Women Health Bull. 2018 October; 5(4):e57194. doi: 10.5812/whb.57194.

Published online 2018 June 25. **Research Article**

Protective Effects of Aerobic Intervention on the Profile of Liver Enzymes with Emphasis on AST to ALT ratio in Adult Females with Obesity

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Received 2017 July 10; **Revised** 2018 February 27; **Accepted** 2018 February 28.

Abstract

Background: Obesity is a worldwide epidemic with a high prevalence of chronic diseases such as metabolic syndrome and fatty liver.
Objectives: The current study aimed at evaluating the role of aerobic exercise program on aspartate aminotransferase (AST) and alanine aminotransferase (ALT) as enzymes indicative of fatty liver in adult females with obesity.
Methods: Twenty-eight inactive females with obesity matched by age (mean: 37 $\pm$ 6 years) and weight (mean: 83 $\pm$ 7 kg) were enrolled in the current study and randomly divided into exercise and control groups. Exercise subjects underwent a three-month aerobic exercise intervention (three sessions per week for up to 45 minutes) as running at 60 - 75 of maximum heart rate in fall 2016, Saveh city, Iran. Before and after the intervention, liver enzymes and their ratio as well as anthropometrical markers were measured in the two groups. Statistical tests were applied using independent and paired t-tests ($P < 0.05$).
Results: There was a significant reduction in the mean values of body weight ($P = 0.001$), body mass index (BMI) ($P = 0.002$), body fat percentage ($P = 0.001$), abdominal circumference ($P = 0.001$), and visceral fat ($P = 0.028$) was observed following the aerobic training in the exercise group. No significant change was observed in AST ($P = 0.096$) and ALT ($P = 0.104$) levels following the training program in the exercise group. Despite unchanged AST and ALT levels, aerobic training resulted in a significant decrease in AST/ALT ratio in the exercise subjects ($P = 0.021$). There were no changes in these variables in the control group.
Conclusions: With emphasis on improved AST/ALT ratio and obesity indicatives, it was concluded that regular aerobic training can be preventing fatty liver in female adults with obesity.

Keywords: Obesity, Aminotransferase, Fatty Liver, Aerobic Intervention

1. Background

Recent scientific literature confirmed obesity as a prelude to the prevalence of chronic diseases associated with metabolic disorders. In this regard, cardiovascular diseases, type-2 diabetes, and some respiratory diseases are introduced as the consequences of obesity (1). Recently, the role of obesity is discussed regarding the prevalence of liver diseases, particularly non-alcoholic fatty liver disease (NAFLD), and extensive studies in this area are underway. Fatty liver is the accumulation of fat in the liver cells, which causes liver inflammation. The possibility of the emergence of NAFLD directly correlates with patients' weight, and given the increase of obesity in various countries such as Iran, the prevalence of NAFLD is also increasing (2). Scientific reports claim that the increase in the prevalence of obesity and the diseases associated with it including diabetes, hypertriglyceridemia, and hypercholesterolemia are the most common reasons for the prevalence of NAFLD (3).

It is also reported that obesity is associated with the increase in serum levels of some liver enzymes (3). Liver enzymes (aspartate aminotransferase (AST) and alanine aminotransferase (ALT) are present in liver cells and destructing liver cells enter the serum of patients. Their increase indicates liver cell destruction (4). Although experimental methods alone are not proper tests to diagnose the disease (4), the measurement of their serum levels is introduced as the preliminary steps in the diagnosis of fatty

liver disease. In fact, the first step in the diagnosis of liver damage is determining the serum levels of these liver enzymes.

In this respect, studies also supported a relationship between the severity of obesity and NAFLD (5). It was also found that hypertriglyceridemia or increase in blood triglyceride often reported in people with obesity is an independent predictive factor for liver diseases in adults with obesity (6). On the other hand, the possibility of prevalence of fatty liver in patients with obesity was reported approximately six times more than its prevalence in individuals with normal weight (7). Moreover, the increase in liver enzyme levels is obvious in individuals with obesity. Hence, it is hypothesized that weight loss or a decline in body fat percentage is associated with the improvement in liver enzyme profile in patients with obesity, though there are few studies in this regard. However, the beneficial effects of weight loss interventions such as diet or exercise on other hormonal and metabolic factors associated with liver damages in healthy or sick individuals with obesity were reported by some researchers, though there are some contradictory findings among them. For example, in a recent study, 10 weeks of aerobic training led to a significant reduction in tumor necrosis factor (TNF)-α in females with obesity (8). In another study, 12 weeks of endurance and resistance training led to a significant reduction in TNF-α in males with obesity (9). However, C-reactive protein (CRP) serum levels did not significantly change after 12 weeks of aerobic training in the mentioned study (9). In the study by Olsan et al., the serum CRP levels after a year of resistance training decreased significantly in females with obesity (10). However, in a recent study, six months aerobic training did not cause a significant change in CRP levels and other inflammatory mediators such as TNF-α and interleukin (IL)-6 in females with overweight or obesity (11).

