The effect of exercise on insulin resistance in obese women with polycystic ovary syndrome

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Introduction
The link of polycystic ovary syndrome (PCOS) with insulin resistance was subsequently established by clinical studies characterizing the profound insulin resistance in obese and lean PCOS patients.

Aim
The aim of this study was to compare the effect of aerobic exercise using an ergonomic treadmill on insulin resistance, body weight, and waist circumference in obese diabetic and nondiabetic women with polycystic ovary.

Patients and methods
Sixty obese women with PCOS, their age ranging from 30 to 40 years, participated in this study. All study participants were recruited from the Gynecology Outpatient Clinic of Kasr Al Aini Hospital. They were assigned into two equal groups: Group A (study group) included 30 obese diabetic women. Group B (control group) included 30 nondiabetic obese women. All patients received a controlled diet program and an aerobic exercise program (each exercise training session included continuous aerobic exercises on a treadmill for 30 min performed three times per week for 24 weeks under the supervision of physicians of the Faculty of Physical Therapy) and were on metformin drug (850 mg every 12 h). Fasting blood glucose, insulin resistance, and waist circumference were measured at the beginning of the study and after the study for both groups.

Results
Statistical analysis revealed a significant improvement in insulin resistance and waist circumference in both groups after the aerobic exercise training program.

Conclusion
Regular aerobic exercises improve insulin resistance, abdominal fat distribution, and body weight in obese diabetic and nondiabetic women with polycystic ovary, and they are advised to perform regular aerobic exercises.

Keywords:
aerobic exercise, obesity, polycystic ovary, type 2 diabetes

Introduction

Polycystic ovary syndrome (PCOS) is one of the common reproductive system disorders with a prevalence estimated to be between 5 and 10% among women in the child-bearing period [1]. An international consensus group proposed that the syndrome can be diagnosed by the determination of at least two of the following criteria: oligo-ovulation or anovulation (usually manifested as oligomenorrhea or amenorrhea), elevated levels of circulating androgens (hyperandrogenemia), or clinical manifestations of androgen excess (hyperandrogenism); it is determined by ultrasonography, after the exclusion of other medical conditions that cause irregular menstrual cycles and androgen excess [2]. Women with the PCOS almost always have some aberration in gonadotropin secretion as compared with women who have normal menstrual cycles [3]. However, gonadotropin concentrations vary over the menstrual cycle and are released in a pulsatile manner into the circulation; thus, in routine clinical practice, abnormal gonadotropin levels need not be documented to diagnose the PCOS [4]. Insulin plays direct and indirect roles in the pathogenesis of hyperandrogenemia in the PCOS. Insulin acts with luteinizing hormone to enhance the androgen production of theca cells. Insulin also inhibits the hepatic synthesis of sex hormone-binding globulin, the key circulating protein that binds to testosterone, and thus, it increases the proportion of testosterone that circulates in the biologically available free-state. Because women with the PCOS typically have hyperinsulinemia, the concentration of free testosterone is often elevated when the total testosterone concentration is at the upper range of normal or just elevated [5].

The relation between hyperinsulinemia and PCOS has been documented for almost 29 years [6]. Later studies

confirmed that 30–40% of women with the PCOS have impaired glucose tolerance, and as many as 10% have type 2 diabetes by their fourth decade. These prevalence rates are among the highest known in women of similar age [7]. Exercise can increase glucose disposal and muscle sensitivity to insulin. In PCOS, women who self-reported 8 h of sports activities per week had improvement in acne and menstrual irregularities. Exercise as the primary intervention without attendant weight loss (<5% weight loss) improved the insulin sensitivity and the free testosterone index, and induced ovulation in obese PCOS patients. Clearly, a reasonable regimen of exercise in addition to modifications of diet is a prudent recommendation for patients with PCOS. Exercise is very important to individuals with diabetes mellitus. It is crucial to educate diabetic patients on the topic of exercise. Exercise increases fuel consumption considerably. As the diabetic population lacks glucoregulatory mechanisms, exercise prevents associated risks [8,9].

Patients and methods
Sixty obese PCOS women, 30 diabetic female patients and 30 nondiabetic female patients, participated in this study; their ages ranged from 30 to 40 years. They were recruited from the Gynecology Outpatient Clinic of Kasr Al Aini Hospital.

Inclusion criteria
(1) Sixty obese PCOS women.
(2) Two of the following three signs were present for the diagnosis of PCOS:
   (a) Clinical (acne or hirsutism) or biochemical hyperandrogenemia.
   (b) Menstrual irregularity.
   (c) Polycystic ovarian morphology on ultrasound defined as increased ovarian mass more than 5.5 cm²/ovary or volume more than 11 cm³/ovary and/or 12 or more follicles measuring 2–9 cm in diameter.
(3) Their ages ranged from 30 to 40 years.
(4) Their BMI ranged from 30 to 39.9 kg/m².
(5) They were able to understand the informed consent.

