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The Effect of 12 Weeks of Aquatic Training on the Quality of Life, Hormonal and Metabolic Indices, Aerobic Power and Physical Performance in Women with Polycystic Ovaries and Hypothyroidism: A Single-Blinded Randomized Clinical Trial

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Original Article

Abstract

Introduction: Polycystic ovary syndrome (PCOS) is a common endocrine and metabolic disorder in reproductive women affecting 15%-20% of women of reproductive age. It induces insulin resistance, hyperinsulinemia, dyslipidemia due to hyperandrogenism. Physical exercise can reduce androgens and mitigate hyperandrogenism by modulating the activity of the hypothalamic-pituitary-adrenal (HPA) axis. This study investigated the effects of aquatic exercise on the quality of life (QoL), as well as hormonal and physical indices, in women with PCOS and hypothyroidism.

Materials and Methods: In this single-blinded randomized clinical trial (RCT), 30 women with PCOS and hypothyroidism were randomly assigned to two groups (n = 15 each). The variables were evaluated at baseline and after 12 weeks. During the 12-week period, the intervention group participated in regular aquatic exercises, while the control group did not engage in any structured exercise. Data normality was examined using the Shapiro-Wilk test, and analysis of covariance (ANCOVA) was employed for data analysis.

Results: Aquatic exercises significantly improved anthropometric indicators and lipid profiles in the intervention group (P = 0.001). Additionally, these exercises had a positive impact on aerobic power, physical performance, and hormonal parameters (P = 0.001), although FSH titers remained unchanged (P = 0.06).

Conclusion: It appears that 12 weeks of regular aquatic exercise can improve anthropometric and hormonal parameters, QoL, aerobic power, and physical performance in women with PCOS and hypothyroidism.

Keywords: Polycystic ovary; Aquatic exercise; Lipid profile; Hypothyroidism

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Introduction

The prevalence of polycystic ovaries varies in different countries and is, on average, 5 to 10%, but in some areas it reaches 26% (1). Regarding the difference in the prevalence of polycystic ovaries, the clinical and biochemical characteristics of this disease may differ according to race and ethnicity. The prevalence of polycystic ovary syndrome is higher in young women than in those over 35 years of age (2). This condition was initially characterized by increased adrenal and

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ovarian androgen secretion, irregular menstruation, fibrotic and enlarged ovaries, increased primary follicles, impaired development of the dominant follicle, and, consequently, impaired ovulation (3, 4). Increased androgen levels (Hyperandrogenism) are the most common hormonal change in women with polycystic ovary syndrome (5, 6). The causes of polycystic ovary syndrome may include a range of endocrine disorders, such as hypothalamus-pituitary-adrenal axis disorders and insulin signalling (7). Neuroendocrine disorders, such as hypothalamic-pituitary-adrenal axis disorders, increase kisspeptin and GABA (Aminobutyric Acid) (5). This leads to increased secretion of gonadotropin-releasing hormone (GnRH), which, in turn, increases luteinizing hormone (LH) secretion and androgen secretion (hyperandrogenism) (8, 6). Impaired insulin signalling occurs due to defects in pancreatic beta cells and excessive phosphorylation of the insulin receptor tyrosine kinase (5); as a result, decreased GLUT4 expression leads to decreased insulin receptor sensitivity and insulin resistance (7). Insulin resistance causes an increase in blood insulin levels (hyperinsulinemia), which subsequently leads to overexpression of the mir93 gene and a decrease in mir145 gene expression, resulting in ovarian cell growth and inhibition of apoptosis, and therefore ovarian hypertrophy and the formation of dysfunctional granule cells (3,4). The level of Follicle Stimulating Hormone (FSH) is reduced to below normal levels and, in addition, prevents the mid-cycle peak secretion of this hormone in patients with this syndrome.

