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The relationship between physical activity and drug treatments and biochemical factors of non-alcoholic fatty liver diseases in firefighters with a history of covid-19

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ABSTRACT

Introduction: The purpose of this study was to investigate the relationship between physical activity and drug treatments with biochemical factors of non-alcoholic fatty liver disease (NAFLD) in firefighters with a history of covid-19.

Material & Methods: In the present study, all firefighters of the Shiraz city fire department were matched based on age and body mass index (BMI) to determine the history of covid-19 infection and the use of related drugs and the prevalence of NAFLD among them was investigated. The statistical sample for this research was 38 people. After identifying people with NAFLD with a history of covid-19, they were asked to complete the Baecke physical activity questionnaire (BPAQ) to record their daily physical activity. After collecting the data, Pearson's test was used to determine the correlation between physical activity levels and biochemical factors related to NAFLD ($P<0.05$).

Results: The findings showed that there was a significant correlation between physical activity and drug treatments. Weight ($P=0.03$), body mass index ($P=0.035$), AST ($P=0.041$), ALP ($P=0.038$), bilirubin ($P=0.039$) and albumin ($P=0.048$) were examined in firefighters with NAFLD with a history of covid-19.

Conclusion: According to the study results, it can be concluded that daily physical activity should be increased in this statistical population to have a greater effect on NAFLD recovery and reduce the use of drugs and their side effects.

Keywords: Physical activity, Non-alcoholic fatty liver disease, Liver enzymes, Covid-19, Firefighters.

