

Effect of Aerobic Exercise Versus Mediterranean Diet on Postmenopausal Metabolic Syndrome: A Randomized Controlled Trial

¹Afaf M. Shahen, ²Khadiga S. Abdulaziz, ³Mohamed F. Abo Elainin and ²Doaa A. Osman

¹Department of Physiotherapy, Tanta Police Hospital, El Gharbeya, Egypt

²Department of Physical Therapy for Woman's Health,

Faculty of Physical Therapy, Cairo University, Giza, Egypt

³Consultant of Obstetrics and Gynecology, Om El-Masryeen Hospital, Giza, Egypt

Abstract: *Aim:* To compare the effect of aerobic exercise versus Mediterranean diet on postmenopausal metabolic syndrome. *Methods:* Forty obese postmenopausal women with metabolic syndrome participated in this study. They were divided into two equal groups. Group (A) received aerobic exercise on for 8 weeks, while group (B) received Mediterranean diet for 8 weeks. The outcome measures, including anthropometric parameters, systolic blood pressure (SBP), diastolic blood pressure (DBP), triglyceride (TG), high density lipoprotein (HDL) and fasting blood glucose (FBG), were evaluated pre- and post-treatment. *Results:* Both groups showed significant reductions in anthropometric parameters, SBP, DBP, TG and FBG ($p < 0.05$), as well as a significant increase in HDL ($p < 0.05$) post-treatment compared to pre-treatment. Comparing both groups post-treatment revealed that there was a significant reduction in SBP ($p < 0.05$) in favour of group (B). However, there were non-significant differences regarding anthropometric parameters, DBP, TG, HDL and FBG between both groups post-treatment ($p > 0.05$). *Conclusions:* Both aerobic exercise and Mediterranean diet are effective in improving postmenopausal metabolic syndrome, with a better effect of Mediterranean diet on reducing systolic blood pressure.

Key words: Aerobic Exercise • Mediterranean Diet • Metabolic Syndrome • Postmenopausal Women

INTRODUCTION

Metabolic syndrome is a combination of several factors including hypertension, dyslipidemia, insulin resistance, obesity and glucose intolerance that increase subjects' risk to develop type 2 diabetes and cardiovascular disease (CVD). Research has shown an increased risk of metabolic syndrome in postmenopausal women which varies from 32.6% to 41.5% [1]. Hormonal changes are considered as one of the main relevant factors regarding CVD as well as some recognized relationships with metabolic syndrome components [2].

Aerobic exercise training may be essential in treating obese patients with metabolic syndrome, even if the exercise does not increase their VO_{2max} . Exercise training contributes to the maintenance of fat-free mass, reduction of visceral adipose tissue and might be more effective for

improving physical fitness and risk factors for coronary heart disease during weight reduction in obese women [3, 4].

The Mediterranean food pattern has acquired an emerging role in cardiovascular epidemiology and reducing the incidence of metabolic syndrome. It is characterized by a high consumption of fruits, vegetables, moderate-to-low consumption of dairy products and meats/meat products and a high monounsaturated-to-saturated fat ratio [5]. Adherence to a Mediterranean-type diet is associated with lower glycosylated hemoglobin (HbA_{1c}) and postprandial glucose levels in type 2 diabetic patients, independent of anthropometric, lifestyle and other health-related variables [6]. It improves inflammation, oxidative stress, as well as insulin resistance and secretion that are considered pathogenic factors in obesity, diabetes and metabolic syndrome [7].

Previous research evaluated the effect of aerobic exercise alone [8, 9], Mediterranean diet alone [10, 11], or both together [12] on metabolic syndrome. However, little is known about which is more effective, aerobic exercise or Mediterranean diet. Therefore, this study aimed to determine the effect of aerobic exercise versus Mediterranean diet on metabolic syndrome in postmenopausal women.

MATERIALS AND METHODS

Study Design: The study was designed as a prospective, randomized, controlled trial. Ethical approval was obtained from the institutional review board at Faculty of Physical Therapy, Cairo University. The study followed the Guidelines of Declaration of Helsinki on the conduct of human research. It was conducted between July 2019 and January 2020.

