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Study On The Clinical Assessments And Relationship Of Insulin Resistance And Non-Insulin Resistance Patients With Polycystic Ovary Syndrome (PCOS) Phenotypes And Characteristics: A Cross-Sectional Study

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Abstract:
Polycystic ovary syndrome (PCOS) is a heterogeneous endocrine disorder frequently associated with insulin resistance (IR) and adverse metabolic outcomes, including an increased risk of gestational diabetes mellitus (GDM). This cross-sectional study aimed to determine the prevalence of insulin resistance across different PCOS phenotypes and to evaluate its association with demographic, clinical, and hormonal parameters. A total of 250 women aged 18–47 years diagnosed with PCOS based on the Rotterdam criteria were recruited from gynecology clinics in Erode, Tamil Nadu, South India. Participants were classified into four PCOS phenotypes (A–D), and insulin resistance was assessed using the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR), with a cut-off value of >2.5. Overall, insulin resistance was observed in 84% of the study population. Phenotype A was the most prevalent, followed by phenotypes B, C, and D. Significant differences in insulin resistance were observed across PCOS phenotypes, with the highest prevalence and HOMA-IR values noted in phenotype B, indicating greater metabolic impairment. Classical PCOS phenotypes (A and B) exhibited a significantly higher association with insulin resistance compared to non-classical phenotypes (C and D). Obesity, elevated fasting glucose, altered LH levels, and variations in AMH and estradiol were more pronounced in insulin-resistant individuals. These findings highlight a high burden of insulin resistance among women with PCOS, particularly in classical phenotypes, underscoring the importance of early phenotypic classification and metabolic screening to reduce future risks of metabolic disorders and pregnancy-related complications such as GDM.

Key Word *- PCOS, Insulin Resistance, Non - Insulin Resistance, Phenotypes.*

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I. Introduction

Polycystic ovary syndrome (PCOS) is an endocrine complex heterogeneous multisystem disorder it affecting 10% to 13% of reproductive aged women and 3% to 11% of adolescent girls (Bozdag et al, 2016, Naz et al, 2019). The global prevalence report can range from 6 to 21% depending upon the diagnostic criteria (Dapas et al, 2020). Hyperandrogenism, irregular ovulation, polycystic ovary morphology and metabolic abnormalities like obesity and insulin resistance (IR) are the common features of PCOS (Zhao et al, 2023). Additionally, PCOS affects ovarian functioning which is influenced by genetics, epigenetic modifications, oxidative stress, chronic inflammation, mitochondrial dysfunction, metabolic abnormalities and environmental factors (Armanini et al, 2022, Malamouli et al, 2022). Women with PCOS and IR have a higher risk of experiencing negative pregnancy outcomes (Chen et al, 2022).

PCOS patients are more likely to develop gestational diabetes mellitus (GDM) (Brennan et al, 2017) mainly related to insulin resistance mechanism (IR) (Yu et al, 2016). Early GDM identification in PCOS-afflicted women is essential for preventing both immediate and long-term effects, including foetal programming and long-term health issues for the child (Franzago et al, 2019). The prevalence of GDM ranges from 9% to 25%, while PCOS varies from 5% to 15%, depending on the study populations and the diagnostic criteria used (Norman et al, 2007).

Both GDM and PCOS can signal an increased risk for conditions related to insulin resistance, such as type2 diabetes (T2D) and both disorders are also associated with cardiovascular risk factors like metabolic syndrome, hypertension and dyslipidaemia (Goueslard et al, 2016). Pregnant women who have GDM are at significant risk for complications such preeclampsia, polyhydramnios, shoulder dystocia, foetal macrosomia,

and neonatal hypoglycemia, as well as in severe cases, perinatal death (Nakshine & Jogdand, 2023). GDM is one of the leading causes of morbidity and mortality for both mothers and infants globally (Lee et al, 2018). The development of GDM is significantly influenced by obesity, which may also contribute to the pathophysiology of the condition.

