Bulletin of Environment, Pharmacology and Life Sciences
Bull. Env. Pharmacol. Life Sci., Vol 3 [10] September 2014: 14-20

Online ISSN 2277-1808
Journal's URL:http://www.bepls.com
CODEN: BEPLAD
Global Impact Factor 0.533
Universal Impact Factor 0.9804

ORIGINAL ARTICLE

Effects of regular swimming on WBC profile, inflammatory mediators and histopathology of pancreatic tissue of high fat-induced diabetes in adult male rats

Rafigheh Ghiasi[1], Farhad Ghadiri Soufi[2], Gisou Mohaddes[3], Mohammad H Somi[1], Hadi Ebrahimi[3],Alireza Alihemmati[4], Fariba Mirzaie Bavil[5], ,Mohammad R Alipour[1]*

[1]Liver and Gastrointestinal Diseases Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.
[2]Research Center for Molecular Medicine, Hormozgan University of Medical Sciences, Bandar-Abbas, Iran.
[3]Neurosciences Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.
[4]Histology & Embryology Department.Medicine Faculty.Tabriz University of Medical Sciences, Tabriz, Iran.
[5]Department of Physiology,Tabriz University of Medical Sciences, Tabriz, Iran

ABSTRACT

As some complications of Type 2 diabetes mellitus (T2DM) are aggravated by low-grade inflammation, and stimulation of the innate immune system, the effects of swim training on WBC profile, inflammatory mediators, and histopathology of pancreatic tissue were investigated in high fat-induced type 2 diabetes. Forty male Wistar rats were randomly divided into four groups (n=10]: sedentary control (Con), sedentary diabetic (Dia), swim trained (Exe), and swim trained diabetic (Dia-Exe). Diabetes was induced by high fat diet (HFD) and a low dose of intraperitoneal streptozotocin (35 mg/kg).In trained groups, one week after induction of diabetes, animals were subjected to swimming (60 min/5 days a week) for 10 weeks. At the end of the training blood samples and pancreatic tissues were collected and used for evaluation of WBC profile, inflammatory mediators in blood and pancreatic histopathololgy. Our findings showed that the WBC, blood lymphocytes, and monocytes significantly (p<0.01) increased in diabetic rats. Whereas the percentage of neutrophils significantly (P<0.01) decreased by induction of diabetes. Swimming significantly (P<0.01) reversed changes in the WBC, lymphocytes, monocytes, and neutrophils count.Serum levels of CRP and IL-6 also increased (P<0.01) in diabetes and swimming decreased these parameters significantly. Induction of diabetes induced a pancreatic damage and swimming alleviated the damage. The present study indicated that the 10-week fifth-weekly swim training was associated with improved WBC profile, IL-6 and CRP levels. Moreover swimming reduced pancreatic damage in T2DM animals

Keywords: *Diabetes; swim training; inflammatory mediators; pancreatic histopathology*

Received 12.05.2014 Revised 29.06.2014 Accepted 21.08. 2014

INTRODUCTION

Type 2 diabetes mellitus (T2DM)is seenaround 80- 90% of diabetes cases. T2DM has several complications such as cardiovascular disease, kidney failure, as well as the premature death([1]. T2DM is a complex heterogeneous group of metabolic conditions characterized by increased levels of blood glucose[2, 3].Obesity, the important regulating risk factor for T2DM, is known to be greatly related to insulin resistance. Obesity, as a result of low physical activity in combination with unhealthy dietary habits such as high fat diets, has an important role in development of pancreatic beta-cell dysfunction and insulin resistance [4-6].Exactly why and how obesity causes insulin resistance is not completely understood.However, the genetic factors and cellular processes are known to be responsible for this phenomenon [1, 7].There is a probability that high fat diet, obesity, and the inflammation of adipose tissue increase the release of inflammatory factors and development of insulin resistance, impaired glucose tolerance and even diabetes [8-10]. Activated adipocytes release many abnormal molecules such as lipids, fatty acids, and inflammatory cytokines such as TNF-α, IL-6, and CRP [11]. Therefore, cytokine levels in obese people are higher than healthy lean people [8, 9]. Release of these cytokines and mediators in long-term results in the recruitment of monocytes to adipose tissue[11].TNF-α, IL-6, and other

mediators produced by macrophages also play an important role in the inflammatory cascade, systemic insulin resistance, and decreased insulin secretion by the beta cells [12, 13]. In addition, activated polymorph nuclear leukocytes, as the main inflammatory cells, release many mediators and lead to the subsequent inflammation [14-17]. Moreover it is known that IL -6 and TNF-α regulate C-reactive protein (CRP) secretion from the liver [18].Altogether enhanced levels of IL-6 and TNF-α impairs glycaemic control in type 2 diabetic individuals [19-21].