Therefore, despite the increase in the number of follicles, the follicles do not mature, and the egg is not released (2). Polycystic ovary morphological indicators are one of the most important and accurate indicators for diagnosing polycystic ovaries. In polycystic ovary ultrasound, an ovarian volume of 10 cubic centimetres or more and the number of follicles measuring 2 to 9 mm are reported as 12 or more (5). This syndrome is a multifactorial disorder that includes genetic, epigenetic, environmental, immune, and other factors (9). In addition to these factors, lifestyle factors also affect the course and pathogenesis of polycystic ovary syndrome. Recent research has shown that several factors, including age, environment, lifestyle, and disease status, can alter the clinical manifestations of PCOS (10). Dysfunctional granulosa cells, caused by weak apoptosis, are common in polycystic ovaries and are usually associated with a lack of ovulation and incomplete or ineffective folliculogenesis (11). Polycystic ovaries cause hyperandrogenism in different ways (12). Hyperandrogenism causes several pathological changes, including insulin resistance (11), hyperinsulinemia, dyslipidemia, and an unbalanced LH/FSH ratio in patients with polycystic ovaries. Women with polycystic ovaries have higher levels of inflammatory factors, such as CRP and interleukin-6, in their blood than other women (13). Some risk factors, such as insulin resistance, dyslipidemia, and oxidative stress, can cause the first occurrence of type 2 diabetes and cardiovascular diseases in patients with polycystic ovaries (14).

Exercise increases hypothalamus-pituitary-adrenal axis activity and subsequently reduces androgen levels, thereby preventing hyperandrogenism (14). Glucocorticoids secreted during exercise inhibit the release of LH from the pituitary gland, and estrogen and progesterone from the ovaries (15). Based on research, moderate-intensity exercise reduces LH secretion (16). As mentioned, water exercises reduce insulin resistance; for this reason, blood glucose and insulin levels drop after water exercise, and subsequently, the secretion of androgens and antimullerian hormone diminishes (17). An increase in the number of follicles and androgen levels in women with PCO leads to increased antimullerian hormone production. At present, the serum level of antimullerian hormone has been proposed as a reliable indicator of ovarian disorder and predicts the possibility of treating infertility (18). However, limited research has examined the effect of exercise training on antimullerian hormone, and existing studies have reported inconsistent results (17, 19).

Another hormone affected by polycystic ovary disease is prolactin. Moderate elevations in serum prolactin levels in both the follicular and luteal phases have been reported in 30% of patients with polycystic ovary syndrome (17). Increased serum prolactin levels are associated with decreased ovarian follicle count and anovulation (19, 20), and it appears that 8 weeks of endurance training significantly alters LH and prolactin levels (21). Despite the large number of studies that have examined hormonal indicators and the effects of various therapeutic interventions in women with polycystic ovaries, no study has simultaneously examined androgen, FSH, LH, anti-Müllerian, and prolactin levels (4).

Thyroid disorders are commonly seen in patients with PCO (20). Thyroid hormones act as insulin agonists in muscle tissue and insulin antagonists in the liver, thereby maintaining normal glucose homeostasis; their decrease or increase leads to hypoglycemia or insulin resistance (22, 23).

Thyroid hormones influence reproductive function by affecting luteal cells in the ovary (3). However,

there is limited evidence examining these two metabolic diseases simultaneously (22, 23). Given the overlap in symptoms, the co-occurrence of these two diseases will influence symptom treatment and control (24). Despite numerous studies investigating the effects of exercise on the treatment of PCO (25), no prescribed exercise regimen has been formulated to date for the treatment of polycystic ovary syndrome (26). According to the mentioned points and the relationship between the polycystic ovary diseases and hypothyroidism as well as the lack of examination of numerous hormonal indicators and metabolic plus morphological indicators in previous studies, and also considering the greater satisfaction of patients with water sports (27), we decided to investigate the effect of aquatic exercise on hormonal indices including prolactin, FSH, LH and other hormones that have been less studied in previous studies or that there is still controversy about the effect of exercise on them (6), along with functional indices and aerobic capacity in women with polycystic ovary syndrome and hypothyroidism. This study aimed to investigate the effects of aquatic exercise on hormonal and metabolic indices, quality of life, aerobic capacity, and physical performance in patients with polycystic ovary syndrome and hypothyroidism.

