ISSN: 2538-5887; Pathobiology Research. 2022;25(2):22-29

The effect of different exercise training modes on serum ferritin and iron levels of type 2 diabetic rats

ARTICLE INFO

Article Type
Original Research

Authors

Ali Heidarianpour*
Mohammad Aghamohamadi
Maryam keshvari

Sport Physiology Department, Sport Sciences Faculty, Bu-Ali Sina University, Hamedan, Iran

***Corresponding authors:**
Ali Heidarianpour, PhD.
Sport Sciences Faculty, Bu -Ali Sina University, Shahid Fahmide Street, Hamedan, Iran. Postal Code: 6517838695.
Phone: +98 (81) 38381422
Fax: +98 (81) 38381421
a.heidarianpour@basu.ac.ir

ABSTRACT

Introduction. Ferritin is an indicator of iron (Fe) storage in the body and plays the main role of cellular oxidation. It is hypothesized that Fe causes insulin resistance and then by reducing insulin secretion leads to type 2 diabetes. Considering the effects of exercise training in increasing insulin sensitivity, this study was designed with the aim of investigating the effect of various resistance, endurance, and combined activities on serum ferritin and Fe levels in diabetic rats.

Methods. Type 2 diabetes was induced by intraperitoneal injection of Nicotinamide solution (120 mg/kg) and Streptozotocin (65 mg/kg). One week after the confirmation of diabetes, the training groups underwent resistance (diabetic resistance group; DR), endurance (diabetic endurance group; DE) and combined activities (diabetic endurance and resistance group; DER) exercises for 10 weeks. After completing the research protocol, blood sampling was done to measure serum ferritin and Fe levels.

Results. Type 2 diabetes caused an adverse increase in blood glucose, insulin levels, increased Homeostasis Model Assessment of Insulin Resistance (HOMA-IR), Fe, serum ferritin and decreased Homeostasis model assessment of insulin secretion (HOMA-IS). Looking to improve glycemic indices after 10 weeks training in DE, DR and DER groups, we saw a decrease in serum Fe and ferritin levels, and training in DER group had a significant decrease in Fe compared to training in DR and DE groups.

Conclusion. This study showed that serum iron and ferritin levels are significantly increased in diabetes and the increment of ferritin may be a reason for insulin resistance in diabetes. Given the importance of iron and ferritin levels in insulin resistance, combined exercise with moderate intensity and time by reducing these biomarkers can reduce glycemic indices in type 2 diabetes.

Keywords: Different exercise, Type 2 diabetes, Ferritin, Iron

INTRODUCTION

An increase in ferritin level as an important independent biological factor may increase the prevalence of diabetes [1]. Ferritin is a protein-iron (Fe)-phosphorus compound and an indicator of body Fe storage. Fe is essential for the transport of oxygen to the tissue and plays the main role of cellular oxidation. A high level of Fe in the serum leads to an increase in the level of ferritin [2]. Insulin affects Fe absorption and storage by increasing transferrin receptors. On the other hand, Fe affects insulin activity by interfering with glucose absorption [3].

It is hypothesized that Fe causes insulin resistance and then leads to type 2 diabetes by reducing insulin secretion [4]. It has been shown that there is a positive relationship between the level of plasma ferritin and type 2 diabetes, but so far, serious studies have not confirmed the hypothesis of increasing Fe reserves in the body and causing

type 2 diabetes [5]. In the study of Jehn et al., although it was found that the level of ferritin in the plasma of diabetic patients is higher than that of healthy people, but according to variables such as gender, age, race and lifestyle, there is no relationship between the level of ferritin and diabetes as a predisposing factor. There is no difference in the development of diabetes [6].

Today, health experts consider physical activity as one of the essential elements in the treatment of diabetes [7]. Physical activity can increase skeletal muscle response to insulin by increasing the expression or activities of proteins involved in insulin metabolism and signaling. So that resistance training increases glycogen synthase activity and GLUT4 expression. Considering the role of fat oxidation in improving insulin action, exercise increases muscle fat reserves and fat oxidation capacity. Also, the physical fitness of people with diabetes can be associated with a decrease in fat oxidation and a shift towards more carbohydrate oxidation in all exercise intensities [8].

