

# The Relationship Between Insulin Resistance and Polycystic Ovary Syndrome in Libyan Women

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#### Abstract

Polycystic ovary syndrome (PCOS) is a heterogeneous endocrine disease that is common in women of reproductive age and is usually caused by androgen excess and ovarian dysfunction. It is often accompanied by insulin resistance (IR) and some manifestations such as hirsutism and fertility problems. The current study was conducted to evaluate the prevalence of polycystic ovary syndrome and its relationship to insulin resistance among Libyan women, Tripoli. This study included 69 patients: 52 diagnosed with PCOS and 17 control women between the ages of 20 and 40. The study was conducted over three months, from January 2024 to March 2024, at Nour Al Hayat Fertility Hospital in Tripoli. a structured questionnaire was utilized to gather data on patient demographics, such as insulin resistance values, HbA1c levels, and various hormone levels, including TSH, FSH, Prolactin, and Testosterone. A 2 ml venous blood sample was collected from each patient for analysis. Insulin and fasting glucose levels were measured using two different assays to calculate the equation: Insulin FBS / 450. Statistical analysis was performed using IBM SPSS version 22 software. The prevalence of polycystic ovary syndrome was 75%, compared to the control group, 25%. Furthermore, there was a significant increase in HOMA IR, HbA1c, Prolactin, and Testosterone levels (p < 0.05), as well as in FSH and TSH levels in the PCOS group compared to the control (P > 0.05). The results also showed that insulin resistance, HOMA IR, was positively correlated with HbA1c levels among both study groups (p < 0.05). In conclusion, Insulin resistance is a common feature of women with PCOS. This study highlights the importance of Insulin resistance and hyperandrogenism, which appear to be interrelated key factors in the pathogenesis of PCOS. Addressing insulin resistance can help improve symptoms and outcomes for individuals with PCOS.

Keywords. Insulin Resistance, PCOS, Hormonal Imbalance, Androgens.

#### Introduction:

Originally known as "Leventhal syndrome" [1], polycystic ovary syndrome (also known as PCOS) is the most prevalent endocrine disorder, affecting 6–10% of women who are at reproductive age [2–3]. It is caused by hyperandrogenism, and its key characteristics include hirsutism, anovulation, irregular menstruation, infertility, and weight gain [4]. As this syndrome affects 48.4 million women between the ages of 20 and 44, infertility is the most common of these complications, which can be short-term or long-term [5]. It is associated with metabolic and reproductive abnormalities, about 90% of PCOS women are not able to uphold pregnancy [6]. The morphological feature of PCOS is due to multiple ovarian cysts appear as a string of pearls on ultrasound examination. These cysts are arrested immature small antral follicles [7].

Women with this syndrome suffer from it as a chronic condition, which makes it widespread, causing several diseases such as obesity, metabolic syndrome, type 2 diabetes, and some endothelial dysfunction, unlike women who do not suffer from this syndrome [8].

Since these defects can be passed down autosomally dominantly, the genetic component of this syndrome plays a significant role in the acquisition of high sex androgens in ovarian cells [9, 10]. Mutations in androgen receptors and sex hormone binding globin [SHBG] may also play a major role in the acquisition of high levels of androgens in the blood [11]. The Rotterdam criteria, which include oligoamenorrhea (OM), hyperandrogenism (HA), and polycystic ovarian morphology (PCOM), are currently the most widely used diagnostic criteria for PCOS [12]. To diagnose hyperandrogenism or oligoamenorrhea, at least two of the three criteria must be met after ruling out other possible causes. The Rotterdam criteria were used to identify four distinct PCOS phenotypes. The most prevalent type, phenotype-A, satisfies all three requirements: OM, HA, and PCOM. OM and HA are present in phenotype-B, HA and PCOM are present in phenotype-C, while OM and PCOM are present in phenotype-D [13].

Numerous cutting-edge medical research studies have demonstrated that insulin resistance is the primary characteristic shared by individuals with this syndrome; approximately 50–70% of women with PCOS exhibit insulin resistance above and beyond what is predicted by their BMI [14]. Insulin resistance (IR) is defined clinically as the inability of a known quantity of exogenous or endogenous insulin to increase glucose uptake and utilization in an individual as much as it does in a normal population [15].

