoneal fat. Abdominal ultrasound was used to evaluate the degree of NAFLD. During the US examination, steatosis severity was categorized as grade 1, 2, or 3.

*Data collection:*Anthropometric data were collected at baseline, at the 3rd month, and at the end of the 6-month calorie restriction-weight reduction plan. Blood specimen were gathered at baseline and at 6 months. Ultrasound tests were employed before the program, at the 3rd month as well as at 6 months.

*Study outcomes:*The main finding of the calorie restriction-weight reduction program was a 10% weight reduction. Other outcomes studied were: (I) advances in metabolic parameters; (II) Drop in grade of NAFLD (III) Drop in grade of NAFPD (e) Decrease in WC (f) improvement in HOMA-IR.

Statistical Analysis

160 cases were gathered for the study. For this study, we used data from 133 total participants. Quantitative variables having a normal distribution were expressed using the mean and standard deviation, whereas skewed distributions were expressed using the median and range. Frequencies with percentages were used to present categorical data. Results below 0.05 were taken as statistically significant.

Results:

A total of 133 ultrasound diagnosed NAFLD & NAFPD individuals, who fulfilled the eligibility criteria were analyzed. In this study, 73 females and 60 males were enrolled. The mean age of individuals was 42.79 ± 10.30 years. Anthropometric measures along with the ultrasound findings of the subjects at baseline and the next three and six months of the calorie restriction-weight reduction program are shown in **Table (1)**.

After three months, the median BMI dropped from 35.0 kg/m2 to 31.5 kg/m2 (p 0.001), and after six months, it dropped to 30.7 kg/m2 (p 0.001). Anthropometric measurements significantly changed along with weight reduction. After three months, the waist circumference dropped from 117 cm to 107 cm (p 0.001), and after six months, it dropped to 103 cm (p 0.001).

The number of NAFLD individuals dropped rapidly with weight reduction, from 31 grade 1 at baseline to 14 after three months ($p < 0.001$) and 17 individuals normalized after six months ($p <$

0.001). In grading after six months of weight reduction, we have 85 of 133 (64%) NAFLD in different grades (14 grade 1, 43 grade 2, and 28 grade 3), with a remaining 48 individuals (36%) without NAFLD (grade 0). In NAFLD grades 2 and 3, no significant change was noticed after three months, but there was a significant change in grading after six months of weight reduction **(Table 1)**.

While NAFLD decreased, the change in grading of NAFPD was not significant after three to six months of weight reduction. In grading after six months of weight reduction, we have 114 of 133 (85.8%) NAFPD in different grades (18 grade 1, 55 grade 2, and 41 grade 3), with a remaining 19 individuals (14.2%) without NAFPD (grade 0). When we compared the change to grade 0 in NAFLD and NAFPD, it showed a significant difference (P =0.001) **(Table 1, Figure 1)**.

As demonstrated in Table 2, most of the laboratory parameters altered greatly with weight reduction. An improvement was found in liver enzymes (ALT and AST), which decreased significantly during the calorie restriction-weight reduction program (ALT: $p < 0.01$, AST: $p = 0.05$). Additionally, the weight reduction was associated with a decrease in triglycerides after six months ($p = 0.01$). whereas in our study, weight loss did not significantly affect the levels of cholesterol, low-density lipoprotein (LDL), or high-density lipoprotein (HDL) cholesterol. HOMA-IR decreased, but the change was not significant after six months **(Table 2)**.

Table (3) showed the correlations of NAFPD and NAFLD with weight, waist circumference, BMI, blood pressure, liver transaminases, and lipid profiles. There were no correlations between NAFPD and anthropometric measurements, blood pressure, or blood biomarkers at rho > 0.4.

