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# Effect of Eight Weeks of Periodic and Resistant Sports Activities with Moderate Severity on TNF-α and IL33 Body Composition Indices in People with Type 2 Diabetes


## Abstract

The purpose of the present study was to evaluate the effect of eight weeks of moderate-intensity intermittent and resistance exercise on TNF-α in individuals with type 2 diabetes. Thirty diabetic women (51.9 09 5.09 years) were randomly divided into three groups (10 people) resistance training, periodic aerobic training, and control. Periodic aerobic exercise with an intensity of 50-75% MHR and resistance exercise with an intensity of 30-75% 1RM was performed for eight weeks and three sessions per week. ELISA measured IL-33. Data were analyzed using paired t-test and one-way ANOVA at the significance level (p≤0.00.05). (Resistance and intermittent aerobic) exercise reduces TNF-α levels. One of the possible reasons for the increase in serum CTRP-12 in the subjects of the present study is a significant decrease in inflammatory factor TNF-a. The results showed that eight weeks of intermittent resistance and aerobic training could significantly increase the serum levels of IL-33 in diabetic women. This increase was greater in the group of resistance training. In the intergroup study, the changes and increases in IL-33 in the resistance training group were much greater than in the periodic aerobic training group and the control group. These differences were also significant.


**Keywords:** *resistance sports activities, Body composition indicators, Inflammatory factor TNF-a, Periodic sports, Type 2 Diabetes*


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## Introduction

Diabetes is a metabolic disorder that results in impaired insulin secretion and function or both. Diabetes results in hyperglycemia with impaired carbohydrate, fat, and protein metabolism (1). This disease has created health, medical and socio-economic problems for human societies. It has been very common in recent decades in societies (2). Researches show that in type II diabetes, the secretion of GLP-1 is impaired. Therefore, increasing and improving blood GLP-1 levels can increase insulin and regulate blood glucose. Today, two types of drugs that enhance the effect of GLP1 are used orally and subcutaneously (3).

Furin is one of the first types of membrane-bound proteases found in all vertebrates and most invertebrates. Overweight and obesity are likely to affect the activity of adipocytokines such as adipokine through furin overexpression in adipose tissue. And reduced adipulin in the blood, thus increasing insulin resistance (4).

Increases in TNF-α, IL-6, and IL-33 predict insulin resistance and endothelial dysfunction and then the development of type 2 diabetes and atherosclerosis (5). It is not yet fully understood to what extent exposure to chronic inflammation with low levels increases or exacerbates insulin resistance (6). TNF-α levels and inflammation observed in pre-diabetic subjects are associated with insulin resistance or impaired insulin secretion. Increased concentrations of proinflammatory molecules in type 2 diabetic patients may be due to high blood sugar and oxidative stress. High blood sugar seems to activate the immune system and the monocyte-macrophage system. Their activation will stimulate the production of cytokines and acute-phase proteins (7).

Systemic inflammation can be an independent risk factor for diabetes in healthy individuals. Inflammatory mediators such as cytokines and TNF-α are increased in diabetic patients. Adipose tissue is one of the tissues that produce inflammatory stokines. Numerous studies have shown that physical activity and cardiorespiratory fitness are inversely related to TNF-α. And that regular exercise decreases plasma levels of TNF-α and other inflammatory markers (8, 9).

Changes in several aspects of life (nutrition, health care, and exercise) have had short-term and long-term positive effects on cardiovascular risk factors (10). Recent studies show that resistance training is associated with a reduced risk of inflammatory diseases such as atherosclerosis, obesity, insulin resistance, and diabetes. These exercises also improve and control insulin resistance and diabetes by reducing systemic inflammation and improving glucose uptake by muscles (11). The importance of moderate-intensity resistance training is such that a comparative study showed that resistance training performed better than aerobic training in glycemic control and improved lipid profile in type 2 diabetics (12).

Moderate-intensity resistance aerobic activity has beneficial effects on the glycemic index and reduces risk factors for cardiovascular disease, including insulin resistance. Moderate-intensity physical activity has beneficial effects on reducing insulin resistance in people with type 2 diabetes (13). Previous research has shown that intensive exercise programs increase

insulin sensitivity in overweight middle-aged men with type 2 diabetes and reduce subcutaneous and visceral adipose tissue.

