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Effect of Moderate Aerobic Exercises on Liver Function in Non-Alcoholic Fatty Liver Disease in University Students

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Abstract:
Purpose: This study aimed to investigate effect of moderate Aerobic Exercises on Liver Function in Non-Alcoholic Fatty Liver Disease in University Students
Methods:sixty patients with non-alcoholic fatty liver disease (NAFLD) with age ranged from 18-28 years old from both sexes.Patients were divided into two equal groups; group A received their standard medications associated with low calorie diet and moderate aerobic exercises 3 times per week for 8weeks while group B received their standard medications and low calorie diet for 8 weeks. Lab investigations of aspartate aminotransferase (AST), alanine aminotransferase (ALT), and triglycerides (TG) were applied to evaluate patients. Fatigue severity scale (FSS) and body mass index BMI were calculated for patients at two intervals (pre-treatment and post-treatment).
Results: there were significant improvement of all variables post-treatment compared to pre-treatment in group (A) with improvement percentage in BMI (8.6%), ALT (15.97%), AST (16.3%), TG (17.99%) and FSS (35.38%). In (group B): there were significant improvement of all variables post-treatment compared to pre-treatment in BMI (5.9%), ALT (11.4%), AST (7.68%), TG (11.15%) and FSS (5.66%). Moreover, there were no significant difference in BMI, ALT, AST and TG between both groups. However, there was significant difference in FSS in favor of group A.
Conclusion: moderate aerobic exercises are not effective strategies in management of liver function of non-alcoholic fatty liver disease in university students when low calorie diet is a part of standard treatment of low calorie diet. Furthermore, aerobic exercise is effective method for improvement fatigue level.
Key words:moderate aerobic exercises, liver function, non-alcoholic fatty liver disease

1. Introduction

Chronic liver disease is a main reason of mortality, morbidity, and health care resource usage worldwide from with mortality dependence on CLD elevated by 46% worldwide which was mostly observed in poor and developmental countries (1).

Definition of Nonalcoholic fatty liver disease (NAFLD) is that a metabolic disorder which characterized by increase triglyceride accretion in hepatocytes while it is

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considered that approximately a 30%of the all population has NAFLD. Several factors seem to affect NAFLD including lifestyle, environment, sexr, steroid hormone metabolism, geneticsusceptibility and metabolic factors play an important a role in the pathology of NAFLD (2).

Types of Non-alcoholic fatty liver disease are non-alcoholic fatty liver (NAFL) and non-alcoholic steato hepatitis (NASH). In NAFL, hepaticsteatosis is characterized with absence of inflammation, whereas in NASH, hepaticsteatosis is characterized with hepatic inflammation .There is no large histological difference between both types (3).

There are varied estimates of NAFLD prevalence in the all population. An estimated 17%-51% of adults have NAFLD (4).

The prevalence of NAFLD in pediatric is approximately 10%, which increase to 17% in adolescents and in obese and overweight children is 40%-70%. While often self-limiting, steatosis can develop and change with injury into no-alcoholic steatohepatitis (NASH) in 3%-5% of all patients. NASH is characterized by lobular and/or portal inflammation, different degrees of fibrosis, hepatocyte death and pathological angiogenesis (5)

The American College of Sports Medicine defines aerobic exercises as any activity which using large muscle groups; is rhythmic in nature; and, can be continuously maintained. Aerobic exercise training place reliance on skeletal muscle's usage of oxygen through aerobic respiration to create energy, in the form of adenosine tri-phosphate or ATP (6).

Diet and exercise-induced weight loss >5% of whole body weight improve NAFLD and reverse hepatic necrotic inflammation and fibrosis (7). Decrease of weight has remained main element of a disease management, the benefits of exercise are more than weight loss alone. Exercise improves NAFLD unrelated to weight loss, however, the accurate dose of exercise and pathophysiologic mechanisms by which exercise produce improvement in NAFLD still unknown (8).

Physical activity, independently from diet change was associated with a significant reduction in intrahepatic fat content, alanine aminotransferase (ALT), and aspartate aminotransferase (AST) (9).

