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How Combined and Separate Aerobic Training and Turmeric Supplementation Alter Lipid Profile and Glycemic Status? A Clinical Trial in Middle-Aged Females with Type 2 Diabetes and Hyperlipidemia

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ABSTRACT

Background: Type 2 Diabetes Mellitus (T2DM) is one of the health problems in all societies. Exercise interventions and supplements are among the non-pharmacological approaches to improve the health status of patients with T2DM and hyperlipidemia.

Objectives: This study aimed to investigate the separate and combined effects of Turmeric Supplementation (TS) and Aerobic Training (AT) on body composition, lipid profile, and glycemic status in patients with T2DM and hyperlipidemia.

Methods: In this randomized, single-blinded, placebo-controlled trial, 42 women with T2DM and hyperlipidemia (age: 45 – 60 years, Body Mass Index (BMI): 25 – 30 kg/m2) were randomly assigned to four groups; i.e., AT + TS (n = 11), AT + placebo (AT; n = 10), TS (n = 11), and Control + placebo (C; n = 10). The AT program consisted of 60 - 75% of HRMax, 20 - 40 min/day, three days/week for eight weeks. The participants in the TS group consumed 2,100 mg powdered rhizome of turmeric daily for eight weeks. Body weight, Fasting Blood Sugar (FBS), insulin, Homeostatic Model Assessment for Insulin Resistance (HOMA-IR), HbA1C, Triglyceride (TG), Total Cholesterol (TC), Low-Density Lipoprotein (LDL), High-Density Lipoprotein (HDL), Apolipoprotein A1 (ApoA1), and Apolipoprotein B (ApoB) were measured before and after the intervention. The data were analyzed using paired sample t-test and Analysis of Co-variance (ANCOVA) followed by Bonferroni test at the signification level of 0.05.

Results: After eight weeks, significant improvements were observed in body composition, lipid profile, and glycemic status in the AT + TS, TS, and AT groups compared to the C group. Additionally, the AT + TS group showed significantly lower TG, TC, LDL, ApoB, FBS, insulin, HOMA-IR, and HbA1C levels and significantly higher HDL and ApoA1 levels compared to the AT and TS groups. The results also revealed a significant difference between the AT and TS groups in terms of TG, TC, LDL, glucose, HOMA-IR, ApoA1, and ApoB levels.

Conclusions: The findings suggested that AT + TS improved body composition, lipid profile, and glycemic status more effectively compared to TS or AT alone in middle-aged females with T2DM and hyperlipidemia.

1. Background

Type 2 Diabetes Mellitus (T2DM) is a chronic disorder caused by a defect in the function and secretion of insulin, which may lead to hyperglycemia (1). According to the World Health Organization (WHO), the number of patients with T2DM will reach 642 million by 2040 (2). However, with a steady incidence rate in Iran, the number of cases with T2DM will reach 5.2 million by 2025 (3). T2DM is more prevalent in middle-aged females due to menopause, inactivity, overweight, and decreased metabolism (4). Increased free reactive species and the induction of oxidative stress cause dyslipidemia in patients with T2DM by increasing Low-Density Lipoprotein (LDL) and decreasing High-Density Lipoprotein (HDL), which may elevate the risks of cardiovascular diseases (5).

Lifestyle changes; i.e., supplementation and exercise, are

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among the complementary treatment approaches in patients suffering from T2DM (6). Evidence has indicated that Aerobic Training (AT) boosts weight loss, improves lipid profile, facilitates skeletal muscle glucose uptake, increases the abundance of GLUT4, and improves the quality of life in these patients (7, 8). AT also alters the lipid profile and reduces body fat by lowering LDL and increasing HDL (9).

Curcumin is a bioactive polyphenol found in turmeric rhizomes and is used in traditional Chinese medicine (10, 11). Evidence has demonstrated that curcumin can decrease Body Mass Index (BMI), weight, and Waist Circumference (WC), improve lipid profile, and reduce blood sugar in people with T2DM (12). In individuals with T2DM, the development of inflammatory mediators is the basis of biological disorders (10, 12). Curcumin plays an inhibitory role in the development of inflammation in these patients (13). Curcumin has also has been found to decrease the release of cytokines and the permeability of macrophages and to improve insulin sensitivity (14).

On the one hand, the effect of AT on lipid profile and glycemic status has not been the same in all the studies performed on patients with T2DM. On the other hand, most studies have explored the separate effects of AT and Turmeric Supplementation (TS) on anthropometric indices, lipid profile, and glycemic status. However, limited studies have investigated the combined effects of AT and TS, and none has compared the separate and interactional effects of AT and TS.