In a study, Rech et al. showed that resistance training led to a significant reduction in TNF-α and IL-1β levels, and in other factors, no significant change was observed in the resistance training group compared to the control group (14). In a study, Bani Talebi et al. showed that the concentration of TNF-α was significantly reduced in the high-intensity interval training group and the combined training group. IL-6 concentration also decreased significantly in the combined exercise group. Insulin resistance was also significantly reduced in both exercise groups (15).

Cassidy et al. (2016) conducted a clinical trial study to investigate the effect of high-intensity intermittent exercise on the function and structure of the cardiovascular system, liver fat, and metabolic status in patients with type 2 diabetes. The results showed that high-intensity resistance training and improving the structure and cardiovascular function in patients led to a significant reduction in hepatic fat and HbA1C in the intervention group compared to the control group (16). Terada et al. investigated the effect of high-intensity interval training in type 2 diabetic patients. The results showed that 12 weeks of high and medium-intensity interval training effectively reduced total body fat (17). Castaneda et al. Conducted a study on the effect of resistance training on glycemic control in adults with type 2 diabetes. The results showed that 16 weeks of increasing intensity training improved glycemic control but did not significantly change the lipid profile (18).

A study performed on diabetics showed a significant relationship between performing different sports activities (aerobic, resistance, and combination) and cardiovascular risk factors. It was shown that aerobic, combination and resistance exercise had the best effect, moderate effect, and weak effect on cardiovascular risk factors, respectively (19). In another study, sports activities did not affect glycemic control and body composition (20). High-intensity intermittent exercise causes structural changes in the heart and reduces liver fat and HbA1c. Combined exercise (aerobic and resistance) reduces (HbA1c, abdominal fat, total cholesterol, triglyceride, HDL-C, LDL-C, and blood pressure) compared to resistance training (21). According to the contents, this study aimed to evaluate the effect of eight weeks of moderate-intensity Periodic and resistance sports activities on TNF-α body composition indices in people with type 2 diabetes.

**Materials and methods:**

The present research was quasi-experimental. Its statistical population consisted of type 2 diabetic women in Baneh with a mean age of 51.9. 5.09 years. In the present research, among the diabetic women referred to the health management of Baneh based on the initial call, 30 women with type 2 diabetes were randomly selected after completing the consent form and health questionnaire. Subjects in three groups of resistance training (n = 10), periodic aerobic exercise (n = 10) and control (n = 10) volunteered to do present research. The subjects of the training groups engaged in selected sports activities for eight weeks and three sessions per week. The control group did not experience any sports activities during the eight weeks.

Inclusion criteria included the following: At least six months have passed since the subjects had diabetes. Having a history of metformin use for at least six months. Their HbA1C is between 9.9-6.6%. They should not have any regular sports activities. The subjects' fasting glucose was equal to or greater than 126 mg / dL.

The research subject was explained to the patients before the start of the study. Written consent was obtained from patients. Subjects were randomly divided into three groups of 8: resistance training group, Interval Exercise Group, and control group. Before starting the study, a general information questionnaire was completed to collect demographic information, including age and sex, marital status, duration of diabetes, type and amount of medication used, history of sports activities, etc. Physical activity was assessed using the International Physical Activity Questionnaire (IPAQ). Also, the food intake of individuals at the beginning and end of the study was determined using a 24-hour recall questionnaire.

Anthropometric measurements, including height and weight, were taken at the beginning and end of the study, and BMI was calculated. cc8 Fasting venous blood samples (12-14 hours) were taken from all subjects before and after the intervention. Biochemical variables were measured using biochemical analyzers, including fasting plasma glucose, serum lipid profile (TG), TC, and HDL-C. The LDL-C calculation was determined using the Friedwald formula.

In this study, after examination and confirmation of unobstructed exercise by the clinic physician and signing of written consent of patients to assess the level of physical fitness at 11-9 am in the pre-test and post-test sessions, and after blood sampling, we performed the following tests:

Increasing interval training:

• It was performed for eight weeks, three sessions per week with a gradual increase in duration (20 to 60 minutes) and intensity of training (75-50% of maximum heart rate (MHR).

• In the first week for 20 minutes with an intensity of 50% MHR and finally in the eighth week for 60 minutes with 75% MHR.

• Each training session included: 10 minutes of warm-up (slow running and stretching), intermittent training with an intensity of 75-50% MHR, and 5 minutes of cooling (slow running and stretching).

