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THE RELATIONSHIP OF FREE ANDROGEN INDEX (FAI) WITH INSULIN RESISTANCE IN DIFFERENT PHENOTYPES OF POLYCYSTIC OVARY SYNDROME

Manoj Prasad Nautiyal[1], Dr. Tariq Masood*[2], Dr. Anjali Choudhary[3]

[1]PhD Scholar, Department of Biochemistry, Shri Guru Ram Rai Institute of Medical and Health Sciences, Shri Mahant Indiresh Hospital, Dehradun, Uttarakhand, India mp.nauti@gmail.com
[2]Professor, Department of Biochemistry, Shri Guru Ram Rai Institute of Medical and Health Sciences, Shri Mahant Indiresh Hospital, Dehradun, Uttarakhand, – 248001, India tariqmas2001@yahoo.co.in
[3]Professor, Department of Obstetrics and Gynaecology, Shri Guru Ram Rai Institute of Medical and Health Sciences, Shri Mahant Indiresh Hospital, Dehradun, Uttarakhand, India mcgsunil@gmail.com
*Corresponding Author: Dr. Tariq Masood

ABSTRACT

Introduction: Polycystic ovary syndrome (PCOS) is a common endocrine and metabolic disorder affecting women of reproductive age. Hyperandrogenism and Hyperinsulinemia are key features of the syndrome. The present study aimed to assess the association between the free androgen index (FAI) and insulin resistance in different phenotypes of PCOS.

Methods: A total of 330 women aged 18–45 years diagnosed with PCOS according to the modified 2003 Rotterdam criteria were included. Participants were classified into phenotypes A, B, C, and D. Clinical, anthropometric, hormonal, biochemical parameters, and ultrasound features of all phenotypes were noted. FAI was calculated as total testosterone/sex hormone binding globulin × 100. Insulin resistance was assessed using homeostatic model assessment of insulin resistance (HOMA-IR). Phenotype wise comparisons and correlations between FAI and HOMA-IR were performed.

Results: Phenotype A was the most prevalent 51% followed by B (31%), C (11%), and D (7%). FAI showed a significant positive correlation with HOMA-IR in the overall study population ($r = 0.255$, $P < 0.001$). Phenotypes A and D showed significant correlations, whereas phenotypes B and C showed non-significant correlations. High FAI levels were observed in 259 participants (78.48%) and were significantly associated with the PCOS phenotypes ($P < 0.001$). Biochemical hyperandrogenism was highest in phenotype A, followed by B, C, and absent in phenotype D.

Conclusion: FAI was significantly associated with insulin resistance in women with PCOS. Phenotype-wise assessment improves the identification of metabolic risk in PCOS and helps in individualized clinical management.

KEYWORDS: Polycystic ovary syndrome, Free androgen index, Insulin resistance, Homeostatic model assessment of insulin resistance, PCOS phenotypes

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a heterogeneous endocrine and metabolic disorder affecting women of reproductive age, with a reported prevalence between 4% to 21% globally, and 2% to 35% in India.[1] It is marked by ovulatory dysfunction (OD), hyperandrogenism (HA) and polycystic ovarian morphology (PCOM). The modified 2003 Rotterdam criteria, which are widely used for diagnosing PCOS, require the presence of any two of the following three features: HA, OD, and PCOM.[2] Based on these criteria, PCOS is classified into four phenotypes: phenotype A (HA+OD+PCOM), phenotype B (HA+OD), phenotype C (HA+PCOM), and phenotype D (OD+PCOM).[3] Other than reproductive health it is also related with obesity, insulin resistance, dyslipidemia, metabolic syndrome, type 2 diabetes mellitus, and increased cardiovascular risk.[4,5] Insulin resistance plays a central role in PCOS pathophysiology by increasing ovarian androgen production and reducing sex hormone-binding globulin (SHBG) synthesis, resulting in elevated free androgen levels.[6]

This interaction highlights the importance of assessing insulin sensitivity in PCOS particularly in relation to the free androgen index (FAI), a reliable marker of biochemical hyperandrogenism calculated from total testosterone and SHBG levels.[7,8] Previous studies have also supported its clinical utility in identifying hyperandrogenism in women with suspected PCOS.[9,7] We hypothesized that hyperandrogenic phenotypes, particularly phenotype A, would exhibit higher insulin resistance and biochemical hyperandrogenism, and that FAI would positively correlate with homeostatic model assessment of insulin resistance (HOMA-IR) across phenotypes. Therefore, present study aimed to evaluate the association between FAI and insulin resistance parameters, including fasting insulin and HOMA-IR across different PCOS phenotypes.