2. Objectives

The present study aims to investigate how combined and separate AT and TS can alter lipid profile and glycemic status in middle-aged females with T2DM and hyperlipidemia.

3. Patients and Methods

3.1. Trial Design and Participants

This single-blind, randomized, placebo-controlled study was performed between May 2021 and July 2021. Considering the power of 0.99, alpha = 0.05, and effect size of 0.85 and using G. POWER 3.1 software, a 36-subject sample size was estimated for the study. To be more conservative, 44 middle-aged females aged 40 – 60 years who suffered from T2DM and hyperlipidemia were selected randomly from the Diabetes Center of Taleghani Hospital, Kermanshah. In fact, all the participants had the same chance of being selected. Then, they were randomly assigned to four groups, namely AT + TS (n = 11), AT + placebo (AT; n = 11), TS (n = 11), and control + placebo (C; n = 11), via a numbered list using the Random Number Generator. However, one participant in the AT group and one in the C group refused to continue cooperation in the research (Figure 1). The inclusion criteria of the study were suffering from non-insulin-dependent (type II) diabetes, HbA1C > 6, Triglycerides (TG) > 150 mg/dL, LDL > 100 mg/dL, and BMI = 25 - 30 kg/m2. The exclusion criteria were exercising on a regular basis, history of heart

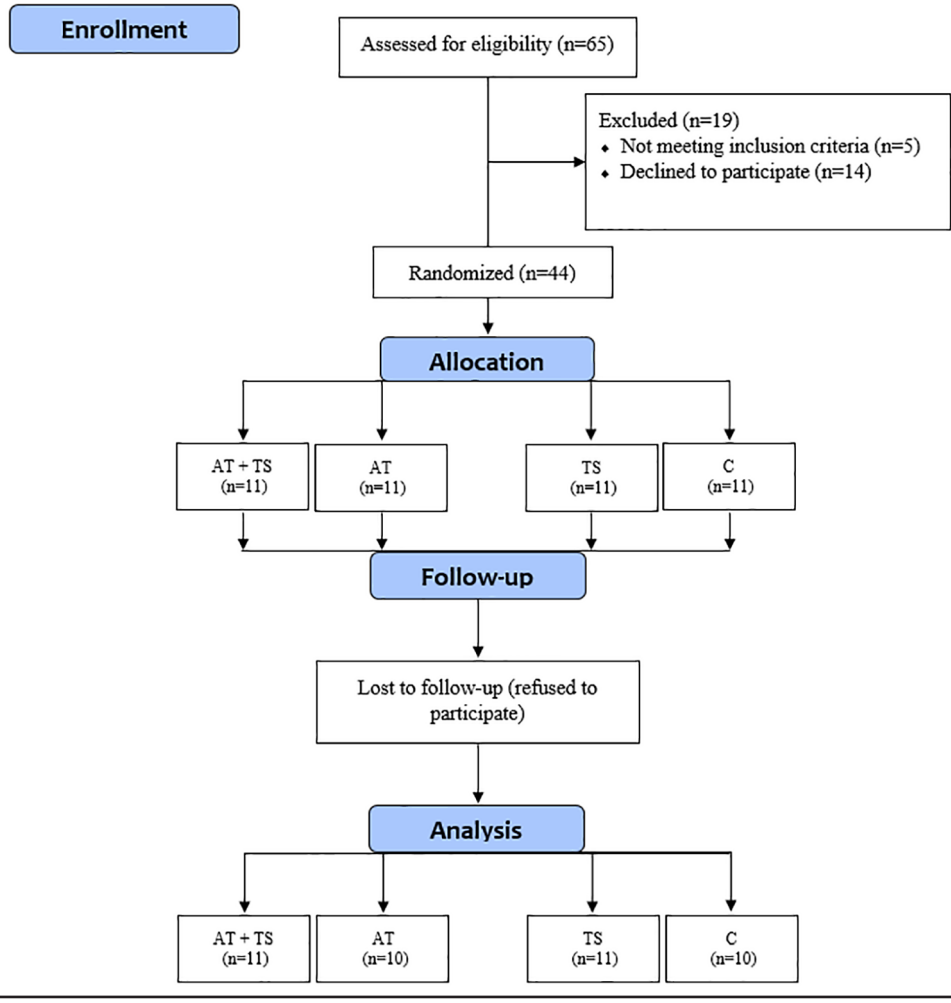


Figure 1. Flow Chart of the Study Population

diseases, hypertension, orthopedic disorders, and smoking, consumption of immunosuppressive drugs, antioxidants, multivitamin supplements, and polyphenols within the past three months, irregular attendance in exercise training and test sessions, muscle injuries, inability to perform the exercises, and COVID-19 infection during the study period.