**Resistance training:**

• For eight weeks, three sessions per week and gradually increasing training intensity (30-30% of a maximum repetition (1RM).

• In the first week with two sets of 10 repetitions and intensity of 30% 1RM and finally in the eighth week with three sets of 8 repetitions and intensity of 75% 1RM.

• Each training session includes 10 minutes of warm-up (slow running and stretching), Resistance training with an intensity of 30-30% 1RM for movements (machine chest press, machine shoulder press, front thigh, recumbent thigh, wire-pulling front arm, wire-pulling rear arm, lying down and sitting, launch and torso extension) And cool for 5 minutes (two slow and stretching movements). The rest time was 1 minute between each set and 3 minutes between movements.

Measuring anthropometric variables includes the following: Height (cm, using a tape measure), weight (kg, with digital scale), body mass index (BMI, using weight-kg formula divided by height squared in meters), waist-to-hip ratio (WHR, with Use of flexible tape measure), Muscle strength and the amount of a maximum repetition (1-RM, using the Brzycki method), Measuring heart rate with a polar heart rate monitor. The formula (age-220) was used to determine the maximum heart rate (MHR).

The Amount of IL-33 Serum was measured using ELISA and a kit (Bioassay Technology Laboratory) made in China with catalog number (Cat. No: E0044Hu) and sensitivity (2.12 ng / L). Serum Forin values were measured using ELISA and a kit (Bioassay Technology Laboratory) made in China with catalog number (Cat. No: E2321Hu) and sensitivity (6.93 ng / L), coefficient of variation within the test (Intra -Assay: CV <8%) and extra-test coefficient of change (Inter-Assay: CV <10%).

The amount of TNF-a serum was measured using ELISA and a kit (Bioassay Technology Laboratory) made in China with catalog number (Cat. No: E0082Hu) and sensitivity (1.52 ng / L), coefficient of variation within the test. (Intra-Assay: CV <8%) and extra-test coefficient of change (Inter-Assay: CV <10%).

Research data were analyzed using SPSS software version 22. The significance level was considered P≤0.05.

**Findings:**

Table 1: Results of dependent t-test (between intragroup pre-test and post-test) of Serum TNF-a

| Resistance exercise group | control group | Variable | |
|---|---|---|---|
| 12.96± 15.18 | 35.18 ±150.1 | pretest | TNF-a) ng/L( |
| 119/48 ± 23/84 | 149/18 ± 42/68 | post-test | |
| 3.081 | 0.055 | value t | |
| 0.013* | 0.957 | P value | |

The correlated t-test for the resistance training group showed that the amount of TNF-α in the post-test compared to the pre-test had a significant decrease in the degree of freedom (df = 9) (p = 0.013). This means that eight weeks of resistance training caused significant changes in serum TNF-a in type 2 diabetic women (Table 1).

Table 2: Results of serum IL-33 dependent t-test (between intragroup pre-test and post-test)

| Resistance exercise group | control group | Variable | |
|---|---|---|---|
| 65.74± 228.01 | 222.1 ±50.25 | pretest | IL-33 )ng/L( |
| 272.27 ±680.31 | 59.87 ±225.59 | posttest | |
| -5.276 | -0.143 | value t | |
| 0.001* | 0.890 | P value | |

The results of the correlated t-test for the resistance training group showed that the amount of IL-33 post-test compared to the pre-test had a significant increase with the degree of freedom (df = 9) (p = 0.001). This means that eight weeks of resistance training has caused significant changes in serum IL-33 in type 2 diabetic women (Table 2).

Table 3: Results of serum TNF-a dependent t-test (between intragroup pre-test and post-test)

| The periodic aerobic exercise group | control group | Variable | |
|---|---|---|---|
| 151.81± 26.70 | 150.1 ±35.18 | pretest | TNF-a) ng/L( |
| 111.14 ±34.35 | 149.18 ±42.68 | posttest | |
| 2.490 | 0.055 | value t | |
| 0.034* | 0. 957 | P value | |

The results of the correlated t-test for the resistance training group showed that the amount of TNF-a post-test compared to the pre-test had a significant decrease with the degree of freedom (df = 9) (p = 0.001). This means that eight weeks of resistance training have caused significant serum TNF-a changes in type 2 diabetic women (Table 3).

