

The Effect of Regular Physical Activities on the Visceral Fat in Diabetic Patients in Iran- Review

Amene Barjaste Yazdi¹, Hassan Matin Homae^{2*}, Maghsoud Peeri³

1. PhD Candidate Department of Exercise physiology, Islamic Azad University Central Tehran Branch, Tehran, Iran.
2. Associate Professor Department of Exercise physiology, Islamic Azad University Central Tehran Branch, Tehran, Iran.
3. Professor Department of Exercise physiology, Islamic Azad University Central Tehran Branch, Tehran, Iran.

*Correspondence:

Hassan Matin Homae, Associate Professor Department of Exercise physiology, Islamic Azad University Central Tehran Branch, Tehran, Iran.
 Tel: (98) 218 807 4871
 Email: hasanmatinhomae@gmail.com

Received: 12 October 2017

Accepted: 07 January 2018

Published in February 2018

Abstract

Objective: The growing prevalence of diabetes makes this disease a health threatening issue. Regular physical activity is a solution in prevention and treatment of diabetes. Therefore, the aim of the present study was to review the effect of exercise trainings on visceral fat tissue in type 2 diabetes patients, based on the studies performed in Iran.

Materials and Methods: The present study is a review concerning the effects of physical training on visceral fat in diabetic patients. The search was performed on SID (Scientific Information Database), Irandoc and Magiran. After the appraisal of the articles, 8 studies carried out between 2005 and 2016 in Iran were included.

Results: A review of the studies indicated that participation in regular physical activities improves blood glucose control. It is effective in secretion and gene expression of adipokines in visceral fat tissues. Moreover, it is able to prevent or delay the onset of type 2 diabetes.

Conclusion: Physical activity has a fundamental role in prevention and control of insulin resistance, pre-diabetic circumstances, type 2 diabetes and its health related complications. Both aerobic and resistance exercises improve the action of insulin and the secretion of adipocytokines of the visceral fat tissue.

Keywords: Diabetes, Visceral fat, Adipokine, Physical activity

Introduction

Obesity and its complications, particularly insulin resistance and diabetes, has become a worldwide epidemic. Obesity is accompanied by an increase in insulin resistance and hyperglycemia and induces several basic and generalized complications in all physiological systems. Ordinarily, adipocytes in both subcutaneous and visceral depots become hypertrophic under these circumstances and

their secretory pattern alters. There is evidence suggesting that the adipose tissue plays an important role in insulin resistance by irregular production and secretion of a number of messenger molecules including the tumor necrosis factor alpha (TNF- α), RBP4, leptin, adiponectin, visfatin, coumarin, omentin-1 and resistin (1). In the past, it was believed that the adipose tissue does not induce any effects and merely stores triglycerides, however, today, it

has been established that the adipose tissue secretes a number of biologically active proteins, known in general as adipokines and through these adipokines, it has a part in energy homeostasis (e.g: adipokine, leptin, omentin-1) and systemic inflammation (e.g: TNF- α), which seem to play key roles in metabolic diseases. (2) Recent evidence suggest that the development of visceral fat is accompanied by a chronic inflammatory condition that is measurable by the level of inflammatory indicators interleukin 6 (IL-6), TNF- α and C-reactive protein (CRP) (3). In fact, chronic inflammation in obese patients in the most important factor relating an increase in adipose tissue mass and insulin resistance since the chemical mediators secreted by adipose tissue, IL-6 and TNF- α , are also significant mediators in the induction of insulin resistance in obese patients (4). Moreover, it has been established that the absorption of macrophages from the circulation by adipose tissue in the most important cause in producing inflammatory processes and the main source of inflammatory factors synthesis in obese patients. It is of note that the macrophages in the visceral adipose tissue have more inclination for diffusion and thus the role of visceral adipose tissue in the pathogenesis of diabetes and its related diseases is quite significant. Regular physical activity along with diet and medications are the basis of managing type 2 diabetes. As a result, international guidelines recommend regular physical activities as 3 or 5 sessions a week for type 2 diabetic patients (5). Regular physical activity reduced mortality rates in diabetic patients and prevents cardiovascular diseases. Although the effectiveness of physical activity in controlling and managing type 2 diabetes has been established, studies show that diabetic patients tend to have less physical activity compared to others (6). Exercise programs and development of daily physical activity have gained much attention due to being inexpensive and lacking the side effects of medications. Thus, physical activities based