3.2. Intervention

3.2.1. AT

The participants in the AT group were required to exercise at home three times per week for eight weeks. All the training sessions were carried out under the supervision of exercise physiologists. In this group, the participants were instructed to do the walking exercise, starting with 20 min at 60% of HRmax per session and increasing up to 40 min at 75% of HRmax per session, which was based on the recommendation of the American Diabetes Association (ADA) (15) (Table 1). Every session also included a 10-min warm-up and a 10-min cool-down. At the outset, the HRmax formula was used to determine the target heart rate [HRmax = 220 − age] (16). The participants were taught to count their pulse rates and heart rates using the pulse palpation method in a training session. Moreover, the 6-20 Rating of Perceived Exertion (RPE) scale was used to ensure that the desired heart rate (exercise intensity) was achieved and maintained during the walking aerobics phase (17) (Table 1).

3.2.2. Turmeric Supplement

The participants were asked to consume the same food and macronutrient composition one day before collecting blood samples in the pre- and post-test. According to a previous research, the TS group participants were required to consume 2100 mg capsules containing turmeric powder daily for eight weeks (18). Dry turmeric powder was prepared after cleaning and grinding turmeric wood prepared by the Traditional Medicine Research Center. Meanwhile, C and AT groups were given 2100 mg capsules containing cornstarch flour with a similar shape, color, and packaging.

3.3. Measurements

3.3.1. Anthropometric and Body Composition

Three days before the beginning of the intervention and at the end of the study, the participants were familiarized with the study procedure and the primary measurements including anthropometric parameters and body composition were done. Height was measured to the nearest 0.5 cm using a stadiometer (DETECTO, Model 3PHTROD-WM, USA), and waist circumference was measured to the nearest 0.5 cm with a non-elastic tape measure. Additionally, the fat mass of the whole body, BMI, and weight were assessed by the INBODY test using bioelectric impedance analysis (Zeus 9.9 PLUS; Jawon Medical Co., Ltd., Kungsang Bukdo, South Korea) at 8-9 A.M. after an at least 12-hour fasting. The participants were asked not to participate in intensive physical activities 48 hours before the test and to refrain from taking diuretics.

3.3.2. Blood Sampling and Biochemical Analysis

After 12 hours of fasting, blood samples were collected at the pre-test and post-test (48 hours before and after the first and the last training sessions, respectively). After resting in a stable state for 30 minutes, 20 cc venous blood was sampled from the antecubital vein using an anticoagulant-treated syringe. The sampled blood was placed in a tube that was not treated for anticoagulation and was then centrifuged at 3,000 rpm using a centrifugal separator for 10 minutes. After extracting the serum from the cellular components, it was poured into a storage tube and was stored in the refrigerator at -70 °C until analysis. Blood lipid profile (TG, Total Cholesterol (TC), HDL, and LDL) was measured enzymatically using Hitachi kits, Tokyo, Japan. Besides, Apolipoprotein A1 (ApoA1) and Apolipoprotein B (ApoB) were measured through the immunoturbidimetric method (Cobasintegra 400, a Roche Company, Germany). Fasting insulin level was also assessed via Enzyme Linked Immunosorbent Assay (ELISA) (Mercodia kits, Sweden). Moreover, glucose level was assayed by the enzymatic method (Pars Azmun Kit, Iran) and HbA1C was evaluated using the ion exchange chromatography method (DS5, Britain). Finally, the insulin resistance index was assessed using the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) equation as follows: resistance (HOMA) = [glucose (mg/dL) × insulin (μU/mL)]/405 (19).

3.4. Data Analysis

The statistical analyses were performed using the IBM SPSS software, version 26.0 (IBM Corp., Armonk, NY, USA). All the data have been presented as mean and standard deviation. The Shapiro–Wilk test was used to check the normal distribution of the continuous variables. Between-group comparisons were made using the Analysis of Covariance (ANCOVA) followed by Bonferroni test. Within-group comparisons were also made using paired sample t-test. P-values less than 0.05 were considered statistically significant.

4. Results

The baseline characteristics of the participants have been presented in Table 2. The results showed no significant differences among the four groups regarding age, medications, and duration of diabetes at baseline ($P > 0.05$).

