Journal of Midwifery & Reproductive Health

JMRH.mums.ac.ir

The Effect of Aerobic Exercise Training on Biochemical and Inflammatory Markers among Young Females Suffering from Polycystic Ovary Syndrome

Soheyla Jafari (MSc)[1], Farzaneh Taghian (PhD)[2]*

[1] MSc in Exercise Physiology, Department of Physical Education and Sport Sciences, Isfahan (Khorasgan) Branch, Islamic Azad University, Isfahan, Iran

[2] Associate Professor in Exercise Physiology, Department of Physical Education and Sport Sciences, Isfahan (Khorasgan) Branch , Islamic Azad University, Isfahan, Iran

ARTICLE INFO

Article type:
Original article

Article History:
Received: 03-Nov-2019
Accepted: 24-Feb-2020

Key words:
Aerobic exercise
Inflammation
Insulin Resistance
Polycystic Ovary Syndrome

ABSTRACT

Background & aim: The present study aimed to investigate the effects of a three-month aerobic exercised training course on inflammatory markers in women with polycystic ovary syndrome (PCOS).

Methods: This quasi-experimental study was conducted on a total of 24 women with diagnosed PCOS in Isfahan, Iran, within May 22nd to September 21st 2018. Participants were randomly assigned into two groups of experimental (n=12) and control groups (n=12). The experimental group underwent 12-week aerobic exercise training, and the control group was only followed in the study. Biochemical markers, including fasting blood glucose, insulin, interleukin-6 (IL-6), C-reactive protein (CRP), tumor necrosis factor-α (TNF-α) were measured in the two groups. Insulin resistance index was also determined by the calculation of the homeostasis model assessment of insulin resistance (HOMA-IR). All the variables were assessed and compared after 12 weeks. The independent t-test was used for comparing the two groups (P<0.05).

Results: There was a significant difference between the experimental and control groups in terms of IL-6 (P=0.003), CRP (P=0.001), insulin (P=0.008), and HOMA-IR (P=0.04) and all were at lower level in intervention than control group. No significant difference was observed regarding TNF-α (P=0.48) and glucose (P=0.09) levels between the two groups.

Conclusion: The findings of the current study showed that aerobic exercise is useful in the management of PCOS. Therefore, it is recommended to perform aerobic exercise as an appropriate modality to control PCOS and reduce its adverse effects.

► *Please cite this paper as*:
Jafari S, Taghian F. Effects of Three-month Aerobic Training on Inflammatory Markers Among Young Females Suffering from Polycystic Ovary Syndrome. Journal of Midwifery and Reproductive Health. 2020; 8(2): 2194-2202. DOI: 10.22038/jmrh.2020.44188.1527

Introduction

The major goal of performing this study was to address polycystic ovary syndrome (PCOS) as the most conventional and complex endocrine disorder affecting the fertility of women in their reproductive age (1, 2). The clinical features of PCOS include hirsutism, androgenic alopecia menstrual irregularity usually from the time of menarche, acne, hyperinsulinemia, insulin resistance (IR), early onset of type II diabetes mellitus, and dyslipidemia (3). The PCOS is underpinned by hormonal disturbances, including IR and hyperandrogenism. In addition, women with PCOS are at a higher risk of obesity (4). Obesity is a commonly present sickness among women with PCOS, and it was shown that between 40-80% of women with this condition are reported to be overweight or obese (5).

Based on the literature, it has been proved that obesity seems to have an additional synergistic impression on the manifestations of PCOS,

* *Corresponding author:* Farzaneh Taghian, Associate Professor of Exercise Physiology, Department of Physical Education and Sport Sciences, Isfahan (Khorasgan) Branch, Islamic Azad University, Isfahan, Iran. Tel: 00989133080241; Email: f_taghian@yahoo.com

including a modifying effect on insulin sensitivity and gonadotrophin secretion, independently and negatively affecting insulin sensitivity, risk of diabetes, and cardiovascular disease (6). Several studies have demonstrated that weight loss of 5-10% in overweight women with PCOS via energy restriction can decrease the circulation of insulin levels and hyperandrogenism (7, 8) and enhance menstrual cyclicity, fertility, and risk factors of cardiovascular disease (7).