Participants: A sample of forty postmenopausal women, suffering from metabolic syndrome, was recruited from Tanta Police Hospital, El-Gharbeya, Egypt. To be included in the study, the participants were chosen postmenopausal women having at least three of the National cholesterol education program's adult treatment panel III criteria for the diagnosis of metabolic syndrome, including abdominal obesity (waist circumference ≥ 88 cm), elevated triglyceride (TG) (≥ 150 mg/dL), reduced high density lipoprotein (HDL) (<50 mg/dL) elevated blood pressure ($\geq 130/\geq 85$ mmHg) and elevated fasting blood glucose (FBG) (≥ 110 mg/dL) [13]. The participants' age ranged from 50-60 years, body mass index (BMI) ranged from 30-35 kg/m² and waist/hip ratio was >0.85 . They had natural menopause and sedentary lifestyle. The participants were excluded if they had history of CVD, epilepsy, infectious diseases, malignant tumors, undiagnosed fever, cardiac pacemaker, or any physical impairment that can prevent following the study program.

Randomization: Each woman was informed about the nature, purpose and benefits of the study, the right to refuse or withdraw at any time and the confidentiality of any obtained data. Women were randomly assigned into 2 equal groups (A and B) with the use of a computer based randomization program. No dropping out of subjects from the study was reported after randomization, Figure (1).

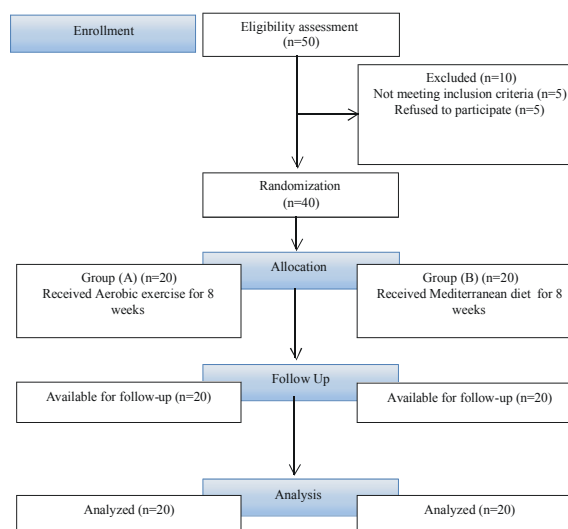


Fig. 1: Flow chart demonstrates the experimental design of the study

Interventions: Group (A) included 20 postmenopausal women who received aerobic exercise for 8 weeks, while group (B) included 20 postmenopausal women who received Mediterranean diet for 8 weeks.

Aerobic Exercise Program: All postmenopausal women in group (A) performed aerobic exercise on a treadmill, 3 times per week, for 8 weeks. The program started with warming up phase through walking on a treadmill for 3-5 minutes at a slow speed. Then, each participant walked on the treadmill at a moderate intensity of 60-70% of target heart rate (THR). It was calculated from the karvonen's equation by using resting heart rate (HR_{rest}), maximum heart rate (HR_{max}) and training fraction. $THR = HR_{rest} + (HR_{max} - HR_{rest}) \times \text{training fraction}$ [14]. The training fraction was 60-70% for moderate intensity. The exercise was progressed from 20-25 minutes in the first week to 55 minutes by the end of sessions. The program ended with 5 minutes of cooling down, during which the treadmill speed was gradually lowered until the heart rate and blood pressure returned to their resting levels.

Mediterranean Diet: All postmenopausal women in group (B) received Mediterranean diet for 8 weeks. They received instructions about consumption of olive oil as added lipid, consumption of nuts and olives as snacks, daily high consumption of vegetables, fruits and whole grain, daily moderate consumption of dairy

product, bi-weekly consumption of legumes, bi-weekly consumption of fish and monthly consumption of meat. The main beneficial components of Mediterranean diet are monounsaturated fats such as oleic acid in olive oil and polyunsaturated fats such as omega-3 (α -linolenic acid found in tree nuts such as walnuts and eicosapentaenoic acid found in oily fish), high amounts of flavonoids and antioxidants found in fruits and vegetables and high amount of fiber found mainly in foods with a low glycemic index [12].

