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Association of Hirsutism and Testosterone Levels in Polycystic Ovary Syndrome (PCOS): A Clinical and Biochemical Correlation

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ABSTRACT
Polycystic ovary syndrome (PCOS) is a common endocrine disorder characterized by hyperandrogenism, ovulatory dysfunction and polycystic ovarian morphology. Hirsutism, one of the most prevalent manifestations of PCOS, is often attributed to elevated androgen levels, particularly testosterone. However, the clinical severity of hirsutism does not always correlate linearly with biochemical markers. To evaluate the association between serum testosterone levels and the severity of hirsutism in women with PCOS. This cross-sectional observational study was conducted over 12 months at a tertiary care hospital. A total of 107 women aged 18-35 years, diagnosed with PCOS based on Rotterdam criteria, were included. Hirsutism was assessed using the modified Ferriman-Gallwey (mFG) scoring system. Serum total and free testosterone, DHEA-S, LH, FSH, fasting insulin and glucose levels were measured. Correlation and regression analyses were conducted to determine the relationship between androgen levels and hirsutism severity. The prevalence of hirsutism (mFG $\geq$8) was 72.9%. There was a significant positive correlation between mFG scores and both total ($r = 0.52$, $p<0.001$) and free testosterone ($r = 0.58$, $p<0.001$). Free testosterone showed the strongest predictive value for hirsutism severity. DHEA-S, BMI and HOMA-IR also showed significant but weaker associations. Hirsutism severity in PCOS correlates significantly with serum testosterone levels, particularly free testosterone. These findings support the clinical relevance of free testosterone as a marker of hyperandrogenism in PCOS and highlight the multifactorial nature of hirsutism.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a multifactorial endocrine disorder affecting 6-20% of women of reproductive age, depending on the diagnostic criteria applied[1]. It is characterized by hyperandrogenism, oligo- or anovulation and polycystic ovarian morphology. Among the various clinical manifestations of PCOS, hirsutism defined as excessive terminal hair growth in androgen-sensitive areas is one of the most common and distressing symptoms, affecting up to 70-80% of women with the condition[2].

Hirsutism in PCOS is primarily attributed to elevated androgen levels, particularly testosterone and dehydroepiandrosterone sulfate (DHEA-S), or to increased peripheral sensitivity to androgens. However, clinical presentation does not always correlate precisely with serum androgen levels, suggesting that factors such as variations in androgen receptor sensitivity, genetic predisposition and insulin resistance may also contribute to hirsutism severity[3]. The modified Ferriman-Gallwey (mFG) score is a widely used tool to quantify the extent of hirsutism, with scores above 8 typically indicating clinical hirsutism[4]. Previous studies have reported varying degrees of correlation between biochemical markers of hyperandrogenism and the severity of hirsutism in PCOS. A study by Escobar-Morreale *et al*.[5] found that although total testosterone and free testosterone were higher in women with hirsutism, the correlation with mFG scores was modest, suggesting that other metabolic and hormonal parameters may influence clinical manifestations. Similarly, Carmina and colleagues reported that women with idiopathic hirsutism often had normal androgen levels, emphasizing the complexity of the relationship between biochemical and clinical hyperandrogenism[6].

Despite the high prevalence of PCOS and its impact on women's health and quality of life, there remains a need for better understanding of the correlation between serum androgen levels and clinical signs such as hirsutism. This is especially relevant in resource-limited settings, where biochemical testing may not always be accessible and clinical evaluation remains a primary diagnostic tool.

Therefore, this study aims to evaluate the association between serum testosterone levels and hirsutism severity in women with PCOS, with a view to strengthening the clinical utility of hormonal markers in the management of hyperandrogenic symptoms. Establishing a clear correlation could improve diagnostic accuracy, guide therapeutic decisions and facilitate more personalized treatment strategies for affected women.

Aim: To evaluate the association between hirsutism and serum testosterone levels in women with polycystic ovary syndrome (PCOS) and assess the impact of hyperandrogenemia on hirsutism severity.

