Impact of Aerobic Exercise and Diet-induced Weight Reduction on Liver Enzymes among Centrally Obese Egyptian Women

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Abstract: Obesity lead to adverse metabolic effects. Obese subjects are at increased risk of liver problems. The incidence of obese patients with fatty liver has increased. This study was conducted to find out the effects of diet restriction and exercise training program on liver enzymes levels (AST and ALT) in centrally obese Egyptian women with fatty liver. Forty eight obese women with BMI 30-39.9 Kg/m² and their ages ranged from 45 to 55 years participated in the study. The patients were randomly assigned to two equal groups. Group 1: (n=24) received weight reduction program (healthy lifestyle control), diet-induced weight loss (1200-1300 Kcal/day) and aerobic exercise for 12 weeks. The exercise intervention consisted of electronic treadmill for 50 minutes, the patients trained to achieve a heart rate of 60–75% of her maximal heart rate for 3 times /week. Group 2: (n=24) were given general information about healthy food choices and low-caloric diet (1200-1300 kg/day) for the same period. Weight, body mass index (BMI), waist circumference (WC) and Liver enzymes (AST and ALT) levels were measured. Results showed no significant differences between groups at the baseline. After 12 weeks, women in group (1) showed a highly significant reduction in weight (p =0.001), BMI (p = 0.001), waist circumference (p = 0.001), AST (p = 0.001) and ALT (p = 0.001). Women in group (2) also demonstrated significant statistically differences in the mean values of weight (p =0.001), BMI (p= 0.01), waist circumference (p=0.001), AST (p = 0.001) and ALT (p = 0.001). The reduction in ALT levels in group (1) and group (2) is 50.8% and 18.58% respectively, AST also decreased in group (1) and group (2) by 54.46 % and 25.59 % respectively. It can be concluded that lifestyle modification, exercise training and low caloric diet resulted in weight reduction and improvement of liver enzymes (AST and ALT) in centrally obese Egyptian women with fatty liver but exercise training and low caloric diet is potentially more valuable than diet restriction only.

Key words: Weight reduction · Aerobic training · Obesity · ALT · AST

INTRODUCTION

The problem of obesity has grown tremendously through the 20th century and into the 21st century, slowly transforming into an epidemic. Along with it, nonalcoholic fatty liver disease (NAFLD) has become one of the major diseases plaguing the nation and world [1].

Centralized distribution of fat is associated with numerous health risks. Central obesity, is an independent and more potent risk factor for insulin resistance, type 2 diabetes, coronary heart disease, stroke and mortality than total body obesity. This may be attributable partially to the role of intra abdominal fat, on metabolic abnormalities. Visceral fat is more metabolically active than subcutaneous fat and is thought to have a stronger influence on adipocytokine production and insulin resistance [2].

The nutrition transition in Egypt has occurred in the context of abundant dietary energy availability, urbanization and moderate fat intakes on average (27% in urban and 22% of dietary energy in rural areas). The prevalence of obesity in adults is very high, particularly among women. The prevalence of hypertension and diabetes mellitus parallel to that of obesity and both are very high. Little information is available on physical activity, but it is likely that a large proportion of the population is quite sedentary, particularly in the cities [3].

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The rates of obesity grew in Egypt since the 1990s mainly because the fats and carbohydrates became more heavily consumed. Furthermore, food is traditionally the center of special occasions and social events in the Egyptian society [4].

Paralleling the increasing prevalence of obesity in the general population the metabolic syndrome is now on the rise. Hypertension, coronary artery disease, diabetes, hypercholesterolemia, osteoarthritis and nonalcoholic fatty liver disease (NAFLD) have become major issues of concern worldwide [5]. The clinical implications of this alarming prevalence of NAFLD are derived from the fact that it may progress to cirrhosis, liver failure and hepatocellular carcinoma [6].

Body mass index (BMI) is used for the measurement of obesity. It compares weight and height that calculated by dividing weight in kilogram onheight (in meters square), an adult who has a BMI of 25-29.9 is considered overweight and an adult who has a BMI over 30 is considered obese [7].

