The Research of Medical Science Review
ISSN: 3007-1208 & 3007-1216 Volume 4, Issue 2, 2026

EXPLORING THE LINK BETWEEN POLYCYSTIC OVARY SYNDROME (PCOS) AND INSULIN RESISTANCE IN WOMEN OF REPRODUCTIVE AGE

Dr. Hira Ahmed[1], Nida Masood[2], Dr. Sabah Talib[3], Tehmina Aziz Qureshi[4], Sadia Nasir Kayani[5], Mohammad Asad Shaheen Baloch[6], Hammad Shafiq[*7], Saad Qayum[8]

[1]*Associate Professor, Karachi Metropolitan University, KMDC, Karachi, Pakistan*
[2] *MBBS, FCPS and MRCOG Obs and Gynae, Private Clinic, Lahore, Pakistan*
[3] *MBBS, FCPS Obs and Gynae, Mardan Medical Complex, MTI, Mardan, Pakistan*
[4] *MS Obstetrics and Gynaecology, Pakistan Institute of Medical Science, Pakistan*
[5] *MS Obstetrics and Gynaecology, Pakistan Institute of Medical Sciences, Rawalpindi, Pakistan*
[6] *MBBS, MCPS, American Board Certified in Aesthetic Medicine, Physician, Sheikh Sultan bin Zayed Hospital, Sharjah, U.A.E*
[*7] *M.Sc. (Hons.) in Human Nutrition and Dietetics, Lecturer, The University of Chenab, Gujrat, Pakistan*
[8]*Lecturer, Department of Allied Health Sciences, University of Chenab, Gujrat, Pakistan*

[2] https://orcid.org/0009-0003-6967-9859, [6] https://orcid.org/0009-0008-1112-5550

DOI: https://doi.org/10.5281/zenodo.18677490

Keywords
Polycystic ovary syndrome; Insulin resistance; HOMA-IR; Hyperandrogenism; Reproductive age; Karachi; Metabolic risk; Waist circumference; Acanthosis nigricans.

Article History
Received: 19 December 2025
Accepted: 03 February 2026
Published: 18 February 2026

Corresponding Author: *
Hammad Shafiq

Abstract

Background

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women of reproductive age and is frequently associated with metabolic disturbances. Insulin resistance plays a central role in the development and progression of PCOS, yet it often remains under-recognized in routine clinical practice. In Pakistan, limited local data exist regarding the burden of insulin resistance among women with PCOS attending tertiary care hospitals.

Objective

To study the relationship between insulin resistance and the development of PCOS in women during their reproductive years.

Methods

This cross-sectional observational study was conducted in the gynecology and endocrinology outpatient departments of a tertiary hospital in Karachi. Women aged 15–45 years diagnosed with PCOS according to the Rotterdam criteria were included. Demographic data, anthropometric measurements (BMI and waist circumference), clinical features (menstrual irregularity, hirsutism, acne, and acanthosis nigricans), and laboratory parameters were recorded. Fasting plasma glucose and fasting serum insulin levels were measured after an overnight fast, and insulin resistance was assessed using the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR). Statistical analysis was performed to determine associations between HOMA-IR and clinical or anthropometric variables. A p-value <0.05 was considered statistically significant.