Outcome Measures

Anthropometric Parameters: Body weight, height, waist and hip circumferences were measured before and after 8 weeks of treatment. Weight was taken using a balance Seca Scale with light clothing and no shoes, while a Holtain anthropometer was used to assess the height. Then, BMI was calculated by dividing weight by height squared (Kg/m^2). Additionally, the waist/hip ratio was calculated after measurement of both waist and hip circumferences. The waist circumference was measured when the tape measure was positioned horizontally just above the iliac crest and exactly under umbilicus, while the hip circumference was measured by a tape measure at the largest buttocks circumference.

Blood Pressure Measures: Systolic and diastolic blood pressures were measured for each participant in both groups (A & B) before and after 8 weeks of treatment, using mercury column sphygmomanometer. After an initial rest of 5 minutes, three sitting blood pressure measurements were taken with intervals of 2 minutes. Measurements were taken from the left arm at the same time of the day. Since it is known that the first measurement is affected by adaptation to the sitting condition, the mean of the second and third measurements were used for analysis [15].

Laboratory Measurements: After a 10-hour overnight fast, venous blood samples were collected from each participant in both groups (A & B) before and after 8 weeks of treatment to measure TG, HDL and FBG levels by BM/Hitachi 747/737 analyzer (Hitachi) using the enzymatic calorimetric method. All samples were drawn between 8 and 10 a.m. [16].

Statistical Analysis: Statistical analysis was conducted using the Statistical Package for the Social Sciences

(SPSS) computer program for windows, version 23 (SPSS, Inc., Chicago, IL). The P-value of ≤ 0.05 was considered significant. Results were expressed as mean \pm standard deviation. Prior to final analysis, data were screened for normality assumption, homogeneity of variance and presence of extreme scores. This exploration was done as a pre-requisite for parametric calculations of the analysis of difference. Preliminary assumption checking revealed that data was normally distributed for anthropometric parameters, SBP, DBP, TG, HDL and FBG, as assessed by Shapiro-Wilk test ($P>0.05$); there were no univariate or multivariate outliers, as assessed by boxplot and Mahalanobis distance ($P>0.05$), respectively; there were linear relationships, as assessed by scatterplot; no multicollinearity. There was homogeneity of variances ($P>0.05$) and covariances ($P>0.05$), as assessed by Levene's test of homogeneity of variances and Box's M test, respectively. Accordingly, 2 \times 2 mixed design MANOVA was used to compare the anthropometric parameters, SBP, DBP, TG, HDL and FBG at different measuring periods at both groups.

RESULTS

At baseline, there were non-significant differences between both groups ($p>0.05$) regarding age, height and all outcome measures (Tables 1-2).

All anthropometric measures (body weight, BMI and waist/hip ratio) showed statistically significant reductions ($p<0.05$) within both groups (A & B). The post-treatment comparison of both groups revealed statistically non-significant differences ($p>0.05$) (Table 2).

The SBP and DBP showed statistically significant reductions ($p<0.05$) within both groups (A & B). The post-treatment comparison of both groups revealed a statistically significant reduction in SBP ($p<0.05$) in favour of group (B), while there was a statistically non-significant difference in DBP ($p>0.05$) between both groups post-treatment (Table 2).

The TG showed a statistically significant reduction ($p<0.05$) within both groups (A & B). The post-treatment comparison of both groups revealed a statistically non-significant difference ($p>0.05$) (Table 2).

The HDL showed a statistically significant increase ($p<0.05$) within both groups (A & B). The post-treatment comparison of both groups revealed a statistically non-significant difference ($p>0.05$) (Table 2).