Studies have also demonstrated that high fat diet leads to pancreatic histological damages. The exact mechanisms of pancreatic damages at cellular and molecular levels are not completely understood; however immigrated inflammatory cells and cytokines secreted from them, as well as reactive oxygen products, have possibly important role in this phenomenon [22].

The beneficial effect of physical activity on T2DM control and alleviation of its complication can be related to reduction of inflammatory markers [23-25]. Long-term exercise has been shown to have an anti-inflammatory effect [26]. This effect of exercise is supported by the observation that individuals subjected to various kind of exercises such as running, bicycling, swimming, and resistance exercises showed decrease in mononuclear cell, TNF-α, IL-6, and CRP production and increase in IL-4 and IL-10 levels [27]. Swim training as a uniform type of activity is less traumatic to animals and is mostly used to recognize the physiological, biochemical, and molecular reactions to exercise [26].

The purpose of the present study is to investigate effects of 10 week swim training on: (1)WBC profile, (2) pro-inflammatory mediators and, (3) histopathological alterations of pancreatic tissue of high fat-diet induced type 2 diabetic rats.

METHODS AND MATERIALS

Animals

Forty male Wistar rats (200-250 g) were obtained from laboratory animal house of Tabriz University of Medical Sciences. They were kept in an animal room at 22-24°C and had free access to rat food and blow water. All the employed experimental processes as well as rat care and handling were in agreement with guidelines provided by the Animal Care Committee of the TabrizUniversity of medical sciences. The animals were randomly divided into four groups (n = 10): control group (Con), diabetic group (Dia), exercise group (Exe) and diabetic- exercise (Dia-Exe) group. Treatment interventions started one week after induction of diabetes.

Induction of type2 diabetes

The rats were fed with high fat diet (HFD) regimens consisting 58% fat, 25% protein, and 17% carbohydrate, for a period of 4 weeks. The composition and preparation of HFD were as described previously [28,29]. After the 4th weeks of dietary manipulation, animals were injected with a low dose of STZ (35 mg/kg, i.p). After 72h, rats with the non-fasting basal plasma glucose (PGL) of ≥ 300 mg/dl were considered diabetic and selected for further studies.

Swim training protocol

Swim training began one week after induction of diabetes. The training was gradually increased during the 12 days from 5 min daily to reach 60 min daily. Thereafter, the rats continued this protocol for 5 days per week for 10 weeks. Swimming exercise carried out in rectangular tanks (100 x 60 cm) with the water maintained at 34–36°C. After swimming, animals were gently dried with towels and placed in the cages.

White blood cell count and assessment of inflammatory mediators

At the end of experiments, all animals were deeply anaesthetized with ketamine (40mg/kg) and Xylazine (5mg/kg), and blood samples were collected from the inferior vena cava. Then, differentiated WBC count performed and percentage of each cell determined.

For assessment of the inflammatory mediators, serum samples were prepared. Then serum levels of CRP were measured by using CRP kit (Cusabio,Biothec,Wuhan, China) and serum levels of IL-6 were measured by using enzyme-linked immune-sorbent assay kits (Boster's rat ELISA Kit). All manufacturers' technical recommendations were followed.

Histological evaluation

After sacrificing of animals, the panceratic tissues were immediately removed and fixed in Bouin's without acid solution, and dehydrated in ascending grades of alcohol and embedded in paraffin. Sections of 5 µm were taken, stained with hematoxylin-eosin (H-E), and examined under light microscope (Olympus BH-2, Tokyo, Japan) in a blinded manner. Panceratic tissues were evaluated in terms of morphological alterations, edema and congestionin sinusoids between islets, leukocytosis infiltration, and deposition of amyloid.