on a regular and specific pattern should be a part of the general strategy of treating type 2 diabetic patients (7). Results of recent studies have presented beneficial effects of physical activity including aerobic or resistance exercises in the treatment of type 2 diabetic patients. Physical activity causes an increase in the number of glucose carriers (GLUT-4) that leads to a decrease in fasting blood sugar and thus a decrease in insulin resistance (8). In addition, physical activity plays a fundamental role in controlling inflammation-related diseases, such as diabetes, by decreasing visceral adipose tissue mass and as a result, decreasing the release of inflammatory cytokines and producing an anti-inflammatory environment (9). Indeed, aerobic exercises alter the effect of insulin on each muscle fiber without increasing the size of the fibers whereas resistance exercises preferably improve glucose absorption by increasing each muscle fiber. Aerobic exercises induce weight loss, improved lipid profile, body fat rate, improved glycemic control, decreased insulin resistance and modulated inflammatory indicators and in total, leads to improved insulin sensitivity (10). A revision of literature on this subject reveals that the atrophy in visceral adipocytes and the alteration in their secretory pattern after regular physical activity, especially aerobic exercises, is one of the main mechanisms in the prevention and treatment of diabetes. Considering that the abundance and prevalence of diabetes in Iran is very high, we have tried to collect and analyze the results of studies by Iranian researchers on the effects of physical activity on visceral adiposity in diabetic conditions in this systematic review.

Materials and Methods

The present study is a review on the studies conducted in order to assess the effects of physical activity on visceral fat in type 2 diabetic patients. The results of this study are based on the articles published in national journals and theses from 2005 to 2016. The articles were selected from information banks

of SID (Scientific Information Database), Irandoc and Magiran. In addition, the resource index of the selected articles was reviewed in order to collect more studies. Totally 145 articles were studied and, 28 were excluded due to duplication and 101 were not relevant. Ultimately, 8 articles were included in the main research process (picture-1). Searching the articles was performed using the Farsi keywords for “diabetes”, “physical activity”, “adypokines”, “visceral adiposity”, “review article” and their combinations.

Beneficial effects of physical activity in diabetes

Various disorders occur in most tissues in diabetic conditions; in the same way, physical activities can reduce the intensity of these disorders. Therefore, considering the metabolic effects of physical activity, it seems