The results of between-group comparisons of the participants' anthropometric indices have been presented in Table 3. The results of t-test revealed no significant differences in the means of Body Weight (BW), BMI, Body

Table 1. The Aerobic Training Protocol

Variables	Week							
	1	2	3	4	5	6	7	8
Intensity (HR_{Max})	60 - 65%	60 - 65%	60 - 65%	65 - 70%	65 - 70%	65 - 70%	70 - 75%	70 - 75%
Time (min)	20	25	30	30	35	35	40	40
Borg scale	10	10	11	11	12	12	13	13

Table 2. The Baseline Characteristics of the Study Participants

Variables	AT + TS (n = 11)	AT (n = 10)	TS (n = 11)	C (n = 10)	P-value [a]
Age (years)	43.02 ± 3.04	42.13 ± 2.39	44.33 ± 1.23	44.22 ± 3.07	0.336
Height (cm)	160.12 ± 4.11	163.13 ± 3.03	159.24 ± 2.79	161.13 ± 5.08	0.393
Blood sugar-lowering agents					0.496
Metformin (%)	5 (50.0)	6 (54.55)	5 (45.46)	7 (70.0)	
Glibenclamide (%)	1 (10.0)	2 (18.18)	2 (18.18)	1 (10.0)	
Metformin + glibenclamide (%)	2 (20.0)	1 (9.09)	2 (18.18)	1 (10.0)	
Gliclazide (%)	1 (10.0)	2 (18.18)	2 (18.18)	1 (10.0)	
Blood lipid-lowering agents					0.577
Atorvastatin (%)	6 (60.0)	6 (54.55)	8 (72.73)	7 (70.0)	
Cholestyramine (%)	2 (20.0)	3 (27.27)	2 (18.18)	2 (20.0)	
Fenofibrate or gemfibrozil (%)	2 (20.0)	2 (18.18)	1 (9.09)	1 (10.0)	
Duration of diabetes					0.367
> 5 years (%)	7 (70.0)	8 (72.73)	7 (63.64)	6 (60.0)	
5 – 10 years (%)	3 (30.0)	3 (27.27)	4 (36.36)	4 (40.0)	

Note: Data of age have been presented as mean ± SD. P<0.05 was considered significant.

Table 3. Mean ± SD of Anthropometric Indices in the Study Groups before the Intervention

Variables	AT + TS (n = 11)	AT (n = 10)	TS (n = 11)	C (n = 10)	P-value [b]
Body weight (Kg)					
Before	73.12 ± 2.91	75.13 ± 2.07	74.13 ± 2.68	75.09 ± 3.20	
After	69.22 ± 3.22	72.16 ± 1.01	72.24 ± 1.76	78.35 ± 4.21	
P†	0.001 *	0.003*	0.002*	0.001*	
Δ	-3.90 ± 0.31 $^{\mu\epsilon\beta}$	-2.97 ± 1.06 $^{\beta}$	-1.89 ± 0.92 $^{\beta}$	3.26 ± 1.01	0.001 ¥
BMI (kg/m^2)					
Before	28.15 ± 1.02	28.12 ± 1.23	29.30 ± 0.30	29.02 ± 1.04	
After	26.99 ± 2.24	27.14 ± 1.07	27.94 ± 0.13	30.12 ± 0.88	
P†	0.001*	0.003*	0.002*	0.001*	
Δ	-1.16 ± 1.22 $^{\beta}$	-0.98 ± 0.16 $^{\beta}$	-1.36 ± 0.17 $^{\beta}$	1.10 ± 0.16	0.002 ¥
Body fat percent (%)					
Before	30.14 ± 1.26	32.09 ± 2.01	29.23 ± 1.27	31.16 ± 2.52	
After	26.09 ± 1.17	28.11 ± 1.84	28.13 ± 0.61	32.11 ± 1.76	
P†	0.001*	0.001*	0.025*	0.001*	
Δ	-4.05 ± 0.09 $^{\mu\epsilon\beta}$	-3.98 ± 0.17 $^{\beta}$	-1.10 ± 0.66 $^{\beta}$	0.95 ± 0.76	0.002 ¥
WHR					
Before	0.90 ± 0.03	0.9 2± 0.04	0.91 ± 0.05	0.92 ± 0.02	
After	0.87 ± 0.01	0.90 ± 0.01 $^{\beta}$	0.90 ± 0.02 $^{\beta}$	0.95 ± 0.02	
P†	0.002*	0.001*	0.001*	0.001*	
Δ	-0.03 ± 0.02 $^{\mu\epsilon\beta}$	-0.2 ± 0.03 $^{\beta}$	-0.01 ± 0.03 $^{\beta}$	0.3 ± 0.0	0.001 ¥

Abbreviations: AT+TS, aerobic training + turmeric supplement; AT, aerobic training group; TS, turmeric supplement group; C, control group. *Data analysis was done by the analysis of covariance and least significant difference post-hoc Bonferroni test after adjustment for baseline values. P†: Statistical analysis was done by paired sample t-test. *: Significantly different in within-group comparisons in the pretest and posttest. ¥: Significant differences between the Δ of the study groups. μ: Significantly different compared to AT. €: Significantly different compared to TS. β: Significantly different compared to C.

