Journal of Exercise and Health Science, Vol. 02, No. 03, Summer 2022, Page 1-14

Research Paper

The Effect of High-Intensity Interval Training on Antioxidant Factors in Women with Type 2 Diabetes

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Received: 2022/06/04 **Accepted: 2022/10/02**

Abstract:

Background: Increased oxidative stress is a significant factor in obesity-related diseases and likely plays a fundamental role in the pathophysiology of diabetes.

Aim: The purpose of this study was to investigate the effect of High-Intensity Interval Training (HIIT) on certain antioxidant biomarkers catalase (CAT) and superoxide dismutase (SOD) in women with type 2 diabetes.

Materials and Methods: This clinical trial was conducted on 30 women aged 50 to 65 with type 2 diabetes. The participants were divided into two groups: experimental and control. The intervention group engaged in HIIT for 8 weeks, three sessions per week. The levels of CAT and SOD were measured by collecting 5 mL of venous blood before and after the intervention. The data were analyzed using dependent t-test in SPSS software version 25, with a significance level of $p < 0.05$.

Results: According to the results, after 8 weeks of intervention, in the HIIT group ($p = 0.00$), (mean difference = 0.540), there was a significant decrease in the variable CAT, while in the control group ($p = 0.32$), (mean difference = 0.390), no significant difference was observed. The data for the SOD variable indicated a significant decrease in the HIIT groups ($p = 0.00$), (mean difference = 9.876). However, in the control group ($p = 0.67$), (mean difference = 0.120), a significant difference was not observed.

Conclusion: HIIT with a prolonged duration leads to cellular stress and destruction of the antioxidants SOD and CAT, thus exerting negative effects on the cellular antioxidant capacity.

Keywords: High-Intensity Interval Training (HIIT), Superoxide Dismutase (SOD), Catalase (CAT) , Type 2 Diabetes

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1. Introduction

Type 2 diabetes is one of the most common chronic non-communicable diseases worldwide (Roy et al., 2023) . It occurs due to three pathophysiological abnormalities, including insulin secretion disorder, environmental resistance to insulin, and excessive production of glucose by the liver. It is predicted to be the seventh leading cause of death in 2030 (Galicia-Garcia et al., 2020). There is a significant relationship between oxidative stress, insulin resistance, and type 2 diabetes (Firuzyar et al., 2023) . In conditions of chronic hyperglycemia or hyperlipidemia, high levels of reactive oxygen species (ROS) are produced. There is increasing clinical and experimental evidence that indicates the elevation of ROS and antioxidants such as glutathione (GSH), superoxide dismutase (SOD), etc., in diabetes, and the onset of diabetes is strongly associated with oxidative stress. In diabetic patients, hyperglycemia generates free radicals and impairs the defensive mechanism of endogenous antioxidants, leading to detrimental effects for the individual (Bhatti et al., 2022).

HIIT is a form of interval training derived from "interval training." Therefore, high-intensity interval training usually involves aerobic-cyclic exercises such as running, cycling, etc. (Kazemi et al., 2023). However, increased metabolism during HIIT may increase the production of reactive oxygen and nitrogen species, which could be associated with inefficient antioxidant defense systems and oxidative stress (Hosseinikahnouj & Bahreini, 2023). Obese individuals have higher levels of reactive oxygen species; therefore, HIIT in obese individuals may lead to exacerbated damage to various molecules, including lipids, proteins, and DNA (Ramos-Tovar & Muriel, 2020). One of the body's defense mechanisms against free radicals is the antioxidant defense system, which exhibits greater defense capacity in tissues with higher oxygen consumption. The antioxidant defense system consists of enzymatic and non-enzymatic components. The enzymatic antioxidant system includes superoxide dismutase (SOD), glutathione peroxidase (GPX), and catalase (CAT). The most important components of the non-enzymatic system are glutathione (GSH), vitamin C, vitamin E, and uric acid (Mirończuk-Chodakowska et al., 2018).

