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Halil DUZOVA, Esin GULLU, Guner ÇIçEK, Burcu K. KOKSAL, Basak KAYHAN, Abdullah GULLU, Ibrahim SAHIN

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The effect of exercise induced weight-loss on myokines and adipokines in overweight sedentary females: steps-aerobics vs. jogging-walking exercises

Halil Duzova[a], Esin Gullu[b], Guner Cicek[c], Burcu K. Koksal[a], Basak Kayhan[d], Abdullah Gullu[b], Ibrahim Sahin[e].

[a] Dept. of Physiology, Medical School, Inonu Univ. Malatya, Turkey
[b] Physical Education and Sports High School, Inonu University, Malatya, Turkey
[c]Physical Education and Sports High School, Hitit University, Corum, Turkey
[d] Dept. of Medical Biology and Genetics, Inonu Univ. Medical School, Malatya, Turkey
[e] Dept. of Endocrinology, Inonu Univ. Medical School, Malatya, Turkey

Author Address: Halil Duzova,
Dept. of Physiology, School of Medicine, Inonu Univ. Malatya, 44280, Turkey
Tel: +90 422 341 0660/1274
e-mail: hduzova@hotmail.com, halil.duzova@inonu.edu.tr

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Abstract

BACKGROUND:The objectives of this study were to verify effects of step-aerobic exercise (SAE) and jogging-walking exercise (JWE) program on myokines and adipokines levels in overweight sedentary females. METHODS:Volunteer subjects (n=25) were assigned to two exercise groups: steps aerobics and jogging-walking. The exercise program given to them was for five days a week and for twelve weeks period. Serum samples were collected from venous blood before and immediately after cardio-respiratory fitness test (CRF) by Bruce protocol and stored at -80 C until they were assayed before 12 weeks exercise program. After 12-weeks training program this procedure was repeated. Serum TNF-α, IL-6, IL-15, IL-17, IL-18, leptin, resistin and adiponectin levels were assayed by ELISA.

RESULTS: Leptin and IL-15 levels were increased whereas resistin levels were decreased after CRF test in JWE training group following 12-weeks exercise program. TNF-α, IL-15 and IL-18 levels were higher and leptin levels were lower in SAE group than JWE group after 12-weeks exercise period. However, both SAE and JWE did not lead to significant change in serum levels of IL-17, IL-6 and adiponectin levels. CONCLUSIONS: What this study has added to existing knowledge that both SAE and JWE may cause weight loss especially in fat mass. But, the effect of SAE and JWE on myokines and adipokines levels may be the different. Further studies are needed to find out clinical importance of these findings.

Keywords: Step aerobics, jogging-walking, female, IL-15, IL-17, IL-18, resistin

Introduction

Physical inactivity has been identified as a strong predictor of different chronic diseases such as obesity, type 2 diabetes mellitus (DM2), stroke, cardiovascular disease (CVD), cancer, hypertension, etc.[1-3] Nowadays due to the industrial development, the incidence of obesity in early life has been increasing because of suffering from lifestyle-related faulty in eating habits, inadequate physical inactivity and lack of exercise. Physical inactivity leads to the accumulation of visceral fat and consequently the activation of a network of chronic low-grade systemic inflammatory pathways, which promote the development of insulin resistance, and thereby the development of the diseases originating from physical inactivity.[2, 4] Regular physical exercise offers protection against many diseases mentioned above and may be useful as a treatment for a wide variety of chronic diseases associated with overweight and obesity.[4] Skeletal muscle as a cytokine producing organ revealed a whole new paradigm: Skeletal muscle is an endocrine organ[2], which by secretion of hormone-like factors such as myokines may influence metabolism (especially oxidative metabolism and fat metabolism)[5, 6] and immune system in tissues via a muscle-to-fat endocrine pathway.[5] Thus, Pedersen's overall idea is that the contracting skeletal muscles release more myokines.[2] Recent findings demonstrate that physical activity induces an increase in the systemic levels of a number of myokines with anti-inflammatory properties which are mainly secreted from skeletal muscle.[1,3] Myokines may be involved in mediating the protective effect of exercise against diseases,[4] health beneficial effects of exercise may also play important roles in the protection against diseases associated with obesity. It has also been demonstrated that exercise increases muscle derived myokines by increasing muscle size and secretory properties.[3] So far, most known secreted myokines are tumor necrosis factor-α (TNF- α), interleukin (IL)-6 and IL-15.[7]

Adipose tissue also displays characteristics of an endocrine organ producing and releasing a number of adipocyte-specific bioactive factors known as 'adipokines', including adiponectin, leptin, and resistin, and cytokines like TNF-α, IL-6[8, 9] and IL-18.[9] It is now regarded that adipokines are regulating fat mass and nutrient, and blood pressure, lipid and glucose metabolism,[10] insulin signalling[11] and inflammation.[10, 12] In a reciprocal signalling pathway factors secreted by skeletal muscle tissue affect adipose tissue metabolism. Adipokines have direct effects on mass and physiological activities of skeletal muscle.[5] In obesity an increase in the obesity-related inflammatory markers (such as TNF-α, IL-6 and IL-18),[13] and a decrease in the anti-inflammatory markers (etc. adiponectin) are observed. It is disregulated secretion of leptin, adiponectin, and resistin with obesity reducing adiponectin levels while weight reduction increases adiponectin.[14]

In everyday life, females make exercise to protect themselves against the diseases mentioned above and from the overweight condition that makes them unhappy. Studies discussing weight-loss interventions up to the present manuscript were broadly classified into two types according to the method of weight loss employed in females; steps-aerobics exercise (SAE) and jogging-walking exercise (JWE). Jogging-walking is an aerobic exercise anyone can apply at almost all ages and sexes. It is within the framework of an exercise program and should be a certain discipline different from daily activities. This type of exercise is easy to

apply and does not require any equipment and is an extremely popular sport. Another weight loss method is steps-aerobics exercise. Steps-aerobics and aerobic dance have been combined with the purpose of achieving maximum aerobic effects. The choreography with music is repeated several times and uses different movements in an appropriate sequence. It is suitable for most groups; levels of activity can be tailored to individual needs in fitness centers which have a group exercise program, from beginners to advanced exercisers, and even to top level athletes. Both SAE and JWE are also recommended by the ACSM (American College of Sport Medicine). In order to improve cardio-respiratory endurance, control of body weight and reducing the risk of premature chronic disease are needed.[15] Olson et al has mentioned that aerobic bench-step exercises provide sufficient cardio-respiratory demand to enhance aerobic fitness and promote weight loss in females.[16]