Fat Percentage (BFP), and Waist-to-Hip Ratio (WHR) after the intervention compared to the pre-test. After eight weeks, BW, BMI, BFP, and WHR significantly decreased in the AT + TS, AT, and TS groups, but significantly increased in the C group.

The results of ANCOVA revealed significant differences among the study groups regarding BW, BMI, BFP, and WHR. The results of Bonferroni post-hoc test showed that BW, BMI, BFP, and WHR changes were significant in the AT + TS, AT, and TS groups compared to the C group. The results also indicated significant differences between the AT + TS group and AT and TS groups concerning BW, BFP, and WHR. However, no significant difference was found between the AT and TS groups with respect to BW, BMI, BFP, and WHR (Table 3).

As detailed in Table 4, the results revealed a significant improvement in insulin, glucose, HOMA-IR, HbA1C, TC, TG, LDL, and HDL levels in the study groups from the pretest to the posttest. Additionally, the results of ANCOVA showed significant differences among the study groups concerning TC, TG, LDL, and HDL levels. Accordingly, a significant difference was found between the AT + ST, AT, and ST groups and the C group regarding insulin, glucose, HOMA-IR, and HbA1C levels. A significant difference was also observed in insulin, glucose, and HOMA-IR in the AT + TS group compared to the AT and TS groups alone. Furthermore, the results revealed a significant difference between AT and TS groups regarding glucose and HOMA-IR, but not insulin and HbA1C. In addition, lipid profile changes were significant in the AT + TS, AT, and TS

Table 4. Mean ± SD of Glycemic Status and Lipid Profile before the Intervention

Variables	AT + TS (n = 11)	AT (n = 10)	TS (n = 11)	C (n = 10)	P-value [a]
Insulin (μU/mL)					
Before	6.69 ± 0.13	6.59 ± 0.08	6.55±0.16	6.63 ± 0.18	
After	5.98 ± 0.19	6.28 ± 0.05	6.41±0.06	6.90 ± 0.13	
P†	0.001*	0.001*	0.015*	0.001*	
Δ	-0.71 ± 0.6 μ€β	-0.31 ± 0.03 €β	-0.14±0.10 β	0.27 ± 0.05	0.001 ¥
FBG (mg/dl)					
Before	152.80 ± 1.75	155.11 ± 1.48	155.08 ± 2.04	153.40 ± 2.50	
After	134.50 ± 2.36	141.54 ± 2.11	147.45 ± 2.06	158.60 ± 1.84	
P†	0.001*	0.001*	0.001*	0.002*	
Δ	-18.30 ± 0.61 μ€β	-13.57 ± 0.63 €β	-7.63 ± 0.02 β	5.20 ± 0.66	0.001 ¥
HOMA-IR					
Before	2.52 ± 0.06	2.52 ± 0.04	2.50 ± 0.06	2.51 ± 0.08	
After	1.98 ± 0.06	2.19 ± 0.02	2.33 ± 0.04	2.70 ± 0.05	
P†	0.001*	0.001*	0.001*	0.001*	
Δ	-0.54 ± 0.0 μ€β	-0.33 ± 0.02 €β	-0.17 ± 0.04 β	0.19 ± 0.03	0.001 ¥
HbA1C%					
Before	7.68 ± 0.48	7.93 ± 0.69	7.70 ± 0.22	7.75 ± 0.13	
After	6.93 ± 0.64	7.06 ± 0.45	7.40 ± 0.16	7.92 ± 0.11	
P†	0.013*	0.003*	0.037*	0.045*	
Δ	-0.75 ± 0.16 €β	-0.87 ± 0.24 β	-0.30 ± 0.06 β	0.17 ± 0.02	0.001 ¥
TC (mg/dl)					
Before	210.08 ± 4.91	216.88 ± 6.02	210.08 ± 3.92	213.32 ± 3.20	
After	183.45 ± 4.34	195.09 ± 3.43	204.42 ± 2.17 β	217.45 ± 5.11	
P†	0.001*	0.001*	0.001*	0.002*	
Δ	-26.63 ± 0.57 μ€β	-21.79 ± 2.59 β	-5.66 ± 1.75 β	4.13 ± 1.91	0.001 ¥
TG (mg/dl)					
Before	181.18 ± 5.28	184.02 ± 6.76	181.69 ± 7.04	183.23 ± 4.51	
After	164.11 ± 2.23 μ€β	173.11 ± 2.33	177.86 ± 4.13 β	186.22 ± 2.88	
P†	0.001*	0.001*	0.001*	0.001*	
Δ	-17.07 ± 3.05 μ€β	-10.91 ± 4.43 €β	-3.83 ± 2.91 β	2.99 ± 1.63	0.011 ¥
LDL (mg/dl)					
Before	133.09 ± 6.23	137.03 ± 3.21	136.13 ± 4.55	135.16 ± 4.55	
After	119.27 ± 3.87	126.09 ± 2.24	131.24 ± 2.60	138.81 ± 3.76	
P†	0.001*	0.001*	0.001*	0.003*	
Δ	-13.82 ± 2.36 μ€β	-10.94 ± 0.97 €β	-4.89 ± 1.95 β	3.65 ± 0.79	0.002 ¥
HDL (mg/dl)					
Before	33.19 ± 4.07	31.13 ± 2.86	32.17 ± 2.66	32.22 ± 2.15	
After	43.21 ± 3.45 μ€β	38.05 ± 1.02 β	36.55 ± 1.82 β	30.19 ± 1.44	
P†	0.001*	0.001*	0.001*	0.002*	
Δ	10.02 ± 0.62 μ€β	6.92 ± 1.84 β	4.38 ± 0.84 β	-2.03 ± 0.71	0.021 ¥