Statistical analysis

Data were statistically analyzed using one-way analysis of variance (ANOVA) followed by Tukey's test. The significant level was set at $p < 0.05$. Results are expressed as Mean ±S.E.M.

RESULTS

White blood cell, lymphocytes, monocytes and eosinophils count in the blood

Diabetic group showed significant ($p<0.01$) increase in WBC, lymphocyte, and monocyte levels, and a significant decrease in neutrophil counts compared to control group (Table1). Exercise could significantly ($p<0.01$) reduce WBC, lymphocyte and monocyte counts, and increased the neutrophil- counts compared to diabetic group. There were no significant differences in intergroup comparisons in eosinophils counts (Table1).

Tabel1.White blood cell count (WBC) and percentage of lymphocytes (Lym), monocytes (Mon), eosinophils (Eos),and neutrophils (Neu) in the blood in sedentary control(Con), sedentary diabetic (Dia), exercised control (Exe), and exercise diabetic (Dia-Exe) rats.

Groups	Con	Exe	Dia	Dia-Exe
WBC ($\times 10^5$)	544.29±2.02	575.71±1.68	811.43±2.38*	591.16±1.50#
Lym (%)	58.84±0.96	61.81±1.47	78.2±0.83*	60±1.97#
Mon (%)	3.14±0.26	3.57±0.20	6.57±0.20*	3.71±0.18#
Eos (%)	1.28±0.18	1.42±0.20	1.85±0.34	1.71±0.35
Neu (%)	35.28±0.86	32.42±1.65	13.71±0.77*	33.83±2.13#

Data are shown as Mean ± SEM, *p < 0.01 vs Control group; # p< 0.01, vs Diabetic group.

Inflammatory mediators

ANOVA showed a significant ($p<0.01$) increase in CRP level in the serum of diabetic and diabetic- exercise groups in comparison with the control group. However, swim training significantly ($p<0.5$) decreased serum CRP level compared with diabetic group (Fig.1). Serum CRP levels in exercise group were also lower in comparison with the control group, although this difference was not significant. Fig. 2 shows a significant ($p<0.01$) elevation in the serum levels of IL-6 in the diabetic compared with the control group. Swim training significantly ($p<0.01$) decreased the serum level of IL-6 in the diabetic rats.

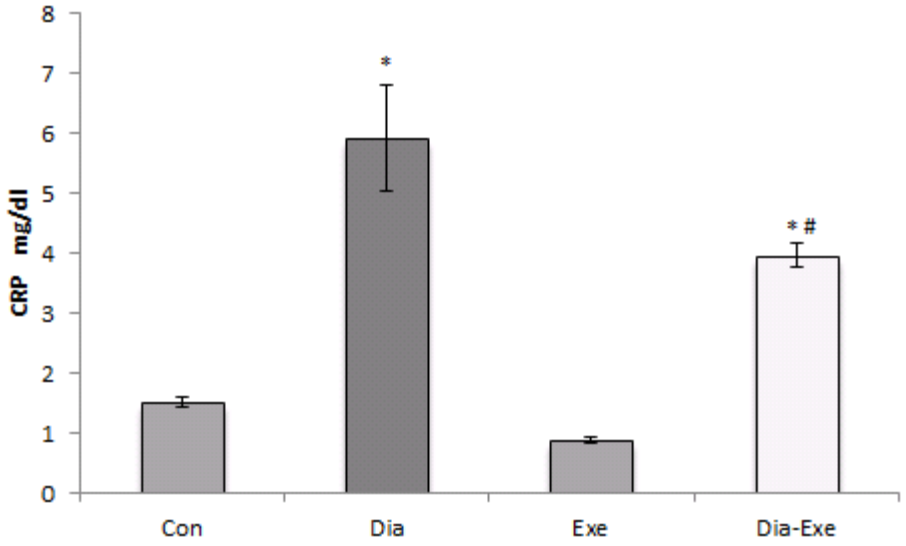

Fig 1.Serum C-reactive protein (CRP) Level in sedentary control (Con), sedentary diabetic (Dia), swim trained control (Exe) and swim trained diabetic rats (Dia-Exe). Data are shown as Mean ± SEM. *p < 0.01 vs Control group; #p < 0.05, vs Diabetic group.

