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Aerobic exercise can improve the beneficial effects of curcumin on PCOS patients

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Abstract

Background: Evidence suggests lifestyle modification, including increased physical activity, should be the first line of therapy for women with Polycystic Ovary Syndrome (PCOS). Combining exercise with herbal medicine can improve health and performance. Exercise and curcumin supplementation can independently improve metabolic and hormonal status in PCOS patients. No data regarding the combined effect of curcumin supplementation and exercise on woman with PCOS.

Objectives: In this study, we examined the combined effect of curcumin supplementation and aerobic exercise on lipid profile, glycemic variables and hormonal parameters in women with PCOS.

Method: In this randomized, 125 woman with PCOS were randomly assigned to four groups: curcumin (CUR, N=31), aerobic training + curcumin (Tr+CUR, N=31), aerobic training + placebo (CUR+PL, N=32), and placebo (PL, N=31). Curcumin or placebo capsules (500 mg/twice/day) were administered for 12 weeks. Anthropometry, glycemic variables, and lipid profiles and hormonal, selected hormones, and were measured pre and post-intervention.

Results: Following the 12 week intervention, Curcumin and aerobic training showed significant reductions in weight, BMI, blood glucose, insulin and HOMA-IR, TG, TC and LDL; and increased HDL-c and DEHA. Curcumin supplementation alone did not have significant effect on WHR, WC, FSH, LH, testosterone and SHBG. Aerobic training, with CUR or PL, had a more significant positive effect on anthropometric parameters, blood glucose, insulin, HOMA-IR, TG, TC, LDL, HDL-c, DEHA, FSH, LH, testosterone and SHBG compare to curcumin and aerobic training alone.

Conclusion: According to the findings of the present study, it seems that the combination of aerobic exercise and curcumin supplementation might be more effective on anthropometric, metabolic and hormonal parameters than either intervention alone in woman with PCOS.

Keywords: Aerobic exercise, Curcumin, polycystic ovary syndrome, hormonal imbalance, Synergism.

Introduction

Polycystic ovary syndrome (PCOS) is a common metabolic and endocrine disorder among females and is a series of indications associated to hormonal imbalance (Essah, Wickham and Nestler 2007, Kempegowda et al. 2020, Velija-Ašimi 2013). Ovulation inconsistencies brought on by this hormonal imbalance may result in the development of cysts in the ovary. This condition, which affects 4–6% of women of reproductive age, is the most prevalent hormonal disease in women (Khmil, Khmil and Marushchak 2020, Torchen et al. 2016). An increase in LH levels, a slight decrease in FSH levels or no change in FSH levels, a slight increase in prolactin, an increase in estradiol and estrogen levels, a potential increase in dehydroepiandrosterone sulfate (DHEAS), androstenedione, and testosterone, and a possible decrease in sex hormone-binding globulin (SHBG) are just a few of the systems in the body that are affected (Choudhary, Jain and Chaudhari 2017, Barbosa et al. 2016). Women with PCOS frequently exhibit metabolic problems such as insulin resistance, dyslipidemia and hyperinsulinemia, making them more likely to develop type 2 diabetes and cardiovascular illnesses (Liu et al. 2019).

Insulin controls the actions of liver and ovary enzymes, which contribute to the generation of androgen and low-grade inflammation, respectively, in PCOS. Insulin resistance, according to reports, frequently results in issues including dyslipidemia as well as cardiovascular and metabolic illnesses (Russell, Wong and Grumbach 2014). Studies indicate that PCOS has a complex and multi-factor etiology that results from the combination of genetic, environmental, and intrauterine variables, while the pathophysiology of PCOS is yet unknown (Chen and Pang 2021).