2. Objectives

Inconsistency in the findings with respect to other metabolic components or inflammatory mediators associated with liver damages in response to exercise trainings in individuals with obesity on one hand and lack of sufficient studies with respect to the response or compatibility of liver damage indicator enzymes to exercise on the other hand, paved the way for the conduction of the current study that aimed at determining the effect of 12 weeks of aerobic training on AST and ALT liver enzyme levels in inactive females with obesity.

3. Methods

3.1. Subjects and Inclusion Criteria

The current semi-experimental study was conducted on 28 inactive females with obesity matched by age (mean: 37 $\pm$ 6 years) and weight (mean: 83 $\pm$ 7 kg) selected first through convenience and purposive sampling and then divided into exercise and control groups based on random allocation using a table of random numbers in fall 2016 in Saveh, Iran. Sample size was decided according to Equation 1.

$$n = \frac{\left(\sigma_1^2 + \sigma_1^2\right)\left(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta}\right)^2}{d^2} \quad (1)$$

Ethics approval was provided by the ethics committee of Islamic Azad University, Iran. The nature and objectives of the study were carefully explained to participants before obtaining a written consent. Participants were non-athletes, non-smokers, and non-alcoholics. Any females with pregnancy or planning a pregnancy were excluded. None of the subjects used drugs or therapies for obesity, and none had an underlying disease or injury that would prevent daily exercise. Exclusion criteria for both groups were presence of symptoms of acute or chronic medical illness during the study. Furthermore, subjects with cardiovascular diseases or overt diabetic and other chronic diseases such as respiratory or kidney diseases were also excluded from the study.

3.2. Anthropometry

Obesity was measured by body mass index (BMI). Body weight and height were measured on the same day to the nearest 0.1 kg and the nearest 0.1 cm, respectively when subjects were in a fasting state before the resting metabolism session. BMI was measured for each individual by division of the body weight (kg) by height (m^2). Waist circumference (WC) was measured with a non-elastic tape at a point midway between the lower border of the rib cage and the iliac crest at the end of normal expiration. Visceral fat and body fat percentage were measured using body composition monitor (OMRON, Finland). Anthropometrical measurements were repeated after exercise program of the two groups.

3.3. Training Protocol and Laboratory Testing

Pre- and post-intervention (48 hours after the last exercise session) of fasting blood samples were collected to measure liver enzymes. Therefore, blood was obtained after an overnight fasting at 8:00 to 9:00 am. Sera were immediately separated to assay AST and ALT activity. The liver enzymes activities were measured by enzymatic methods

(Pars Azmoon kit, Tehran) with a Roche COBAS MIRA auto-analyzer (Germany).

Endurance training lasted a 12-week, three sessions weekly consisting of warm-up (10 minutes), main exercise, and cooling down (5 - 10 minutes). Main exercise in each session was 30 - 45 minutes running at a work intensity of 60% - 75% heart rate maximum (HRmax). The first two weeks at 60% - 65% of HRmax, third and fourth weeks at 65% - 70% of HRmax, and fifth and sixth weeks at 70% - 75% of HRmax. After that, the subjects continued aerobic exercise for 6six weeks until the 12th week at 70% - 75% of HRmax. Heart rate in each session was controlled by polar telemetry. The heart rate, used to calculate the intensity of exercise, was determined by counting heart beats by polar telemetry. Control subjects were instructed to maintain their habitual activities. Participants were instructed to maintain their usual diet throughout the study.

3.4. Data Collection

Normal distribution of data was analyzed by the Kolmogorov-Smirnov normality test. The comparison between the means of the groups and homogeneity of groups were examined using independent t test. Paired t-test was used to determine the mean differences between baseline and post-intervention values on liver enzymes and anthropometric variables. All statistical analyses were performed with SPSS version 15.0 (SPSS Inc., IL, USA). P value < 0.05 was considered as statistically significant.

4. Results

Means and standard deviations (SD) were calculated for all variables. Age and anthropometric characteristics of the study participants are shown in Table 1. At baseline (pre-intervention), no significant differences were observed between the groups in terms of anthropometrical indexes.