The efficacy of Moderate aerobic exercise has not been investigated. Thus, we aimed to find out the effect of moderate aerobic exercise on liver function tests and fatigue severity scale in university students with NAFLD, aiming to add another perspective regarding which method is more beneficial.

2. Patients and Methods

2.1. Participants

Sixty patients with NAFLD were recruited from outpatient clinics of internal medicine of Zagazig University Hospital and student hospital in Zagazig City with following inclusion criteria; BMI between 25-35 kg/m^2 and age between 18 and 28 years while patients were free from any immunodeficiency disorders or diseases that can affect the treatment process.

2.2. Inclusion and exclusion criteria:

2.2.1. Inclusion criteria:

Sixty patients suffering from Nonalcoholic fatty liver disease (NAFLD), their age will be ranged from 18-28years old, all patients are students of university, patients will be included as they have Nonalcoholic fatty liver disease (NAFLD), that will be assessed clinically by investigations including Plain ultrasound, body mass index (25– 35) and all patients are medically stable.

2.2.2. Exclusion criteria:

Patients who will meet one of the following criteria will be excluded from the study:

Patients with Hepatitis C & b, acute and chronic significant illnesses that may interfere with, moderate aerobic exercises severe ventricular arrhythmia, hemodynamic, co-morbidities that limit exercise tolerance (chronic obstructive pulmonary disease with FEV1 50%), cardio vascular disorders (Pacemakers), genetic disorders(down syndrome), epileptic Seizures, pregnancy and cancer.

2.3. Instrumentation:

2.3.1. Assessment equipment:

Height and weight scale: RGZ 220 (China). Liver enzyme measuring machine : Hermle/ made in Germany, Liver enzyme measuring kits machine .Semi-automatic, single-beam filter photometer 5010 v5+ Made in Germany, Ultrasonography: logiq p3/ Made in China.

2.3.2. Therapeutic equipment:

Electronic treadmill: Grand Fit AC 999 (China).

Aerobic means 'with oxygen', involves or improves oxygen utilization by the body, and refers to the usage of oxygen in a muscle's energy-producing process. Many types of exercises are aerobic and by definition are performed at moderate intensity level for extended duration (10).

2.4. Procedures of the study:

All patients were randomly enrolled into 8-week blinded randomized clinical trial. This study was approved by the Ethics Committee for Scientific Research of the Faculty of Physical Therapy, Cairo

University. Instructions and details of the study were explained for each patient. Patients who accepted to participate in the study were asked to sign a consent form.

Both groups underwent an identical number of tests: baseline (before training) and after 8 weeks (after training). Initially, patients underwent plan ultrasound examination to ensure that he/she had non-alcoholic fatty liver disease. Data on the participants' characteristics were collected in the first session, including BMI, alanine aminotransferase (ALT), aspartate aminotransferase (AST), triglyceride (TG) and fatigue severity scale (FSS). Weight was measured using a standard weight scale. Height was measured with the participant standing in an erect position against a vertical scale.

Initial medical screening was performed for every patient by the physician, diagnosed as NAFLD using abdominal ultrasound by the radiologist. Initially, 113 patients were selected from the outpatient clinic of internal medicine of Zagazig University Hospital and students hospital in Zagazig City from March, 2019 to January, 2020 and identified as potentially eligible for the study as NAFLD patients with BMI between 25and 35 kg/m2. Measuring liver enzymes and triglyceride obtained through blood samples. Also, fatigue severity scale was identified for each patient, 53 patients were found to be ineligible according to inclusion and exclusion criteria and therefore excluded. Sixty patients were found to be eligible and already participated in the study. All 60 participants had completed the 8 weeks' program to the end.

The 60 eligible participants were randomly assigned to two groups equal in number, groups A and B. Group A received a standard medication and low calorie diet in addition to program of moderate intensity aerobic exercise. Group B followed standard medication and a program of low-caloric diet. Each patient had been re-evaluated after 8 weeks of their treatment program for BMI, ALT, AST, TG and FSS.

