Original Article

Anti-Inflammatory Effects of a Period of Aerobic Training and Vitamin D Supplementation in Postmenopausal Women with Metabolic Syndrome

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Abstract

Background: Inflammatory markers of blood are critical predictors of chronic diseases as well as exacerbating risk factors. Exercise is a well-known strategy to reduce the risk of inflammation and chronic disease. The present study aimed to investigate the anti-inflammatory effects of a period of aerobic training and vitamin D supplementation (AT + Vit D) in postmenopausal women with metabolic syndrome. **Methods:** This quasi-experimental research was performed on forty-six patients with metabolic syndrome who were selected according to the available sampling method, and were randomly divided into four groups: AT + Vit D (50,000 IU), AT, Vit D (50,000 IU), and control (C). The training protocol consisted of 40–60 min of AT 60–75% of maximal heart rate, three times a week, for 8 weeks. One-way Analysis of variance (ANOVA) and *t*-test were used to compare the between and within groups; the Bonferroni *post hoc* test was used if significant differences were found. **Results:** The combination of exercise and vitamin D significantly reduced C-reactive protein (CRP) ($P = 0.001$), interleukin-6 (IL-6) ($P = 0.001$), and improved the metabolic syndrome indices ($P = 0.001$ in all indices). The results also show that the improvement in the metabolic syndrome indices, CRP, and IL-6 was more significant in AT + Vit D, compared to AT or Vit D alone. **Conclusions:** The findings from the present study suggested that a sedentary lifestyle and vitamin D deficiency accelerated the occurrence of metabolic syndrome probably by increasing the anti-inflammatory. Additionally, adequate levels of plasma vitamin D are necessary to achieve the beneficial metabolic effects of AT.

Keywords: *Exercise, inflammatory markers, metabolic syndrome, vitamin D*

Introduction

Metabolic syndrome is a condition known as mild inflammation. It can cause insulin resistance and the consequence is the development of metabolic diseases, such as diabetes and cardiovascular disease.[1,2] The exact etiology of the metabolic syndrome is unclear[3]. Probably, it is caused by the interaction of genetic, metabolic, and environmental factors (including diet and physical activity).[2,4] The prevalence of metabolic syndrome is associated with increased levels of inflammatory cytokines such as C-reactive protein (CRP) and interleukin-6 (IL-6) in menopause.[1,5] Based on the results of the studies, increased concentrations of CRP and IL-6 are known to be predictive factors of diabetes and the metabolic syndrome.[5,6] Accordingly, numerous therapeutic drug approaches have been proposed to counter the oxidative stress in the primary stage of inflammation. Many of these methods are medicinal and have side effects.[7,8] Therefore, many researchers believe that a combination of aerobic training (AT) and a suitable diet reduces inflammation.[9,10] According to the results of the studies, AT has an important role in modulating inflammatory responses at both the acute and chronic levels.[11,12] Recently, vitamin D (Vit D) has been considered due to its antioxidant role and some researchers have pointed to the role of Vit D in modulating inflammation.[13,14]

However, evidence regarding the anti-inflammatory effect of Vit D is scarce in human clinical studies; more importantly, there is no convincing evidence of the simultaneous effect of AT and Vit D supplementation on the improvement of immune deficits in postmenopausal women with metabolic syndrome. This study aimed to evaluate the anti-inflammatory effects of AT + Vit D supplementation in postmenopausal women with metabolic syndrome.

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Methods

Study population and design

This is a semi-experimental study. The target population of this study was postmenopausal women with metabolic syndrome (50–60 years old) of Kermanshah. Forty-six patients with metabolic syndrome were selected according to the available sampling method and were randomly (using a random number table) divided into four groups: AT + Vit D (50,000 IU), AT, Vit D (50,000 IU), and control (C) [Figure 1]. The inclusion criteria included the metabolic syndrome based on adult Treatment Panel III (NCEP: ATP III) criteria,[15] 25-hydroxyvitamin D3 (25(OH)D serum levels between 10 and 20 ng/mL, not having a specific diet, regular exercise program in the past year, and more than a year of complete menstrual cycle cessation. The exclusion criteria included failure to participate in an intervention program for more than one session, failure to follow the recommended diet plan, and other disorders.[16,17] It is worth mentioning that one subject in the AT + Vit D group and one subject in the C group refused to continue the program.