**Received**: 06/05/25 **Accepted**: 04/07/25 **Published**: 12/07/25

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Compensatory hyperinsulinemia is a physiological response of the body to maintain the balance of fats and carbohydrates to reduce insulin sensitivity [16]. This response leads to the depletion of cells and the emergence of a series of side effects and diseases mentioned above for polycystic ovary syndrome [17]. The production of ovarian androgens is stimulated by IR and hyperinsulinemia, which also increases the effect of LH on ovarian androgen production. These factors together determine hyperandrogenemia. Inhibiting SHBG secretion is a common action of androgens and insulin, which raises levels of free and bioactive androgens and exacerbates clinical androgen excess. Furthermore, it is believed that treating IR, which includes lifestyle modifications, insulin-sensitizing medications, and bariatric surgery, is crucial for both reducing IR and mitigating its effects because it plays a critical role in the development of metabolic syndrome and cardiovascular diseases in PCOS women [18].

Carmina et al. [19] examined three groups of twenty-five women with PCOS. They found that the prevalence of IR, as determined by the results of an insulin tolerance test are varies from 68 to 76 percent in these regions (mainly Hispanic Americans), southern Italy, and Japan. There is currently a large population study to determine the prevalence of IR in PCOS at Birmingham. Catherine et al. have noticed that 64.4% of PCOS patients were insulin resistant according to HOMA/IR measurement, and 2.6% had  $\beta$ -cell dysfunction [20]. That is a clear observation that patients with IR were more clinically affected. Although IR is more common in PCOS women, its dose seems to be a universal feature.

Since several reports have shown a clear correlation between PCOS and insulin resistance, highlighting the importance of insulin, particularly for females in the reproductive age range thus in order to enable appropriate treatment and prevent the emergence of potential complications screening for insulin resistance is crucial for PCOS patients. This study aims to reduce the risk of developing polycystic ovarian syndrome PCOS among Libyan patients by assessing the prevalence of insulin resistance and finding out the relationship between IR and reproductive hormones.

# Methods

#### Study design and area

This study was conducted on PCOS patients aged between 20 and 40 years and covered a period of approximately three months from January 2024 to March 2024 and was conducted at Nour Al Hayat Fertility Hospital in Tripoli.

## Study subjects

There were 69 cases who visited the hospital during the study period, some of whom probably had polycystic ovary syndrome according to the Rotterdam criteria [12]. We used a questionnaire to collect information such as age, insulin resistance values, HBA1c, and some hormones including: Prolactin, Testosterone, TSH and FSH. Pregnant and breastfeeding women and those with uterine fibroids or breast cells were excluded from this study.

## Sample collection

HOMA IR (Homeostasis Model Assessment of Insulin Resistance) was used to find out insulin resistance in the body and whether the patient suffers from what is called prediabetes. The procedure that required for this test is that the patient must fast for 8 to 12 hours. A 2ml venous blood sample was taken from the patients. In this test, two types of analyzes were used to calculate the equation: Insulin FBS /450. Measuring insulin and Fasting Blood Sugar FBS: to measure insulin, we used a white tube "clot activator" and to measure FBS, a fluoride tube was used. The two samples were separated in a centrifuge at 4000 rpm for 5 to 7 minutes, and a serum sample was taken. The insulin and FBS levels were measured by using the absorbance photometry measurement method with the cobasE411 reader from Roche company. The normal range of insulin resistance is 0.5-1.5.

## Statistical analysis

Statistical analysis was performed using IBM SPSS version 26. To determine whether there was a significant difference between groups (women with PCOS and women without PCOS) we used an independent (unpaired) t test. Data were expressed as mean  $\pm$  standard deviation (SD). The Pearson correlation test between HOMA IR and other variables between (women with PCOS and women without PCOS). A P value <0.05 was considered statistically significant.

## Results

The study was conducted on 69 participating women, divided into 52 (75%) women with polycystic ovary syndrome and 17 (25%) women without polycystic ovary syndrome (the control group). and their mean ages, were 31.7 years and 26.4 years respectively (Fig1).