The results of a systematic review revealed that lifestyle modifications, such as performing exercise and physical activity, are the first medical measurements in the improvement of health outcomes in PCOS. The most frequently observed refinements included improved ovulation, reduced IR (9-30%), and weight loss (4.5-10%) (9). The inflammatory mediators in PCOS have been linked to hyperandrogenism, IR, type II diabetes, and cardiovascular risk factors. Recent studies indicated that PCOS is a pro-inflammatory condition with the increased levels of plasminogen activator inhibitor, tumor necrosis factor-α (TNF-α), and interleukin (10). Circulating levels of TNF-α, interleukin-6 (IL-6), high-sensitivity C-reactive protein (hs-CRP), white blood cell (WBC) count, and neutrophil count have been observed to be elevated in patients with PCOS according to age and body mass index (BMI)-matched controls (11). According to the evidence, hyperglycemia is linked to systemic inflammation as observed in glucose-intolerant PCOS women.

Hyperglycemia and IR could effectively prompt an increase in the concentration of reactive oxygen species (ROS) (12). The ROS activates the nuclear factor kappa-light-chain-enhancer of activated B cells, which can stimulate the synthesis of inflammatory factor (i.e., TNF-α) that is a mediator of IR and is highly expressed in PCOS patients (13). One investigation proved that all women with PCOS tend to have some sort of IR (14). Another study indicated that exercise-induced improvement in both autonomic and cardiopulmonary functions negatively corresponds with the inflammatory markers (i.e., C-reactive protein [CRP] levels and WBC count), strengthening the role of exercise in improving the cardiovascular risk profile in young PCOS women (15).

The results of some studies revealed that aerobic exercise reduces inflammation in women with PCOS. Vasheghani-Farahani et al. demonstrated the impact of their training course (i.e., strengthening aerobic exercises) on diminishing waist-to-hip ratio (WHR), along with the blood level of insulin, fasting blood sugar, hs-CRP, and homeostasis model assessment of insulin resistance (HOMA-IR) index. They all decreased drastically in the exercise group, compared to those reported in the control group (16). The results of another study showed a noteworthy reduction in CRP following a three-month exercise training program (15). The results of a contrasting study carried out by Jeffrey et al. revealed no significant change in CRP and TNF-α (17). Circulating IL-6 concentration corresponded with obesity, as well as with IR, which is common in PCOS (18, 19).

As expressed in previous studies, obesity worsens the signs of PCOS; however, reducing weight or doing exercise causes improvement in reproductive function in women with PCOS but with still unknown mechanisms (20). Regardless of the potential advantage of physical exercise in PCOS, there have been a small number of studies investigating the independent effects of exercise on inflammatory factors. Therefore, the present study aimed to examine the effects of a three-month aerobic training course on inflammatory markers in young women with PCOS.

Materials and Methods

This quasi-experimental study was carried out on a total of 24 participants selected from obese women within the age range of 20-30 years affected by PCOS who referred to the outpatient gynecologic clinics of Isfahan University and Shahinshahr Branch, Iran, within May 22nd to September 21st 2018. The presence of this syndrome was confirmed using ultrasound, blood test, and clinical examination performed by gynecologists.

As the first step in screening the subjects, the researchers checked the medical cases of the patients admitted to Shahid Beheshti Hospital in Isfahan, Iran, followed by contacting the potential subjects via telephone calls, sending them invitations, or using notice banners in order to introduce the present study. The age, height, weight, BMI, and fat percentage of the subjects were assessed in order to ensure the homogeneity of the participants in both groups.

Before the treatment, the independent t-test was performed for the respective mean scores of the two groups. Table 1 tabulates the results of the t-test showing that there are no statistically significant differences between the two means at the beginning of the study.