The intra-group changes of all anthropometrical markers were analyzed by paired samples t test. Data showed significant decrease in body weight (Figure 1) and BMI (Figure 2) and the other anthropometrical markers after aerobic intervention when compared with pre-intervention in exercise group, but these variables remained unchanged in the control subjects (Table 2).

There were no statistically significant differences between the exercise and control subjects with regard to AST (P = 0.933), ALT (P = 0.944), and AST/ALT ratio (P = 0.268) at baseline.

No difference in AST activity was observed after aerobic intervention compared with baseline values in the exercise group (P = 0.096, Figure 3). Moreover, ALT activity did not change by aerobic intervention compared with baseline (P = 0.104, Figure 4).

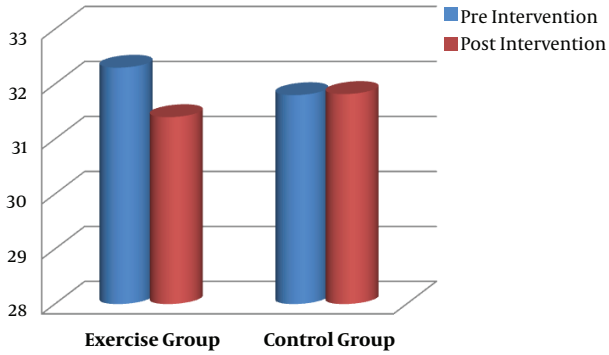

Figure 1. Pre- and post-training body weight of the study groups; aerobic intervention resulted in significant decrease in weight in the exercise group

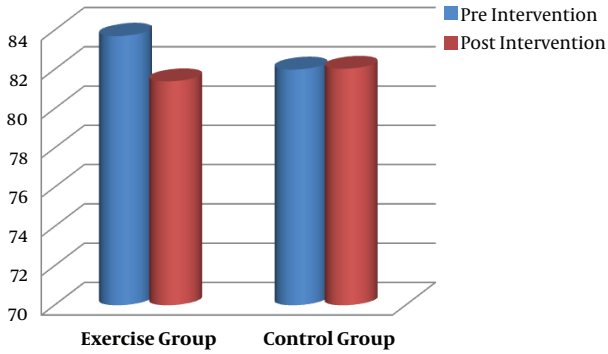

Figure 2. Pre- and post-training BMI of the study groups; aerobic intervention resulted in significant decrease in BMI of the exercise group

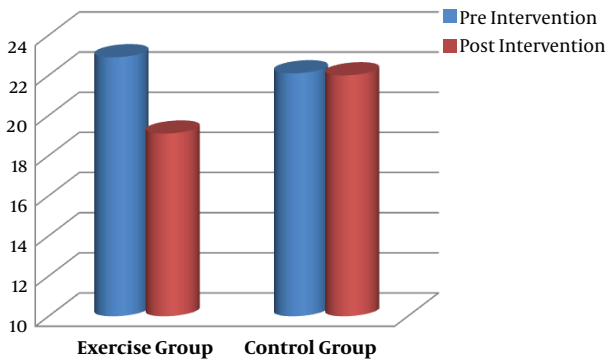

Figure 3. Pre- and post-training AST activity of the study groups; no significant changes in AST activity following aerobic intervention

Despite no changes in AST and ALT levels, aerobic inter-

Table 1. General Anthropometrical Characteristics of the Study Groups Before Intervention[a,b]

Group	Age, y	Weight, kg	Height, cm	BMI, kg/m^2	AC, cm	BF, %	Visceral Fat, mm
Exercise	37.9 ± 5.59	83.7 ± 6.6	161 ± 5.8	32.3 ± 2.60	111 ± 8.29	46 ± 3.66	8.6 ± 1.1
Control	36.6 ± 3.33	82 ± 4.9	161 ± 4.2	31.8 ± 1.18	110 ± 7.55	44.4 ± 1.78	8.07 ± 0.80
P value	0.46	0.46	0.78	0.55	0.67	0.14	0.13

Abbreviation: AC, Abdominal Circumference; BF, Body Fat Percentage; BMI, Body Mass Index.
[a]Values are expressed as mean ± SD.
[b]Data based on t test for independent samples (P < 0.05).