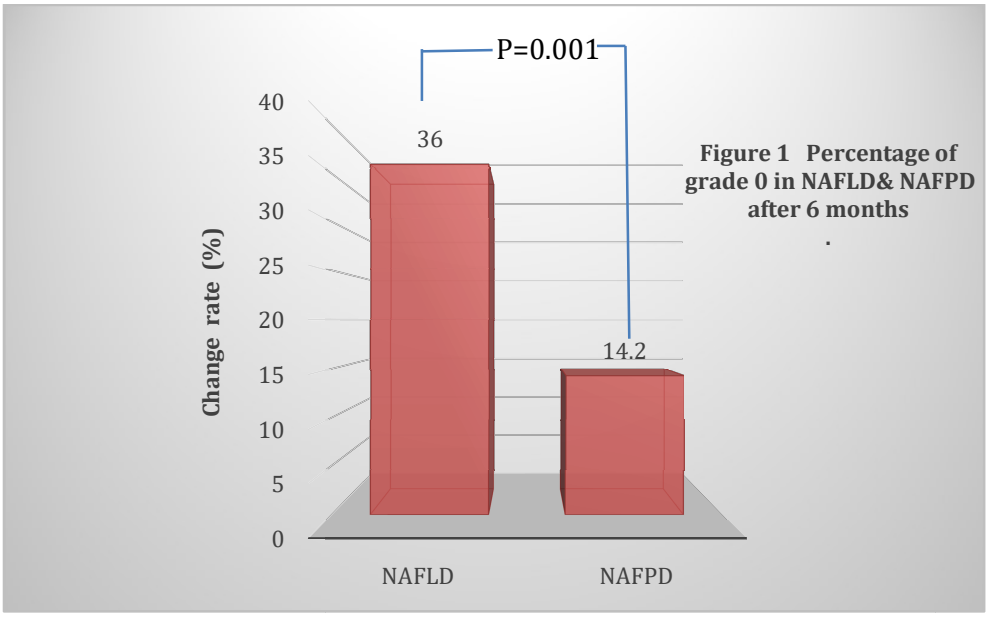

Fig. 1:Percentage of grade 0 in NAFLD& NAFPD after 6 months.

Table (1): Anthropometric measures, and ultrasound findings at baseline and after three and six months.

	Baseline	After 3 months	After 6 months	Changes at 3 months	P	Changes at 6 months	P
Anthropometric measures							
Weight [kg]	106.1 (89.1; 118.1)	97.7 (85.3; 109.4)	92.4 (82.2; 103.7)	-8.4.0 (-13.7; -10.0)	< 0.001	-13.7 (-19.9; -9.1)	< 0.001
Body mass index [kg/m2]	35.0 (32.1; 40.8)	31.5 (28.8; 37.0)	30.7 (27.8; 34.1)	3.2 (-4.1; -2.8)	< 0.001	4.6 (-6.2; -2.6)	< 0.001
Waist circumference [cm]	117.0 (102.; 124.0)	107.0 (94.0; 118.0)	103.0 (92.0; 112.0)	-10.0 (-11.0; -7.0)	< 0.001	-14.0 (-16.0; -8.0)	< 0.001
Grade of NAFLD							
Grade 1 n (%)	31	17	14	14 (45.1%)	<0.01	17 (54.8%)	< 0.001
Grade 2 n (%)	59	47	43	12 (20.3%)	0.13	16 (27.1%)	<0.01
Grade 3 n (%)	43	39	28	4 (9.3%)	0.32	15 (34.8%)	< 0.001
Grade of NAFPD							
Grade 1 n (%)	22	20	18	2 (9.09%)	0.31	4 (18.1 %)	0.21
Grade 2 n (%)	63	57	55	6 (9.5%)	0.42	8 (12.6%)	0.39
Grade 3 n (%)	48	44	41	4 (8.3%)	0.38	7 (14.5%)	0.33

Table (2): Blood pressure, metabolic parameters, and laboratory data, at baseline and after six months.

Outcome measure	Baseline	After 6 months	p
SBP (mmHg)	139.6 ± 11.0	132.2 ± 14.0	<0.01
DBP (mmHg)	90.1 ± 8.1	86.0 ± 81	<0.01
Metabolic syndrome [n (%)]	43 (32.3)	37 (27.8&)	< 0.001
AST	41.9 ± 32.3	28.6 ± 10.8	<0.05
ALT	51.7 ± 41.6	34.1 ± 14.8	< 0.01
Cholesterol [mg/dL]	211.4 ± 34.1	203.3 ± 34.5	0.23
Triglycerides [mg/dL]	139.4 ± 64.9	108.3 ± 53.5	0.01
HDL [mg/dL]	54.0 ± 15.0	52.9 ± 14.9	0.41
LDL [mg/dL]	129.5 ± 26.0	128.7 ± 29.5	0.42
HbA1c [%]	5.5 ± 0.4	5.4 ± 0.3	0.38
HOMA-IR	3.4 ± 1.9	2.6 ± 1.3	0.11
Glucose [mg/dL]	93.4 ± 8.0	91.8 ± 8.0	0.23

Table (3): Parameters associating with NAFPD and NAFLD by Spearman's correlation coefficient.