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1. Introduction

Corona virus 2019 (Covid-19) is one of the epidemic diseases associated with high complications for the affected person. These complications include respiratory, cardiovascular and metabolic problems. Following the spread of this virus all over the world, different countries formulated various national programs to prevent its spread and also to reduce the pressure on the national health system of each country. These programs were based on general and individual quarantine and social distance to reduce virus spread. However, these types of programs have had significant negative consequences for public health. Among these negative consequences, we can mention a decrease in physical activity and an increase in immobility during public and individual quarantine. The aforementioned consequences caused an increase in weight and visceral fat in both men and women (1). On the other hand, today's car lifestyle has also increased physical inactivity (2). Due to the rules of public quarantine and social distancing, many public and specific sports activities in parks, clubs and medical centers were restricted or prohibited (3). So that under the conditions of Corona restrictions, about thirty percent of people spent their daily time sitting and about forty percent of people had a very severe decrease in physical activity. According to a previous study, sedentary people had more fatty liver symptoms than active people during the general quarantine period (4). As a result of overeating and inactivity in the 21st century, obesity, metabolic syndrome, and non-alcoholic fatty liver disease (NAFLD) have increased in both adults and children. NAFLD is a liver manifestation of metabolic syndrome and is a clinical condition that encompasses a wide range of liver damage (from simple steatosis to steatohepatitis, advanced fibrosis, and cirrhosis) as well as increased levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and fat accumulation in liver cells. Liver enzymes are a sensitive indicator of liver damage, an independent risk factor for type 2 diabetes, and an indicator of hepatic and visceral fat accumulation. Various methods have been proposed to prevent fatty liver from progressing to steatohepatitis and advanced liver disease. There are several ways to lose weight, including changing your diet, exercising, or taking certain medications. There is, however, no general agreement on what type of exercise should be prescribed. Although the main causes of NAFLD are not well known, factors like genetics, increasing age, inactivity, pre-inflammatory status, and hormonal changes indirectly affect it. The occurrence of this disease has been associated with central obesity, visceral fat accumulation, and insulin resistance, and insulin resistance is sometimes even suggested as its cause (5). Job stress is one of the most significant factors in accelerating the prevalence of NAFLD, so that in the USA, the prevalence of cardiovascular diseases in jobs such as firefighting has been estimated as high as 45% (6). Job stressors, along with problems such as obesity, by reducing physical efficiency, increasing the risk of heat-related diseases, and enhancing the negative impact of potential hepatotoxins, accelerate the incidence of NAFLD and its related complications in firefighters (7). Until today, the positive effects of increasing physical activity on enhancing the performance of the respiratory and cardiovascular systems, as well as the metabolic systems, have been identified in patients and healthy people at all levels (8). Regular daily physical activity causes beneficial effects on the metabolic system and improves obesity and reduces visceral fat, as well as improves liver function (9). After investigating the prevalence of metabolic syndrome and fatty liver disease among firefighters in Tabriz city, it has been determined that this type of disease is common among firefighters and administrative workers, and it is suggested to raise awareness by focusing on a healthier lifestyle, such as the level of physical activity and nutrition (10). Chatripour et al. (2022) determined and compared the prevalence of metabolic syndrome and non-alcoholic fatty liver disease in military and civilian employees and its relationship to lifestyle. Their findings indicated that military personnel's active lifestyle reduces the prevalence of this disease in them (11). Mansouri et al. (2017) determined the effect of increasing age and overweight on biomotor indicators and cardiovascular risk factors for three age groups of firefighters in Mashhad city. Their results showed that with increasing age, Mashhad firefighters suffer from overweight and obesity and related complications, including liver enzyme disorders. As a result, their fitness and physical health are at risk of decline (12). Shirvani and Rostam Khani (2019) stated that performing moderate-intensity sports activity improves the metabolic system and liver tissue. Therefore, regular exercise is one of the ways to prevent inactivity's harms and disadvantages, especially preventing obesity and its complications, including NAFLD (13). On the other hand, people suffering from Corona disease should use anti-inflammatory drugs such as dexamethasone and antibiotics such as amoxicillin and azithromycin to improve their condition. Since these types of drugs have side effects such as lethargy, drowsiness, etc., during the illness, in addition to improving patients with Corona, they can increase the immobility caused by the side effects of the drugs, and this results in an increase in the incidence and severity of metabolic syndrome symptoms in these people. Also, due to the spread of the Corona virus and the closure of sports activities, including sports clubs, it has changed people's lifestyle. This lifestyle change, along with the increase in drug consumption during this illness, has caused obesity and associated complications, including NAFLD. On the other hand, due to the increased prevalence of non-alcoholic fatty liver disease among firefighters, as well as the increase in the spread of Corona virus and the application of restrictions and the use of related drugs to treat Corona virus disease, it is considered a contributing factor in the prevalence of non-alcoholic fatty liver disease among firefighters (14,15). In light of the importance

of physical activity, the question arises as to how much physical activity firefighters who have recovered from covid-19 are able to perform in order to prevent and improve the symptoms of NAFLD. The aim of this study was to determine the relationship between physical activity, drug treatment, and biochemical factors of NAFLD in firefighters with a history of covid-19.

2. Methodology

2.1. Materials and methods

The present study was causal-comparative or post-event research.

2.2. Participants

Ethical principles (IR-KHU.KRC.1000.181). The study was conducted in accordance with the principles of working with humans approved by the Institute of Movement Sciences. The research population included all Shiraz firemen, and 38 people were selected from the statistical population. Firefighters with NAFLD (based on Table 1) were identified through occupational medicine information.

2.3. Measurements

The results of tests such as weight, height, BMI, AST, ALP, bilirubin, albumin, and total protein were recorded for these people. Then, during a face-to-face interview or phone call, individual characteristics such as age, work experience, physical activity level, history of chronic diseases in the family, smoking, and history of covid-19 infection and daily medication use, as well as the conditions for entering the study, were examined. All the subjects used the same drug treatment when infected with Covid-19.

2.4. Intervention

Medicines include montelukast (in tablet form, every 8 hours), dexamethasone (in injection vial, every 24 hours, 5 CC), amoxicillin (in tablet form, every 8 hours), diphenhydramine (in tablet form, every 8 hours), alprazolam (in tablet form, once every 24 hours), acetaminophen, codeine (in tablet form, every 8 hours) and levothyroxine (1 tablet daily or half a tablet daily).