Three days before the start of the study, explanations about research conduction were provided for subjects and consent forms were provided and signed by all 48 subjects. Also, the physical activity readiness questionnaire (PARQ), 3-day dietary questionnaire, nutritional questionnaire, and health history questionnaire (HHQ) were completed. On the first day, the height was measured to the nearest 0.5 cm using a stadiometer (DETECTO, Model 3PHTROD-WM, USA) and waist circumference (WC) was measured with a tape measure. The body weight (BW), body mass index (BMI), and body fat percentage (BFP) were obtained by a bioelectric impedance body composition analyzer (Zeus 9.9 PLUS; Jawon Medical Co., Ltd., Kungsang Bukdo, South Korea) in the fasting state, with minimum clothes possible, and without shoes. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) measurements took place each day between 8.00 a.m. and 10.00 a.m. under the protocol of the American Heart Association. The mean arterial pressure (MAP) was calculated as DBP + (0.333 [SBP – DBP]).[18]

Aerobic training

The 8-week AT program consisted of a total of 45–60 min at 60–75% of maximum heart rate (MHR), three sessions per week (135–180 min/week) [Table 1]. The aerobic exercise consisted of three phases: Warm-up (10 min), aerobic exercise (20–40 min), and cool down (10 min). The warm-up protocol consisted of stretching movements, walking, and jogging. Then, it was followed by the aerobic exercise phase. At the baseline, the training phase commenced with 20 min of walking and jogging at 60% HR_{Max} in the first week and increased to 40-minute running at 75% HR_{Max} R per week by the final week of training [Table 1]. To assure the maintenance of the desired heart rate (exercise intensity) during the aerobic exercise phase, each participant underwent heart-rate monitoring with polar (model: FT1). Also, the 6–20 Borg scale was used to ensure the actual heart rate at 10–13 of the rating of perceived exertion (RPE).[19] The HR_{Max} formula was used to determine the target heart rate [HR_{Max} = 220−age].

Vitamin D supplementation

In this study, both the AT + Vit D group and Vit D group received 50,000 units of Vit D supplement once per week at the beginning of the week made by the Zahravi Pharmaceutical Company in Iran. The C and AT groups also received placebo weekly (made by the Zahravi Pharmaceutical Company, Iran) with the same shape, color, smell, and tastes as Vit D supplement pills, over a period of 8 weeks.[20]

Blood sampling

Blood samples were taken twice a day before the first training session (pre-test) and all the subjects arrived at 8:00 a.m. on the day of the test in the clinical laboratory with a fasting state of more than 12 h. After maintaining the subjects in a stable state for 30 min, 20 mL of venous blood was sampled from the antecubital vein using an anticoagulant treated syringe. Blood lipid profile (triglycerides [TG], and high-density lipoprotein [HDL]) were measured enzymatically with the Hitachi Kit, Tokyo, Japan. Glucose with the enzymatic method (Pars Azmun kit made in Iran) to evaluate CRP was used (human kit Diagnostics Biochem, made in Canada by ELISA) with the coefficient of variation and sensitivity of measurement method 5.7 and 8.9 ng/mL, respectively, and to evaluate IL-6 human immunodeficiency kit eBioscience, made in Australia by ELISA was used, with a sensitivity of 0.05 pg/mL.

Ethical considerations

Informed consent was obtained from all the subjects. The present project was approved by the ethics committee of Kurdistan University of Medical Sciences (code number: IR.MUK.REC.1398.241) and registered in the Iranian Clinical Trial Registration Center under the code IRCT20200122046217N1.

Statistical analysis

All statistical analyses were performed using the SPSS statistical software (version 21; SPSS Inc., Chicago, IL, USA) and were used at a significant level of $P < 0.05$. The Shapiro–Wilk's test was used for evaluating the normality of the

Table 1: Aerobic training program

Stage	Mode	Duration	Intensity
Warm-up	Stretching	15 min	HRR 45~55%
Main Exercise	1~4 week	20~30 min	HRR 60~65%
	5~8 week	30~40 min	HRR 65-75%
Cool Down	Stretching	10 min	HRR 40~50%

distribution. In order to compare the mean metabolic syndrome risk factors between and within the groups, one-way ANOVA and *t*-test were used, respectively. The Bonferroni *post hoc* test was used if significant differences were found.