Table 1. Mean±standard deviation of weight, fat percentage, and body mass index in pretest and posttest

	Group	Pretest	Posttest	Mean±standard deviation	Difference of mean changes between control and experimental groups± standard deviation	T	P-value
Weight (kg)	Control	74.28±10.07	74.38±9.93	0.1±0.14	1.64±0.47	3.45	P≤0.001
	Experimental	77.14±11.23	75.76±11.87	01.38±0.64			
Fat percentage	Control	35.62±2.23	35.83±2.43	-0.21±0.2	1.4±0.48	5.58	P≤0.001
	Experimental	36.66±5.23	33.62±4.81	3.04±0.36			
Body mass index (kg/m²)	Control	29.21±2.67	30.38±3.59	-1.17±1.32	1.4±0.16	8.52	P≤0.001
	Experimental	30.52±3.78	29.73±3.81	0.79±0.03			

To determine the sample size, the included factors were a) the two independent groups, b) 5% type I error, c) 20% type II error, d) 80% power of the statistical test, and e) 0.9 effect size. Considering the aforementioned parameters, G*Power software (version 3.0.10) was used to calculate a total sample size of 26 subjects (13 women per group) in line with an anticipated dropout rate of 20%. A total of 24 women affected by PCOS were randomly selected for the two control and experimental groups, with the mean values of BMI and age reported as 29.86±3.22 Kg/cm^2 and 26.87±4.43 years, respectively.

The subjects were not affected by cardiovascular, renal, and liver diseases or diabetes and did not receive medications, such as contraceptives, progesterone, metformin, and clomiphene citrate. The participants did not also smoke or drink alcohol. While being under investigation, the subjects in the control group just performed their ordinary daily activities and were also asked not to participate in any exercise program during the study period. In order to maintain the calorie intake during the study, the subjects' dietary data were recorded by a 24-hour dietary recall questionnaire on three days (i.e., Saturday, Sunday, and Friday) by the subjects themselves.

They were not trained and had no regular exercise. The plan included 12 weeks of aerobic exercise at a moderate level (60-70% of maximum heart rate), three 60-minute sessions a week. The plan also consisted of a warm-up for 10 min, main phase (i.e., aerobic exercise) for 40 min, and cooling down for 10 min. A Polar pulse measuring device (Polar, England) was used to control exercise intensity.

The protocol of the present study was approved by the Local Ethics Committee of Islamic Azad University, Isfahan (Khorasgan) Branch, Isfahan, Iran, and informed consent was obtained from all the patients before they entered the study. Both groups were well informed that no change should be made in their diet. Then, 5 ml of venous blood was taken from the left hands of the subjects by a laboratory technician. All of the participants were recommended not to have carbohydrate-rich foods 12-14 h before undergoing the blood sampling test and abstain from all or some kinds of food or drink up to the next morning during the sampling. Two days after the blood sampling, the patients were assessed by body composition (3.0; Biospace Co., Korea) as an analyzing device for determining their weight, BMI, and fat percentage. After 12 weeks of exercise, another test was performed on the patients (observing all the items in the pretest). Two days after collecting the samples of the second phase, another analysis was carried out on the patients.

Body composition analyzer (3.0; Biospace Co., Korea) was employed to determine body compositions. The height of the patients was obtained by the height measuring device (SEGA, USA); however, Polar S-series Toolkit (Polar, England) was used to determine the heart rate. For the determination of biochemical variables, 5 ml of blood samples were taken in a resting situation. The subjects were asked not to perform exercise 12 h before the blood test. A specific kit (Bender MedSystems, Australia) was used to determine the level of IL-6 and TNF-α, and an ELISA kit (Bender MedSystems, Australia) was employed to measure CRP. Then, the participants in the experimental group took part in a three-month training program after which all the aforementioned variables were measured again.

Before the initiation of the study, the subjects were asked to fill a testimonial attesting their consent and then participate in the study. The subjects were explained about the research process and their role. The results of the experiments were reported to the participants, and the data were gathered for the researchers. The participants were assured that they could withdraw from the study freely.

Both descriptive and inferential statistics were used to analyze the data. After investigating the normality of data distributions using the Kolmogorov-Smirnov test, an independent sample t-test was used to assess intergroup and intragroup differences, respectively. It is worth noting that SPSS software (version 21, IBM Corporation, Corporation, Armonk, NY, USA) was utilized for data analysis. P-value less than 0.05 was considered statistically significant.