Aerobic exercise is a crucial component in the prevention and treatment of many diseases since it is a powerful nonpharmaceutical intervention. It enhances metabolic processes and the immunological, cardiovascular, and respiratory systems within the body (Sawant and Bhide 2019). Exercise is an essential first step in treating overweight and obese PCOS patients because it not only reduces hyperandrogenism and menstrual irregularities

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but also has a significant positive impact on the cardiometabolic profile and cardiopulmonary function of PCOS patients (Bellver et al. 2018, Barber et al. 2019). Women with PCOS are only advised to alter their lifestyles as a form of treatment because there is currently no cure for the condition (Ee et al. 2021). The majority of these therapies concentrate on improving weight loss, physical activity, and eating behaviors (Brennan et al. 2017, Hajivandi et al. 2020). However, recent research on medicinal herbs and complementary medicine has produced encouraging findings for the treatment of PCOS. Curcumin is one of the auxiliary antioxidant components that has received a lot of attention recently. The ginger family member turmeric, which contains phenol and quinone groups, is used to make curcumin, a natural medication. It is widely recognized as a secure dietary supplement (Pachiappan et al. 2017, Kamal et al. 2021, Jabczyk et al. 2021). Patients with PCOS were given curcumin (in doses of 500–1500 mg three times a day for 1-3 months) or a placebo in various randomized, double-blinded clinical trials. It has been hypothesized that curcumin can significantly reduce hyperandrogenism, insulin resistance and serum glucose levels in PCOS (Jabczyk et al. 2021, Jamilian et al. 2020).

Curcumin and exercise have each been proven in a number of trials to have positive effects on PCOS, although it is unclear how well they work together. In this regard, Zhang et al. demonstrated that exercise and curcumin together had beneficial effects on follicular dysfunction in rats with PCOS-like conditions. However, no human study has yet looked into the combined effects of curcumin and exercise on PCOS, so this research looked into the combined effects of curcumin and exercise for the first time in women with PCOS as one of the potential mechanisms of PCOS pathogenesis.

Material and methods

A double-blind, randomized, placebo-controlled clinical trial was used to construct this investigation. The study methodology included 88 consecutive young, overweight, nonsmoking women with PCOS. PCOS was identified using the National Institutes of Health criteria (Fauser et al. 2012) Pregnancy, glucose intolerance (as detected by a 2-hour oral glucose tolerance test), diabetes, hypothyroidism, hyperprolactinemia, Cushing's syndrome, nonclassical congenital adrenal hyperplasia, and use of oral contraceptives, glucocorticoids, antiandrogens, ovulation inducers, antidiabetic, or antiobesity medications within the previous 6 months were all exclusion criteria. The study also excluded participants with neoplastic, hepatic, respiratory, cardiovascular, or any other concurrent medical conditions (such as heart failure, lung disease, or renal disease). This study was approved by the Ethics Committee of Yan 'an University, China (Ethical committee reference code: YDYIG2019035)

Study design

Fig. 01 displays a flowchart of the study protocol. The subjects (n = 125) were divided into four groups at random using a list generated by a random number generator: curcumin supplementation (CUR, N=31), aerobic training + curcumin supplementation (Tr+CUR, N=31), aerobic training + placebo (Tr+PL, N=32) and placebo (PL, N=31) for a period of 12 weeks, while the Tr+PL and PL groups received a placebo daily. Before and 12 weeks after the intervention, questionnaires about the menstrual cycle characteristics were completed (Fig. 01).