Exclusion criteria
Participants who met one of the following criteria were excluded from the study:

(1) Unwilling to accept randomization.
(2) Any medical condition that would be a contraindication to exercise.
(3) Unwilling to travel to/participate in the exercise program as defined by the protocol.

(4) Uncontrolled hypertension, cardiac illness or psychiatric condition.
(5) Cognitive dysfunction.
(6) Patients with morbid obesity (BMI>40 kg/m²).
(7) Patients suffering from any other endocrine disorder were excluded to avoid the effect on measures of insulin secretion and the sex steroid assay.

Patients were divided into two groups, equal in number:

(1) Group A (study group): 30 obese diabetic women.
(2) Group B (control group): 30 nondiabetic obese women.

All participants of both groups received a controlled diet program under the supervision of physicians of the Faculty of Physical Therapy and an aerobic exercise program; each exercise training session included continuous aerobic exercises on a treadmill for 30 min performed three times per week for 24 weeks under the supervision of physicians of the Faculty of Physical Therapy in the faculty department and they were on metformin drug (850 mg every 12 h) for diabetes treatment.

All patients were subjected to the measurement of weight, height, and BMI and the measurement of the waist circumference using the NIH protocol; the waist circumference measurement was taken at the top of the iliac crest. The tape was positioned directly around the abdomen so that the inferior edge of the tape was at the level of the landmarked point [10]; a pelvic ultrasonography was performed in all cases.

Laboratory assessment of fasting insulin and fasting blood glucose, followed by the calculation of the Homeostasis Model Assessment (HOMA) were performed. The HOMA-IR index was calculated as follows: HOMA-IR = $0.0555 \times$ fasting glucose (mg/dl) $\times$ fasting insulin (µIU/ml)/22.5. A HOMA number of more than 4.0 was taken as a sensitive indicator of insulin resistance [11].

Because there is no generalized consensus on a HOMA cutoff for insulin resistance, interpretation of the HOMA was based on the statistical stratification of the participants included in the study.

Both groups were on metformin drug (850 mg every 12 h) for polycystic ovary (PCO) treatment.

Both groups performed the moderate-intensity aerobic exercise program on a treadmill three times per week for 24 weeks.

Statistical analysis

(1) Descriptive statistics:

On the basis of the raw data, the mean, and SDs were calculated for each component of the dependent variables for all patients.

(2) Inferential statistics:

   (a) The paired '*t*' test was used to determine the differences between pretest and post-test evaluations of the same group.

   (b) The unpaired '*t*' test was used to determine the differences between post-test and pretest evaluations of both groups.

Results

Table 1 shows demographic data and anthropometric measures in both obese diabetic and non-diabetic groups. Table 2 shows that on within-group comparison, the mean ± SD of fasting insulin level values in the 'pre' and 'post' tests were 27.03 ± 4.67 and 23.9 ± 3.9 IU/ml, respectively, in the diabetic group (group A). This indicates a significant reduction of the fasting insulin level ($P = 0.01$). However, in group B, the mean ± SD values of the fasting insulin level in the 'pre' and the 'post' tests were 27.16 ± 4.17 and 24.63 ± 3.83 IU/ml, respectively, in the nondiabetic group (group B). This indicates a significant reduction of the fasting insulin level ($P = 0.05$).

Between-group (group A vs. group B) comparisons showed no significant differences in the pretest fasting insulin level ($P = 0.908$); post-test comparisons also showed no significant differences in the fasting insulin level in both groups ($P = 0.466$).

Table 3 shows the comparison within group A, in which the mean ± SD values of the weight in the 'pre' and the 'post' tests were 101.4 ± 8.69 and 94.93 ± 8.41 kg, respectively, in the diabetic group (group A). There was a significant decrease in the weight after treatment ($P = 0.001$).

In the nondiabetic group (group B), the mean ± ± SD values of the weight in the 'pre' and the 'post' tests were 104.5 ± 14.69 and 94.73 ± 13.76 kg, respectively. This indicates a significant reduction of weight after treatment ($P = 0.001$).

Comparison of the two groups showed that the weight was not statistically different before the test ($P = 0.324$); the post-test comparison also showed no significant differences of weight in both groups ($P = 0.946$).

Table 4 shows the comparative study of pretest and post-test waist circumferences between both groups. In the

within-group A comparison 'pre' and 'post' tests, there was a significant reduction of the waist circumference after treatment ($P = 0.05$). In the nondiabetic group (group B), there was significant reduction of waist circumference after treatment ($P = 0.01$). Comparison of the two groups showed no statistical difference in the waist circumference before the test ($P = 0.170$); the post-test comparison also showed no significant differences in the waist circumference in both groups ($P = 0.677$).