Results

Tables 1 and 2 tabulate the results of the independent t-test for comparing the average subtraction of pretest and posttest values of the variables in the experimental and control groups before and after 12 weeks of aerobic exercises. The collected data on weight, fat percentage, and BMI are presented in Table 1. A significant difference was observed between the control and experimental groups regarding bodyweight ($t=3.45$, $P<0.05$). There was also a significant difference in terms of fat percentage between the two groups ($t=5.58$, $P<0.05$). Likewise, regarding BMI, a significant difference was noticed between the control and experimental groups ($t=8.52$, $P<0.05$).

The collected data about glucose, insulin, and HOMA-IR are shown in Table 2. A significant difference was observed between the control and experimental groups in terms of insulin level ($t=-2.98$, $P<0.05$). There was also a significant difference regarding HOMA-IR between the two groups ($t=-2.17$, $P<0.05$). However, concerning glucose level, no significant difference was shown between the two groups of the study ($t=-1.75$, $P\geq0.05$).

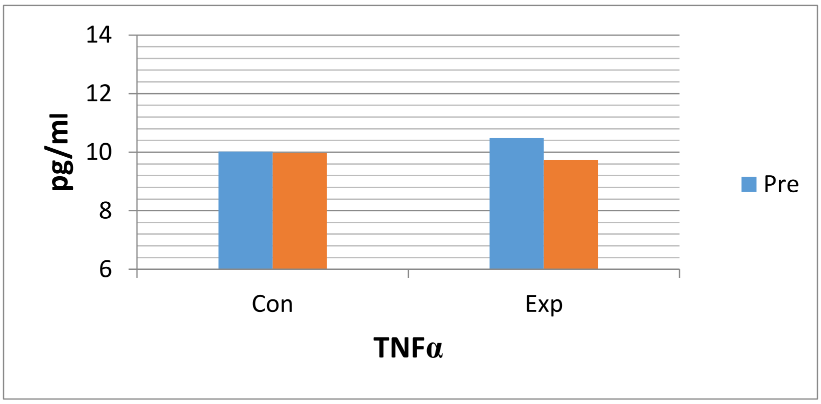

Figure 1. Levels of tumor necrosis factor-α before and after exercise intervention

As depicted in Figure 1, no significant difference was noticed regarding TNF-α between the experimental and control groups ($t=-0.72$; $P>0.05$). There was also a significant difference in terms of the mean IL-6 between the control and experimental groups ($t=-3.50$, $P<0.05$). The IL-6 decreased significantly in the experimental group ($P=0.006$) but not in the control group (Figure 2; $P=0.64$).

Regarding CRP, significant differences were observed between the control and experimental groups (t=-6.98, P<0.05), as CRP decreased significantly in the experimental group (P≤0.0001) but not in the control group (P=0.42) presented in Figure 3.

Table 2. Mean±standard deviation of glucose, insulin, homeostasis model assessment of insulin resistance, interleukin-6, tumor necrosis factor-α, and C-reactive protein in pretest and posttest

	Group	Pretest	Posttest	Mean difference±standard deviation	Difference of mean changes between control and experimental groups±standard deviation	T	P-value
Glucose (mmol/liter)	Control	78.00±9.83	79.00±9.16	-1.14±.09	-7.9±3.5	-1.75	P≥0.001
	Experimental	84.10±10.86	77.00±5.94	7.1±4.92			
Insulin (mU/liter)	Control	18.83±7.66	19.20±7.79	-0.37±0.24	-3.6±2.1	-2.98	P≤0.001
	Experimental	14.28±7.96	10.99±7.09	3.29±0.9			
Homeostasis model assessment of insulin resistance	Control	3.66±1.72	3.64±1.26	0.2±0.46	-0.91±0.4	-2.17	P≤0.001
	Experimental	3.08±1.94	2.15±1.44	0.94±0.5			
Interleukin-6 (pg/ml	Control	8.06±13.72	8.22±12.72	0.16±1	-3.68±2.4	-3.50	P≤0.001
	Experimental	5.53±3.14	2.01±1.85	3.52±1.29			
Tumor necrosis factor-α (pg/ml)	Control	10.02±3.21	9.97±2.90	0.05±0.31	-0.7±0.21	-0.72	P≥0.001
	Experimental	10.48±4.05	9.73±2.09	0.75±2.04			
C-reactive protein	Control	0.92±1.42	0.77±1.42	0.15±0.1	-2.2±0.86	-6.98	P≤0.001
	Experimental	3.43±0.93	1.08±0.93	2.35±0.1			