Zuniga et al suggested that IL-17, mainly Th17 cell-expressed cytokine plays a role in the regulation of body weight, adipocyte differentiation, and insulin and glucose homeostasis.[13] Zuniga et al reported that serum IL-17 is upregulated in obese human patients, and obesity is positively correlated with enhanced IL-17 expression and increased severity of inflammation in IL-17 dependent mouse models.[13] IL-17 is thought to be inter-related between muscle tissue and fat tissue in females who practice different aerobic exercises.[17]

However, it has been hypothesized that the reduction in the diseases risk with obesity seen in response to reduce adipose tissue and increase skeletal ratio muscle could be as a result of an improved myokine profile associated with a decrease in the adipokines.[14] This is due to metabolic and hormonal interactions between muscle and adipose tissues that can potentially alter peripheral insulin sensitivity.[18] As we know that the JWA is done mostly with leg muscles while SAE is performed mostly by legs, buttocks, abdomen, chest head and arm muscles. For this reason, SAE may spent more energy than JWA. That's the aim of this study; we firstly intended to figure out which aerobic exercise method is more effective to skeletal muscle and adipose tissue both of which have been accepted as endocrine organs. Likewise, the relationships between myokines, adipokines, and insulin resistance have been investigated in these exercise programs. Secondly we examined the effect of SAE or JWE programs on metabolic capacity, weight loss, myokines, and adipokines levels in overweight sedentary female at the end of 12 weeks. Thirdly, it is worthwhile to investigate serum IL-17 levels in different aerobic exercises in order to elucidate the roles of IL-17 in glucose metabolism and insulin resistance.

Material and Methods

Subjects

Twenty five healthy sedentary females voluntarily participated in this study. All candidates did not attend regularly sports activities (more than one hour per week) before the study. Smokers and patients receiving lipid-lowering medications, insulin, or thiazolidinediones were rejected. None of the subjects had been ill within the previous month. Those with

diabetic vascular complications, life-threatening diseases, orthopedic problems, or liver and renal impairment were also excluded. They were assigned to either of two exercise groups, based on their preference. One group (n=10, age 38,30±0,42) performed steps aerobics exercise (SAE) and the second group (n=15, age 38,73±0,99) made jogging-walking exercise (JWE) for five days a week for twelve weeks period. The study was approved by the Local Ethical Committee and performed according to the Declaration of Helsinki. All subjects completed a medical questionnaire and were informed about the possible risks and discomfort involved before giving their written consent to participate.

Research design

All participants agreed to avoid the use of vitamin/mineral supplements, herbs, and medications from the previous day until after the last sampling point. All participants attended the same breakfast at 08:00. As the subjects rested quietly, the pre-Bruce protocol blood samples (Pre) were collected at 12.00. Laboratory and clinical measurements of all participants were made after the subjects refrained from any rigorous physical activity 24 h before measurements. The post-Bruce protocol blood samples were collected immediately after the test. Therefore, measurements were taken immediately after and within 10 min after the work out. Peripheral blood samples were drawn by antecubital venipuncture from the participants in the sitting position. All participants drank the same quantity of fluid during exercise. After a warm-up, they each drank 500 ml of fluid before the test, but were not permitted to consume any food or drink after the provided liquid and then rested in a supine position.

Cardio-respiratory fitness

Cardio-respiratory fitness (CRF) was measured using symptom-limited maximal treadmill exercise testing, heart rate recording was done by M22 Polar Heart Monitor (Finland) and estimation of oxygen consumption (metabolic equivalents (METS)) was done according to the Bruce protocol. The participants were encouraged to continue exercise until volitional exhaustion; even after exceeding 85% of their maximum predicted heart rate (maximal predicted heart rate is defined as 220 minus age). The cohort achieved an average of 97.9% (SD 6.6) of maximal age-predicted heart rate on these tests. During the exercise test CRF was determined from the maximum or peak METS achieved at peak exercise. Heart rate recovery in one minute (HHR1) was calculated as peak heart rate minus heart rate in one minute, during recovery following the test.[19]

Data collection

Height was measured to the nearest 0.1cm on a stadiometer when the participants were shoesless. Body weight, fat mass and predicted muscle mass was measured to the nearest 0.1kg using a pre-calibrated body composition monitors (model TBF-305; Tanita, Arlington Heights, IL) electronic scale. BMI was calculated as weight in kilograms divided by height squared (kg/m^2) in meters. The subjects were asked to breathe out for measurement of their waist circumference (WC), which was measured to the nearest 0.1cm at the iliac crest. When viewed from the side, hip circumference was evaluated at the level of the maximum extension

of the thigh, and waist-hip ratio (WHR) equals the WC divided by the hip circumference (HC); WC (cm)/height (m).

Applied Training Programs

SAE was applied to the first group and JWE was applied to the second group for five days a week, throughout 12-week. Training intensity was calculated separately for each subject: 1) the maximal heart rate (MHR) was calculated by using of the 220-Age formula, and 2) MHR was multiplied by the percentage of 80 % to find out target heart rate (THR) zone. The THR was controlled by portable heart rate monitor to ensure desired intensity of the training program for each participant. The JWE involved gradually increasing the distance in bi-weekly, as shown with in the exercise time available (see Table 1). The SAE also involved gradually increasing the number of repeats in bi-weekly, as shown within the exercise time available (see Table 3).

Maximal Heart Rate (MHR): calculated using the formula; (220-Age).
Target Heart Rate (THR): calculated using the formula; (MHR) x (0.80).

Jogging-walking Exercise (JWE) Group: JWE was applied in outdoor exercise park of the university campus. Exercise modality was based on the recent recommendations of ACMS. The workload was individualized according to the initial physical fitness assessment and gradually increased with continuous heart rate monitor. Aerobic exercise consisted mainly of jogging-walking on soil road and calisthenics involving upper and lower limbs. Moreover, subjects in the exercise group were encouraged to increase daily physical activities (e.g. brisk walking, etc.). JWE program was applied according to Table 1, as follows. Last 10-minute cool-down exercises were applied with isometric stretching exercises in lower intensity for upper and lower extremities.