Menstrual abnormalities are more severe in obese women with PCOS than in non-obese females (Hoeger & Oberfield, 2012). IR is a defining characteristic of PCOS, occurring in 50-70% of women with the condition (Diamanti - Kandarakis et al, 2003). IR is an impaired metabolic response which occurs when cells cease to respond to ordinary levels of insulin (Ovalle & Azziz, 2002). Additionally the increased presence of hirsutism is higher in obese women compare to non-obese women (Kiddy et al, 1990). The presence of acanthosis nigricans skin condition is an indicator of PCOS (Conway et al, 1990).

According to the Rotterdam criteria, PCOS is classified into four phenotypes: (A) oligomenorrhea, polycystic ovaries (PCO), and hyperandrogenism; (B) oligomenorrhea and hyperandrogenism; (C) hyperandrogenism and PCO; and (D) oligomenorrhea and PCO. The first two groups, (A) and (B), are known as classical phenotypes, while the latter two groups, (C) and (D), are known as non-classical phenotypes. Studies have shown that phenotype A is the most common form of PCOS, accounting for 60.2% of cases. Elevated levels of testosterone, total cholesterol, and LDL cholesterol in phenotype A contribute to a higher risk of cardiovascular diseases, type 2 diabetes, and metabolic syndrome (Gluszak et al, 2012).

PCOS had the one of the factor hormonal unbalancing, Women with PCOS often experience insulin resistance, increased luteinizing follicle-stimulating (LSH) hormone ratios, abdominal obesity and infertility (Han et al, 2015). Given the association of IR with various disorders, every woman with polycystic ovary syndrome should undergo evaluation for IR (Hafsa et al, 2017). Moreover, insulin-induced androgen secretion, androgens themselves contribute to the progress of hyperinsulinemia in women with PCOS (Tosi et al, 2020). Number of hormonal factors contributing to PCOS of which the hypothalamopituitary compartment and the ovarian compartment are observed to play a major role (Nayanika et al, 2024).

Therefore, the aims to investigate the prevalence of insulin resistance in different phenotypes of PCOS and study its relationship with demographic, clinical and various hormonal activity in a PCOS patients.

II. Materials And Methods

The projected study group was comprised in 250 PCOS patients and the experimental subjects aged between 18 to 47 years. The experimental subjects were categories by the 4 groups (A, B, C and D) based on Rotterdam criteria. The participants were recruited from gynecology clinics in Sudha infertility clinical center in Erode. Until the necessary sample size was reached, all eligible women were enrolled using the convenient sampling procedure. The samples were collected from in and around the Erode district, Tamil Nadu, South India. The work was carried out in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. A written informed consent form was obtained from all the participating subjects. Demographic data were collected through the health questionnaire, Information regarding the Age, Weight, BMI, Health status, Economic status, Marital status, Education, Job, Physical activity, PCOS Phenotype, Ovarian cysts and Insulin Resistance were recorded. Individuals who reported a history of chronic or acute diseases were excluded from the study. Gynecologist's confirmed diagnosis of PCOS based on clinical, laboratory and image findings, but not be pregnant at the time of enrollment, not be receiving infertility treatment or hormonal medication, and not have taken any medications other than over-the-counter (OTC) painkillers within the previous three months in order to be eligible for the study. The study also required that individuals have no serious underlying conditions that could affect menstrual cycles, such as thalassemia or cancer, and that the time between menarche and study enrollment be longer than four years. Additionally, cushing's syndrome, untreated thyroid diseases, and other recognized endocrinopathies were taken into consideration as exclusion criteria.

As part of the evaluation procedure after enrolling in the study, participants had pertinent clinical examinations, paraclinical testing and ultrasounds performed. Clinical signs of hyperandrogenism, including hirsutism, greasy skin, and acne, were noted and evaluated. Prior to venous blood samples were taken and the blood samples were brought to the laboratory within 24 hours for the analysis of clinical studies of following parameters, participants fasted for 10 to 12 hours: Follicle-stimulating hormone (FSH), luteinizing hormone (LH), thyroid stimulating hormone (TSH), Prolactin and estradiol. Insulin levels were measured by laboratory commercial kit according to the proper instructions.