MATERIALS AND METHODS

This cross-sectional study was conducted over 18 months, from August 2024 to February 2026. Women attending the outpatient department of Obstetrics and Gynaecology at a tertiary care multispecialty and superspecialty teaching hospital, who fulfilled the modified 2003 Rotterdam criteria for PCOS, were included in the study. A consecutive sampling technique was employed. A total of 330 PCOS women age 18-45 years who met with the inclusion criteria and provided written informed consent during the study period were recruited. Exclusion criteria for this study were 1) women with a history of treatment with insulin sensitizers 2) endocrine disorders such as thyroid diseases, hyperprolactinemia, and Cushing's syndrome 3) women with a history of ovarian drilling. The sample size was calculated based on the reported prevalence of insulin resistance among women with PCOS.[10] Considering a prevalence of 31%, precision of 5%, and a 95% confidence level, the required sample size was calculated accordingly.

At the baseline visit, participants underwent all general anthropometric and physical examination as well as systolic and diastolic blood pressure were measured. Body mass index (BMI) was determined by dividing body weight in kilograms by height in meters squared (kg/m²). Clinical examination included menstrual history, gynecological and family history and current use of medication.

The presence of hirsutism was assessed using the modified Ferriman–Gallwey (mFG) scoring system, with a score ≥8 considered significant. A standardized clinical screening was performed by trained gynecologist. Ovulatory dysfunction (OD) was defined as the presence of oligo-amenorrhea (cycles > 35 days apart or <8 cycles per year).[11] PCOM was defined as the presence of either 20 or more follicles each ovary and/or an ovarian volume of ≥10cm^3 on either ovary, using transvaginal ultrasound transducer with a frequency of 8MH_Z or more.[11]

For biochemical measurements, participants were called on the days 2-3 of their next menstrual cycle in the fasting state. Five millilitres of venous blood was collected from each participant under all aseptic condition in the plain vacutainer vial by venepuncture. The biochemical parameters estimated were total testosterone, SHBG, fasting glucose and insulin, follicle stimulating hormone (FSH), luteinizing hormone (LH), free T_3 and T_4, Thyroid Stimulating hormone (TSH), and Prolactin. Serum SHBG was estimated by electrochemiluminescence immunoassay (ECLIA) using the Roche Cobas e 411 analyzer (Roche Diagnostics, Germany). The remaining biochemical parameters were analyzed on the VITROS 5600 and VITROS XT 7600 integrated systems based on dry chemistry and immunodiagnostic technology (QuidelOrtho™ Corporation, San Diego, CA, USA). Calibration and internal quality control procedures were performed regularly according to the manufacturer's instructions to ensure accuracy and precision of the test results. FAI was used for biochemical hyperandrogenism. FAI was calculated as ratio of total testosterone to SHBG multiplied by 100.[12] In our study, an FAI cutoff value of ≥2.56 was used as the diagnostic threshold for biochemical hyperandrogenism. The FAI cutoff value was based on evidence from a systematic review and diagnostic meta-analysis conducted to inform the 2023 International PCOS Evidence-based Guidelines,[8] which reported a median FAI cutoff of 2.56, with a reported pooled sensitivity of 0.78, specificity of 0.85, and area under the curve (AUC) of 0.87 for detecting biochemical hyperandrogenism in PCOS. The homeostasis model assessment of insulin resistance (HOMA-IR) was used as a marker of insulin resistance in our study. A HOMA-IR cut-off of ≥2.5[13] was used to define insulin resistance. After evaluating all the parameters, participants were classified into their respective PCOS phenotypes based on the modified 2003 Rotterdam criteria.[11] As to the criteria, PCOS has four different possible phenotypes. Phenotype A (Full-Blown or Classic PCOS): HA) + OD + PCO. Phenotype B (Non - PCO PCOS) – HA + OD. Phenotype C (Ovulatory PCOS) – HA + PCO. Phenotype D (Non - hyperandrogenic PCOS)- OD+PCO.[14]