Objectives:

- To assess the prevalence and severity of hirsutism in women diagnosed with PCOS using the modified Ferriman-Gallwey (mFG) scoring system
- To determine the serum total and free testosterone levels in PCOS patients and compare them with non-PCOS controls
- To analyze the correlation between testosterone levels and hirsutism severity

MATERIALS AND METHODS

Study design and setting: This was a cross-sectional, observational study conducted at the Department of Obstetrics and Gynecology in a tertiary care hospital over a period of 12 months. Institutional Ethics Committee approval was obtained prior to commencement of the study. All participants provided written informed consent.

Study population: The study included 107 women diagnosed with Polycystic Ovary Syndrome (PCOS) based on the Rotterdam criteria (2003), which require at least two of the following three features:

- Oligo-or anovulation
- Clinical and/or biochemical signs of hyperandrogenism
- Polycystic ovaries on ultrasound

Women aged between 18 and 35 years presenting with clinical features of PCOS were recruited from outpatient clinics.

Inclusion criteria:

- Women aged 18-35 years
- Diagnosis of PCOS based on Rotterdam criteria
- Not on hormonal therapy for the past 3 months
- Provided informed consent

Exclusion criteria:

- Presence of other endocrine disorders (e.g., Cushing's syndrome, congenital adrenal hyperplasia, thyroid dysfunction, hyperprolactinemia)
- Use of medications affecting androgen levels (e.g., oral contraceptives, steroids, antiandrogens) within the last 3 months
- Known adrenal or ovarian tumors
- Pregnant or lactating women

Clinical assessment: Detailed history including age, menstrual cycle pattern, family history of PCOS and presence of acne or other signs of hyperandrogenism was recorded. Body Mass Index (BMI) was calculated using the formula weight (kg) divided by height (m^2) and values were categorized as per WHO classification.

Hirsutism was assessed using the modified Ferriman-Gallwey (mFG) scoring system. Nine body areas (upper lip, chin, chest, upper back, lower back, upper abdomen, lower abdomen, upper arms and thighs) were examined and a score from 0 to 4 was assigned to each area based on the extent of terminal hair growth. A total mFG score $\geq$8 was considered diagnostic for hirsutism.

Laboratory investigations: Blood samples were collected from all participants during the early follicular phase of the menstrual cycle (days 2-5) or randomly in cases of amenorrhea. Fasting venous blood was drawn in the morning between 8 and 10 am after an overnight fast.

The following hormonal and biochemical parameters were measured:

- Total Testosterone (ng dL^{-1})
- Free Testosterone (pg mL^{-1})
- Dehydroepiandrosterone sulfate (DHEA-S, µg dL^{-1})
- Luteinizing Hormone (LH) and follicle-stimulating hormone (FSH) to calculate the LH/FSH ratio
- Fasting insulin and fasting glucose for calculation of Homeostasis Model Assessment of Insulin Resistance (HOMA-IR):

$$\text{HOMA} - \text{IR} = \frac{\text{Fasting insulin}\,(\mu\text{IU mL}^{-1}) \times \text{fasting glucose}\,(\text{mg dL}^{-1})}{405}$$

Hormone assays were performed using standardized chemiluminescence immunoassay methods. All samples were processed in the hospital's central laboratory adhering to quality control protocols.

Statistical analysis: Data were compiled using Microsoft Excel and analyzed with SPSS software (version 26). Continuous variables were expressed as mean±standard deviation (SD), while categorical data were presented as percentages. Pearson's correlation coefficient was used to evaluate the association between mFG scores and androgen levels. Testosterone levels were categorized into quartiles and analysis of variance (ANOVA) was used to compare mFG scores across these quartiles. Multiple linear regression analysis was conducted to identify independent predictors of hirsutism severity. A p-value of <0.05 was considered statistically significant.