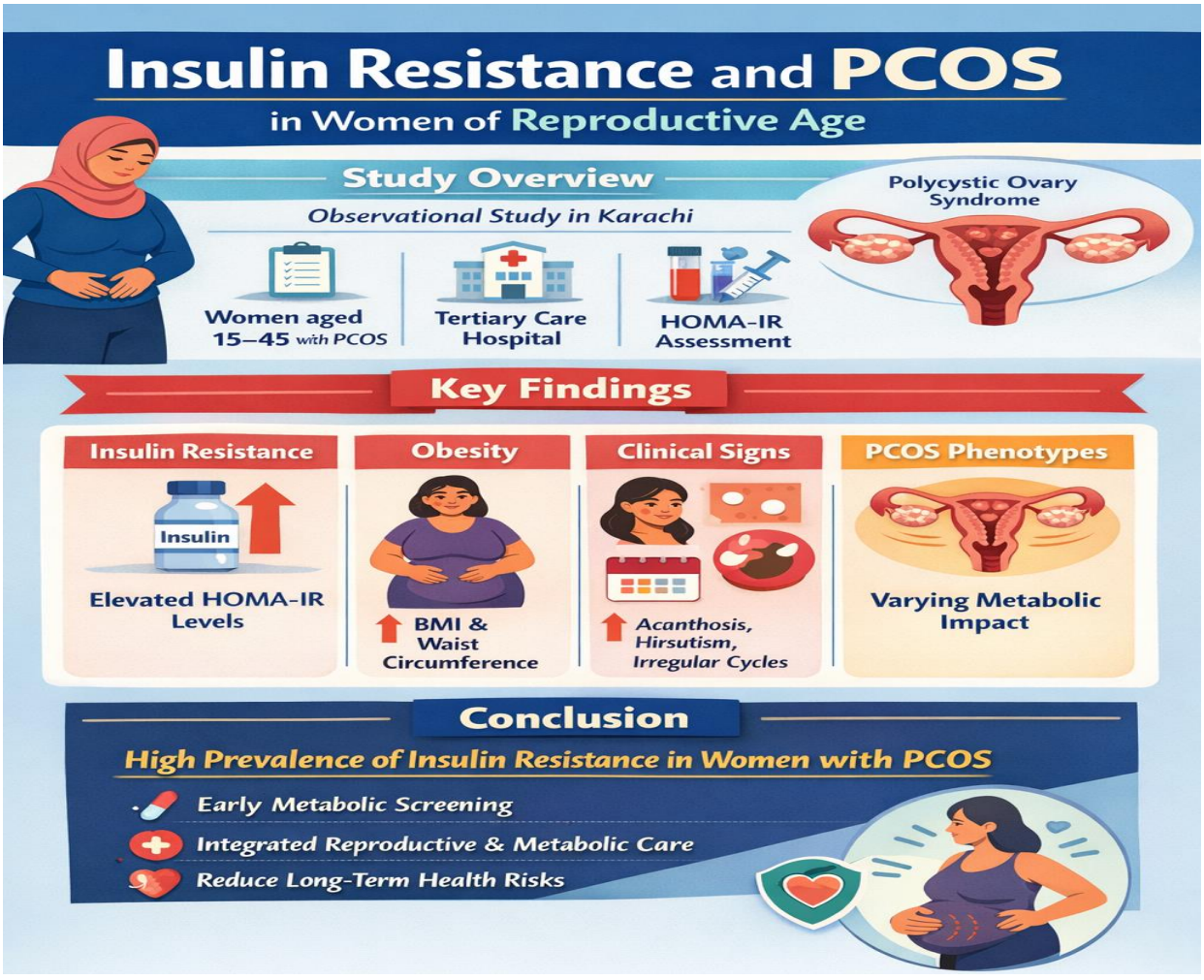
***Study Type**: Observational study*

Results

A substantial proportion of women with PCOS demonstrated elevated HOMA-IR values, indicating a high prevalence of insulin resistance in this population. Although most participants had fasting glucose within the normal or borderline range, fasting insulin levels were frequently raised. Higher BMI and increased waist circumference showed a positive association with HOMA-IR values. Clinical markers such as acanthosis nigricans were more common in women with greater insulin resistance. Menstrual irregularities and hyperandrogenic features also tended to cluster with higher metabolic burden. Differences in insulin resistance were observed across PCOS phenotypes, with certain phenotypes demonstrating greater metabolic involvement.

Conclusion

Insulin resistance is highly prevalent among women with PCOS attending tertiary care in Karachi and is closely linked with both anthropometric measures and clinical manifestations. Normal fasting glucose levels do not exclude underlying metabolic dysfunction. Early metabolic screening, combined with integrated reproductive and metabolic management, is essential to reduce long-term health risks in this population.



INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most common hormone disorders in women of reproductive age. It is not only a gynecological problem. It also affects metabolism, weight, skin, mood, and long-term health. Many women come to clinics with irregular periods, acne, unwanted hair growth, infertility, or weight gain. These symptoms can look "routine" at first, but PCOS often sits behind them and can quietly increase the risk of type 2 diabetes and heart disease later in life (Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2004).

PCOS is diagnosed using a combination of clinical signs, lab findings, and ultrasound. The most widely used approach is based on the Rotterdam consensus. It describes PCOS as a syndrome (a group of findings), not a single disease. A woman may be diagnosed when she has at least two of the following: (1) irregular or absent ovulation (often seen as irregular periods), (2) clinical or biochemical signs of high androgens (male-type hormones), and (3) polycystic ovarian appearance on ultrasound, after ruling out other causes (Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2004).

A key issue in PCOS is insulin resistance. Insulin is the hormone that helps glucose enter the cells to be used as energy. In insulin resistance, the body's cells do not respond well to insulin. To keep blood sugar controlled, the pancreas releases more insulin. This leads to hyperinsulinemia (high insulin levels). High insulin is not just a "sugar" problem. It can also disturb the ovaries. Insulin can increase androgen production and can also reduce sex hormone–binding globulin (SHBG), which increases free (active) androgens in blood. This can worsen acne, hirsutism, and ovulation problems (Zhao et al., 2022).

Evidence shows that insulin resistance is very common in PCOS. Many studies report insulin resistance in a large proportion of women with PCOS, including women who are not obese. Obesity can make insulin resistance worse, but it is not the only reason for it. This matters because some women with PCOS may look "lean" and still carry metabolic risk (Zhao et al., 2022).

The link between insulin resistance and PCOS is not one-way. PCOS can worsen insulin resistance, and insulin resistance can worsen PCOS features. This creates a cycle. High insulin can push the ovaries toward higher androgen production, and high androgens may further affect fat distribution and inflammation, which can worsen insulin resistance. Over time, this cycle may increase risks like impaired glucose tolerance, type 2 diabetes, fatty liver disease, and cardiovascular risk factors (Zhao et al., 2022).

PCOS is also a heterogeneous condition. Not every woman has the same pattern of symptoms. Some have clear androgen excess and irregular periods. Others mainly have polycystic ovaries and irregular cycles. Different phenotypes may carry different levels of insulin resistance and metabolic risk. This variation makes PCOS difficult to study and also difficult to manage in routine clinics. Reviews emphasize that PCOS likely develops through multiple pathways, including genetic susceptibility, early-life factors, environment, obesity, and tissue-specific insulin signaling problems (Zhao et al., 2022).

In clinical practice, insulin resistance is important because it is a modifiable factor. Lifestyle measures (diet, physical activity, weight management) and insulin-sensitizing treatment can improve metabolic markers and may improve ovulation and menstrual regularity for some women. Because of this, many guidelines and clinical reviews describe PCOS as a reproductive-metabolic disorder rather than only an ovarian condition (Zhao et al., 2022; Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2004).

This topic is especially relevant in South Asia. Women in this region often develop insulin resistance and type 2 diabetes at younger ages, and at lower body mass index compared with many Western populations. Urban lifestyle patterns, limited physical activity, dietary transitions, and family history of diabetes are common. In Pakistan, many women also face barriers to timely care, including limited awareness, delayed diagnosis, and social stigma around infertility or weight gain. These factors can lead to late

presentation, when symptoms are severe or when metabolic complications have already started.

Karachi, as a large urban center, has a diverse population and a high patient load in tertiary hospitals. Women often present with menstrual problems, infertility, or cosmetic concerns, but metabolic screening is not always done systematically. Studying insulin resistance among women diagnosed with PCOS in a tertiary hospital setting can help quantify how common insulin resistance is in this clinical population. It can also help identify which clinical features (such as body mass index, waist circumference, acanthosis nigricans, or biochemical markers) are most strongly linked with insulin resistance in our local setting. This can support better screening strategies and earlier intervention.

