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Correlation of visual (modified Ferriman–Gallwey scoring) and biochemical evaluation of hirsutism in polycystic ovary syndrome patients in a tertiary hospital: A cross-sectional study

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Abstract:

BACKGROUND: Polycystic ovarian syndrome (PCOS) is a common gynecologic endocrine disorder affecting between 2.2% and 26% of the population. It is typically characterized by hirsutism and signs of ovulatory dysfunction. Hirsutism is defined as the presence of excess body or facial terminal hair growth in females, following a male-like pattern. It is diagnosed using visual assessment methods, such as the modified Ferriman–Gallwey (mFG) scoring system, and biochemical tests, including measurements of total testosterone (tT) and the free androgen index (FAI).

OBJECTIVES: The general objective of the study is to identify the correlation of visual scoring with the biochemical evaluation of hirsutism. Specific objectives include (1) to describe the visual and biochemical scores of hirsutism in PCOS patients and (2) to determine a cutoff score for the visual scoring of hirsutism among Filipinos.

METHODOLOGY: This is a cross-sectional study done in a tertiary hospital. Ethical approval was obtained for this study. Patients who satisfied the inclusion criteria were included in the study. Age, height, weight, body mass index (BMI), and OB score were noted. Visual scoring for hirsutism using the mFG scoring system was performed. Blood extraction was done for testosterone and sex hormone-binding globulin tests. FAI was then computed and correlated with the mFG scores.

RESULTS: A total of 52 patients were identified. A positive correlation is noted between the mFG with testosterone and FAI. A positive correlation was also noted between the BMI with testosterone and FAI. An mFG value of >4 is an acceptable cutoff for Filipinos.

CONCLUSION: The study showed as the mFG score increases, FAI and tT levels also increase. It was also noted that as BMI increases, the FAI and tT levels are also expected to increase. It can also be concluded that a lower mFG cutoff value, >4, is applicable for Filipinos.

Keywords:

Hirsutism, hyperandrogenism, polycystic ovary syndrome

Introduction

Polycystic ovarian syndrome (PCOS) is the most common gynecological

endocrinopathy, characterized by a variable presentation of hyperandrogenism and ovulatory dysfunction. Women with PCOS are at increased risk of reproductive

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problems including infertility, endometrial cancer, and also metabolic problems including cardiovascular disease, insulin resistance, type 2 diabetes mellitus, and dyslipidemia.^[1,2] Consequently, PCOS represents a significant public health concern that requires accurate diagnosis to determine the proportion of affected women.

Despite its impact on reproduction and women's health, estimates of its prevalence are limited. Reported prevalence rates of PCOS range from 2.2% to as high as 26%.^[3] The high variability can be attributed to the difficulties in diagnosing the disorder – such as the need for blood tests or ultrasound – and to the heterogeneity in symptom presentation, which leads to disagreements over the diagnostic criteria used to define the condition.^[3] Various criteria have been developed, but existing prevalence estimates have primarily relied on the National Institutes of Health (NIH) criteria (The Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group).^[3]

Several diagnostic criteria for PCOS have been formulated. The NIH diagnostic criteria are based on the consensus that women with PCOS usually present with a combination of chronic oligo- or anovulation (ANOVU) and clinical or biochemical signs of hyperandrogenism, with the exclusion of related disorders.^[2-5] In contrast, the Rotterdam criteria, developed in Rotterdam, The Netherlands, define PCOS by the presence of two or more of the following: (1) oligo/anovulation (ANOVU), (2) clinical or biochemical signs of hyperandrogenism, with the exclusion of related disorders, and (3) the presence of polycystic ovaries (PCOs).^[2-4,6] The 2003 Rotterdam criteria broadened the scope of PCOS diagnosis rather than replacing the previous NIH criteria.^[4] The Androgen Excess Society, on the other hand, emphasizes androgen excess is the central feature of PCOS and should be defined by the presence of hyperandrogenism (clinical and/or biochemical) in combination with ovarian dysfunction (oligo-anovulation and/or PCOs) excluding related disorders from other causes.^[1,2]

Hyperandrogenism can be diagnosed through biochemical and clinical examinations. Azziz *et al.*^[1] noted that elevated circulating androgen levels are observed in approximately 60%–80% of PCOS patients. Biochemical hyperandrogenism (hyperandrogenemia) is defined as an elevation of serum androgen levels, including total testosterone (tT), androstenedione (A4), dehydroepiandrosterone sulfate (DHEAS), and/or free androgen index (FAI), exceeding the 95th percentile of 216 healthy, nonhirsute, eumenorrheic women without PCO.^[7] The specific upper normal limit for tT, A4, DHEAS, and FAI was 54.7 ng/dL (1.9 nmol/L), 2.97 ng/mL (10.4 nmol/L), 3257.4 ng/mL (8840.6 nmol/L), and 4.94, respectively.^[7]

