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ORIGINAL ARTICLE

Association between Insulin Resistance and Hyperandrogenism among Women with PCOS in Pakistan

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ABSTRACT

Background: Polycystic Ovary Syndrome (PCOS) is a common endocrine disorder in women of reproductive age and is frequently associated with insulin resistance and hyperandrogenism. Insulin resistance plays a pivotal role in aggravating androgen excess and contributes to both reproductive and metabolic complications. Evidence from Pakistani populations regarding this relationship remains limited.

Objective: To assess the association between insulin resistance and hyperandrogenism among women diagnosed with PCOS in Pakistan.

Methods: This cross-sectional analytical study was conducted at Sheikh Zayed Hospital, Lahore, and Arif Memorial Teaching Hospital, Pakistan, from January 2023 to May 2024. A total of 90 women aged 18–40 years diagnosed with PCOS according to the Rotterdam criteria were included. Clinical hyperandrogenism was assessed using the modified Ferriman–Gallwey score, while biochemical evaluation included fasting glucose, insulin, total testosterone, and sex hormone-binding globulin levels. Insulin resistance was determined using the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR). Statistical analysis was performed to evaluate correlations between insulin resistance and hyperandrogenic parameters.

Results: Insulin resistance was observed in 64.4% of participants. Significant positive correlations were found between HOMA-IR and total testosterone, free androgen index, and modified Ferriman–Gallwey score, while a significant inverse correlation was observed with sex hormone-binding globulin levels ($p < 0.001$). These associations remained significant after adjustment for body mass index.

Conclusion: Insulin resistance is highly prevalent among Pakistani women with PCOS and shows a strong independent association with hyperandrogenism. Early metabolic screening and targeted interventions may help reduce disease severity and long-term metabolic complications.

Keywords: Polycystic, Insulin, Hyperandrogenism, Resistance, Metabolism.

INTRODUCTION

Polycystic Ovary Syndrome (PCOS) is one of the most common endocrine disorders affecting women of reproductive age and represents a major cause of menstrual irregularities, infertility, and metabolic dysfunction worldwide[1]. The syndrome is clinically heterogeneous and is characterized by a combination of ovulatory dysfunction, hyperandrogenism, and polycystic ovarian morphology. Beyond its reproductive manifestations, PCOS is increasingly recognized as a systemic metabolic disorder with long-term implications for glucose metabolism, cardiovascular health, and overall quality of life[2].

Insulin resistance is considered a central pathophysiological feature of PCOS and is observed in a substantial proportion of affected women, independent of obesity. Reduced insulin sensitivity leads to compensatory hyperinsulinemia, which plays a pivotal role in amplifying ovarian androgen production and disrupting normal follicular development[3]. Hyperandrogenism, another defining feature of PCOS, manifests clinically as hirsutism, acne, and androgenic alopecia, and biochemically through elevated circulating androgen levels. The interaction between insulin resistance and androgen excess forms a self-perpetuating cycle that worsens both metabolic and reproductive abnormalities in PCOS[4].

In South Asian populations, including Pakistan, the burden of PCOS is compounded by a high prevalence of insulin resistance, central obesity, and sedentary lifestyles. Pakistani women with PCOS often present at a younger age and exhibit more pronounced metabolic derangements compared to Western populations[5]. Cultural, genetic, and environmental factors may further influence disease expression, yet region-specific data exploring the metabolic–hormonal interplay in PCOS remain limited. Understanding this relationship is particularly important in Pakistan, where early metabolic screening is not routinely emphasized in reproductive health settings[6].

Given the strong biological link between insulin resistance and hyperandrogenism and their collective impact on disease severity and long-term health outcomes, evaluating this association in Pakistani women with PCOS is of significant clinical relevance. Clarifying this relationship may aid in early diagnosis, risk stratification, and the development of integrated management strategies targeting both metabolic and endocrine components of PCOS. Therefore, this study focuses on examining the association between insulin resistance and hyperandrogenism among women with PCOS in Pakistan[7,8].

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MATERIALS AND METHODS

Study Design and Setting: This cross-sectional analytical study was conducted at two tertiary care centers in Pakistan: Sheikh Zayed Hospital, Lahore, and Arif Memorial Teaching Hospital, Pakistan. The study was carried out over a period of 17 months, from January 2023 to May 2024, and aimed to evaluate the association between insulin resistance and hyperandrogenism among women diagnosed with Polycystic Ovary Syndrome (PCOS).

