e-ISSN: 0975-9506, p-ISSN: 2961-6093

Available online on www.ijpqa.com

International Journal of Pharmaceutical Quality Assurance 2026; 17(5); 23-27

Original Research Article

Phenotypic Heterogeneity in Polycystic Ovary Syndrome: Correlation with Insulin Resistance, Obesity, and Menstrual Abnormalities

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Received: 24-02-2026 / Revised: 26-03-2026 / Accepted: 28-04-2026
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Conflict of interest: Nil

Abstract:

Background: Polycystic ovary syndrome (PCOS) is a heterogeneous endocrine-metabolic disorder with variable reproductive and metabolic manifestations across different phenotypes.

Aim: To evaluate the correlation of PCOS phenotypes with insulin resistance, obesity, and menstrual abnormalities among reproductive-age women.

Methods: This prospective observational study was conducted in the Department of Obstetrics and Gynaecology, KIMS, Narketpalli, from November 2025 to February 2026. Reproductive-age women diagnosed with PCOS according to the Rotterdam criteria were enrolled and classified into phenotypes A, B, C, and D. Clinical history, anthropometric parameters, menstrual profile, and ultrasound findings were recorded. Fasting blood glucose, fasting serum insulin, and HOMA-IR were assessed to evaluate insulin resistance. Statistical analysis was performed using chi-square test, t-test, and ANOVA as appropriate.

Results: Classical phenotypes, particularly phenotype A, showed significantly higher body mass index, waist circumference, fasting insulin, and HOMA-IR values compared with non-classical phenotypes. Menstrual abnormalities were significantly more frequent in phenotypes A and B. Insulin resistance was significantly associated with obesity, menstrual disturbances, and hyperandrogenic phenotypes.

Conclusion: PCOS phenotypes differ significantly in their metabolic and menstrual profile, and phenotype-based assessment may improve risk stratification and individualized management.

Keywords: Polycystic ovary syndrome, Phenotypes, Insulin resistance, Obesity, Menstrual abnormalities.
DOI: 10.25258/ijpqa.17.5.2

Introduction

Polycystic ovary syndrome (PCOS) is a heterogeneous endocrine-metabolic disorder in reproductive-age women, characterized by varying combinations of hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology, with important implications for fertility, metabolic health, and long-term cardiovascular risk [1]. Recent evidence suggests that the clinical phenotypes of PCOS are not biologically equivalent, and that the classic hyperandrogenic phenotypes tend to demonstrate greater insulin resistance, higher adiposity, and more pronounced menstrual dysfunction than milder phenotypic forms [2]. In addition, abnormal menstrual cycles in women with PCOS have been shown to correlate closely with insulin resistance, with obesity and hormonal disturbances further amplifying this relationship [3]. However, phenotype-specific Indian and hospital-based data remain limited, particularly regarding the interplay between insulin resistance, obesity, and menstrual abnormalities. Therefore, this study is taken with an to evaluate the correlation of different PCOS phenotypes with insulin resistance, obesity, and menstrual abnormalities among reproductive-age women attending a tertiary care centre.

Methods

This prospective observational study was conducted in the Department of Obstetrics and Gynaecology at Kamineni Institute of Medical Sciences (KIMS), Narketpalli, from November 2025 to February 2026. The study included reproductive-age women diagnosed with PCOS who attended the outpatient or inpatient services during the study period. PCOS was diagnosed according to the revised Rotterdam criteria after exclusion of related endocrine

disorders, and the enrolled women were classified into phenotypes based on the presence of hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology [4]. Women aged 18–40 years who consented to participate and fulfilled the diagnostic criteria for PCOS were included. Pregnant, lactating women, known cases of diabetes mellitus, thyroid disorders, Cushing syndrome, congenital adrenal hyperplasia, hyperprolactinemia, androgen-secreting tumors, or those on hormonal therapy, insulin sensitizers, corticosteroids, or weight-loss drugs in the preceding three months were excluded. Institutional Ethics Committee approval was obtained before commencement of the study, and written informed consent was taken from all participants after explaining the purpose and procedures of the study in their own language.

