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Effect of Ketogenic Diet and Exercise on Lipid Profile on Obese Postmenopausal women

Hala M. Hanafy[1], Enas M. Kamar[2], Sara M. Ahmed[3], Hossam Eldin H. Kamel[4]

[1,3]Department of Woman's Health, Faculty of physical therapy, Cairo University, Egypt.

[2]Master of physical therapy, Faculty of Physical Therapy, Cairo University, Egypt.

[4]Department of Obstetrics and Gynecology, Faculty of Medicine, El-Azhar University, Egypt.

***Correspondence to**
Hala M. Hanafy
Department of Women Health, Faculty of Physical Therapy, Cairo University, Egypt.

Tel:01222105163

Email;
Emara.hala@yahoo.com

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Background: postmenopausal obesity leads to many serious health risks such as cardiovascular disease, diabetes and psychological disorder.

Purpose: This study aimed to determine the effect of ketogenic diet and exercise on lipid profile in obese postmenopausal women.

Subjects: Forty obese postmenopausal women participated in this study, aged from 50-55 years, with body mass index (BMI) of 30-35 kg/m^2,were selected from outpatient clinic of El Mahalla General Hospital, El Mahalla El Kobra city, El Gharbia Governorate, Egypt. They received very low carbohydrate ketogenic diet for 4 weeks and aerobic exercises in form of walking on the treadmill for 30 min, three times per week for 4 weeks.

Material and method: anthropometric measures (body weight, BMI and waist and hip circumference), and lipid profile were assessed pre and post treatment program.

Result: comparing pre and post treatment result, there was a significant improvement in body weight, body mass index, waist hip ratio, total cholesterol, triglyceride, low density lipoprotein cholesterol and high density lipoprotein cholesterol after treatment program than pre-treatment values.

Conclusion: combined therapy of ketogenic diet and aerobic exercise is an effective method in improving lipid profile and body weight in obese postmenopausal women

Key words: Postmenopausal women, Obesity, Ketogenic diet, Aerobic exercise, Lipid profile.

1.Introduction:

Menopause is a period in a woman's life when maintaining her weight can be hard. During the premenopausal transition, women gain an average of 1–2 kg, while during the menopausal transition, fat distribution and storage shifts from the buttocks to the abdomen (1).

It has been reported that 70% of women of age 45-54 years are overweight or obese. As a result, it's possible to infer that obesity is more common in postmenopausal women than in premenopausal women. (2).

The menopause transition (MT), along with shifts in the hypothalamic-pituitary-ovarian axis, may be an underappreciated contributor. A number of hormonal shifts, such as decreased oestrogen levels and increased levels of circulating androgens, contribute to weight gain, especially visceral fat. As a result, visceral fat mass increases by 44 percent during menopause,

while gynoid fat mass increases by around 32 percent (3).

In addition to hormonal differences, Lifestyle factors such as lack of physical activity, Westernized eating habits, and emotional eating disorders linked to psychological distress should be considered (4). As a result, a variety of lipid metabolic disorders can lead to metabolic syndromes like cardiovascular disease and type 2 diabetes. As a result, metabolic syndrome is three times more common in postmenopausal women than it was prior to menopause (5).

Obesity has a wide range of negative consequences, including an increased risk of premature mortality, a lower quality of life, and chronic diseases. Obesity is a risk factor for cancers such as endometrial and breast cancer in women, and it also raises the risk of depression due to negative body image (6).

After menopause, adipose tissue is the primary source of sex hormones and an immunologically and metabolically active endocrine organ that produces inflammatory cytokines, adipokines, and oxidative stress (7).

Obesity can be determined by different methods, some of which are quite simple, while others are complex or sophisticated. Methods of assessment include the body mass index (BMI), waist-to-hip ratio (WHR), waist circumference (WC), waist-to-height ratio (WHtR), skin fold calipers, dual energy x-ray absorptiometry (DEXA), bioelectric impedance analysis (BIA), computerized axial tomography scan (CAT scan), magnetic resonance imaging (MRI), ultrasound, and near -infrared interactome (8).