Species of reactive oxygen species (ROS) are produced through regular metabolic processes in cellular mitochondria and can initiate damage to macromolecules (Silva & Lima, 2015). Oxidative stress is an inevitable consequence of aerobic exercise, and there is growing evidence suggesting that internal ROS molecules play a significant role in aging and many pathological conditions (Ye et al., 2021). These antioxidant defense systems maintain homeostasis for normal cellular functions during rest and under normal physiological conditions. However, during intense exercises, disease processes, and aging, the production of ROS may overwhelm the antioxidant defense capacity, leading to cellular and tissue damage. Because of the double lipid layer of cell membranes, proteins, and even DNA can suffer oxidative damage (Banerjee et al., 2003). Physical exercise is a complex biological activity that challenges homeostasis at the cellular, tissue, organ, and whole-body levels. Numerous reports provide reasonable support for the idea that exercise increases ROS production (Thomas et al., 2022) . Regarding exercise, the increase in oxidative stress is not entirely clear. However, the primary factor causing oxidative damage during exercise appears to be increased oxygen consumption (Radak et al., 2007). Therefore, it is essential to maintain a balance between antioxidants and pro-oxidants so that reactive oxygen species behave as modulators and do not have pathological effects (Shi et al., 2007). During physical exercise, there is a redistribution of blood flow due to increased metabolism in active cells, particularly in skeletal muscle fibers. Additionally, there is less blood flow to visceral organs. Although blood flow to the muscle's increases, they may experience short periods of hypoxia followed by reperfusion. This is because muscle contractions exceeding 50% of the muscle's functional capacity can cause short-lived vessel occlusion. This situation can lead to an increase in the contradictory production of mitochondrial ROS since without oxygen; Complex III of the electron transport chain can produce superoxide anions in a controlled manner. Superoxide anions, in turn, increase the reactivity of other oxygen species, and hydrogen peroxide becomes the primary intracellular signaling messenger (second messenger) (Andrés et al., 2023). Immediately after a high-intensity interval training session, reactive oxygen species increase compared to 24 hours after exercise, regardless of the individual's physical conditions (Martins et al., 2008). The reactive oxygen species generated during and after a workout can activate various intracellular signaling pathways associated with gene regulation processes. Therefore, the aim of this study was to investigate the effect of HIIT on some antioxidant factors in women with type 2 diabetes.

2. Materials and Methods

2.1. Participants

The present study was conducted with an applied and clinical trial objective in the form of a quasi-experimental two-group design (an experimental group and a control group) in the city of Hamedan. After obtaining permission from the Ethics Committee of the Sports Sciences Research Institute (IR.SSRI.REC.1401.1870) and registering on the Clinical Trials website (IRCT20221120056548N3), a total of 30 participants aged 50 to 65 years were selected through convenience sampling and met all inclusion criteria. They were placed on the research participant list after completing the consent form.

Additionally, the research participants were requested to adhere to natural sleep patterns (minimum of 8 hours of sleep), daily activity patterns, and dietary regimen (12-hour fasting state before the test) during the study. They were also asked to refrain from intense physical activity, dietary supplements, medication, coffee, tobacco, and cocoa for up to 48 hours before the test and until the collection of blood samples, which could affect their immune system and performance. To familiarize the participants with the movements and equipment used, they were called to the fitness and bodybuilding center one week before the start of the research protocol to become acquainted with the research process, proper use of supplements, and exercise techniques.

The inclusion criteria for participating in the study were as follows: no physical or mental illnesses, absence of specific dietary regimens, menopause, no physical or movement problems, fasting blood sugar level above 120, not being pregnant, and not engaging in regular physical activity. The exclusion criteria included intolerance to exercise (expressing discomfort, severe fatigue, lack of balance, and dizziness), cardiovascular diseases, irregular participation in exercises, incorrect use of supplements, pregnancy and lactation, and failure to complete the study duration.

All ethical principles were observed while working with these individuals during exercise and experiments. After receiving medical information, the participants were homogenized based on age, blood sugar, and weight and divided equally into two groups (1. High-Intensity Interval Training [HIIT] group with 15 participants, 2. Control group with 15 participants). The exercise sessions were conducted in a sports club under the supervision of an approved sports physician and trainer. The participants were required to have sports insurance and a COVID-19 vaccination card. The control group did not experience any physical activity or supplementation during this period. All stages of the research were carried out over an eight-week period.

The age of all participants was recorded based on their identification documents. For body weight measurement, the participants stood on a digital scale (OMRON) with minimal clothing. Body weight was recorded to the nearest tenth of a kilogram. Body weight measurements were taken with at least three hours of fasting after consuming a meal. For height measurement, the participants stood straight with their backs against the wall, and their heels, buttocks, and shoulder blades were in contact with the wall. The head had to be positioned in alignment with the Frankfurt plane, with the upper border of the ear hole and the lower border of the eye socket resting on a horizontal plane. The participants took a deep breath before measurement and held it during measurement (Naderifar et al., 2022).

