## **ORIGINAL ARTICLE**

# Insulin Resistance in Patients with Polycystic Ovary Syndrome

SHAZIA HAIDER<sup>1</sup>, MUHAMMAD AYYAZ<sup>2</sup>, NEHA AHUJA<sup>3</sup>, MARIA DHAHRI<sup>4</sup>, ATIQ AHMAD<sup>5</sup>, MUHAMMAD FAHEEM SIDDIQUI<sup>6</sup>

<sup>1</sup>Assistant Professor, Department of Obstetrics & Gynaecology, Fatima Jinnah Medical University, Lahore

<sup>2</sup>Assistant Professor, <sup>5</sup>Associate Professor, Department of Medicine, M. Islam Medical & Dental College, Gujranwala

<sup>3</sup>Medical Officer, Ali Hospital, Wagan Road, Larkana

<sup>4</sup>Consultant OBGY, Indus Hospital & Health Network (IHHN), District Headquarter Hospital, Badin

<sup>6</sup>Assistant Professor, Department of Biochemistry, Pak Red Crescent Medical & Dental College, Dina Nath

Correspondence to: Shazia Hiader, Email: shaziahaider05@gmail.com, Cell: 0333-4072329

### **ABSTRACT**

**Background:** Polycystic ovary syndrome is a common endocrine disorder affecting women of reproductive age, characterized by hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology.

**Objective:** To determine the frequency of insulin resistance in patients with Polycystic ovary syndrome and evaluate its association with clinical features and biochemical markers.

Study Design: Descriptive cross-sectional study

Place and Duration of Study: Department of Obstetrics & Gynaecology, Fatima Jinnah Medical University, Lahore from 1st February 2023 to 31st July 2023.

**Methodology:** One hundred female patients diagnosed with polycystic ovary syndrome were enrolled.

**Results:** The mean age was 26.4±4.8 years, and mean body mass index was 29.3±5.2 kg/m². Insulin resistance was present in 68% of the patients. A significant association was observed between insulin resistance and higher body mass index (p<0.001), menstrual irregularity (p<0.01), and lipid abnormalities (p<0.05). The mean Homeostatic Model Assessment for insulin resistance in the insulin-resistant group was 4.3±1.2 compared to 2.1±0.5 in the non-resistant group. Pearson correlation showed a strong positive correlation between body mass index and Homeostatic Model Assessment for insulin resistance (r = 0.61, p<0.001).

**Conclusion:** The insulin resistance is prevalent among women with polycystic ovary syndrome and is significantly associated with obesity, menstrual irregularities, and dyslipidemia. Routine screening for insulin resistance and early intervention are essential to prevent long-term metabolic and reproductive complications.

Keywords: Insulin resistance, Polycystic ovary syndrome, Clinical features, Biochemical markers

#### INTRODUCTION

Worldwide polycystic ovary syndrome (PCOS) stands as one of the common endocrine diseases affecting 5 to 10 percent of women who are capable of having children. The disease shows multiple symptoms that cluster as ovulatory problems and elevated testosterone levels and ultrasound detected cysts in ovaries.¹ Polycystic ovary syndromes reproductive and androgen-related symptoms receive primary attention from clinicians yet metabolic problems possess equal importance by supporting pathophysiological development of the syndrome. The primary pathogenic mechanism in PCOS produces two important effects because insulin resistance both initiates the syndrome development and worsens its clinical characteristics and long-term medical problems.²

A physiologic condition known as insulin resistance will affect peripheral organs like skeletal muscle tissue and adipose tissue but also liver tissue rendering their insulin response insufficient. Glucose homeostasis requires progressively increasing levels of insulin because of which patients develop compensatory hyperinsulinemia.<sup>3</sup> The presence of insulin resistance in women who have PCOS stands as a primary characteristic of the illness because it occurs independently from weight status. Research shows that insulin resistance afflicts between 50-70% of individuals with PCOS since it strongly influences the reproductive and metabolic dysfunctions of this condition.<sup>4</sup>

Polycystic ovary syndrome-related hormonal imbalance becomes worsened because of the elevated insulin levels that occur during insulin resistance. Insulin stimulates ovarian androgen production by directly influencing theca cells and by limiting hepatic sex hormone-binding globulin synthesis thus raising free androgen blood levels. The condition leads to hirsutism as well as acne and menstrual irregularities among affected patients. Women with insulin resistance encounter problems with normal follicular development and ovulation while their ovaries become polycystic due to these interference effects.