Table 1: Demographic data of postmenopausal women in both groups

	Group (A) (n = 20)	Group (B) (n = 20)	P value
Age (yrs.)	56.25±3.29	56.45±3.28	0.848 ^{NS}
Height (m)	1.6±0.06	1.62±0.065	0.308 ^{NS}

^{NS}P > 0.05 = non-significant, P = Probability

Table 2: The anthropometric parameters, SBP, DBP, TG, HDL and FBG for both groups

		Group (A) (n = 20)	Group (B) (n = 20)	P value*
Body weight (Kg)	Pre-treatment	94.85±7.3	98.25 ±7.73	0.161 ^{NS}
	Post-treatment	87.32 ±6.93	88.82±6.66	0.49 ^{NS}
	P value**	0.0001 ^S	0.0001 ^S	
BMI (Kg/m ²)	Pre-treatment	37.03±1.62	37.35 ±1.21	0.483 ^{NS}
	Post-treatment	34.07±1.55	33.79±1.23	0.525 ^{NS}
	P value**	0.0001 ^S	0.0001 ^S	
Waist/hip ratio	Pre-treatment	0.91±0.04	0.93 ±0.03	0.262 ^{NS}
	Post-treatment	0.9 ±0.04	0.91±0.03	0.311 ^{NS}
	P value**	0.0001 ^S	0.0001 ^S	
SBP (mmHg)	Pre-treatment	141.5±7.45	137 ±6.56	0.051 ^{NS}
	Post-treatment	133.25 ±6.54	127.5±6.38	0.008 ^S
	P value**	0.0001 ^S	0.0001 ^S	
DBP (mmHg)	Pre-treatment	91.25±6.25	90.25 ±4.72	0.572 ^{NS}
	Post-treatment	85.5±4.55	84.75±4.43	0.601 ^{NS}
	P value**	0.0001 ^S	0.0001 ^S	
TG (mg/dL)	Pre-treatment	177.15±22.89	178.85 ±15.18	0.783 ^{NS}
	Post-treatment	166.2 ±19.47	162.7±14.47	0.523 ^{NS}
	P value**	0.0001 ^S	0.0001 ^S	
HDL (mg/dL)	Pre-treatment	39.2±6.11	38.25 ±4.58	0.582 ^{NS}
	Post-treatment	44.75 ±5.3	42.8±3.7	0.186 ^{NS}
	P value**	0.0001 ^S	0.0001 ^S	
FBG (mg/dL)	Pre-treatment	200.75±19.58	187.7 ±21.63	0.053 ^{NS}
	Post-treatment	192.55 ±19.22	181.05±21.87	0.085 ^{NS}
	P value**	0.0001 ^S	0.0001 ^S	

* Inter-group comparison; ** intra-group comparison of the results pre- and post-treatment.

^{NS} P > 0.05 = non-significant, ^S P < 0.05 = significant, P = Probability

The FBG showed a statistically significant reduction (p<0.5) within both groups (A & B). The post-treatment comparison of both groups revealed a statistically non-significant difference (p>0.05) (Table 2).

DISCUSSION

Metabolic syndrome is an important cluster of risk factors for atherosclerotic disease and characterized by a group of metabolic risk factors, associated with development of type 2 diabetes and CVD, which represents the leading cause of morbidity and mortality. In addition to predisposing factors, lifestyle, physical inactivity, atherogenic dietary habits and genetic factors play important roles in the development of this disease [17, 18]. Therefore, this study was the first one which aimed to compare the effect of aerobic exercise versus Mediterranean diet on metabolic syndrome in postmenopausal women.

Regarding group (A), the results showed statistically significant reductions in anthropometric parameters, SBP, DBP, TG and FBG, as well as a significant increase in HDL between pre- and post-treatment.

These results agreed with a systematic review and meta-analysis by Wewege *et al.* [19] that revealed the significant improving effects of aerobic exercise on waist circumference, TG, HDL, DBP and FBG in persons having metabolic syndrome. In addition, El-Refayea and Younis [20] investigated the efficacy of aerobic exercise in reducing both SBP and DBP in postmenopausal hypertension. Moreover, a meta-analysis of randomized controlled trials examined the effects of aerobic exercise on lipids and lipoproteins in women aged ≥18 years. It reported that aerobic exercise is effective in decreasing TG and increasing HDL levels in women [21].

The valuable effect of aerobic exercise on the metabolic syndrome could be attributed to its influence on reducing body weight and BMI, as well as body

composition, lipid profile, glucose and energy metabolism [22]. Additionally, the beneficial impact of aerobic exercise on reducing blood pressure could be mediated by peripheral resistance reduction and arterial vasodilatation increase in trained subjects [20].