Insert Table 1

Steps-Aerobics Exercise (SAE) Group: SAE was applied in health center of the Inonu University. The exercises were choreographed by a professional step-aerobics dance coach. The movements were simplified and made easy to learn, and required the use of both the upper and lower extremities and the back. Verbal and tactile prompts were given during each step-aerobic dance exercise class. The choreographed exercise program consisted of stretching exercises, walking exercises and progressive step-aerobic movements. It was performed with music, and required the continuous use of extended arm movements and the involvement of the major muscle groups. The outline of the step-aerobic dance exercise program is shown in Table 2 and 3 (modified from Arslan, 2011).[15]

Insert Table 2

SAE training program was applied according to Table 3, as follows. Last 10-minute cool-down exercises were applied with isometric stretching exercises in lower intensity for upper and lower extremities.

Insert Table 3

Measurement of Myokines and Adipokines

Blood samples for cytokine measurement were drawn into polypropylene tubes. The tubes were spun in 2500 g for 15 min at 4°C. The serum was stored at -80°C until analyses were performed. TNF-α, IL-6, IL-15, leptin and adiponectin ELISA kits from Boster Biological Technology Co. Ltd, IL-17 and IL-18 ELISA kits from E-Bioscience Co. and resistin kit from ASSAYPRO are provided. High sensitive ELISA reader from Titertek Multiscan Plus (Icn Flow) Systems (Minneapolis, MN, USA) was used for measurement. Serum glucose levels were analyzed by photometric method using an Architect C 16000. Serum insulin levels were measured by chemiluminescence immunoassay (CLIA) using an Immulate 2000 auto analyser (Siemens, USA). The insulin resistance index was calculated using fasting values of plasma glucose and insulin, according to the HOMA model formula:

Insulin resistance or HOMA-IR = fasting insulin (IU/mL) x fasting glucose (mg/dL) / 405.
As previously recommended, insulin resistance was arbitrarily considered when it was higher than 2.

Statistical analysis

Statistical analyses were performed using SPSS 17.0. A power analysis was conducted prior to the beginning of the study and found that 10 subjects per group would produce a power of ≥ .80. All data were reported as mean ± standart error. Normality for continued variables in groups was determined by Shapiro –Wilk test. Some variables were normal distributions ($p<0.05$) or were not ($p>0.05$). So comparisons within groups were performed by paired t test or Wilcoxon test. Comparisons between the groups were performed by unpaired t test or Mann-Whitney U test. Correlations among variables were calculated by Pearson or Spearman correlation test. A value of $p<0.05$ was considered significant.

Results

As shown in table 4, there were significant differences in body weight, body mass index (BMI) and VO_{2max} in between the JWE and SAE groups both pre-(respectively $p<0,010$, $p<0,044$, $p<0,026$) and post-training (respectively $p<0,011$, $p<0,030$, $p<0,007$). However, there were no significant differences in fat mass (%) and waist/hip ratio (WHR) between two groups neither pre- nor post training ($p>0,05$).

Insert table 4

As indicated in table 5, there were significant differences in serum TNF-α levels between the JWE and SAE groups in both pre- ($p<0,006$) and post-training after CRF test ($p<0,04$). Also, there were significant differences in post-training serum TNF-α levels between the JWE and

SAE groups, before Bruce test ($p<0,01$). As shown in table 5, there were significant differences in pre-training serum IL-15 levels between the JWE and the SAE groups after CRF test ($p<0,01$). There were significant differences in serum IL-18 levels between the JWE and the SAE groups, both pre-($p<0,016$) and post-training after ($p<0,01$) subject had completed the Bruce protocol. CRF test, 12-week training programs, as well as SAE and JWE did not cause significant changes in the serum IL-6, IL-17 and adiponectin levels at the sedentary overweight females.

As shown in table 5, Serum leptin levels were significantly increased after subjects had completed the Bruce protocol, post-training of JWE females ($p<0,023$). There were significant differences in serum IL-15 levels between pre-training and post-training samples after the Bruce protocol at JWE females ($p<0,019$). As shown in table 5, there were also significant differences in serum resistin levels between pre-training and post-training samples before CRF test of JWE females ($p<0,047$).

Insert Table 5

In table 6, serum levels of myokines and adipokines and correlation values are given for Female Jogging-walking and Step-aerobics exercise groups. There was a negative correlation between serum TNFα levels and waist/hip ratio (WHR) after the cardio-respiratory fitness test (CRF) ($p<0,050$, -0,511) at pre-training jogging-walking exercise (JWE) of female group. Serum resistin levels were also negatively correlated with WHR ($p<0,034$, -0,550) after the CRF of JWE female group post-training.

Serum IL-6 levels were negatively correlated with VO_{2max} ($p<0,021$, -0,591) before CRF whereas it was positively correlated with weight ($p<0,018$, -0,600) after CRF in JWE female group post-trainingly. Serum HOMA-IR had positive correlation with serum IL-6 levels ($p<0,047$, -0,714), as well as IL-18 level ($p<0,010$, 0,833) but it had negative correlation with serum IL-15 levels ($p<0,048$, -0,518) and resistin levels ($p<0,050$, -0,750) of this group after CRF post-trainingly.

Insert Table 6

Female weights were positively correlated with serum Il-6 ($p<0,033$, 0,673) and resistin levels ($p<0,025$, 0,697) after the CRF in pre-training of SAE group females. There was a positive correlation between serum leptin levels and BMI before the CRF ($p<0,043$, -0,648) in pre-training step aerobic exercise (SAE) group. There was a positive correlation between serum adiponectin levels and VO_{2max} before CRF($p<0,029$, -0,683).

BMI were positively correlated with serum IL-6 ($p<0,042$, -0,650) and IL-18 levels ($p<0,042$, -0,650) before the CRF post-training of SAE groupe. Serum leptin levels were positively correlated with weight before the CRF ($p<0,038$, -0,661) post-trainingly. VO_{2max} was negatively correlated with serum resistin levels ($p<0,018$, -0,724) whereas it was positively correlated with serum IL-15 levels ($p<0,008$, 0,777) before the CRF in the post-training of SAE females. Serum IL-17 levels had negative correlation with WHR ($p<0,019$, -0,721) and

serum TNF-α levels had positive correlation with fat mass (p<0,034, -0,671) after the CRF test in the post-training of the same group.