Materials and Methods

This randomized clinical trial was conducted in Isfahan, Iran, with 1402 participants. The research plan was approved by the Ethics Committee of Khorasgan Azad University and registered in the Iranian Clinical Trials Registration System. Based on previous studies (17, 28, 29), with a statistical power of 80% and an alpha of 5%, a total of 15 participants per group were required. Women aged 18 to 30 were invited to participate in the study through advertisements posted in government, charity, and private clinics and gynaecologists' offices in Isfahan. Before the study began, volunteers were informed of the study's objectives and assured that the collected information would be kept confidential. Volunteers who wished to participate in the study signed an informed consent form. The participants in the research were selected non-randomly (conveniently) from women aged 18 to 30 who referred to women's clinics in Isfahan, Iran, and were diagnosed and clinically examined by a gynaecologist, based on the entry and exit criteria. The conditions for entering the study included having at least 2 of the 3 Rotterdam criteria, suffering from subclinical hypothyroidism, a BMI < 23, no regular sports activity in the last 3 months, and an age range of 18 to 30 years. Exclusion criteria included having cardiovascular diseases, skin diseases, rheumatism, kidney and liver diseases, BMI > 23, having muscular and skeletal diseases or physical disabilities, taking contraceptive pills of any kind, and being an athlete. The study volunteers were randomly divided into two groups of 15 each (intervention and control) using a random number table. In this study, the analyst was unaware of the study groups.

Evaluation method: Anthropometric measurements, including Height, weight (kg), body mass index (BMI) as kg/m^2, Hip and waist circumference, and waist-to-hip ratio (WHR), were taken twice: at baseline, after 12 weeks, and at the end of the study.

The WHO Quality of Life Questionnaire (WHOQOL-BREF) is a 26-item instrument that assesses a person's overall quality of life. The Persian version of this questionnaire was published in 2020, and its validity and reliability were confirmed (32).

Aerobic capacity was assessed using the Rockport One Mile Walk Test (33), and physical performance was assessed using the One Minute Sit-Stand Test, with good reliability and adequate validity (34). Insulin resistance was assessed by the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) index and by measuring fasting blood glucose and insulin levels. After blood samples were collected, the researcher assessed physical performance and aerobic capacity in both groups on the same day. All measurements and assessments were repeated after 12 weeks and 48 hours after the end of the training sessions in both groups.

The participants' blood samples were collected from the antecubital vein after overnight fasting, between 8:00 AM and 10:00 AM, during the early follicular phase on days 2 to 4. The samples were allowed to clot completely at room temperature, and then centrifuged within 30 min at 1500 rpm for 4 min. Hormonal indicators and lipid profiles were assessed by laboratory personnel in the medical diagnosis laboratory of one Clinic, under the supervision of the laboratory's technical pathologist, using blood samples from patients. Diagnostic kits from Ayriktech Pishtaz Medical Company, made in Iran, were used to measure hormones (TSH) and other indicators (Glucose, Insulin, LDL, HDL, Triglycerides). All the mentioned tests were repeated after 12 weeks in both the control and intervention groups. Moreover, the results were recorded.

Exercise intervention: The intervention group participated in regular water exercises for 12 weeks, 3 sessions per week. The exercise group was advised not to engage in any other exercise except the exercise program recommended by the researcher.

The control group did not receive any exercise during this period. The control group was informed that they should not participate in any exercise program during this period, as it would distort the study's results. The water exercise protocol was performed for 12 weeks, including 20 minutes of walking forward, backwards, sideways, and jogging in the shallow part of the pool, where the water height was up to neck level. Next, plyometric exercises in water were performed for 10 minutes, including high jump, throwing a soccer ball, and climbing the pool stairs, with each movement repeated 10 times and a 30-second rest between exercises (33). Each training session lasted 45 minutes, including warm-up and cool-down (35). Aquatic exercises were taught to patients by a physiotherapist, and all stages were performed under the physiotherapist's supervision. During this period, the control group did not engage in any specific exercise or physical activity beyond their usual daily activities.

For statistical data analysis, SPSS software (version 16, SPSS Inc., Chicago, IL, USA) was used. Using the Shapiro-Wilk test, the normality of the sample distributions in the research groups was assessed. To analyze the data and determine the difference between pre-test and post-test scores across the two groups, analysis of covariance (ANCOVA) was used. The significance level was considered $\alpha < 0.05$. The study power was determined using G*Power software (G*Power 3.1.9.7 freeware, Released 17 March 2020, University of Düsseldorf, Düsseldorf, Germany).

Results

In the present study, all participants completed all stages (attrition rate: 0%). Therefore, the CONSORT diagram was not prepared, and the intention-to-treat (ITT) analysis was not performed. The means of the study variables are presented in table 1, separated into case and control groups.