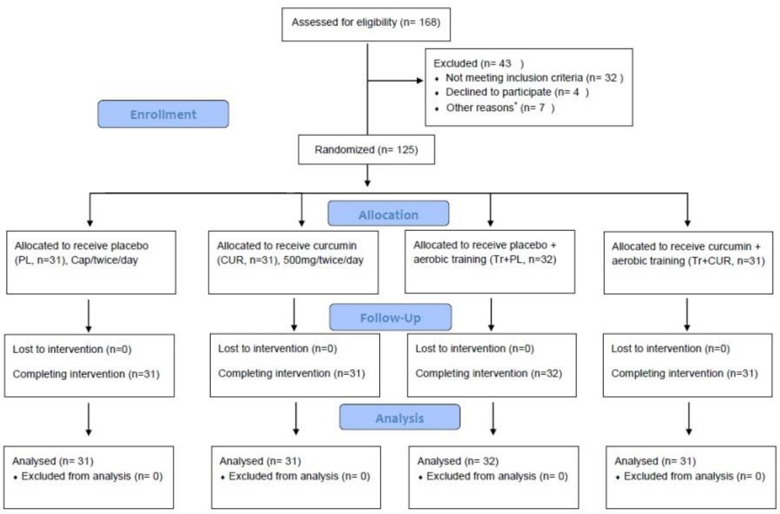

Fig 01. A flowchart of the study protocol

Supplementation

The turmeric extract used in the curcumin supplement, known as BCM95®, commonly referred to as Curcugreen®, was standardized to contain at least 65% curcumin, at least 95% curcuminoids, and naturally occurring quantities of turmerones. It contained 500 mg of this extract. The dry rhizomes of turmeric were used to make the turmeric extract, which was then turned into turmeric oleoresin by extracting it with ethyl acetate. The curcumin supplement is made more accessible by combining curcuminoid crystals that were precipitated at low temperatures with turmeric essential oil that was obtained through steam distillation. Roasted rice powder was used to make the curcumin placebo capsules. M/s Arjuna Natural Pvt. Ltd., India, provided the curcumin supplement and its placebo capsules. The texture and look of the placebos matched those of the relevant active supplement.

Aerobic training

The subjects in the Tr+CUR and Tr+PL groups engaged in aerobic exercise in a gym three times per week for a period of 12 weeks. The 6-minute Rockport test was used to gauge each subject's level of aerobic fitness. Each person's maximum heart rate was calculated to be 208−0.7×(age) (Tanaka, Monahan and Seals 2001). During the training session, the subjects stretched for 6 minutes to warm up before running continuously on the treadmill for 20 minutes at a speed of 7 km/hr and a heart rate of 50% to 80% of maximum. To ensure that they ran at the desired intensity, a Polar polarimeter (within 5% of a heartbeat error rate) measured their heart rate. This level of intensity was unique. Everybody had a certain intensity. The younger participants ran harder, while the older participants ran less. The running time was increased by 90 seconds in each of the ensuing sessions. Using a belt heart rate sensor (Polar Beat, Kempele, Finland), the exercise intensity was managed. CUR and PL group participants were told not to alter their level of physical activity.

Anthropometric measurements

One observer (SD) measured the anthropometric indexes. With subjects wearing minimal clothing and no shoes, body weight was measured using electronic digital scales, which were accurate to 0.1 kg. A flexible stadiometer was used to measure height in standing posture to the nearest 0.1 cm. By dividing body weight (kg) by the square of height (m), the BMI was computed. According to established protocols, measurements of the waist and hip circumferences (HC; to the nearest 0.5 cm) were taken while the subjects were standing (Rahimi et al. 2016). Using a regular measuring tape, the WC was measured from the front at the narrowest point between the rib cage and iliac crest following complete expiration, and the HC was measured from the side at the maximum extension of the buttocks. The formula used to compute the waist-to-hip ratio (WHR) was WC (cm) divided by HC (cm).

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Biochemical assessment

12 hours of fasting were followed by the collection of blood samples. Using original kits and an Abbott-Aeroset autoanalyser (Architect C-8000, Chicago, Illinois, USA), glucose, total cholesterol, high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL), and triacylglycerols were determined. Utilizing data from fasting serum tests, the homeostasis model assessment-insulin resistance (HOMA-IR) was used to evaluate insulin resistance. A chemiluminescent microparticle immunoassay (Architect Abbott Lab, IL, USA) was used to measure luteinizing hormone (LH), follicle-stimulating hormone (FSH), total testosterone, Sex Hormone Binding Globulin (SHBG) and dehydroepiandrosterone (DHEA).

HOMA-IR=fasting insulin (μU/mL)×fasting blood glucose (mmol/L)/22.5

Statistical analysis

The statistical analyses were performed using IBM SPSS version 22.0 (IBM Corp., Armonk, NY, USA). All data are presented as mean±standard deviation. The Kolmogorov-Smirnov test was used to check the normal distributions of continuous variables. Between-group comparisons were performed using the analysis of covariance followed by the least significant difference post-hoc test (Bonferroni test). Within-group comparisons were performed using paired sample t-tests. A P-value less than 0.05 was considered statistically significant.