Table 1 Demographic data and anthropometric measures in obese diabetic (group A) and nondiabetic (group B) groups

Variables	$\overline{X}$ ± SD		P-value
	Group A	Group B	
Age (years)	37.63 ± 2.26	35.36 ± 4.49	0.637
Height (cm)	160.27 ± 5.7	161.35 ± 7.19	0.529
Weight (kg)	101.4 ± 8.69	104.5 ± 14.69	0.324
BMI (kg/m²)	39-84 ± 2.3	41 ± 1.7	0.251
Waist circumference (cm)	100.35 ± 9.4	104.26 ± 2.21	0.170

Table 2 Comparative study of the fasting insulin level pretest and post-test in groups A and B

Insulin level (IU/ml)	Means ± SD		P-value
	Pretest	Post-test	
Diabetic (group A)	27.03 ± 4.67	23.9 ± 3.9	0.01*
Nondiabetic (group B)	27.16 ± 4.17	24.63 ± 3.83	0.05*
P-value	0.908	0.466	

*Significant level, $P < 0.05$.

Table 3 Comparison of the weight pretest and post-test in groups A and B

Weight (kg)	Means ± SD		P-value
	Pretest	Post-test	
Diabetic	101.4 ± 8.69	94.93 ± 8.41	0.001*
Nondiabetic	104.5 ± 14.69	94.73 ± 13.76	0.001*
P-value	0.324	0.946	

*Significant level, $P < 0.05$.

Table 4 Comparative study of the waist circumference pretest and post-test between both groups

Waist circumference (cm)	Means ± SD		P-value
	Pretest	Post-test	
Diabetic	100.35 ± 9.4	95.6 ± 9.51	0.05*
Nondiabetic	104.26 ± 2.21	96.83 ± 13.02	0.01*
P-value	0.170	0.677	

*Significant level, $P < 0.05$.

Table 5 Comparison of the fasting glucose pretest and post-test in groups A and B

Fasting glucose (mg/dl)	Means ± SD		P-value
	Pretest	Post-test	
Diabetic	130.73 ± 17.56	121.5 ± 14.11	0.001*
Nondiabetic	96.46 ± 8.62	90.8 ± 6.72	0.001*
P-value	0.0001*	0.0001*	

*Significant level, $P < 0.05$.

Table 5 shows that on within-group comparison, the mean ± SD of the fasting glucose in the 'pre' and the 'post' tests were 130.73 ± 17.56 and 121.5 ± 14.11 mg/dl, respectively, in the diabetic group (group A). There was significant reduction of the fasting glucose after treatment ($P = 0.001$). In the nondiabetic group (group B), the mean ± SD values of the fasting glucose in the 'pre' and the 'post' tests were 96.46 ± 8.62 and 90.8 ± 6.72 mg/dl, respectively. This indicates a significant reduction of the fasting glucose after treatment ($P = 0.001$). Pretest comparisons of the two groups showed a very highly significant difference of the fasting glucose ($P = 0.0001$); the post-test comparison showed a very highly significant difference of fasting glucose in both groups ($P = 0.0001$).

Table 6 shows a comparative study between groups A and B regarding the insulin resistance calculated by HOMA: in the within-group comparison, the mean ± SD of the insulin resistance level in the 'pre' and the 'post' tests were 7.88 ± 1.93 and 6.49 ± 1.3, respectively, in the diabetic group (group A). This indicates a significant reduction of the insulin resistance level as assessed by HOMA ($P = 0.05$).

Also within-group comparison of group B showed that the mean ± SD values of the insulin resistance level in the 'pre' and the 'post' tests were 5.87 ± 1.1 and 4.98 ± 0.88, respectively, in the nondiabetic group (group B). This indicates a significant reduction of the insulin resistance level as assessed by HOMA ($P = 0.05$).

Between both groups (group A vs. group B), comparisons showed a significantly higher insulin resistance (assessed by HOMA) in diabetic women than in nondiabetic women with PCO both before and after termination of the exercise program ($P = 0.01$).

Discussion

PCOS is one of the most common reproductive system disorders with a prevalence estimated to be between 5 and 10% among women in the child-bearing age [1]. Approximately over 60% of patients with PCOS are insulin resistant and obese. Furthermore, 20–40% of

Table 6 Comparative study of the insulin resistance level pretest and post-test in groups A and B

Insulin resistance level (HOMA)	Means ± SD		P-value
	Pretest	Post-test	
Diabetic (group A)	7.88 ± 1.93	6.49 ± 1.3	0.05*
Nondiabetic (group B)	5.87 ± 1.1	4.98 ± 0.88	0.05*
P-value	0.01*	0.01*	

HOMA, Homeostasis model assessment; *Significant level, $P < 0.05$.

nonobese PCOS patients have evidence of insulin resistance [12]. Chronic exposure to high insulin levels leads to the development of acanthosis, increased body fat, and glucose intolerance [13].