Study Population and Sample Size: A total of 90 women of reproductive age diagnosed with PCOS were enrolled in the study. Participants were recruited from the outpatient gynecology and endocrinology clinics of the participating hospitals using a non-probability consecutive sampling technique. The diagnosis of PCOS was established according to the Rotterdam criteria, requiring the presence of at least two of the following features: oligo- or anovulation, clinical and/or biochemical hyperandrogenism, and polycystic ovarian morphology on ultrasonography, after exclusion of other endocrine disorders.

Inclusion and Exclusion Criteria: Women aged 18–40 years with a confirmed diagnosis of PCOS were included in the study. Patients with known diabetes mellitus, thyroid dysfunction, Cushing's syndrome, congenital adrenal hyperplasia, hyperprolactinemia, pregnancy, or those receiving hormonal therapy, insulin-sensitizing drugs, or anti-androgen medications within the preceding three months were excluded to avoid confounding effects on metabolic and hormonal parameters.

Data Collection and Clinical Assessment: Detailed demographic and clinical data were collected using a structured proforma, including age, menstrual history, duration of symptoms, and family history of metabolic disorders. Anthropometric measurements such as height, weight, and body mass index (BMI) were recorded following standard protocols. Clinical hyperandrogenism was assessed using the modified Ferriman–Gallwey (mFG) score, with a score ≥8 considered indicative of hirsutism.

Biochemical Analysis: After an overnight fast of at least 8–10 hours, venous blood samples were obtained from all participants. Fasting plasma glucose and fasting serum insulin levels were measured using standard enzymatic and immunoassay methods, respectively. Insulin resistance was assessed using the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR), calculated as:

HOMA-IR = (Fasting insulin [μIU/mL] × Fasting glucose [mg/dL]) / 405

A HOMA-IR value above the established cut-off was considered indicative of insulin resistance. Serum total testosterone levels were measured to evaluate biochemical hyperandrogenism, and sex hormone-binding globulin (SHBG) levels were assessed where available to calculate the free androgen index (FAI).

Statistical Analysis: Data were entered and analyzed using Statistical Package for the Social Sciences (SPSS) version 25.0. Continuous variables were expressed as mean ± standard deviation or median with interquartile range, depending on data distribution, while categorical variables were presented as frequencies and percentages. The association between insulin resistance (HOMA-IR) and hyperandrogenic parameters (mFG score, total testosterone, and FAI) was evaluated using Pearson or Spearman correlation tests as appropriate. A p-value of <0.05 was considered statistically significant.

Ethical Considerations: The study protocol was reviewed and approved by the Institutional Ethical Review Committees of both participating hospitals. Written informed consent was obtained from all participants prior to enrollment, and confidentiality of patient data was strictly maintained throughout the study.

RESULTS

A total of 90 women diagnosed with PCOS were included in the final analysis. The mean age of the participants was 26.8 ± 4.9 years, with the majority of women falling within the 21–30-year age group. Most participants presented with menstrual irregularities, and a substantial proportion demonstrated clinical features of hyperandrogenism. Based on body mass index (BMI), 48.9% of women were classified as overweight or obese, reflecting the high metabolic burden in this population. The baseline demographic and anthropometric characteristics of the study population are summarized in Table 1.

Table 1. Baseline demographic and anthropometric characteristics of study participants (n = 90)

Variable	Mean ± SD / n (%)
Age (years)	26.8 ± 4.9
BMI (kg/m²)	27.4 ± 5.1
Normal BMI (<25)	46 (51.1%)
Overweight (25–29.9)	27 (30.0%)
Obese (≥30)	17 (18.9%)
Menstrual irregularities	78 (86.7%)
Clinical hirsutism (mFG ≥8)	55 (61.1%)

Biochemical evaluation revealed a high prevalence of insulin resistance among the study participants. The mean fasting glucose level was 96.3 ± 12.7 mg/dL, while mean fasting insulin was 17.9 ± 6.8 μIU/mL. The calculated mean HOMA-IR value was 4.26 ± 1.81, and based on the predefined cut-off, 64.4% (n = 58) of women were classified as insulin resistant. These findings indicate that insulin resistance was a predominant metabolic abnormality even in women who were not overtly obese. Detailed metabolic and hormonal parameters are presented in Table 2.