Discussion

Determining the skeletal muscle as a cytokine-producing organ led to the discovery that muscle-derived cytokines could account not only for exercise-associated immune changes, but also they played a role in mediating the exercise associated metabolic changes, as well as the metabolic changes following training adaptation.[3] The obesity and overweight are characterized by myokines/adipokines imbalance, which is suggested to be of importance for low-grade chronic inflammatory and the metabolic syndrome. Haaland et al reported that aerobic training plays a significant role in prevention of the chronic diseases in obesity which result in significant reduction in circulating proinflammatory cytokines and their receptors even after 8 weeks of training period.[21] Conversely, proinflammatory cytokine levels are changed in a variety of tissues with acute physical exercise.[22]

Cardio-respiratory fitness test (CRF), 12-week training programs, as well as SAE and JWE did not cause significant changes in the serum levels of IL-17 of the sedentary overweight females.[23] Anderson et al (2010) showed that immediately after the first soccer's matches, a significant elevation occurred in plasma concentrations of IL-17 in female elite soccer's[23]. Duzova et al showed that a single bout of strenuous exercise increases serum IL-17 level in heavy trained rats without muscle damage whereas it creates no change in its production in moderate trained and control male rats.[22] Sugama et al found that plasma concentrations of IL-17 were decreased significantly immediately after the fourteen male triathletes participated in a duathlon race, but they were significantly higher at 1.5 h and 3 h compared with values at 0 h post-exercise.[24] In this study , IL-17 level of SAE training females was negatively correlated with IL-6 after the CRF test; conversely it was positively correlated with IL-6 of JWE training females.[24] Sugama et al suggested that since IL-6 increases dramatically following long-lasting endurance exercise, this response may also stimulate the induction of IL-17 after exercise.[24] While Gaffen reported that IL-17 synergizes with TNF-α to promote IL-6 production.[25] Until today elevations in plasma IL-17 as a result of exercise have been observed only after soccer matches,[23] heavy trained rats,[22] duathlon race[24] and hyperthermia and hypoxia during acute exercise[26] and not after other forms of strenuous or prolonged exercises.

Prior investigations have provided controversial findings; some have investigated the effect of exercise on IL-6 and TNF-α. Despite in SAE females with a lower fat mass, their serum TNF-α levels were higher than JWE females in pre-training after the test and post-training pre- as well as post the test's with no significant changes in IL-6. Christiansen et al found that the increment in circulating IL-6 and TNF-α was significantly higher in overweight and obese subjects than lean subjects after acute ergometer cycling exercise.[27] Pedersen reported a negative association between the amount of regular physical activity and the basal plasma IL-6 and TNF-α level.[28] In spite of the plasma TNF-α is generally unchanged by a single bout of exercise, Lakhdar et al showed that in the exercise-diet group of obese females, three sessions per week of walking/running on a treadmill, circulating levels of TNF-α, IL- 6 and HOMA-IR were decreased after 24 weeks.[29] Ambeba et al reported IL-6 was significantly decreased after 6 months of weight loss treatment in overweight individuals and but decrease in weight loss did not lead to any significant changes in TNF-α.[30] Some researchers reported small elevations in plasma TNF-α as a result of exercise have been observed only after highly strenuous and prolonged exercise such marathon running and not after other forms of strenuous or prolonged exercise.[3, 31] In contrast, Borgers et al showed that TNF-α levels were slightly lower in kayakers than controls.[4] TNF-α significantly was also decreased with weight loss but weight loss did not lead to significant changes in IL-6.[4] Ambeba et al suggested that methodological differences among these studies may have contributed to the variability of the results.[30] Although Raschke and Eckel reported human serum and skeletal muscle biopsy data, IL-6 has been shown to be secreted by primary human skeletal muscle cells in vitro and its secretion was increased during contraction and after exercise.[32] Gokhale et al suggested that regular physical training may be expected to attenuate such a response.[33] Pedersen et al (34) reported a decrease in association between the amount of regular physical activity and the basal plasma IL-6 levels: the more the participants are physically active, the lower their IL-6 levels are the under resting conditions.[34] Contrary to IL-6,level of muscle IL-6 receptor mRNA is increased with training, potentially improving the sensitivity of muscle to the positive metabolic effects of IL-6.[18]

While Jung et al also showed that IL-6 is significantly correlated with baseline TNF-α after exercise for 12 weeks training, in this study TNF-α level of the females wasn't correlated with IL-6.[35] As Christiansen et al showed that the absolute increase in IL-6 after acute exercise was found to be positively correlated with the body fat percentage, there was a positive correlation between IL-6 and body weights of the females in this study .[27] In addition, at TNF α level of females in SAE training group was also correlated with fat mass, whereas TNFα level of

females in JWE training group was negatively correlated with WHR. Rubin et al also showed that BMI was positively correlated with IL-6 in mid-pubertal adolescent girls.[12] Piva et al also showed that IL-6 concentrations were higher in the obese group than those in the normal weight group and the BMI showed a positive correlation with IL-6.[36]

In previous studies, conflicting data are published whether physical activity affects IL-15 expression, protein level, and secretion from skeletal muscle. In this study, only SAE females' serum IL-15 level was higher than the JWE female's level in pre-training after the Bruce test. It was increased in 12-wk-trained JWE females after the CRF test. Christiansen et al showed that in both obese and lean subjects, circulating levels of IL-15 were also significantly increased after acute exercise.[27] Tamura et al found a significant increase in circulating IL-15 concentration after the exercise in untrained male subjects underwent 30-min treadmill running.[37] Rinnov et al also showed that 12 weeks of endurance training resulted in an elevation of IL-15 protein in skeletal muscle of male volunteers, even though mRNA expression and IL-15 plasma levels remained unchanged.[38] Quinn reported plasma IL-15 protein levels from both untrained and 10-wk-trained human subjects were increased acutely by whole-body resistance exercise.[5] Riechman et al showed that plasma IL-15 was significantly increased immediately after both at the first and last (30th) session of 10 weeks of resistance exercise training but did not change with training.[39] They also reported resting concentrations, and acute and chronic training changes in IL-15 were not significantly correlated to muscle mass, strength, or quality at baseline or in response to resistance.[39] Raschke and Eckel reported that blood IL-15 level was significantly more enhanced after 8 weeks of moderate intensity resistance training than high intensity.[32] It is unclear if the differences among these studies was due to the use of highly trained vs. relatively untrained human or to the difference between aerobic vs. resistance exercise[5] and the mode of exercise. In this study healthy female subjects performed only JWE showed an increase in plasma IL-15 immediately after acute exercise. Other researchers studying healthy male subjects showed that resistance exercise increased plasma IL-15 levels after training and the lack of plasma sampling immediately after exercise may explain the failure to show a significant change in plasma IL-15,[27, 37, 39] as observed by our study.