Table 1. *Normal and abnormal range of liver biochemical factors*

Variable	Normal range
AST (U/L)	5 to 40
ALP (U/L)	20 to 140
Bilirubin (mg/L)	0.3 to 1.2
Albumin (gr/dL)	3.6 to 5.2
Total protein (U/L)	6.4 to 8.3

After identifying people with fatty liver disease with a history of covid-19, they were asked to complete the Baecke physical activity questionnaire (BPAQ) to record their daily physical activity. This questionnaire was used to assess physical activity in three different domains: physical activity at work, sports practice, and leisure time/commuting physical activities, and provides a dimensionless score for the habitual practice of physical activity (16). This instrument is composed of 16 questions scored on a Likert scale from 1 to 5 for each question. A specific formula uses provides a score between 1 and 5 for each assessed domain, with a total physical activity score ranging from 3 to 15 (the sum of the three domains score) (16).

2.5. Statistical Methods

The Kolmogorov-Smirnov test was used to determine the normal distribution of the data. Pearson's test was used to determine the correlation between physical activity and fatty liver disease symptoms. A significant level ($P>0.05$) was considered. All statistical methods were performed with SPSS version 26 software.

3. Results

Table 2 presents descriptive data related to firefighters subjects with NAFLD. There was a significant correlation between daily physical activity along with drug treatments and body weight in this disease ($r=0.74$, $p=0.03$) and according to the value of r, the intensity of the relationship between these two variables was strong. Also, a significant correlation between daily physical activity levels along with drug treatments and BMI ($r=0.68$, $p=0.035$); serum levels of AST ($r=0.62$, $p=0.041$); serum levels of ALP ($r=0.589$, $p=0.038$); serum levels of albumin ($r=0.45$, $p=0.048$) and serum levels of bilirubin ($r=0.54$, $p=0.039$) was present in this disease. According to r, the intensity of the relationship between these two variables was moderate. There was no significant correlation between the level of daily physical activity along with drug treatment and the total protein level of

blood serum (r=0.25, p=0.482), and according to the value of r, the intensity of the relationship between these two variables was relatively weak.

Table 2. *Descriptive findings related to subjects*

Variable	Mean	SD	Min	Max
Age (years)	34.0	4.5	26	46
Height (cm)	176.2	4.3	165	185
Weight (kg)	82.8	8.6	70	98
BMI (kg/m^2)	26.6	2.5	22.2	32
Physical activity	9.6	0.8	8.3	11.6
Total protein (U/L)	7.2	0.5	6.2	8
Albumin (gr/dL)	4.5	0.5	3.2	5.6
Bilirubin (mg/L)	1.2	0.6	0.4	2.8
ALP (U/L)	173.5	39.3	108	272
AST (U/L)	49.8	14.6	35.5	80.3