Table 2. Anthropometrical Characteristics of the Study Population Before and After the Exercise Intervention[a,b]

Variables	Exercise Group			Control Group		
	Pre-Intervention	Post-Intervention	P Value	Pre-Intervention	Post-Intervention	P Value
Weight, kg	83.7 ± 6.6	81.4 ± 7.34	< 0.01	82 ± 4.91	82.04 ± 4.99	0.541
AC, cm	111 ± 8.29	108 ± 7.99	0.01	110 ± 7.55	110 ± 7.69	0.77
BMI, kg/m^2	32.3 ± 2.60	31.4 ± 2.54	< 0.01	31.85 ± 1.18	31.82 ± 1.22	0.53
Body fat, %	46 ± 3.66	44.5 ± 3.67	< 0.01	44.4 ± 1.78	44.3 ± 1.83	0.40
Visceral fat	8.6 ± 1.1	8.2 ± 1.21	0.021	8.07 ± 0.80	8 ± 0.76	0.58

Abbreviations: AC, Abdominal Circumference; BMI, Body Mass Index.
[a]Values are expressed as mean ± SD.
[b]Data based on t test for paired samples (P < 0.05).

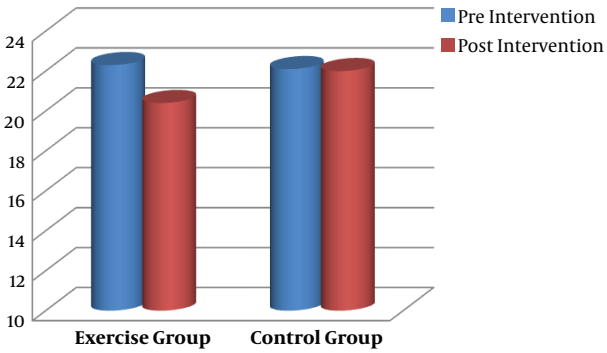

Figure 4. Pre- and post-training ALT activity of the study groups; no significant changes in ALT activity following aerobic intervention

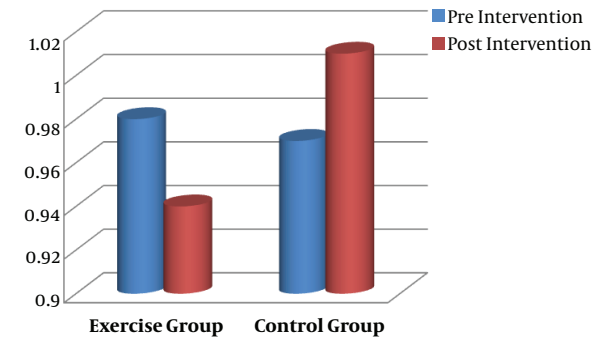

Figure 5. Pre- and post-training ALT/ALT of the study groups; aerobic intervention resulted in significant decrease in AST/ALT in the exercise group

vention resulted in a significant decrease in AST/ALT ratio in the exercise group (P = 0.021, Figure 5).

All variables remained unchanged in the control group (Table 3).

5. Discussion

In the current study, although obesity indicator indexes such as weight and body fat levels decreased in response to aerobic intervention, the training program was not associated with a significant change in AST and ALT liver enzymes. However, previous clinical studies introduced weight loss as one of the most important ways of treating liver diseases in people with obesity. Although achieving and maintaining a normal weight seems difficult for individuals with obesity, physical activity can also affect liver fat levels (12). In this regard, some studies noted that long-term aerobic exercises along with diet control lead to a reduction in ALT activity (13). In another study, aerobic and combined (aerobic + resistance) training led to the reduction of visceral and liver fat stores, insulin resistance, and ALT, but resistance training did not affect the

Table 3. Liver Enzymes Activity of the Study Population Before and After the Exercise Intervention[a,b]

Variables	Exercise Group			Control Group		
	Pre-Intervention	Post-Intervention	P Value	Pre-Intervention	Post-Intervention	P Value
AST, U/L	22.9 ± 8.91	19. 1 ± 6.78	0.10	22.1 ± 1.56	22 ± 5.70	0.26
ALT, U/L	23.3 ± 4.87	20.4 ± 4.75	0.10	22.8 ± 3.38	21.9 ± 2.81	0.34
AST/ALT	0.98 ± 0.08	0.94 ± 0.11	0.02	0.97 ± 0.14	1.01 ± 0.14	0.54

Abbreviations: ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase.
[a]Values are expressed as mean ± SD.
[b]Data based on t test for paired samples ($P < 0.05$).

levels of these variables (14).