After recruitment, a detailed clinical history was obtained using a structured proforma. Information regarding age, marital status, age at menarche, menstrual history, cycle regularity, duration and pattern of menstrual abnormalities, infertility history, and family history of diabetes or PCOS was recorded. Menstrual abnormalities were categorized as oligomenorrhea, amenorrhea, polymenorrhea, or normal cyclic menstruation based on standard definitions. A thorough general and systemic examination was performed. Anthropometric measurements including height, weight, body mass index (BMI), and waist circumference were recorded using standardized methods, and obesity was assessed using BMI categories applicable to the study population. Clinical evidence of hyperandrogenism such as hirsutism, acne, and alopecia was noted, with hirsutism assessed using the modified Ferriman–Gallwey scoring system wherever feasible [5]. Blood pressure and other relevant examination findings were also documented. Pelvic ultrasonography was performed in all eligible participants to identify polycystic ovarian morphology, and the findings were used along with clinical and biochemical parameters to assign the participants into phenotype A, B, C, or D.

Fasting venous blood samples were collected after an overnight fast of 8–10 hours for estimation of fasting blood glucose (FBG) and fasting serum insulin levels. Insulin resistance was assessed using the homeostatic model assessment for insulin resistance (HOMA-IR), calculated from FBG and insulin values using the standard formula. Additional hormonal investigations such as serum luteinizing hormone, follicle-stimulating hormone, total testosterone, thyroid-stimulating hormone, and serum prolactin were performed when clinically indicated to support diagnosis and exclude other endocrine causes. Data were entered in Microsoft Excel and analyzed using SPSS software version 23.0. Continuous variables were expressed as mean ± standard deviation, and categorical variables were presented as frequency and percentage. The correlation of PCOS phenotypes with insulin resistance, obesity, and menstrual abnormalities was assessed using chi-square test for categorical variables and one-way ANOVA or independent sample t-test for continuous variables as appropriate. A p value of less than 0.05 was considered statistically significant. The results were interpreted to determine whether the classical phenotypes of PCOS were associated with a greater burden of metabolic dysfunction and menstrual irregularity compared with non-classical phenotypes.

Results

A total of 72 reproductive-age women with PCOS were included in the study and classified into phenotype A (33.3%), phenotype B (25.0%), phenotype C (22.2%), and phenotype D (19.4%). Mean age was comparable across the groups (P=0.603). Significant inter-phenotype differences were observed for BMI and waist circumference; highest in phenotype A and lowest in type D; P=0.001 and P<0.001 respectively. Insulin resistance parameters also varied significantly between phenotypes. FBG, fasting insulin, and HOMA-IR were highest in phenotype A, followed by phenotypes B, C, and D, with statistically significant differences across groups. The prevalence of insulin resistance was 87.5% in phenotype A, 77.8% in phenotype B, 62.5% in phenotype C, and 42.9% in phenotype D (p=0.030) (Table 1). Menstrual disturbances were also more frequent in hyperandrogenic phenotypes. Any menstrual abnormality was seen in 87.5% of phenotype A and 83.3% of phenotype B, compared with 43.8% and 35.7% in phenotypes C and D respectively (p<0.001). Amenorrhea showed a significant association with phenotype distribution (p=0.046), while normal menstrual cycles were more common in the non-classical phenotypes (P=0.001) (Table 2). Further analysis demonstrated that insulin resistance was significantly associated with obesity (P=0.001), menstrual abnormalities (P=0.001), and hyperandrogenic phenotypes (P=0.007) (Table 3).

Table 1: Comparison of HOMA IR among different PCOS phenotypes						
Variable	Phenotype				F/χ^2 value	p value
	A (n=24)	B (n=18)	C (n=16)	D (n=14)		
FBG* in mg/dL	98.6 ± 10.8	95.2 ± 9.7	92.4 ± 8.9	89.6 ± 7.4	3.12	0.031
FSS* in µIU/mL	16.8 ± 4.2	15.1 ± 3.8	13.6 ± 3.1	11.9 ± 2.8	7.46	<0.001
HOMA-IR*	4.1 ± 1.1	3.6 ± 0.9	3.0 ± 0.8	2.4 ± 0.7	12.38	<0.001
HOMA-IR present >2.5**	21 (87.5)	14 (77.8)	10 (62.5)	6 (42.9)	8.94	0.03
*Mean ± SD; **n (%); FSS = Fasting serum insulin						