2.2. Training protocol

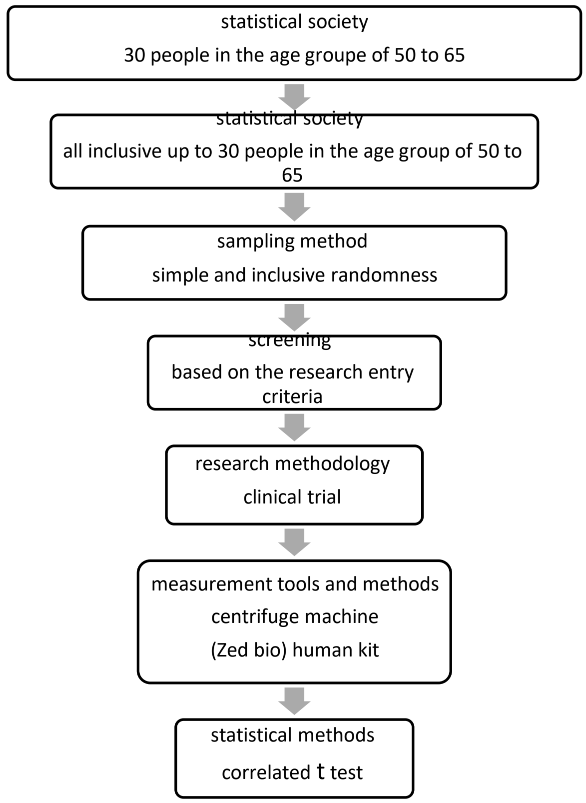
The HIIT group engaged in high-intensity interval aerobic exercise, alternating brisk walking and running with two active recovery periods at a moderate pace as described follow: participants run for 3 min, 3 times/session (Those who could not run were instructed to walk as quickly as possible) at 80–90% of maximum heart rate (HRmax). An active recovery time was implemented to interrupt the high-intensity period, during which participants walked at a moderate pace for 3 minutes at 55-65% of their HRmax. The HRmax was estimated equation ((208 – age) ∗ 0.7)(Kazemi et al., 2023)

2.3. Blood Sampling

Sampling was done in two stages: one day before the first training session and 48 hours after the last training session in the eighth week. All samples were fasted for 12 hours. Before each draw, the subjects rested for a few minutes in a sitting position. Approximately 5 mL of blood was collected from the participants' arm veins during each sampling stage (two stages during the study) and transferred to test tubes. The samples were immediately centrifuged at 3000 rpm for 10 minutes, and the serum samples were separated and collected in microtubes and kept frozen at -20°C for further examination and testing. For oxidative stress laboratory samples, a human Zell bio kit with a sensitivity of 0.03 u/ml (manufactured in Germany) was used.

2.4. Data analysis

Descriptive statistics such as mean and standard deviation are used to describe the research data. After ensuring the normality of the data using the Kolmogorov-Smirnov test, the dependent t-test is used to test hypotheses within groups, and one-way analysis of variance (ANOVA) is used to compare between groups at a significance level of 0.05 in SPSS software version 25.



3.Results

Table 1- Mean and standard deviation of demographic variables for the population.

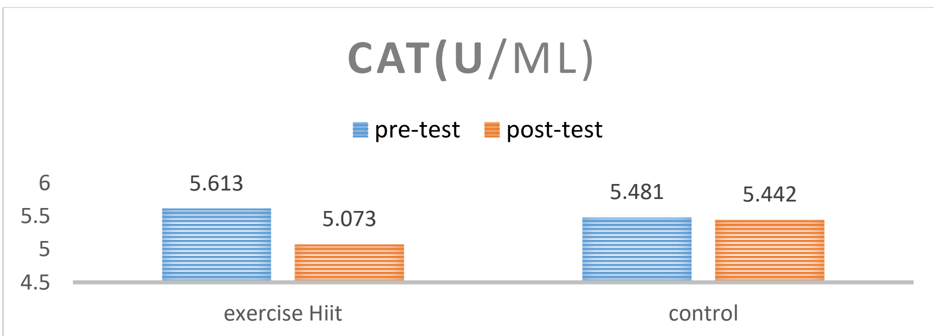
Variable	Group	mean±standard deviation	p-value
Age	HIIT	54.12±3.68	0.358
	control	59.6±3.76	0.134
Weight	HIIT	68.59±4.25	0.210
	control	72.16±4.03	0.718
Fasting blood sugar	HIIT	145.32±9.37	0.134
	control	139.30±7.94	0.211