Weight loss by lifestyle changes, dietary interventions, and enhanced physical activity, as well as behavioural approaches, is the cornerstone of therapeutic care (9).

Dietary treatments have been shown to reduce body weight and body composition profile parameters in premenopausal and postmenopausal women more effectively than exercise alone, according to studies. The addition of exercise to dietary interventions improves the impact of dietary interventions on body weight and composition (10).

Obesity and type 2 diabetes can be treated with a ketogenic diet as a first-line therapy. A ketogenic diet can also help with a variety of other chronic, often complicated, metabolic disorders, including neurodegenerative disease, cancer, type 1 diabetes, and steatohepatitis (11).

A previous 12-week study of a 90-minute integrated exercise session consisting of a 10-minute warm-up, 40 minutes of aerobic exercise, 30 minutes of resistance exercise, and a 10-minute cool-down for middle-aged postmenopausal women with abdominal obesity concluded an improvement in percentage of body fat and health-related activity, as well as an enhancement of immune function and a decrease in visceral fat and endotoxin concentrations (12).

Aerobic exercise practice improves adipocyte lipolysis in vitro (13). In addition, aerobic exercise training mitigates the effects of caloric restriction on abdominal and gluteal adipocyte lipolysis in postmenopausal women (14)

Obesity is a multifaceted, complex disorder that results from the combination between genotype and environment. However, physical, behavioural, cultural, physiological, metabolic, and genetic factors all play a role (15).

The regional fat distribution differs depending on the gender. Female sex hormones are thought to induce fat accumulation in women's buttocks, thighs, and hips; this typical female fat storage may be essential for normal reproductive function (16). Fat migrates from the buttocks, hips, and thighs to the belly as women enter menopause and the oestrogen released by the ovaries decreases(17).

A high-fat, polyunsaturated-fatty-acid-rich diet (ketogenic diet) is beneficial in lowering body weight and risk factors with chronic diseases (18). The positive effects of a ketogenic diet after a long period of use. It decreases body weight and BMI by a considerable amount. Furthermore, it lowers triglyceride and LDL cholesterol levels (19).

There has been little research done on the effects of aerobic exercise training in women, who have an elevated risk of cardiovascular disease after menopause (20, 21) **,** and sedentary activity has been suggested as a cardiovascular risk factor (22).

2. Materials and Methods

This research included forty obese postmenopausal women who volunteered to take part without any drop out. They were chosen from El Mahalla General Hospital's Outpatient Clinic. The aim of the study is to investigate the efficacy of ketogenic diet and aerobic exercise on obese

postmenopausal women. The duration of the study was six months from beginning of April 2020 to the end of September 2020.

Their age ranged from (50 to 55) years, their body mass index (BMI) ranged from (30-35) Kg/ m^2 . They all had hyperlipidemia (Cholesterol above 240 µg/dl, Triglycerides above 150 µg/dl, HDL below 30 µg/dl, LDL above 150µg/dl). They all had natural menopause.

They all were medically stable. Participants were excluded if they had diabetes, hypertension, heart disease, kidney disease, liver disease, and hyperthyroidism or hypothyroidism.

They were all in one group pre-test post-test design. It consisted of forty obese postmenopausal women who received aerobic exercise 30 minutes per session, three times per week for 4 weeks and ketogenic diet regimen for 4 weeks. All participants were given a full explanation of the assessment and treatment procedures. Before participating in this study, each woman had to sign an informed consent form. Ethical committee acceptance was obtained from the institutional review board at Faculty of Physical Therapy, Cairo University before the study commencement with number REC/012/002816.

Before and after the treatment programme (one month), all of the patients were assessed for measurements of body mass index (BMI), body weight, waist and hip ratio (WHR), and measurement of lipid profile (Serum Triglyceride, HDL and LDL) after fasting for 12 hours.