Both sedentary lifestyle and decreasing physical activity play a major role in obesity worldwide. At least 30% of the world's population gets insufficient exercise [8]. Commonly, obesity is caused by a combination of excessive food energy intake, lack of physical activity and genetic susceptibility, although a few cases are caused primarily by genes, endocrine disorders, medications or psychiatric illness [9].

Obesity increases the risk of various diseases, particularly heart disease, type 2 diabetes, obstructive sleep apnea, certain types of cancer and osteoarthritis [10]. Most patients with NAFLD have few or no symptoms. Patients may complain of fatigue, malaise and dull right upper quadrant abdominal discomfort. Mild jaundice may be noticed although this is rare. More commonly NAFLD is diagnosed following abnormal liver function tests during routine blood tests [11].

When large vacuoles of triglycerides accumulate in the cells of liver through steatosis (i.e., abnormal retention of the lipids within a cell), it leads to fatty liver disease which is a reversible condition. Although having multiple causes, fatty liver can be considered a single disease which occurs worldwide in those who are obese (without or with effects of insulin resistance). Fatty liver disease (FLD) is commonly associated with metabolic syndrome (hypertension, diabetes, obesity and dyslipidemia) or with alcohol. In the Western countries, the FLD is considered one of the most common causes of elevated liver enzymes and chronic liver disease [12].

It was found that fatty liver disease is the commonest liver disorders in developed countries. Steatosis is the less severity form and characterized by an accumulation of triglycerides in the hepatocytes while steatohepatitis (SH) is the more advanced form and characterized by injury of liver cells [13].

It was reported that individuals with fatty liver have higher calories intake especially cholesterol and saturated fat compared with healthy controls. They also have lower polyunsaturated fat intake, antioxidant vitamins (such as vitamin E and C) and fibers [14].

Hepatic steatosis is strongly associated with centralobesity. So, lifestyle modification which includes exercise and dietary restriction to achieve weight loss, beside risk factors control such as obesity, T2DM and dyslipidemia, are recommended as the most and first important approach for NAFLD (Nonalcoholic fatty liver disease) management [15].

Exercise has a positive direct impact on liver fat. Habitual physical activity is negatively associated with liver fat independent of BMI [16]. Studies on the changes in body weight and lifestyle with changes in serum ALT levels revealed that weight loss and regular exercise were significantly associated with improvement in serum ALT and increased the odds of ALT normalization. They suggested that reducing body weight by at least 5% with subsequent weight control and exercising regularly may be beneficial in treating fatty liver [17].

The aim of this study was to find out the efficacy of lifestyle modification and weight reduction program on liver enzymes (ALT and AST) in centrally obese women with fatty liver.

**MATERIAL AND METHODS**

**Subjects:** This study was conducted on forty eight obese (BMI, 30-39.9 Kg/m²) women with elevated liver enzymes aged 45 to 55 years. Women were recruited from the outpatient department of the obesity unit at October 6th University Hospital, Giza, Egypt. This study was conducted at October 6th University Hospital.

**Inclusion Criteria:**
- Body mass index (BMI) range from 30-39.9 kg/ m².
- Centrally obese (Waist circumference >88 cm)
- Patients with echogenic liver on ultrasonography suggestive of fatty liver (steatosis) and/or persistently elevated liver enzymes (AST > 40 units per liter of serum, ALT > 56 units per liter of serum)
Their age ranged from 45 to 55 years old.
Able to follow instructions of diet.
Sign in a consent form.
Women were sedentary (< 1 h/week of physical activity), with no evidence of participation in any diet reduction program.

**Exclusion Criteria:**
- Cardiovascular instability.
- Hypo or hyperthyroidism.
- Unstable metabolic disorders
- Chronic diseases: Diabetes mellitus, renal failure, visual impairment, liver cirrhosis or any known etiology for liver disease.
- Orthopedic problems interfere with the aerobic exercise program.
- Evidence of any other systemic or malignant diseases.

