



Original Research Article

Correlation of clinical profile and anthropometry factors with free androgen index in evaluation of polycystic ovarian syndrome

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Abstract

Background: Polycystic ovarian syndrome (PCOS) is a common endocrine disorder affecting women of reproductive age leading to subfertility and presenting with symptoms such as menstrual irregularities, hirsutism, acne, and obesity. It is also linked with metabolic condition like insulin resistance and metabolic syndrome. This study aimed to evaluate the clinical profile and anthropometric factors in women with PCOS and their correlation with Free Androgen Index (FAI) levels.

Materials and Methods: A cross-sectional study included 92 PCOS women in tertiary care centre. FAI levels were measured from blood samples, clinical features, anthropometric data were measured and recorded. Statistical analysis was performed using SPSS-23, with a significance level set at 5%.

Results: Significant associations were found between FAI levels and clinical features. Higher FAI values correlated with irregular menstrual cycles ($p = 0.0001$), hirsutism ($p = 0.00001$), acne ($p = 0.0001$), androgen alopecia ($p = 0.0001$), acanthosis nigricans ($p < 0.05$), a mixed diet ($p = 0.00001$), physical inactivity ($p = 0.00001$), obesity ($p = 0.00001$), increased waist-hip ratio ($p = 0.0001$) and PCOM on ultrasound ($p = 0.00001$). Elevated FAI levels were notably associated with the metabolic phenotype of PCOS.

Conclusion: FAI is a significant diagnostic marker for PCOS, strongly associated with clinical symptoms and metabolic risk factors. The study highlights the need for larger, multicentric research to validate these findings and improve PCOS screening and management strategies.

Keywords: Polycystic ovary syndrome, Free androgen index, Hyperandrogenism, Metabolic syndrome, Total testosterone, Free testosterone.

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1. Introduction

PCOS prevalence varies globally with higher rates observed among Indian women compared to other populations characterized by a variety of symptoms and health complications.¹ PCOS is associated with high levels of androgenic hormones and presents a spectrum of clinical manifestations.² Historically PCOS was first described by Michael Leo Leventhal and Irving Freiler Stein in 1935 and despite various modifications to its diagnostic criteria over the decades, the concept remains complex and evolving.

According to pooled data, the prevalence is approximately 10% when using the AES and Rotterdam criteria, compared to 5.8% with the NIH criteria.³ The Rotterdam criteria established in 2003, is currently the most widely used and require at least two of the following three

criteria for diagnosis: chronic anovulation, biochemical and/or clinical hyperandrogenism and polycystic ovarian morphology (PCOM) on ultrasound.⁴ For adolescents, all three criteria must be met. Exclusion of other disorders such as cushing syndrome and congenital adrenal hyperplasia is necessary.

During puberty, hormonal changes include rising levels of cortical androgen stimulating hormones with increased GnRH release leading to elevated LH and FSH levels. This hormonal surge stimulates the ovaries promoting the development of Graafian follicles and the onset of menarche.¹ The physiology of the ovary involves the growth of one dominant follicle which matures under the influence of FSH and LH, with androgens produced by the theca interna cells being aromatized into estrogen by granulosa cells.⁶

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PCOS involves several key pathophysiological aspects like ovarian androgen production, hyperinsulinemia, elevated LH levels and abnormal ovarian morphology. The ovaries in PCOS typically have numerous small follicles and increased stromal volume with an imbalance in follicle development and a high rate of atresia inhibition.⁷ Insulin resistance plays a crucial role, contributing to the overall pathology of PCOS and increasing the risk of associated conditions like diabetes and cardiovascular disease.⁸

PCOS presents with a diverse range of clinical features primarily affecting menstrual regularity, androgen levels and overall metabolic health. Menstrual irregularities are among the most common manifestations with patients often experiencing oligo/amenorrhea due to inhibited ovulation, which can result in infertility.⁹ Hyperandrogenism, characterized by elevated levels of androgens such as testosterone and androstenedione often accompanies irregular menstrual cycles. This imbalance can lead to additional issues like endometrial hyperplasia due to unopposed estrogen.¹⁰