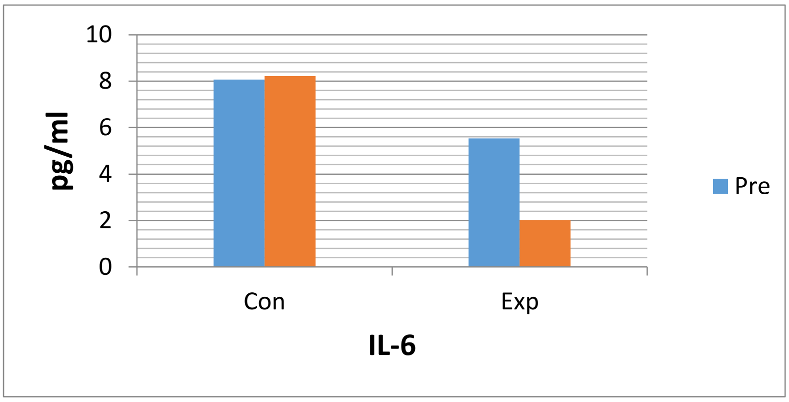

Figure 2. Levels of interleukin-6 before and after exercise intervention

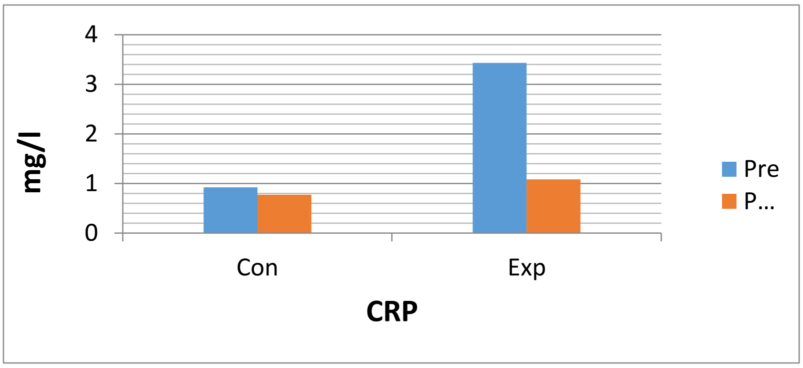

Figure 3. Levels of C-reactive protein before and after exercise intervention

Discussion

The results of the present study indicated that BMI and fat percentage reduced remarkably after 12 weeks of performing aerobic exercise.

Exercise and physical activities decrease the body fat that stores estrogens and provides the production of steroid hormones (21). The findings of the current study confirmed the effect of aerobic exercise on the reduction of body compositions. The previous studies have reported that exercise with or without dietary energy restriction improves IR in PCOS (9, 22). Three studies previously mentioned all reported reduced IR and showed improvements within 12 weeks of exercise (15, 20, 23).

A study was carried out by Giallauria F. et al. in 2008 regarding the improvement of the immune system independently by physical exercises in women affected by PCOS. In the aforementioned study, there were 62 individuals in the experimental group with an average age of 22.8 years and BMI of 29.2Kg/m^2. In addition, there were 62 subjects in the control group with an average age of 22.6 years and BMI of 29.5kg/M^2. The exercises of the experimental (i.e., exercise-included) group consisted of fixed cycling (3×30 min/week) with medium intensity (60-70% VO_2 max) performed for 12 weeks. Finally, the subjects in the experimental group had a considerable reduction in BMI and WHR, compared to those reported in the control group (15).

Regular moderate-intensity aerobic exercise over a short period boosts reproductive outcomes, such as ovulation and menstrual cycle regulation. Furthermore, it decreases weight and IR in young overweight females suffering from PCOS (9). Similarly, the researchers observed a decrease in BMI, fat percentage, and IR after 12 weeks of performing aerobic exercise. The allocated time for exercising can be referred to as one of the probable factors contributing to this attainment.