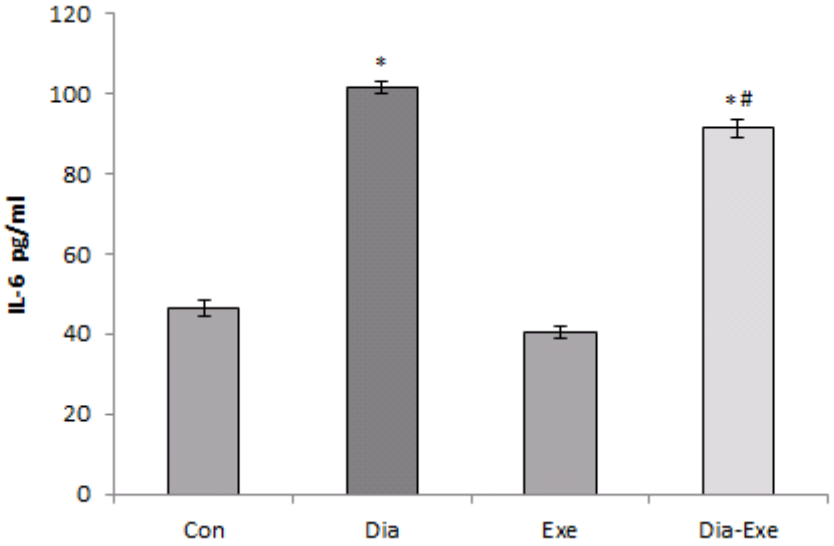

Fig2. Serum Interlukine-6 (IL-6) level in sedentary control (Con), sedentary diabetic (Dia), swim trained control (Exe) and swim trained diabetic rats (Dia-Exe). Data are shown as Mean ± SEM. *p < 0.01 vs Control group; #p < 0.01, vs Diabetic group.

Histopathological findings:

Histological examination of the panceras showed that there were no histological changes in the swim trained group compared to the control group (Fig 3a, 3b). In the sedentary diabetic group, appearance of pancreatic islets had atrophic changes, irrigular morphology, leukocyte infiltration, vasodilated, and congested sinusoids. Inaddition, Langerhans cells had picnotic, necrotic nuclei, and degenerated vacuoles with acidophilic cytoplasm. Also, deposition of amyloid in some areas of pancreatic islets was seen. Swim training resulted in a marked attenuation of morphological alterations, leukocyte infiltration, and vasodilatation and congestion in sinusoids between islets in diabetic animals (Fig 3d). Also, deposition of amyloid in the pancreatic islets was milder in swim trained diabetic rats than sedentary diabetic rats (Fig 3d).