Hyperandrogenism in PCOS can be attributed to multiple factors including ovarian, adrenal gland abnormalities, elevated insulinemia and conditions like hypothyroidism. Ovarian hyperandrogenism is commonly linked to cortical stromal hyperplasia and overproduction of androgens by the theca cells of the ovaries.¹¹ This excess androgen contributes to symptoms such as hirsutism, acne and androgenic alopecia. Hirsutism characterized by excessive hair growth in a masculine distribution pattern is scored based on the extent of hair growth with a score of 8 or more indicating significant hirsutism.¹² Acne severity is assessed using a grading scale from 0 to 5 with high grades reflecting severe cases.¹³ Acanthosis nigricans, a condition marked by velvety skin changes is observed in about 5% of PCOS patients and is linked to insulin resistance.¹⁴

Obesity exacerbates PCOS symptoms by decreasing Sex hormone binding globulin (SHBG) and increasing levels of estradiol and free testosterone thereby contributing to dyslipidemia and an elevated risk of cardiovascular diseases. Insulin resistance prevalent in many PCOS patients further complicates the condition often leading to hyperinsulinemia which affects ovulation and exacerbates hyperandrogenism. Managing these diverse symptoms requires a comprehensive approach including lifestyle modifications, pharmacological interventions, and regular monitoring to address the multifaceted nature of PCOS.¹⁵

Hormonal measurements are crucial for diagnosing and managing Polycystic Ovary Syndrome. Follicle-Stimulating Hormone (FSH) and Luteinizing Hormone (LH) are key indicators of reproductive health, with their levels varying throughout the menstrual cycle. FSH a glycoprotein dimer with a half-life of 3–4 hours shows peak value at 0.2–17.2 mIU/mL mid-cycle. LH another glycoprotein hormone with a 20-minute half-life peaks at 21–56.6 mIU/mL mid-cycle.¹⁶

Androgens such as testosterone, dehydroepiandrosterone (DHEA) and dehydroepiandrosterone sulfate (DHEAS) play significant roles in PCOS. The adrenal glands produce about 25% of circulating testosterone and 80% of DHEA while ovaries produce androstenedione and testosterone. Elevated levels of these androgens particularly free testosterone are associated with hyperandrogenism, a hallmark of PCOS.¹⁷ Free testosterone is more indicative of hyperandrogenism compared to total testosterone due to its direct impact on symptoms like hirsutism.

Sex Hormone Binding Globulin (SHBG) regulates the availability of free testosterone in the bloodstream. SHBG levels are often decreased in PCOS with a normal range of 16–120 nmol/L.¹⁸ The Free Androgen Index (FAI) calculated by dividing total testosterone by SHBG is a valuable diagnostic marker for hyperandrogenism. An FAI greater than 10 indicates elevated levels of free testosterone which correlates with PCOS symptoms such as hirsutism and acne.¹⁹ Thus measuring these hormones and indices provides critical insights into diagnosing and managing PCOS effectively.

Transvaginal sonography (TVS) and transabdominal sonography (TAS) are used to diagnose polycystic ovaries with TVS considered the gold standard due to its higher resolution and ability to avoid interference from fatty tissue, making it especially useful for obese patients.²⁰ TVS using a 5 MHz vaginal probe eliminates the need for a full bladder and provides detailed images of the ovaries. Diagnostic criteria for PCOS include the presence of at least 12 follicles each 2–9 mm in diameter and/or an ovarian volume greater than 10 cc. An ultrasound should be conducted outside of the menstrual cycle if a corpus luteal cyst or dominant follicle is present. The presence of either criterion is sufficient for a PCOS diagnosis although the use of oral contraceptive pills can reduce ovarian size and must be considered when interpreting results.²¹

2. Materials and Methods

A cross-sectional study was performed in tertiary care centre to analyse various factors associated with polycystic ovary syndrome in women aged 15–35. Study done over an 18-month period a sample size of 92. Sample size was determined using a formula accounting for a 6% precision error and a 10% non-response rate. Participants selected through simple random sampling were assessed for age, menstrual cycle regularity, dietary patterns, physical activity and various clinical features such as hirsutism, acne and BMI index. Key study variables also include waist-hip ratio, free androgen levels and ultrasound features of polycystic ovarian morphology (PCOM). Inclusion criteria encompassed women with PCOS aged 15–35 and those with a history of infertility. Exclusion criteria ruled out individuals with other causes of hyperandrogenism, pregnant, lactating women, with pre-existing endocrine disorders, hyperprolactinemia and oral contraceptive usage. Data collection involved patient

consent, medical history, systemic and gynecological examinations and biochemical and ultrasound assessments, with subsequent analysis using SPSS-23 software for descriptive statistics and significance testing at a 5% level.