Continuous variables were expressed as median (IQR), while categorical variables were presented as frequencies and percentages. Data were analyzed using IBM SPSS STATISTICS version 31. The variables were tested for normality using the Kolmogorov-Smirnov and Shapiro-Wilk test. As the quantitative variables were not normally distributed, the Mann–Whitney *U* test was used to compare two groups. The Kruskal– Wallis test was used for comparisons among more than two groups. When statistically significant differences were observed, post-hoc pairwise comparisons were conducted using Bonferroni correction. Correlation between continuous variables were assessed using Spearman rank correlation coefficient. Associations between categorical variables were evaluated using the Chi-square test or Fisher's exact test when expected cell frequencies were less than five. A *P*-value of <0.05 was considered statistically significant.

RESULT

Table - 1 Descriptive characteristics of anthropometric, clinical and biochemical parameters of the study participants [Median (IQR)]

Characteristic (Qualitative)	**Grouping**	***n* (%)**	**Characteristic (Quantitative)**	**Median (IQR)**
PCOS Phenotype	A	169 (51.2)	Age (years)	27.00 (23.00–31.00)

	B	103 (31.2)	Height (cm)	157.00 (151.00–161.75)
	C	37 (11.2)	Weight (kg)	62.00 (54.00–70.00)
	D	21 (6.4)	BMI[1] (kg/m²)	24.85 (22.29–28.07)
FAI[2] Category	Low (<2.56)	71 (21.5)	m-FG[3] score	11.00 (8.00–13.75)
	High (≥2.56)	259 (78.5)	FBS[4] (mg/dL)	89.00 (81.00–100.00)
Insulin Resistance (IR)	No (HOMA-IR[5] <2.5)	102 (30.9)	Fasting insulin (pmol/L)	90.00 (64.20–120.00)
	Yes (HOMA-IR[5] ≥2.5)	228 (69.1)	HOMA-IR[5]	3.30 (2.25–4.40)
BMI[1] Category	Normal (<25 kg/m²)	172 (52.1)	TT[6] (nmol/L)	2.43 (1.84–3.02)
	Overweight/obese (≥25 kg/m²)	158 (47.9)	SHBG[7] (nmol/L)	54.67 (35.10–87.11)
Polycystic Ovarian Morphology	Normal	103 (31.21)	FAI[2]	4.37 (2.86–7.77)
	Polycystic ovaries	227 (68.79)	LH[8] (mIU/L)	10.50 (8.16–13.45)
			FSH[9] (mIU/L)	5.60 (4.41–6.69)
			LH:FSH ratio	1.94 (1.33–2.73)
			FT3[10] (pmol/L)	6.22 (5.36–7.01)
			FT4[11] (pmol/L)	18.25 (14.30–22.48)
			TSH[12] (mIU/L)	2.10 (1.18–3.00)
			PRL[13] (ng/mL)	235.55 (163.33–307.00)

[1]BMI: Body mass index, [2]FAI: Free androgen index, [3]m-FG: Modified Ferriman–Gallwey, [4]FBS: Fasting blood sugar, [5]HOMA-IR: Homeostatic model assessment for insulin resistance, [6]TT: Total testosterone, [7]SHBG: Sex hormone-binding globulin, [8]LH: Luteinizing hormone, [9]FSH: Follicle-stimulating hormone, [10]FT3: Free triiodothyronine, [11]FT4: Free thyroxine, [12]TSH: Thyroid-stimulating hormone, [13]PRL: Prolactin.

Table - 2 Comparison of anthropometric, metabolic, and hormonal parameters among different phenotypes of PCOS

Variable	**Phenotype A (*n* = 169)**	**Phenotype B (*n* = 103)**	**Phenotype C (*n* = 37)**	**Phenotype D (*n* = 21)**	***P*-value**
Age (years)	26 (23–31)	27 (23–30)	30 (26–33)	26 (24–33)	0.083 *
Weight (kg)	63 (54–70)	61 (54–72)	60 (53–67)	61 (52–64)	0.551 *
Height (cm)	157 (152–162)	157 (151–162)	157 (152–159)	154 (151–162)	0.879 *
BMI[1] (kg/m²)	25.32 (22.35–28.57)	24.35 (22.21–27.85)	23.92 (22.27–26.71)	24.39 (22.81–25.72)	0.558 *
Waist circumference (cm)	35 (32–38)	33 (30–36)	31 (30–34)	33 (30–36)	<0.001*
Hip circumference (cm)	39 (36–42)	39 (35–41)	37 (34–40)	38 (33–41)	0.022 *