Received on 10-08-2023 Accepted on 20-09-2023 The metabolic issues associated with PCOS become more severe when patients have insulin resistance since this condition leads to multiple persistent medical complications. The metabolic conditions related to PCOS include type 2 diabetes mellitus, dyslipidemia, impaired glucose tolerance, non-alcoholic fatty liver disease and hypertension. Women with PCOS have an elevated cardiovascular disease risk because of their multiple comorbidities which appear earlier in age than in the rest of the female population. The property of the service of the service of the service of the service of the female population.

The development of type 2 diabetes shows a five-fold risk increase in women who have PCOS as compared to women without the disorder. A complex combination of biological factors creates multiple pathways that result in insulin resistance among women with PCOS.8 Multiple studies indicate that impairment of insulin signalling pathways alongside chronic inflammation and oxidative stress and altered adipokine such as leptin and adiponectin levels exist as suspected factors in this condition.9 Both mitochondrial dysfunction and irregularities of the gut microbiome contribute to insulin resistance development. The link between PCOS and insulin resistance together with genetic and epigenetic factors requires further study to establish associations since these factors appear to predispose particular individuals to the conditions. Because insulin resistance exists in PCOS patients the clinical approach requires attention. 10 Weight reduction efforts combined with changes in diet and physical activity enhance both reproductive function and insulin sensitivity according to documented research.<sup>11</sup> A small amount of weight loss leads to both the recovery of ovulatory cycles and lower androgen hormone levels. The medical treatment of PCOS is supported through pharmacological methods. Metformin serves as an insulinsensitizing drug which physicians commonly prescribe to treat both PCOS metabolic symptoms together with reproductive conditions.12

# **MATERIALS AND METHODS**

This descriptive cross-sectional study was conducted at Department of Obstetrics & Gynaecology, Fatima Jinnah Medical University Lahore from 1st February 2023 to 31st July 2023. A total of 100 female patients diagnosed with polycystic ovary syndrome

were enrolled. All women aged 18 to 35 years who met the Rotterdam diagnostic criteria for PCOS, which requires at least two of the following: (1) oligo- or anovulation, (2) clinical and/or biochemical signs of hyperandrogenism, and (3) polycystic ovarian morphology on transabdominal or transvaginal ultrasound were included. Patients with a prior diagnosis of diabetes mellitus, Cushing's syndrome, congenital adrenal hyperplasia, thyroid dysfunction, or those currently on insulin sensitizers, hormonal therapy, corticosteroids, or weight reduction medications, pregnant and lactating women were excluded. Each participant underwent a comprehensive clinical evaluation, which included demographic details, medical history, menstrual pattern, and physical examination. Anthropometric measurements such as height and weight were recorded. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters (kg/m²). Fasting blood samples were collected after an 8-12 hour overnight fast. The investigations were performed as fasting blood glucose (measured in mmol/L), fasting serum insulin (measured in μIU/mL) and lipid profile (including total cholesterol, HDL, LDL, and triglycerides). All biochemical analyses were conducted using standardized laboratory methods at the hospital's central laboratory. Fasting insulin levels were determined using chemiluminescent immunoassay. Insulin resistance was assessed using the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR). Data were analyzed using SPSS-25.0. Student's t test was applied and p-value < 0.05 considered statistically significant.