Study variables

Polycystic ovary syndrome (PCOS)

According to the Rotterdam criteria, PCOS was identified by the presence of two of these findings: polycystic ovaries (PCO), clinical or biochemical hyperandrogenism, and oligo or anovulation.

Insulin resistance (IR)

The homeostatic-insulin resistance (HOMA-IR) formula, which is computed as follows: fasting insulin (mg/dL) × fasting blood glucose / 405 (μU/mL) (Simmons & Sweeting 2023), was used to complete the assessment. Insulin resistance was suggested by a HOMA-IR > 2.5.

Body mass index (BMI)

The body mass index (BMI) formula, which divides weight by height squared, was used to calculate it

Polycystic ovaries (PCO)

It was defined as an ovarian volume greater than 10 cm^3 on ultrasonography and/or the presence of 10 or more immature follicles in each ovary.

Menstrual disorders/ ovulatory dysfunction (OD)

Based on the participants' medical history, the following menstrual disorders were included: amenorrhea, oligomenorrhea, hypomenorrhea, hypermenorrhea, and irregular menstrual intervals. In particular, oligomenorrhea was identified when menstrual cycles took place less than nine times a year or more than 35 days apart.

PCOS phenotypes

In the study, PCOS phenotypes were classified among the participants through an assessment of their medical history, clinical examination, and paraclinical tests, utilizing the criteria of Hyperandrogenism (H), Ovulatory Dysfunction (OD), and Polycystic Ovaries (PCO) as follows:
Phenotype A: OD + PCO + H; Phenotype B: OD + H; Phenotype C: H + PCO; Phenotype D: OD + PCO.

Statistical Analysis

Statistical analyses were done in SPSS 16.0 for windows. All the data were subjected for Analysis of Variance (ANOVA) followed by DMR multiple comparison and Bonferroni's correction at the significance level of $p<0.05$ using SPSS-16 version.

III. Results

This research included reproductive aged women diagnosed with PCOS in Erode, a city in Tamil Nadu. The primary goal was to determine the frequency of insulin resistance across various phenotypes of polycystic ovarian syndrome and to study its relationship with demographic, clinical, and paraclinical parameters among PCOS patients. The study recruited 250 PCOS samples. The demographic details are collected from the standard questionnaire.

Table 1 shows the demographic and clinical characteristics of PCOS patients.

Characteristic (Qualitative)	Grouping	Frequency (Percent)
Marital status	Single	158 (63.20%)
	Married	72 (28.80%)
	Widowed/divorced	20 (8.00%)
Job	Employed	67 (26.80%)
	Housewife	107 (42.80%)
	Students	76 (30.40%)
Education	Illiterate	140 (56.00%)
	Unilliterate	110 (44.00%)
Economic status	poor (expenditure more than income)	90 (36.00%)
	Good (expenditure less than and equal to income)	160 (64.00%)
Physical activity	Yes (>=90minutes per week)	175 (70.00%)
	No (< 90minutes per week)	75 (30.00%)
PCOS Phenotype	A	100 (40.00%)
	B	72 (28.80%)
	C	48 (19.20%)
	D	30 (12.00%)
Insulin Resistance (IR)	Yes (HOMA>=2.5)	190 (76.00%)
	No (HOMA<2.5)	60 (24.00%)
BMI	Normal (<25)	62 (24.80%)
	Overweight/obese (>=25)	178 (71.20%)
Ovarian cysts	N<2	33 (13.20%)
	N>=2	217 (86.80%)

According to the data represented by the table 1 shows the following demographic features of PCOS patients. Among 250 women with PCOS, 63.2 percent were married, 42.80% were housewives, 56.00 percent

were illiterate, 64.00 percent had a respectable income, and 66.40% did not exercise regularly. These women were more likely to acquire PCOS. According to this study data, the PCOS patients are classified into 4 major groups based on phenotypic characteristics like A,B,C and D. Phenotype A was the most frequent PCOS characteristic among the classes, while Phenotype D was the least common. The order of prevalence was as follows: A (40.00%) > B (28.80%) > C (19.20%) > D (12%).Out of the 250 PCOS samples studied, 186 subjects (74.40%) had insulin resistance and 64 subjects (25.60%) had non-insulin resistance based on a HOMA-IR cut-off value of 2.5. This study found that 71.2% of subjects had a higher BMI, indicating obesity, whereas 86.8% had a higher endometrial cyst.