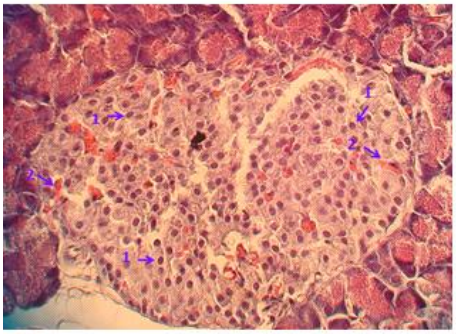
Fig 3a

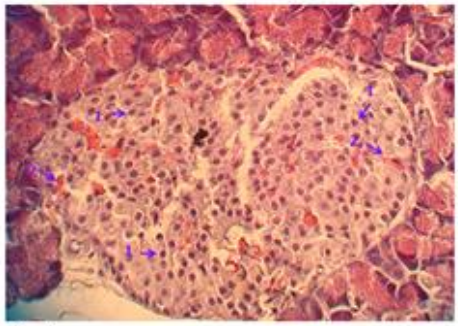
fig 3b

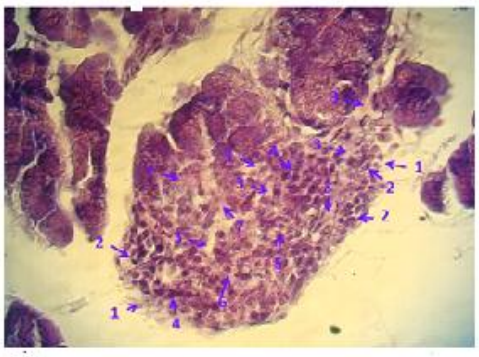
fig 3c

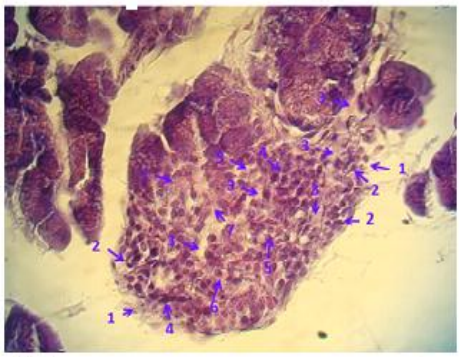
fig 3d

Fig 3: Histopathological evaluation of rat pacceratic tissue after 10 weeks. Panceratic sections are stained by hematoxylin and eosin (HE) and examined by a light microscope(40 × HE).

Fig 3 (a, b): The normal panceratic tissue in sedentary control and in swim trained control group. Healthy appearance of pancreatic islets: normal morphology, without inflammatory cells, endocrine cells with distinct nuclear (vector1) and sinusoids containing erythrocytes (vector 2)

Fig3c: The panceratic tissue in sedentary diabetic group: atrophic size, irrigular morphology (vector1), leukocytes infiltration (vector2), Sinusoids between islets were vasodilated and congested (vector3), Langerhans cells with picnotic and necrotic nuclei (vector 4), degenerated vacuoles (vector 5), acidophilic cytoplasm (vector 6), and deposition of amyloid in some areas of pancreatic islets (vector 7).

Fig3d: The panceratic tissue in swim trained diabetic atrophic size and distinct border, few inflammatory cells (vector 1), Sinusoids between islets were mildly vasodilated and congested (vector 2), deposition of amyloid in focal areas of pancreatic islets (vector 3).

DISCUSSION

HFD induced diabetic rats are extensively used as an animal model of humanT2DM to investigate its pathophysiology [28, 29]. In this study, we found that HFD and low dose (35mg/kg) of streptozotocin injection in rats lead to induction of type 2 diabetes, an inflammatory response and pancreatic damage. Diabetic rats subjected to exercise training for 10 weeks showed improvement in inflammatory response and pancreatic histological damages.

In the present study, significant increases in the WBC counts, lymphocytes and monocytes were observed in the diabetic rats. Our findings about the WBC counts, lymphocytes and monocytes are consistent with the resultsof previous studies on diabetes [30-32]. However, some studies have shown no change or reduction in lymphocytes after induction of type 1 diabetes induced by the alloxan monohydrate and diabetic patients [33, 34]. Possibly, the type of study, the induced diabetes method, and time of blood sampling have caused this discrepancy. The important change that we found in diabetic rats was a significant reduction in neutrophils that swim training reversed it. Some studies, unlike the present study, have shown an increase in the number of neutrophil count in diabetic animals [35].Reduction of neutrophils count in our study is probably due to the relocation and Immigration of these cells to the inflamed tissues [33]. Another possible reason is the