4. Discussion

This study investigated the relationship between physical activity and drug treatments and biochemical factors of NAFLD in firefighters with a history of covid-19. The findings of this research showed that there was a significant correlation between the level of physical activity along with drug treatments with weight (p=0.03), BMI (p=0.035), AST (p=0.041), ALP (p=0.038), bilirubin (p=0.039) and albumin (p=0.048) in firefighters with fatty liver with a history of covid-19 and the intensity of the relationship between them. Except for the weight variable, it was average. This is while the relationship intensity was strong for the weight variable. In line with the present study results, Eslami et al. (2013) observed that after performing eight weeks of regular physical activity of low to moderate intensity in middle-aged men with fatty livers, liver enzymes including AST decreased and liver function improved. These researchers also stated that physical activity independent of weight loss can improve liver function and reduce liver enzymes (17). Minaeifar et al. (2020) after examining the physical activity of 15 workers of Mibod Tile Factory in Yazd through Beck's physical activity questionnaire and comparing them with 15 inactive employees of the same factory, they concluded that liver enzymes and bilirubin are more reduced in active people than in inactive people. Also, blood factors including hemoglobin were more active in people than inactive people. They concluded that physical activity can improve blood factors, liver enzymes and fat profiles in workers. They stated that employees and workers could improve blood and liver biochemical variables through minimal physical activity (18). Sediqhi et al. (2019), following an eight-week period of physical activity with low to moderate intensity, concluded that physical activity decreases the liver enzymes AST and ALP. They stated that physical activity has a direct relationship with these enzymes (19). In a study by Shamsoddini et al. (2015). By examining the effect of resistance activity on overweight people suffering from non-alcoholic fatty liver disease, they concluded that resistance activity significantly decreases liver enzymes (20). Hallsworth et al. (2015), found that eight weeks of resistance exercise led to an improvement in blood lipids in obese adults with non-alcoholic fatty liver disease independent of any change in body weight. Also, they did not observe a significant decrease in AST levels after eight weeks of resistance activity (21). The findings of Hallsworth's study showed that the level of physical activity does not have much relationship with the amount of weight or the level of liver enzymes. These findings are inconsistent with the present research findings. In present research, there was a significant relationship between the levels of physical activity, body weight and liver enzymes. Among the reasons for the discrepancy between the findings of the current research and Hallsworth's research, we can mention factors such as the type of subjects, the disease history and sports background of the research samples, the type of occupation of the subjects and their race. One of the most significant effects of sports activities on the liver is changes in liver enzymes. Based on the research, the liver is one of the vital organs involved in various sports activities. This may increase the amount of enzymes in the blood as a result of these activities. That is, the increase in serum ALT and AST causes liver and muscle enzymes to enter the blood circulation. Therefore, the concentration of these enzymes can change due to muscle damage. Factors that can affect the change in enzyme amount are the type, duration and intensity of sports activity. This means that long-term and endurance activities (low to moderate intensity activities) whose energy production is mostly aerobic affect the activity level of liver enzymes in the serum. Therefore, liver enzymes are of particular importance during exercise, rest and return to the initial state, so that changes in serum enzymes are a suitable indicator for determining injury, tissue and cell destruction. There is many evidence that various exercise interventions are effective in reducing liver fat and hepatic steatosis. However, the main mechanisms of improving liver function that can improve liver function after exercise are not completely clear. They probably include changes in energy balance, circulating lipids, fat

oxidation, and insulin sensitivity (22). Contrary to the findings of the present study, we can refer to the study by Zar et al. (2015). They observed no significant changes in the aspartate aminotransferase enzyme after eight weeks of moderate intensity aerobic exercise (22). The findings of the present research show that physical activity has a significant effect on AST enzyme amount. Among the reasons for the disparity between the findings of the current research and Zar et al.In Zar et al's research, we can mention disease background (fatty liver patients vs. healthy and active people), gender (male vs. female), sports background, level of physical fitness, and difference in job type.