Lutz and Quinn suggested that IL-15 inhibits insulin resistance.[40] In this study IL-15 was correlated with IL-6 and TNF-α in 12-wk-trained JWE females but negatively correlated with HOMA-IR after the CRF test. Pre-trainingly in the same group, IL-15 was associated with IL-18 after the CRF test. Activity of IL-15 was also related to other cytokines such as TNF-α, with a regulatory effect over their secretion and a potentialisation of effects in the presence of

these cytokines. One such mechanism involves the muscular production of IL-15, which can modulate the negative effects of TNF-α, primarily at the intermediate metabolism level. IL-15 improves insulin sensitivity in tissues, especially in skeletal muscle.[41]

In this study IL-18 levels of females in JWE training group were lower than those for females in SAE training group both pre-trainingly and post-trainingly. Kadoglou et al showed that this is the first study to provide evidence of decreased IL-18 without weight decline after long-term supervised exercise.[42] In our study there was a positive correlation between serum IL-18 levels and BMI of SAE group females, while there is a positive correlation between IL-18 and WHR of JWE females. Leick et al also showed mRNA of IL-18 is expressed in human AT, and both AT IL-18 mRNA content and systemic levels of IL-18 show a relationship with low limb fat content and high WHR in patients with lipodystrophy.[43] They also showed that plasma IL-18 concentrations were higher in the obese group than those for the non-obese group.[43]

In this study, as in the study by Jung et al resistin levels are decreased in females of JWE group at the end of 12 weeks training.[35] Kadoglou et al reported that sub-group analysis indicated a remarkable decline of resistin in exercise-trained male subjects, whereas this difference became less marked among female subjects.[42] Resistin level was negatively correlated with IL-15 level in 12-wk-trained SAE females after the CRF test but it was positively correlated with IL-15 in pre-training. In this study, resistin levels were also correlated with body weight of SAE females in post-training. Luo et al reported that resistin concentrations in overweight subjects disclosed a significant positive correlation with BMI.[44]

Resistin, TNF-α and IL-18 were implicated in impairing insulin sensitivity of humans and rodents; conversely, two other adipokines, leptin and adiponectin, increased insulin sensitivity of lean and obese rodents.[45] Although it was well-described that the weight-loss was associated with increases in adiponectin, there were inconsistent changes regarding to the other cytokines' association with weight loss. Despite, Ambeba et al showed that femal having a higher percent increase in adiponectin with weight loss[30], in this study adiponectin levels did not change in both groups female with significant weight loss by exercise and traning Since adiponectin is secreted exclusively from white adipose tissue and is an abundant plasma protein, there is a strongly negative correlation between plasma adiponectin concentrations of human and adiposity.[8, 10] Various researchers reported adiponectin levels were associated variably with increased BMI, insulin resistance-related traits, and type 2 DM[10, 46] with obesity reducing adiponectin levels while weight reduction increases

adiponectin.[8] In this study adiponectin levels of JWE female group, had negative association with serum TNF-α level after the CRF test, results which are as expected in general opinions. Gueugnon et al showed that on regular exercise and a balanced diet on adiponectin increased plasma levels.[47] Although Storgaard et al also suggested that plasma adiponectin level was negatively associated with abdominal fat, in our study adiponetctin levels were not correlated with WHR.[6] Adiponectin and TNF-α control each other's synthesis and activity, thus create a balanced physiological situations.[10] Adiponectin inhibits the production of TNF-α and IL-6 whereas TNF-α inhibits the production of adiponectin but stimulates IL-6. On the contrary IL-6 attenuates TNF-α expression.[18] In contrast to our study, Gueugnon et al showed that in obese adolescents, a long-term combination of aerobic exercise and a balanced diet, inducing change in body composition and improving insulin sensitivity, markedly increased adiponectin.[47] Rubin et al also showed that HOMA-IR was significantly negatively associated with adiponectin in the mid-pubertal adolescent girls.[12] Simons et al reported that diet-induced weight loss in obese individuals resulted in augmented adiponectin expression.[48] In this study adiponectin level of JWE group females was weakly correlated with resistin. Gueugnon et al reported that the lack of association between resistin and adiponectin is an interesting finding in studies investigating adults.[47] In our study , Il-17 level of SAE female group was strongly negatively correlated with both WHR and adiponectin after the CRF test, whereas it was positively correlated with leptin before the CRF test.

While IL-17 level of SAE female group was strongly positively correlated with serum IL-18 after CRF test both pre-and post-trainingly, IL-17 level of JWE female group was only positively correlated with serum IL-18 after CRF test post-trainingly. That's the reason that adipose tissue may be an important target in the role of IL-17 in the pathogenesis of insulin resistance. Zuniga et al showed that IL-17 expressed of genes encoding proadipogenic transcription factors, adiponectin, and molecules linking lipid and glucose metabolism.[13] Therefore, IL-17 could play pivotal roles in the pathogenesis of insulin resistance[17] both before and after training in JWE females since there is a strong positive correlation between IL-17 and glucose levels. Although, Zuniga et al showed that IL-17 deficiency was also associated with a significant reduction in serum insulin, in our study there was no correlation among IL-17 ,insulin and HOMA-IR.[13] Ohshima et al showed that IL-17-antibody treatment increased serum adiponectin concentration, decreased serum TNF-α level. that was well known to directly inhibit insulin signaling as a result in insulin resistance.[17] For these reasons, we thought that IL-17, a new hormone such as IL-6, is increasing the level of blood glucose. IL-17 also mediates immune responses by triggering the production of other proinflammatory

cytokines, such as IL-6, IL-18 and TNF-α which is involved in the pathogenesis of insulin resistance.[13] Recent studies have also shown IL-18, in synergy with IL-23, can promote IL-17-production from Th17 cells.[49] Ahn et al detected a direct interaction between IL-18 and Th17 differentiation.[50]