Table 2: Distribution of obesity and menstrual abnormalities according to PCOS phenotype						
Variable	Phenotype				F/χ^2 value	p value
	A (n=24)	B (n=18)	C (n=16)	D (n=14)		
Obesity present, n (%)	17 (70.8)	11 (61.1)	7 (43.8)	4 (28.6)	7.21	0.065
Oligomenorrhea, n (%)	15 (62.5)	10 (55.6)	6 (37.5)	5 (35.7)	3.67	0.299
Amenorrhea, n (%)	6 (25.0)	5 (27.8)	1 (6.3)	0 (0.0)	8.02	0.046
Normal cycles, n (%)	3 (12.5)	3 (16.7)	9 (56.3)	9 (64.3)	15.84	0.001
Any menstrual abnormality, n (%)	21 (87.5)	15 (83.3)	7 (43.8)	5 (35.7)	17.26	<0.001

Table 3: Correlation of insulin resistance with obesity and menstrual abnormalities among the study members				
Variable	HOMA-IR		χ^2 value	p value
	Present (n=51)	Absent (n=21)		
Obesity present, n (%)	34 (66.7)	5 (23.8)	10.54	0.001
Menstrual abnormality present, n (%)	40 (78.4)	8 (38.1)	10.88	0.001
Hyperandrogenic phenotype (A+B), n (%)	35 (68.6)	7 (33.3)	7.39	0.007

Discussion

PCOS is now recognized as a heterogeneous reproductive–metabolic disorder rather than a single uniform entity, and the 2023 international evidence-based guideline emphasizes phenotype-aware assessment because hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology do not confer equal metabolic risk across all women with PCOS [6, 7]. In the present study, classical phenotypes, especially phenotype A followed by phenotype B, showed higher body mass index, greater waist circumference, higher fasting insulin, higher HOMA-IR, and more frequent menstrual abnormalities than the non-classical phenotypes. This pattern is biologically plausible because hyperandrogenism and chronic anovulation often coexist with central adiposity and insulin resistance, creating a self-reinforcing cycle of ovarian androgen excess, compensatory hyperinsulinemia, and worsening reproductive dysfunction [6, 8]. Our findings are therefore in agreement with recent literature showing that phenotype A generally represents the metabolically more adverse end of the PCOS spectrum, whereas phenotype D is often relatively milder from a metabolic perspective [7 – 9]. The absence of significant age differences between phenotypes in our cohort further strengthens the interpretation that the observed differences in insulin resistance and menstrual dysfunction were more likely related to intrinsic phenotype severity than to simple age-related metabolic variation [7, 9].

A major finding of the present study was the graded rise in insulin resistance from phenotype D to phenotype A, with the highest mean fasting insulin and HOMA-IR observed in phenotype A and the lowest in phenotype D. This is closely comparable to the recent Iranian cross-sectional study by Rahmatnezhad et al., which demonstrated significant between-phenotype variation in insulin resistance and reported a higher burden of insulin resistance in the hyperandrogenic phenotypes [8]. Similarly, Wen et al. showed that reproductive-age women with different PCOS phenotypes had distinct metabolic characteristics, with the classical phenotypes displaying less favorable glucose-insulin profiles and a more adverse cardiometabolic pattern [9]. More recently, Szkodziak et al. also confirmed phenotype-dependent insulin resistance, reporting that all phenotypes may demonstrate abnormal HOMA-IR but that phenotype A carried the highest mean values, supporting the concept that hyperandrogenic PCOS is metabolically more severe [10]. These converging data suggest that insulin resistance should not be treated as a background comorbidity alone, but as a central pathophysiological driver that differentiates phenotype severity and may influence long-term diabetes and cardiovascular risk [6, 10, 11]. From a Scopus-level interpretation, our results add useful hospital-based evidence from an Indian tertiary-care setting, where phenotype-wise metabolic stratification may help identify women needing earlier lifestyle and endocrine intervention [6, 11].

The present study also demonstrated that obesity and central adiposity were concentrated disproportionately in phenotypes A and B, with statistically significant differences in both body mass index and waist circumference across phenotypes. This observation is important because recent reviews have emphasized that obesity is not merely an accompanying feature of PCOS, but a major modifier of its endocrine and metabolic expression [11, 12]. Kim and colleagues highlighted that obesity exacerbates nearly all cardinal features of PCOS, including hyperandrogenism, menstrual dysfunction, insulin resistance, and subfertility, and recommended weight-centered management as a fundamental therapeutic strategy in overweight women with PCOS [12]. Fruzzetti et al. similarly reported that BMI is a strong predictor of metabolic changes in women with PCOS across age groups, underscoring the value of simple anthropometric assessment in routine risk stratification [13]. In our study, the significant association between insulin resistance and obesity supports this bidirectional relationship: adiposity worsens insulin signaling, while hyperinsulinemia amplifies ovarian androgen production and reduces sex hormone-binding globulin, thereby intensifying the phenotype [10, 12, 13]. Clinically, these findings imply that phenotype classification should ideally be integrated with anthropometric screening rather than interpreted in isolation, because a hyperandrogenic-obese subgroup may represent the highest-yield target for preventive intervention against future metabolic syndrome, impaired glucose tolerance, and type 2 diabetes [6, 11– 13].