The individuals in the two groups did not show significant differences in hormonal variables, quality of life, and performance and aerobic power indices at the beginning of the study. Therefore, any difference between the groups after 12 weeks can be attributed to the effect of water exercise. The results of the covariance analysis showed that the effect of the pre-test on the post-test was significant at the 5% level (P = 0.001), and that controlling the pre-test factor made the F value for the difference between the two groups significant (P = 0.001). Table 2 shows the investigated variables in the two groups before and after the study period.

Examination of Anthropometric Variables: The results showed a significant decrease in the exercise group's weight values and no change in the control group after 12 weeks of intervention compared with baseline (P = 0.001). The mean weight of the exercise group was lower than that of the control group. The Eta squared value was 0.91, indicating that about 91% of the weight changes were due to differences between the experimental groups, and the test power to detect this difference was 100%.

Table 1. Comparison of Investigated Variables in the Intervention and Control Groups at the Beginning of the Study

Variable type	Variable	Control group	Intervention group	Total	P (between groups)
Anthropometric	Age (years)	26.20 ± 3.83	26.53 ± 2.87	26.37 ± 3.33	0.74
	Height (meters)	1.59 ± 0.03	1.59 ± 0.03	1.59 ± 0.03	0.81
	Weight (kilograms)	57.69 ± 2.44	58.01 ± 2.46	57.85 ± 2.42	0.72
	BMI (kg/m²)	22.63 ± 0.28	22.79 ± 0.17	22.71 ± 0.24	0.98
	Waist circumference (cm)	79.63 ± 1.65	78.86 ± 2.81	79.25 ± 2.30	0.71
Blood Sugar	FBS (mg/dL)	92.27 ± 6.49	90.80 ± 5.94	91.54 ± 6.16	0.13
	Fasting insulin (mIU/L)	25.32 ± 0.36	25.24 ± 0.45	25.28 ± 0.40	0.06
	Insulin resistance (HOMA-IR)	5.76 ± 0.47	5.65 ± 0.38	5.71 ± 0.43	0.06
Hormonal	TSH (mIU/L)	8.27 ± 1.45	7.96 ± 1.25	8.12 ± 1.34	0.06
Variables	LH (IU/L)	16.68 ± 4.06	13.56 ± 3.58	15.12 ± 4.08	0.06
	FSH (IU/L)	9.006 ± 2.33	7.53 ± 2.54	8.27 ± 2.51	0.93
Lipid Profile	Triglycerides (mg/dL)	200.20 ± 1.65	198.27 ± 11.78	199.24 ± 8.32	0.86
	LDL (mg/dL)	103.73 ± 13.13	103.07 ± 16.52	103.40 ± 14.67	0.11
	HDL (mg/dL)	37.00 ± 2.75	35.20 ± 3.50	36.10 ± 3.23	0.106
Exercise	Aerobic power (mL/kg/min)	40.19 ± 5.10	37.05 ± 5.80	38.62 ± 5.60	0.35
System Indices	Physical performance (reps/min)	25.87 ± 3.29	26.80 ± 3.40	26.34 ± 3.32	0.61
Quality of Life	SF26 questionnaire score	27.29 ± 4.98	26.97 ± 5.28	27.13 ± 5.09	0.70

BMI: Body mass index; FBS: Fasting blood sugar; TSH: Thyroid stimulating hormone; LH: Luteinizing hormone; FSH: Follicle stimulating hormone; LDL: Low-density lipoprotein; HDL: High-density lipoprotein

Table 2. Comparison of Investigated Variables before and after Intervention in the Two Groups