movement of neutrophils(a process called *infiltration*) into adipose tissue in animals receiving HFD [36]. Since exercise reduces body lipid content, it seems that it could result in an increase of neutrophils in the circulation. Chronic low-grade systemic inflammation is a feature of chronic diseases such as type2 diabetes [37].The circulating levels of TNF-α, IL-6, and CRP increase in T2DM [18].Elevated CRP, IL-6 and TNF-α levels are also associated with visceral adiposity [38]. Indeed adipose tissue could be the source of this enhanced release of IL-6 and TNF-α, which consequently induces insulin resistance [10]. It is known that physical activity has beneficial effects in preventing and protection against complications of T2DM [23, 24]. Exercise by increasing the energy output decreases the body lipid content, and therefore diminishes the production of pro-inflammatory production. Weight loss in morbidly obese patients induces a significant decrease of CRP and IL-6 concentrations in association with an improvement of the insulin receptor sensitivity [39]. Bradley's study also proposes that exercise decreases adiposity, improves insulin resistance, and reduces adipose tissue inflammation in diet-induced obese mice [40]. These findings are supported by our results that 10 week swim training decreases chronic inflammation markers as well as lymphocyte, monocyte counts, and serum levels of CRP and IL-6. Also, in accordance with our findings, 12-week thrice-weekly swim training improved chronic inflammation markers as indicated by an increase in the levels of adiponectin and a reduction in CRP and IL-6. Recent studies have also emphasized on the beneficial effects of exercise in the prevention of leukocyte and platelet activation. Suppression of the inflammatory mediators by swimming, believed to be related to improvement of insulin sensitivity [41]. Histological findings of our study showed amyloid deposits, increased cell death and other damages in pancreatic tissue which are related to the infiltration of inflammatory cells and cytokines secreted from them.These findings are consistent with other studies [42, 43]. Exercise training in diabetic- exercise group, improved previously mentioned histopathological alterations. Exercise also has pleiotropic effects such as correction of dysglycaemia and dyslipidaemia, increase of antioxidant defense, and decrease of pro-inflammatory cytokines [43]. In conclusion, the present study indicated that 10 week swim training has antiinfillammatory effect in T2DMby reducing the number of WBC, lymphocytes, monocyte and production of pro-inflammatory cytokines such as CRP andIL-6. Our findings also proposed that swim training improves pancreatic histopathological alterations of typ2 DM.