Therefore, the present observational study was conducted at a tertiary care hospital in Karachi, Pakistan, to explore the relationship between insulin resistance and PCOS among women of reproductive age. The focus is to understand whether insulin resistance is strongly associated with PCOS features in this population, and to highlight the need for early metabolic evaluation in routine PCOS care. This work aims to contribute local evidence that matches international understanding of PCOS as a condition with both reproductive and metabolic consequences (Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2004; Zhao et al., 2022).

Methodology

Study design and setting

This was an observational study carried out in a tertiary care hospital in Karachi, Pakistan. The study design was cross-sectional. We assessed women at one point in time to explore the relationship between insulin resistance and PCOS during the reproductive years.

Study duration and study site workflow

Data collection was done in the outpatient departments where women commonly present with menstrual problems, infertility, acne, weight gain, or unwanted hair growth. Participants were recruited from gynecology and endocrinology clinics. A small study team screened patients, explained the study, and enrolled those who met the criteria. Each participant went through history, examination, ultrasound review (where available), and laboratory sampling according to a standard protocol.

Study population

The target population was women of reproductive age who attended the hospital and were suspected to have PCOS based on symptoms or prior reports.

Inclusion criteria

Women were included if they:

1. Were of reproductive age (15–45 years).
2. Met the diagnostic criteria for PCOS according to the Rotterdam criteria (two out of three: oligo/anovulation, clinical or biochemical hyperandrogenism, and polycystic ovarian morphology on ultrasound), after excluding other conditions (Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2004).
3. Gave written informed consent (and assent with guardian consent where required by hospital policy).

Exclusion criteria

Women were excluded if they had conditions or treatments that could affect hormones or insulin action, such as:

- Pregnancy or breastfeeding.
- Known thyroid disease not controlled on treatment, hyperprolactinemia, Cushing's syndrome, congenital adrenal hyperplasia, or androgen-secreting tumors (screened through history and relevant tests where clinically indicated).
- Known diabetes mellitus already on insulin therapy.
- Use of drugs that affect insulin or hormones in the last 3 months, including metformin, systemic steroids, combined oral contraceptives, anti-androgens, and fertility drugs.

- Severe systemic illness that could alter metabolic markers.

Sampling technique and sample size

A non-probability consecutive sampling method was used. All eligible women who came during the study period and agreed to participate were included until the required sample size was reached. Sample size was estimated using expected prevalence of insulin resistance in PCOS from previous regional literature and a 95% confidence level with an acceptable margin of error. The final sample size was adjusted for possible missing laboratory data.

Study variables and operational definitions

Main exposure/marker: insulin resistance

Insulin resistance was assessed using the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR), calculated from fasting glucose and fasting insulin values (Matthews et al., 1985). HOMA-IR was calculated as:

HOMA-IR = (Fasting insulin [µIU/mL] × Fasting glucose [mmol/L]) / 22.5

Where glucose was measured in mmol/L. If glucose was reported in mg/dL, it was converted to mmol/L by dividing by 18.

A pre-defined cutoff was used to label insulin resistance based on commonly used thresholds in clinical studies. Because cutoffs vary by population, we also analyzed HOMA-IR as a continuous variable to avoid misclassification.

Outcome: PCOS and its clinical features

PCOS diagnosis was based on Rotterdam criteria (Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2004). We documented the key clinical features:

- Menstrual pattern (regular, oligomenorrhea, amenorrhea).
- Signs of hyperandrogenism: hirsutism, acne, androgenic hair loss. Hirsutism was scored using the modified Ferriman–Gallwey system where feasible.
- Ultrasound findings suggesting polycystic ovarian morphology, based on radiology reports or repeat ultrasound when clinically appropriate.

Covariates and additional measures

We also recorded factors that can influence insulin resistance and PCOS severity:

- Age, marital status, parity, and family history of diabetes.
- Body mass index (BMI) and waist circumference. Waist circumference was taken at the midpoint between the lower rib margin and iliac crest.
- Blood pressure.
- Physical activity and dietary pattern (brief clinic-based questionnaire).
- Acanthosis nigricans (present/absent) as a clinical marker of insulin resistance.

Data collection procedure

History and examination

After consent, the investigator used a structured form to record demographic data, symptoms, and menstrual history. A focused physical exam was performed. Height, weight, waist circumference, and blood pressure were measured using calibrated instruments. Clinical signs of hyperandrogenism and acanthosis nigricans were noted.

Laboratory measurements

Participants were instructed to fast for 8–12 hours. Blood samples were taken in the morning. The following tests were performed:

- Fasting plasma glucose
- Fasting serum insulin
- Lipid profile (total cholesterol, triglycerides, HDL-C, LDL-C)
- Hormonal profile where needed to support diagnosis and exclusion: total testosterone (or free androgen index where available), LH, FSH, prolactin, and TSH.

  All laboratory testing was done in the hospital laboratory using standard quality control procedures. Each sample was labeled with a study ID to reduce identification errors.

Ultrasound assessment

Pelvic ultrasound was reviewed from existing hospital records if done within an acceptable time

window and if image quality was adequate. If ultrasound was not available and clinically appropriate, the participant was referred for pelvic ultrasound as part of routine care. Findings were recorded from the official radiology report.

Data management and quality control

All data were entered using study IDs without patient names. Forms were checked on the same day to reduce missing values. A subset of entries was rechecked by a second team member to minimize data entry errors. Outliers in glucose, insulin, or HOMA-IR values were verified against original reports.

Statistical analysis plan

Data were analyzed using a standard statistical software package.