It has been shown that diabetic patients who have defects in insulin function, regular physical exercises increase the entry of glucose into muscle cells in the absence of insulin through increasing insulin sensitivity. In addition, resistance exercises are able to increase the activity of antioxidant enzymes against stressful complications and protect body organs from the complications of diabetes [9].

Also, exercise has been reported to have a profound effect on protein turnover. Muscle and whole-body protein synthesis increases during recovery after endurance exercise. Resistance training has also been shown to increase total body protein synthesis 50-100% above resting levels early in recovery and up to 24 hours post-exercise. Whole-body protein breakdown, as measured by stable isotope tracers, is also increased by endurance exercise [10]. Considering the different responses of the body's metabolism to endurance and resistance exercises, this study was designed with the aim of investigating the effect of resistance, endurance exercises and the combination of these exercises on serum ferritin and Fe metabolism in type 2 diabetic male rats.

MATERIALS AND METHODS

Animals

This experimental study was conducted on 40 Wistar rats (10 weeks old) that were purchased from the Animal Breeding Center of Arak University of Medical Sciences. Rats were kept under conditions of 12 h of light /12 h dark in a temperature range of 23-25 C and free access to food and water. This study was carried out in compliance with all the ethical issues of working with laboratory animals approved by Arak University of Medical Sciences (IR.ARAKMU.REC.1394.329). One week after familiarizing the rats with the laboratory environment, they were randomly were divided into 5 groups (n=8): healthy control (HC), diabetic control (DC), training groups underwent resistance (diabetic resistance group; DR), endurance (diabetic endurance group; DE) and combined activities (diabetic endurance and resistance group; DER).

Induction and confirmation of type 2 diabetes

In order to induce type 2 diabetes after 12 hours of fasting, Nicotinamide (Sigma, USA) dissolved in normal saline at a dose of 120 mg/kg and after 15 min of streptozotocin (STZ) (Sigma, USA) solution in 0.1 M citrate buffer with a dose of 65 mg/kg was used as an intraperitoneal injection. 72 h after the injection to ensure the diabetes induction, rats whose blood glucose level was more than 250 mg/dl were considered as diabetic [11]. The blood glucose level in rats was measured by a glucometer every time after 12 h of fasting.

Endurance training

The endurance training program was implemented on a 5-channel treadmill due to the easier control of speed and duration of running. The entire training period was divided into 3 stages of familiarization, overloading, saving and fixing the work intensity. In the familiarization phase (first week), the mice walked on the treadmill every day for 10-15 min at a speed of 10 m/min. In the overload phase (second to fourth week), the rats first ran on the treadmill for 20 min at a speed of 27 m/min, and gradually over the course of 3 weeks, the duration of the activity was increased (2 min/session) until the final level 60 min arrived, and finally, in the phase of saving

Table 1. Endurance training protocol during 10 weeks on the treadmill

	Familiarization	week1	week2	week3	week4	week5-10
Exercise duration (min)	15	20-30	30-40	40-50	50-60	60
Speed (m/min)	27	27	27	27	27	27
Intensity equivalent (vo_2max) %	75	75	75	75	75	75

and fixing the work intensity (Fifth to tenth week), they performed endurance training (60 min at a speed of 27 m/min) (approximately equivalent to 75% VO2max) for 3 weeks. At the same time, in each training session, at the beginning, they worked for 5 min to warm up (with an intensity of 16 m/min) and at the end for 5 min to cool down (with an intensity of 16 m/min and gradually reducing the intensity to the lowest value (See Table 1) [12].

Resistance training

First, the animals climbed a 36-step ladder without weights for 1 week and repeated three sessions to get familiar. Then the regular exercise protocol started with 5 days a week and 3 sets of 4 with 3 min rest between sets and 15 sec between repetitions for 10 weeks. In the second three weeks, the target animals were trained with a weight of 30% of their body weight and in the second three weeks with a weight of 70, 100 and 120% of their body weight and finally in the last week with a weight of 200% of their body weight (See **Table 2**) [13].

Combined exercise

The exercises of the combined diabetic group included resistance and endurance exercises in such a way that resistance and endurance exercises are performed with a frequency of 5 days a week and alternately 1 session of resistance exercise and 1 session of endurance exercise according to the protocols of resistance and endurance exercise.