## **RESULTS**

The mean age of participants was  $26.4\pm4.8$  years and mean body mass index was  $29.3\pm5.2$  kg/m², with 62% of participants categorized as overweight or obese (BMI  $\geq$ 25 kg/m²). The majority of patients 71% reported irregular menstrual cycles, and clinical signs of hyperandrogenism (hirsutism and/or acne) were observed in 68% of participants. The mean fasting blood glucose level was  $5.4\pm0.6$  mmol/L, and the mean fasting serum insulin was  $15.8\pm6.3$  µIU/mL. The mean HOMA-IR score was  $3.8\pm1.7$ . A total of 68 patients (68%) were found to have insulin resistance (HOMA-IR >2.5) [Tables 1-2].

Among the study participants, insulin resistance was significantly more prevalent in those with a BMI ≥25 kg/m². Of the 62 overweight or obese individuals, 52 (83.9%) were insulin resistant, compared to only 14 (36.8%) among the 38 participants with a BMI <25 kg/m². This association was statistically significant (p<0.001), indicating that higher BMI is strongly correlated with increased risk of insulin resistance in PCOS patients (Table 3).

Correlation analysis revealed a strong positive relationship between BMI and HOMA-IR (r = 0.61, p<0.001), indicating that increased body mass index is significantly associated with higher insulin resistance. Fasting insulin levels also showed a strong correlation with HOMA-IR (r = 0.73, p<0.001), suggesting that elevated insulin levels are closely linked with insulin resistance (Table 4).

The distribution of HOMA-IR values among the study participants showed that the majority of patients (68%) had a HOMA-IR score greater than 2.5, indicating insulin resistance. Only 24% of patients fell within the normal range (1.5–2.5), while a small proportion (8%) had low insulin sensitivity with HOMA-IR values below 1.5 (Table 5).

Table 1: Frequency of clinical and biochemical characteristics of women (n=100)

(11-100)		
Parameter	No.	%
Overweight/Obese (BMI ≥25)	62	62.0
Irregular menstrual cycles	71	71.0
Clinical hyperandrogenism	68	68.0
Patients with IR (HOMA-IR >2.5)	68	68.0

Comparison of lipid profiles between insulin-resistant and non-insulin-resistant groups revealed significant differences. The IR group had higher levels of total cholesterol (198.6 vs. 178.4

mg/dL, p = 0.02), LDL (125.7 vs. 106.3 mg/dL, p = 0.03), and triglycerides (172.4 vs. 141.2 mg/dL, p = 0.04), along with lower HDL levels (39.2 vs. 48.5 mg/dL, p = 0.01) [Table 6].

Table 2: Descriptive statistics of the women (n=100)

Parameter	Mean±SD
Age (years)	26.4±4.8
Body mass index (kg/m²)	29.3±5.2
Fasting blood glucose (mmol/L)	5.4±0.6
Fasting insulin (µIU/mL)	15.8±6.3
HOMA-IR Score	3.8±1.7

Table 3: Association between body mass index and insulin resistance (n=100)

Body mass index	No.	IR Present	p-value
<25 kg/m²	38	14 (36.8%)	<0.001
≥25 kg/m²	62	52 (83.9%)	<0.001

Table 4: Correlation of HOMA-IR with Clinical Parameters

Variable	Pearson's correlation value (r)	P value
Body mass index	0.61	<0.001
Fasting Insulin	0.73	<0.001
Fasting Glucose	0.35	0.001

Table 5: Distribution of patients according to HOMA-IR categories

HOMA-IR Category	No.	%
<1.5 (Low)	8	8.0
1.5-2.5 (Normal)	24	24.0
>2.5 (Insulin resistant)	68	68.0

Table 6: Comparison of lipid profile between IR and Non-IR Groups

Lipid Parameter	IR Group (n = 68)	Non-IR Group (n = 32)	p-value
Total cholesterol (mg/dL)	198.6	178.4	0.02
HDL (mg/dL)	39.2	48.5	0.01
LDL (mg/dL)	125.7	106.3	0.03
Triglycerides (mg/dL)	172.4	141.2	0.04