Abbreviations: AT+TS, aerobic training + turmeric supplement; AT, aerobic training group; TS, turmeric supplement group; C, control group. *Data analysis was done by the analysis of covariance and least significant difference post-hoc Bonferroni test after adjustment for baseline values. P†: Statistical analysis was done by paired sample t-test. *: Significantly different in within-group comparisons at pre and posttests. ¥: Significant differences between the Δ of the study groups. μ: Significantly different compared to AT. €: Significantly different compared to TS. β: Significantly different compared to C.

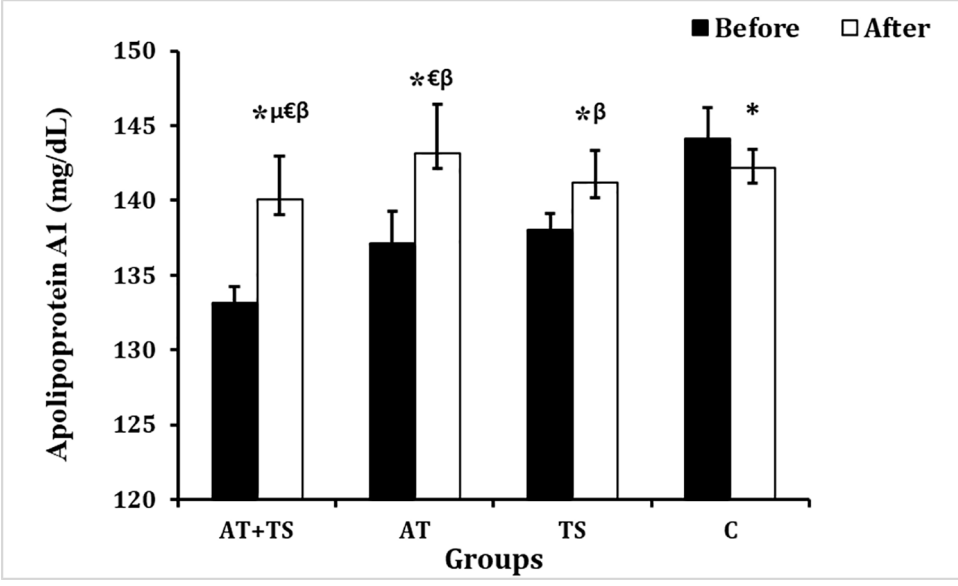
groups compared to the C group. Besides, the AT + TS group had significantly lower TC, TG, and LDL levels and significantly higher HDL levels compared to the AT and TS groups. The results also showed a significant difference between the AT and TS groups regarding all the variables, except for insulin (P = 0.215), HbA1C (P = 0.994), and HDL (P = 0.440).