Results

Anthropometric parameters

After intervention, weight and BMI considerably decreased in all intervention groups when compared to baseline, according to intragroup analysis. Contrary to what would be expected, there was no significant difference between the Tr+CUR and Tr+PL groups in terms of weight or BMI compared to the CUR group. The post-test CUR and PL groups' WHR and WC did not significantly decline from their pre-test levels. While there was no discernible change in mean WHR and WC between the Tr+CUR and Tr+PL groups, they were

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considerably lower in the Tr+CUR and Tr+PL groups than in the CUR and PL groups (p 0.05). Additionally, analysis of WHR and WC reduction revealed no discernible differences between the CUR and PL groups (Table 01).

Table 01. Anthropometric parameters before and after 12-week of intervention.

Variables		PL	CUR	Tr+PL	Tr+CUR	P-value
Weight (kg)	Before	73.23±7.36	72.36±8.25	68.87±8.13	69.13±6.57	0.823
	After	71.92±8.56	70.82±6.08[a]	65.71±8.51[ab]	64.24±7.02[ab]	-
	P-value	0.903	0.034	0.013	0.036	
BMI ($kg.m^{-2}$)	Before	29.23±1.36	29.32±1.74	29.68±2.01	28.81±1.23	0.716
	After	29.41±1.62	28.68±1.01[a]	28.72±1.83[ab]	27.63±1.52[ab]	-
	P-value	0.521	0.046	0.038	0.014	
WC (cm)	Before	93.56±6.33	96.98±5.20	94.33±5.74	93.14±6.77	0.778
	After	92.24±6.02	95.63±4.87	89.29±5.12[ab]	87.84±5.38[ab]	-
	P-value	0.638	0.415	0.029	0.023	
WHR (cm)	Before	0.93±0.02	0.81±0.06	0.91±0.08	0.94±0.03	0.641
	After	0.92±0.06	0.79±0.01	0.86±0.05[ab]	0.85±0.04[ab]	-
	P-value	0.377	0.629	0.031	0.012	

BMI: Body Mass Index; *WC*: Waist Circumference; WHR: Waist-to-Hip Ratio. *Values are showed as mean ± SD. a: Significantly different compared to PL. b: Significantly different compared to CUR. c: Significantly different compared to Tr+PL.*

Biochemical parameters

Glycemic indicators, such as serum glucose, insulin levels, and HOMA-IR post-intervention, were lower in all intervention groups as compared to the pre-intervention group. The CUR and Tr+PL groups significantly reduced glycemic indices more than the Tr+CUR group. Combining curcumin with aerobic exercise significantly improved HDL-c and lowered basal serum TG, TC, and LDL. Even when compared to the PL group, serum levels of TG, TC, and LDL were all lower. Tr+CUR significantly decreased levels of these indices compared to Tr+PL and CUR groups, while the levels of these lipid indices were similar across Tr+PL and CUR groups. In comparison to the PL groups, serum HDL-c levels were higher in all of the examined groups. Comparing the Tr+CUR group to the Tr+PL and CUR groups, a significant rise in HDL-c was observed (Table 02).

Table 02. Biochemical parameters before and after 12-week of intervention.