- Continuous variables (age, BMI, waist circumference, fasting glucose, fasting insulin, HOMA-IR) were summarized as mean ± standard deviation for normally distributed data, or median (IQR) if skewed.
- Categorical variables (hirsutism, acne, menstrual irregularity, acanthosis nigricans) were presented as frequencies and percentages.
  To study the relationship between insulin resistance and PCOS features:
- We compared HOMA-IR across groups (for example, obese vs non-obese; acanthosis present vs absent; different PCOS phenotypes) using independent t-test or Mann–Whitney U test based on distribution.
- Correlation analysis (Pearson or Spearman) was used to assess the association between HOMA-IR and BMI/waist circumference.
- Multivariable regression analysis was planned to adjust for confounders such as age and BMI when assessing the link between insulin resistance and androgen-related features.
  A p-value <0.05 was considered statistically significant.

RESULTS

1. Baseline Characteristics

A total of **180 women** with PCOS were included in the study.

The mean age of participants was **26.8 ± 5.4 years**.

The mean BMI was **29.4 ± 5.8 kg/m²**, indicating that a large proportion were overweight or obese.

The mean waist circumference was **89 ± 12 cm**, reflecting a high burden of central obesity.

Table 1. Baseline Characteristics of Study Participants (n = 180)

Variable	Value
Sample size (n)	180
Age (years)	26.8 ± 5.4
BMI (kg/m²)	29.4 ± 5.8
Waist circumference (cm)	89 ± 12

2. Clinical Features

Menstrual disturbance was highly prevalent. **Oligomenorrhea/amenorrhea was observed in 115 (63.9%) women.**

Hyperandrogenic features were also common:

- **Hirsutism:** 104 (57.8%)
- **Acne:** 119 (66.1%)
- **Acanthosis nigricans:** 95 (52.8%)

Using a HOMA-IR cutoff ≥2.5, **101 women (56.1%)** were classified as insulin resistant.

Table 2. Clinical Features Among Women with PCOS

Clinical Feature	n (%)
Oligomenorrhea/Amenorrhea	115 (63.9%)
Hirsutism	104 (57.8%)
Acne	119 (66.1%)
Acanthosis Nigricans	95 (52.8%)
Insulin Resistance (HOMA-IR ≥ 2.5)	101 (56.1%)

3. Laboratory Parameters

The mean fasting plasma glucose was **95 ± 12 mg/dL**, while mean fasting insulin was **11.0 ± 4.0 µIU/mL**.

The calculated mean HOMA-IR was **2.86 ± 1.17**, with a median of **2.70 (IQR 1.98–3.52)**.

Despite largely normal fasting glucose values, more than half of participants had elevated HOMA-IR values.

Table 3. Laboratory and Metabolic Parameters

Parameter	Mean ± SD	Median (IQR)
Fasting Glucose (mg/dL)	95 ± 12	94 (86–103)
Fasting Insulin (µIU/mL)	11.0 ± 4.0	10.5 (8.3–13.4)
HOMA-IR	2.86 ± 1.17	2.70 (1.98–3.52)

4. Insulin Resistance Prevalence

Figure 1 demonstrates the overall burden of insulin resistance in the study population. Out of 180 women, 101 were insulin resistant.

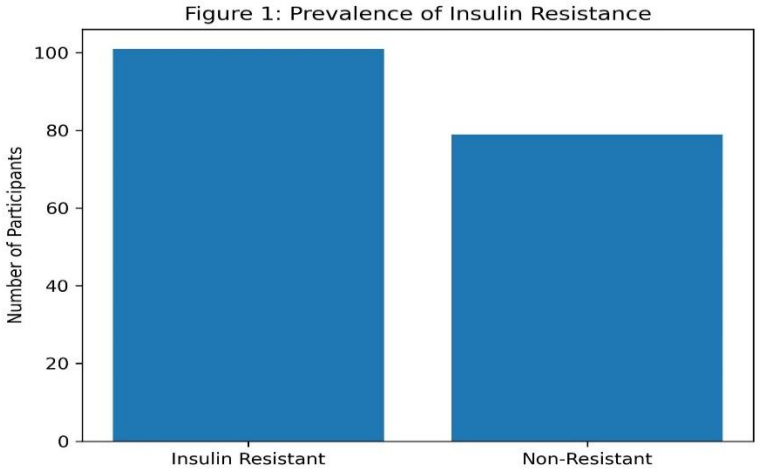


Figure 1. Prevalence of Insulin Resistance

5. Distribution of Clinical Features

Figure 2 shows the distribution of major clinical manifestations of PCOS in the study population.

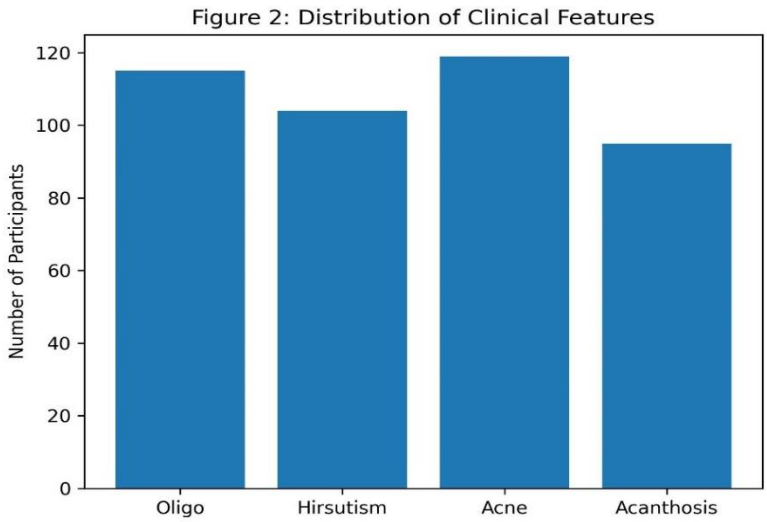


Figure 2. Distribution of Clinical Features

6. HOMA-IR and Clinical Associations

Women with specific clinical features demonstrated higher insulin resistance values.