Biochemical assays

72 h after the last training session, all rats were anesthetized with chloroform and samples were taken. After clotting, the blood samples were placed in a centrifuge and their serum was extracted at 3500 rpm for 10 min and kept at -70 C until the study variables were measured. Using the ELISA sandwich method, serum of FIns (Mercodia Rat Insulin ELISA Kit, Uppsala, Sweden), Ferritin (ELISA Kit, Eastbiopharm Company) and Fe (Selctra E auto laser device) was measured in the ELISA reader (BioTek-ELx808) according to the manufacturer's guidelines. The homeostasis model assessment of insulin resistance (HOMA-IR) and homeostasis model assessment of insulin secretion (HOMA-IS) were calculated based on the formula HOMA-IR= (FIns, μU/ml) × (FBG, mmol/L) /22.5 and HOMA-IS = (20 × FIns (μU/ml)) / (FBG (mmol/L) - 3.5).

Statistical analysis

The results were reported as mean ± SD for the studied variables in each group. The normality of the data was checked using the Shapiro-Wilk test, and the Levene's test was used to check the assumption of equality of variances. In order to statistically analyze the data and compare between groups, one-way ANOVA and Tukey's post hoc test with a significance level of $P<0.05$ was used. All statistical calculations were done using SPSS 22 statistical software.

RESULTS

Following the adverse changes in blood glucose and insulin levels in type 2 diabetic rats, we observed an increase in HOMA-IR and a decrease

Table 2. Resistance training protocol during 10 weeks on the treadmill

Week	1	2	3	4	5	6	7	8	9	10
Load (body weight/)	Familiarization	30	70	100	120	140	160	180	190	200