It has been well established that the ovarian dysfunction associated with PCOS responds to treatment by insulin-sensitizing agents such as metformin and thiazolidinediones [14,15]. Therefore, insulin resistance and PCOS are closely related to each other [16].

The aim of this study was to investigate the effect of aerobic exercise on insulin resistance and waist circumference in diabetic and nondiabetic women with PCO.

The present study included 60 obese women recruited from the Gynecology Outpatient Clinic of Kasr Al Aini Hospital. They were assigned into two groups equal in number: group A (30 diabetic obese woman) received a controlled diet and aerobic exercise program and were on metformin drug (850 mg every 12 h) for diabetes treatment, and group B (30 nondiabetic obese women) received a controlled diet and aerobic exercise program performed three times per week for 24 weeks and were on metformin drug (850 mg every 12 h) for PCO treatment. The training program for patients in both groups was three times per week for 24 weeks; insulin resistance and waist circumference were measured at the beginning and after 24 weeks of training program for both groups.

To judge the glucose tolerance status of the patients against that of the control group, this study measured fasting glucose and insulin; we found no statistically significant difference in the fasting insulin level between both groups before and after the test, whereas there was a highly statistically significant difference in patients compared with in controls regarding fasting glucose.

This was in agreement with the study of Sir-Petermann *et al.* [17] and El Mkadem *et al.* [18], who found a significant difference in both groups regarding the glucose level, whereas in contrast to our result, they found an increased insulin level in the patient group compared with the control group.

In our study, insulin resistance calculated by HOMA was found to be significantly reduced post-test in both groups A and B ($P = 0.01$), and also significantly reduced within both groups comparison post-test ($P = 0.05$).

Similarly, Bhattacharya [19], Lin *et al.* [20], and Villuendas *et al.* [19–21] showed that PCOS patients have higher HOMA results and less tolerance to glucose.

This was also in agreement with the study by Nelson *et al.* [22], who stated that daily moderate-to-vigorous physical activity had a significant and positive effect on insulin resistance (IR).

These results were supported by Bunt *et al.* [23], who found that both the physical activity behavior and the physical activity level were significantly and directly related to the insulin sensitivity.

The results of this study agreed with results obtained by Strong *et al.* [24], who found that overweight youth who participate in a structured exercise program can significantly improve their insulin resistance.

Also, our results were supported by Nassis *et al.* [25], who examined the effects of 12 weeks of aerobic exercise training on insulin response to an oral glucose challenge in overweight adolescent girls. The program consisted of three 40-min supervised sessions per week at moderate exercise intensity; the girls exhibited a decrease in serum insulin concentrations in response to a 2-h oral glucose tolerance test. Collectively, the lower insulin concentrations resulted in a 23% reduction in the insulin area under the curve ($P < 0.05$): an indication of improved whole-body insulin sensitivity.

The results of this study coincided with the results achieved by Hutchison *et al.* [26], who reported that higher IR in PCOS compared with non-PCOS women at baseline and after 3 months of supervised intensified exercise training decreases insulin resistance.

The results of this study agreed with results obtained by Taghavi *et al.* [27], who studied twenty obese PCOS patients aged 15–30 years who underwent a 12-week aerobic training program. After the 12-week training program, they revealed a significant reduction in body weight and the percentage of body fat.

This was also in agreement with Garcia-Hermoso *et al.* [9], who reported improvements (only in fasting insulin) after an aerobic exercise program for more than 12 weeks, three sessions per week, and over 60 min of aerobic exercise per session. This meta-analysis provides insight about the effectiveness of aerobic exercise interventions on insulin resistance markers in the obese youth population.

Also, this was consistent with Phillips and Cobbold [28], who studied the effects of exercise on the fluctuating concentrations of the inflammatory markers adipokines, with an increase in the secretion of adiponectin produced by increased physical activity. Increases in adiponectin can help reduce risk factors of cardio vascular disease (CVD) by decreasing inflammation and increasing microvascular blood flow and insulin sensitivity.

Finally, it was concluded that aerobic exercise has potent effect in women with PCOS by its direct effect on improving insulin resistance through mitochondrial biogenesis and by improving glucose tolerance and insulin action. Also, aerobic exercise helps in weight reduction, which decreased lipolysis, resulting in decreased plasma free fatty acids, which in turn improves insulin-mediated glucose uptake.

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