In the current study, it was also observed that insulin and HOMA-IR reduced significantly; however, there were no changes in glucose level after 12 weeks of performing aerobic exercise. It is obvious that exercise acts through two mechanisms, including the stimulation of glucose transport through activating an insulin-independent pathway and protection against mitochondrial dysfunction-induced IR through increasing muscle antioxidant defense and mitochondrial biogenesis (24).

In the present study, the initial level of glucose was determined as normal. In the experimental group, it decreased after the intervention from an average of 84.10 to 77. Moreover, the insulin level showed a statistically significant decrease from 14.28 to 10.99, demonstrating a significant reduction in IR. It is noteworthy that although a decrease was also observed in glucose level, it was not proved to be statistically significant (P=0.09). As for the intervention resulting in weight loss, the decrease in IR led to the regulation of the blood sugar using the insulin of less density.

The findings of the current study demonstrated that a three-month aerobic training program improved the inflammatory factors (i.e., CRP levels and IL-6) in young PCOS women. The degree of elevation in the circulating levels of CRP and IL-6 in PCOS was much greater when obesity was also present (19). Regular exercise training also reduces basal IL-6 production. In addition, the results showed that contracting skeletal muscle leads to increased cytosolic Ca^{2+} and activation of p38 mitogen-activated protein kinases and/or calcineurin, which results in the activation of transcription factors depending on these upstream events. The IL-6 has anti-inflammatory effects as it inhibits TNF production (25).

The main result of a systematic review was that physical activity/exercise has positive nonacute effects on several key factors in the atherosclerosis process in patients with risk factors of cardiovascular diseases or established diseases. The findings of the aforementioned review showed that there is sufficient evidence that physical activity decreases cytokines, particularly TNF-α, and to some extent IL-6 (26). The results of the present study are consistent with the findings of a study conducted by Giallauria et al. (2008) demonstrating a significant decrease in CRP levels in the trained group. The aforementioned study indicated that exercise-induced improvement in both autonomic and cardiopulmonary functions negatively correlates with the inflammatory markers (i.e., CRP levels and WBC count), supporting the role of exercise in improving the cardiovascular risk profile in young PCOS women (15). Morreale et al. proved that CRP levels are higher in PCOS; however, multiple studies proved that CRP levels are also high in obese patients (19, 27, 28).

In the meta-analysis of the most comparable studies performed by Escobar-Morreale et al. (2011), it was demonstrated that circulating CRP was boosted in PCOS and indicative of the chronic low-grade inflammation present in the disorder. In contrast, the trend toward slightly greater circulating levels of IL-6 and TNF-α among women with PCOS was far from reaching a statistical significance. Because the CRP elevation attributable to PCOS was relatively small, caution should be exercised in using CRP to attribute metabolic and cardiovascular risk to PCOS (19). Esposito et al. also demonstrated significantly reduced CRP and IL-6 levels after 2 years of a low-energy Mediterranean diet and increased physical activity (29).

The TNF-α appears to be linked with hyperandrogenism, increased IR, and obesity, which were common features noted with PCOS (30). It was observed that the serum levels of TNF-α would increase in patients with PCOS (19, 30). In the current study, there were no changes in TNF-α after exercise training. These results are not in line with the findings of a previous study that demonstrated a reduction in TNF-α after 7 months of aerobic exercise (31). The present study examined the effect of performing aerobic exercise within a period of only 12 weeks. Studies with a longer duration, such as a study carried out by Kondo et al. (2006), may show different results regarding TNF-α.

In a study carried out by Jeffery et al. in 2016, it was revealed that the level of TNF after 16 weeks of exercise did not demonstrate a significant difference in women with PCOS. It should also be mentioned that in the aforementioned study, the initial level of TNF in patients with PCOS did not differ significantly with the level of TNF reported for normal people. Moreover, the results of a similar study showed no significant difference between patients with PCOS and normal people in terms of the gene expression of TNF. There were several limitations in the current study, including participants' nutrition and emotions. In addition, it is essential to consider the number of participants while elucidating and generalizing its outcomes.