Variables		PL	CUR	Tr+PL	Tr+CUR	P-value
FBS (mg/dL)	Before	98.38±6.13	100.28±5.87	99.88±5.21	102.12±7.40	0.344
	After	97.23±7.28	93.30±5.43[a]	91.28±5.87[ab]	88.34±5.12[abc]	-
	P-value	0.829	0.531	0.638	0.422	
Insulin (μU/mL)	Before	17.57±3.52	16.38±3.26	18.11±4.33	17.93±5.26	0.482
	After	16.42±3.18	14.01±3.12[a]	14.21±3.52[a]	12.56±5.68[abc]	-
	P-value	0.192	0.34	0.029	0.003	
HOMA-IR	Before	3.99±1.48	4.15±1.11	4.31±1.23	4.03±1.24	0.549
	After	3.66±1.03	3.33±1.26[a]	3.15±1.42[a]	2.80±1.63[abc]	-
	P-value	0.835	0.028	0.016	0.001	
TC (mg/dL)	Before	200.15±18.31	197.99±17.74	208.52±17.81	207.67±16.56	0.762
	After	203.48±13.89	182.29±15.92[a]	183.87±14.93[ab]	169.44±19.82[abc]	-
	P-value	0.719	0.019	0.009	0.0001	
TG (mg/dL)	Before	141.77±9.11	139.84±9.25	140.39±8.17	138.22±9.70	0.276
	After	142.86±8.56	121.66±8.77[a]	123.63±9.75[a]	119.34±7.82[a]	-
	P-value	0.492	0.013	0.008	0.0001	
HDL-c (mg/dL)	Before	47.32±3.29	48.95±5.74	47.28±5.22	48.28±6.02	0.533
	After	48.73±4.64	53.63±5.29[a]	53.04±5.86[a]	56.82±5.54[ab]	-
	P-value	0.633	0.032	0.024	0.001	
LDL-c (mg/dL)	Before	101.32±8.46	103.12±7.02	103.87±7.84	107.88±5.28	0.744
	After	99.87±7.09	97.59±6.28[a]	94.34±7.11[ab]	92.36±5.62[abc]	-
	P-value	0.829	0.046	0.022	0.0001	

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FBS: Fasting blood glucose; HOMA-IR, homeostatic model assessment for insulin resistance;; HDL-c: high-density lipoprotein cholesterol; LDL-c: low-density lipoprotein cholesterol; TG: triglyceride; TC: total cholesterol. *Values are showed as mean ± SD. a: Significantly different compared to PL. b: Significantly different compared to CUR. c: Significantly different compared to Tr+PL..*

Hormonal parameters

Serum DHEA increased significantly in intervention groups compared to the baseline. Furthermore, LH, and testosterone levels were significantly lower in post-tests than pre-tests in the Tr+CUR and Tr+PL groups. Also, LH and testosterone levels were significantly lower in Tr+CUR and Tr+PL groups compared to PL groups ($p < 0.05$) , However, No significant difference was observed in these parameters between Tr+CUR and Tr+PL groups. As shown in Table 03, FSH and SHBG levels were significantly higher in Tr+CUR and Tr+PL groups than in PL group, but this effect was significantly abolished by exercise plus curcumin more than by exercise alone. We observed no significant alterations in LH, FSH, SHBG and testosterone levels in CUR group compared to the PL group (Table 03).

Table 03. Hormonal parameters before and after 12-week of intervention.

Variables		PL	CUR	Tr+PL	Tr+CUR	P-value
LH (mg/dL)	Before	12.81±4.92	13.11±5.11	11.78±5.43	12.13±4.02	0.512
	After	12.03±4.36	11.76±4.93	8.13±4.29[ab]	7.23±4.35[ab]	-
	P-value	0.821	0.128	0.032	0.0001	
FSH (IU/mL)	Before	9.28±2.72	8.77±3.92	10.11±3.87	10.13±4.10	0.819
	After	9.54±2.91	10.01±2.67	13.19±3.95[ab]	15.28±4.62[ab]	-
	P-value	0.910	0.193	0.018	0.010	
Testosterone (ng/dl)	Before	63.94±10.48	68.15±11.16	64.14±9.91	63.54±11.32	0.922
	After	64.11±11.02	65.53±12.43	54.10±10.17[ab]	48.81±10.13[abc]	-
	P-value	0.536	0.149	0.034	0.001	
DHEA (µg/dl)	Before	189.23±11.20	192.39±9.86	191.42±12.63	193.67±8.35	0.622
	After	180.06±10.93	161.57±11.38[a]	164.49±12.78[a]	156.26±10.45[a]	-
	P-value	0.485	0.032	0.021	0.013	
SHBG (nmol/l)	Before	84.59±20.29	80.16±22.32	86.35±23.17	87.33±19.70	0.235
	After	80.93±21.37	83.84±24.25	107.24±19.92[ab]	124.92±21.83[abc]	-
	P-value	0.317	0.422	0.008	0.0001	