# **DISCUSSION**

An evaluation of insulin resistance frequency together with its clinical relationships occurred among women who received a PCOS diagnosis. This study demonstrated that insulin resistance occurs in 68% of participants thus confirming its essential role as a metabolic irregularity in PCOS. Research literature confirms that insulin resistance affects 50% to 75% of women diagnosed with PCOS according to variable criteria and demographic factors. Among our participants 68 patients displayed insulin resistance defined as values greater than 2.5 based on a HOMA-IR measurement of 3.8±1.7. The research findings match what Dunaif et al<sup>13</sup> and Legro et al<sup>14</sup> presented about elevated HOMA-IR scores in both lean and obese PCOS patients. This study showed insulin resistance occurring among individuals of all weight categories. The association between BMI and insulin resistance (p<0.001) existed nonetheless 36.8% of lean patients displayed insulin resistance thus demonstrating insulin resistance in PCOS results from inherent insulin signaling pathway defects beyond adiposity alone.15

The menstrual irregularity occurred in 71% of participants while men experienced insulin resistance at a statistically significant rate (p<0.01). Insulin resistance appeared in 78.9% of women who experienced irregular cycles but 41.4% of women who experienced regular cycles. This research conducted lipid parameters analysis between groups with insulin resistance and those without insulin resistance. <sup>16</sup> Significant statistical differences revealed that total cholesterol, LDL and triglyceride levels were elevated along with HDL being decreased in the IR group as compared to other groups (all p<0.05). The results confirm how PCOS patients with insulin resistance typically develop atherogenic lipid levels leading to increased cardiovascular danger in this affected population. Insulin-resistant PCOS women show higher rates of dyslipidemia together with metabolic syndrome according to research from Wild et al. <sup>17</sup> and Shirazi et al. <sup>18</sup>

The medical world deals with these findings because of their major practical consequences. Early detection of IR in PCOS patients requires the implementation of basic cost-effective evaluation using HOMA-IR particularly for people experiencing menstrual problems, obesity and hyperandrogenism.<sup>19</sup> Insulin sensitizing drugs like metformin or inositol-based agents together with lifestyle modification provide the best therapy options for higher risk metabolically managed patients.<sup>20</sup> This study has two major limitations because it used a cross-sectional research design that prevents identifying cause-effect relationships. Although HOMA-IR provides practical results it functions as an indirect assessment method which might not encompass the complete spectrum of insulin steroid hormone interaction. Research studies must include extended observational assessments and should consider adopting clamp-based assessment protocols for establishing the validity of identified results.

#### CONCLUSION

The insulin resistance is highly prevalent among patients with polycystic ovary syndrome, affecting approximately two-thirds of the study population. The presence of insulin resistance was significantly associated with higher body mass index, irregular menstrual cycles, and adverse lipid profiles, emphasizing its role as a core metabolic disturbance in PCOS. These findings reinforce the importance of early identification and management of insulin resistance to prevent long-term complications such as type 2 diabetes, cardiovascular disease, and persistent reproductive dysfunction.

## **REFERENCES**

- Schröder AK, Tauchert S, Ortmann O, Diedrich K, Weiss JM. Insulin resistance in patients with polycystic ovary syndrome. Ann Med 2004; 36(6): 426-39
- Morey S, Raziel A, Friedler S, Strassburger D, Bern O, Ron-E RI. Insulin resistance in patients with polycystic ovary syndrome is associated with elevated plasma homocysteine. Human Reprod 2003: 18/41: 721-7.
- Toprak S, Yönem A, Cakir B, Güler S, Azal O, Ozata M, Corakçi A. Insulin resistance in nonobese patients with polycystic ovary syndrome. Horm Res 2001;55(2):65-70.
- Chang RJ, Nakamura RM, Judd HL, Kaplan SA. Insulin resistance in nonobese patients with polycystic ovarian disease. J Clin Endocrinol Metab 1983; 57(2): 356-9.
- Moghetti P. Insulin resistance and polycystic ovary syndrome. Curr Pharmaceut Design 2016; 22(36): 5526-34.
- Shoupe D, Kumar DD, Lobo RA. Insulin resistance in polycystic ovary syndrome. Am J Obstet Gynecol 1983; 147(5): 588-92.