Results

There was no significant change in the physical activity level and diet within and between the groups before and after the intervention; therefore, the results are not mentioned. The findings on some demographic information and anthropometric indices of the subjects and their between-group comparison are presented in Table 2. Based on the results, there were significant differences in the mean of BW, BMI, and BFP between the pre-test and post-test conditions. After 8 weeks, the BW, BMI, and BFP significantly decreased in AT + Vit D, AT, Vit D groups, while in the C group, a significant increase in BW, BMI, and BFP levels was observed [Table 2].

The results of one-way ANOVA showed no significant difference in BW, BMI, and BFP between the groups in the pre-test, however in the post-test, there was a significant difference in the above variables between the groups. The results of the Bonferroni *post hoc* test shows that the lowest anthropometric indices (BW, BMI, and Body Fat Percentage (BFP)) were observed in the AT + Vit D group. Also, the AT group showed better improvement in the PBF compared to the Vit D group [Table 2].

There were significant differences in the metabolic syndrome factors between the pre-test and post-test conditions, as detailed in Table 3. The results of one-way ANOVA showed no significant difference in the metabolic syndrome factors between the groups in the pre-test, however, in the post-test, there was a significant difference in the metabolic syndrome factors between the groups. The results of the Bonferroni *post hoc* test showed that compared to the C group, significant differences were observed in all the metabolic syndrome factors in all the intervention groups; while significant differences were observed in all the metabolic syndrome factors (except for WC) between AT + Vit D compared with the other groups [Table 3]. Also, significant differences were observed in TG, and glucose between AT compared with Vit D groups ($P = 0.001$, $P = 0.001$) [Table 3].

Figures 2 and 3 show that there were significant differences in the CRP and IL-6 between the pre-test and post-test conditions. The CRP and IL-6 changes were significant in AT + Vit D, AT, and Vit D compared to C. Also, AT + Vit D had significantly lower CRP, and IL-6 compared with AT, Vit D groups. Also, a significantly lower amount of CRP was observed in AT compared to Vit D ($P = 0.001$).

Discussion

The results showed that 8 weeks of AT + Vit D had a significant effect on metabolic syndrome in elderly women

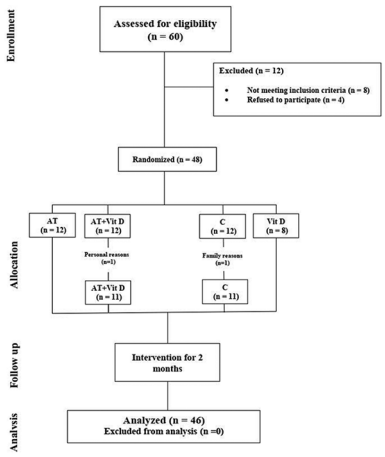

Figure 1: Flow diagram of the progress through the phases of a parallel randomized trial of four groups

with metabolic syndrome. However, Vit D and AT alone had significant effects on the metabolic syndrome indices. They had less effect compared to the concurrent effect of AT + Vit D. These results are consistent with the results of Babaei *et al*.[21] (2014), Hosseini *et al*. (2017),[22] and Hosseini *et al*. (2020).[20] According to the results of the studies, regular AT increases daily energy intake, improves and increases fat oxidation in the skeletal muscles and mitochondria, and ultimately improves the metabolic syndrome parameters.[23,24]