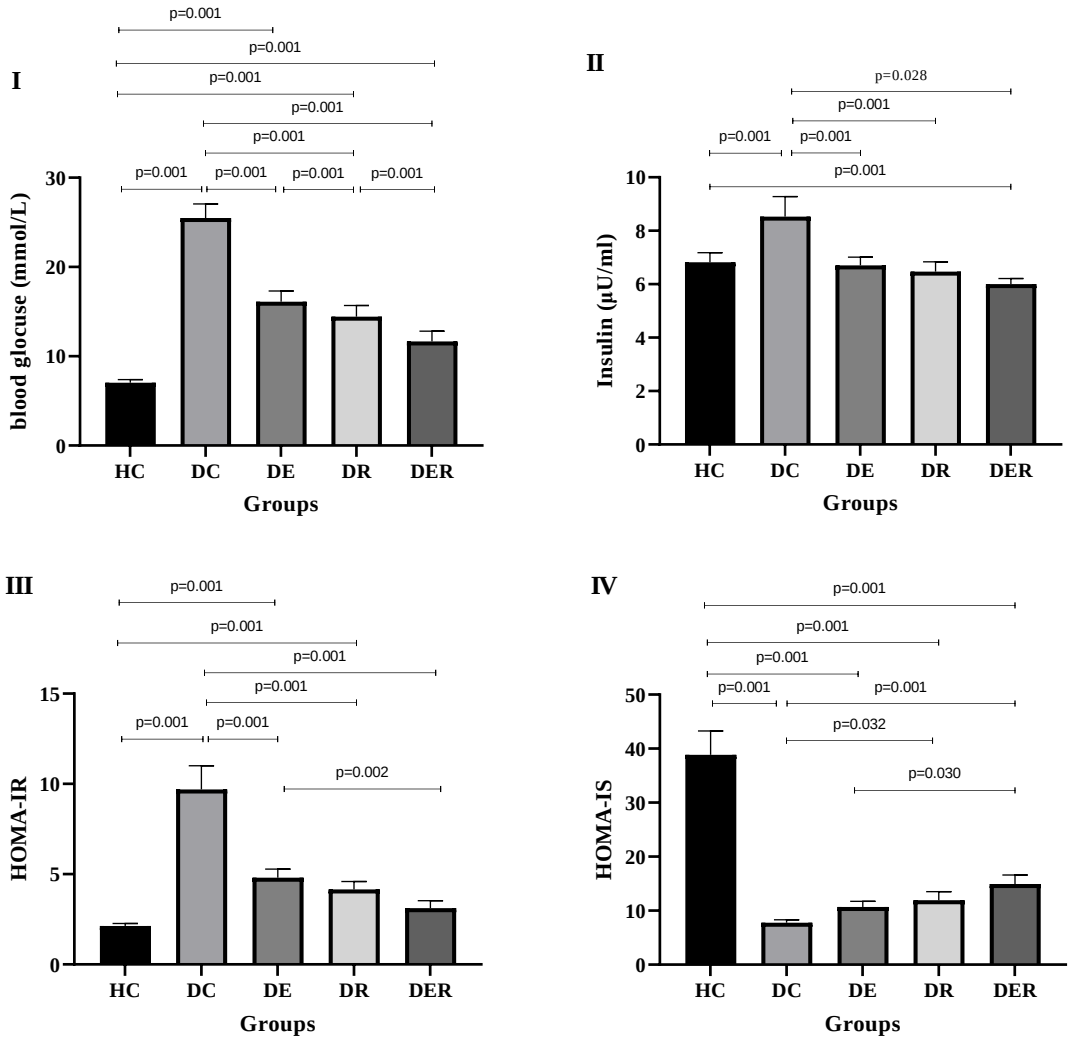

Fig 1. The simultaneous implementation of resistance and endurance exercises improved the glycemic indexes in type 2 diabetic rats. Changes of blood glucose (I), insulin (II), HOMA-IR (III), and HOMA-IS (IV) in diabetic rats following 10 weeks of resistance, endurance and combined exercises. The significance level was P<0.05. Abbreviations: healthy control (HC), diabetic control (DC), training groups underwent resistance (diabetic resistance group; DR), endurance (diabetic endurance group; DE) and combined activities (diabetic endurance and resistance group; DER).

in HOMA-IS. So that there is a significant difference between the studied groups in blood glucose ($F=202.504$, $p<0.001$), insulin ($F=28.655$, $p<0.001$), HOMA-IR ($F=110.472$, $p<0.001$) and HOMA-IS ($F= 178.344$, $p<0.001$) was observed. Comparison of groups showed that ten weeks of DE and DR groups was able to reduce blood glucose and insulin levels in DE and DR groups compared to DC group ($p<0.001$). The significant effect of combined exercise (DER group) in reducing blood glucose level was significant ($p<0.001$), but there was no difference between DER, DR and DE groups in reducing insulin level ($p\geq0.05$). In addition, HOMA-IR decreased in the exercise groups, so that the reduction of HOMA-IR in the DER group was not different from DR ($p\geq0.05$), but it was different from DE ($p=0.002$). No difference was observed