- Park KH, Kim JY, Ahn CW, Song YD, Lim SK, Lee HC. Polycystic ovarian syndrome (PCOS) and insulin resistance. Int J Gynecol Obstet 2001; 74(3): 261-7.
- Lankarani M, Valizadeh N, Heshmat R, Peimani M, Sohrabvand F. Evaluation of insulin resistance and metabolic syndrome in patients with polycystic ovary syndrome. Gynecol Endocrinol 2009;25(8):504-7.
- Noyan V, Yucel A, Sagsoz N. The association of bone mineral density with insulin resistance in patients with polycystic ovary syndrome. Eur J Obstet Gynecol Reprod Biol 2004;115(2):200-5.
- Purwar A, Nagpure S. Insulin Resistance in Polycystic Ovarian Syndrome. Cureus 2022; 14(10):e30351.
- Pasquali R, Casimirri F, Venturoli S, Paradisi R, Mattioli L, Capelli M, et al. Insulin resistance in patients with polycystic ovaries: its relationship to body weight and androgen levels. Acta Endocrinol (Copenh) 1983;104(1):110-6.
- Ashkar F, Rezaei S, Salahshoornezhad S, Vahid F, Gholamalizadeh M, Dahka SM, et al. The Role of medicinal herbs in treatment of insulin resistance in patients with polycystic ovary syndrome: a literature review. Biomol Concepts 2020;11(1):57-75.
- Dunaif A. 1997. Insulin resistance and the polycystic ovary syndrome: mechanism and implications for pathogenesis. Endocr Rev 1997; 18:774-800
- Legro RS, Daniel CV, Kauffman RP. Detecting insulin resistance in polycystic ovary syndrome: purposes and pitfalls. Obstet Gynecol Survey 2004; 59(2): 141-54.
- Feng Y, Li M, Li X, Tang Q, Li X, Ji X, Tian W, Zhang H. Characteristics of different obesity metabolic indexes and their correlation with insulin resistance in patients with polycystic ovary syndrome. Reprod Sci 2023; 31(9):2829-35.
- Hemati T, Moghadami-Tabrizi N, Davari-Tanha F, Salmanian B, Javadian P. High plasma homocysteine and insulin resistance in patients with polycystic ovarian syndrome. Iranian J Reprod Med 2011; 9(3): 223.
- Wild RA, Painter PC, Coulson PB, Carruth KB, Ranney GB. Lipoprotein lipid concentrations and cardiovascular risk in women with polycystic ovary syndrome. J Clin Endocrinol Metab. 1985;61:946–951.
- Shirazi FKH, Khodamoradi Z, Jeddi M. Insulin resistance and high molecular weight adiponectin in obese and non-obese patients with polycystic ovarian syndrome (PCOS). BMC Endocrine Disord 2021; 21: 1-7.
- Panidis D, Tziomalos K, Misichronis G, Papadakis E, Betsas G, Katsikis I, Macut D. Insulin resistance and endocrine characteristics of the different phenotypes of polycystic ovary syndrome: a prospective study. Hum Reprod 2012;27(2):541-9.
- Behboudi-Gandevani S, Ramezani Tehrani F, Rostami Dovom M, Farahmand M, Bahri Khomami M, Noroozzadeh M, et al. Insulin resistance in obesity and polycystic ovary syndrome: systematic review and meta-analysis of observational studies. Gynecol Endocrinol 2016;32(5):343-53.

This article may be cited as: Haider S, Ayyaz M, Ahuja N, Dhahri M, Ahmad A, Siddiqui MF: Insulin Resistance in Patients with Polycystic Ovary Syndrome. Pak J Med Health Sci, 2023; 17(10): 157-159.