On the other hand, studies have reported that Vit D deficiency is linked to the prevalence of diabetes, impaired glucose tolerance, and metabolic syndrome.[25,26] Scragg *et al*. (2004) showed that elevated serum 25-hydroxyvitamin D levels in obese individuals were significantly lower than in healthy weight individuals.[27] Hosseini *et al*. (2017) reported that a high intake of Vit D may improve the metabolic syndrome indices.[22] The underlying mechanism might be that hypovitaminosis D leads to increased parathyroid hormone (PTH), which in turn increases intracellular Ca^{++}. In turn, this increase blocks the insulin receptors in the target tissues and blocks the Glut-4 channel. On the other hand, the insulin release from pancreatic beta cells depends on intracellular calcium concentration. Consequently, hypovitaminosis D can impair the insulin function, glucose metabolism, and other metabolic processes in the adipose tissue.[13,21] Based on the results of the present study, AT caused a little improvement in the metabolic syndrome indices. However, the effect of AT + Vit D was greater than the other interventions in the present study in improving the metabolic syndrome indices. It might likely be due to the higher sensitivity of visceral adipocytes, which stimulate the lipolytic process in response to catecholamine. Also, AT + Vit D may have a direct effect on the insulin sensitivity and beta-cell function.[28,29]

The results showed that 8 weeks of AT + Vit D had a significant effect on the anti-inflammatory factors in elderly

Table 2: Mean±SD of demographic information and anthropometric indices

Variables	AT + Vit D (*n*=11)	AT (*n*=12)	Vit D (*n*=12)	C (*n*=11)	*P*[a]
Age (years)	56.01±2.23	45.25±2.22	55.25±2.01	56.36±1.91	*P*=0.651
Height	158.81±2.75	161±2.89	157.33±1.66	159.27±1.48	*P*=0.782
BW (kg)					
Before	87±1.94	87.91±1.92	86.16±1.99	87.27±1.48	0.546
After	83.09±1.30[€¥µ]	85±1.34[µ]	84.58±1.67[µ]	89.81±1.25	0.001[¥]
P[b]	*P*=0.001*	*P*=0.002*	*P*=0.003*	*P*=0.001*	
BMI (kg/m^2)					
Before	34.51±1.21	33.94±1.24	34.82±1.20	34.41±1.01	0.632
After	32.95±0.92[¥µ]	32.81±1.20 [µ]	34.18±1.26[µ]	35.41±0.89	0.001[¥]
P[b]	*P*=0.001*	*P*=0.002*	*P*=0.003*	*P*=0.001*	
BFP (%)					
Before	42.90±1.57	42.25±1.35	41.50±1.44	42.62±1.40	0.584
After	37.63±1.36[¥µ]	38.91±1.08[¥µ]	40.58±1.67[µ]	45.01±0.89	0.001[¥]
P[b]	*P*=0.001*	*P*=0.001*	*P*=0.049*	*P*=0.001*	

AT + Vit D group, Aerobic training and vitamin D supplementation, AT group, Aerobic training; Vit D group, vitamin D supplementation; C group, that had neither aerobic training nor Vit D. *P* values with superscript "a" are calculated using one-way analysis of variance test followed by *post hoc* Bonferroni test; superscript letter "b" indicates that values are calculated using paired *t*-test. *Significantly different in comparison pre- and post-test within the groups. [£]Significantly different in the comparison between the groups. [¥]Significantly different in comparison with pre- and post-test between groups. [€]Significance different between AT + Vit D group compared to AT. [¥]Significance different between AT + Vit D group compared to Vit D group. [µ]Significant difference between AT + Vit D, AT, and Vit D groups compared to C group