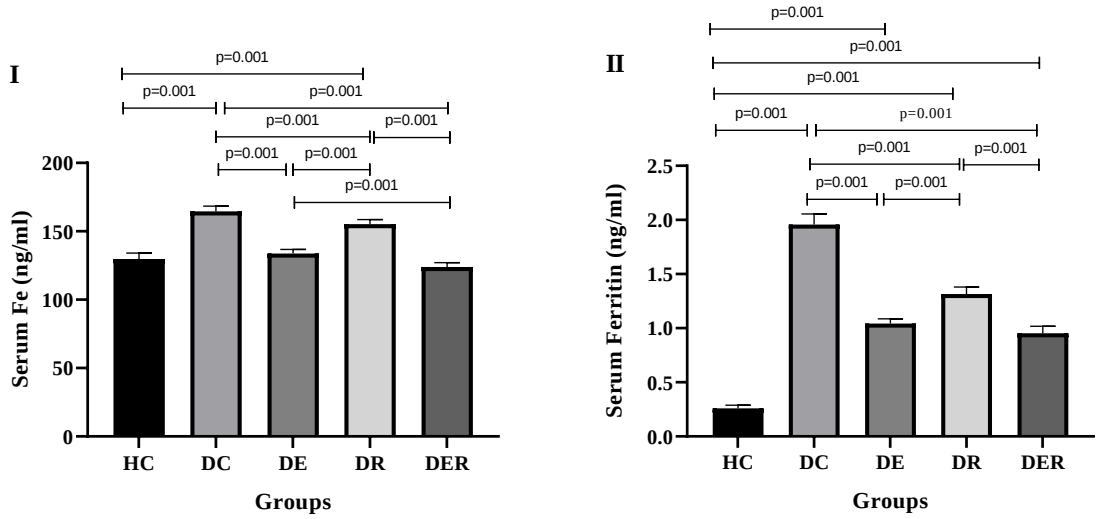

Fig 2. The simultaneous implementation of resistance and endurance exercises decreased serum iron (Fe) and ferritin levels in type 2 diabetic rats. Changes of Fe (I), and ferritin (II) in diabetic rats following 10 weeks of resistance, endurance and combined exercises. The significance level was P<0.05. Abbreviations: healthy control (HC), diabetic control (DC), training groups underwent resistance (diabetic resistance group; DR), endurance (diabetic endurance group; DE) and combined activities (diabetic endurance and resistance group; DER).

between DR and DE groups in reducing HOMA-IR ($p \geq 0.05$). Also, resistance and combined exercises increased HOMA-IS in the DR ($p=0.032$) and DER ($p<0.001$) groups compared to the DC group. No difference was observed between DER and DR groups ($p \geq 0.05$) (See Fig. 1).

Diabetes caused a significant change in serum Fe and ferritin levels in diabetic rats, so that a significant difference between groups was observed in Fe ($F=141.839$, $p<0.001$) and ferritin ($F=541.001$, $p<0.001$) levels. The comparison of the grooves showed that ten weeks of DR and DE groups decreased serum Fe, and DER groups had a significant reduction in Fe compared to DR and DE (See Fig. 2).

DISCUSSION

Our results showed that type 2 diabetes, in addition to adverse changes in glycemic indices, including increased levels of blood glucose, insulin, insulin resistance, and decreased insulin sensitivity, caused an increase in Fe and ferritin serum levels. Increased body Fe and oxidative stress play a role in the pathogenesis and increased risk of type 2 diabetes and other disorders. It has been found that Fe affects glucose metabolism even in the absence of Fe. Oxidative stress and inflammatory cytokines expand and strengthen these events [14]. Laboratory studies showed that Fe deficiency and excess cause mitochondrial damage by free radicals [15]. In addition, chronic inflammation with oxidative stress is another pathological factor for diabetes, which develops through the effects of pro-inflammatory cytokines such as c-reactive protein (CRP), interleukin-6 factor (IL-6) and TNF-a [16].

On the other hand, one of the mechanisms involved in the relationship between Fe and the increase in complications of diabetes is that the increase in Fe reserves may cause disruption of insulin secretion through oxidative damage of pancreatic beta cells, which, as a result, can increase glucose Serum, insulin increase and insulin resistance are related [17]. For unknown reasons, liver Fe overload is associated with increased serum ferritin, which is associated with increased insulin resistance syndrome [18]. It has been seen that in frequent blood donors who have less Fe reserves, hyperinsulinemia after meals is reduced, and this increases insulin sensitivity and creates preventive factors for diabetes [19]. In a study of women with high ferritin levels (greater than 107 ng/ml), the incidence of type 2 diabetes over 10 years was threefold independent of other risk factors, including body mass index, age, and race [20].

It has been proven that increased serum ferritin concentration is associated with insulin resistance and diabetes in the general population [21]. The level of serum ferritin is a direct indicator of the amount of stored Fe in the body. In general, a serum ferritin level of less than 12 μg/L indicates depletion of Fe reserves [22]. Although the mechanism of Fe -induced diabetes is not known in general, studies conducted on animal models consider 1) insulin deficiency, 2) insulin resistance, and 3) liver dysfunction as possible key mechanisms [23].

A small prospective study from Finland, 1481 people with blood samples collected before the diagnosis of diabetes showed a direct relationship between increased Fe stores, as the ratio of serum transferrin receptor concentration to serum ferritin concentration, and the prevalence of type 2 diabetes in men [5]. In a meta-analysis, they concluded that there is a direct relationship between elevated serum ferritin and increased risk of type 2 diabetes [24].