Waist–hip ratio	0.89 (0.87–0.91)	0.87 (0.84–0.89)	0.86 (0.84–0.88)	0.88 (0.87–0.89)	<0.001*
SBP[2] (mmHg)	119.00 (112.68–124.92)	116.53 (108.19–122.12)	117.12 (109.37–121.29)	116.40 (111.50–120.49)	0.010*
DBP[3] (mmHg)	77.54 (72.14–81.52)	74.50 (70.38–77.91)	74.56 (70.74–81.75)	71.60 (69.40–76.23)	<0.001*
m-FG[4] score	13.00 (7.00–15.00)	11.00 (9.00–12.00)	10.00 (8.00–12.00)	4.00 (1.00–5.00)	<0.001*
TT[5] (nmol/L)	2.75 (2.25–3.47)	2.12 (1.76–2.71)	2.08 (1.42–2.91)	2.15 (1.39–2.32)	<0.001*
SHBG[6] (nmol/L)	47.25 (32.00–74.60)	54.74 (34.00–87.26)	61.20 (37.50–86.70)	111.50 (94.10–128.70)	<0.001*
FAI[7] (%)	5.82 (3.80–9.73)	3.82 (2.57–6.17)	3.54 (1.90–6.92)	1.75 (1.26–1.99)	<0.001*
FBS[8] (mg/dL)	91 (83–101)	87 (76–99)	89 (80–99)	85 (80–97)	0.078*
Fasting insulin (pmol/L)	98.06 (71.20–129.00)	90.00 (66.00–112.00)	78.90 (58.00–103.20)	64.00 (31.00–102.00)	0.002*
HOMA-IR[9]	3.62 (2.57–4.81)	3.11 (2.27–4.07)	2.89 (1.90–3.78)	2.47 (1.16–3.44)	<0.001*
LH[10] (mIU/L)	10.19 (8.39–12.88)	11.71 (7.92–16.30)	11.46 (8.32–13.72)	6.68 (4.86–9.68)	<0.001*
FSH[11] (mIU/L)	5.10 (4.12–6.21)	6.79 (5.59–7.54)	5.10 (4.26–6.20)	3.33 (2.62–5.18)	<0.001*
LH:FSH ratio	2.08 (1.39–2.86)	1.71 (1.20–2.38)	2.38 (1.62–2.86)	1.87 (1.28–2.15)	0.008*
FT3[12] (pmol/L)	6.18 (5.32–6.91)	6.14 (5.42–7.04)	6.62 (5.68–7.19)	6.43 (4.92–7.00)	0.447*
FT4[13] (pmol/L)	18.10 (14.10–22.40)	19.40 (13.70–22.50)	18.30 (15.30–21.70)	17.60 (15.40–23.80)	0.870*
TSH[14] (mIU/L)	2.00 (1.13–2.97)	2.22 (1.13–3.02)	2.32 (1.34–3.00)	1.91 (1.48–2.88)	0.809*
PRL[15] (ng/mL)	237.00 (167.10–307.00)	244.70 (174.50–319.70)	223.50 (122.10–310.80)	203.20 (158.50–262.20)	0.301*

*Kruskal–Wallis test, [1]BMI: Body mass index, [2]SBP: Systolic blood pressure, [3]DBP: Diastolic blood pressure, [4]m-FG: Modified Ferriman–Gallwey, [5]TT: Total testosterone, [6]SHBG: Sex hormone-binding globulin, [7]FAI: Free androgen index, [8]FBS: Fasting blood sugar, [9]HOMA-IR: Homeostatic Model Assessment for Insulin Resistance, [10]LH: Luteinizing hormone, [11]FSH: Follicle-stimulating hormone, [12]FT3: Free triiodothyronine, [13]FT4: Free thyroxine, [14]TSH: Thyroid-stimulating hormone, [15]PRL: Prolactin.