Table 3: Mean±SD of metabolic syndrome indices

Variables	AT + Vit D (*n*=11)	AT (*n*=12)	Vit D (*n*=12)	C (*n*=11)	*P*[a]
WC (cm)					
Before	97.63±1.02	97.33±1.87	96.33±1.07	97.63±1.12	0.467
After	95.09±1.86[µ]	95.16±2.03[µ]	95.25±0.96[µ]	100.18±1.25	0.001[¥]
P[b]	*P*=0.002*	*P*=0.001*	*P*=0.001*	*P*=0.001*	
MAP (mmHg)					
Before	101.56±1.41	102.23±1.31	102.90±0.68	101.22±1.09	0.816
After	96.71±0.74[€¥µ]	99.37±1.31[µ]	100.29±1.06[µ]	103.37±0.66	0.001[¥]
P[b]	0.001*	*P*=0.001*	*P*=0.001*	*P*=0.002*	
TG (mg/dL)					
Before	191.45±2.38	193.08±2.57	192.25±2.22	192.09±1.92	0.622
After	174.54±2.50[€¥µ]	182.75±3.88[¥µ]	187.41±1.72[µ]	196.27±2.24	0.001[¥]
P[b]	*P*=0.001*	*P*=0.001*	*P*=0.001*	*P*=0.001*	
HDL (mg/dL)					
Before	34.18±1.94	34.08±1.88	35.08±1.37	34.36±1.85	0.743
After	45.45±1.69[€¥µ]	39.91±2.42[µ]	39.75±1.48[µ]	31.54±1.96	0.001[¥]
P[b]	*P*=0.001*	*P*=0.001*	*P*=0.001*	*P*=0.001*	
Glucose (mg/dl)					
Before	143.45±1.21	144.83±1.52	145.08±1.88	145.36±1.50	0.631
After	125.27±1.67[€¥µ]	130.83±2.97[¥µ]	137.33±2.10[µ]	148.45±0.93	0.001[¥]
P[b]	*P*=0.001*	*P*=0.001*	*P*=0.001*	*P*=0.001*	

AT + Vit D group, Aerobic training and vitamin D supplementation, AT group, Aerobic training; Vit D group, vitamin D supplementation; C group, that had neither aerobic training nor Vit D. *P*-values with superscript "a" are calculated using one-way analysis of variance test followed by *post hoc* Bonferroni test; superscript letter "b" indicates values are calculated using paired *t*-test. *Significantly different in comparison pre- and post-test within the groups. [£]Significantly different in the comparison between the groups. [¥]Significantly different in comparison with pre- and post-test between groups. [€]Significance different between AT + Vit D group compared to AT. [¥]Significance different between AT + Vit D group compared to Vit D group. [µ]Significant difference between AT + Vit D, AT, and Vit D groups compared to C group

women with the metabolic syndrome. Although Vit D and AT alone had a significant effect on CRP and IL-6, they were less effective than the concurrent effect of AT + Vit D. Also, according to the results of the present study, AT + Vit D had a significant effect on reducing BFP.

These results are important in interpreting CRP and IL-6 levels since the adipose tissue is one of the major tissues influencing the secretion process of CRP and IL-6. These results are consistent with the results of Matinhomaee *et al.* (2017)[30] and Chandler *et al.* (2014).[30] while

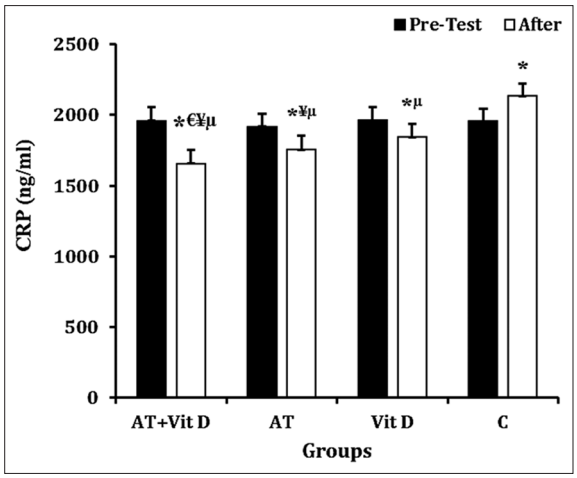

Figure 2: Comparison between mean ± SD of CRP between groups. AT + Vit D group, Aerobic training and vitamin D supplementation, AT group, Aerobic training; Vit D group, vitamin D supplementation; C group, that had neither aerobic training nor Vit D. *P* values with a superscript "a" is calculated using paired *t*-test; superscript letter "b" indicates that values are calculated using two-way ANOVA of variance test followed by *post hoc* Bonferroni test. *: Significantly different in comparison pre- and post-test within the groups. £: Significantly different in the comparison between the groups. ¥: significantly different in comparison with pre- and post-test between groups. €: Significance different between AT + Vit D group compared to AT. ¥: Significance different between AT + Vit D group compared to Vit D group. µ: Significant difference between AT + Vit D, AT, and Vit D groups compared to C group