Training Program

The purpose of training program was explained to each patient. Aerobic exercises training program consisted of treadmill walking, 3 days per week for 8 weeks moderate Aerobic training consists of 10 minutes warm-up, followed by 45-minutes aerobic training with heart rate at 60-75% of maximum heart rate exercise session terminates by 10 minutes cool-down. (16).

Maximum heart rate was calculated for each participant by (Karvonen formula)

HRmax=220-age (20).

Data analysis

The statistical analysis was conducted by using statistical SPSS Package program version 23 for Windows (SPSS, Inc., Chicago, IL).

The following statistical procedures were conducted: Descriptive statistics is including the mean and standard deviation for age, weight, height, BMI, ALT, AST, TG, and FSS variables. - Paired t-test to compare between pre and post-treatment within diet (control) group and exercise (study) group for BMI, ALT, AST, TG, and FSS variables. - Unpaired (Independent) t-test to compare between diet(control)and exercise(study) groups for age, weight, height, BMI, ALT, AST, TG, and FSS variables. - Statistical level all statistical analyses were significant at level of probability less than an equal 0.05 ($P \leq 0.05$).

3. Results

There were no statistically significant differences between the two groups at baseline in the mean values of age, height, and weight.

Table (1) Comparison of demographic data mean values between diet group and exercise group.

	Age	Height	Weight
Diet group	22.72 ±3.2	168±8.86	82.53±10.18
Exercises group	22.60 ±2.61 years	162±30.28	87.12±13.34
P value	0.923	0.871	0.616
Significance	NS	Ns	NS

S= Significant NS= Non significant

1-BMI:

Within-group comparison showed that in the exercise group, there was statistically significant difference in the mean value of BMI measured before treatment (30.76±2.91 kg/cm^2) when compared with its corresponding value after treatment (28.11 ±2.48 kg/cm2) (P=0.001).

In the diet group, there was statistically significant difference between the mean value of BMI measured before treatment (28.79 ±1.8kg/cm2) and its corresponding value after treatment (27.1±1.6 kg/cm2) (P=0.001). The percentage of decrease in BMI in both the exercise and diet groups was 8.6%. And 5.9% .respectively.

Between group difference showed that Before treatment, there was no statistically significant difference between the mean value of BMI in the exercise group (30.76±2.91 kg/cm^2) and its corresponding value in the diet group (28.79

±1.8 kg/cm2) (P=0.342). After treatment, there was no statistically significant difference between the mean value of BMI in the exercise group 28.11 ±2.48 (kg/cm2) and its corresponding value in the diet group (27.1±1.6 kg/cm2) (P=0.05).

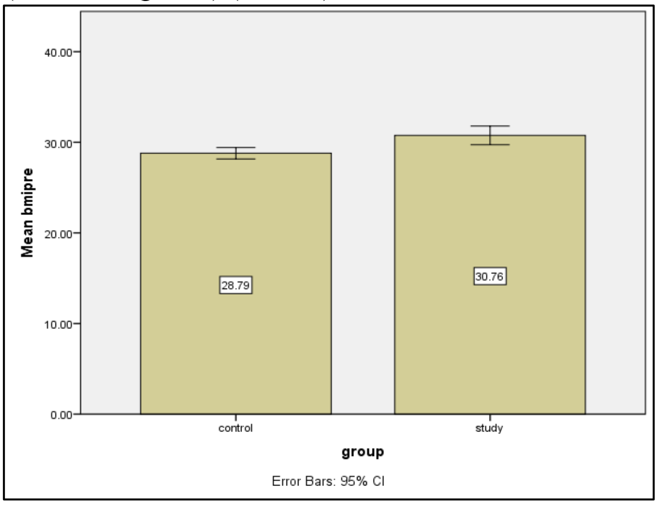

Fig (1): Comparison mean values of pre- BMI between both groups.