In recent years, the amount of time spent doing sedentary activities such as sitting at a computer or watching TV has increased dramatically. Despite health-enhancing benefits, physical activity alone may not reduce disease risk. Physical activity and inactivity may be opposite each other. Excessive sitting may cause metabolic disturbances in cellular processes and have a different effect than systematic exercise. This has already been studied in exercise physiology. In fact, recent epidemiologic studies show that the longer time spent being sedentary increases the risk of obesity, diabetes, insulin resistance, metabolic syndrome, cardiovascular disease, cancer, and mortality. This is independent of time spent exercising. So far, there has only been one study that reported a positive association between sitting time and NAFLD among 74 people in the UK (23). For adults, it is recommended to do at least 150 minutes of physical activity per week in periods of no more than 10 minutes. It is known that the intensity of this type of physical activity is one of the key features of primary and secondary health prevention. This prevents obesity, diabetes and cardiovascular diseases. An increasing number of epidemiological studies have suggested a link between insufficient physical activity and adverse outcomes such as diabetes, coronary heart disease, stroke, and increased cardiovascular mortality. However, the association between physical activity and NAFLD remains unknown. In this study, an inverse and significant linear relationship between physical activity and NAFLD prevalence was observed. This finding is consistent with previous studies (22). Data from the National Health and Nutrition Examination Survey (2006-2003) indicated that people with NAFLD had low physical activity levels. A small cross-sectional study of 74 British subjects reported an inverse association between physical activity levels and NAFLD (23). A cross-sectional study of 3718 Korean people also showed an inverse relationship between different types of physical activity and NAFLD independent of visceral obesity and insulin resistance (24). Overall, these results show that increasing physical activity and reducing seated time are independently significant in decreasing NAFLD risk. Sitting time may be offset by alternating seated with standing and physical activity. Some experimental studies have also suggested that replacing seated activity with light activity and standing has favorable effects on glucose and insulin sensitivity. Therefore, replacing prolonged sitting with periods of light activity in older people with prolonged sitting may reduce NAFLD risk (25). The exact mechanisms by which seated time independently of physical activity level contributes to NAFLD prevalence remain to be elucidated. The positive association between sitting time and NAFLD may be explained by high caloric intake. In Ryu et al.'s (2015) study, individuals who reported seated for 10 hours per day were more likely to have a higher total caloric intake than those who reported less than 5 hours per day (26). However, the association between sitting time and NAFLD remains statistically significant even after accounting for total caloric intake. Another possible mechanism is that this association may be due to lower energy intake. This in turn may lead to obesity, weight gain, and an increased risk of NAFLD. In one study, no association was found between sitting time and NAFLD after adjusting for either BMI or HOMA-IR, but an association was found after adjusting for percent fat mass. This suggests that the association between sedentary time and NAFLD occurs with increased fat mass. This discrepancy between BMI and percent fat mass may be because BMI is an imperfect measure of body fat. This is mainly because it does not directly measure fat mass. Lower body musculoskeletal mass may explain the possible association between prolonged sitting and NAFLD. Data from the Korean National Health and Nutrition Examination Survey (2011-2008) showed that Sarcopenia was associated with NAFLD independently of obesity and insulin resistance (26). The mechanism by which physical activity levels were inversely associated with NAFLD prevalence was not determined in this study. Obesity, which is partly influenced by physical activity and is a major risk factor for NAFLD, may represent a possible mechanism related to physical activity in NAFLD. Obesity may be a mediator or confounder in this relationship. In Ryu et al.'s (2015) study, physical activity was inversely linked with NAFLD even with a BMI of less than 23 kg/m2. However, in the current study, the average BMI of the statistical samples was about 27 kg/m2. The association between physical activity and NAFLD may be mediated through increased insulin sensitivity due to increased GLUT-4 levels and muscle glycogen synthase activity, decreased serum triglyceride concentrations, and a stronger muscle capillary network. In fact, NAFLD is now considered one of the hepatic symptoms of insulin resistance and one of the characteristics of metabolic syndrome. Low skeletal muscle mass may indicate a possible association between physical activity and NAFLD. These findings suggest that physical activity may directly affect NAFLD through biological pathways independently of obesity or insulin resistance (27).

5. Conclusion

The findings of the present research indicate that the amount of daily physical activity can be a very influential factor in the symptoms of non-alcoholic fatty liver disease. It can also be concluded that the amount of weight and body mass index has a significant and inverse relationship with physical activity. This can have a potential impact on this type of disease in firefighters. This study shows that both increased participation in physical activity and reducing sedentary time may be independently effective in reducing the risk of NAFLD. Finally, the subjects in this study were male firemen of Shiraz city with different educational levels, young and middle-aged, who regularly participate in the annual health screening examinations of the fire department, often as part of work-related health screening programs. They participated. Therefore, the results of the current research may not be generalizable to the general population of firefighters in the country or other populations with a different demographic composition. More research should be done in this field, and one should act cautiously in using these findings until a definitive result is obtained.

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