2.1. Evaluative procedures:

All the participants were assessed before starting and after the treatment program through:

2.1.1. History taking: A full history was taken from each woman in the study before starting this study and recorded in a data recording sheet.

2.1.2. Weight (body mass) and height measurements: To determine BMI, each woman in the study had her height and weight measured before and after the interventional programme. The participant stood perfectly still on the scale as her weight and height were measured in kilograms and meters, respectively. BMI was calculated by the weight in kilograms divided by the height in meters square according to the formula: **BMI=Weight (Kg) /Height (m) ^{2}.**

Also, body weight of each participant was measured before and after intervention program.

For measuring of abdominal muscle thickness: The participants assumed a supported and relaxed crook lying position. Ultrasound gel was freely applied to the areas of imaging to validate good sonic coupling between the transducer and skin. Then ultrasonic probe was placed perpendicular on intersection between umbilicus line level and mid intercostal line perpendicularly on it. The ultrasound image was captured at the end of expiration. Measuring was done first on right side then left side for the rectus abdominis and then for external oblique muscles.

2.1.3. Waist to hip ratio: Waist circumference and hip circumference were measured for each woman in the study before and after interventional program to calculate WHR. With the subject standing and breathing normally, the waist circumference (cm) was measured with a tape measure at the point halfway between the costal margin and iliac crest in the mid-axillary line. The hip circumference (cm) was measured around the greater trochanter at its widest point. The waist-to-hip ratio was calculated as the waist measurement divided by the hip measurement.

2.1.4. Measurement of lipid profile: After a written consent and use of local antiseptic for the skin, a fasting sample of venous blood (3mls) was collected from each participant included in the study before and after treatment program, from the arm directly in a centrifuge tube for serum preparation. Serum levels of total cholesterol (TC), triglyceride (TG), low density (LDL), and high density lipoproteins(HDL) were measured by using reagents, ELISA Kits, and ELISA reader (stat fax -2100).

2.2. Treatment procedures

All women were informed and instructed about the treatment procedures to gain their confidence and cooperation throughout the study course. Each woman in this study received:

2.2.1. Ketogenic diet: In form of very low carbohydrate ketogenic diet, classic 4:1 diet (ratio of grams of fat to grams of protein plus carbohydrate) according to the Johns Hopkins protocol

2.2.2 Aerobic exercise (treadmill training): To prevent unnecessary loss of body water during the workout, both participants were encouraged to drink plenty of water before and after the workout. Comfortable clothing and flat, light shoes were required of each woman. During exercise, the

therapist position should be close to the patient to monitor and identify signals that the exercise should be stopped, such as dexterity, discomfort, and fatigue **(figure 1).**

Treadmill training was for 30 minutes per session, 3 sessions per week for 4 weeks. The session was divided into 3 stages. Warming up stages consisted of five minutes on the treadmill at a low intensity 40% of maximum heart rate (MHR), actual stages consisted of 20 minutes on the treadmill with moderate intensity 60% of (MHR), and finally cooling stages consisted of five minutes on the treadmill with low intensity 40% of (MHR). Maximum heart rate was calculated according to equation: MHR = 210 – age (years).

Fig. (1): Obese postmenopausal woman during treadmill training

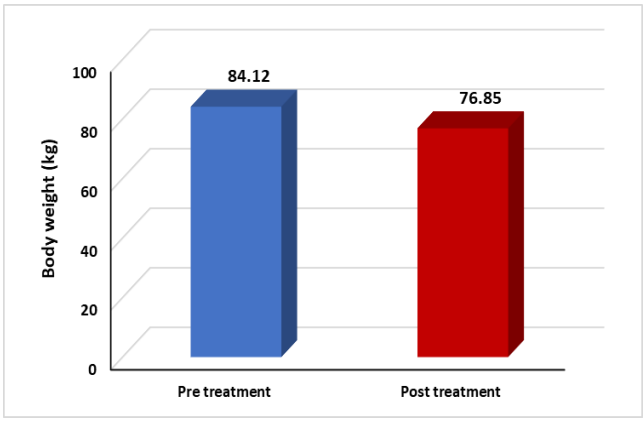
Statistical analysis:

Data was collected and statically analyzed using descriptive statics (mean and stander deviation) for comparing BMI, body weight, WHR, and lipid profile before and after treatment program. Analysis of variance (T-Test) was used to determine the effect of ketogenic diet and aerobic exercise on obese postmenopausal women with level of significance ($P<0.05$).

3.Results

- General characteristics of the subjects:

The mean ± SD age, weight, height and BMI of the study group were 52.17 ± 1.59 years, 84.12 ± 6.88 kg, 161.9 ± 5.97 cm and 32.09 ± 1.32 kg/m² respectively **(Table 1) (figure 2).**



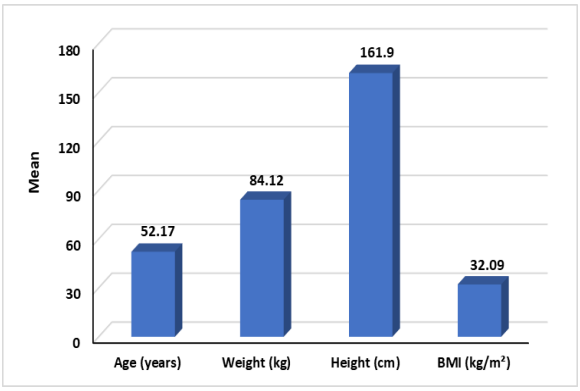


Figure (2). Mean age, weight, height and BMI of the study group.

Table 1. Descriptive statistics for the mean age, weight, height and BMI of the study group.

Range	Maximum	Minimum	$\overline{X}$ ±SD	Items
5	55	50	52.17 ± 1.59	**Age (years)**
29	101	72	84.12 ± 6.88	**Weight (kg)**
25	175	150	161.9 ± 5.97	**Height (cm)**
4.88	35	30.12	32.09 ± 1.32	**BMI (kg/m²)**

$\overline{X}$ **: Mean**
SD: Standard Deviation

I- Comparison of body weight between pre and post treatment:

The mean ± SD body weight of the study group before treatment was 84.12 ± 6.88 kg while after treatment was 76.85 ± 6.06 kg. The mean difference between before and after treatment was 7.27 kg and the percent of change was 8.64%. There was a significant decrease in the body weight after treatment compared with that

of before treatment (p = 0.0001) (**Table 2**) **(figure 3).**

Table 2. Comparison of body weight between pre and post treatment of the study group:

Items	Body weight (kg) $\bar{X}$ ±SD	MD	% of change	t-value	p-value	Sig
before treatment	84.12 ± 6.88	7.27	8.64	9.34	0.0001	S
after treatment	76.85 ± 6.06					

$\bar{X}$: Mean MD: Mean difference SD: Standard deviation
S: Significant p value: Probability value t value : Paired t value

Figure (3). Mean body weight pre and post treatment of the study

II- Comparison of BMI between pre and post treatment:

The mean ± SD BMI of the study group before treatment was 32.09 ± 1.32 kg/cm² while after treatment was 29.39 ± 1.68 kg/cm². The mean difference between before and after treatment was 2.7 kg/cm² and the percent of change was 8.41%. There was a significant decrease in the BMI after treatment compared with that of before treatment (p = 0.0001). (**Table 3) (figure 4**).