Conclusion

The obtained results of the present study showed that women with PCOS benefit from performing aerobic exercise for a long time to reduce their bodyweight, BMI, IR, and inflammatory factors. The findings of the current study suggested that aerobic exercise is useful in the management of PCOS and should be recommended as an appropriate modality to control PCOS and reduce its adverse cardiovascular effects.

Acknowledgements

This study was approved by the Ethics Committee of Biomedical School of Islamic Azad University, Isfahan Branch (Khorasgan) with the ethics code of IR.IAU.KHUISF.REC.1398.094. The authors would like to thank all the participants and those who helped with this project. This study was carried out by the personal budget of the corresponding author.

Conflicts of interest

Authors declared no conflicts of interest.

References

1. Talbott EO, Zborowski JV, Boudreaux MY, McHugh-Pemu KP, Sutton-Tyrrell K, Guzick DS. The relationship between C-reactive protein and carotid intima-media wall thickness in middle-aged women with PCOS. The Journal of Clinical Endocrinology and Metabolism. 2004; 89(12):6061-6067.
2. Sadeghi A, Djafarian K, Mohammadi H, Shab-Bidar S. Effect of omega-3 fatty acids supplementation on insulin resistance in women with polycystic ovary syndrome: Meta-analysis of randomized controlled trials. Diabetes & Metabolic Syndrome. 2017; 11(2):157-162.
3. Al-Jefout M, Alnawaiseh N, Al-Qtaitat A. Insulin resistance and obesity among infertile women with different polycystic ovary syndrome phenotypes. Scientific Reports. 2017; 7(1):1-9.
4. Naderpoor N, Shorakae S, Joham A, Boyle J, De Courten B, Teede HJ. Obesity and polycystic ovary syndrome. Minerva Endocrinologica. 2015; 40(1):37-51.
5. Sam S. Obesity and polycystic ovary syndrome. Obesity Management. 2007; 3(2):69-73.
6. Alvarez-Blasco F, Luque-Ramirez M, Escobar-Morreale HF. Obesity impairs general health-related quality of life (HR-QoL) in premenopausal women to a greater extent than polycystic ovary syndrome (PCOS). Clinical Endocrinology. 2010; 73(5):595-601.
7. Moran LJ, Harrison CL, Hutchison SK, Stepto NK, Strauss BJ, Teede HJ. Exercise decreases anti-mullerian hormone in anovulatory overweight women with polycystic ovary syndrome: a pilot study. Hormone and Metabolic Research. 2011; 43(13):977-979.
8. Hoeger KM. Exercise therapy in polycystic ovary syndrome. Seminars in Reproductive Medicine. 2008; 26(1):93-100.
9. Harrison CL, Lombard CB, Moran LJ, Teede HJ. Exercise therapy in polycystic ovary syndrome: a systematic review. Human Reproduction Update. 2011; 17(2):171-183.
10. Cakiroglu Y, Vural F, Vural B. The inflammatory markers in polycystic ovary syndrome: association with obesity and IVF outcomes. Journal of Endocrinological Investigation. 2016; 39(8):899-907.
11. Linscheid P, Seboek D, Schaer DJ, Zulewski H, Keller U, Muller B. Expression and secretion of procalcitonin and calcitonin gene-related peptide by adherent monocytes and by macrophage-activated adipocytes. Critical Care Medicine. 2004; 32(8):1715-1721.
12. Gonzalez F, Rote NS, Minium J, Kirwan JP. Reactive oxygen species-induced oxidative stress in the development of insulin resistance and hyperandrogenism in polycystic ovary syndrome. The Journal of Clinical Endocrinology and Metabolism. 2006; 91(1):336-340.
13. Scicchitano P, Dentamaro I, Carbonara R, Bulzis G, Dachille A, Caputo P, et al. Cardiovascular risk in women with PCOS. International Journal of Endocrinology and Metabolism. 2012; 10(4):611-618.
14. Vrbikova J, Cibula D, Dvorakova K, Stanicka S, Sindelka G, Hill M, et al. Insulin sensitivity in women with polycystic ovary syndrome. The Journal of Clinical Endocrinology and Metabolism. 2004; 89(6):2942-2945.
15. Giallauria F, Palomba S, Maresca L, Vuolo L, Tafuri D, Lombardi G, et al. Exercise training improves autonomic function and inflammatory pattern in women with polycystic ovary syndrome (PCOS). Clinical Endocrinology. 2008; 69(5):792-798.
16. Vasheghani-Farahani F, Khosravi S, Yekta1 AH, Rostami M, Mansournia MA. The effect of home based exercise on treatment of women with poly cystic ovary syndrom; a single-blind randomized controlled trial. Novelty in Biomedicine. 2017; 5(1):8-15.
17. Covington JD, Tam CS, Pasarica M, Redman LM. Higher circulating leukocytes in women with PCOS is reversed by aerobic exercise. Biochimie. 2016; 124:27-33.
18. Mohlig M, Spranger J, Osterhoff M, Ristow M, Pfeiffer A, Schill T, et al. The polycystic ovary syndrome per se is not associated with increased chronic inflammation. European Journal of Endocrinology. 2004; 150(4):525-532.
19. Escobar-Morreale HF, Luque-Ramírez M, González F. Circulating inflammatory markers in polycystic ovary syndrome: a systematic review and metaanalysis. Fertility and Sterility. 2011; 95(3):1048-1058.
20. Palomba S, Giallauria F, Falbo A, Russo T, Oppedisano R, Tolino A, et al. Structured exercise training programme versus hypocaloric hyperproteic diet in obese polycystic ovary syndrome patients with anovulatory infertility: a 24-week pilot study. Human Reproduction. 2008; 23(3):642-650.
21. Abazar E, Taghian F, Mardanian F, Forozandeh D. Effects of aerobic exercise on plasma lipoproteins in overweight and obese women with polycystic ovary syndrome. Advanced Biomedical Research.