In contrast to these observations, some studies reported no effects for short- or long-term training programs on the enzymatic and non-enzymatic components of liver disease indicators. For example, in a study, levels of serum bilirubin, the activity of ALT, and other liver enzymes did not significantly change in response to 12 weeks of aerobic exercises in patients with obesity (15). In another study, despite a significant reduction in ALP activity after eight weeks of resistance training, AST and ALT activity did not significantly change (16). These findings are also reported on people with overweight or obesity by some other studies (14, 17). On the other hand, another study reported a significant increase in liver enzymes such as AST, ALT, and alkaline phosphatase (ALP) after six and twelve weeks of continuous and alternative training courses (18). Tartibian et al., reported a significant increase in the concentration of ALP after nine weeks of aerobic training (19).

In a review, some scientific studies demonstrated no changes (15, 20, 21), an improvement (12, 13), and a significant increase (18) in indicator enzymes of fatty liver in response to different training practices in athletes or non-athletes and healthy or sick individuals. Hence, providing a comprehensive and systematic conclusion for their response to aerobic or resistance exercises with different training courses in these populations is somewhat difficult and controversial, since the findings are often contradictory. It is also possible that the beneficial effects of long-term training courses appear on the activity of liver enzymes along with other external stimuli such as diet. For instance, in one study, 30 minutes of aerobic exercise for three months along with calorie intake restrictions by diet control led to a significant reduction in ALT and cholesterol in patients with fatty liver (22).

Another study noted the beneficial effects of regular aerobic trainings along with diet manipulation on the severity of the disease in mice with fatty liver (23). On the other hand, Bahari et al., found that although environmental intervention within eight weeks of resistance training without diet manipulation significantly reduced liver enzymes such as AST, ALT, and gamma-glutamyl transferase (GGT) in patients with type-2 diabetes, statistical analyses did not show any significant differences between the experimental and control groups (24) in this regard. In another study, despite a significant reduction in abdominal fat following aerobic or resistance exercises, the serum levels of liver enzymes and insulin resistance did not change significantly (25).

Accordingly, some researchers, based on their findings, attributed the improvement in the effective factors on liver diseases primarily to diet control or nutritional therapies, but not to endurance exercises (26). However, some scientific resources introduced AST/ALT ratio as the criteria for the severity of liver damages. These studies considered the increase in AST/ALT as one of the symptoms of the increase in severity of liver damages (27). In other words, the ratio of AST/ALT is used in the differential diagnosis of liver diseases. In this regard, values < 1 indicate mild liver damages, and values > 1 indicate severe liver damages (27). Some studies reported no change in AST/ALT (28) or an increase in AST/ALT (29) in response to long-term endurance and resistance training programs. In the current study, although the activity of AST and ALT enzymes did not change significantly in response to the training program, the statistical findings indicated a decrease in AST/ALT due to aerobic trainings when compared with the state prior to the intervention. These findings support the beneficial effects of the long-term aerobic trainings as well as the reduction in the severity of liver damages in response to these kinds of trainings. Thus, from a clinical perspective, aerobic training intervention is important to improve the profile of liver diseases in people with obesity. Finally, it should be noted that other liver damage factors such as GGT, ALP, and low-density lipoprotein (LDH) or non-enzymatic factors such as bilirubin were not considered in the current study, which is counted as one of its limitations. Investigating the changes in the so-called indicators in response to aerobic intervention may lead to more results. For example, some studies indicated that ALT had a minor role in the recognition of liver diseases such as NAFLD (30) and

reported a stronger link between GGT (compared to ALT) and obesity-related diseases such as type-2 diabetes (31). In this regard, clinical trials revealed that GGT predicts the development of type-2 diabetes independent of body mass and alcohol consumption, and it is thought that GGT, as a marker of liver and visceral fat storage, is a good predictor of obesity complications such as insulin resistance, type-2 diabetes, and metabolic syndrome (32).

5.1. Conclusion

Despite the potential role of obesity in liver damages and the prevalence of fatty liver, the findings of the current study suggested no changes in AST and ALT levels in response to relatively long-term aerobic training in middle-aged females with obesity. However, training programs associated with the reduction in AST/ALT ratio, as one of the most obvious criteria to determine the severity of liver damages in the females with obesity, is significant from a clinical perspective. To achieve a comprehensive conclusion regarding the response of liver damages to aerobic intervention in individuals with obesity, other diagnostic indicators of liver damage such as GGT, ALP, or LDH should be measured.

Acknowledgments

The authors acknowledge their gratitude to all the subjects for their participation in the study.

Footnote

Funding/Support: The research was financially supported by Islamic Azad University, Iran.

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