Variable type	Variable	Measurement time	Control group	Intervention group	Eta squared [95% CI]	P (between groups)
Anthropometric	Weight (kg)	Pre-test	57.69 ± 2.44	58.01 ± 2.46	0.5	0.720
		Post-test	57.91 ± 2.39	56.16 ± 2.40	0.98	0.001
	P (Within-group comparison)		0.680	0.001		
	Eta squared [95% CI]		0.025	0.980		
	BMI(kg/m²)	Pre-test	22.63 ± 0.28	22.79 ± 0.17	0.5	0.980
		Post-test	22.75 ± 0.25	22.07 ± 0.25	0.8	0.001
	P (Within-group comparison)		0.100	0.001		
	Eta squared [95% CI]		0.080	0.790		
	Waist circumference (meters)	Pre-test	79.63 ± 1.65	78.86 ± 2.81	0.026	0.710
		Post-test	79.73 ± 1.66	76.26 ± 2.96	0.02	0.196
	P (Within-group comparison)		0.190	0.196		
	Eta squared [95% CI]		0.060	0.090		
Blood sugar	FBS (mg/dL)	Pre-test	92.27 ± 6.49	90.80 ± 5.94	0.020	0.130
		Post-test	92.40 ± 6.81	78.40 ± 6.24	0.657	0.001
	P (Within-group comparison)		0.520	0.001		
	Eta squared [95% CI]		0.020	0.200		
	Fasting insulin (mIU/L)	Pre-test	25.32 ± 0.36	25.24 ± 0.45	0.200	0.060
		Post-test	25.28 ± 0.31	11.40 ± 1.90	0.978	0.001
	P (Within-group comparison)		0.600	0.001		
	Eta squared [95% CI]		0.056	0.978		
	Insulin resistance (HOMA-IR)	Pre-test	5.76 ± 0.47	5.65 ± 0.38	0.30	0.060
		Post-test	5.76 ± 0.44	2.21 ± 0.46	0.970	0.001
	P (Within-group comparison)		0.950	0.001		
	Eta squared [95% CI]		0.550	0.980		
Hormonal variables	TSH (mIU/L)	Pre-test	8.22 ± 1.45	7.96 ± 1.25	0.020	0.060
		Post-test	8.22 ± 1.49	3.90 ± 0.88	0.98	0.001
	P (Within-group comparison)		0.600	0.001		
	Eta squared [95% CI]		0.350	0.970		
	LH (IU/L)	Pre-test	16.68 ± 4.06	13.56 ± 3.58	0.800	0.060
		Post-test	16.48 ± 4.06	8.91 ± 3.15	0.990	0.001
	P (Within-group comparison)		0.250	0.001		
	Eta squared [95% CI]		0.006	0.930		
	FSH (IU/L)	Pre-test	9.006 ± 2.33	7.53 ± 2.54	0.920	0.930
		Post-test	9.11 ± 2.20	6.74 ± 2.53	0.350	0.001
	P (Within-group comparison)		0.320	0.001		
	Eta squared [95% CI]		0.040	0.940		
Lipid profile	Triglycerides (mg/dL)	Pre-test	200.20 ± 1.65	198.27 ± 11.78	0.24	0.86
		Post-test	199.87 ± 1.88	128.47 ± 35.98	0.71	0.001
	P (Within-group comparison)		0.31	0.001		
	Eta squared [95% CI]		0.24	0.75		
	LDL (mg/dL)	Pre-test	103.73 ± 13.13	103.07 ± 16.52	0.21	0.11
		Post-test	102.13 ± 14.53	85.13 ± 6.67	0.63	0.001
	P (Within-group comparison)		0.1	0.001		
	Eta squared [95% CI]		0.11	0.66		

Table 2. Comparison of Investigated Variables before and after Intervention in the Two Groups (continue)

Variable type	Variable	Measurement time	Control group	Intervention group	Eta squared [95% CI]	P (between groups)
	HDL (mg/dL)	Pre-test	37.2 ± 2.75	35.20 ± 3.50	0.600	0.106
		Post-test	37.47 ± 2.66	48.87 ± 4.20	0.790	0.001
	P (Within-group comparison)		0.680	0.001		
	Eta squared [95% CI]		0.180	0.790		
Exercise system indices	Aerobic power (mL/kg/min)	Pre-test	40.19 ± 5.10	37.05 ± 5.80	0.79	0.35
		Post-test	38.96 ± 5.62	46.34 ± 4.83	0.86	0.001
	P (Within-group comparison)		0.14	0.001		
	Eta squared [95% CI]		0.24	0.81		
	Physical performance (reps/min)	Pre-test	25.80 ± 3.40	26.3 ± 4.43	0.1	0.61
		Post-test	25.33 ± 3.24	33.4 ± 3.29	0.84	0.001
	P (Within-group comparison)		0.45	0.001		
	Eta squared [95% CI]		0.44	0.92		
Quality of Life	SF26 questionnaire score	Pre-test	27.29 ± 4.98	26.97 ± 4.93	0.93	0.70
		Post-test	27.4 ± 4.93	21.08 ± 4.93	0.92	0.001
	P (Within-group comparison)		0.01	0.001		
	Eta squared [95% CI]		0.19	0.81		

Therefore, 12 weeks of water exercise had an effect on weight in women with PCOS and subclinical hypothyroidism.