FSH: Follicle-stimulating hormone; LH: luteinizing hormone; DHEA: Dehydroepiandrosterone; SHBG: Sex Hormone Binding Globulin. *showed as mean ± SD. a: Significantly different compared to PL. b: Significantly different compared to CUR. c: Significantly different compared to Tr+PL.. †Statistical analysis was done by paired sample t-test. *Statistical analysis were determined using One-way ANOVA.*

Menstrual characteristics

The results showed no significant differences among the four groups regarding amenorrhea and oligomenorrhea frequency at baseline. Amenorrhea and oligomenorrhea frequency changes were significant in the intervention groups compared to the PL group (Table 04).

Table 04. Menstrual characteristics before and after 12-week of intervention.

Menstrual characteristics		PL	CUR	Tr+PL	Tr+CUR	P-value
Before	Amenorrhea	3 (27.27)	4 (36.36)	4 (33.33)	3 (27.27)	0.795
	Regular	3 (27.27)	2 (18.18)	2 (16.17)	4 (36.36)	
	Oligomenorrhea	5 (45.45)	5 (45.45)	6 (50.00)	4 (36.36)	
After	Amenorrhea	2 (27.27)	2 (18.18)	2 (16.17)	2 (18.18)	0.038
	Regular	4 (36.36)	6 (54.54)	7 (58.33)	7 (63.63)	
	Oligomenorrhea	5 (45.45	3 (27.27)	2 (25.00)	2 (18.18)	

Discussion

This study looked at how aerobic exercise alone and in combination with curcumin supplementation affected a woman with PCOS's body composition, glycemic status, lipid profiles, and hormonal factors. According to the current study's findings, PCOS women who participated in aerobic exercise for 12 weeks lost weight and had lower BMIs. WHR and WC were improved by aerobic exercise using CUR or PL. Supplementing with

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curcumin did not change WHR or WC in any way. Aerobic exercise appears to have been the sole element that reduced WHR and WC. Numerous studies have shown that weight loss following exercise can improve body composition in PCOS individuals by lowering waist circumference (Woodward, Klonizakis and Broom 2020, Tiwari, Pasrija and Jain 2019). Better waist circumference preservation has significant potential consequences for long-term weight loss and maintenance because it helps sustain weight loss and/or maintenance and maintains the resting metabolic rate (Woodward et al. 2020, Tiwari et al. 2019). Similar to the findings of this investigation, weight and BMI in diabetes patients were reduced dramatically in the Panahi et al. trial that used 1,000 mg of curcumin administration over 3 months (Panahi et al. 2017). Uncertainty surrounds the process by which curcumin affects anthropometric parameters. However, curcumin inhibits the kinase enzyme, which has been implicated in the etiology of obesity. By inhibiting adipocyte development by suppressing the transcription factor peroxisome proliferator-activated receptor, a high dose of curcumin also lessens obesity (Bradford 2013, Jin et al. 2018)

According to the findings, all groups' glucose, insulin, and HOMA-IR values were lower than those of the PL group. Additionally, the Tr+CUR group's glucose and insulin levels were much lower than those of the CUR group. Numerous studies have demonstrated the distinct impacts of aerobic exercise and curcumin on glycemic indicators. Our findings were somewhat in line with those of earlier research; one human study found that taking 500 mg of curcumin daily for three months reduced HOMA-IR, FBS, and insulin levels in people with PCOS (Jamilian et al. 2020). Contrarily, a randomized trial on PCOS-affected women who received 500 mg of curcumin three times per day for 12 weeks only demonstrated a decrease in fasting blood glucose; no effect was observed on fasting insulin or HOMA-IR (Heshmati et al. 2021).