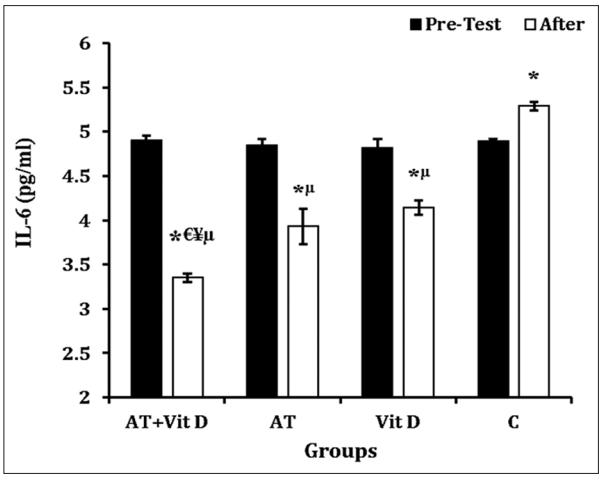

Figure 3: Comparison between mean ± SD of IL-6 between groups. AT + Vit D group, Aerobic training and vitamin D supplementation, AT group, Aerobic training; Vit D group, vitamin D supplementation; C group, that had neither aerobic training nor Vit D. *P* values with a superscript "a" is calculated using paired *t*-test; superscript letter "b" indicates that values are calculated using two-way ANOVA of variance test followed by *post hoc* Bonferroni test. *: Significantly different in comparison pre- and post-test within the groups. £: Significantly different in the comparison between the groups. ¥: Significantly different in comparison with pre- and post-test between groups. €: Significance different between AT + Vit D group compared to AT. ¥: Significance different between AT + Vit D group compared to Vit D group. µ: Significant difference between AT + Vit D, AT, and Vit D groups compared to C group

contradictory to the findings of Donges *et al*. (2010)[31] and Carrillo *et al*. (2012).[32] It seems that contradictory results might be due to the differences in the blood sampling time (the last interval between AT and blood sampling), cytokine measurement methods (ELISA vs. flow cytometry), different training protocols (especially training intensity), and gender and age of the subjects. According to the results of the studies, AT reduces inflammatory markers directly by decreasing the production of cytokines from the adipose tissue, muscle, and mononuclear cells, and indirectly by increasing the insulin sensitivity, increasing the body's antioxidant capacity, improving endothelial function, and reducing body weight and fat.[33,34] Moreover, inflammatory factors are often associated with insulin resistance and beta-cell dysfunction.[22,35] The mechanism by which Vit D affects the inflammatory markers (CRP and IL-6) is still uncertain. However, *in vitro* evidence suggests that by pairing with the Vit D receptors, the active Vit D metabolites (25-hydroxyvitamin D3) and the related compounds can downregulate or reduce CRP, IL-6, and granulocyte macrophage-stimulating macrophages translation and production.[36] Although the findings should be interpreted with caution, the key strength of the present study was the comprehensive examination of the metabolic state in the patient with the metabolic syndrome, and investigating the separate and interactional effect of AT and vitamin D supplementation.

Limitations of the study

The small sample size due to the lack of available volunteers is one of the limitations of this study. Therefore, we suggest investigating the same intervention in larger sample sizes. Finally, we considered non-exercise physical activities and diet data base on the self-reported information, which might affect the results.

Conclusions

The findings from the present study suggested that a sedentary lifestyle and Vit D deficiency accelerated the occurrence of the metabolic syndrome probably by increasing the anti-inflammatory. The combination of exercise and Vit D significantly reduced CRP, IL-6, and improved the metabolic syndrome indices. Additionally, adequate levels of plasma vitamin D are necessary to achieve the beneficial metabolic effects of AT.