ACKNOWLEDGEMENT

This study was financially supported by Liver and Gastrointestinal Diseases Research Center of Tabriz University of Medical Sciences (project No: 5/4/610). This article is derived from PhD dissertation of MS. Rafigheh Ghiasi, entitled "Evaluating the effect of swimming exercise onpanceratic inflammatory miRs signaling (miR-34a and miR146a) in type 2 diabetic male rats".

ETHICAL ISSUES

The study protocol was designed in accordance with NIH guidelines and Ethics Committee for the Use of Animals in Research at Tabriz University of Medical Sciences.

CONFLICT OF INTEREST

The authors have declared that there is no conflict of interest.

REFERENCES

1. Virally, M., Blickle, J.F., Girard, J., Halimi, S., Simon. D., & Guillausseau, P.J. (2007). Type 2 diabetes mellitus: epidemiology, pathophysiology, unmet needs and therapeutical perspectives. Diabetes. Metab. 33:231-44.
2. Frances, D. E., Ingaramo, P. I ., Ronco, M. T., & Carnovale, C. E. (2013). Diabetes, an inflammatory process: Oxidative Stress and TNF-alpha involved in hepatic complication. J. Biomedical Science and Engineering., 6:645-653.
3. Zimmet, P., Alberti, K.G., & Shaw, J. (2001). Global and societal implications of the diabetes epidemic. Nature., 414:782-787.
4. Gregor , M. F., & Hotamisligi G s. (2011). Inflammatory Mechanisms in Obesity. Annu. Rev. Immunol., 29:415–45.
5. Olefsky, J.M., &Glass CK .(2010). Macrophages, inflammation, and insulin resistance.*Annual review of physiology.,72*: 219-46.
6. Xu, H., Barnes G.T., Yang, Q., Tan, G., Yang ,D., &et al.(2003). Chronic inflammation in fat plays a crucial role in the development of obesity-related insulin resistance. J .Clin . Invest., 112:1821–1830, 2003.
7. Arkan, M.C., Hevener, A.L., Greten, F.R., Maeda, S., Li, Z.W., &et al. (2005). IKK-beta links inflammation to obesity-induced insulin resistance. Nat. Med., 11:191–198.
8. Kraegen, E.W., Clark, P.W., Jenkins, A.B., Daley, E.A., Chisholm, D.J.,& et al. (1991). Development of muscle insulin resistance after liver insulin resistance in high f at-fed rats. Diabetes., 40:1 397–1403 .
9. Fernandez-Sanchez, A., Santillan, E., Bautista, M., Esquivel-Soto, J., Morales-González, A., Esquivel-Chirino,C.,.& et al. (2011). Inflammation, Oxidative Stress, and Obesity. Int. J. Mol. Sci., 12:3117-3132.
10. Dandona, P., Aljada, A., & Bandyopadhyay, A. (2004). inflammation: the link between insulin resistance, obesity and diabetes. TRENDS in Immunology., 25(1): 4-7.
11. Vachharajani, V., & Granger, D.N. (2009). Adipose tissue: A motor for the inflammation associated with obesity. IUBMB Life. 61(4): 424–430.
12. Swirski, R.S., Sela, S., Shasha, S., Shapiro, G., & Nasser, L. (2001).Involvement of Peripheral Polymorphonuclear Leukocytes in Oxidative Stress and Inflammation in type 2 Diabetic Patients. Diabetes Care., 24(1):104-110.
13. Weisberg, S.P., McCann. D., Desai, M., & Rosenbaum, M. (2003).Obesity is associated with macrophage accumulation in adipose tissue. Clin Invest ., 112:1796 –1808, .
14. Ford, E.S. (2002). Leukocyte Count, Erythrocyte Sedimentation Rate, and Diabetes Incidence in a National Sample of US Adults. Am J Epidemiol., 155:57–64.
15. Kapperta, K., Meyborgb, H., Clemenza, M., Grafb, K., Fleckb, E., Kintschera, U., & Stawowy, P. (2008). Insulin facilitates monocyte migration: A possible link to tissue inflammation in insulin –resistance. Biochemical and Biophysical Research Communications., 365 : 503–508.
16. Bastard J.P, Maachi M, Lagathu C, Kim M.J, Caron M, & Feve B. (2006). Recent advances in the relationship between obesity, inflammation, and insulin resistance. Eur. Cytokine Netw., 17 (1):4-12.
17. Hu, F.B., .Meigs, J.B., Li, T. Y., Rifai, N., & Manso, J.E. (2004). Inflammatory markers and risk of developing type 2 diabetes in women. diabetes., 53:693–700.
18. Donath M.Y, & Shoelson S E.(2011). Type 2 diabetes as an inflammatory disease.Immunology., 11: 98-107.
19. Vandanmagsar, B., Youm, Y.H., Ravussin, A., Galgan,i J.E., Stadler, K. , & et al. (2011). The NLRP3 inflammasome instigates obesity-induced inflammation and insulin resistance. Nature medicine., 17:179–188.
20. Claycombe, K., King, L.E., & Fraker, P.J. (2008). A role for leptin in sustaining lymphopoiesis and myelopoiesis. Proceedings of the National Academy of Sciences of the United States of America., 105:2017–2021.
21. Zarkesh-Esfahani, H. ,Pockley, A.G., Wu, Z., Hellewell, P.G., Weetman, A.P., & et al. (2004). Leptin indirectly activates human neutrophils via induction of TNF-alpha. J Immanol ., 172: 1809–1814.
22. Zhang, X., Cui, Y., Fang, L., & Li, F. (2008). Chronic high-fat diets induce oxide injuries and fibrogenesis of pancreatic cells in rats .Pancreas., 37(3):e31- e39.
23. Helle, B. (2005). Physical activity and modulation of systemic low-level inflammation. Journal of Leukocyte Biology., 78: 819-835.
24. Bente, K.P. 2006). The anti-inflammatory effect of exercise: its role in diabetes and cardiovascular disease control. Essays in Biochemistry., 42: 105-117.
25. Woods, J.A., Vieira, V.J., & Keylock, K.Todd. (2013). Exercise, inflammation, and innate immunity.*Immunology and allergy clinics of north american*., 29 (2):381-393.