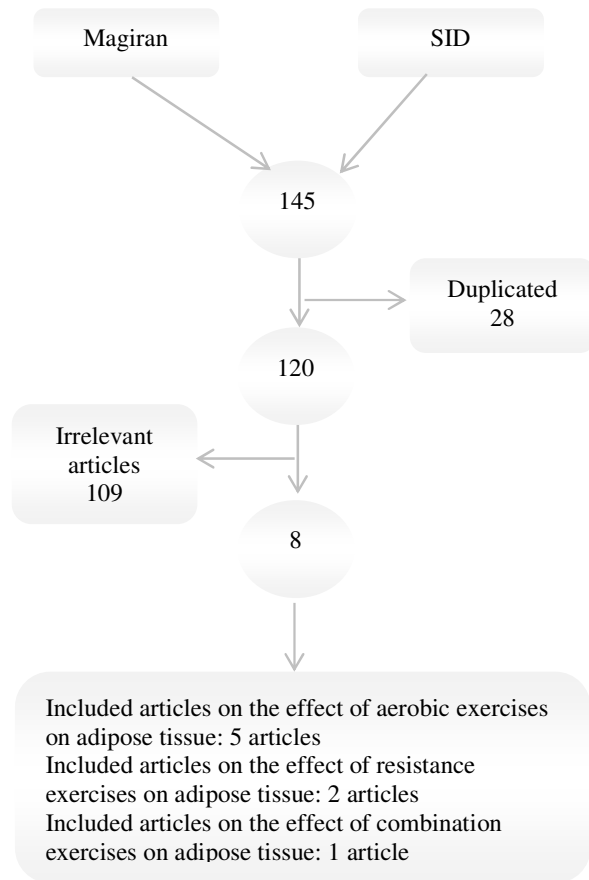


Figure 1. The flow diagram of articles selection

that regular physical exercise is one of the effective factors in type 2 diabetes and its management (11). Evidence suggests that physical activity is an efficacious treatment for prevention and management of type 2 diabetes. A 60 percent reduction in the development risk of diabetes has been reported in patients with insulin resistance after regular physical exercises. There is a strong correlation between aerobic fitness and improvement in glycemic control and insulin sensitivity. These effects are modulated through alterations in visceral fat by the secretion of adipocytokines. These adipocytokines are not only influential in controlling the balance of body weight, but also they justify the relation of obesity, insulin resistance and diabetes by their effect on metabolic, inflammatory and lipid profiles (12). Regarding the manner of glucose uptake by skeletal muscle cellules, research evidence has been concentrated on two cellular pathways. When recovering from physical activities, the uptake of glucose by the muscle is dependent on insulin and its main role is to restore muscular glycogen resources. During the activity, molecular mechanisms as a result of muscular contractions increase the uptake glucose from the circulation in order to provide for the growing craving in the muscle for glucose, independent of insulin action mechanism. Since the mechanism of glucose uptake through muscular contraction is independent of molecular path of insulin receptor, muscular absorption of glucose occurs naturally during activity in type 2 diabetic patients whose insulin-dependent absorption of glucose has become dysfunctional. This phenomenon is an important mechanism in modulating blood glucose in insulin resistance conditions. Muscular glucose absorption remains in higher levels even after stopping the exercise compared to the resting time before the activity. The reason for this phenomenon is the increased coupling tendency of insulin receptors to insulin and reinforcement of signaling pathways after the insulin receptor in

skeletal muscle (13). There is evidence suggesting that the concentration and circulation of GLUT-4 increases with physical activity, specifically with aerobic exercises. Furthermore, in trained muscles, GLUT-4 transporting mechanisms such as the activation of AMP-activated protein kinase, adenosine, Calcium ion and nitric oxide leads to the transportation of GLUT-4 from depth to the surface of the cellule. Generally, this transportation of GLUT-4 from depth to the surface of the cellule, which is stimulated by insulin, is dysfunctional in type 2 diabetic patients and does not occur normally. Both aerobic and resistance exercises increase the amount of GLUT-4 and glucose absorption, even in type 2 diabetic patients (14).

Analysis of available studies concerning the effect of resistance physical exercises on the secretory characteristics of visceral fat in diabetic conditions

The modulating effects of regular physical activities, specifically resistance exercises, on the immune system may have positive influences on the innate immune system and thus induce other benefits other than improvement of strength and functional capacity (15). The higher glucose uptake and hypertrophy as a result of muscular contractions, show physical activities as a treatment method in managing many chronic diseases and it has been indicated that these exercises are effective and safe for the elderly and the obese. Suitable resistance exercises such as aerobics, lead to higher insulin sensitivity, increase in energy consumption and improvement of life quality. In addition, resistance exercises can decrease the base levels of cytokines in long term (16). Cytokines such as IL-6 and TNF- α are able to alter insulin sensitivity by influencing different phases of insulin signaling pathways (17). Some researchers believe physical activity with high-energy consumption to play a vital role in regulation, production and secretion of adipokines secreted from visceral adipose tissue (resistin and coumarin). Studies show a

decrease in resistin after regular exercises in obese and diabetic patients. It has been reported that 8 weeks of circular resistance training induces a significant reduction in plasma concentrations of resistin, blood insulin, blood glucose, glycated hemoglobin and insulin resistance in male type 2 diabetic patients (18). Even in some studies, it was reported that 3 months of strength training without a diet can lead to the reduction of metabolic syndrome symptoms (including total cholesterol, triglyceride, glucose and insulin resistance index) and this improvement is accompanied by lower levels of coumarin and CRP. On one hand, these changes as a result of training were coincident with a decrease in abdominal fat mass (especially visceral fat). This finding shows that when physical activity or diet leads to a decrease in abdominal fat mass (especially visceral fat), it reduces the risk factors of metabolic diseases (19). On this matter, it could be stated that coumarin is effective on fat cellular differentiation stimulation of lipolysis (20). This adipokine facilitates the uptake of insulin-stimulated glucose and apparently coumarin has a role in insulin sensitivity and could be considered as a therapeutic target in diabetes, especially type 2 diabetes (21). As a conclusion, it seems that resistance exercises with their beneficial effects specifically increasing muscular mass and decreasing the expression of visceral adiposity-secreted resistin and coumarin genes could lead to improvement of insulin sensitivity in active tissues. On the other hand, the increase in muscular mass could lead to a higher basic metabolism rate and thus higher consumption of body fat and as a result, weight loss (22).