	NAFPD		NAFLD	
	rho	**p-Value**	**rho**	**p-Value**
Weight	0.281	0.001 *	0.412	0.001 *
BMI	0.258	0.002 *	0.521	0.001 *
Waist circumference	0.241	0.004 *	0.496	0.001 *
NAFPD	1.000		0.185	0.025

NAFLD	0.185	0.025	1.000	
SBP (mmHg)	0.042	0.691	0.142	0.080
DBP (mmHg)	0.026	0.421	0.312	0.024
AST	0.067	0.479	0.189	0.024
ALT	0.141	0.072	0.457	0.001 *
Cholesterol [mg/dL]	−0.092	0.697	0.087	0.239
Triglycerides [mg/dL]	0.107	0.351	0.329	0.001 *
HDL [mg/dL]	−0.169	0.041	−0.368	0.001 *
LDL [mg/dL]	−0.004	0.850	0.079	0.421
HbA1c [%]	0.048	0.567	0.223	0.001 *
HOMA-IR	0.073	0.431	0.325	0.001 *
Glucose [mg/dL]	0.076	0.327	0.245	0.002 *

Discussion

Despite the widespread acceptance of diet and lifestyle changes as treatments for NAFLD, diabetes, and cardiovascular disease, there is scant evidence to support making the same recommendation for NAFPD [25–28]. In the present study, we used ultrasound to evaluate changes in NAFLD and NAFPD following a standardized caloric restriction-weight-reduction of 10 % or more in overweight or obese non-diabetics. Triglycerides and transaminases, two laboratory parameters, decreased noticeably by the end of six months. Our ultrasound findings suggest that in non-diabetic individuals who are overweight or obese, losing weight significantly reduces NAFLD while leaving NAFPD unaffected.

Obese patients with and without diabetes have been studied for the impact of weight loss on the grading of NAFLD [29–35]. These studies found that different dietary programs reduced NAFLD grading by percentages ranging from 43.0 to 84.1 %, which is comparable to our finding that NAFLD had decreased by approximately 36 percent to grade 0 by the end of six months. We observed that in NAFLD grades 2 and 3, no significant change had occurred after three months, but there was a significant change in grading after six months of weight reduction. This finding conflicts with that of ***Colles et al.***,[33] who found that 80% of liver fat reduction was during the

first two weeks of a diet. This is because in that study they used a very-low-energy diet, and the individuals were morbidly obese (BMI > 40).

Weight reduction had a minor influence on the grading of NAFPD measured by ultrasound. NAFPD remained at a different grade by the end of six-month caloric restriction -weight reduction, and only 14.2 % reached grade 0 by the end of six months.The change of NAFLD to grade 0 was significantly higher than the change in NAFPD (36% vs. 14.2%). In NAFPD, when correlated with anthroprometric parameters, blood pressure, and a number of metabolic indicators (cholesterol, triglycerides, or insulin), there were no correlations.

NAFPD did not change significantly because, in contrast to the liver, in NAFLD the fat accumulates intra-hepatocytes, while in NAFPD, intra-pancreatic fat is located within adipocytes [37].Since the pancreas goes through the same processes of fat buildup and infiltration as other organs, weight loss may be the decisive factor in whether NAFPD worsens or improves.

The importance of NAFPD in clinical practice is currently being discussed. Age and body mass index have both been linked to an increase in fat in the pancreas [38–40]. However, the link between pancreatic fat and type 2 diabetes remains controversial. Researchers ***Van der Zijl et al.***[41] found that pancreatic fat in people with impaired glucose metabolism was unrelated to beta-cell function. Pancreatic steatosis was not linked to diabetes risk in a study by ***Kühn et al.***[42]. Pancreatic fat has not been shown to increase in type 2 diabetes patients in other studies [39]. More research is needed to know pancreatic fat's role in the metabolic syndrome, especially any potential connections to insulin resistance.

When we examined the effect of weight reduction on liver enzymes in subjects who already had abnormal liver enzymes and NAFLD at baseline, we noticed a significant decrease in ALT and AST concentrations after a dietary-induced weight reduction. Moreover, we observed an important decrease in blood pressure, triglycerides, and metabolic syndrome by the end of the 6-month weight reduction program. Overall, the findings of our study offer empirical evidence for the claim that moderate weight decreases of more than 10% are required to significantly reduce NAFPD and metabolic syndrome. These results are in accordance with previous reports [43].

Conclusion

This study demonstrates that in overweight and obese non-diabetics, losing weight significantly lowers the risk of developing NAFLD. On the other hand, losing weight does not seem to have any effect on the NAFPD.

Conflict of interest: None.

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