As depicted in Figures 2 and 3, there were significant differences in ApoA1 and ApoB levels in the pretest and posttest in all the study groups. The results of ANCOVA showed significant differences among the study groups with regard to ApoA1 and ApoB levels. Accordingly, ApoA1 and ApoB changes were significant in AT + TS, AT, and TS groups compared to the C group. Based on the results presented in Figure 2, the AT + TS group exhibited a significantly higher ApoA1 level and lower ApoB level compared to the AT and TS groups. Additionally, the AT group presented significantly lower ApoA1 and ApoB levels (P = 0.011 and P = 0.021, respectively) compared to the TS group.

5. Discussion

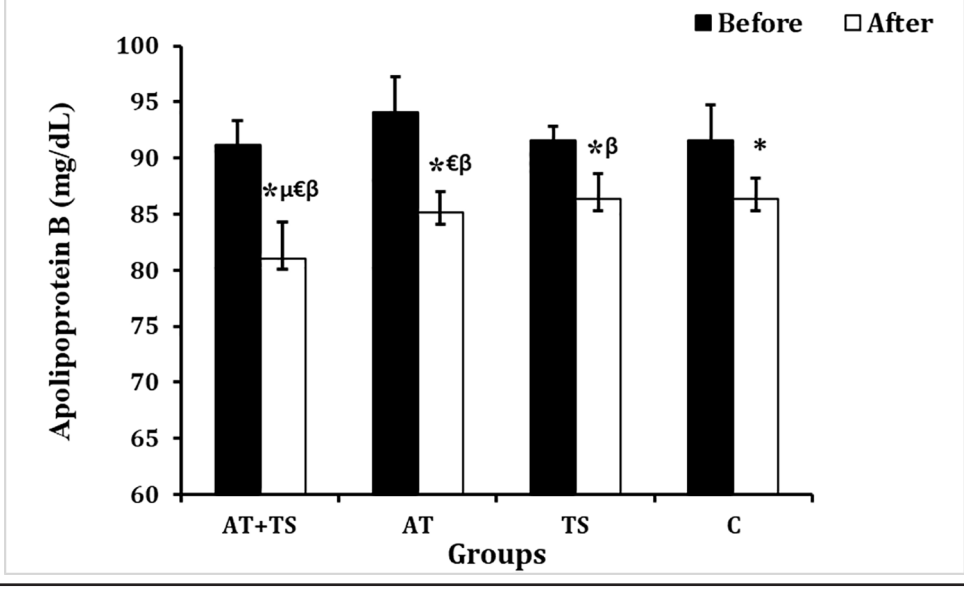
The results of the present study indicated that eight weeks of AT and TS led to a significant decrease in anthropometric indices (BW, BMI, and BFP) in hyperlipidemic females with T2DM. Although this decrease was significant in the AT and TS groups alone, it was more prominent in the AT + TS group. However, a significant increase was found in anthropometric indices in the C group. In the same line, Adab et al. (2019) reported that the daily consumption of

Figure 2. Comparison of the Study Groups regarding the Mean ± SD of Apolipoprotein A1



Abbreviations: AT+TS, aerobic training + turmeric supplement; AT, aerobic training group; TS, turmeric supplement group; C, control group. *: Significantly different in within-group comparisons at pre and posttests. µ: Significantly different compared to AT. €: Significantly different compared to TS. β: Significantly different compared to C.

Figure 3. Comparison of the Study Groups regarding the Mean ± SD of Apolipoprotein B



Abbreviations: AT+TS, aerobic training + turmeric supplement; AT, aerobic training group; TS, turmeric supplement group; C, control group. *: Significantly different in within-group comparisons at pre and posttests. µ: Significantly different compared to AT. €: Significantly different compared to TS. β: Significantly different compared to C.

2100 mg of turmeric powder (700 mg capsules) resulted in a significant reduction in weight and BMI (20). Ho et al. (2012) also assessed the anti-obesity effects of turmeric in obese rats and revealed a significant reduction in weight (21). The main mechanism by which turmeric improves anthropometric parameters might be increased free fatty acid oxidation, increased basal metabolic rate, and decreased levels of inflammatory cytokines (21). Consistent with the results of the present study, Banitalebi et al. (2019) (22) and Jiang et al. (2020) (23) stated that AT reduced BW and BFP by increasing maximal fat oxidation in patients with T2DM. Therefore, regular AT in these patients might improve anthropometric indices by increasing the gene expression of lipolytic, beta-oxidation, Krebs cycle, electron transfer chain enzymes, mitochondrial density, and fat uptake as the energy supply (22, 23).