26. Lemos, E.T., Reis, F., .Pinto, R. Sepodes, B., Vala, H., Rocha-Pereira, P., & Silva, G.C. (2009). Exercise training decreases proinflammatory profile in Zucker diabetic type 2 fatty rats. Nutrition., 25:330 –339.
27. Oberbach, A., Tonjes, A., Kloting, N., Fasshauer, M., Kratzsch, J., Busse, M.W., & et al. (2006). Effect of a 4 week physical training program on plasma concentrations of inflammatory markers in patients with abnormal glucose tolerance. European Journal of Endocrinology., 15477–585.
28. Zhang, M., Zhang, X.Y., Li, J. & Chen L. (2008). The Characterization of High-fat diet and multiple low-dose streptozotocin induced type 2 diabetes rat model. *Experimental Diabetes Research*., 25:1-9.
29. Srinivasan, K., Viswanad, B., & Ramarao, K. (2005). Combination of high-fat diet-fed and low-dose streptozotocin-treated rat: A model for type 2 diabetes and pharmacological screening. *Pharmacological Research.,*52:313–320.
30. Nikseresht, A., FehrestiHaghighi, S., Solhjoo, K., & Kargar –Jahromy, H. (2012). Effect of maximum activity on the immune system cells in diabetic rats. Journal of Jahrom University of Medical Sciences.,10 (4):42-47.
31. Vozarova, B., Weyer,C., Lindsay, R.S., . Pratley, R.E., Bogardus, C., & Tataranni, P.A. (2002). High white blood cell count is associated with a worsening of insulin sensitivity and predicts the development of type 2 diabetes. Diabetes., 51:455– 461.
32. Gkrania- Klotsas, E., Ye, Z., Cooper, A.J., Sharp, S.J., Luben, R., & et al. (2010). Differential white blood cell count and type 2 diabetes: systematic review and meta-analysis of cross- sectional and prospective studies. PLoS ONE., 5(10):e13405.
33. Mansoori, D., Jamaati, H.R., Arami, S., Zadsar, M., Abbasian, L., & et al. (2002). Comparison of Lymphocyte Number and Their Subsets in Patients with Diabetes Mellitus Type II, Tuberculosis and Concomitant TB and Diabetes. Tanaffos., 1(4):45-50.
34. Otton, R., Soriano, F.G., Verlengia, R. & Curi R. (2004). Diabetes induces apoptosis in lymphocytes. Journal of Endocrinology.,182: 145–156.
35. Kim, S.Y., Johnson, M.A., McLeod, D.S., Alexander, T., Hansen, B.C., & Lutty, G.A. (2005). Neutrophils are associated with capillary closure in spontaneously diabetic monkey retinas. Diabetes., 54 (5): 51534-1542.
36. Talukdar, S., Oh, D.Y., Bandyopadhyay, G., Li, D., Xu, J., & et al. (2012). Neutrophils mediate insulin resistance in mice fed a high-fat diet through secreted elastase. *Nature Medicine.,* PMID: 22863787
37. Pedersen, B.K. (2006).The anti-inflammatory effect of exercise: its role in diabetes and cardiovascular disease control. The Biochemical Society., 42:106-117.
38. Licastro, F., Candore, G., Lio, D., Porcellini, E., Colonna-Romano, G., & et al. (2014). Innate immunity and inflammation in ageing: a key for understanding age-related diseases. Immunity & Ageing., 2:8.1-14.
39. H.P. Kopp, H.P., Kopp,C.W., Festa,A., Krzyzanowska,K., Kriwanek,S., & et al. (2003). Impact of weight loss on inflammatory proteins and their association with the insulin resistance syndrome in morbidly obese patients. Arterioscler Thromb Vasc Biol., 23:1042-1047.
40. Bradley, R.L., , Jeon ,J.Y., Liu, F.F., & Maratos-Flie, E. (2008). Voluntary exercise improves insulin sensitivity and adipose tissue inflammation in diet-induced obese mice. American Journal of Physiology Endocrinology and Metabolism,. 295(3):E586-E594
41. Lemoe, E.T., Reis, F., Baptista, S., Pinto, R., & Sepodes, B. (2007). Exercise training is associated with improved levels of C-reactive protein and adiponectin in ZDF (type 2) diabetic rats. Med Sci Monit., 13(8). BR168-74.
42. Donath, M.Y., Dalmas, E., Sauter, N.S., & BoniSchnetzler, M. (2013). Inflammation in Obesity and Diabetes: Islet Dysfunction and Therapeutic Opportunity. Cell Metabolism.17:860- 872.
43. Teixeira-Lemos, E., Nunes, S., Teixeira, F., & Reis, F. (2011). Regular physical exercise training assists in preventing type 2 diabetes development: focus on its antioxidant and anti-inflammatory properties. Cardiovascular Diabetology.,10(12):1-15.

Citation of This Article

Rafigheh G, Farhad G S, Gisou M, Mohammad H S, Hadi E, Alireza A, Fariba Mirzaie B, ,Mohammad R A. Effects of regular swimming on WBC profile, inflammatory mediators and histopathology of pancreatic tissue of high fat-induced diabetes in adult male rats. Bull. Env. Pharmacol. Life Sci., Vol 3 [10] September 2014: 14-20