Analysis of available studies concerning the effect of aerobic physical exercises on the secretory characteristics of visceral fat in diabetic conditions

An effective exercise program requires a combination of intensity, duration, number of sessions and exercise type in order to impose extra weight on different body organs and

induce adaptation. Regular aerobic exercises lead to physiological adaptations such as increased oxidation enzymes, reduced adipose tissue, decreased inflammatory agents, increased anabolic hormones, higher capillary density, increased number of mitochondria, elevated maximum consumed oxygen and competence of the cardiovascular system (23). Many epidemiological studies have indicated that visceral obesity imposes a greater risk for obesity-related diseases, such as insulin resistance, type 2 diabetes, cardiovascular diseases and dyslipidemia compared to peripheral obesity (24). In principle, blood lipid disorders and increased adipose tissue in a central accumulation pattern are observed in diabetic patients (25). Increased plasma level of RBP4 (visceral adiposity adipokine) has been established as an effective factor in development and emergence of disorders in glucose tolerance and its consequent diabetes in both humans and animals (16). Studies have shown that after 8 weeks of alternative aerobic exercises, the level of serum RBP4 is reduced by 28 percent in diabetic patients. In addition, alterations of RBP4 are accompanied by changes in serum TG and this decrease leads to the improvement of insulin resistance (26). Furthermore, after 7 weeks of aerobic exercises in diabetic mice, significant decrease of RBP4 in EDL muscle, visceral and subcutaneous fat has been reported as well as a significant reduction in weight and central obesity. Moreover, endurance exercises reduce the expression of RBP4 in visceral and subcutaneous adiposity (27). 8 weeks of aerobic exercises result in elevated concentrations of serum omentin-1 and improvement of lipid profile in obese and overweight participants. However, the improved insulin sensitivity as a result of weight loss is the probable cause of increased omentin-1 (28). In another study, it was indicated that 8 weeks of rhythmical aerobic exercises could be effective in the reduction of plasma visfatin in obese women by the decrease in body fat mass, waist and hip circumference, weight loss and improvement

of lipid profile including the decrease in LDL, triglyceride, cholesterol, and the increase in HDL (29). Researchers also observed the reduction of plasma visfatin in obese women after 9 weeks of aerobic exercises and attributed this change to weight loss and reduction in abdominal fat due to exercise. Alteration in the production of inflammatory factors by the adipose tissue (specifically abdominal) might play an important role in insulin resistance and metabolic disorders related to obesity (30). Regular aerobic exercises could have an essential role in reducing the risk of cardiovascular diseases and improvement of glucose metabolism process in diabetic patients because of decreasing insulin resistance and increasing glucose metabolism on one hand, and reducing RBP4 and visfatin rates and elevating visceral fat omentin and thus increasing insulin sensitivity on the other.

Analysis of available studies concerning the effect of combination physical exercises on the secretory characteristics of visceral fat in diabetic conditions

In recent years, weight loss and increased physical activity have been proposed as solutions to control diabetes and insulin resistance (31). Based on the guidelines today, type 2 diabetic patients must take aerobic exercises for at least 150 minutes with medium intensity per week, and undergo resistance exercises 3 times weekly (32). American Diabetes Association and American College of Sports Medicine have confirmed that the rehabilitation program for diabetic patients should be a combination of aerobic and resistance exercises in order to produce the beneficial effects of both exercise types (33). Long aerobic activity along with resistance activities are more effective in reducing inflammatory indicators that each activity performed separately (34), and are known as the more effective type of activity in controlling blood glucose, insulin activity and risk factor improvement in cardiovascular disorders (35), and are more effective in

improving insulin resistance than aerobic or resistance exercises separately (36). In one study, a significant reduction was observed in insulin resistance index and fasting blood sugar in type 2 diabetic patients after 8 weeks of aerobic and combination (aerobic-resistance) exercises, and it was concluded that 8 weeks of aerobic or combination exercises could be beneficial for type 2 diabetic patients by improving insulin resistance and fasting blood glucose (37). The combination of aerobic and resistance exercises is identified as the more effective type of activity in controlling glucose and insulin activity (33). Regular aerobic and resistance physical activities are helpful factors with the same power in controlling the metabolic side effects of type 2 diabetes (38).

Conclusions

Physical activities are able to reduce cytokine levels in circulation directly by decreasing the production of inflammatory cytokines in the adipose tissue, muscle and mononuclear cells, and indirectly by increasing insulin sensitivity and improving endothelial function. Physical activity plays a key role in prevention and control of insulin resistance, pre-diabetic conditions, pregnancy diabetes, type 2 diabetes and health issues related to diabetes. Both aerobic and resistance exercises improve insulin function and secretion of adipocytokines secreted from visceral adipose tissue and are effective in the management of blood glucose, blood lipids, hypertension, cardiovascular mortality risk and quality of life. It must be noted that in order to benefit from these effects, exercises should be performed regularly and consistently.