The patients were divided into two groups:-

**Group 1:** (n=24) received weight reduction program (healthy lifestyle control, diet-induced weight loss (1200-1300 Kcal/day) and aerobic exercise 50 minutes, 3 sessions / week for 12 weeks. Their mean ± SD age, weight, WC and BMI were 49.7±2.63 years, 94.5±4.03 kg, 105.6± 6.4 cm and 37.9±5.9 kg/m² respectively.

**Group 2:** (n=24) was given general information about healthy food choices and low-caloric diet (1200-1300 kg/m² /day) for the same period. Their mean ± SD age, weight, WC and BMI were 49.6 ± 2.82 years, 93.8±9.6 kg, 106.2±7.8 cm and 37.4±6.74 kg/m² respectively.

**Instrumentation**

**Evaluation Instruments:**
- Body Weight and Height Scale (Seca 200, Hamburg, made in Germany) to measure the patient’s weight and height and body mass index (BMI) according to the following formula: BMI= Weight (kg) /Height (m2) [18].
- Standardized Flexible tape measurement used to measure waist circumference.
- Disposable plastic syringes were used for drawing venous blood samples, polypropylene tubes with EDTA to keep blood samples and kits supplied by "Diamond Diagnostics".
- Ultrasound Toshiba Xario device to evaluate the steatosis.

**Treatment Program:**
- Both groups received low caloric diet provides 1200-1300 Kcal / day. A diet with low saturated fat and no trans –fats and high fiber diets (such as fruits, vegetables, whole grains, non-refined complex carbohydrates) were emphasized.

**Methods:** Before starting the study, the procedures and the study protocol were explained in details for each patient and a written informed consent was signed by each patient before participation in the study as an agreement to be included in the present study. This study was reviewed and was approved by the Ethics Committee of Faculty of Physical therapy, Cairo University.

**Evaluation Methods:** All patients were subjected to all of the following evaluation protocol:
- Detailed medical history and physical examinations.
- Anthropometric measurements: weight, height, BMI and waist circumference.
- Analysis of Liver enzymes (ALT and AST): Sterile syringes, tourniquet and cotton were used to draw the venous blood samples (6ml) from the ante-cubital vein from all patients of both groups to be assayed later for measurement of serum alanine aminotransferase and aspartate aminotransferase before and after the study (i.e.12 weeks).

**Treatment Instruments:**
- Electronic treadmill (Delux motorized screened treadmill, USA) with electronic digital heart rate monitor was used for the aerobic training program for the study group (1).
(65%-75% of their maximal heart rate) in bouts with a total time of 40 minutes, then the patient ending the session by cool-down phase which continued 5 minutes during which the workload gradually decreased (30-40% of maximal heart rate) until HR had nearly returned to their resting levels.

**Group 2:** were given general oral and written information about healthy food choices and low-caloric diet (1200-1300 kg/m²/day) at baseline and at subsequent weekly visits for food exchange list, but no specific individualized exercise programs were offered to them.

**Statistical Analysis:** The data obtained were analyzed using descriptive statistics of mean and standard deviation for all the variables. Inferential statistics of dependent and independent t-tests were used to explore differences in mean values of BMI, WC, ALT and AST between the two groups and within each group. The Statistical analysis was conducted through Statistical package for social sciences (SPSS 19) version 19.

### RESULTS

The effect of aerobic exercise and diet-induced weight reduction on liver enzymes in 48 centrally obese Egyptian women was assessed after 12 weeks. The demographic data of both groups are shown in (Table 1). There was no statistically significant difference between both groups.

Results revealed a statistical significant improvement (decrease) in the anthropometric measurements in both groups with more improvement in group (1), as shown in (Table 2).

**Regarding the Results of Liver Enzymes (ALT and AST) in Both Groups:** Before the study, there was no statistically significant difference between both groups regarding mean values of Liver enzymes (ALT and AST). After lifestyle, exercise intervention and diet restriction in group (1) and diet-induced weight loss in group (2), a significance improvement (decrease) was found in both groups post treatment compared to pretreatment with more improvement in group (1) as shown in (Table 3).