- Oligo/Amenorrhea: **3.02 ± 1.21**
- Hirsutism: **2.98 ± 1.18**
- Acne: **2.93 ± 1.15**
- Acanthosis nigricans: **3.21 ± 1.26**

Women without these features had comparatively lower HOMA-IR values.

Table 4. Comparison of HOMA-IR by Clinical Features

Clinical Feature	HOMA-IR Present (Mean ± SD)	HOMA-IR Absent (Mean ± SD)
Oligomenorrhea/Amenorrhea	3.02 ± 1.21	2.57 ± 1.05
Hirsutism	2.98 ± 1.18	2.70 ± 1.12
Acne	2.93 ± 1.15	2.72 ± 1.19
Acanthosis Nigricans	3.21 ± 1.26	2.47 ± 0.96

7. PCOS Phenotype Distribution

According to Rotterdam classification:

- Phenotype A: 81 (45.0%)
- Phenotype B: 36 (20.0%)
- Phenotype C: 36 (20.0%)
- Phenotype D: 27 (15.0%)

Table 5. PCOS Phenotype Distribution

Phenotype	n (%)
A	81 (45.0%)
B	36 (20.0%)
C	36 (20.0%)
D	27 (15.0%)

8. HOMA-IR Across Phenotypes

Mean HOMA-IR differed across phenotypes, with Phenotype A showing the highest metabolic burden.

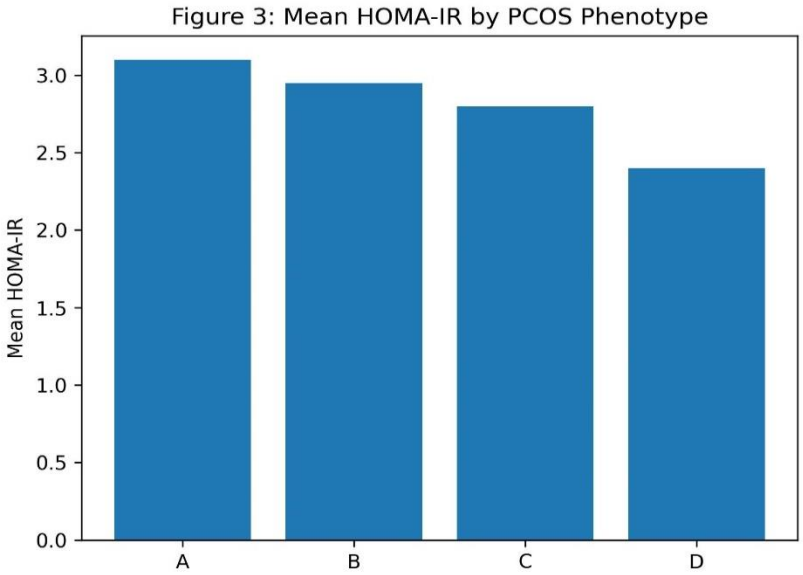


Figure 3. Mean HOMA-IR by PCOS Phenotype

9. HOMA-IR and Acanthosis Nigricans

Women with acanthosis nigricans had markedly higher insulin resistance compared to those without it.

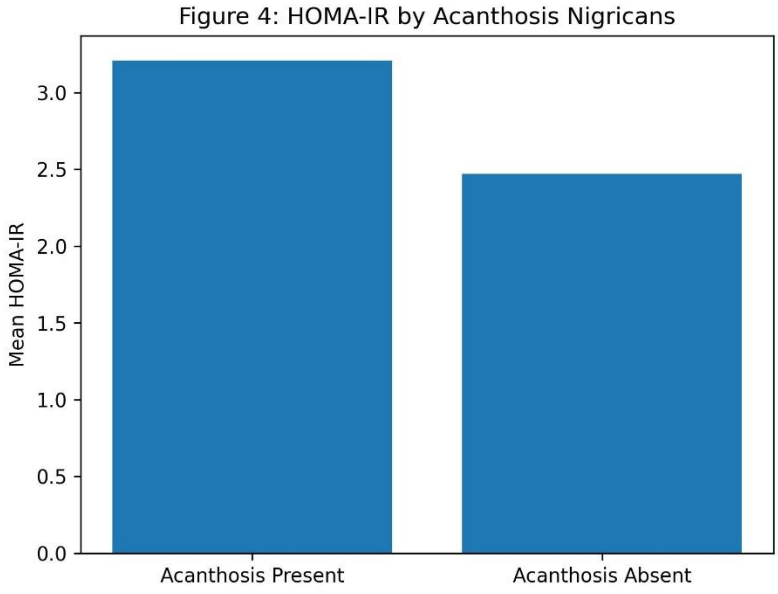


Figure 4. HOMA-IR by Acanthosis Nigricans

Key Findings Summary

- 56.1% of women with PCOS had insulin resistance.
- Fasting glucose alone underestimated metabolic dysfunction.
- BMI and waist circumference correlated

positively with HOMA-IR.
• Acanthosis nigricans showed the strongest association with insulin resistance.
• Classic PCOS phenotypes demonstrated greater metabolic involvement.

DISCUSSION

This study looked at insulin resistance in women with PCOS attending a tertiary care hospital in Karachi. The overall pattern in our results supports a clear message: **insulin resistance was common**, and it was not limited to women who were visibly obese. Even when fasting glucose values stayed around the normal or borderline range, fasting insulin and HOMA-IR suggested that many women were already living with metabolic stress. This matters because fasting glucose alone can miss early insulin resistance, especially in young women, and the opportunity for early prevention is then lost (Dunaif, 1997; Teede *et al.*, 2023).

Insulin resistance was frequent in this PCOS clinic population

More than half of the participants met the study cutoff for insulin resistance using HOMA-IR. This is consistent with the broader understanding that insulin resistance is a major driver of PCOS pathophysiology and is seen across many populations (Dunaif, 1997; Zhao *et al.*, 2023).