Table 2. Metabolic and hormonal parameters of women with PCOS

Parameter	Mean ± SD
Fasting glucose (mg/dL)	96.3 ± 12.7
Fasting insulin (μIU/mL)	17.9 ± 6.8
HOMA-IR	4.26 ± 1.81
Total testosterone (ng/dL)	71.5 ± 24.3
SHBG (nmol/L)	29.6 ± 11.2
Free androgen index (FAI)	9.8 ± 4.1

Assessment of hyperandrogenism showed that both clinical and biochemical markers were markedly elevated. Clinical hyperandrogenism, assessed using the modified Ferriman–Gallwey (mFG) score, demonstrated a mean score of 10.7 ± 3.9, with 61.1% of women exceeding the diagnostic threshold for hirsutism. Biochemically, mean serum total testosterone levels were elevated beyond normal reference ranges in a significant proportion of participants, and reduced SHBG levels contributed to increased free androgen index (FAI). These findings highlight the coexistence of clinical and biochemical hyperandrogenism in Pakistani women with PCOS.

To further explore the relationship between insulin resistance and hyperandrogenism, correlation analysis was performed between HOMA-IR and androgenic parameters. A strong positive correlation was observed between HOMA-IR and serum total testosterone ($r = 0.48$, $p < 0.001$), indicating that higher degrees of insulin resistance were associated with increased androgen levels. Similarly, HOMA-IR showed a moderate positive correlation with mFG score ($r = 0.41$, $p < 0.001$), suggesting that worsening insulin resistance was linked with greater clinical severity of hirsutism. An inverse correlation was noted between HOMA-IR and SHBG levels ($r = –0.46$, $p < 0.001$), reflecting the suppressive effect of hyperinsulinemia on hepatic SHBG production. These correlations are detailed in Table 3.

Table 3. Correlation between insulin resistance and hyperandrogenic parameters

Parameter	Correlation with HOMA-IR (r)	p-value
Total testosterone	0.48	<0.001
mFG score	0.41	<0.001
SHBG	–0.46	<0.001
Free androgen index	0.52	<0.001

When participants were stratified into insulin-resistant and non-insulin-resistant groups, women with insulin resistance demonstrated significantly higher mean testosterone levels, higher FAI values, and more severe clinical hirsutism compared to those without insulin resistance ($p < 0.05$ for all comparisons). Notably, this difference remained significant even after adjusting for BMI, indicating that insulin resistance independently contributed to androgen excess rather than acting solely through obesity.

Overall, the results clearly demonstrate a strong and clinically meaningful association between insulin resistance and hyperandrogenism among women with PCOS in Pakistan. The findings support the concept that metabolic dysfunction plays a central role in amplifying androgen excess, thereby worsening both reproductive and dermatological manifestations of PCOS. These results emphasize the importance of routine metabolic screening in women presenting with hyperandrogenic features to enable early intervention and prevent long-term cardiometabolic complications.

DISCUSSION

The present study demonstrates a strong and clinically significant association between insulin resistance and hyperandrogenism among women with Polycystic Ovary Syndrome (PCOS) in Pakistan[8-10]. The findings highlight that insulin resistance is highly prevalent in this population and closely linked with both clinical and biochemical manifestations of androgen excess. This relationship persisted even after considering body mass index, underscoring the fact that insulin resistance in PCOS is not merely a consequence of obesity but an intrinsic component of the syndrome. These results align with the growing understanding of PCOS as a complex endocrino-metabolic disorder rather than a purely reproductive condition[11].

In this cohort, nearly two-thirds of the participants exhibited insulin resistance as assessed by HOMA-IR. This prevalence is comparable to reports from other South Asian and Middle Eastern populations, where insulin resistance has been documented in 60–70% of women with PCOS[12]. The relatively young mean age of the study participants suggests that metabolic abnormalities develop early in the disease course, emphasizing the need for early metabolic screening in clinical practice. The high burden of insulin resistance observed even among women with normal or moderately elevated BMI further supports the hypothesis of a primary defect in insulin signaling in PCOS, potentially influenced by genetic and ethnic susceptibility in Pakistani women[13].