Through a variety of processes, including enhancing the absorption of glucose and glycolysis and glycogen synthesis in skeletal muscles or reducing gluconeogenesis in the liver, curcumin lowers serum glucose levels (Greenberg et al. 2006, Jabczyk et al. 2021). Curcumin has also been demonstrated to be able to boost glucose absorption by raising AMP-activated protein kinase (AMPK) phosphorylation The AMPK cascade, downstream signaling pathways, and mitogen-activated protein kinase (MAPK) and kinase 3/6-p38 signaling pathways all function better when curcumin is present, increasing cellular glucose uptake (Heshmati et al. 2021, Naeini et al. 2019, Ghanbarzadeh-Ghashti et al. 2023). Curcumin increases adenosine monophosphate-activated protein kinase, which inhibits phosphoenolpyruvate carboxykinase and glucose-6 phosphatase to reduce gluconeogenesis (Soltani et al. 2019, Lian et al. 2016) . Numerous investigations on the impact of exercise on insulin sensitivity found a significant reduction in insulin resistance in the exercise group, while a small number of studies found no significant difference in HOMA-IR before and after exercise (Whillier 2020, DiMenna and Arad 2021, Borghouts and Keizer 2000). Exercise enhances insulin sensitivity by increasing muscle mass and the quantity of glucose transporter proteins, while improving glucose elimination by increasing skeletal muscle capillarization, blood flow, and hexokinase and glycogen synthase activities (Covington et al. 2016).

Women with PCOS may have abnormal lipid levels. Women with PCOS often have moderate hypercholesterolemia, according to a recent study (Macut, Bjekić-Macut and Savić-Radojević 2013, Pergialiotis et al. 2018) According to our findings, exercise and curcumin both help PCOS patients with their lipid profiles. However, when used together, the lipid profiles of these individuals improved more than when the two were used separately. According to a study by Sohaei et al., administering curcumin could dramatically lower triglycerides, total cholesterol, and LDL cholesterol while raising HDL cholesterol levels (Shojaei-Zarghani, Molani-Gol and Rafraf 2022). The treatment of curcumin, in contrast, had no discernible impact on levels of triglycerides, total cholesterol, LDL cholesterol, or HDL cholesterol, according to a meta-analysis (Sahebkar 2014). Curcumin reduced TG, LDL, and cholesterol levels in the blood and elevated HDL, according to a number of studies conducted on PCOS-affected women (Chien et al. 2021, Sohaei et al. 2019, Reddy et al. 2016). Both humans and animals cholesterol levels are lowered by curcumin. By lowering dietary cholesterol absorption, it prevents the accumulation of blood cholesterol concentrations in animal tests (Jabczyk et al. 2021, Shojaei-Zarghani et al. 2022). By inhibiting the enzyme 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase (HMG-CoA reductase), curcumin primarily decreases blood and liver cholesterol levels (Silva et al. 2021). According to a recent study, curcumin suppressed the expression and activity of the gene for the sterol regulatory element-binding protein-2 (SREBP-2) to prevent the formation of the LDL receptor and reduce the absorption of extracellular LDL (Zingg, Hasan and Meydani 2013).

In a group of PCOS patients participating in aerobic activity, Sprung et al. observed a substantial reduction in Total cholesterol and LDL within 16 weeks (Sprung et al. 2013). The research of Abazar et al., demonstrated that after 12 weeks of exercise, triglycerides significantly decreased and HDL significantly increased. however LDL, VLDL, and cholesterol levels did not decrease significantly (Abazar et al. 2015).

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Numerous methods by which regular exercise alters the lipid profile have been proposed in earlier investigations (Mann, Beedie and Jimenez 2014). The reversible cholesterol route is one potential mechanism that could modify HDL-c levels (Rocco et al. 2011). Furthermore, it is well known that regular exercise enhances the expression and activity of the lipoprotein lipase (LPL) gene in skeletal muscle, resulting in a reduction in plasma triglyceride levels (Wang and Xu 2017). Additionally, the hepatic triglyceride lipase enzyme's decreased activity during prolonged exercise may be responsible for the decline in LDL-c levels (Lira et al. 2010).