Table -3 Association of FAI with the demographic, clinical, and paraclinical characteristics of the study participants

Quantitative variable	**High FAI (*n* = 259) median (IQR)**	**Normal FAI (*n* = 71) median (IQR)**	***P*-value (Mann–Whitney)**
Age	27.0 (23.0–32.0)	27.0 (24.0–31.0)	0.629
Weight (Kg)	62.0 (54.0–70.0)	61.0 (52.0–68.0)	0.544
Height (cm)	157.0 (152.0–162.0)	156.0 (151.0–160.0)	0.343
BMI[1]	24.91 (22.43–28.07)	24.46 (22.11–28.12)	0.588
m-FG Score[2]	10.0 (8.0–12.0)	8.0 (6.5–9.0)	<0.001*
F-Insulin[3] (pmol/L)	91.0 (67.05–122.21)	82.41 (43.9–110.8)	0.006*
FBS[4] (mg/dl)	90.0 (81.0–101.0)	86.0 (80.0–98.0)	0.070
HOMA-IR[5]	3.41 (2.42–4.54)	2.97 (1.58–3.81)	0.001*
TT[6] (nmol/l)	2.63 (2.12–3.37)	1.78 (1.08–2.22)	<0.001*
SHBG[7] (nmol/L)	46.6 (31.35–65.37)	103.4 (86.98–128.85)	<0.001*

FT3[8] (pmol/L)	6.22 (5.38–7.01)	6.18 (5.23–6.8)	0.410
FT4[9] (pmol/L)	18.3 (14.3–22.25)	18.0 (14.65–23.1)	0.342
TSH[10] (mIU/L)	2.1 (1.18–3.0)	2.12 (1.18–2.97)	0.889
PRL[11] (ng/ml)	240.5 (172.75–312.0)	222.8 (151.2–284.55)	0.149

*Significant, [1]BMI: Body mass index, [2]m-FG: Modified Ferriman–Gallwey, [3]F-Insulin: Fasting insulin, [4]FBS: Fasting blood sugar, [5]HOMA-IR: Homeostatic model assessment for insulin resistance, [6]TT: Total testosterone, [7]SHBG: Sex hormone-binding globulin, [8]FT3: Free triiodothyronine, [9]FT4: Free thyroxine, TSH: [10]Thyroid-stimulating hormone, [11]PRL: Prolactin.

Table 4- Correlation of FAI with demographic, clinical, and paraclinical characteristics of the participants.

Variable (quantitative)	FAI	
	Correlation coefficient (*r*)	*P*-value (Spearman's test)
Age	-0.052	0.344
Weight (Kg)	0.039	0.481
Height (cm)	0.069	0.212
BMI[1]	0.026	0.634
m-FG[2] Score	0.509	<0.001*
FBS[3] (mg/dl)	0.019	0.736
F-Insulin[4] (pmol/L)	0.252	<0.001*
HOMA-IR[5]	0.255	<0.001*
TT[6] (nmol/l)	0.592	<0.001*
SHBG[7] (nmol/L)	-0.698	<0.001*
FT3[8] (pmol/L)	0.009	0.867
FT4[9] (pmol/L)	-0.016	0.767
TSH[10] (mIU/L)	-0.044	0.426
PRL[11] (ng/ml)	0.049	0.373

*Significant, [1]BMI: Body mass index, [2]m-FG: Modified Ferriman–Gallwey, [3]F-Insulin: Fasting insulin, [4]FBS: Fasting blood sugar, [5]HOMA-IR: Homeostatic model assessment for insulin resistance, [6]TT: Total testosterone, [7]SHBG: Sex hormone-binding globulin, [8]FT3: Free triiodothyronine, [9]FT4: Free thyroxine, TSH: [10]Thyroid-stimulating hormone, [11]PRL: Prolactin.

A total of 330 women with PCOS were recruited for this study. The median age of the participants was 27.00 (23.0–31.00) years and the median body mass index (BMI) was 24.85 (22.29–28.07) kg/m². The median HOMA-IR was 3.30 (2.25–4.40). The median serum testosterone and free androgen index (FAI) were 2.43 (1.84–3.02) nmol/L and 4.37 (2.86–7.77), respectively. Among the PCOS phenotypes, phenotype A (51%) was the most common, followed by phenotype B (31%), phenotype C (11%), and phenotype D (7%) Baseline characteristics of the study participants are summarized in Table -1

No significant differences were observed in age, height, weight and BMI among the PCOS phenotypes ($P > 0.005$). However, significant differences were observed in systolic blood pressure, diastolic blood pressure, waist circumference, and waist-hip ratio across the phenotypes ($P < 0.005$).