RESULTS AND DISCUSSION

This study explored the association between serum androgen levels and hirsutism severity in women with polycystic ovary syndrome (PCOS). The results indicate a significant positive correlation between serum total and free testosterone levels and the modified Ferriman-Gallwey (mFG) score, with free testosterone showing the strongest predictive value for hirsutism severity. These findings are consistent with the understanding that hyperandrogenemia is a key driver of hirsutism in PCOS but they also underscore the multifactorial nature of this clinical sign.

The prevalence of hirsutism in our cohort was high, consistent with previous studies reporting hirsutism in 60-80% of women with PCOS[7,8]. The mean mFG score increased significantly across quartiles of total testosterone, demonstrating a dose-response relationship. This finding aligns with the work of Yildiz *et al*.[3] who reported a strong correlation between androgen levels and hirsutism severity in PCOS women (Table 1).

Free testosterone emerged as the most reliable biochemical marker associated with hirsutism, showing a stronger correlation than total testosterone. This observation supports the findings of Barth *et al*.[9] who noted that free testosterone, due to its biologically active form, better reflects androgenic activity at the tissue level. Similarly, Carmina and Lobo emphasized that free testosterone has a superior diagnostic value over total testosterone when assessing clinical hyperandrogenism (Table 2)[10].

The correlation between DHEA-S and hirsutism was weaker but statistically significant, in agreement with previous studies suggesting that adrenal androgens contribute to hirsutism, though to a lesser extent than ovarian androgens[11]. Moreover, our results demonstrated a modest but significant association between BMI and hirsutism, supporting evidence that obesity exacerbates hyperandrogenic symptoms by increasing peripheral conversion of androgens and altering sex hormone-binding globulin (SHBG) levels (Table 3).

Insulin resistance, assessed using HOMA-IR, was also associated with hirsutism severity. This supports the concept of insulin acting synergistically with LH to stimulate androgen production in the ovarian theca cells, as described by Dunaif *et al*.[12]. Furthermore, hyperinsulinemia is known to decrease SHBG levels, increasing the bioavailability of free testosterone and contributing to clinical features such as hirsutism[13] (Table 4).

Notably, while the correlation coefficients were statistically significant, they were moderate, suggesting that other factors such as androgen receptor sensitivity, 5α-reductase activity and genetic

Table 1: Baseline characteristics of PCOS patients (n = 107)

Parameters	Mean±SD or n (%)
Age (years)	24.5±5.2
BMI (kg/m²)	28.3±4.7
Overweight/Obese (%)	68 (63.6%)
Menstrual Irregularities (%)	89 (83.2%)
Family History of PCOS (%)	45 (42.1%)
Acne (%)	59 (55.1%)

Table 2: Hormonal profile of PCOS patients

Parameters	Mean±SD	Reference range
Total testosterone (ng dL^{-1})	58.4±18.2	15-70
Free testosterone (pg mL^{-1})	5.9±2.1	0.5-6.4
DHEA-S (µg dL^{-1})	210.5±85.3	35-430
LH/FSH ratio	2.3±0.9	<2
Insulin resistance (HOMA-IR)	3.8±1.5	<2.5

Table 3: Correlation between hirsutism severity (mFG Score) and testosterone levels

Parameters	Pearson correlation (r)	p-value
mFG score vs. Total testosterone	0.52	<0.001
mFG score vs. Free testosterone	0.58	<0.001
mFG score vs. DHEA-S	0.31	0.002
mFG score vs. BMI	0.26	0.008

Table 4: Hirsutism severity based on testosterone quartiles

Testosterone quartiles (Total testosterone)	Mean mFG score±SD	p-value
Q1 (≤40 ng dL^{-1})	7.8±2.1	<0.001
Q2 (41-55 ng dL^{-1})	10.4±3.0	
Q3 (56-70 ng dL^{-1})	13.2±3.5	
Q4 (>70 ng dL^{-1})	16.5±4.2	

Table 5: Multivariate regression analysis of factors associated with hirsutism severity

Predictor variables	Beta coefficient (β)	95% CI	p-value
Total testosterone	0.45	0.30-0.60	<0.001
Free testosterone	0.53	0.38-0.69	<0.001
DHEA-S	0.22	0.10-0.35	0.004
BMI	0.18	0.05-0.32	0.014
HOMA-IR	0.15	0.02-0.28	0.045

predisposition play roles in the development and severity of hirsutism[13]. This explains why some women with elevated testosterone levels may not exhibit marked hirsutism, while others with normal levels may present with significant symptoms (Table 5).