Although the underlying mechanisms of these changes have not yet been fully elucidated, due to the positive effects of AT + Vit D, it seems likely that this intervention might be appropriate to recommend for these patients.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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References

1. Mokhayeri Y, Riahi SM, Rahimzadeh S, Pourhoseingholi MA, Hashemi-Nazari SS. Metabolic syndrome prevalence in the Iranian adult's general population and its trend: A systematic review and meta-analysis of observational studies. Diabetes Metab Syndr 2018;12:441-53.
2. Peterson JM, Clark WA, Marrs J-A, Alamian A. Serum adipokines and metabolic syndrome risk factors in hispanic children. Federation of American Societies for Experimental Biology (FASEB).
3. Deen JF, Krieger EV, Slee AE, Arslan A, Arterburn D, Stout KK, *et al*. Metabolic syndrome in adults with congenital heart disease. J Am Heart Assoc 2016;5:e001132.
4. Choi JR, Kim JY, Huh JH, Kim SH, Koh SB. Contribution of obesity as an effect regulator to an association between serum leptin and incident metabolic syndrome. Clin Chim Acta 2018;487:275-80.
5. Darooghegi Mofrad M, Milajerdi A, Koohdani F, Surkan PJ, Azadbakht L. Garlic supplementation reduces circulating C-reactive protein, tumor necrosis factor, and Interleukin-6 in adults: A systematic review and meta-analysis of randomized controlled trials. J Nutr 2019;149:605-18.
6. Ridker PM. From C-reactive protein to interleukin-6 to interleukin-1: Moving upstream to identify novel targets for atheroprotection. Circ Res 2016;118:145-56.
7. Ridker PM, Buring JE, Cook NR, Rifai N. C-reactive protein, the metabolic syndrome, and risk of incident cardiovascular events: An 8-year follow-up of 14 719 initially healthy American women. Circulation 2003;107:391-7.
8. Naci H, Ioannidis JP. Comparative effectiveness of exercise and drug interventions on mortality outcomes: Metaepidemiological study. Br J Sports Med 2015;49:1414-22.
9. Lundberg JO, Carlström M, Weitzberg E. Metabolic effects of dietary nitrate in health and disease. Cell Metab 2018;28:9-22.
10. Wang J, Leung K-S, Chow SK-H, Cheung W-H. Inflammation and age-associated skeletal muscle deterioration (sarcopaenia). J Orthop Translat 2017;10:94-101.
11. Atashak S. The effect of the eight-week progressive concurrent training on inflammatory index of cardiovascular disease predictor, and body composition in sedentary middle-age men. Iran Cardiovasc Res J 2013;2:16-25.
12. Beavers KM, Brinkley TE, Nicklas BJ. Effect of exercise training on chronic inflammation. Clin Chim Acta 2010;411:785-93.
13. Barker T, Martins TB, Hill HR, Kjeldsberg CR, Dixon BM, Schneider ED, *et al*. Circulating pro-inflammatory cytokines are elevated and peak power output correlates with 25-hydroxyvitamin D in vitamin D insufficient adults. Eur J Appl Physiol 2013;113:1523-34.
14. Zhang M, Tan X, Yin C, Wang L, Tie Y, Xiao Y. Serum levels of omentin-1 are increased after weight loss and are particularly associated with increases in obese children with metabolic syndrome. Acta Paediatr 2017;106:1851-6.
15. Grundy SM, Cleeman JI, Bairey Merz CN, Brewer HB Jr, Clark LT, Hunninghake DB, *et al*. Implications of recent clinical trials for the national cholesterol education program adult treatment panel III guidelines. J Am Coll Cardiol 2004;44:720-32.
16. Al-Jiffri O, Al-Sharif F, El-Kader S, Ashmawy E. Weight reduction improves markers of hepatic function and insulin resistance in type-2 diabetic patients with non-alcoholic fatty liver. Afr Health Sci 2013;13:667-72.
17. Johnson NA, Sachinwalla T, Walton DW, Smith K, Armstrong A, Thompson MW, *et al*. Aerobic exercise training reduces hepatic and visceral lipids in obese individuals without weight loss. Hepatology 2009;50:1105-12.
18. Townsend RR, Wilkinson IB, Schiffrin EL, Avolio AP, Chirinos JA, Cockcroft JR, *et al*. Recommendations for improving and standardizing vascular research on arterial stiffness: A scientific statement from the American heart association. Hypertension 2015;66:698-722.
19. Heil DP. ACSM's guidelines for exercise testing and prescription. Med Sci Sports Exerc 2001;33:343.
20. Hoseini Z, Behpour N, Hoseini R. Co-treatment with vitamin D supplementation and aerobic training in elderly women with Vit D deficiency and NAFLD: A single-blind controlled trial. Hepat Mon 2020;20:e96437.
21. Babaei *P*, Damirchi A, Hoseini R. The interaction effects of aerobic exercise training and vitamin D supplementation on plasma lipid profiles and insulin resistance in ovariectomized rats. J Exerc Nutrition Biochem 2015;19:173-82.
22. Hoseini R, Damirchi A, Babaei P. Vitamin D increases PPARγ expression and promotes beneficial effects of physical activity in metabolic syndrome. Nutrition 2017;36:54-9.
23. Smart N, King N, McFarlane JR, Graham P, Dieberg G. Effect of exercise training on liver function in adults who are overweight or exhibit fatty liver disease: A systematic review and meta-analysis. Br J Sports Med 2018;52:834-43.
24. Van Gemert WA, May AM, Schuit AJ, Oosterhof BY, Peeters PH, Monninkhof EM. Effect of weight loss with or without exercise on inflammatory markers and adipokines in postmenopausal women: The SHAPE-2 trial, a randomized controlled trial. Cancer Epidemiol Biomarkers Prev. 2016;25:799-806.
25. Nakhl S, Sleilaty G, El Samad S, Saliba Y, Chahine R, Farès N. Association between vitamin D deficiency and lipid and non-lipid markers of cardiovascular diseases in the middle east region. Eur J Clin Nutr 2019;73:850-8.
26. Mogili KD, Karuppusami R, Thomas S, Chandy A, Kamath MS, Aleyamma T. Prevalence of vitamin D deficiency in infertile women with polycystic ovarian syndrome and its association with metabolic syndrome–A prospective observational study. Eur J Obstet Gynecol Reprod Biol 2018;229:15-9.
27. Scragg R, Sowers M, Bell C. Serum 25-hydroxyvitamin D, diabetes, and ethnicity in the Third national health and nutrition examination survey. Diabetes Care 2004;27:2813-8.
28. Barker T, Martins TB, Hill HR, Kjeldsberg CR, Dixon BM, Schneider ED, *et al*. Vitamin D sufficiency associates with an increase in anti-inflammatory cytokines after intense exercise in humans. Cytokine 2014;65:134-7.
29. Holick MF, Chen TC. Vitamin D deficiency: A worldwide problem with health consequences. Am J Clin Nutr