References

1. Spiegelman BM, Flier JS. Adipogenesis and obesity: rounding out the big picture. *Cell* 1996;87:377-89.
2. Maury E, Brichard SM. Adipokine dysregulation, adipose tissue inflammation and metabolic syndrome. *Mol Cell Endocrinol* 2010;314:1-16.
3. Nakayama Y, Komuro R, Yamamoto A, Miyata Y, Tanaka M, Matsuda M, et al. Rho A induces expression of inflammatory cytokine in adipocytes. *Biochem Biophys Res Commun* 2009;379:288-92.
4. Bastard JP, Maachi M, Lagathu C, Kim MJ, Caron M, Vidal H, et al. Recent advances in the relationship between obesity, inflammation, and insulin resistance. *Eur Cytokine Netw* 2006;17:4-12.
5. Kirk A, Barnett J, Leese G, Mutrie N. A randomized trial investigating the 12-month changes in physical activity and health outcomes following a physical activity consultation delivered by a person or in written form in Type 2 diabetes: Time2Act. *Diabet Med* 2009;26(3):293-301.
6. Kahn EB, Ramsey LT, Brownson RC, Heath GW, Howze EH, Powell KE, et al. The effectiveness of interventions to increase physical activity. A systematic review. *Am J Prev Med* 2002;22(4):73-107.
7. Zanuso S, Jimenez A, Pugliese G, Corigliano G, Balducci S. Exercise for the management of type 2 diabetes: a review of the evidence. *Acta Diabetol* 2010;47(1):15-22.
8. Kern M, Wells A, Stephens J, Ehon CW, Friedman JE, Tapscott EB, et al. Insulin responsiveness in skeletal muscle is determined by glucose transporter (GLUT4) protein level. *Biochem J* 1990;270(2):397-400.
9. Gleeson M, Bishop NC, Stensel DJ, Lindley MR, Mastana SS, Nimmo MA. The anti-inflammatory effects of exercise: mechanisms and implications for the prevention and treatment of disease. *Nat Rev Immunol* 2011;11:607-15.
10. Oberbach A, Lehmann S, Kirsch K, Krist J, Sonnabend M, Linke A, et al. Long-term exercise training decreases interleukin-6 (IL-6) serum levels in subjects with impaired glucose tolerance: effect of the K174G/C variant in IL-6 gene. *Eur J Endocrinol* 2008;159(2):129-36.
11. Poirier P, Tremblay A, Broderick T, Catellier C, Tancrède G, Nadeau A. Impact of moderate aerobic exercise training on insulin sensitivity in type 2 diabetic men treated with oral hypoglycemic agents: is insulin sensitivity enhanced only in nonobese subjects? *Med Sci Monit*. 2002 Feb;8(2):59-65.
12. Trayhurn P, Wood IS. Adipokines: inflammation and the pleiotropic role of white adipose tissue. *Br J Nutr* 2004;92(3):347-55.
13. Goodyear LJ, Kahn BB. Exercise, glucose transport, and insulin sensitivity. *Annu Rev Med*. 1998;49:235-61.