Different authors suggested that resistin has been shown to play a significant role in obesity-induced insulin resistance.[8, 47] However, a lot of authors reported no change in the resistin levels of obese individuals and HOMA-IR after a hypo-energetic diet and moderate physical activity.[44, 47, 51] Our findings suggest that resistin may play an important role in the improvement often observed in female HOMA-IR levels with exercise. In animals, studies have shown an inhibitory effect of resistin on insulin-stimulated glucose uptake, and in human beings resistin is proposed to link obesity and insulin.[50] However, Gueugnon et al showed no significant correlation between resistin levels and markers of insulin resistance.[47] Despite the fact that in the present study, resistin was negatively correlated with serum TNF-α, WHR and HOMA-IR levels of JWE female group post-trainingly, no correlation was established in the study by Jung et al.[35] Resistin is associated with obesity and type 2 DM in animal models, but its role in humans remains intricate.[44] Rabe et al suggested that expression of resistin is increased by TNF-α and IL-6. Conversely, resistin upregulates the production of TNF-α and IL-6.[10] This correlation between glucose intolerance and resistin concentrations might be explained by the fact that adipocytes are the major source of resistin in humans. The association between serum resistin and TNF-α concentration in the current study supports the hypothesis that circulating resistin may play both metabolic and inflammatory role in females. Galic et al suggested plasma IL-6 levels are increased in type 2 DM and are positively correlated with body mass.[8] In this study , HOMA-IR level of JWE group females was positively correlated with TNF-α, conversely it was negatively correlated with IL-6. This finding supports the idea that exercise-induced elevation of IL-6 plasma levels lead to increased circulating levels of several potent anti-inflammatory cytokines, suggesting that IL-6 may also have anti-inflammatory properties.[52] Rubin et al showed that the HOMA-IR was not associated with neither TNF-α or IL-6 of mid-pubertal adolescent girls.[12] It appears that healthy, well-trained humans are more sensitive to IL-6, whereas untrained people have impaired IL-6 signaling and compensatory high circulating IL-6 levels.[53] Schnyder and Handschin hypothesized that IL-6 stimulates the secretion of glucagon-like peptide-1 (GLP-1), which results in an enhanced secretion of insulin.[52] It is also demonstrated that IL-6 increases insulin-stimulated glucose uptake in vitro.[28] In addition, Schnyder and Handschin

reported that overexpression of IL-6 in transgenic mice results in reduced body mass and impaired insulin-stimulated glucose uptake by skeletal muscle.[52] However, a lot of studies demonstrating that IL-6 is released from skeletal muscle have shed a different light on the role of IL-6 in the aetiology of insulin resistance since insulin action is known to be enhanced in the period immediately after exercise.[8] Muscle-derived IL-6 is likely to inhibit low-level proinflammatory production such as TNF-α, resistin and IL-18 and to increase production such as IL-15, thereby these adipokines induce insulin resistance and thus become an important player in mediating the beneficial health effects of exercise.

As expected, IL-18, which is known to be important for insulin resistance, is correlated with resistin in JWE group females in pre-training after the test and also TNF α level of SAE group females in post-training. Leick et al reported that IL-18 was correlated with insulin resistance. It suggests that training induced reduction in adipose tissue (AT) IL-18 expression and it may be a contributing mechanism to improve insulin sensitivity after training.[43] But in their study, while acute exercise did not affect IL-18 mRNA expression at the studied time-points, exercise training reduced the AT IL-18 mRNA content. Hence they suggested that the training-induced reduced IL-18 which may play a role in improved insulin sensitivity with regular physical activity and IL-18 concentration was positively correlated with insulin resistance.[43] Somewhat paradoxically, there were negative correlations between IL-18 both IL-6 and HOMA-IR levels of JWE female group. These results may be due to the fact that IL-18 is added to a growing list of catabolic, proinflammatory cytokines that paradoxically required to maintain pathways which are important for fatty acid oxidation, and thus prevent insulin resistance.[54]

Although Storgaard et al showed that a positive effect of acute and chronic training on expression of these receptors exists in skeletal muscle and it is consistent with the positive association between VO_{2max} and adiponectin receptors.[6] In the present study there was a positive correlation between serum adiponectin levels and VO_{2max} levels of SAE female group pre-trainingly but this relationship disappeared after the training. This result might be related to sample size of the study. In our study, IL-17 serum level was also positively correlated with IL-15 which was thought to be associated with muscle mass and strength, in pre-training of SAE group after the CRF test. Dufresne et al showed that FEV1 and BMI were negatively correlated with IL-17.[10] They also showed that some negative correlations were found for limb muscle (e.g., between biceps strength and quadriceps) cross-sectional area and IL-17.[55]

In this study serum IL-15 level of SAE female group was strongly correlated with VO_{2max} in the post-training period, whereas Christiansen et al have found no correlation between

changes in IL-15 and VO_{2max}.[27] Although, IL-6 level of JWE female group was positively correlated with VO_{2max}, but not with TNF-α, serum concentration of resistin was positively correlated with body weights. However they were negatively correlated with VO_{2max} level of SAE female group after training. Christiansen et al found that VO_{2max} was found to be inversely correlated with circulating IL-6 at baseline but not with TNF-α, whereas no association was found between changes in IL-6 and VO_{2max}.[27] On the contrary, Rubin et al found that VO_{2max} was negatively correlated with TNF-α in the girls but not with IL-6.[12] Gokhale et al suggested that plasma IL-6 increases in an exponential fashion with exercise and is related to exercise intensity, the mass of muscle recruited, and one's endurance capacity, especially duration of the exercise,[33] whereas the mode of exercise has little effect.[28] While Jung et al showed that at the end of 12 weeks, serum leptin level had significantly been decreased[35], serum leptin levels didn't changed after training in both groups in this study. As shown in table 5, in JWE female group, serum leptin level increased after the CRF test. Christiansen et al showed that both diet-induced weight loss and exercise-diet-induced weight-loss combined obese in healthy males and females' leptin mRNA was decreased in adipose tissue but with pure exercise no changes observed.[56] Simons et al reported that diet-induced weight loss in obese individuals resulted in diminished leptin concentrations.[48] As shown in table 6, serum leptin level of SAE female group was only correlated with body mass. Galic et al also showed that there is a positive linear correlation between circulating levels of serum leptin and total body fat mass.[8] Sjögren et al showed that even after a 6-month period of increased physical activity in overweight elderly individuals, circulating leptin concentrations were decreased despite increased levels of leptin mRNA in adipose tissue.[57] Our studies showed that since leptin is correlated with IL-17 in SAE female group, leptin is known as an immune stimulator and should increase IL-17.[58]

Conclusion

In this study, there was no extra advantage of both of the aerobic training programs, but aerobics training programs led to significant changes in VO_{2max} capacity. 12-week training programs, as well as step aerobics and jogging-walking did not cause significant changes in the level of serum IL-17 in sedentary females. TNF-α, IL-15 and IL-18 levels were higher in step-aerobics female group than jogging-running female group either in pre-training and post-training period while leptin decreased more in step-aerobics female group than jogging-walking female group after cardio-respiratory fitness test. But serum resistin decreased significantly in jogging-walking female group only after training. Jogging-walking female

group was also found to have increased leptin and IL-15 levels by cardio-respiratory fitness test while step-aerobics female group had increased only TNF-α level by the test. These may be of clinical interest and add to previous findings that we and others have shown that weight loss in fat mass and improvement in skeletal muscle mass by aerobics exercises and it has beneficial versus deterimetal effects, might depend on the intensity, frequency, type, mode, duration and other variables in secretion..