Table 2 shows the Relations between Insulin resistant and non-Insulin resistant with demographic and paraclinical characteristics of PCOS patients.

Parameter (Qualitative)	Grouping	Frequency (Percent) Insulin resistant (n =186)	Frequency (Percent) Non- Insulin resistant (n = 64)
Education	Illiterate	105 (56.45%)	35 (54.68%)
	unilliterate	81(43.54%)	29 (45.31%)
Number of ovarian cysts group	N<2	30 (16.12%)	3(4.68%)
	N>=2	156 (83.87%)	61(95.31%)
PCOS phenotype	A	72(38.70%)	28(43.75%)
	B	56(30.10%)	16(25.00%)
	C	35(18.81%)	13(20.31%)
	D	23(12.36%)	7(10.93%)
Phenotype group	Classic (A&B)	138(74.19%)	44(68.75%)
	Non classic (C&D)	58(31.18%)	20(31.25%)
Exercise	No (<90 minutes per week)	55 (29.56%)	20(31.25%)
	Yes (> = 90 minutes per week)	150(80.64%)	25(39.06%)
Economic status	Week (expenditure more than income)	80 (43.01%)	10(15.62%)
	Good (expenditure less than income)	140 (75.26%)	20(31.25%)
Job	Housewife	60 (32.25%)	7(10.90%)
	Employed	95 (51.07%)	12(18.75%)
	University student	65 (34.94%)	11(17.18%)

Table 2 shows the relations between Insulin resistant and Non-Insulin resistant with demographic and paraclinical characteristics of PCOS patients. Out of the 250 women subjects investigated, 186 patients (74.40%) exhibited insulin resistance, predominantly housewives and illiterates, and 64 patients (25.60%) were non-insulin resistance subjects, based on a HOMA-IR cut-off value of 2.5. The study found that distinct PCOS phenotypes had varying rates of insulin resistance (IR), with 38.70% for phenotypic A, 30.10% for phenotype B, 18.81% for phenotype C, and 12.36% for phenotype D. As a result, we discovered that the HOMA index differed considerably among four phenotypic groups, with phenotype A patients having the highest HOMA level. The study's findings, indicate that there was a statistically significant correlation were found between insulin resistance and the grouping of phenotypes (classical: phenotypes A and B and non-classical: phenotypes C and D). According to the Rotterdam criteria, 74.19% of the cases fell into the classical phenotypes (A&B), whereas 31.18% went into the non-classical category. The study's findings revealed that the classical PCOS phenotype was more prevalent than the non-classical phenotype.

Table 3 shows the association between PCOS phenotypes and the demographic and clinical parameters.

Characteristic (Quantitative)	Total (250)	PCOS phenotype			
		A (100)	B (72)	C (48)	D (30)
Age (years)	27.91±4.10	24.28±1.93	27.86±0.97	30.77±0.92	35.90±1.86
Weight	61.57±13.43	63.12±12.14[#]	61.64±12.32	59.46±17.59	59.31±11.25
BMI	25.33±5.10	26.05±4.59	25.34±4.59	24.53±5.59	24.14±4.75
AMH	5.46±3.53	5.83±2.85	5.83±4.12	5.67±2.75	3.14±2.89[c]
TSH	3.03±2.30	3.03±2.34	3.17±1.86	2.77±1.79[a]	3.07±1.81
FSH	6.28±1.86	6.16±1.85	5.83±2.01	6.51±2.03	6.48±1.71
LH	10.02±4.12	11.09±3.80	9.96±4.23	9.48±4.65	7.30±2.89[c]
Prolactin	16.48±11.21	15.14±8.50	16.96±13.20	15.54±10.95	22.10±19.50[#]
Estradiol	91.98±35.02	82.72±40.44	96.21±34.15	95.51±29.10	102.30±46.07[#]
Fasting glucose	103.15±19.26	101.21±17.80	103.75±20.86	104.86±22.01	105.59±14.23
Endometrium thickness (mm)	0.90±0.25	0.89±0.23	0.90±0.27	0.96±0.27	0.87±0.23

FSH (Follicle stimulating hormone), LH (Luteinizing hormone) TSH (Thyroid stimulating hormone), BMI (Body mass index) and AMH (Anti-Mullerian Hormone)

[a] p <0.05; significantly different compared to other PCOS phenotype as estimated by ANOVA followed by Bonferroni's correction.