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<tr>
<th>Table 1: Demographic data of patients of both groups (group 1 and group 2) before the study</th>
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<td><strong>Group 1</strong></td>
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<td>Weight (kg)</td>
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<td>BMI (kg/m²)</td>
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<td>WC (cm)</td>
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:mean, BMI = body mass index, WC = waist circumference, p-value=probability value, SD: Standard Deviation, t-value: unpaired t value, NS: Non significant

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<th>Table 2: Comparison between mean values of anthropometric measurements before and after treatment in both groups</th>
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<td><strong>Group 1 (Mean± SD)</strong></td>
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<td><strong>Variable</strong></td>
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<td>Weight (Kg)</td>
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<td>BMI (Kg/m²)</td>
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<td>WC (cm)</td>
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BMI = body mass index, WC = waist circumference, *: decrease, p-value=probability value, SD: Standard Deviation, *Significance

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<th>Table 3: Comparison between mean values of Liver enzymes (ALT and AST) before and after treatment in both groups</th>
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<td><strong>Groups</strong></td>
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SD: Standard Deviation, *: decrease, P-value: Probability Level,
DISCUSSION

Obesity is an increasingly important public health concern in Egypt. An estimated (35 %.) of Egyptian adults (18.7 % males and 48.1 % females) are considered to be obese [20].

It is increasingly recognized that the location of excess adiposity, particularly increased deposition of visceral adipose tissue, is important when determining the adverse health effects of obesity [21]. So, this study was done to find out the effect of moderate aerobic exercise and diet-induced weight reduction on 48 Egyptian women with central obesity and elevated liver enzymes, their age ranged from 45 to 55 years. They were assigned into two groups equal in number; Group 1: (n=24) received weight reduction program (healthy lifestyle control, diet-induced weight loss (1200-1300 Kcal/day) and aerobic exercise for 12 weeks. Group 2: was given general information about healthy food choices and low-caloric diet (1200-1300 kg/day) for the same period.

The results of this study Revealeda significant improvement (decrease) in ALT and AST in both groups with more improvement in group 1, as ALT levels decreased by 50.8% and 18.58% in group 1 and group 2 respectively. AST levels decreased in group 1 and group 2 by 54.46% and 25.59% respectively.

The results of current study revealed also significant decrease in BMI and waist circumference in both groups with more improvement in group 1 in which BMI decreased by 12.13 % and 7.75 % in group 1 and group 2 respectively. Where, WC decreased in group 1 and group 2 by 17.14 % and 16.29 % respectively.

In this study, the decrease in WC in these groups is likely to be due to a decrease in the abdominal fat stores which supported by [21] who reported that exercise seems to redistribute the fat stores in the body, which ultimately leads to a decrease in visceral obesity and improve the insulin responsiveness in adipose tissue. Regular physical exercise also increases the level of serum HDL and reduces the risk of developing non-insulin dependent diabetes mellitus, both of themare considered significant risk factors for NASH.

Wang et al. [22] postulated that obesity, particularly central obesity, is strongly associated with hepatic steatosis. So, lifestyle modification that includes dietary restriction to achieve weight loss, in addition to the control of risk factors such as T2DM, obesity and dyslipidemia, is recommended as the first and most important approach to managing people with NAFLD.

The results of Suzuki et al. [11] agree with the result of the current study as they found that changes in body weight and lifestyle associated with changes in serum ALT levels. They found also that regular exercise and weight loss were significantly associated with improvement in serum ALT. They suggested that reducing body weight by at least 5% with subsequent weight control and exercising regularly may be beneficial in treating fatty liver.

Adams et al. [23] demonstrated that, a sedentary lifestyle with reduced physical activity, independent of diet, represents a risk factors for fatty liver. Although these risk factors may successfully be modified by moderate lifestyle interventions, the existence of other risk factors most probably may necessitate more intense treatment. Among them, a disproportionate fat distribution, particularly with increased visceral adiposity releasing humoral factors regulating liver fat. Liver fat measure is closely and positively correlated with measures of total adiposity such as body mass index (BMI) or percentage body fat.