Table 4: ANOVA test results for TNF-a

| P | F | average of squares | Degrees of freedom | Squares | Source of change | Variable |
|---|---|---|---|---|---|---|
| 0.050* | 3.359 | 3997.812 | 2 | 7995.624 | Intergroup | TNF-a (ng/L) |
| | | 1190.289 | 27 | 32137.796 | Intragroup | |
| | | | 29 | 40133/420 | total | |

The results of the ANOVA test related to TNF-a of different research groups after eight weeks are shown in Table (4). It is observed that the value (p = 0.050) and the degree of freedom (df = 29) are equal to the alpha level of 0.05. That is, there is no significant difference between the mean of TNF-α in different research groups. The Tukey post hoc test results are shown in Table (5).

Table 5: Results of TNF-a variable Tukey follow-up test

| **Sig** | Group | group | Variable |
|---|---|---|---|
| **0.151** | Resistance | Control | **TNF-a )ng/mL(** |
| **0.050*** | Periodic aerobics | | |
| 0.852 | Periodic aerobics | Resistance | |

Table 6: ANOVA test results for IL-33

| P | F | average of squares | Degrees of freedom | Squares | Source of change | Variable |
|---|---|---|---|---|---|---|
| 0.001* | 12.784 | 518369.216 | 2 | 1036738.433 | Intergroup | IL-33 (ng/L) |
| | | 40549.031 | 27 | 1094823.842 | Intragroup | |
| | | | 29 | 2131562.275 | total | |

The results of the ANOVA test related to IL-33 of different research groups after eight weeks are shown in Table (6). It is observed that the value (p = 0.001) and the degree of freedom (df = 29) are less than the alpha level of 0.05. There is no significant difference between the mean of IL-33 in different research groups. The results of the Tukey follow-up test are shown in Table (7).

Table 7: Results of IL-33 variable Tukey follow-up test

| **Sig** | Group | group | Variable |
|---|---|---|---|
| **0.001*** | Resistance | Control | **IL-33 ) ng/mL(** |
| **0.074** | Periodic aerobics | | |
| **0.027*** | Periodic aerobics | Resistance | |

**Conclusion:**

Disruption of glycemic balance due to diabetes increases the risk of cardiovascular disease. Exercise improves glucose metabolism and regulates glycemic homeostasis with various protective factors. This study aimed to evaluate the effect of eight weeks of intermittent and resistance sports activities on body composition indices and TNF-a in people with type 2 diabetes. The results showed that eight weeks of resistance training caused significant changes in serum TNF-a in type 2 diabetic women. Also, eight weeks of resistance training has caused significant changes in serum IL-33 in type 2 diabetic women. On the other hand, eight weeks of periodic aerobic exercise caused significant changes in serum TNF-a in type 2 diabetic women. There is no significant difference between the mean of TNF-α in different groups. The results showed that there was no significant difference between the mean of IL-33 in different groups.

Studies have shown that by inducing TNF-α and endoplasmic reticulum stress into the adipocyte culture medium, serum levels and CTRP-12 gene expression are reduced (22).

Inflammatory factor TNF-a is one of the proinflammatory adipo ines derived from adipose tissue and a negative regulator of CTRP-12 (22). This factor is affected by exercise (22). The results of the present study were consistent with these results. Exercise (resistance and intermittent aerobics) reduces TNF-α levels. One of the possible reasons for the increase in serum CTRP-12 of the subjects in the present study is a significant decrease in the inflammatory factor TNF-a. In this regard, it has been stated that TNF-a reduces this factor by degrading the signaling pathways of upregulation (positive regulation) of CTRP-12 because TNF-α has been shown to reduce the transcription factor KLF-15 (Krüppel-like factor 15) by activating c-Jun N-terminal kinase, followed by CTRP-12 levels in adipocytes. Decreases (KLF-15) stimulate CTRP12 promoter activity in 293 cells and positively regulate CTRP-12) (23). TNF-α reduction strategy has been effective in increasing CTRP-12 in the present study. The present study results also showed that eight weeks of resistance training and periodic aerobic exercise reduce TNF-α levels. Reducing fat mass seems to be a necessity to reduce the number of anti-inflammatory adipokines (24); reducing the content of adipose tissue in the body while reducing the volume of fat cells due to reduced penetration of macrophages into adipose tissue is reduced the synthesis and secretion of TNF-a. The anti-inflammatory role of IL-6 (myokine) is among the mechanisms involved in controlling TNF-a. The positive effects of long-term, regular exercise are due to its anti-inflammatory benefits, which are produced by IL-6 secreted from muscle tissue (myokine). Physiological concentrations of IL-6 stimulate the release of anti-inflammatory cytokines IL-1ra and IL-10 and inhibit the production of proinflammatory cytokines TNF-α. The anti-inflammatory effects of exercise may also be related to its protective role against TNF-induced insulin resistance. In relation to the present study's periodic and resistance aerobic training modalities, these two types of exercises appear to be effective in controlling TNF-α by increasing muscle IL-6. IL-6 levels were not measured in the present study (25).