Hyperandrogenism was highly prevalent in the study population, with more than half of the women exhibiting clinical hirsutism and elevated androgen levels[14]. The strong positive correlations between HOMA-IR and total testosterone, free androgen index, and mFG score indicate that worsening insulin resistance is associated with increasing androgen excess and greater clinical severity. These findings are biologically plausible, as hyperinsulinemia enhances ovarian theca cell androgen production and suppresses hepatic synthesis of sex hormone-binding globulin, leading to increased bioavailability of circulating androgens. The inverse relationship between HOMA-IR and SHBG observed in this study further supports this mechanism[15].

Importantly, stratified analysis revealed that women with insulin resistance had significantly higher androgen levels and more severe hirsutism compared to non-insulin-resistant women, independent of BMI[16]. This suggests that insulin resistance acts as an independent driver of hyperandrogenism in PCOS. Similar observations have been reported in international literature, reinforcing the concept of a self-perpetuating cycle in which insulin resistance exacerbates androgen excess, and elevated androgens further impair insulin sensitivity. This vicious cycle contributes to disease progression and increases the risk of long-term complications such as type 2 diabetes mellitus, metabolic syndrome, and cardiovascular disease[17].

The findings of this study have important clinical implications in the Pakistani context, where metabolic screening is often underemphasized in women presenting with reproductive or dermatological symptoms[18]. Early identification of insulin resistance in women with PCOS, particularly those with hyperandrogenic features, may allow timely intervention through lifestyle modification and insulin-sensitizing therapies, potentially improving both metabolic and reproductive outcomes. Despite its strengths, this study has certain limitations, including its cross-sectional design, which precludes causal inference, and the relatively modest sample size. Longitudinal and multicenter studies are needed to further elucidate the temporal relationship between insulin resistance and hyperandrogenism and to explore genetic and environmental modifiers specific to the Pakistani population[19].

CONCLUSION

This study concludes that insulin resistance is highly prevalent among Pakistani women with PCOS and is strongly associated with both clinical and biochemical hyperandrogenism. The results indicate that insulin resistance plays a central and independent role in driving androgen excess, irrespective of obesity status. These findings underscore the importance of integrating metabolic evaluation into the routine assessment of women with PCOS, particularly those presenting with hyperandrogenic features. Early recognition and targeted management of insulin resistance may not only reduce androgen-related symptoms but also lower the long-term risk of metabolic and cardiovascular complications. Future large-scale and longitudinal studies are warranted to refine screening strategies and optimize individualized treatment approaches for women with PCOS in Pakistan.

Declarations

Authors' Contributions: MF[1] conceived and designed the study. MBS[2] contributed to data collection and patient recruitment. LA[3] and MI[4] performed laboratory and biochemical analyses. AN[5] assisted in data entry and statistical analysis. ASI[6] contributed to literature review and manuscript drafting. HZC[7] critically reviewed the manuscript and approved the final version.

Conflict of Interest: The authors declare no conflict of interest.

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Ethical Approval: The study was approved by the Institutional Ethical Review Committees of the participating hospitals.

Informed Consent: Written informed consent was obtained from all participants prior to enrollment.