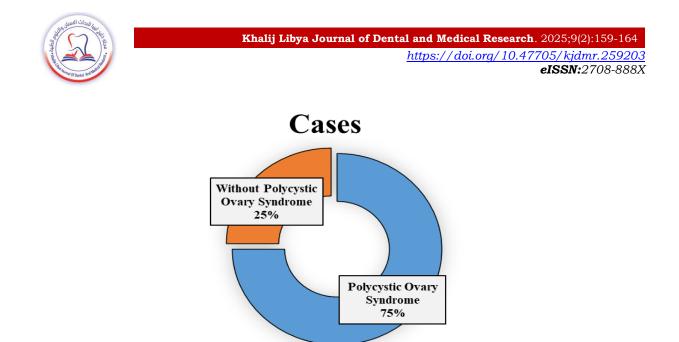


Figure 1. Distribution of study population

The results showed that HOMA IR, HBA1c, Prolactin and Testosterone were statistically significantly higher in PCOS women ( $1.788 \pm 0.692$ ,  $5.417 \pm 0.611$ ,  $24.705 \pm 4.341$  and  $1.061 \pm 0.434$ ) respectively, compared with control group ( $0.823 \pm 0.311$ ,  $4.917 \pm 0.329$ ,  $1.775 \pm 0.958$ ,  $7.448 \pm 1.945$ ,  $18.017 \pm 5.897$ ,  $0.479 \pm 0.213$ ) (p < 0.05) (Table 1). However, there was no statistically significant difference in TSH and FSH levels among women with PCOS compared to women with non-polycystic ovary syndrome (P > 0.05) (Table 1).

Table 1. Comparison of Age	e, HOMA IR, HBA1c	, TSH, FSH,	Prolactin, a	nd Testoster	rone values
betwe	en women with PC	OS and the	control grou	р.	

	Women with PCOS	Women without PCOS	_ <b>T</b>	Р
Parameters	Mean ± SD Mean ± SD		Test	Value
Age(years)	26.470 ± 4.515	31.764 ± 5.437	3.021	0.008
HOMA IR	$1.788 \pm 0.692$	$0.823 \pm 0.311$	5.240	0.001
HBA1c%	$5.417 \pm 0.611$	$4.917 \pm 0.329$	3.529	0.003
TSH (mIU/ml)	$2.117 \pm 1.406$	$1.775 \pm 0.958$	0.892	0.385
FSH (mIU/ml)	8.486 ± 1.660	$7.448 \pm 1.945$	1.753	0.099
Prolactin(ng/ml)	$24.705 \pm 4.341$	$18.017 \pm 5.897$	3.423	0.003
Testosterone (ng/ml)	$1.061 \pm 0.434$	$0.479 \pm 0.213$	5.325	0.001

Table 2 shows that there was a strong positive correlation between HOMA IR and HbA1c in both study groups, PCOS women (r= 0.796, p= 0.001) and the control group (r= 0.704, p= 0.002). Furthermore, HOMA IR was correlated negatively with FSH in PCOS and control groups (r=-0.166, r=-0.013), respectively, but it was not statistically significant (Fig. 3).

Moreover, among PCOS women there was a weak correlation between HOMA IR: and age is (r = 0.174), prolactin (r = 0.124) and testosterone (r = 0.162) with statistical significance (p = 0.216), (p = 0.383), (p = 0.253) respectively (P > 0.05). Whereas, HOMA IR was correlated negatively with the same variables, age (r = -0.033), prolactin (r = -0.364), and testosterone (r = -0.284) in women without PCOS, and also it was not statistically significant (Table 2). Also, the results show that TSH is correlated negatively with HOMA IR (r = -0.091) in the patient' group while there is a positive relationship between TSH and HOMA IR in control women (r = 0.426) (P > 0.05) (Table 2).

Table 2. The correlation between	HOMA IR with values of Ag	e, HbA1c, TSH, FSH, Prolactin, and			
Testosterone					

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HOMA IR	Women with PCOS		Women without PCOS		
	R	Р	r	Р	
Age	0.174	0.216	-0.033	0.899	
HBA1c	0.796**	0.001	0.704**	0.002	
TSH	-0.091	0.520	0.426	0.089	
FSH	-0.166	0.240	-0.013	0.961	
Prolactin	0.124	0.383	-0.364	0.151	
Testosterone	0.162	0.253	-0.284	0.270	

# Discussion

Women with PCOS (polycystic ovary syndrome) and insulin resistance are closely linked. Insulin resistance is thought to be a major contributing factor in the development of PCOS. Insulin resistance and type 2 diabetes are more common in women with PCOS. High insulin levels can stimulate the ovaries to produce more androgens. In this study, the prevalence of polycystic ovary syndrome was 75%, and they were insulin resistant compared to the control group (p = 0.001). A study conducted in 2016 in Italy found that insulin resistance affects up to 70% of women with PCOS [21]. This result is similar to another study that found 33% of the study population in Iraq had polycystic ovary syndrome [22].