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Tables

Table 1: Jogging-walking exercise (JWE) program (20).

Week	Contents of Exercise	Duration of exercise (min)	Intensity of training (%)	Number of exercise (day/week)	Distance of exercise (km)	Speed of running (km/h)
1-2	Warm-up	5	80	5	3.5	6
	Main period	35				
	Cool-down	10				
3-4	Warm-up	5	80	5	4	6.9
	Main period	35				
	Cool-down	10				
5-6	Warm-up	5	80	5	4.8	7.2
	Main period	40				
	Cool-down	10				
7-8	Warm-up	5	80	5	5	7.5
	Main period	40				
	Cool-down	10				
9-10	Warm-up	5	80	5	5.8	7.7
	Main period	45				
	Cool-down	10				
11-12	Warm-up	5	80	5	6	8
	Main period	45				
	Cool-down	10				

NOTE: The distance of JWE was increased by adding of 500-meter in biweekly, to ensure desired exercise intensity.

Table 2: Step-aerobics drills

Basic movements for aerobics	Basic movements for step	Repetitions
March	Basic step	8
Running	Wide step	8
Step touch	Tap up, tap down	8
Step touches front and back	Knee lift	8
Double step touch	Leg curl	8
Grapevine	Leg opening side and back	8
Side to side	Kick	8
Knee lift	Knee lift and Leg curl repeater	8
Leg curl	Straddle up-do	8
Leg opening side and back	Turn step	8
Kick side and front	Turn travel	8
Lunge side and back	Over the top	8
Squat	Across the top	8
Slide	Corner to corner	8
Jumping jacks	Lunge	8
Jumping (knee to chest)	Reverse step	8

Table 3: Step-aerobics exercise (SAE) program.

Week	Contents of Exercise	Duration of exercise (min.)	Intensity of training (%)	Number of exercise (day/week)	Number of set (times)	Number of repeat (times)
1-2	Warm-up	10	80	5	2	256
	Main period	30				
	Cool-down	10				
3-4	Warm-up	10	80	5	2	320
	Main period	30				
	Cool-down	10				
5-6	Warm-up	10	80	5	2	384
	Main period	35				
	Cool-down	10				
7-8	Warm-up	10	80	5	2	448
	Main period	35				
	Cool-down	10				
9-10	Warm-up	10	80	5	2	512
	Main period	40				
	Cool-down	10				
11-12	Warm-up	10	80	5	2	576
	Main period	40				
	Cool-down	10				

NOTE: The number of repetitions of SAE was increased by adding of 8-repeats for every drill in bi-weekly, to ensure desired exercise intensity.[15]

Table 4: Comparison of the jogging-walking and steps-aerobics groups in pre-training and post-training respectively

	Jogging-walking exercise (n=15)		Steps aerobics exercise(n=10)	
	Pre-training	Post training	Pre-training	Post training
Weight (kg)	74,70±3,44[a]	70,90±3,29[b]	63,37±2,23[a]	59,88±2,15[b]
Body mass index (BMI)	29,08±1,29[c]	27,59±1,23[d]	25,76±0,84[c]	24,31±0,69[d]
Fat mass (%)	35,81±1,76	32,67±1,91	31,23±1,76	27,33±1,96
Waist-to hip ratio (WHR)	78, 70±1,81	78,38±1,81	80,25±1,26	79,51±1,93
VO_{2max}	30,86±2,03[e]	44,10±1,61[f]	38,30±2,32[e]	52,65±2,32[f]

a=p<0,010, b=p<0.011, c= p<0,044, d=p<0,030, e=p0.026, f=p<00.007.

Table 5: Comparison of the myokines, adipokines and HOMA-IR of jogging-walking and steps-aerobics groups in pre-training and post-training respectively.

	Jogging-walking exercise (n=15)				Steps aerobic exercise (n=10)			
	Pre-training		Post-training		Pre-training		Post-training	
	Pre- CRF test	Post-CRF test	Pre- CRF test	Post- CRF test	Pre- CRF test	Post CRF test	Pre- CRF test	Post- CRF test
TNF-α	57,48±14,28	55,23±10,50[a]	56,07±13,79[b]	62,90±12,86[c]	95,65±18,57	106,48±13,80[a]	102,87±18,55[b]	116,67±20,28[c]
IL-6	9,40±0,67	9,96±0,86	16,65±6,09	17,91±7,30	11,24±1,32	11,89±1,43	10,55±1,37	22,62±11,25
IL-15	21,57±4,18	18,53±3,37[b, e]	24,23±4,05	26,00±4,64[e]	30,80±5,79	32,00±2,34[b]	29,15±2,80	26,90±5,04
IL-17	26,90±2,70	26,02±3,02	29,52±3,64	27,91±3,14	48,30±21,46	56,52±32,84	60,92±37,63	69,37±42,32
IL-18	992,67±105,54	850,67±94,93[d]	896,00±126,35	865,33±67,38[x]	1906,00±734,06	2177,00±864,15[d]	1947,00±917,60	1869,00±590,35[x]
Leptin	3105,60±142,64	3043,47±202,48	2973,33±117,65[y]	3196,67±72,20[y]	2811,50±224,55	2853,90±247,06	2528,40±279,18	2875,80±191,21
Adiponectin	6,06±0,69	5,45±0,81	7,18±0,80	6,89±0,57	5,93±0,75	5,18±0,75	6,61±1,00	6,09±0,80
Resistin	25089,33±1156,60[z]	23928,00±1869,53	22196,00±1278,23[z]	23551,33±1235,98	24589,00±1223,61	24329,00±2317,77	21850,00±1588,07	21338,00±1356,20
HOMA-IR	2,06±0,26	1,72±0,10	2,88±0,70	2,14±0,22	2,42±0,35	1,39±0,21	1,28±0,29	3,11±0,95

a=p<0,006, b=p<0, 01, c= p<0, 04, d=p<0.016, e=p<0.019, x=p<0.01, y=p<0.023, z=p<0.047.