The current study results demonstrated significant changes in the glycemic index after AT + TS. Accordingly, insulin, FBS, HOMA-IR, and HbA1C levels decreased significantly after the eight-week intervention. Although this decrease was observed after AT and TS alone, the interactive effect of AT + TS was significantly stronger. The possible exercise-induced mechanisms might be increased Glucose Transport Protein (GLUT-4), insulin receptor signaling, glycogen synthase and hexokinase enzymes activity, muscular capillaries, and mitochondria and glucose uptake,

consequently increasing free fatty acid metabolism in serum and muscle tissue and increasing adipokine levels (24). Moreover, turmeric activates glycolysis, inhibits hepatic gluconeogenesis, and reduces lipid metabolism, eventually reducing insulin resistance and improving the glycemic status (25, 26).

The findings of the present study showed the lowest levels of TC, TG, and LDL and the highest levels of HDL in the AT + TS group after eight weeks. Therefore, AT + TS was more effective in improving blood lipid profile compared to TS or AT alone. Consistently, Hoseini et al. (2019) and Dolati et al. (2020) reported that the combination of TS and AT improved the glycemic and lipid statuses more effectively in comparison to TS or AT alone (27, 28). Although the mechanism of exercise-induced lipid changes is unclear, AT may increase serum lipid consumption, thereby decreasing lipid levels (29). Other mechanisms may involve the increased activity of Lipoprotein Lipase (LPL) that is responsible for chylomicrons and Very Low Density Lipoprotein (VLDL) and Triacylglycerol (TAG) hydrolysis in granules (29), increased expression of ATP-Binding Cassette Transporter A-1 (ABCA1), plasma HDL formation, and protection against atherosclerosis (30). The effective mechanism of TS in improving the lipid profile in females with T2DM may be partly due to the upregulation of cholesterol catabolism by increasing the activity of cholesterol 7-hydroxylase enzyme in the liver. Increased cholesterol activity (by increasing the activity of hepatic cholesterol enzyme 7-hydroxylase) may also be related to the effect of turmeric on the LDL receptors (by inhibiting the absorption of dietary cholesterol) (31, 32).

The results of the present study showed that eight weeks of AT + TS resulted in a significant increase in the ApoA1 level as well as a significant decrease in the ApoB level in females with T2DM. TS and AT alone also had significant effects on increasing the ApoA1 level and decreasing the ApoB level. However, the combination of AT and TS had a more prominent effect. Low ApoA1 levels are directly related to the development of atherosclerosis, especially when coincided with increased ApoB levels (33, 34). However, studies have indicated that regular AT increases ApoA1 and decreases ApoB by decreasing HDL, increasing the activation of LPL, listin, and acyltransferase, and decreasing hepatic lipase, ultimately reversing cholesterol transfer and reducing the risk of cardiovascular diseases in patients with T2DM (34, 35). TS has also been shown to increase fatty acid beta-oxidation by inhibiting the Fatty Acid Synthase (FAS) activity. As a result, it leads to an effective reduction in fat storage, which regulates lipid metabolism by increasing ApoA1 and decreasing ApoB (22).

The strengths of the present study were the successful blinding of the participants, accurate control of AT intensity, and high rate of compliance (all the participants reported that they had taken the capsules through the study). However, one of the study limitations was that it was a short-term trial, and it is unknown whether longer durations of supplementation could cause further improvements. Additionally, the impact of different doses was not investigated in this research. Finally, the small number of the participants could affect the generalizability of the results.

5.1. Conclusion

Based on the findings, AT + TS is recommended as a convincing lifestyle approach due to its great effect on lipid profile, glycemic status, and ApoA1 and ApoB levels in middle-aged hyperlipidemic females with T2DM. Yet, further studies are suggested to determine the most efficient TS dose and exercise type (High Intensity Interval Training (HIIT), Moderate Intensity Continuous Training (MICT), and Low Intensity Continuous Training (LICT)) in different age groups in the long run.

5.2. Ethical Approval

This study was approved by the Ethics Committee of Razi University of Kermanshah (IR.RAZI.REC.1400.013) and was registered in the Iranian Clinical Trial Registration Center (code: IRCT20201129049524N1).

5.3. Informed Consent

Written informed consent approved by the local Ethics Committee of the institute was obtained from all the participants. In this form, the participants were informed about the voluntary nature of the research as well as their right to leave the study.

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Authors' Contribution

RH designed the study. MAD did the experiments. SG analyzed the data and wrote the manuscript. EA was involved in the interpretation of the data and reviewed and edited the manuscript. All authors read and approved the final manuscript.

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