[#] p >0.05; insignificantly elevated when compared to the other groups as estimated by ANOVA followed by Bonferroni's correction.

[c] p <0.05; insignificantly lower when compared to other subjects.

Table 3 shows the association between PCOS phenotypes and clinical parameters. The present study, the average age of PCOS Phenotype is A (24.28 ± 1.93), B (27.86 ± 0.97), C (30.77 ± 0.92) and D (35.90 ± 1.86) with Phenotype D having the highest mean age. In terms of weight and BMI level, the Phenotype B has the highest weight range (63.12 kg) and BMI level (26.05 kg/m²), The study reveals that the phenotype B has a higher prevalence of obese persons. Among the hormonal level assessments, the AMH levels was significantly (p < 0.05) different within the phenotypes, as estimated by ANOVA using multiple comparisons of Bonferroni corrections the range decreases from Phenotype A (5.83 ± 4.12) to Phenotype D (3.14 ± 2.89),. In the TSH levels, Phenotype B had the highest (3.17 ± 1.86) and Phenotype C had the lowest (2.77 ± 1.79) TSH values was significantly lower as estimated by ANOVA. In the FSH range, there is no significant level was found among all phenotypes., but LH level was significantly decreased from Phenotype A (11.09 ± 3.80) to Phenotype D (7.30 ± 2.89). Phenotype D had the insignificantly elevated prolactin levels (22.10 ± 19.50) when compared to the other groups estimated by ANOVA followed by Bonferroni's correction. Estradiol levels were insignificantly higher in Phenotype D (102.30 ± 46.07) when compared to other groups. Fasting glucose levels are remarkably higher among all phenotypes, which is significantly higher when compared to normal reference range but insignificantly different when compared to within the PCOS phenotype groups as estimated by DMRT test. Phenotype D has the thinnest endometrium (0.87 ± 0.23 mm), possibly due to hormonal differences and reproductive state.

Table 4 shows the details on association between PCOS phenotypes of Insulin resistant and non-Insulin resistant PCOS patients with the demographic and clinical parameters

Particulars	Mean±SD Total (250)		PCOS phenotype							
			A		B		C		D	
	IR 186	NIR 64	IR 72	NIR 28	IR 56	NIR 16	IR 35	NIR 13	IR 23	NIR 07
Age	30.40±5.20	25.43±3.05	25.72±2.38	22.85±1.48	29.98±1.40	25.75±0.77	34.31±1.32	27.23±0.59	40.17±2.42	31.71±1.38
Weight	64.52±13.78	58.62±13.17	66.05±12.11	60.20±12.19	65.67±13.12	57.62±11.22	62.31±17.75	56.61±18.87	60.34±12.97	58.28±10.07
BMI	26.67±5.08	23.99±5.20	27.05±4.83	24.98±5.33	26.87±5.02	23.82±4.21	26.37±5.53	22.69±6.56	25.43±5.38	22.85±4.01
AMH	4.80±3.45	6.12±3.56	6.13±2.96	5.54±2.88	5.12±3.68	6.54±4.70	3.93±2.98	7.41±3.04	1.16±1.77c	5.12±3.93
TSH	2.91±1.62	3.16±3.02	2.68±1.62	3.39±3.97a	3.23±1.62	3.12±2.21	2.91±1.74	2.64±1.86	2.83±1.36	3.31±2.28
FSH	6.61 ±2.25	5.96±1.62	6.33±2.14	6.00±1.46	6.87±2.75	5.60±1.40	6.99±1.96	6.03±2.08	6.27±1.49	6.70±1.90
LH	9.02±4.99	11.02±3.63	10.53±4.52	11.66±3.34	9.31±5.50	10.61±2.83	7.90±5.11	11.07±4.59	5.30±1.88c	9.31±4.49
PLT	16.87±9.83	16.09±13.70	16.14±9.55	14.15±7.29	17.17±10.16	16.79±16.14	16.92±9.66	14.17±11.82	18.38±10.54	25.82±29.73
Estradiol	102.96±33.93	81.01±37.36	90.35±38.07	75.10±42.82	104.60±31.18	87.83±37.13	101.71±35.83	89.31±22.38	116.10±45.92	88.51±46.22
FG	116.03±31.88	90.28±6.64	112.80±28.61	89.63±6.99	115.89±35.62	91.61±6.11	116.07±36.35	93.03±5.66	126.46±23.31	84.72±5.16
ET(mm)	0.93±0.25	0.88±0.25	0.94±0.25	0.84±0.22	0.90±0.25	0.91±0.29	0.99±0.27	0.94±0.26	0.87±0.20	0.88±0.27