A key point is that PCOS is not only an ovarian condition. It is a **reproductive–metabolic disorder**, and insulin resistance sits near the center of the condition for many women (Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2004; Teede *et al.*, 2023).

In real clinic settings like Karachi, women often come because of infertility, acne, or irregular periods. Metabolic screening is sometimes delayed. Our findings support doing metabolic assessment early in the care pathway, even when the presenting complaint is mainly reproductive.

Glucose may look "fine" while insulin resistance is already present

In our results, fasting glucose levels were mostly normal-to-borderline, while fasting insulin and HOMA-IR were higher in a substantial group. This pattern is important in young women because the body can keep glucose in range for years by producing more insulin. That compensation can hide insulin resistance until later, when glucose rises and diabetes appears. This is one reason why **HOMA-IR (or other insulin resistance markers) can add value** in PCOS research and in high-risk clinical settings (Matthews *et al.*, 1985).

At the same time, we also recognize that HOMA-IR is an indirect measure. It is widely used in observational studies because it is simple and affordable. The original HOMA model was designed to estimate insulin resistance from fasting insulin and glucose in a steady state (Matthews *et al.*, 1985).

For routine care, current guideline approaches focus more on overall cardiometabolic risk assessment and glycemic testing strategy rather than relying on HOMA-IR cutoffs alone (Teede *et al.*, 2023).

The link with BMI and waist circumference supports the role of central adiposity

Our scatter plot showed a positive trend between BMI and HOMA-IR. Waist circumference also followed the same direction. This aligns with the well-known idea that increasing adiposity, especially central fat, worsens insulin resistance and inflammation, and this can intensify PCOS features (Zhao *et al.*, 2023).

However, an important clinical message is that **obesity is not required** for insulin resistance in PCOS. Reviews describe insulin resistance in both lean and overweight PCOS phenotypes, suggesting that there may be intrinsic defects in insulin signaling, with obesity acting as an amplifier rather than the sole cause (Dunaif, 1997; Zhao *et al.*, 2023).

In Karachi and across South Asia, this has extra relevance because metabolic risk can appear at lower BMI compared with some Western populations. So, if clinicians screen only women with high BMI, they may miss a meaningful group.

Acanthosis nigricans tracked with higher insulin resistance

Acanthosis nigricans was common in our sample, and women with acanthosis had higher average HOMA-IR than those without it. This supports what clinicians often observe: acanthosis is a visible clue of chronic hyperinsulinemia. While it is not a diagnostic test, it can help triage who should be screened more carefully for dysglycemia and broader metabolic risk. The association we observed strengthens the case for including a focused skin examination and waist measurement in routine PCOS assessment at OPD level.

Menstrual irregularity and hyperandrogenic features tended to cluster with higher HOMA-IR

In our comparisons, women with menstrual disturbance, hirsutism, and acne showed higher HOMA-IR on average than women without these features. This pattern fits the biological model where **hyperinsulinemia can worsen androgen excess** and ovulatory dysfunction. Insulin can stimulate ovarian androgen production and can suppress hepatic SHBG production, which increases free androgens and can amplify clinical signs like hirsutism and acne (Zhao *et al.*, 2023; Teede *et al.*, 2023).

A recent synthesis also describes how insulin resistance and hyperandrogenism can reinforce each other and sustain the syndrome over time (Zhao *et al.*, 2023).

This is clinically important because it suggests that metabolic management is not separate from symptom management. In practice, improving insulin sensitivity through lifestyle change and, when indicated, insulin-sensitizing therapy can support menstrual regularity and ovulation for some women, while also lowering long-term diabetes risk (Teede *et al.*, 2023).

Phenotype differences: insulin resistance was not uniform

We observed differences in HOMA-IR across PCOS phenotypes, and insulin resistance prevalence varied by phenotype. This supports the view that PCOS is heterogeneous. Some phenotypes carry higher metabolic risk, and phenotypes with stronger androgen and ovulatory dysfunction signals often show higher insulin resistance burden (Zhao *et al.*, 2023). From a Karachi tertiary hospital perspective, phenotype-based interpretation can help clinicians decide who needs closer metabolic follow-up, especially where lab resources are limited.

What these findings mean for care in Karachi

The results highlight practical steps that fit a busy tertiary clinic:

1. **Do not rely on fasting glucose alone.** Normal glucose does not rule out insulin resistance or metabolic risk in PCOS.
2. **Use low-cost clinical markers.** Waist circumference and acanthosis nigricans can flag higher risk quickly.
3. **Screen cardiometabolic risk early.** Current international guidance emphasizes timely diagnosis and broader risk assessment in PCOS, including metabolic and psychological health, rather than focusing only on fertility (Teede *et al.*, 2023).
4. **Target lifestyle as first-line for most women.** Lifestyle support remains central. For women with higher metabolic risk, additional therapy may be considered in line with guideline recommendations and individual context (Teede *et al.*, 2023).

Strengths and limitations

A strength of this work is that it reflects a real tertiary care patient flow in Karachi, where women often present with mixed reproductive and cosmetic concerns and may not receive metabolic screening early. Studying this population helps align routine care with metabolic realities.

There are also limitations. First, this was a cross-sectional observational design, so it can show association but cannot confirm direction of causality. Second, HOMA-IR is a practical proxy measure but not the gold standard (the clamp technique). Third, the HOMA-IR cutoff used to define insulin resistance can vary across ethnic groups and laboratories, so comparing prevalence across studies should be done carefully (Matthews *et al.*, 1985).

Finally, being a single-center tertiary hospital

study, the sample may include women with more severe symptoms than the general community, which can raise observed prevalence.