Regarding group (B), the results showed statistically significant reductions in anthropometric parameters, SBP, DBP, TG and FBG, as well as a significant increase in HDL between pre- and post-treatment.

These results were consistent with Fiore *et al.* [23] who showed that higher adherence to Mediterranean diet is associated with better metabolic status in postmenopausal women. Also, a recent systematic review and meta-analysis concluded that Mediterranean diet has beneficial effects on all components and most risk factors of metabolic syndrome [24]. Moreover, studies reported that Mediterranean diet represents a healthy and sustainable lifestyle whose adoption plays a key role in primary and secondary prevention of metabolic syndrome and its components [25, 26].

The mechanisms underlying the healthy properties of the Mediterranean diet cannot be limited to any single nutrient, food or food component, but they are attributed to the synergy or interactions of bioactive compounds and other nutrients in whole foods. The high consumption of fruits, vegetables and whole grain in the Mediterranean diet provide a unique blend of bioactive components including resistant starches, vitamins, minerals, phytochemicals, antioxidants and flavonoids that may provide desirable health benefits reducing the risk of the development of chronic diseases. Additionally, the consumption of low glycemic index foods decreases the prevalence of metabolic syndrome by reducing blood pressure and insulin resistance. Moreover, the Mediterranean diet is rich of monounsaturated and polyunsaturated fats. The monounsaturated fats improve insulin sensitivity and glucose concentrations, as well as reduce the risk of weight gain. The polyunsaturated fats are inversely related to inflammatory markers and oxidative stress. Furthermore, Mediterranean diet represents a possible therapy for metabolic syndrome, preventing adiposopathy or sick fat formation [25, 27].

Regarding the comparison between both groups post-treatment, the results revealed statistically non-significant differences in all outcome measures, except SBP that revealed a statistically significant reduction post-treatment in favour of group (B).

The review of literature did not detect any study comparing the effect of aerobic exercise versus Mediterranean diet on postmenopausal metabolic

syndrome. Therefore, the present work is considered the first study on this point. Accordingly, the results cannot be compared or discussed with other research outcomes but showed a significant better effect of Mediterranean diet on reducing SBP in postmenopausal metabolic syndrome. This finding could be explained by Finicelli *et al.* [28] who revealed the ameliorating effects of polyphenolic anthocyanins (found in fruits such as blueberries) on SBP because of significantly increase of endothelial nitric oxide synthase levels and decrease of vasoconstriction, via nitric oxide-mediate pathway and the reduction of renal oxidative stress. Likewise, polyphenolic compounds (found in virgin olive oil) are associated with SBP reduction in hypertensive and coronary heart disease patients [29].

CONCLUSION

Aerobic exercise and Mediterranean diet exhibited similar positive effects on metabolic syndrome risk factors in postmenopausal women, with a greater improving effect of Mediterranean diet on systolic blood pressure.

Source of Funding: This study received no financial support.

Conflict of Interest: The authors have no conflict of interest to declare

ACKNOWLEDGMENTS

The authors would like to thank all postmenopausal women who participated in the study.

REFERENCES

1. Jouyandeh, Z., F. Nayebezhadeh, M. Qorbanim and A. Mojgan, 2013. Metabolic syndrome and menopause. *J. Diabetes Metab Disord*, 12: 1.
2. Heidari, R., M. Sadeghi, M. Talaei, K. Rabiei, N. Mohammadifard and N. Sarrafzadegan, 2010. Metabolic syndrome in menopausal transition: Isfahan Healthy Heart Program, a population based study. *Diabetol Metab Syndr*, 2: 59.
3. Okura, T., Y. Nakata, K. Ohkawara, S. Numao, Y. Katayama, T. Matsuo and K. Tanaka, 2007. Effects of aerobic exercise on metabolic syndrome improvement in response to weight reduction. *Obesity (Silver Spring)*, 15(10): 2478-2484.