The results showed a significant decrease in the BMI values of the exercise group (P = 0.001) and no change in the control group (P = 0.100) after twelve weeks of intervention compared to the baseline, and the mean BMI of the exercise group was lower than that of the control group. The Eta squared value was 0.79, indicating that about 79% of the BMI changes were due to the difference between the experimental groups, and the test power to detect this difference was 96%. Therefore, 12 weeks of water exercise affected the BMI level in women with PCOS and subclinical hypothyroidism. It is worth mentioning that in this study, changes in patients' waist circumference were examined in both groups. Statistical analyses showed that after 12 weeks of water exercise, the intervention group's mean waist circumference decreased from 78.86 to 76.26. However, the changes compared to the control group were not statistically significant (P = 0.196).

Examination of Insulin Resistance Variable: The fasting blood sugar (FBS) levels of the studied patients were measured over 12 weeks. The results showed that aquatic exercises effectively reduced FBS, Insulin, and insulin resistance in the patients (P=0.001). Insulin resistance in the control group did not change after 12 weeks without intervention compared with baseline (P=0.95). The mean insulin resistance in the exercise group was significantly lower than in the control group. According to the Eta squared value, about 97% of the changes in insulin resistance were attributable to the difference between the experimental groups, and the test power to detect this difference was 100%. 12 weeks of water exercise had an effect on insulin resistance in women with PCOS and subclinical hypothyroidism.

Examination of Hormonal Indices Variables: In all hormonal indices (including FSH, LH, and TSH), a significant decrease was reported in the exercise group (P=0.001) and no change in the control group (P = 0.25) in the post-test phase. Also, the mean levels of all three hormones at the end of the study were significantly lower in the exercise group than in the control group. According to the Eta squared for these variables, 35%, 99%, and 98% of the changes in these hormones were due to the use of aquatic exercises in the intervention group (i.e., differences between the two groups). The test power for detecting this difference ranged from 96% to 100%. Therefore, 12 weeks of aquatic training affected the levels of FSH, LH, and TSH hormones in women with PCOS and subclinical hypothyroidism.

Examination of Lipid Profile: Based on the results of the present study, after 12 weeks from the start of the exercise program in the training group, a significant decrease in the level of High-density Lipoprotein (HDL), Low-density Lipoprotein (LDL), and triglycerides was reported in the exercise group

(P = 0.001) and no change in the control group (P = 0.100). The mean LDL and triglycerides were lower than those of the control group, and the mean HDL was significantly higher. According to the Eta squared for these variables, 79%, 63%, and 71% of the changes in these hormones were due to the use of aquatic exercises in the intervention group, and the test power to detect this difference ranged from 80% to 100%.

Examination of VO_2max Changes: The results showed a significant increase in VO_2max in the exercise group (P=0.001) and no change in the control group (P=0.14) after 12 weeks of intervention compared with baseline. The mean VO_2max of the exercise group was higher than that of the control group. The Eta squared value was 0.81, indicating that about 81% of the VO_2max changes were due to differences between the experimental groups, and the test power to detect this difference was 100%.

Examination of Functional Index Changes (Sit to Stand Test Results): A significant improvement in physical performance was observed in the exercise group (P=0.001) but not in the control group (P=0.44) after 12 weeks of intervention compared with baseline. After controlling for the pre-test, a significant difference in physical performance was observed between the two groups, with the exercise group showing a higher mean physical performance test score than the control group. The Eta squared value indicated that about 84% of the changes in physical performance were due to differences between the experimental groups, and the test power to detect this difference was 100%.

Examination of Quality of Life Changes: Compared with the baseline, after 12 weeks of intervention, the exercise group showed a significant increase in quality-of-life scores (P=0.001), whereas the control group showed no change (P=0.48). By controlling for the pre-test, a significant difference in quality of life was observed between the two groups, with the exercise group showing a higher mean quality of life than the control group. Eta squared was 0.81; in other words, about 81% of the changes in quality of life were due to the difference in the experimental groups, and the test power for detecting this difference was 100%.