14. Frosig C, Richter E. Improved insulin sensitivity after exercise: focus on insulin signaling. *Obesity* 2009;17:15-20.
15. Li ZZ, Liu JB, Li L, Jiao L, Chen L. Intensive therapy for diabetes through influence on innate immune system. *Med Hypotheses* 2009;72:675-6.
16. Fontana L, Eagon JC, Trujillo ME, Scherer PE, Klein S. Visceral fat adipokine secretion is associated with systemic inflammation in obese humans. *Diabetes* 2007;56:1010-3.
17. Hotamisligil GS. Inflammation and metabolic disorders. *Nature* 2006; 444: 860-7.
18. AfshounPour MT, Davoodi Z, Habibi A, Ranjbar R, Shakerian S. The effect of circuit resistance exercise on plasma resistin concentration and insulin resistance in type 2 diabetic men. *J Shahid Sadoughi Univ Med Sci* 2015;23(8):770-81.
19. Saremi A, Moslehabadi M, Parastesh M. Effects of Twelve-week Strength Training on Serum Chemerin, TNF- α and CRP Level in Subjects with the Metabolic Syndrome. *Iranian Journal of Endocrinology and Metabolism* 2011;12(5).
20. Bozaoglu K, Bolton K, McMillan J. Chemerin is a novel adipokine associated with obesity and metabolic syndrome. *Endocrinology* 2007;148:4687-94.
21. Goralski KB, McCarthy TC, Hanniman EA. Chemerin, a novel adipokine that regulates adipogenesis and adipocyte metabolism. *J Biol Chem* 2007;282:28175-88.
22. Winnick JJ, Gaillard T, Schuster DP. Resistance training differentially affects weight loss and glucose metabolism of white and African American patients with type 2 diabetes mellitus. *Ethn Dis* 2008;18:152-6.
23. Kriketos AD, Gan SK, Poynten AM, Furler SM, Chisholm DJ, Campbell LV. Exercise increase adiponectin levels and insulin sensitivity in humans. *Diabet Care* 2007;27:629-30.
24. Bee KT, Raghunad S, Farhatullah Kris C, Paul OH, Hendrik L, Harpal S. Omentin-1, a novel adipokine, is decreased in overweight insulin resistant women with polycystic ovary syndrome. *Diabetes* 2008;57:801-8.
25. Sam S, Haffner S, Davidson MH, Dagostino RB, Feinstein S, Kondos G, et al. Relationship of abdominal visceral and subcutaneous adipose tissue with lipoprotein particle number and size in type 2 diabetes. *Diabetes* 2008;57:2022-7.
26. Soory R, Hassani Ranjbar SH, Vahabi K, Shabkhiz F. Effect of aerobic exercise on serum RBP4 and insulin resistance index in patients with type 2 diabetes. *Iranian journal of Diabetes and Lipid* 2011;10(4): 388-397.
27. Aveseh M, Nikooie R, Atabi F, Mirzaie zadeh Z, Omidfar K, Larijani B. The effect of seven weeks endurance training on RBP4 gene expression in skeletal muscle in type 2 diabetic rats. *Iranian journal of Diabetes and Metabolism* 2014;13(2).
28. Namazi zadeh M, Fathollahy Shorabe F, Jalaly Dehkordi KH, Sheikh Saraf B. The effect of aerobic training on the changes Omentin-1, insulin resistance, CRP and lipid profile in overweight and obese older women. *Journal of Sports Medicine and Physical Fitness* 2013;1:1-20.
29. Faramarzi M, Azimian Jazi A, Bagheri Harouee N. Effect of rhythmic aerobic exercise on resting levels of visfatin and metabolic risk factors in overweight women. *Sporting Life Sciences* 2011;11:23-38.
30. Haghghi A, Yarahmadi H, shojaei M. Effect of 9 weeks of aerobic training on serum visfatin level and insulin resistance index in obese women. *Quarterly Journal of Sabzevar University of Medical Sciences* 2014;20(5).
31. Dubnov G, Brzezinski A, Berry EM. Weight control and the management of obesity after menopause: the role of physical activity. *The Maturitas* 2003;44:89-101.
32. Umpierre D, Schaan B, Ribeiro P, Kramer C, Leitao C, Gross J, et al. Physical activity advise only or structured exercise training and association with HbA1C levels in type 2 diabetes: A systematic review and meta-analysis. *JAMA* 2011;305(17):1790-9.
34. Tokmakidis SP, Zois CE, Volaklis KA, Kotsa K, Touvra AM. The effects of a combined strength and aerobic exercise program on glucose control and insulin action in women with type 2 diabetes. *Eur J Appl Physiol* 2004;92(4-5):437-42.
35. Hopps E, Canino B, Caimi G. Effects of exercise on inflammation markers in type 2 diabetic subjects. *Acta Diabetol* 2011;48(3):183-9.
36. Sigal R, Kenny GP, Wassermann DH, Castaneda-Sceppa C, White RD. Physical activity/exercise and type 2 diabetes: a consensus statement from the American Diabetes Association. *Diabetes Care* 2006;29(6):1433-8.
37. Sigal RJ, Kenny GP. Combined aerobic and resistance exercise for patients with type 2 diabetes. *JAMA* 2010;304(20):2298-9.
38. Yousefipoor P, Tadibi V, Behpoor N, Parnow A, Delbari M, Rashidi S. The effect of 8-week aerobic and concurrent (aerobic- resistance) exercise training on serum il-6 levels and insulin resistance in type 2 diabetic patients. *J Shahid Sadoughi Univ Med Sci* 2013;21(5):619-31.
39. Castaneda C, Layne JE, Munoz-Orians L, Gordon PL, Walsmith J, Foldvari M, et al. A randomized controlled trial of resistance exercise training to improve glycemic control in older adults with type 2 diabetes. *Diabetes care* 2002;25(12):23.11-51.