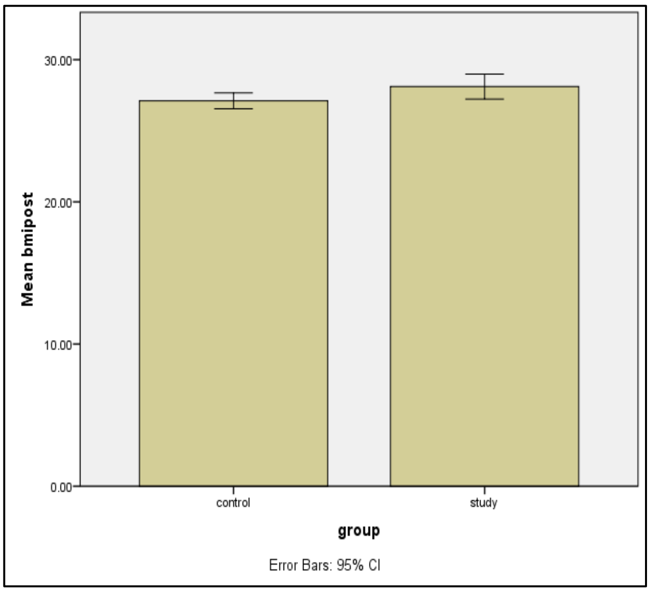

Fig (2): Comparison mean values of post- BMI between both groups

2-ALT

Within-group comparison showed that In the exercise group, there was a statistically significant difference in the mean value of ALT measured before treatment (73.52±20.95IU/l) when compared with its corresponding value after treatment (61.78±17.92IU IU/l) (P=0.001).

In the diet group, there was a statistically significant difference between the mean value of ALT measured before treatment (66.18±12.99IU/l) and its corresponding value after treatment (58.62± 11.72 IU/l) (P=0.001).

The percentage of decrease in ALT in both the exercise and diet groups was15.97%, and11.4%, respectively. Between group difference showed that Before treatment, there was no statistically significant difference between the mean value of ALT in the exercise group (73.52±20.95IU/l) and its corresponding value in the diet group (66.18±12.99IU/l) (P=0.867.). After treatment, there was no statistically significant difference between the mean value of ALT in the exercise group (61.78±17.92IU) and its corresponding value in the diet group (58.62± 11.72 IU/l) (P=0.393)