Discussion

This study, by examining 30 women with PCOS and subclinical hypothyroidism, investigated changes in anthropometric indices, physical function, quality of life, lipid profile, and hormonal levels. The findings of this study indicated the significant effect of 12 weeks of water exercise on improving metabolic, hormonal, physical function, and quality of life parameters in women with PCOS and subclinical hypothyroidism. These results are consistent with previous studies that emphasized the role of exercise in managing metabolic and hormonal disorders.

The lack of significant change in waist circumference might be due to the short duration of the intervention or the need for combined exercises (aerobic + resistance) to reduce visceral fat. The reduction in FBS and Insulin confirms that water exercises, by improving insulin sensitivity, can reduce the metabolic complications of PCOS, such as type 2 diabetes. These results are similar to those of research on the effects of exercise on glucose homeostasis. The decrease in TSH and improvement in thyroid function may be due to reduced oxidative stress and inflammation. The decrease in LH and FSH indicates that the hypothalamic-pituitary-gonadal axis is disrupted in PCOS. The increase in HDL and the decrease in LDL and triglycerides support the positive effect of exercise on lipid metabolism. These changes can reduce the risk of cardiovascular diseases. The improvement in VO_2max and the Sit-to-Stand test score indicates increased cardiorespiratory capacity and muscle strength, which are crucial for patients with movement limitations (due to obesity or chronic fatigue). The significant improvement in quality of life is likely due to reduced metabolic symptoms, increased energy, and improved body image. This finding aligns with studies suggesting exercise as an intervention for mental health in PCOS.

The investigations in this study showed that 12 weeks of water exercise significantly reduced BMI in patients with PCOS and hypothyroidism. The significant reductions in weight and BMI in the exercise group demonstrate the strong impact of water-based exercise on weight control. The results of this study are consistent with those of Samadi et al. (36) and indicate the importance of regular physical exercise for weight and body mass index.

Nasiri et al. (28) in 2022 investigated the effects of high-intensity interval training (HIIT) and combined resistance training on anthropometric indices, such as BMI and waist circumference, in women with PCOS. In their study, combined resistance training significantly reduced the patients' waist circumference. The lack of change in waist circumference after 12 weeks of water exercise is probably due to differences in the types of exercise between the two studies: HIIT is a short-term, high-intensity exercise that promotes greater fat burning than other forms (37). This type of exercise reduces fat stored in the abdominal and flank

areas of patients. Furthermore, the participants in our study had a BMI below 23, indicating little abdominal fat accumulation. On the other hand, consistent with Nasiri et al.'s study, 12 weeks of water exercise led to a reduction in BMI in patients—water-based exercise results in higher energy expenditure than land-based exercise.

The present study, by examining TSH in patients with PCOS and subclinical hypothyroidism, showed that regular water exercise can effectively reduce TSH levels and thereby reduce the need for thyroid medications. Based on the obtained results, the dosage of received medications and changes in TSH levels in these patients should be considered by relevant specialists. Regular exercise, independent of weight change, can help improve metabolic status. Exercise reduces oxidative stress and systemic inflammation, improves hormonal balance, and enhances cellular metabolic efficiency (31).

Smith et al. (7) concluded in a 2022 systematic review that exercise significantly improves cardiorespiratory fitness. Waist circumference, systolic blood pressure, fasting blood sugar, insulin resistance, and lipid profile remained unchanged in the studies included in this systematic review. However, the present study showed that FBS in patients decreased significantly after 12 weeks of continuous water exercise, as per a standard protocol. Since the type of exercise performed in the underlying studies was not discussed in this systematic review, differences in results between the two studies could be due to differences in the type and duration of the exercise, which should be considered. Moreover, the patients in the present study were simultaneously dealing with two metabolic diseases, PCOS and hypothyroidism; therefore, this issue could also be a reason for the difference in the obtained results. In any case, exercise increases glucocorticoid levels, such as cortisol, which in turn increases lipolysis. Cortisol reduces the activity of the hypothalamic-pituitary-ovarian axis, decreases LH levels, and consequently reduces androgens. Exercise, by stimulating the sympathetic system, increases insulin sensitivity, increases GLUT4 and glucose reuptake, and decreases blood sugar levels.