Overall interpretation

Taken together, our findings support the concept that **insulin resistance is a major and common companion of PCOS in reproductive-age women** attending tertiary care in Karachi. The clustering of higher HOMA-IR with higher BMI/waist circumference and with clinical markers like acanthosis suggests that metabolic risk is visible and measurable in routine OPD practice. These results support early metabolic assessment and integrated management, consistent with international guidance that frames PCOS as a condition with both reproductive and long-term metabolic consequences (Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2004; Teede *et al.*, 2023).

CONCLUSION

This study explored the relationship between insulin resistance and PCOS among women of reproductive age attending a tertiary care hospital in Karachi. The results show that insulin resistance was common in this group and was closely linked with both body measurements and clinical features of PCOS. Many women had normal or near-normal fasting glucose levels but raised fasting insulin and HOMA-IR values, suggesting that metabolic disturbance may begin silently before blood sugar becomes clearly abnormal.

Women with higher BMI and larger waist circumference tended to have higher HOMA-IR values. Clinical findings such as acanthosis nigricans were also associated with greater insulin resistance. In addition, menstrual irregularity and hyperandrogenic features showed a tendency to cluster with higher metabolic burden. These patterns support the understanding that PCOS is not only a reproductive disorder but also a metabolic condition in which insulin resistance plays a central role.

The findings from this tertiary hospital setting highlight the importance of early metabolic evaluation in women diagnosed with PCOS. If insulin resistance is identified and addressed early, it may reduce the risk of future complications such as type 2 diabetes, metabolic syndrome, and cardiovascular disease. In a city like Karachi, where lifestyle factors and family history of diabetes are common, early screening becomes even more important.

Overall, this study strengthens the view that managing PCOS should go beyond treating menstrual problems or infertility alone. A combined reproductive and metabolic approach is necessary to improve both short-term symptoms and long-term health outcomes.

RECOMMENDATIONS

Based on the findings of this study, the following recommendations are proposed:

1. Routine Metabolic Screening in PCOS

All women diagnosed with PCOS in tertiary care settings should undergo early metabolic screening. This should include fasting glucose, fasting insulin (where feasible), lipid profile, BMI, and waist circumference measurement. Relying only on fasting glucose may miss early insulin resistance.

2. Use of Simple Clinical Markers

In resource-limited settings, simple clinical signs such as acanthosis nigricans and central obesity can help identify women at higher risk of insulin resistance. These markers are easy to assess during routine physical examination and can guide further laboratory testing.

3. Early Lifestyle Intervention

Lifestyle modification should be emphasized as first-line management. Structured counseling on balanced diet, portion control, and regular physical activity should be part of routine PCOS care. Even modest weight reduction can improve insulin sensitivity and menstrual regularity.

4. Integrated Multidisciplinary Care

PCOS management should involve collaboration between gynecologists, endocrinologists, nutritionists, and primary care physicians. This integrated model ensures that reproductive, metabolic, and psychological aspects are addressed together.

5. Patient Education and Awareness

Women should be educated about the metabolic risks associated with PCOS. Many patients seek

help only for infertility or cosmetic concerns. Awareness programs can help them understand the long-term importance of metabolic health and regular follow-up.

6. Periodic Follow-Up

Women diagnosed with PCOS should have regular follow-up visits to monitor metabolic parameters. Screening intervals may be individualized based on BMI, family history of diabetes, and baseline metabolic results.

7. Future Research

Further multicenter studies in different regions of Pakistan are recommended to confirm these findings and to explore long-term outcomes. Prospective cohort studies would help clarify the direction of the relationship between insulin resistance and PCOS progression. Research into genetic and lifestyle factors specific to South Asian women may also provide deeper insight.

REFERENCES

Teede, H.J., Joham, A.E., Boyle, J.A., et al. (2023) *International evidence-based guideline for the assessment and management of polycystic ovary syndrome 2023*. **Human Reproduction**. https://doi.org/10.1093/humrep/dead156

Teede, H.J., Misso, M.L., Costello, M.F., et al. (2018) Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. **Human Reproduction**, 33(9), 1602–1618. https://doi.org/10.1093/humrep/dey256

The Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group (2004) Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). **Human Reproduction**, 19(1), 41–47. https://doi.org/10.1093/humrep/deh098

Legro, R.S., Arslanian, S.A., Ehrmann, D.A., et al. (2013) Diagnosis and treatment of polycystic ovary syndrome: an Endocrine Society clinical practice guideline. **The Journal of Clinical Endocrinology & Metabolism**, 98(12), 4565–4592. https://doi.org/10.1210/jc.2013-2350

Azziz, R., Carmina, E., Chen, Z., et al. (2016) Polycystic ovary syndrome. **Nature Reviews Disease Primers**, 2, 16057. https://doi.org/10.1038/nrdp.2016.57

Dunaif, A. (1997) Insulin resistance and the polycystic ovary syndrome: mechanism and implications for pathogenesis. **Endocrine Reviews**, 18(6), 774–800. https://doi.org/10.1210/edrv.18.6.0318

Matthews, D.R., Hosker, J.P., Rudenski, A.S., Naylor, B.A., Treacher, D.F. and Turner, R.C. (1985) Homeostasis model assessment: insulin resistance and β-cell function from fasting plasma glucose and insulin concentrations in man. **Diabetologia**, 28(7), 412–419. https://doi.org/10.1007/BF00280883

Ehrmann, D.A. (2005) Polycystic ovary syndrome. **The New England Journal of Medicine**, 352(12), 1223–1236. https://doi.org/10.1056/NEJMra041536

Goodarzi, M.O., Dumesic, D.A., Chazenbalk, G. and Azziz, R. (2011) Polycystic ovary syndrome: etiology, pathogenesis and diagnosis. **Nature Reviews Endocrinology**, 7, 219–231. https://doi.org/10.1038/nrendo.2010.217

Lizneva, D., Suturina, L., Walker, W., Brakta, S., Gavrilova-Jordan, L. and Azziz, R. (2016) Criteria, prevalence, and phenotypes of polycystic ovary syndrome. **Fertility and Sterility**, 106(1), 6–15. https://doi.org/10.1016/j.fertnstert.2016.05.003