Clinical and biochemical hyperandrogenism was predominant in phenotype A, followed by phenotypes B, C, and D. The median m-FG score was highest in phenotype A [13.00 (7.00–15.00)] and lowest in phenotype D [4.00 (1.00–5.00)]. Serum total testosterone (nmol/L) levels differed significantly across the phenotypes, with median values of 2.75 (2.25–3.47) in phenotype A, 2.12 (1.76–2.71) in phenotype B, 2.08 (1.42–2.91) in phenotype C, and 2.15 (1.39–2.32) in phenotype D ($P < 0.001$). In contrast SHBG (nmol/L) levels showed a significant opposite pattern, being lowest in phenotype A [47.25 (32.00–74.60)] and highest in phenotype D [111.50 (94.10–128.70)] ($P < 0.001$). Consequently, median FAI was significantly higher in phenotype A [5.82 (3.80–9.73)] than in phenotype B [3.82 (2.57–6.17)], phenotype C [3.54 (1.90–6.92)] and phenotype D [1.75 (1.26–1.99)] ($P < 0.001$). Comparison of clinical and biochemical parameters across PCOS phenotypes are presented in Table-2

Based on the FAI cut-off value of 2.56%, 259 participants (78.48%) had high FAI. The median FAI among the study participants was 4.26 (2.76–7.82). Biochemical hyperandrogenism (FAI ≥ 2.56) was significantly associated with PCOS phenotype (χ^2 = 93.723, P < 0.001). Among the total study population, the highest proportion of biochemical hyperandrogenism was observed in phenotype A 46.7% (154), followed by phenotype B 23.6% (78) and phenotype C 8.2% (27), whereas no participant with phenotype D showed biochemical hyperandrogenism. Additionally, 172 patients (52.12%) had normal BMI. The association of FAI with the demographic, clinical, and paraclinical characteristics of the participants are summarized in Table -3

Other hormonal parameters, LH and FSH, were significantly higher in phenotype B than in other phenotypes (P < 0.005), whereas the LH:FSH ratio was significantly higher in phenotype C (P = 0.008). In contrast, thyroid profile parameters and prolactin levels were similar among the PCOS phenotypes, with no significant differences [FT3 (P = 0.447), FT4 (P = 0.870), TSH (P = 0.809), and prolactin (P = 0.301)].

Fasting insulin and HOMA-IR were both statistically significant among the phenotypes (P = 0.002, P < 0.005, respectively). Phenotype A showed the highest fasting insulin [98.06 (71.20–129.00)] and HOMA-IR [3.62 (2.57–4.81)]. However, fasting blood glucose was not statistically significant across the phenotypes (P = 0.078). Considering a HOMA-IR cut-off of 2.50, 228 participants (69.09%) were classified as having insulin resistance, while 102 participants (30.91%) were categorized as non-insulin resistance. The distribution of insulin resistance differed significantly across the PCOS phenotypes (χ^2 = 10.094, P = 0.018). In the overall study population, phenotype A had highest percentage 38.79% (128) of insulin resistance followed by phenotype B 20.61% (68), phenotype C 6.67% (22) and 3.03% (10) of phenotype D.

Correlation analysis demonstrated significant associations between FAI and several clinical and biochemical parameters as shown in Table 4. FAI was significantly correlated with the m-FG score (r = 0.509), total testosterone (r = 0.592), and HOMA-IR (r = 0.255), whereas a strong negative correlation was observed with SHBG levels (r = −0.698).

DISCUSSION

The present study evaluates the association between free androgen index (FAI) and insulin resistance across different phenotypes of polycystic ovary syndrome (PCOS). A significant positive correlation between FAI and HOMA-IR was observed in the overall study, with stronger associations in phenotypes A and significant correlation in phenotype D. However, no significant correlation was found in phenotypes B and C. Similar findings were reported by Savran *et al*. [15]