Table 3. Comparison of BMI between pre and post treatment of the study group:

	BMI (kg/cm²) $\bar{X}$ ±SD	MD	% of change	t-value	p-value	Sig
before treatment	32.09 ± 1.32	2.7	8.41	9.34	0.0001	S
After treatment	29.39 ± 1.68					

$\bar{X}$: Mean MD: Mean difference p value: Probability value
SD: Standard deviation S: Significant t value : Paired t value

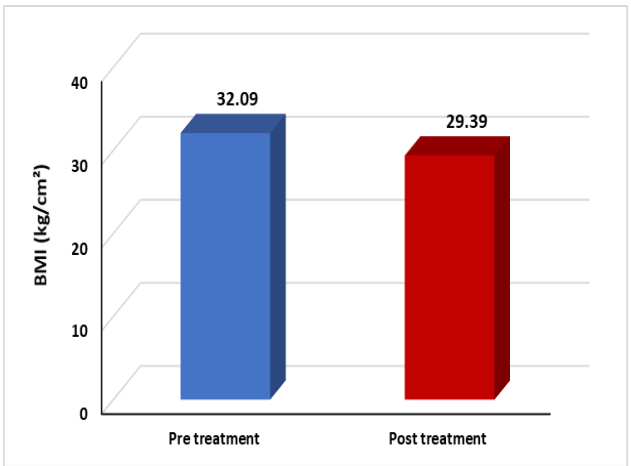


Figure (4). Mean BMI pre and post treatment of the study group.

III- Comparison of WHR between pre and post treatment:

The mean ± SD WHR of the study group before treatment was 1.01 ± 0.06 while after treatment was 0.96 ± 0.15. The mean difference between before and after treatment was 0.05 and the percent of change was 4.95%. There was a significant decrease in the WHR after treatment compared with that of before treatment (p = 0.0001). **(Table 4) (Figure 5).**

Table 4. ***Comparison of WHR between pre and post treatment of the study group:***

Items	WHR $\bar{X}$ ±SD	MD	% of change	t-value	p-value	Sig
before treatment	1.01 ± 0.06	0.05	4.95	2.36	0.02	S
after treatment	0.96 ± 0.15					

$\bar{X}$: Mean MD: Mean difference
p value: Probability value SD: Standard deviation
t value : Paired t value S: Significant

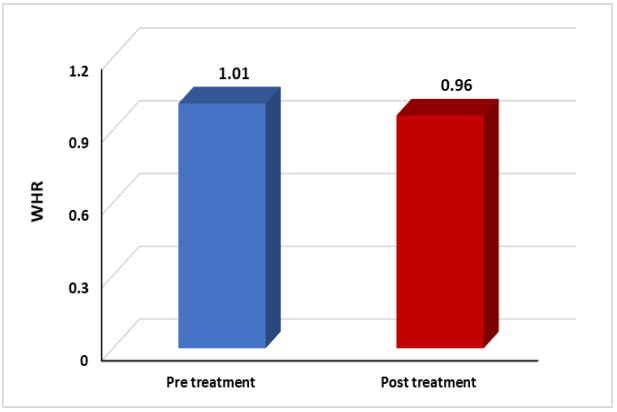


Figure (5). **Mean WHR pre and post treatment of the study group**

IV- Comparison of TC between pre and post treatment:

The mean ± SD TC of the study group before treatment was 275.57 ± 33.39 mg/dl while after treatment was 222.55 ± 24.02 mg/dl. The mean difference between before and after treatment was 53.02 mg/dl and the percent of change was 19.24%. There was a significant decrease in the TC after treatment compared with that of before treatment (p = 0.0001). (**Table 5) (figure 6**).