2008;87:1080S-6S.

30. Matinhomaee H, Zobeiri M, Azarbayjani MA, Azizbeigi K. The effect of vitamin D supplementation during resistance training on the markers of systemic inflammation in untrained males. Sci J Kurd Univ Med Sci 2017;21:89-98.
31. Donges CE, Duffield R, Drinkwater EJ. Effects of resistance or aerobic exercise training on interleukin-6, C-reactive protein, and body composition. Med Sci Sports Exerc 2010;42:304-13.
32. Carrillo AE, Flynn MG, Pinkston C, Markofski MM, Jiang Y, Donkin SS, *et al*. Vitamin D supplementation during exercise training does not alter inflammatory biomarkers in overweight and obese subjects. Eur J Appl Physiol 2012;112:3045-52.
33. Meyer JD, Hayney MS, Coe CL, Ninos CL, Barrett BP. Differential reduction of IP-10 and C-reactive protein via aerobic exercise or mindfulness-based stress-reduction training in a large randomized controlled trial. J Sport Exerc Psychol 2019;41:96-106.
34. Hosseini F, Abdollahpur N, Bahrami Abdehgah E. Effect of eight weeks high intensity aerobic exercise on C-reactive protein levels in obese middle-aged men. J Phys Act Health 2019;2:14-25.
35. Kjalarsdottir L, Tersey SA, Vishwanath M, Chuang J-C, Posner BA, Mirmira RG, *et al*. 1,25-Dihydroxyvitamin D3 enhances glucose-stimulated insulin secretion in mouse and human islets: A role for transcriptional regulation of voltage-gated calcium channels by the vitamin D receptor. J Steroid Biochem Mol Biol 2019;185:17-26.
36. Nagpal S, Na S, Rathnachalam R. Noncalcemic actions of vitamin D receptor ligands. Endocr Rev 2005;26:662-87.