The results of Kadayifci et al. [24] agree with the result of the current study as they revealed that weight reduction results in the loss of white adipose tissue, which decreases insulin resistance (IR). Exercise can also improve muscular insulin sensitivity, which may improve the impact of IR on NAFLD. The weight reduction with a calorie-restricted diet, with or without exercise, results in a significant biochemical improvement in overweight and obese adults and significant reduction in ALT values in patients with biopsy proven NAFLD.

The results of this study were consistent also with the findings of Chalasani et al. [25] who stated that moderate amounts of weight loss as well as exercise are associated with improvement in insulin sensitivity and thus are logical treatment modalities for patients with NAFLD who are overweight or obese. Weight reduction may be achieved by caloric restriction from dieting and physical exercise. Habitual leisure-time physical activity, may play a protective role in NAFLD. This association appears to be mediated by a reduced rate of abdominal obesity [26].

A study by Thomas et al. [27] stated that weight reduction program can improve liver histology and liver function results in patient with nonalcoholic steatohepatitis. With a weight loss of 4.5 to 6.8 kg, the liver transaminase levels also often return to normal.
Martins et al. [28] reported that, visceral adiposity is known to play a major role in developing NAFLD by secreting adipokines, hormones and free fatty acids, which drain directly into the portal vein and overload hepatocytes with lipids. So, diet-induced weight Reduction leads to decrease in visceral fat which in turn leads to a reduced portal free fatty acid supply, favoring changes in the secretion of adipokines.

The results of this study come coincided with results of Angulo [29] who reported that both weight loss and exercise improve insulin resistance and are recommended in conjunction with the treatment of associated metabolic abnormalities. Patients following a restricted diet and exercise regimen over 3 months had reduced liver enzymes levels and hepatic steatosis compared with control subjects.

It was found that exercise have many benefits on secondary vascular and metabolic co-morbidities associated with NAFLD, including insulin resistance, dyslipidemia, inflammation and hypertension [30] and endothelial dysfunction which reduces the risk of liver-related and cardiovascular morbidity and mortality. It was found that a one Metabolic Equivalent improvement in cardiorespiratory fitness (3.5 ml/kg/min) is associated with a 15% and 13% reduction risk of cardiovascular events and in all-cause mortality, respectively [31].

Petersen et al. [32] stated that moderate amounts of weight loss as well as exercise are associated with improvement in insulin sensitivity and thus are logical treatment modalities for patients with NAFLD who are overweight or obese. Weight reduction may be achieved by caloric restriction from dieting and physical exercise.

Sreenivasa Baba et al. [33] showed that calorie restriction and regular aerobic exercise (moderate aerobic exercise) for 3 minutes aday for 3 months resulted in normalization of liver biochemistry (ALT and AST) in patients with nonalcoholic steatohepatitis.

The chronic aerobic exercise significantly decreases the fat content of the liver and improves the outcomes of patients with NAFLD via different mechanisms. include: (i) decreasing hepatic oxidative stress through modulating of the reactive oxygen species and enhancing antioxidant enzymes such as catalase and glutathione peroxidase; (ii) reducing intrahepatic fat content by down-regulating sterol regulatory element-binding protein-1c and up-regulating peroxisome proliferator-activated receptor gamma expression levels; (iii) ameliorating hepatic inflammation via the inhibition of pro-inflammatory mediators such as tumor necrosis factor-alpha and interleukin-1 beta; (iv) attenuating mitochondrial dependent apoptosis by reducing cytochrome C released from the mitochondria to the cytosol; and (v) inducing hepato-protective autophagy [34].

The results of this study come in agreement with Gill and Wu [25], who found that a 500 kCal-restricted diet regime for 6 months, can improve liver function tests and change body fat deposits in patients with NAFLD, even though the average body weight reduction was only 4%. A low glycemic index diet regimens have been shown to cause more short-term weight loss, greater lowering of BMI and greater improvement in insulin sensitivity than low-fat diets.

CONCLUSION

In conclusion, individualized aerobic exercise, diet intervention and lifestyle modification are effective methods in the prevention and treatment of central obesity and improvement of liver enzymes in patients with nonalcoholic fatty liver.

REFERENCES