Another result of this study was the improvement of glycemic indices after ten weeks of endurance, resistance, and combined training. Following the favorable changes in glycemic indices, we saw a decrease in serum Fe and ferritin levels and combined training compared to resistance and aerobic training had a significant effect in reducing serum Fe. In general, regular exercise is known as an effective strategy in the management and treatment of type 2 diabetes [25]. One of the remarkable results of the effects of sports activities in diabetics is the effect on blood glucose collection. Exercise increases glucose uptake in body muscles, which changes are dependent on insulin signaling and increased protein content (GULT4) [26].

It has been reported that the trained muscle uses glucose 7-20 times more than the untrained muscle. Exercising and physical activity play an important role in fueling cell reserves and rebuilding them. It also reduces plasma insulin concentration and increases insulin sensitivity [27, 28]. Aerobic or resistance exercises alone improve blood glucose in diabetic patients, but the greatest effect of these exercises is when they are combined [29].

Since ferritin is classified in the acute phase protein class, it increases in response to inflammatory cytokines, and as a result, it may increase in response to oxidative stress caused by endurance exercise [30]. Endurance sports are often compared to the acute phase such as infections and inflammations [31]. Although many endurance athletes experience a decrease in ferritin levels, many factors cause the ferritin concentration to remain elevated for several days after exercise [32]. Also, IL-6 is an inflammatory cytokine that is secreted by fat tissue and reduces insulin sensitivity [33].

Sports activities can cause changes in inflammatory markers and ultimately improve insulin sensitivity [34]. High-intensity exercises also increase the inflammatory response. These exercises increase the process of ferritin synthesis, and damage to the cell membrane of ferritin-storing tissues such as the liver causes excessive ferritin to be released into the serum, and excess ferritin is most likely a mild form of exercise-induced hemolysis [35]. They have also shown that aerobic exercise causes a decrease in IL-6 levels [33].

Some other studies have reported IL-6 reduction in combined activities in diabetic patients more than aerobic or resistance exercises [36]. So there is a possibility that the exercise activities used in this study decreased the amount of ferritin and serum Fe in diabetic rats after 72 hours from the last training session by modulating factors such as inflammatory cytokines and oxidative stress. Also, in this regard, it is possible to mention intravascular hemolysis, which is responsible for the reduction of ferritin during exercise. During intravascular hemolysis, hemoglobin is released from the hemolysis cell and is released by the hemolysis haptoglobin, then it is transported to the liver by the haptoglobin, and the hemoglobin Fe is discharged from the Fe reserves through urine or sweat and finally, my ferritin goes down. In endurance athletes, the phenomenon of intravascular hemolysis is common because the concentration of haptoglobin is inversely related to the running distance or the time of sports performance.

This suggests the possibility of a close relationship between intravascular hemolysis and depletion of body Fe stores. Hemolysis occurs in the walls of blood vessels, the soles of the feet that are in contact with the ground, and even in the

heart valve, causing the destruction of old and fragile hemoglobins [37]. A lot of research has been done on the changes of Fe parameters in connection with exercise, but unfortunately, these parameters have received less attention in people with diabetes. It seems that long-term exercise sessions with moderate intensity can lower the serum ferritin and Fe levels of type 2 diabetic rats in a chronic state, and this decrease causes a decrease in insulin resistance.

CONCLUSION

The results of this study showed that induction of type 2 diabetes increased Fe and ferritin levels of diabetic ranks and decreased these variables for ten weeks of endurance, resistance and hybrid training. Compared to the types of exercise exercises in this study, combined exercises have had a significant impact on reducing Fe levels of diabetic ranks. Therefore, due to the use of the exercise, the researchers suggest the implementation of the combined training method. Finally, given the important role of Fe and ferritin in metabolic disorder as well as the beneficial effects of exercise exercises on diabetes, this requires further studies.

DECLARATIONS

none

COMPETING INTERESTS

The authors declare that they have no competing interests.

REFERENCES

[1] Forouhi N, Harding A, Allison M, Sandhu M, Welch A, Luben R, et al. Elevated serum ferritin levels predict new-onset type 2 diabetes: results from the EPIC-Norfolk prospective study. Diabetologia. 2007;50(5):949-56.

[2] Bae S, Le TD, Singh KP, Blair SN, Morrow JR, editors. Association between serum ferritin, cardiorespiratory fitness and risk of type 2 diabetes: aerobics center longitudinal study. 18th world IMACS. MODSIM Congress, Cairns, Australia; 2009: Citeseer.