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REFERENCES

1. Manique ME, Ferreira AM. Polycystic ovary syndrome in adolescence: challenges in diagnosis and management. Rev Bras Ginecol Obstet. 2022;44(4):425-433. doi:10.1055/s-0042-1742292
2. Tay C, Hart R, Hickey M, Moran L, Earnest A, Doherty D, et al. Updated adolescent diagnostic criteria for polycystic ovary syndrome: impact on prevalence and longitudinal body mass index trajectories from birth to adulthood. BMC Med. 2020;18(1):1-11. doi:10.1186/s12916-020-01861-x
3. Yasmin A, Roychoudhury S, Paul Choudhury A, Ahmed A, Dutta S, Mottola F, et al. Polycystic ovary syndrome: an updated overview foregrounding impacts of ethnicities and geographic variations. Life (Basel). 2022;12(12):1974. doi:10.3390/life12121974
4. Barber TM, Joharatnam J, Franks S. Pathogenesis and management of adiposity and insulin resistance in polycystic ovary syndrome. In: Pediatric Obesity: Etiology, Pathogenesis and Treatment. Cham: Springer; 2018. p. 629-642. doi:10.1007/978-3-319-68192-4
5. Kadhim SM, Al-Fartusie FS, Klichkhanov NK. Evaluation of adiponectin and hepcidin with some biochemical parameters in sera of women with polycystic ovary syndrome. Al Mustansiriyah J Sci. 2023;34(1):52-57. doi:10.23851/mjs.v34i1.1299
6. Armanini D, Boscaro M, Bordin L, Sabbadin C. Controversies in the pathogenesis, diagnosis and treatment of PCOS: focus on insulin resistance, inflammation, and hyperandrogenism. Int J Mol Sci. 2022;23(8):4110. doi:10.3390/ijms23084110
7. Hernández-Jiménez JL, Barrera D, Espinoza-Simón E, González J, Ortíz-Hernández R, Escobar L, et al. Polycystic ovarian syndrome: signs and feedback effects of hyperandrogenism and insulin resistance. Gynecol Endocrinol. 2022;38(1):2-9. doi:10.1080/09513590.2021.2003326
8. Sanchez-Garrido MA, Tena-Sempere M. Metabolic dysfunction in polycystic ovary syndrome: pathogenic role of androgen excess and potential therapeutic strategies. Mol Metab. 2020;35:100937. doi:10.1016/j.molmet.2020.01.001
9. Pal L, Pathy S. Polycystic ovarian syndrome. In: Evidence-Based Obstetrics and Gynecology. Hoboken: Wiley-Blackwell; 2019. p. 117-129. doi:10.1002/9781119072980.ch12
10. Arif A, Waheed P, Anees R, Rashid A, Khan SA. A comparative study of insulin resistance in patients of polycystic ovary syndrome. Pak Armed Forces Med J. 2021;71(5):1746-1750. doi:10.51253/pafmj.v71i5.2633
11. Hussein SR, Sadiq AM, Johar SA, Nasrawi AJ. Insulin level, lipid profile, and HOMA index in lean and obese patients with polycystic ovary syndrome. J Med Life. 2023;16(8):1258-1265. doi:10.25122/jml-2023-0040
12. HOMA-IR insulin resistance calculator. The Blood Code. Available from: https://thebloodcode.com/homa-ir-calculator/. Accessed January 29, 2019.

13. Khan MJ, Ullah A, Basit S. Genetic basis of polycystic ovary syndrome (PCOS): current perspectives. Appl Clin Genet. 2019;12:249-260. doi:10.2147/TACG.S200341
14. Chen W, Pang Y. Metabolic syndrome and PCOS: pathogenesis and the role of metabolites. Metabolites. 2021;11(12):869. doi:10.3390/metabo11120869
15. Barber TM, Hanson P, Weickert MO, Franks S. Obesity and polycystic ovary syndrome: implications for pathogenesis and novel management strategies. Clin Med Insights Reprod Health. 2019;13:1179558119874042. doi:10.1177/1179558119874042
16. Shirazi FK, Khodamoradi Z, Jeddi M. Insulin resistance and high-molecular-weight adiponectin in obese and non-obese patients with polycystic ovary syndrome. Pak Armed Forces Med J. 2024;74(5):1387-1392.
17. Baldani DP, Skrgatic L, Kasum M, Zlopasa G, Kralik Oguic S, Herman M. Altered leptin, adiponectin, resistin and ghrelin secretion may represent an intrinsic polycystic ovary syndrome abnormality. Gynecol Endocrinol. 2019;35(5):401-405. doi:10.1080/09513590.2018.1534096
18. Amisi CA. Markers of insulin resistance in polycystic ovary syndrome women: an update. World J Diabetes. 2022;13(3):129-142. doi:10.4239/wjd.v13.i3.129
19. Borzan V, Lerchbaum E, Missbrenner C, Heijboer AC, Goschnik M, Trummer C, et al. Risk of insulin resistance and metabolic syndrome in women with hyperandrogenemia: a comparison between PCOS phenotypes and beyond. J Clin Med. 2021;10(4):829. doi:10.3390/jcm10040829

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