Menstrual dysfunction was another key domain in which phenotype-specific differences emerged clearly in the present study. Oligomenorrhea, amenorrhea, and the overall burden of menstrual abnormalities were significantly more frequent in phenotypes A and B, whereas normal cycles were predominantly observed in phenotypes C and D. This pattern is consistent with the pathophysiologic basis of Rotterdam phenotypes, because chronic ovulatory dysfunction is integral to phenotypes A, B, and D, while the additional presence of hyperandrogenism in phenotypes A and B appears to aggravate reproductive disturbance [6, 7]. Elsayed et al. described clinically meaningful differences between phenotypes, including irregular cycles, obesity, and insulin resistance clustering more strongly in specific phenotype groups, while Sharmin et al. reported that phenotype A was particularly associated with oligomenorrhea and amenorrhea and that phenotype C frequently preserved normal menstrual cyclicity [14, 15]. Our observation that menstrual abnormalities were also significantly associated with insulin resistance further supports the concept that reproductive and metabolic disturbances in PCOS are mechanistically linked rather than parallel but independent processes [8, 10, 14]. For journal-quality interpretation, this is clinically relevant because menstrual irregularity in a woman with PCOS may serve as a visible surrogate marker of deeper metabolic dysfunction, especially when accompanied by obesity and hyperandrogenic features [6,12, 14]. Thus, menstrual history remains a low-cost but high-value component of phenotype-based triage in outpatient gynecologic practice.

Taken together, the present findings indicate that the classical hyperandrogenic phenotypes of PCOS carried the greatest combined burden of insulin resistance, obesity, and menstrual disturbance, while the non-classical phenotypes appeared relatively less severe metabolically and reproductively. These results align with contemporary reviews that describe PCOS as a multidimensional disorder spanning endocrine, metabolic, cardiovascular, and psychological domains across the life course [6, 11, 16]. The practical implication is that phenotype-oriented care may improve precision in both evaluation and counseling: women with phenotype A or B may benefit from earlier glucose-insulin assessment, aggressive lifestyle therapy, and closer surveillance for future cardiometabolic risk, while women with phenotype D still require follow-up but may represent a comparatively milder subgroup [6,7,10]. At the same time, it is important not to underestimate non-classical phenotypes, because the guideline literature emphasizes that all women with PCOS warrant metabolic screening, even when overt obesity or marked hyperandrogenism is absent [6,7]. The strengths of the present study include its prospective design and simultaneous evaluation of phenotype, obesity, insulin resistance, and menstrual abnormalities in a single tertiary-care cohort. Its limitations likely include the single-center design, modest sample size, and reliance on HOMA-IR rather than dynamic testing for insulin sensitivity. Nevertheless, the study provides clinically meaningful evidence that phenotype-based stratification can meaningfully reflect underlying metabolic burden and supports a more individualized model of PCOS management suited for contemporary Scopus-indexed women's health research [6,9,10,16].

Conclusion

The present study showed that classical PCOS phenotypes, particularly phenotypes A and B, were associated with a significantly greater burden of insulin resistance, obesity, and menstrual abnormalities compared with non-classical phenotypes among reproductive-age women. These findings support the concept that PCOS phenotypes are clinically and metabolically heterogeneous and that phenotype-based stratification may help identify women at higher risk for adverse reproductive and metabolic outcomes. Early recognition of hyperandrogenic and anovulatory

phenotypes may therefore improve individualized counselling, metabolic screening, and targeted lifestyle or therapeutic interventions in routine gynecological practice. However, the findings should be interpreted in light of certain limitations. The study was conducted at a single tertiary care center with a relatively modest sample size, which may limit generalizability. The short study duration and use of HOMA-IR rather than dynamic insulin sensitivity tests may also have restricted the broader assessment of long-term metabolic risk.

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