[3] Gohel M, Sirajwala H, Chacko A. Serum free iron concentration in patients with type 2 diabetes mellitus with good and poor control and its correlation with glycemic control. Int J Diab Res. 2013;2(2):33-8.

[4] Galan P, Noisette N, Estaquio C, Czernichow S, Mennen L, Renversez J-C, et al. Serum ferritin, cardiovascular risk factors and ischaemic heart diseases: a prospective analysis in the SU. VI. MAX (SUpplementation en VItamines et Mineraux AntioXydants) cohort. Public Health Nutrition. 2006;9(1):70-4.

[5] Jiang R, Manson JE, Meigs JB, Ma J, Rifai N, Hu FB. Body iron stores in relation to risk of type 2 diabetes in apparently healthy women. Jama. 2004;291(6):711-7.

[6] Jehn ML, Guallar E, Clark JM, Couper D, Duncan BB, Ballantyne CM, et al. A prospective study of plasma ferritin level and incident diabetes: the Atherosclerosis Risk in Communities (ARIC) Study. American journal of epidemiology. 2007;165(9):1047-54.

[7] Rhee MK, Slocum W, Ziemer DC, Culler SD, Cook CB, El-Kebbi IM, et al. Patient adherence improves glycemic control. The Diabetes Educator. 2005;31(2):240-50.

[8] Brooks N, Layne JE, Gordon PL, Roubenoff R, Nelson ME, Castaneda-Sceppa C. Strength training improves muscle quality and insulin sensitivity in Hispanic older adults with type 2 diabetes. International journal of medical sciences. 2007;4(1):19.

[9] Radak Z, Chung HY, Goto S. Systemic adaptation to oxidative challenge induced by regular exercise. Free Radical Biology and Medicine. 2008;44(2):153-9.

[10] Tipton KD, Ferrando AA, Williams BD, Wolfe RR. Muscle protein metabolism in female swimmers after a combination of resistance and endurance exercise. Journal of Applied Physiology. 1996;81(5):2034-8.

[11] Punitha I, Rajendran K, Shirwaikar A, Shirwaikar A. Alcoholic stem extract of Coscinium fenestratum regulates carbohydrate metabolism and improves antioxidant status in streptozotocin–nicotinamide induced diabetic rats. Evidence-Based Complementary and Alternative Medicine. 2005;2(3):375-81.

[12] Afzalpour ME, Chadorneshin HT, Foadoddini M, Eivari HA. Comparing interval and continuous exercise training regimens on neurotrophic factors in rat brain. Physiology & behavior. 2015;147:78-83.

[13] Nadi Z, Abbasi Y, Jalali Mashayekhi F, Bayat M, Bayat P, Baazm M. Effect of Resistance and Endurance Trainings on Nrf2/Keap1 Signaling Pathway in Testicular Tissue of Type 2 Diabetic Rats. Journal of Mazandaran University of Medical Sciences. 2022;32(214):24-34.

[14] Barbieri M, Ragno E, Benvenuti E, Zito G, Corsi A, Ferrucci L, et al. New aspects of the insulin resistance syndrome: impact on haematological parameters. Diabetologia. 2001;44(10):1232-7.

[15] Srigiridhar K, Madhavan Nair K, Subramanian R, Singotamu L. Oral repletion of iron induces free