4. Eskicioğlu, F., S.E. Muhammet and Ö Beyhan, 2019. Are visceral adiposity index and ultrasonographic visceral fat thickness measurements correlated to endometrial thickness in postmenopausal women? *Journal of Gynecological Research and Obstetrics*, 5(1): 9-12.
5. Tortosa, A., M. Bes-Rastrollo, A. Sanchez-Villegas, F.J. Basterra-Gortari, J.M. Nuñez-Cordoba and M.A. Martinez-Gonzalez, 2007. Mediterranean diet inversely associated with the incidence of metabolic syndrome: the SUN prospective cohort. *Diabetes Care*, 30(11): 2957-2959.
6. Esposito, K., M.I. Maiorino, C. Di Palo and D. Giugliano, 2009. Adherence to a Mediterranean diet and glycaemic control in Type 2 diabetes mellitus. *Diabetic Medicine*, 26(9): 900-907.
7. Calder, P.C., N. Ahluwalia, F. Brouns, T. Buetler, K. Clement, K. Cunningham, K. Esposito, L.S. Jönsson, H. Kolb, M. Lansink, A. Marcos, A. Margioris, N. Matusheski, H. Nordmann, J. O'Brien, G. Pugliese, S. Rizkalla, C. Schalkwijk, J. Tuomilehto, J. Wärnberg and B.M. Winklhofer-Roob, 2011. Dietary factors and low-grade inflammation in relation to overweight and obesity. *The British Journal of Nutrition*, 106 Suppl 3: S5-S78.
8. Kang, S., E. Kim and K. Ko, 2016. Effects of aerobic exercise on the resting heart rate, physical fitness and arterial stiffness of female patients with metabolic syndrome. *J. Phys. Ther. Sci.*, 28: 1764-1768.
9. Ciolac, E.G., A.B. Edimar, A.B. Luiz, O.C. Vitor, G. Julia and V.G. Guilherme, 2010. Effects of high-intensity aerobic interval training vs. moderate exercise on hemodynamic, metabolic and neuro-humoral abnormalities of young normotensive women at high familial risk for hypertension. *Hypertension Research*, 33: 836-843.
10. Garcia, M., J. Bihuniak, J. Shook, A. Kenny, J. Kerstetter and T. Huedo-Medina, 2016. The effect of the traditional Mediterranean-style diet on metabolic risk factors: A meta-analysis. *Nutrients*, 8(3): 168.
11. Babio, N., E. Toledo, R. Estruch; E. Ros, M. Martinez-Gonzalez, O. Castaner, M. Bullo, D. Corella, F. Aros, E. Gomez-Gracia, V. Ruiz-Gutiérrez, M. Fiol, J. Lapetra, R. Lamuela-Raventos, L. Serra-Majem, X. Pintó, J. Basora, J. Sorlí, J. Salas-Salvadó and Predimed Study Investigators, 2014. Mediterranean diets and metabolic syndrome status in the PREDIMED randomized trial. *CMAJ*, 186(17): E649-E657.
12. Alkhatib, A., 2015. Effective intervention strategies combining Mediterranean diet and exercise for reducing obesity, metabolic and cardiovascular risks in high-risk populations: Mini review. *Obes Res. Open J.*, 2(1): 4-9.
13. Anık İlhan, G. and B. Yıldızhan, 2019. Visceral adiposity indicators as predictors of metabolic syndrome in postmenopausal women. *Turk J. Obstet Gynecol.*, 16(3): 164-168.
14. Casillas, J.M., A. Gudjoncik, V. Gremaux, J. Aulagne, D. Besson and D. Laroche, 2017. Assessment tools for personalizing training intensity during cardiac rehabilitation: Literature review and practical proposals. *Ann. Phys. Rehabil Med.*, 60(1): 43-49.
15. Jaeschke, L., A. Steinbrecher and T. Pischon, 2015. Measurement of waist and hip circumference with a body surface scanner: feasibility, validity, reliability and correlations with markers of the metabolic syndrome. *PLoS One*, 10(3): e0119430.
16. Lin, W.Y., W.S. Yang, L.T. Lee, C.Y. Chen, C.S. Liu, C.C. Lin and K.C. Huang, 2006. Insulin resistance, obesity and metabolic syndrome among non-diabetic pre- and post-menopausal women in North Taiwan. *International Journal of Obesity*, 30(1): 912-917.
17. Katherine, E., C. Miryam and G. Dario, 2007. Mediterranean diet and the metabolic syndrome. *Molecular Nutrition*, 51(10): 1268-1274.
18. Meydani, M., 2005. A Mediterranean-style diet and metabolic syndrome. *Nutrition Reviews*, 63(9): 312-314.
19. Wewege, M.A., J.M. Thom, K.A. Rye and B.J. Parmenter, 2018. Aerobic, resistance or combined training: A systematic review and meta-analysis of exercise to reduce cardiovascular risk in adults with metabolic syndrome. *Atherosclerosis*, 274: 162-171.
20. El-Refayea, G.E. and H.A. Younis, 2019. The effect of 12 weeks of resistive exercises versus aerobic exercises in overweight hypertensive postmenopausal women. *Bulletin of Faculty of Physical Therapy*, 24: 40-48.
21. Kelley, G.A., K.S. Kelley and Z.V. Tran, 2004. Aerobic exercise and lipids and lipoproteins in women: a meta-analysis of randomized controlled trials. *Journal of women's health (Larchmt)*, 13(10): 1148-1164.
22. Kim, J.W. and D.Y. Kim, 2012. Effects of aerobic exercise training on serum sex hormone binding globulin, body fat index and metabolic syndrome factors in obese postmenopausal women. *Metabolic syndrome and related disorders*, 10(6): 452-457.