This table presents the mean and standard deviation of age and height variables in the four research groups (Table 1)**.**

Table 2- The paired t-test to compare pre-test and post-test scores on the CAT variable.

group	average pre-test	average post-test	average difference	t	degrees of freedom	significance level
HIIT	5.613	5.073	-0.540	4.176	14	0.00
control	5.481	4.442	0.390	0.671	14	0.32

According to Table 2, the results of the paired t-test indicate that in groups with significance values less than 0.05=P and t-values greater than the standard value of 1.96, there is a significant difference between the pre-test and post-test. Therefore, based on this evaluation, the HIIT group showed a significant decrease in the antioxidant (CAT) with a mean difference of 0.540- and t-value of 4.176 at a significance level of 0.05>P, while no significant effect was observed in the control group.

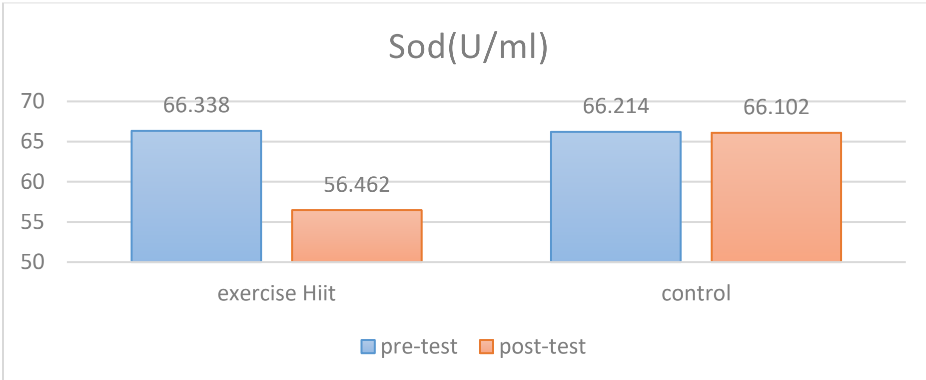


Graph 1- Comparison of pre-test and post-test for the CAT variable.

Table 3- The paired t-test to compare pre-test and post-test scores on the SOD variable.

group	average pre-test	average post-test	average difference	t	degrees of freedom	significance level
HIIT	66.338	56.462	-9.876	7.994	14	0.00
control	66.214	66.102	0.120	0.864	14	0.67

According to Table 3, the results of the paired t-test indicate that in the HIIT group, there is a significant decrease in the post-test. No significant difference was observed in the Control group. 0.05<P.



Graph 2- Comparison of pre-test and post-test for the SOD variable.

4. Discussion

This study aimed to investigate the effect of 8 weeks of high-intensity interval training (HIIT) on some antioxidant biomarkers (CAT and SOD) in women with type 2 diabetes. The research findings showed that eight weeks of HIIT had negative effects and reduced the levels of antioxidant CAT and SOD in women with diabetes.

Koyuncuoğlu et al. (2021)_conducted a study entitled “High-Intensity Interval Training on Stress-Induced Cognitive Impairment” where after a period of intense interval training, the levels of malondialdehyde (MDA), glutathione (GSH), luminal and lucigenin luminescence, and myeloperoxidase (MPO) were measured, and histopathological damage was evaluated. The results indicated that exercise had negative effects on CAT and MDA in the post-test and positive effects on SOD, MPO, and GSH. Overall, the exercises improved physical performance in individuals (Koyuncuoğlu et al., 2021).

Akgul et al. (2019)_ in a study titled “The Effect of High-Intensity Interval Training under Hypoxic Conditions on the Antioxidant Status of Students with Moderate Exercise” stated that there was no significant interaction effect (time × group) for SOD, CAT, GPX, and MDA, indicating no meaningful change in response to repeated measures. Therefore, although 8 weeks of high-intensity interval training only significantly affected SOD and GPX ($p < 0.05$), leading to a decrease in SOD and CAT in the post-test, thermoxic and hypoxic conditions did not show significant changes among individuals.

This study suggests that HIIT induce antioxidant activity in the body and create a strong anti-atherogenic and effective treatment against hypercholesterolemia. Thus, the “redox state” of an individual can serve as an additional indicator in physical exercise and prevention of damage to the body. Lipid peroxidation activates cellular compounds through active oxidation or radical chain reactions, leading ultimately to membrane integrity loss (Wang et al., 2021).