Table 5. ***Comparison of TC between pre and post treatment of the study group:***

	TC (mg/dl) $\overline{X}$ ±SD	MD	% of change	t-value	p-value	Sig
before treatment	275.57 ± 33.39	53.02	19.24	12.45	0.0001	S
After treatment	222.55 ± 24.02					

$\overline{X}$: Mean MD: Mean difference p value: Probability value
SD: Standard deviation t value : Paired t value S: Significant

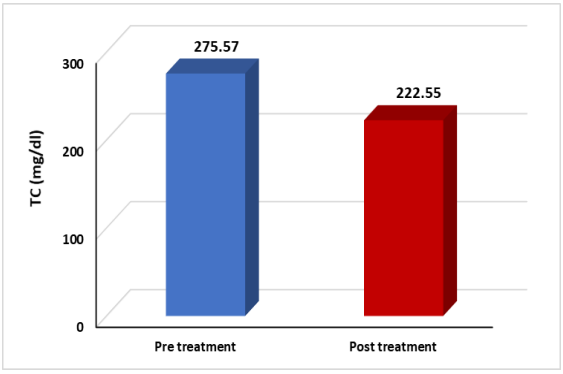


Figure (6). **Mean TC pre and post treatment of the study group.**

V- Comparison of LDL between pre and post treatment:

The mean ± SD LDL of the study group before treatment was 229.87 ± 23.73 mg/dl while after treatment was 192.57 ± 26.7 mg/dl. The mean difference between before and after treatment was 37.3 mg/dl and the percent of change was 16.23%. There was a significant decrease in the LDL after treatment compared with that of before treatment (p = 0.0001). **(Table 6) (figure 7)**.

Table 6. ***Comparison of LDL between pre and post treatment of the study group:***

	LDL(mg/dl) $\overline{X}$ ±SD	MD	% of change	t-value	p-value	Sig
before treatment	229.87 ± 23.73	37.3	16.23	9.27	0.0001	S
after treatment	192.57 ± 26.7					

$\overline{X}$: Mean MD: Mean difference p value: Probability value
SD: Standard deviation t value : Paired t value S: Significant

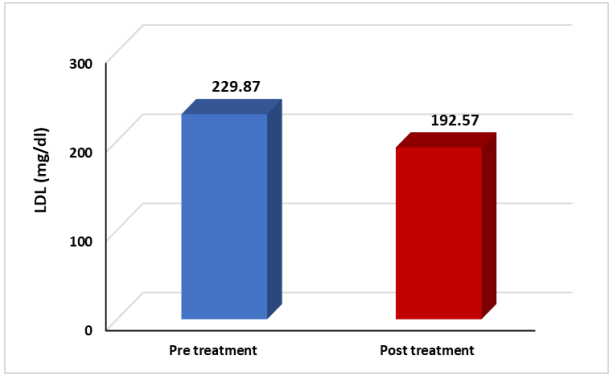


Figure (7). **Mean LDL pre and post treatment of the study group**

VI- Comparison of HDL between pre and post treatment:

The mean ± SD HDL of the study group before treatment was 42.11 ± 5.67 mg/dl while after treatment was 46.72 ± 5.51 mg/dl. The mean difference between before and after treatment was -4.61 mg/dl and the percent of change was 10.95%. There was a significant increase in the HDL after treatment compared with that of before treatment (p = 0.0001). (**Table 7) (figure 8).**

Table 7. ***Comparison of HDL between pre and post treatment of the study group:***

Items	HDL (mg/dl) $\overline{X}$ ±SD	MD	% of change	t-value	p-value	Sig
before treatment	42.11 ± 5.67	-4.61	10.95	-8.03	0.0001	S
after treatment	46.72 ± 5.51					

$\overline{X}$: Mean MD: Mean difference p value: Probability value
SD: Standard deviation t value : Paired t value S: Significant