2015; 4:68.
22. Hutchinson JC, Sherman T, Martinovic N, Tenenbaum G. The effect of manipulated self-ef fi cacy on perceived and sustained effort. Journal of Applied Sport Psychology. 2008; 20(4):457-472.
23. Vigorito C, Giallauria F, Palomba S, Cascella T, Manguso F, Lucci R, et al. Beneficial effects of a three-month structured exercise training program on cardiopulmonary functional capacity in young women with polycystic ovary syndrome. The Journal of Clinical Endocrinology and Metabolism. 2007; 92(4):1379-1384.
24. Di Meo S, Iossa S, Venditti P. Improvement of obesity-linked skeletal muscle insulin resistance by strength and endurance training. The Journal of Endocrinology. 2017; 234(3):R159-R181.
25. Pedersen BK. Anti-inflammatory effects of exercise: role in diabetes and cardiovascular disease. European Journal of Clinical Investigation. 2017; 47(8):600-611.
26. Palmefors H, DuttaRoy S, Rundqvist B, Börjesson M. The effect of physical activity or exercise on key biomarkers in atherosclerosis–a systematic review. Atherosclerosis. 2014; 235(1):150-161.
27. Yilmaz MA, Duran C, Basaran M. The mean platelet volume and neutrophil to lymphocyte ratio in obese and lean patients with polycystic ovary syndrome. Journal of Endocrinological Investigation. 2016; 39(1):45-53.
28. Agacayak E, Tunc SY, Sak S, Basaranoglu S, Yuksel H, Turgut A, et al. Levels of neopterin and other inflammatory markers in obese and non-obese patients with polycystic ovary syndrome. Medical Science Monitor: International Medical Journal of Experimental and Clinical Research. 2015; 21:2446-2455.
29. Esposito K, Pontillo A, Di Palo C, Giugliano G, Masella M, Marfella R, et al. Effect of weight loss and lifestyle changes on vascular inflammatory markers in obese women: a randomized trial. JAMA. 2003; 289(14):1799-1804.
30. Thathapudi S, Kodati V, Erukkambattu J, Katragadda A, Addepally U, Hasan Q. Tumor necrosis factor-alpha and polycystic ovarian syndrome: a clinical, biochemical, and molecular genetic study. Genetic Testing and Molecular Biomarkers. 2014; 18(9):605-609.
31. Kondo T, Kobayashi I, Murakami M. Effect of exercise on circulating adipokine levels in obese young women. Endocrine Journal. 2006; 53(2):189-195.