23. Fiore, V., M. Capraro, R. Ragusa, J. Godos, A. Mistretta and M. Marranzano, 2019. Mediterranean diet and metabolic status in post-menopausal women living in a mediterranean area. *Nutrition and Healthy Aging*, 5(1): 53-60.
24. Papadaki, A., E. Nolen-Doerr and C.S. Mantzoros, 2020. The Effect of the Mediterranean Diet on Metabolic Health: A Systematic Review and Meta-Analysis of Controlled Trials in Adults. *Nutrients*, 12(11): 3342.
25. Innocenti, A., C. Giampietro, J. Fusi, F. Galetta, F. Franzoni and O. Giampietro, 2015. Can Mediterranean Diet Counteract Metabolic Syndrome Diffusion? *Journal of Cardiol Ther.*, 2(6): 452-455.
26. Kastorini, C.M., H.J. Milionis, K. Esposito, D. Giugliano, J.A. Goudevenos and D.B. Panagiotakos, 2011. The effect of Mediterranean diet on metabolic syndrome and its components: a meta-analysis of 50 studies and 534,906 individuals. *Journal of the American College of Cardiology*, 57(11): 1299-1313.
27. Di Daniele, N., A. Noce, M.F. Vidiri, E. Moriconi, G. Marrone, M. Annicchiarico-Petruzzelli, G. D'Urso, M. Tesauro, V. Rovella and A. De Lorenzo, 2017. Impact of Mediterranean diet on metabolic syndrome, cancer and longevity. *Oncotarget*, 8(5): 8947-8979.
28. Finicelli, M., T. Squillaro, F. Di Cristo, A. Di Salle, M. Melone, U. Galderisi and G. Peluso, 2019. Metabolic syndrome, Mediterranean diet and polyphenols: Evidence and perspectives. *Journal of Cellular Physiology*, 234(5): 5807-5826.
29. Gaforio, J.J., F. Visioli, C. Alarcón-de-la-Lastra, O. Castañer, M. Delgado-Rodríguez, M. Fitó, A.F. Hernández, J.R. Huertas, M.A. Martínez-González, J.A. Menendez, J. Osada, A. Papadaki, T. Parrón, J.E. Pereira, M.A. Rosillo, C. Sánchez-Quesada, L. Schwingshackl, E. Toledo and A.M. Tsatsakis, 2019. Virgin Olive Oil and Health: Summary of the III International Conference on Virgin Olive Oil and Health Consensus Report, JAEN (Spain) 2018. *Nutrients*, 11(9): 2039.