Tr+CUR co-administration may improve the antioxidant-oxidant ratio, boost triglyceride lipolysis Positive changes in lipid profile induced by co-administration of Tr+CUR may occur via an increase in triglyceride lipolysis (Ravi Kiran et al. 2006), affect LDL-c synthesis (Burneiko et al. 2006), or speed at which LDL-c is removed from the plasma by tissues, all of which may result in positive changes to the lipid profile. (Saedmocheshi 2014).

The etiology of PCOS, which lasts the entirety of a woman's reproductive life, is thought to be significantly mediated by hyperandrogenism (Walters 2016). Pathogenesis could involve IR-induced hyperinsulinism and aberrant gonadotropin production. In patients with PCOS, abnormally elevated LH pulse frequency and amplitude further boost androgen production in ovarian theca cells and cause hyperandrogenemia (Coutinho and Kauffman 2019). Through stimulation of LH secretion and a reduction in SHBG production, hyperinsulinemia may increase androgen production in the adrenal cortex and follicles, resulting in elevated androgen levels that may cause recognizable clinical manifestations like amenorrhea, oligomenorrhea, and hirsutism(Shannon and Wang 2012).

The results showed that curcumin and aerobic training improved DHEA, but curcumin has no effect on LH, FSH, testosterone and SHBG compared to the control group. The results also showed that serum LH, DHEA and testosterone levels decreased significantly in Tr+CUR and Tr+PL groups compared to the control group. Similar to our findings, curcumin extract or compounds suppressed insulin and dehydroepiandrosterone (DHEA) in a clinical experiment on women with PCOS (Chien et al. 2021). Curcumin (1500 mg/day for 12 weeks) repressed DHEA and boosted estradiol instead of repressing it in women with PCOS who had experienced it for at least two years, according to research by Heshmati et al. (Heshmati et al. 2021). From these, curcumin may have an impact on people with PCOS by reducing androgen levels.

In this context, Sweatt et al. demonstrated that consistent exercise could result in higher levels of FSH and lower levels of LH (Sweatt et al. 2015). According to Ennour-Idrissi et al.'s meta-analysis, exercise causes a statistically significant rise in SHBG but a statistical drop in free testosterone, DHEAS, androstenedione, and adiposity indicators (Ennour-Idrissi, Maunsell and Diorio 2015). Researchers believe that due to exercise pressure and activation of the hypothalamus–pituitary– adrenal axis there was inhibitory effects on function of the female reproductive system. Thus the growth hormone (GH) prevents the release of the gonadotropin (GnRH) releasing hormone. Additionally, the glucocorticoid secreted during exercise stops the pituitary gland from releasing the hormone LH and causes the ovaries to release estrogen and progesterone

Our findings support McBreairty et al.'s finding that exercise has no impact on a woman's testosterone levels (McBreairty et al. 2016). Although Lopes et al. found reduced testosterone levels following 16 weeks of intermittent aerobic exercise, these women with PCOS reported enhanced sexual function (Lopes et al. 2018). Through reduced insulin and increased insulin sensitivity, long-term exercise appears to decrease the production of adrenal androgens, lower serum androgen levels, and lessen their negative effects on ovarian follicles (Kite et al. 2019). Weight loss brought on by exercise is another factor that lowers testosterone levels in these patients after exercise (Scarfò et al. 2022).

Also, the results of this study showed that SHBG significantly increased in exercise groups compared to PL group. Women with polycystic ovarian syndrome showed an increase in SHBG after exercise, according to Bruner et al. Since insulin suppresses SHBG formation in human hepatoma cells in addition to its direct influence on enhanced androgen production, this appears to be one of the physiological explanations for the increase in SHBG levels following the intervention in the current investigation (Bruner, Chad and Chizen 2006).

Conclusion:

According to the findings of the present study, it seems that the combination of aerobic exercise and curcumin supplementation might be more effective on anthropometric, metabolic and hormonal parameters than either intervention alone in woman with PCOS.

Declarations

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Conflict of interest The authors declare no conflict of interest.

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