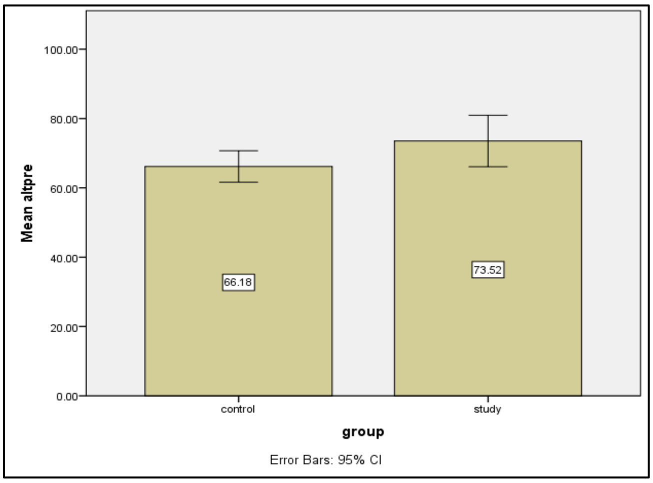

Fig (3): Comparison mean values of pre- Alt between both groups

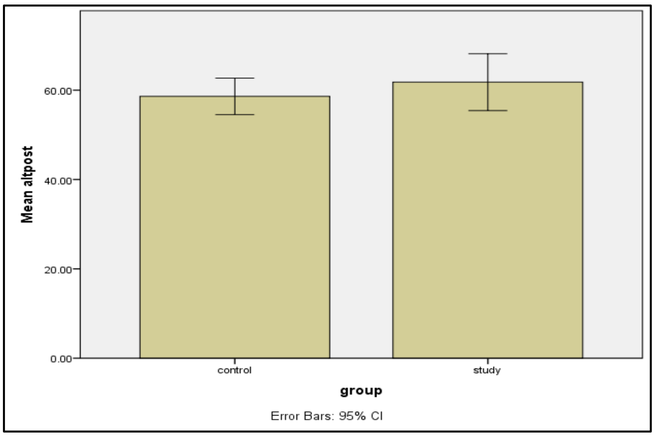

Fig (4): Comparison mean values of post- ALT between both groups

3-AST

Within-group comparison showed that in the exercise group, there was a statistically significant difference in the mean value of AST measured at after treatment (57.9±18.7 IU/l) when compared with its corresponding value after treatment (48.57 ±15.69IIU/l) (P=0.001).

In the diet group, there was a statistically significant difference between the mean values of AST measured before treatment (52.05±11U/l) and its corresponding value after treatment 48.05 ±10.22 (IU/l) (P=0.001). The percentage of decrease in AST in both the exercise and diet groups was 16.3%and 7.68%. , respectively.

Between group difference showed that before treatment, there was no statistically significant difference between the mean value of AST in the exercise group (57.9±18.7 IU/l) and its corresponding value in the diet group (52.05±11lu/l) (P=0.933). After treatment, there was no statistically significant difference between the mean value of serum glutamic-pyruvic transaminase in the exercise group (48.57 ±15.69IU/l) and its corresponding value in the diet group (48.05 ±10.22 IU/l) (P=0.873)

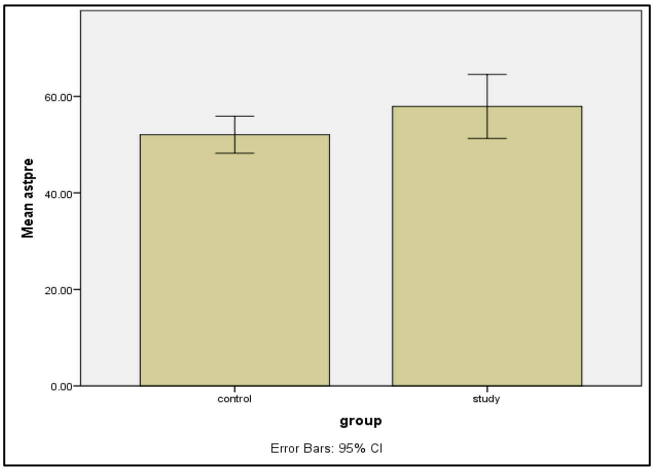

Fig (5): Comparison mean values of pre- AST between both groups

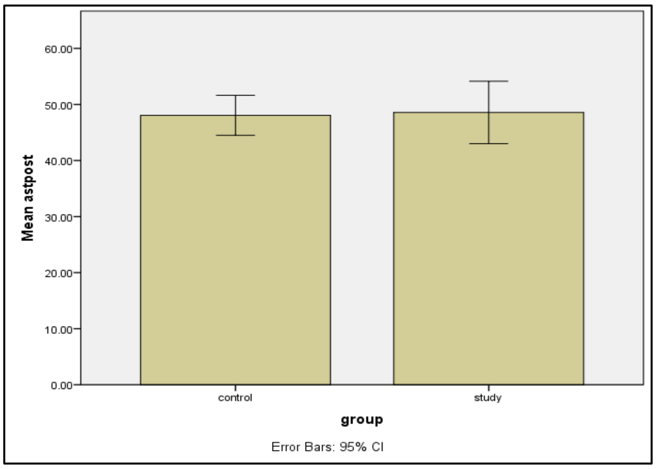

Fig (6): Comparison mean values of post- AST between both groups

4-Triglycerides

Within-group comparison showed that in the exercise group, there was a statistically significant difference in the mean value of TG measured at before treatment (155.63 ±47.51 IU/l) when compared with its corresponding value after treatment (127.63 ±41.60 IU/l) (P=0.001).