3. Result

In our study done among 92 PCOS women where majority mean age of the PCOS women were 26.45 ± 4.71 years, 38% of PCOS women belong to upper middle class and 44% of PCOS women had completed degree.

Table 1:

| Characteristic | Number | Percentage % |
|--|--------|--------------|
| Between 15 – 20 years age group | 12 | 13.04 |
| Between 21 - 25 years age group | 20 | 21.74 |
| Between 26– 30 years age group | 45 | 48.91 |
| Between 31 – 35 years age group | 15 | 16.30 |
| Upto higher secondary Educational status | 20 | 21.74 |
| Degree | 41 | 44.57 |
| Professional | 31 | 33.70 |
| Lower Socio-economic class | 9 | 9.78 |
| Middle Socio-economic class | 17 | 18.48 |
| Lower middle Socio-economic class | 15 | 16.30 |
| Upper middle | 35 | 38.04 |
| Upper | 16 | 17.39 |
| Regular menstrual cycle | 32 | 34.78 |
| Irregular menstrual cycle | 60 | 65.22 |
| With Acanthosis nigricans | 31 | 33.69 |
| Without Acanthosis nigricans | 61 | 66.31 |
| With Hirsutism | 69 | 75.00 |
| Without Hirsutism | 23 | 25.00 |
| With acne | 66 | 71.74 |
| Without acne | 26 | 28.26 |
| With androgen alopecia | 51 | 55.43 |
| Without androgen alopecia | 41 | 44.57 |
| Normal BMI | 12 | 13.04 |
| Overweight | 40 | 43.48 |
| Obesity | 40 | 43.48 |
| Normal free androgen index | 39 | 42.39 |
| Elevated free androgen index | 53 | 57.61 |

This **Table 1** summarizes the distribution and characteristics of PCOS women in the study, including age,

educational status, socio-economic class, menstrual cycle pattern, presence of acanthosis nigricans, hirsutism, acne, androgen alopecia, BMI, FAI levels, and PCOM features.

Table 2: Comparison between Hirsutism grading and FAI

| Menstrual Cycle | FAI | |
|-----------------|--------|-------|
| | Mean | SD |
| Regular | 1.62 | 11.65 |
| Irregular | 11.71 | 3.62 |
| T value | 15.35 | |
| P value | 0.0001 | |

PCOS women with irregular menstrual cycle had higher FAI mean values (11.71 ± 3.62) than PCOS women with regular cycles 1.62 ± 11.65 as given in **Table 2** which was statistically significant ($p\text{-value } 0.0001 < 0.05$).

Table 3: Comparison between Hirsutism grading and FAI

| Hirsutism grading | FAI | |
|-------------------|-------|------|
| | Mean | SD |
| Mild | 3.58 | 4.59 |
| Moderate | 8.98 | 5.46 |
| Severe | 10.76 | 5.01 |
| X2 value | 5.72 | |
| P value | 0.005 | |

PCOS women with increased severity of Hirsutism had higher FAI mean values (10.76 ± 5.01) were calculated and given in **Table 3** and was statistically significant ($p\text{-value } 0.005 < 0.05$).

Table 4: Comparison between Acne grading and FAI

| Acne Grading | FAI | |
|--------------|-------|------|
| | Mean | SD |
| Mild | 8.08 | 5.9 |
| Moderate | 10.96 | 4.32 |
| Severe | 12.76 | 1.51 |
| Very severe | 15.2 | 0 |
| f value | 3.79 | |
| P value | 0.029 | |

PCOS women with increased severity of Acne had higher mean FAI values (15.2 ± 0) as given in **Table 4** which was ($p\text{-value } 0.029 < 0.05$) statistically significant.