The observed association between FAI and insulin resistance may be explained by the bidirectional interaction between hyperinsulinemia and androgen excess. Insulin resistance leads to compensatory hyperinsulinemia, which stimulates ovarian androgen production and suppresses hepatic SHBG synthesis, thereby increasing the free androgen levels. Elevated androgen levels may further impair insulin sensitivity, creating a vicious cycle between hyperandrogenism and metabolic dysfunction in PCOS.[16] This interaction between high insulin and elevated androgen levels may explain the positive relationship between FAI and HOMA-IR in the present study. Phenotype A (51%) had the highest prevalence among the phenotypes, followed by B (31%), C (11%), and D (7%). Our findings were consistent with those of Rahmatnezhad *et al*. [13], where phenotype A (51.9%) was the most prevalent among the study population. Phenotype A exhibited the most adverse clinical, biochemical, and metabolic profiles. This phenotype demonstrates higher central adiposity, greater clinical and biochemical hyperandrogenism, lower SHBG levels, and higher fasting insulin and HOMA-IR values compared with other phenotypes. Our findings are consistent with those of previous studies that reported phenotype A as the most severe form of PCOS. [14]

Hyperandrogenic phenotypes B and C showed higher m-FG score and FAI, in contrast, phenotype D had the least androgenic and metabolic abnormalities. Similar findings were reported by Polak *et al*. [17] Despite similar BMI across phenotypes, phenotype A showed higher central adiposity indices, suggesting that fat distribution may be more important than overall obesity in determining metabolic risk in PCOS. The presence of insulin resistance even in women with normal BMI further indicates that metabolic dysfunction in PCOS may occur independently of obesity. This observation is supported by previous studies demonstrating insulin resistance in non-obese women with PCOS,[18] due to intrinsic defects in insulin signalling, genetic susceptibility, or increased visceral adiposity.

The present findings support the heterogeneous nature of PCOS, in which endocrine disorders and metabolic abnormalities differ across phenotypes. The significant positive relationship between FAI and HOMA-IR suggests an association between biochemical hyperandrogenism and insulin resistance. Our findings are supported by several PCOS studies showing significant positive correlations between FAI and HOMA-IR, supporting an association between biochemical hyperandrogenism and insulin resistance.[2] However, the weak correlation indicates that insulin resistance may be influenced by multiple factors other than androgen excess. Other contributing factors, such as adiposity, lifestyle variation, and genetic predisposition, may also play important roles.

The metabolic risk in patients with PCOS may vary among different phenotypes. Differences in study population, diagnostic criteria, and methods used to measure androgen levels may explain variations in findings across studies. These findings have important clinical implications. Assessment of FAI with phenotypic classification may help identify women at a higher risk of metabolic complications, even in the absence of clinical obesity. Early identification of high-risk phenotypes, particularly phenotype A, may facilitate timely interventions, such as lifestyle modifications and insulin-sensitizing therapy, thereby reducing the long-term risk of cardiometabolic complications. Similar phenotype-related differences in insulin resistance and metabolic risk among PCOS phenotypes were also reported by Paolo Moghetti *et al*. [19]

The present study had certain limitations. The cross-sectional design limits the causal interpretation between FAI and insulin resistance. Unequal phenotype distribution, particularly the small sample size of phenotype D, may reduce the precision of subgroup analyses. In addition, FAI was used as a surrogate marker rather than a direct measurement of free testosterone. Therefore, the findings should be interpreted with carefully and require validation in larger, prospective studies.

This study provides a comprehensive comparison of the four PCOS phenotypes and highlights the clinical significance of phenotype-based classification. Phenotypic classification of women with PCOS and related comorbidities can help in assessing disease severity and expected outcomes. The significant association between FAI and insulin resistance supports the role of biochemical hyperandrogenism in the metabolic dysfunction of PCOS.[20] Incorporating FAI into routine clinical assessment, along with phenotypic classification, may improve risk stratification and guide individualized management strategies for women with PCOS.

CONCLUSION

The present study highlights the clinical, endocrine, and metabolic profiles of women with PCOS across the four phenotypes using the modified 2003 Rotterdam criteria. Phenotype A was the most common phenotype and showed a greater burden of hyperandrogenism and insulin resistance compared with the other phenotypes. A significant association between FAI and HOMA-IR in the overall cohort indicates a possible link between biochemical hyperandrogenism and insulin resistance. However, the weak strength of correlation suggests that insulin resistance in PCOS is multifactorial and may also be influenced by adiposity, lifestyle and genetic predisposition factors. Overall, phenotype-wise assessment of PCOS may help in better understanding disease severity, identifying women at higher metabolic risk, and guiding individualized clinical management of the condition. Early screening for insulin resistance and biochemical hyperandrogenism should be considered, particularly in women with hyperandrogenic phenotypes.

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