In 2011, Taghavi et al. (29) investigated the effect of aerobic exercise on obesity and insulin resistance in women with PCOS. In this study, 20 obese women aged 15 to 30 years underwent 12 weeks of aerobic exercise, and anthropometric parameters (weight, Height, maximum oxygen consumption, waist circumference, waist-to-hip ratio, and body fat percentage) and hormonal and metabolic profiles (glucose and Insulin) were evaluated and compared before and after the intervention. Their results showed that changes in glucose, fasting blood sugar, and Insulin were not significant, which is inconsistent with the present findings of significant reductions in weight, FBS, and insulin resistance. The types of exercise can also explain the differences in the results of these two studies. Furthermore, the patients in Taghavi et al.'s study were obese, which itself is a metabolic disease. The factor of obesity increases insulin resistance, insulin levels, androgen levels, and cholesterol levels, and also increases the likelihood of depression in these patients (35). Based on the present results, regular exercise can increase insulin sensitivity and reduce insulin resistance, both of which are important underlying factors for PCOS. On the other hand, improved insulin sensitivity, by any method, can also lead to better regulation of sex hormone levels (29).

Ghilani et al. (16) in 2019, in a study titled "The effect of 8 weeks of endurance training on androgen levels in women with PCOS," concluded that 8 weeks of endurance training had a significant effect on LH and prolactin levels but did not significantly affect testosterone and FSH levels. The results of the present study, in terms of reduced LH and prolactin levels, are also consistent with those of this study. According to researchers, exercise activates the hypothalamic-pituitary-adrenal axis, thereby affecting the function of the female reproductive system. The secretion of Growth Hormone (GH) following exercise can lead to a decrease in the secretion of Gonadotropin-Releasing Hormone (GnRH) (5). Glucocorticoids produced during exercise also prevent the secretion of LH from the pituitary gland and stimulate the secretion of estrogen and progesterone from the ovaries. Through this mechanism, exercise can decrease LH (38), as confirmed by the present study. Contrary to Ghilani et al.'s study, FSH changes were not significant, which contradicts the present findings; this may be due to the timing of blood sampling from the patients, i.e., at which point in their menstrual cycle they were sampled.

You et al. (26) in 2016 investigated the effect of endurance exercise on the quality of life of women with hypothyroidism. The exercises included 16 weeks of aerobic exercise (stationary bike or treadmill) three times a week. Quality of life was assessed using the SF-36 questionnaire, and the study concluded that 16 weeks of aerobic exercise resulted in a significant improvement in the quality of life of women with hypothyroidism. The results of this study, consistent with the aforementioned study, showed that water exercises can increase the quality-of-life index. Given

the differences in the types of exercise in the two studies, it might be said that regular physical activity, regardless of type, can improve quality of life.

Consistent with this study's results, Oktas et al. (37) conducted a 2022 study investigating the effects of 12 weeks of HIIT on visfatin, adiponectin, and leptin levels in women with PCOS. Leptin and visfatin levels did not change, while adiponectin levels increased compared to the control group. Additionally, serum levels of Insulin, triglycerides, cholesterol, and LDL decreased, and serum HDL levels increased. As might be expected, continuous physical exercise effectively improves the lipid profile in patients.

Limitations

Physical activity level, diet, and psychological stress affect hormonal and metabolic indices. Although this study, as a clinical trial, has important strengths, the lack of recording variables during the follow-up phase and the inability to control patients' physical activity levels, diet, and psychological stress affect the results.

Recommendations

It is suggested that in future studies, patients should be controlled for diet, physical activity level, and psychological stress. By recording data during the follow-up phase, the sustainability of the effects of water exercises on hormonal, metabolic, and functional indices can be analyzed. It is also suggested that the effect of these exercises on hormonal, metabolic, and functional indices in patients with other hormonal disorders be investigated in future studies.

Conclusion

Overall, the results of this study showed that water exercise with the proposed protocol can likely effectively improve anthropometric indices, lipid profile, functional indices, and aerobic capacity in patients. Also, it seems these exercises can cause positive hormonal changes in patients with PCOS combined with subclinical hypothyroidism. The results of this study showed that changes in TSH following these exercises should be specifically monitored and investigated by relevant specialists. Therefore, it is recommended that aquatic training be used as a non-pharmacological treatment method to improve the symptoms of PCOS and hypothyroidism in women.

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Conflict of Interest

The authors did not have a conflict of interest.

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