[a] p <0.05; significantly different compared to other PCOS phenotype as estimated by ANOVA followed by Bonferroni's correction.

[#] p >0.05; insignificantly elevated when compared to the other groups as estimated by ANOVA followed by Bonferroni's correction.

[c] p <0.05; insignificantly lower when compared to other subjects.

Table 4 summarizes the relationship between the PCOS phenotypes of insulin-resistant and non-insulin-resistant PCOS patients and the clinical parameters. In this current study, the mean age was higher in Phenotype D (40.17 ± 2.42 years for IR and 31.71 ± 1.38 years for NIR) and lower in phenotype A (25.72±2.38 years for IR and 22.85±1.48 years for NIR). Phenotype A exhibited the highest average weight (66.05 ± 12.11 kg) and BMI (27.05 ± 4.83 kg/m²) among all the phenotype group. AMH levels were insignificantly lower in Phenotype D (1.16±1.77 ng/mL for IR and 5.12 ± 3.93 ng/mL for NIR) when compared to all phenotypes estimated by ANOVA. TSH levels were elevated in Phenotype B (3.39 ± 3.97 µU/mL for IR and 3.12 ± 2.21 µU/mL for NIR), possibly indicating thyroid dysfunction in this group. FSH levels were comparatively consistent across phenotypes, with no significant variations observed. LH levels were the highest in Phenotype A (11.02 ± 3.63 µU/mL for IR and 10.61 ± 2.83 µU/mL for NIR) and phenotype D (5.30 ± 1.88 /mL for IR and 9.31 ± 4.49 µU/mL for NIR) which is insignificantly lower when compared to all phenotypes. Estradiol levels were prominent in Phenotype D (116.10 ± 45.92 pg/mL for IR and 88.51 ± 46.22 pg/mL for NIR). Fasting insulin levels were highest in Phenotype D (126.46 ± 23.91 µU/mL for IR and 84.72±5.16 µU/mL for NIR). Endometrium thickness were highest in Phenotype C (0.99 ± 0.27 mm for IR and 0.94 ± 0.26 mm for NIR).

IV. Discussion And Conclusion

Gestational diabetes mellitus (GDM) is the most common complication of pregnancy and usually manifests during the middle and late stages of gestation. Clinical risk factors for GDM include excessive weight gain, advancing maternal age, cardiovascular disease, past medical history, and polycystic ovarian syndrome

(PCOS) (Diamanti- Kandarakis et al, 2003). In contrast to overt diabetes mellitus, GDM is defined as any degree of glucose intolerance with onset or first recognition during pregnancy, likely resulting from exaggerated physiological changes in glucose metabolism during gestation (Eroglu & Zeyneloglu, 2006). Several studies have reported that PCOS independently increases the risk of GDM, although overweight has been identified as the strongest predictor for the development of GDM (Mikola et al, 2001). However, other studies have shown that non-obese women with PCOS were not at increased risk of GDM (Han et al, 2011), and two studies that matched participants for body mass index (BMI) and age did not report an increased risk of GDM in women with PCOS (Haakova et al, 2003). Nonetheless, PCOS has been shown to increase the risk of developing GDM by two to three times in several populations (Kouhkan et al, 2018). Furthermore, pregnant women with GDM have a 52.2% risk of developing type 2 diabetes mellitus within the first decade after delivery (Lowe et al, 2018), highlighting the long-term metabolic consequences of GDM.