Furthermore, the research findings demonstrated that eight weeks of HIIT had significant effects on reducing the levels of antioxidant SOD in women with diabetes. Therefore, it aligns with the results of the following studies:

Martinovic et al. (2011) conducted a study to determine the effect of long-term training on elite female volleyball players and identify parameters that could differentiate them based on stress oxidative-related adaptability. These results indicate that long-term light exercises lead to a significant increase in oxidative stress parameters in athletes (Martinovic et al., 2011).

In addition, Koyuncuoğlu et al. stated that high-intensity interval training protects against cognitive impairment-induced stress disorder. The study's findings showed that high-intensity interval training reduces antioxidant levels (SOD, CAT)(Koyuncuoğlu et al., 2021).

Furthermore, Sudarsono investigated the effect of combined high-intensity interval and resistance training on blood glucose control and oxidative stress in type 2 diabetes. The results indicated that the combined HIIT and strength training program did not significantly improve blood glucose control but reduced oxidative stress while the SOD level significantly increased (Sudarsono et al., 2019).

However, Norouzi et al. examined the effects of two types of intervals and intense endurance exercise along with pomegranate supplement consumption on oxidative stress status and antioxidant capacities in rats. The results of the present study showed that interval and intense endurance exercises led to a decrease in oxidative pressure and a significant increase in antioxidant enzyme activities (SOD, TAC) in immature rats, which is one of the possible causes of the different effects of Intense exercises on rats and humans (Karimiasl et al., 2023).

Diabetes leads to increased oxidative stress due to various factors. Hyperglycemia produces reactive oxygen species (ROS), resulting in lipid peroxidation and membrane damage through glucose oxidation. Exercise intensity can generate free radicals, stimulating the metabolic pathways of antioxidants (Rösen et al., 2001).

At the beginning of low-intensity exercise, when the production of free radicals is minimal, superoxide dismutase (SOD) is activated as the primary defense line (Alghadir et al., 2016).

In the initial stage, when free radicals are generated, they are immediately converted to superoxide anions through SOD and then transformed into H2O2. As long as the exercise is performed at a level that does not require excessive disposal of free radicals, SOD continues its activity. However, with increasing exercise intensity, GPX and catalase become active and neutralize H2O2.

Therefore, high GPX activity will be associated with less SOD activity (Ficker et al., 2010). Regular exercise is considered an important means of prevention and treatment in modern medicine. Although intense exercise increases oxidative stress, it has been shown that regular exercise strengthens the antioxidant defense system (Shanmugam et al., 2011). Given that excessive tissue oxygen supply is one of the most important causes of increased oxidative stress, and the response of oxidative stress to exercise is influenced by factors such as individual health status, age, race, genetics, tissue-specific differences, muscle fibers, and a decrease in the intake of antioxidant compounds in daily nutrition, along with repeated exposure to exercise stress leading to enzymatic adaptation that reduces the consequences of stress, and possibly one of the justifications for enhancing the antioxidant system resulting from intense exercises, the results of this study are not unexpected. The enhancement of the antioxidant system and the reduction of oxidative stress highlight the important role of supplementation and exercise in increasing and strengthening the antioxidant system to overcome adverse tissue and cellular conditions in cases of obesity and overweight (Firuzyar et al., 2023). However, increasing the intensity of training increases the number of free radicals, and this process causes suppression of the antioxidant defense system. Therefore, the process of increasing the levels of oxidative stress is directly related to the intensity and type of exercise (Bloomer, 2008).

5. Conclusion

The results obtained from this research showed that the amounts of antioxidants (SOD, CAT) in the HIIT group had negative effects, and the post-test had lower averages than the pre-test. According to the study’s findings, it can be said that high-intensity interval training can weaken the antioxidant function in people with diabetes.

Conflict of interest

The authors declared no conflicts of interest.

Authors' contributions

All authors contributed to the original idea, study design.

Ethical considerations

All research participants provided written informed consent forms. Moreover, the study was approved by the Research Ethics Committee of the Sports Sciences Research Institute (IR.SSRI.REC.1401.1870).

Data availability

The dataset generated and analyzed during the current study is available from the corresponding author on reasonable request.

Funding

This work was funded by the faculty of physical education and sports science of the Danesh Alborz University, Iran.

Acknowledgments

We would like to extend our gratitude to all participants of this study. The above article is the result of a master's thesis conducted at Danesh Alborz University, and we express our appreciation to the officials and research participants involved.

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