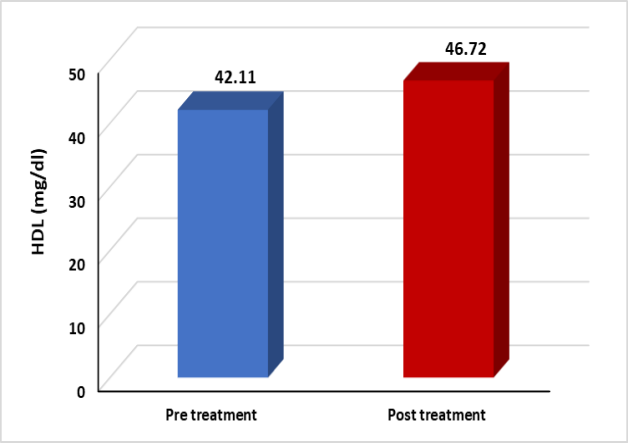


Figure (8). **Mean HDL pre and post treatment of the study group**

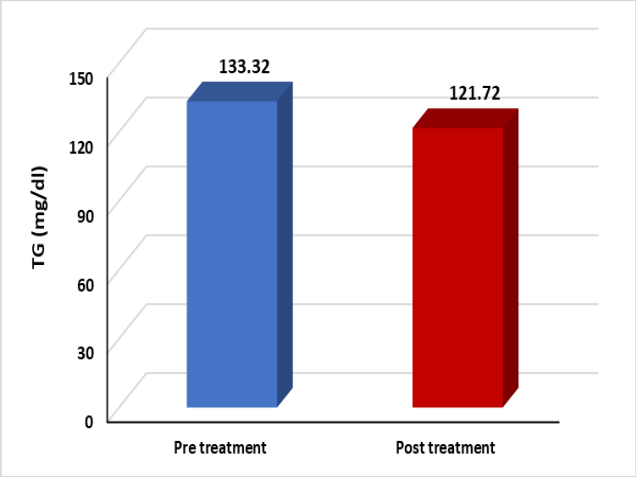


Figure (9). **Mean TG pre and post treatment of the study group**

VII- Comparison of TG between pre and post treatment:

The mean ± SD TG of the study group before treatment was 133.32 ± 8.11 mg/dl while after treatment was 121.72 ± 8.81 mg/dl. The mean difference between before and after treatment was 11.6 mg/dl and the percent of change was 8.7%. There was a significant decrease in the TG after treatment compared with that of before treatment (p = 0.0001). **(Table 8) (figure 9).**

Table 8. ***Comparison of TG between pre and post treatment of the study group:***

Items	TG (mg/dl) $\overline{X}$ ±SD	MD	% of change	t-value	p-value	Sig
before treatment	133.32 ± 8.11	11.6	8.7	10.48	0.0001	S
after treatment	121.72 ± 8.81					

$\overline{X}$: Mean MD: Mean difference p value: Probability value
SD: Standard deviation t value : Paired t value S: Significant

4. Discussion:

Overweight and obesity are becoming more common across the world, according to health organizations (23).Which is concerning given that obesity, especially abdominal obesity, is a risk factor for heart disease and is highly correlated to dyslipidemia and metabolic syndrome (24). Therefor current study aimed to investigate the effect of ketogenic diet and exercise on obese postmenopausal women**.**

The present study was conducted on forty obese postmenopausal women who were selected randomly from outpatient clinic of El Mahalla General Hospital, Egypt and agreed to participate in the study; their age ranged from 50 to 55 years old with mean value of 52.17 ± 1.59. They were diagnosed with hyperlipidemia (Cholesterol above 200 µg/dl, Triglycerides above 150 µg/dl, HDL below 30 µg/dl, LDL above 150µg/dl); they were not under any medical treatment.

For one month, each patient followed a very low carbohydrate ketogenic diet and aerobic activities that included 30 minutes of treadmill walking divided into 3 stages. Warming-up stages consisted of five minutes on the treadmill at a low intensity (40 percent of MHR), actual stages consisted of 20 minutes on the treadmill at a moderate intensity (60-75 percent of MHR), and cooling stages consisted of five minutes on the treadmill at a low intensity (40 percent of MHR) (40 percent of MHR). The frequency of exercise will be three times per week for one month.

Assessment of each patient was done through assessing body weight by weight height scale, body mass index by dividing body weight on height per meter square, waist hip ratio by dividing waist round measurement on hip round measurement and lipid profile which consist of total cholesterol, triglycerides, high density lipoprotein and low density lipoprotein before and after treatment program.