In the diet group, there was a statistically significant difference between the mean value of TG measured before treatment (146.88±42.77 1U/l) and its corresponding value after treatment (130.50 ±40.43 IU/l) (P=0.001). The percentage of decrease in TG in both the exercise and diet groups' was17.99% and 11.15%. , respectively.

Between group difference showed that before treatment, there was no statistically significant difference between the mean value of TG in the exercise group (155.63 ±47.51IU/l) and its corresponding value in the diet group (146.88±42.77lu/l) (P=0.0.814). After treatment, there was no statistically significant difference between the mean value of serum glutamic-pyruvic transaminase in the exercise group (127.63 ±41.60 IU/l) and its corresponding value in the diet group (130.50 ±40.43IU/l) (P=0. 776)

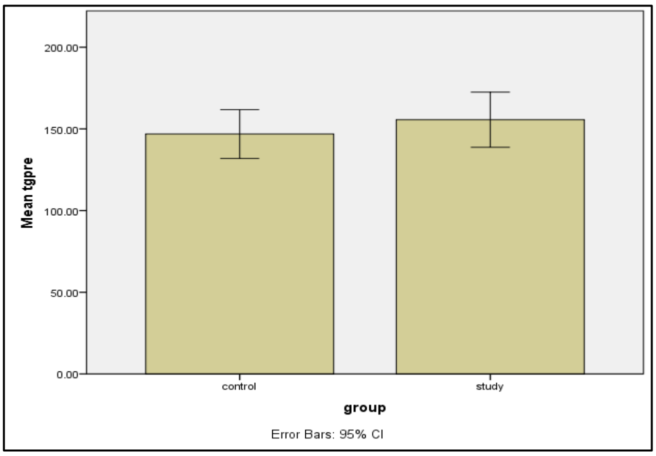

Fig (7): Comparison mean values of pre- TG between both groups

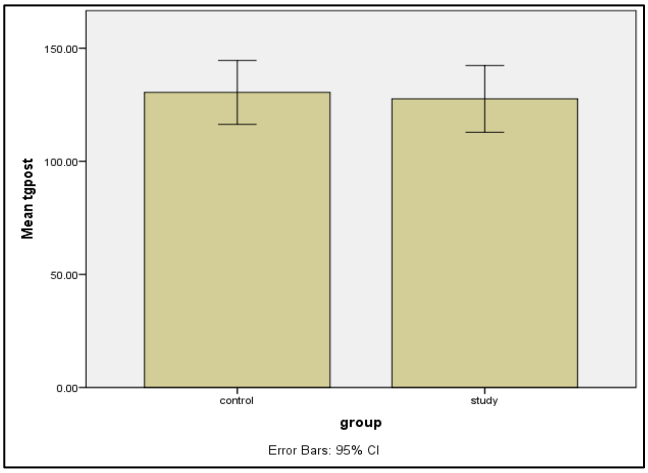

Fig (8): Comparison mean values of post- TG between both groups

5-Fatigue severity scale (FSS)
Within-group comparison showed that in the exercise group, there was a statistically significant difference in the mean value of FSS measured at after treatment (36.15 ± 4.60) when compared with its corresponding value after treatment (23.36±3.26) (P=0.001).

In the diet group, there was a statistically significant difference between the mean value of FSS measured before treatment (37.41 ±4.91) and its corresponding value after treatment (35.29±3.75) (P=0.001). The percentage of decrease in FSS in both the exercise and diet groups was35.38%, and5.66%., respectively.