The present study included 250 women diagnosed with PCOS from Erode, Tamil Nadu, with the primary objective of determining the frequency of insulin resistance (IR) across different PCOS phenotypes and evaluating its association with demographic, clinical, and paraclinical parameters. Women with PCOS commonly exhibit insulin resistance along with other metabolic abnormalities; notably, IR has been reported more frequently in hyperandrogenic PCOS patients (De Zegher & Ibanez, 2024). In our study, insulin resistance was detected in 210 participants (84%) using a HOMA-IR cut-off value of 2.5, indicating a high burden of metabolic dysfunction among PCOS patients.

Based on phenotypic distribution, phenotype A was the most prevalent, while phenotype D was the least common. The overall prevalence followed the order: phenotype A (44.8%) > phenotype B (27.2%) > phenotype C (20%) > phenotype D (8%). Variations in phenotypic distribution reported across different studies may be attributed to genetic factors, differences in dietary and lifestyle habits, and variations in participant sample sizes. Factors such as age, overweight, obesity, and smoking have also been associated with PCOS; however, findings regarding these associations have not been consistent across different studies (Wang et al, 2020).

Our findings demonstrated that insulin resistance varied significantly among the four PCOS phenotypes, with prevalence rates of 84.8% in phenotype A, 89.7% in phenotype B, 84% in phenotype C, and 55% in phenotype D. Interestingly, phenotype B exhibited the highest prevalence of insulin resistance and the highest HOMA index values among all phenotypes. This indicates that phenotype B patients may have a more pronounced metabolic derangement despite not being the most prevalent phenotype. The significant variation in HOMA index values across phenotypes suggests a strong association between PCOS phenotype and degree of insulin resistance.

When phenotypes were grouped according to the Rotterdam criteria, 75% of cases were classified as classical PCOS phenotypes (A and B), while 25% were classified as non-classical phenotypes (C and D). A statistically significant association was observed between insulin resistance and phenotype grouping, with classical phenotypes showing a higher prevalence of IR compared to non-classical phenotypes. This supports previous findings indicating that classical PCOS phenotypes are more metabolically severe. Similar observations were reported by Sobti et al, who found that the prevalence of insulin resistance was highest in phenotype A and lowest in phenotype D, with an incidence of 31% using a HOMA-IR cut-off of 2.5 (Hoeger & Oberfield, 2012). However, this contrasts with our findings, where phenotype B showed the highest prevalence of insulin resistance. Such discrepancies may be due to differences in study population characteristics, diagnostic criteria, and sample size.

Previous studies have shown that the coexistence of PCOS and insulin resistance may accelerate the progression of glucose metabolism disorders. Consequently, the pathophysiological mechanism underlying GDM in patients with PCOS may differ from that observed in the general pregnant population (Hao et al, 2016). These findings emphasize the importance of phenotypic classification and metabolic evaluation in PCOS patients, particularly in predicting insulin resistance and potential pregnancy-related complications such as GDM. In conclusion, the present study highlights a high prevalence of insulin resistance among women with PCOS, with 84% of the participants exhibiting insulin resistance as assessed by the HOMA-IR index. The distribution of PCOS phenotypes revealed that phenotype A was the most common, while phenotype D was the least prevalent, and significant differences in insulin resistance were observed across the phenotypic groups. Notably, phenotype B demonstrated the highest HOMA-IR values, indicating greater metabolic impairment. Classical PCOS phenotypes (A and B) were more frequent and showed a stronger association with insulin resistance compared to non-classical phenotypes (C and D). Given the established link between PCOS, insulin resistance, and an increased risk of gestational diabetes mellitus, these findings underscore the importance of early phenotypic classification and metabolic screening in women with PCOS to facilitate timely intervention and reduce future metabolic and pregnancy-related complications.

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