Table 6: Correlations of the myokines and adipokines in jogging-walking and steps-aerobics during pre-training and post-training of sedentary females

	Steps-aerobics exercise group (n=10)				Jogging-walking exercise group (n=15)			
	Pre-training		Post-training		Pre-training		Post-training	
	Pretest	Posttest	Pretest	Posttest	Pretest	Posttest	Pretest	Posttest
IL-6 IL-15	r=,200 p>,580	r=,442 p>,200	r=,588 p>,074	r=,624* p<,050	r=-,032 p>,909	r=,375 p>,169	r=,014 p>,960	r=-,245 p>,379
IL-6 IL-17	r=-,139 p>,701	r=,340 p>,336	r=,297 p>,405	r=,668* p>,035	r=-,238 p>,394	r=-,306 p>,268	r=-,256 p>,358	r=,507 p>,050
IL-6 IL-18	r=,152 p>,676	r=,188 p>,603	r=,406 p>,244	r=-,389 p>,266	r=-,143 p>,611	r=-,496 p>,060	r=-,599* p>,018	r=,152 p>,589
IL-6 TNF-α	r=-,345 p>,328	r=,292 p>,413	r=,061 p>,867	r=,335 p>,343	r=-,463 p>,082	r=-,071 p>,800	r=-,079 p>,781	r=-,186 p>,508
IL-6 leptin	r=-,139 p>,701	r=-,055 p>,881	r=,442 p>,200	r=,115 p>,751	r=-,141 p>,616	r=,207 p>,459	r=,429 p>,111	r=,475 p>074
IL-6 adiponectin	r=,261 p>,467	r=,345 p>,328	r=,200 p>,580	r=,479 p>,162	r=-,182 p>,515	r=-,311 p>,260	r=,250 p>,369	r=,291 p>,292
IL-6 resistin	r=-,200 p>,580	r=,333 p>,347	r=-,261 p>,467	r=-,455 p>,187	r=,148 p>,598	r=-,257 p>,355	r=-,229 p>,413	r=,382 p>,160
IL-15 IL-17	r=,455 p>,187	r=,888* p<,001	r=,539 p>,108	r=,418 p>,229	r=,073 p>,795	r=-,222 p>,427	r=,166 p>,554	r=,027 p>,924
IL-15 IL-18	r=,527 p>,117	r=,782* p<,008	r=,394 p>,260	r=-,146 p>,688	r=,350 p>,201	r=-,072 p>,799	r=,095 p>,737	r=-,127 p>,651
IL-15 TNF-α	r=,127 p>,726	r=,328 p>,354	r=,061 p>,867	r=,110 p>,763	r=,483 p>,069	r=,359 p>,189	r=,582* p<023	r=,438 p>,102
IL-15 leptin	r=,042 p>,907	r=,188 p>,603	r=,,285 p>,425	r=,552 p>,098	r=-,032 p>,909	r=-,029 p>,919	r=,243 p>,383	r=,224 p>,423
IL-15 adiponectin	r=-,030 p>,934	r=-,030 p>,934	r=-,103 p>,777	r=-,055 p>,881	r=-,190 p>,498	r=,009 p>,975	r=-,057 p>,840	r=-,303 p>,273
IL-15 resistin	r=-,018 p>,960	r=-,636* p<,048	r=-,358 p>,310	r=-,721* p>,019	r=-,059 p>,835	r=-,083 p>,770	r=-,393 p>,147	r=-,079 p>,780
IL-17 IL-18	r=,345 p>,328	r=,778* p<,008	r=,273 p>,446	r=,122 p>,738	r=,386 p>,156	r=-,011 p>,970	r=,136 p>,629	r=,718* p<,003
IL-17 TNF-α	r=,-,139 p>,701	r=,390 p>,265	r=,207 p>,565	r=-,488 p>,153	r=,082 p>,770	r=-,318 p>,247	r=-,113 p>,689	r=-,422 p>,117
IL-17 leptin	r=-,139 p>,701	r=,195 p>,590	r=0, 685* p<0,029	r=,527 p>,117	r=,011 p>,970	r=,434 p>,106	r=,152 p>,589	r=-,014 p>,960
IL-17 adiponectin	r=-,152 p>,676	r=-,024 p>,947	r=-,382 p>,276	r=-,638* p<,047	r=,163 p>,562	r=-,089 p>,751	r=,275 p>,321	r=-,110 p>,696
IL-17 resistin	r=-,,358 p>,310	r=,608 p>,062	r=,200 p>,580	r=-,164 p>,651	r=,032 p>,909	r=,009 p>,975	r=,134 p>,634	r=,238 p>,394
IL-18 TNF-α	r=-,-,030 p>,934	r=,188 p>,602	r=,726* p<0,018	r=-,278 p>,436	r=,129 p>,647	r=-,021 p>,940	r=,343 p>,210	r=-,420 p>,119
IL-18 leptin	r=-,042 p>,907	r=,273 p>,446	r=,030 p>,934	r=,067 p>,854	r=-,061 p>,830	r=,086 p>,761	r=-,336 p>,221	r=,267 p>,337
IL-18 adiponectin	r=-,515 p>,128	r=,394 p>,260	r=,261 p>,467	r=-,450 p>,192	r=,007 p>,980	r=,157 p>,576	r=-,048 p>,864	r=,442 p,099
IL-18 resistin	r=,321 p>,365	r=,794* p<,006	r=,164 p>,651	r=,067 p>,854	r=-,275 p>,321	r=-,129 p>,648	r=-,143 p>,611	r=,550* p<,034
TNF-α leptin	r=0, 661* p<0,038	*r=-,231* *p>,521*	r=,049 p>,894	r=,213 p>,554	r=-,075 p>,790	r=-,313 p>,256	r=-,164 p>,558	r=,121 p>,666
TNF-α adiponectin	r=,236 p>,511	r=,049 p>,894	r=-,061 p>,867	r=,518 p>,125	r=-,165 p>,557	r=-,282 p>,308	r=-,571* p<,026	r=-,206 p>,462
TNF-α resistin	r=,345 p>,328	r=,067 p>,854	r=,262 p>,464	r=,274 p>,443	r=-,251 p>,367	r=-,159 p>,571	r=-,714* p<,003	r=-,518* p<,048
leptin adiponectin	r=-,103 p>,777	r=,139 p>,701	r=,006 p>,987	r=,030 p>,934	r=-,093 p>,742	r=,300 p>,277	r=,396 p>,143	r=,475 p>,073

leptin resistin	r=,091 p>,803	r=,600 p>,067	r=,261 p>,467	r=-,152 p>,676	r=,018 p>,950	r=,250 p>,369	r=,175 p>,533	r=,068 p>,810
Adiponectin resistin	r=,067 p>,855	r=-,261 p>,467	r=-,588 p>,074	r=,006 p>,987	r=,157 p>,576	r=,246 p>,376	r=,571* p<026	r=-,127 p>,652