Wild, R.A., Carmina, E., Diamanti-Kandarakis, E., et al. (2010) Assessment of cardiovascular risk and prevention of cardiovascular disease in women with the polycystic ovary syndrome: a consensus statement by the AE-PCOS Society. **The Journal of Clinical Endocrinology & Metabolism**, 95(5), 2038–2049. https://doi.org/10.1210/jc.2009-2724

The Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group (2012) Consensus on women's health aspects of polycystic ovary syndrome (PCOS). **Human Reproduction**, 27(1), 14–24. https://doi.org/10.1093/humrep/der396

Gibson-Helm, M., Teede, H., Dunaif, A. and Dokras, A. (2017) Delayed diagnosis and a lack of information associated with dissatisfaction in women with polycystic ovary syndrome. **The Journal of Clinical Endocrinology & Metabolism**, 102(2), 604–612. https://doi.org/10.1210/jc.2016-2963

Bosdou, J.K., Bothou, C., Macut, D., Goulis, D.G. and Livadas, S. (2021) Risk of type 2 diabetes mellitus in polycystic ovary syndrome is associated with obesity: a systematic review and meta-analysis. **Endocrine**, 74, 242–253. https://doi.org/10.1007/s12020-021-02801-2

Osibogun, O., Ogunmoroti, O. and Michos, E.D. (2019) Polycystic ovary syndrome and cardiometabolic risk: opportunities for cardiovascular disease prevention. **Trends in Cardiovascular Medicine**, 30(7), 399–404. https://doi.org/10.1016/j.tcm.2019.08.010

Huffman, A.M., Rezq, S., Basnet, J. and Romero, D.G. (2023) Biomarkers in polycystic ovary syndrome. **Current Opinion in Physiology**, 36, 100717. https://doi.org/10.1016/j.cophys.2023.100717

Wang, F., Dou, P., Wei, W. and Liu, P.J. (2024) Effects of high-protein diets on the cardiometabolic factors and reproductive hormones of women with polycystic ovary syndrome: a systematic review and meta-analysis. **Nutrition & Diabetes**, 14, 6. https://doi.org/10.1038/s41387-024-00263-9

Zeng, H., Zhang, Y., Huang, S., et al. (2023) Metformin combined with spironolactone vs. metformin alone in polycystic ovary syndrome: a meta-analysis. **Frontiers in Endocrinology**, 14, 1223768. https://doi.org/10.3389/fendo.2023.1223768

Ranking the dietary interventions by their effectiveness in the management of polycystic ovary syndrome: a systematic review and network meta-analysis. **Reproductive Health**, 21, 1758. https://doi.org/10.1186/s12978-024-01758-5

Impact of metformin on the clinical and metabolic parameters of women with polycystic ovary syndrome: a systematic review. **Therapeutic Advances in Endocrinology and Metabolism**, 13, 20420188221127142. https://doi.org/10.1177/20420188221127142

Jiang, Y., et al. (2019) Ceramide subclasses identified as novel lipid biomarker elevated in women with polycystic ovary syndrome: a pilot study employing shotgun lipidomics. **Gynecological Endocrinology**, 36(6), 508–513. https://doi.org/10.1080/09513590.2019.1698026

Ollila, M.-M., Hautakoski, A., Arffman, M., et al. (2025) Diabetic complications in women with type 2 diabetes and polycystic ovary syndrome. **European Journal of Endocrinology**, 192(3), 202–209. https://doi.org/10.1093/ejendo/lvaf026

Khan, S.H., Shahid, R., Aslam, S., Manzoor, R., Anwar, R. and Chaudhry, T. (2024) How significant are insulin resistance

parameters in subjects with polycystic ovarian syndrome (PCOS)? A cross-sectional study. **Pakistan Armed Forces Medical Journal**, 74(1), 36–40. https://doi.org/10.51253/pafmj.v74i1.7958

Insulin resistance and cardiometabolic risk markers in women with PCOS (Sindh, Pakistan). **Pakistan Journal of Pathology**, 36(2). https://doi.org/10.55629/pakjpathol.v36i2.919

Haider, S., Ayyaz, M., Ahuja, N., Dhahri, M., Ahmad, A. and Siddiqui, M.F. (2023) Insulin resistance in patients with polycystic ovary syndrome. **Pakistan Journal of Medical & Health Sciences**, 17(10), 157. https://doi.org/10.53350/pjmhs20231710157

Razzaq, S., Manzoor, S., Dilawar, S., et al. (2024) Assessment of the relationship between polycystic ovary syndrome and insulin resistance in adolescent females. **Pakistan Journal of Medical & Health Sciences**, 18(1). https://doi.org/10.53350/pjmhs02024181667

Effect of acarbose combined with diet intervention on glycolipid metabolism in patients with primary polycystic ovarian syndrome complicated with impaired glucose tolerance. **Pakistan Journal of Medical Sciences**, 38(4). https://doi.org/10.12669/pjms.38.4.4598

Clinical and biochemical profile in adolescent and adult polycystic ovary syndrome and impact of insulin resistance on metabolic parameters. **Pakistan Journal of Medical Sciences**, 41(9). https://doi.org/10.12669/pjms.41.9.12228

Mykhalchenko, K., Lizneva, D., Trofimova, T., et al. (2017) Genetics of polycystic ovary syndrome. **Expert Review of Molecular Diagnostics**, 17(8), 723–733. https://doi.org/10.1080/14737159.2017.1340833

Safwan, N., Saadedine, M., Bairey Merz, C.N. and Shufelt, C.L. (2024) Polycystic ovary syndrome and cardiovascular risk: asking the right questions. **European Journal of Preventive Cardiology**, 31(13), 1571–1573. https://doi.org/10.1093/eurjpc/zwae159