Table 5: Comparison between androgen alopecia grading and FAI

| Androgen Alopecia Grading | FAI | |
|---------------------------|-------|------|
| | Mean | SD |
| Grade I | 3.66 | 4.59 |
| Grade II | 9.34 | 5.08 |
| Grade III | 10.29 | 4.99 |
| f Value | 7.97 | |
| P Value | 0.001 | |

PCOS women with increased severity of androgen alopecia had higher FAI mean values (10.29 ± 4.99) given in **Table 5**. This difference was (p -value $0.001 < 0.05$) statistically significant.

Table 6: Comparison between acanthosis nigricans and FAI

| Acanthosis nigricans | FAI | |
|----------------------|---------|------|
| | Mean | SD |
| Yes | 12.41 | 2.26 |
| No | 6.07 | 5.65 |
| T value | 5.93 | |
| P value | 0.00001 | |

PCOS women with acanthosis nigricans had higher mean FAI value (12.41 ± 2.26) than PCOS women without acanthosis nigricans given in **Table 6**. This difference was (p -value $0.00001 < 0.05$) statistically significant.

Table 7: Comparison between BMI and FAI

| BMI | FAI | |
|-------------|---------|------|
| | Mean | SD |
| Normal | 1.64 | 1.14 |
| Over weight | 6.82 | 5.69 |
| Obesity | 11.56 | 3.96 |
| f Value | 24.58 | |
| P Value | 0.00001 | |

Obese PCOS women had higher mean FAI value (11.56 ± 3.96) than PCOS women with normal weight given in **Table 7**. This difference was (p -value $0.00001 < 0.05$) statistically significant.

4. Discussion

In our study 48% of PCOS women were among age group of 26–30 years. In study conducted by Chitme et al.,²² a sizeable percentage of PCOS women are within reproductive age range between 25 to 30 years and similarly Haq et al.²³ found that the greatest incidence of PCOS was found among those aged 25–29 years, which was similar with our study. About 38.04% PCOS women were in upper middle socio-economic group and 17.39% were in upper socio-economic group, Geatana et al.,²⁴ conducted a study in 2008 concluded that PCOS women among high income are more prone to PCOS than PCOS women with low income.

Zangenah et al.,²⁵ in their study concluded that about 68.24% of PCOS women had irregular cycles similar to our study where 65.22% were having irregular menstrual cycle. Also Shuying Wei et al.,²⁶ in their study concluded that SHBG, FAI has direct influence ($p < 0.01$) on association between obesity and irregular cycles similarly in our study free androgen index of PCOS women with irregular cycle had mean FAI of 11.2 and regular cycle PCOS women had FAI of 1.62.

PCOS women with severe hirsutism and PCOS women mild hirsutism had FAI 10.16 vs 3.58. In a study conducted in 2023 with 256 PCOS women which compared hirsutism by modified F-G score and biochemical androgen levels significant positive correlation was seen with FAI, DHEA, DHEA-S and hirsutism

In the study by Usma et al.,²⁸ they found androgen levels were not correlating with severity of acne. However in our study PCOS women with acne had higher FAI compared to PCOS women without acne (10.5 vs 1.7).

In a study by Pathak et al.,²⁹ it was found that serum testosterone and FAI increased in androgen alopecia, similarly to this study with mean FAI value in PCOS women having androgen alopecia was 12.98

Khan et al.,³⁰ in his study concluded that PCOS adolescent girls with acanthosis nigricans had elevated FAI levels of 10.1 when compared to PCOS adolescent without acanthosis nigricans similar to our study PCOS women with acanthosis nigricans had mean FAI of 12.41.

FAI in overweight PCOS women was lower when compared to obese PCOS women (6.82 vs 11.56). Similarly Abdalla et al.,³¹ in their study in 2021 had mean BMI of 33.3 with mean FAI - 6 concluded that FAI had increased correlation with BMI ($p < 0.005$).

Overall, the study underscores the multifaceted nature of PCOS, where age, socioeconomic status, lifestyle choices, and clinical symptoms intersect with hormonal profiles such as FAI. Our study supports previous studies that free androgen index is robust marker for diagnosis of PCOS as it is found to be elevated with various clinical manifestation of PCOS.

5. Source of Funding

None.

6. Conflict of Interest

None.

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