Exercise therapy is one of the treatments for diabetes that is recommended for diabetics. Regular exercise improves lipid metabolism and insulin resistance, which minimizes the complications associated with diabetes. Exercise improves Chronic inflammation (26). Exercise Therapy can improve chronic inflammatory diseases such as obesity, metabolic syndrome, diabetes mellitus, etc. (27).

Exercise controls blood glucose levels through various mechanisms that are effective in regulating glycemic control. Immune factors affect glycemic control of IL-33 (28). The present study results showed that eight weeks of intermittent resistance training and aerobics could significantly increase the serum levels of IL-33 in diabetic women. This increase was greater in the authority training group. In the intergroup study, the changes and increases in IL-33 in the resistance training group were much greater than in the periodic aerobic training group and the control group. These differences were also significant. IL-33 is a protective cytokine that is reduced in diabetic patients. Recently, IL-33 has also been expressed in human adipocytes and has metabolic protective effects in obesity and diabetes (29). It seems that the increase of IL-33 in the exercise groups of the present study is related to the protective role of IL-33. In other words, exercise by inducing and increasing IL-33 has a protective role against diabetes. Numerous mechanisms have been proposed regarding the protective role of IL-33 in obesity and diabetes. Treatment of murine fat cells with IL-33 has been shown to induce the production of cytokine T helper cell -2 (TH2), reducing lipid stores. And reduces the expression of several genes associated with lipid metabolism and adiposeness. (C / EBPα[1], SREBP-1c[2], LXRα[3], LXRβ and PPARγ[4]).The distribution of IL-33 in obese (genetic) diabetic mice leads to a decrease in fat cells, a decrease in fasting glucose, and an improvement in insulin sensitivity (29). In the present study, glycemic index (glucose, insulin, and insulin resistance) in the training groups decreased with increasing IL-33. In addition, IL-33 has been shown to affect macrophages. Macrophages are divided into two categories, which are: Classical macrophage (M1, inflammatory) and Alternative (M2, anti-inflammatory), Each of which has its own characteristics. Macrophages M1 and M2 have different functions against infections. It is stated that IL-33 induces local accumulation of Th2 cells (CD4 + ST2 + IL-5 +) and cytokines in adipose tissue. It causes polarization of adipose tissue macrophages to the active phenotype of the protective (anti-inflammatory) variable M2 (macrophage M2) (CD206 +). In addition, ST2 - / - (cardiac stress biomarker) increased body weight and fat mass in mice on a high-fat diet. Insulin secretion and glucose regulation are also impaired compared to the control group. In conclusion, IL-33 may have a protective role against obesity and diabetes by inducing Th2 cytokine and M2 anti-inflammatory macrophages in adipose tissue and controlling ST2 - / - (29). The effects of exercise on improving the function of cytokines and macrophages have been proven. In this regard, Ji Young et al. (2015) investigated the effect of exercise on macrophage infiltration and change of M1 to M2 macrophage in mice with a high-fat diet. Their results showed that moderate-intensity exercise prevents macrophage infiltration and positively regulates CD163 expression (30). However, research on the IL-33 signal pathway on macrophages has been limited to exercise. It seems

[1] . CCAAT-enhancer-binding proteins

[2] Sterol regulatory element-binding protein 1

[3] . Liver X receptor alpha

[4] Peroxisome proliferator-activated receptor

that the intermittent resistance training and aerobic exercise of the present study are effective in improving the immune function in type 2 diabetic patients with incremental changes in IL-33. However, we did not evaluate the immunological parameters in the present research.

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