The results of this study revealed that after treatment, body weight, BMI, waist hip ratio, total cholesterol, triglyceride, and low density lipoprotein cholesterol all decreased significantly, while high density lipoprotein cholesterol increased significantly.

The result of the present study came in consentient with (25) who reported that a ketogenic diet would help people lose weightand reduce their risk of developing a number of chronic diseases. Also, (26) concluded that a low-carbohydrate diet reduced fasting triglycerides, as well as the ratio of triglycerides to high-density lipoprotein, and improved blood sugar levels while also lowering body weight.

The result of the study in agreement with (27-28-29), Have confirmed that The ketogenic diet is a successful treatment for obesity. In addition to the fact that an equivalent number of calories are achieving fat loss than the traditional high carbohydrate/low-fat diets. Low-carbohydrate diets have also been shown to be more beneficial than standard diets for more selective fat loss and muscle preservation; additionally, some longer-term studies have shown changes in body composition on a higher protein diet despite comparable weight loss (30).

These findings came in accordance with (31). who reported that use of ketogenic diet in 15 women there was a 14.3 percent decrease in body weight ($p = 0.008$) and a decrease in fasting serum insulin from 24.2 μIU/ml to 12.2 μIU/ml from baseline to 24 weeks ($p < 0.005$). In that study, there was a 12.1% decrease in body weight ($p = 0.006$), and a reduction in insulin from 23.5 μIU/ml to 8.2 μIU/ml ($p = 0.002$).

The result of the present study came in consentient with (32). who reported that Long-term administration of a ketogenic diet substantially decreases body weight and body mass index. Additionally, it lowers triglycerides and LDL cholesterol levels.

The results of the present study could be explained by the results of (33) who reported that if saturated fatty acids are replaced in the diet, unsaturated fatty acids can reduce the risk of chronic heart disease (CHD), as long as the unsaturated fatty acids are not from trans-fatty acids. Also, according to (34), a diet relatively high in monounsaturated fatty acids oleic acid, promoted a lipid profile associated with a decrease in coronary heart disease (CHD).

This recommendation was found to increase the risk of developing cardiovascular diseases (CVD), by increasing plasma triacylglycerol, lipoprotein-a, decrease HDL-C and LDL particle size (35).

A reevaluation of dietary saturated fatty acids was done after these findings, showing the effects it had on CVD (35).

The results of the present study could be explained by the results of (36) who reported After a single session of aerobic exercise, findings showed an increase in blood HDL-C, as well as a decrease in triglycerides and LDL-C, with the results lasting up to 48 hours after the exercise session was completed.

Also, according to (37), who found that a decrease in atherogenic lipid profile was associated with both exercise training and acute physical activity.

(38)who stated that the progression of cardiovascular disease (CVD) in women can be slowed by doing moderately intensive exercise for 30 minutes. A correlation has been noted between physical activity and HDL-C.

The result of the present study came in consentient with that there is a decrease of HDL-C after menopause, (39), stated that even one session of physical activity has the potential to increase HDL-C in postmenopausal women.

Findings of this study agreed with (40), who reported that the blood lipid profile was enhanced by moderate or intensive aerobic exercise.

In agreement with the results of this study (41), who investigated the effectiveness of combined regular exercises and dietary alterations on metabolic profile, and they found that combined program (regular exercises and

dietary alterations) achieving a significant improvement in oxidative damage, nitric oxide availability and improved the overall lipid metabolism .

These findings are confirmed by (42), who found that exercise affect HDL-C structure, TC efflux, and TC transmission to receptor. Findings of this study agreed with (43), who demonstrated that aerobic exercise raised HDL while lowering LD L, TG, and TC levels.

5. Conclusion

So, it can be concluded that ketogenic diet and aerobic exercise is an effective method in improving body weight, body mass index, waist hip ratio and lipid prof**.**

Conflict of Interests

The authors declare no conflict of interest.

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