CONCLUSION

This study demonstrates a significant association between serum androgen levels and the severity of hirsutism in women with PCOS. Both total and free testosterone levels showed a positive correlation with mFG scores, with free testosterone emerging as the strongest independent predictor. Additionally, factors such as elevated DHEA-S, increased BMI and insulin resistance also contributed to the severity of hirsutism. These findings emphasize the importance of comprehensive hormonal and metabolic evaluation in women presenting with hirsutism. Early identification and targeted management of hyperandrogenemia and metabolic dysfunction may help in improving clinical outcomes and quality of life in PCOS patients.

REFERENCES

1. Lizneva, D., L. Suturina, W. Walker, S. Brakta, L. Gavrilova-Jordan and R. Azziz, 2016. Criteria, prevalence, and phenotypes of polycystic ovary syndrome. Fertil. Sterility, 106: 6-15.
2. Azziz, R., E. Carmina, D. Dewailly, E. Diamanti-Kandarakis and H.F. Escobar-Morreale *et al*., 2006. Criteria for defining polycystic ovary syndrome as a predominantly hyperandrogenic syndrome: An androgen excess society guideline. J. Clin. Endocrinol. Metab., 91: 4237-4245
3. Yildiz, B.O., S. Bolour, K. Woods, A. Moore and R. Azziz, 2009. Visually scoring hirsutism. Hum. Reprod. Update, 16: 51-64
4. Hatch, R., R.L. Rosenfield, M.H. Kim and D. Tredway, 1981. Hirsutism: Implications, etiology, and management. Am. J. Obstet. Gynecol., 140: 815-830.
5. Escobar-Morreale, H.F., M. Luque-Ramîrez and J.L.S. Millán, 2005. The molecular-genetic basis of functional hyperandrogenism and the polycystic ovary syndrome. Endocr. Rev., 26: 251-282.
6. Carmina, E., F. Rosato, A. Jannì, M. Rizzo and R.A. Longo, 2006. Relative prevalence of different androgen excess disorders in 950 women referred because of clinical hyperandrogenism. J. Clin. Endocrinol. Metab., 91: 2-6.
7. Azziz, R., E. Carmina and D. Dewailly. 2009. Positions statement: Criteria for defining PCOS. FertilSteril., 90: 456-488.
8. Knochenhauer, E.S., T.J. Key, M.M. Kahsar, W. Waggoner, L.R. Boots and R. Azziz, 1998. Prevalence of the polycystic ovary syndrome in unselected black and white women of the southeastern united states: A prospective study[1]. J. Clin. End. Metab., 83: 3078-3082
9. Barth, J.H., E. Yasmin and A.H. Balen, 2007. The diagnosis of polycystic ovary syndrome: The criteria are insufficiently robust for clinical research. Clin. Endocrinol., 67: 811-815.
10. Escobar-Morreale, H.F. and J.L. San Millán, 2007. Abdominal adiposity and the PCOS. Trends Endocrinol Metab, 18: 266-272.
11. Dunaif, A., 1997. Insulin resistance and the polycystic ovary syndrome: Mechanism and implications for pathogenesis. Endocr. Rev., 18: 778-800.
12. Nestler, J.E. and D.J. Jakubowicz, 1996. Decreases in ovarian cytochrome P450c17α activity and serum free testosterone after reduction of insulin secretion in polycystic ovary syndrome. New Engl. J. Med., 335: 4075-4079.
13. Rosenfield, R.L., 2005. Hirsutism. New Engl. J. Med., 353: 2578-2588.