A study conducted in Benghazi, Libya, in 2016 found that 67% of female polycystic ovary syndrome patients were between 20 and 29 years old [23]. Another cross-sectional study was conducted on 258 female students registered in the fourth year at the Faculty of Medicine at the University of Tripoli. The mean study age was 23.81 ± 1.13, with an age range of 22 to 29 years [24].

The current results were obtained indicating a strong relationship in patients with polycystic ovary syndrome and type 2 diabetes, which explains that patients suffer from a condition called pre-diabetes, which makes insulin resistance necessary. A health problem that must be addressed. This condition means that the body cannot use insulin properly. PCOS is associated with a high prevalence of type 2 diabetes) T2D .(In line with the results of a study conducted at Chengdu University Hospital of Traditional Chinese Medicine, Chengdu, China, 2022 and previous descriptive findings, approximately 21% of women with type 2 diabetes have PCOS overall. Subgroup analysis revealed that female patients between the ages of 25 and 45 years had a higher incidence of PCOS compared to patients younger than this age. The incidence of PCOS was highest among women with T2DM in Oceania, Europe, and Asia, and lowest among women with T2DM in North America [25].

Women with polycystic ovary syndrome, hyperprolactinemia, or high prolactin levels can experience interference with a regular menstrual cycle and ovulation. This may lead to irregular menstruation, difficulty getting pregnant, and other symptoms of polycystic ovary syndrome [4]. This is what our study has shown that an increase in the hormone prolactin in patients with polycystic ovary syndrome is possible and closely linked to this condition. These results are consistent with a study conducted at the University of Medical Sciences in Iran/Tehran in 2022, which showed that prolactin levels were significantly higher in the PCOS group, while this was not observed in the group. The exact mechanism by which prolactin may be associated with PCOS remains unknown. However, several plausible mechanisms have been proposed. There is evidence demonstrating that physical, psychological, and environmental factors can play a role in regulating prolactin secretion [26].

The results of this study showed an increase in the level of testosterone, which is common in patients with polycystic ovary syndrome. It explains the disturbance of androgenic hormones and related phenomena. These were clear manifestations, such as hirsutism and acne. This is consistent with one study conducted in Benghazi/Libya in 2016, where free testosterone was high in patients with polycystic ovary syndrome [23]. On the other hand, a study conducted in America Testosterone was low in women with polycystic ovary syndrome, and this decrease coincided with increasing age (ages were 37 to 42 years). The cause of decreased testosterone concentrations with age in women with polycystic ovary syndrome is currently unknown. Since decreased testosterone levels are not associated with SHBG but SHBG levels are unchanged, it is suggested that a decrease in testosterone production occurs [27].

The main mechanism of polycystic ovary syndrome is insulin resistance. The study discovered that hormonal changes associated with subclinical hypothyroidism include high levels of TSH and FSH ratios, but in the current study, we did not obtain a clear change in either hormone. This may be because the diagnosis of polycystic ovary syndrome is not based on hypothyroidism. These findings were in agreement with a previous study conducted in the Gynecology Outpatient Department of Ziauddin Kemmari Hospital, Karachi, Pakistan, in 2019 [28]. Regarding hormones ,the value was less than 0.05no significant difference was found in FSH levels. In addition, there was no correlation between TSH and FSH levels .Furthermore ,these results are similar to the study conducted in Benghazi [23], where there were no significant differences in TSH or FSH. This is because in the presence of normal levels of FSH and TSH, it can sometimes lead to grade 1 polycystic ovary syndrome, or it can be caused by hypothyroidism.

# Limitations of this study

Women who have been diagnosed with polycystic ovary syndrome should check their insulin regularly, so that it in turn affects the likelihood of developing this syndrome and better improving its symptoms. Lifestyle modification, weight control, and a healthy approach, such as a balanced diet and exercise, may reduce allergies. Insulin resistance, which in turn affects the reduction in the incidence of this syndrome or its non-development, if present. Some medications, such as metformin, may be prescribed to help control the regulation of insulin levels. Reducing the symptoms of polycystic ovary syndrome.



# Conclusion

In conclusion, the relationship between insulin resistance and polycystic ovary syndrome is complex, and its management is important, as insulin resistance is contributed with pathogenesis of polycystic ovary syndrome, which in turn affects hormonal disturbance, ovarian function, and metabolism. To control polycystic ovary syndrome, insulin resistance must first be controlled by lifestyle changing, such as improving diet, exercising, and properly managing medications. More research is needed to understand the mechanism and reasons behind this relationship to develop and better understand the disease mechanism for more effective results and treatment.

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