radical mediated alterations in the gastrointestinal tract of rat. Molecular and cellular biochemistry. 2001;219(1):91-8.
[16] Pickup JC. Inflammation and activated innate immunity in the pathogenesis of type 2 diabetes. Diabetes care. 2004;27(3):813-23.
[17] Gao W, Li X, Gao Z, Li H. Iron increases diabetes-induced kidney injury and oxidative stress in rats. Biological trace element research. 2014;160(3):368-75.
[18] Wrede CE, Buettner R, Bollheimer L, Scholmerich J, Palitzsch K, Hellerbrand C. Association between serum ferritin and the insulin resistance syndrome in a representative population. European journal of endocrinology. 2006;154(2):333-40.
[19] Ascherio A, Rimm EB, Giovannucci E, Willett WC, Stampfer MJ. Blood donations and risk of coronary heart disease in men. Circulation. 2001;103(1):52-7.
[20] Scholl TO. Iron status during pregnancy: setting the stage for mother and infant. The American journal of clinical nutrition. 2005;81(5):1218S-22S.
[21] Tuomainen T-P, Nyyssönen K, Salonen R, Tervahauta A, Korpela H, Lakka T, et al. Body iron stores are associated with serum insulin and blood glucose concentrations: population study in 1,013 eastern Finnish men. Diabetes care. 1997;20(3):426-8.
[22] Cook JD, Lipschitz DA, Miles LE, Finch CA. Serum ferritin as a measure of iron stores in normal subjects. The American journal of clinical nutrition. 1974;27(7):681-7.
[23] Raghavani PH, Sirajwala H. Serum ferritin level in patients with type-2 diabetes mellitus. Intern J Biomed Adv Res. 2014;5(6):272-4.
[24] Kunutsor SK, Apekey TA, Walley J, Kain K. Ferritin levels and risk of type 2 diabetes mellitus: an updated systematic review and meta-analysis of prospective evidence. Diabetes/metabolism research and reviews. 2013;29(4):308-18.
[25] Bassuk SS, Manson JE. Epidemiological evidence for the role of physical activity in reducing risk of type 2 diabetes and cardiovascular disease. Journal of applied physiology. 2005.
[26] Jorge MLMP, de Oliveira VN, Resende NM, Paraiso LF, Calixto A, Diniz ALD, et al. The effects of aerobic, resistance, and combined exercise on metabolic control, inflammatory markers, adipocytokines, and muscle insulin signaling in patients with type 2 diabetes mellitus. Metabolism. 2011;60(9):1244-52.
[27] Chen S-R, Lee Y-J, Chiu H-W, Jeng C. Impact of glycemic control, disease duration, and exercise on heart rate variability in children with type 1 diabetes mellitus. Journal of the Formosan Medical Association. 2007;106(11):935-42.
[28] Davison GW, George L, Jackson SK, Young IS, Davies B, Bailey DM, et al. Exercise, free radicals, and lipid peroxidation in type 1 diabetes mellitus. Free Radical Biology and Medicine. 2002;33(11):1543-51.
[29] Sigal RJ, Kenny GP, Boulé NG, Wells GA, Prud'homme D, Fortier M, et al. Effects of aerobic training, resistance training, or both on glycemic control in type 2 diabetes: a randomized trial. Annals of internal medicine. 2007;147(6):357-69.
[30] Arosio P, Levi S. Ferritin, iron homeostasis, and oxidative damage. Free Radical Biology and Medicine. 2002;33(4):457-63.
[31] Fallon KE. The acute phase response and exercise: the ultramarathon as prototype exercise. Clinical Journal of Sport Medicine. 2001;11(1):38-43.
[32] Fallon K, Sivyer G, Sivyer K, Dare A. Changes in haematological parameters and iron metabolism associated with a 1600 kilometre ultramarathon. British Journal of Sports Medicine. 1999;33(1):27-31.
[33] Lindstrom J, Louheranta A, Mannelin M, Rastas M, Salminen V, Eriksson J, et al. The Finnish Diabetes Prevention Study (DPS) Lifestyle intervention and 3-year results on diet and physical activity. Diabetes care. 2003;26(12):3230-6.
[34] McGarry JD. Banting lecture 2001: dysregulation of fatty acid metabolism in the etiology of type 2 diabetes. Diabetes. 2002;51(1):7-18.
[35] Pattini A, Schena F, Guidi G. Serum ferritin and serum iron changes after cross-country and roller ski endurance races. European journal of applied physiology and occupational physiology. 1990;61(1):55-60.
[36] Balducci S, Zanuso S, Nicolucci A, Fernando F, Cavallo S, Cardelli P, et al. Anti-inflammatory effect of exercise training in subjects with type 2 diabetes and the metabolic syndrome is dependent on exercise modalities and independent of weight loss. Nutrition, Metabolism and Cardiovascular Diseases. 2010;20(8):608-17.
[37] Hegenauer J, Strause L, Saltman P, Dann D, White J, Green R. Transitory hematologic effects of moderate exercise are not influenced by iron supplementation. European journal of applied physiology and occupational physiology. 1983;52(1):57-61.