Between group difference showed that before treatment, there was no statistically significant difference between the mean value of FSS in the exercise group (36.15 ± 4.60) and its corresponding value in the diet group (37.41 ±4.91) (P=0.0.941). After treatment, there was statistically significant difference between the mean value of FSS in the exercise group (23.36±3.26) and its corresponding value in the diet group (35.29±3.75) (P=0.oo1)

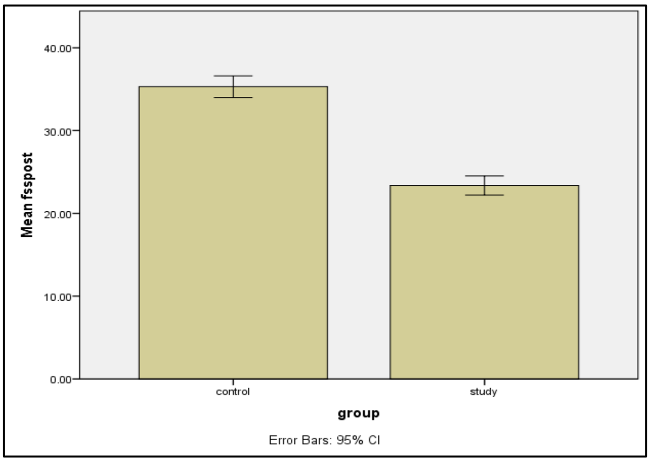

Fig (9): Comparison mean values of pre- FSS between both groups

4. Discussion

For both groups, BMI, ALT, AST, TG and FSS were significantly different pre and post intervention either in diet group or diet and aerobic exercise group. Furthermore, there is no significant difference between groups regarding all parameters except FSS that favors aerobic exercise group.
NAFLD patients have higher fatigue levels and decreased physical activity despite comparable BMI, and this appears to be unrelated to depression. Symptoms such as fatigue are related entirely to increase weight and obesity, and may now allow directed studies into the pathogenesis of fatigue in NAFLD (11).

Many of researches supported our results, eight weeks of exercise and/or dietary exercise intervention lead to significant decrease of liver weight and improvement of liver TG. In both training and/or dietary change groups (12).

Also, both diet and exercise counseling are often recommended for patients with NAFLD to achieve weight reduction aims. Unfortunately, data evaluating the effect of combination between diet and exercise on NAFLD are limited. When concentrate on weight loss alone in a pooled analysis of 18 trials, combination diet and exercise resulted in a 1.14 kg greater weight loss than diet alone (13).

Suzuki et al.2005, showed that decrease of weight and lifestyle change with diet changes and improvement physical activity are advised as the first step in the control of NAFLD. Achieving and maintaining weight reduction may improve NAFLD (14).

The effect of aerobic exercise on ALT and AST were not related to weight loss. Overall, the available evidence suggests that 8–12 weeks of aerobic activities can improve ALT and AST levels in subjects with NAFLD or NASH. However, normal ALT values have been noted across the spectrum of NAFLD, and carefulness should be used when interpreting whether AST and ALT are apposite substitute markers for finding out differentiations in NAFLD with exercise training (15)

Shamsoddini et al. 2015, showed that moderate-intensity treadmill training significantly improved mean ALT from 36.9 ± 16.4 U/L to 24.4 ± 7.2 U/L, p = 0.002; and improved AST from 29.7 ± 9.0 U/L to 20.9 ± 4.4 U/L, p = 0.02 in an eight-week aerobic training intervention in 10 ultrasound-confirmed NAFLD patients (16).

Smith et al., 2001, conducted a study on sixty patients who completed a 3 months under supervision exercise program and concluded that supervised aerobic training safely lower fatigue, weight, Body mass index, subcutaneous fat and abdominal girth (central fat) in HIV-1-infected individuals (17).

Maniam et al., 2014, suggested a training program for hemodialysis patients, three times per week for3months and concluded that low-to-moderate-intensity exercise is effective for reducing fatigue, sleep problems and the overall quality of life among hemodialysis patients (18).

El-Kader et al., 2015, showed that a program of aerobic exercise training with moderate intensity between 60–

70% of maximum heart rate for twelveweeks can get better symptoms of fatigue depend on inflammatory cytokines in obese and overweight patients with type 2 diabetes (19).

5. Conclusion

Moderate aerobic exercises has no effect on ALT, AST, TG BMI when low calorie diet is a part of standard management of non-alcoholic fatty liver in students of university .while it is effective method for decreasing fatigue level .

Conflict of Interests

The authors proclaim no conflict of interest.

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