Clinical features of hyperandrogenism include hirsutism, acne, and androgenic alopecia. Hirsutism is the most commonly used clinical diagnostic criterion of androgen excess.^[7] Hirsutism is characterized by excess body or facial terminal (coarse) hair growth in females in a male-like pattern.^[8,9] According to Cook *et al.*,^[9] it affects approximately 5%–8% of the population and is present in up to 70% of PCOS patients.^[10] The most commonly used scoring system for assessing hirsutism was developed by Ferriman and Gallwey in 1961, involving the tabulation of terminal hair growth in various body areas.^[8] The original Ferriman–Gallwey system included 11 body areas, including the lip, chin, chest, upper abdomen, lower abdomen, upper arm, forearm, thigh, lower leg, upper back, and lower back.^[8,9] This scoring system was later modified (modified Ferriman–Gallwey system [mFg]) to include only nine body areas, excluding the forearm and the lower leg. In the mFG, each body area is visually scored on a scale of 0–4.^[8,9] A score of 0 indicates no terminal hair growth, a score of 1 indicates minimal terminal hair growth, a score of 2 indicates more than minimal but less than that of a man, a score of 3 indicates a moderately hairy man, and a score of 4 indicates a typical man.^[8] Total scores of >8 indicate hirsutism, but due to variations in hair follicle density and hair growth rates across races and ethnicities, a cutoff value per race and ethnicity is more appropriate.

Ewing and Rouse^[11] noted that individuals of East Asian origin, such as those from Japan, China, Korea, and Vietnam, are generally less hairy than their Euro-American counterparts, despite having the same level of androgen. Asian descent individuals were found to have fewer scalp hair follicles than Black or White individuals.^[12] A study by Cheewadhanaraks *et al.*,^[13] involving 531 Thai women who underwent annual gynecologic examinations, revealed that 97.8% had an mFG score of 2 or less. Another study by Zhao *et al.*,^[14] involving 623 women from Shandong, China, showed that an mFG score of >2 was observed in 48% of PCOS patients.^[11] Karimah and Hestiantoro^[10] found that in 30 Indonesian women, the cutoff value for mFG is >5. It has also been suggested that an mFG score of 6 is applicable for Japanese women, 3 for Thai women, 8 for Caucasian women, and 10 for Turkish women.^[10] This indicates that a lower cutoff for Asian descent, including Filipinos, is needed for diagnosing hirsutism.

The general objective of this study was to identify the correlation of visual (mFg scoring) and biochemical evaluation of hirsutism in PCO syndrome patients in a tertiary hospital. The specific objectives include: to describe the visual and biochemical scores of hirsutism in PCOS patients and to determine a cutoff score for the visual scoring of hirsutism among Filipinos.

Methodology

This was a cross-sectional study for the correlation of visual (mFG scoring) and biochemical evaluation of hirsutism in PCO syndrome patients in a tertiary.

Ethical approval was obtained for the study from the Research Institute for the Health Sciences Ethics Review Committee.

Patients

Criteria for inclusion of patients to the study were the following: (a) reproductive-aged women and (b) women with any two of the following criteria (Rotterdam criteria): (i) oligomenorrhea, (ii) clinical hyperandrogenism, and (iii) PCOs on ultrasound.

Patients excluded were: (a) pregnant patients; (b) patients who were premenarchal or postmenopausal; (c) patients who had undergone prior hysterectomy, bilateral oophorectomy; (d) patients with Cushing syndrome, hyperprolactinemia, untreated hypothyroidism, congenital adrenal hyperplasia, or androgen-secreting ovarian/adrenal tumor; (e) patients who are taking corticosteroids, antiepileptic, antipsychotic drugs or hormonal contraception; and (f) patients who had undergone hair waxing or shaving <4 weeks from data collection.

The study defines the following terms, operationally as:

- Oligomenorrhea – absence of menstruation for >35 days^[15]
- Amenorrhea – no menstruation for 6 months^[15]
- PCOs on ultrasound (PCO) – an antral follicle count of >12 in 2–9 mm diameter and/or ovarian volume of >10 cm³ at least in a single ovary^[6,7]
- Clinical hyperandrogenism – mFG score >8 with or without acne and/or androgenic alopecia^[6]
- Biochemical hyperandrogenism – patients with FAI of >4.94.^[7]

Sample size estimation

The sample size was calculated using the following formula for one population problem:

$$N_0 = \frac{k^2 pq}{d^2} = \frac{(1.96)^2 \times (0.1) \times (0.52)}{0.05^2} = 79.90 \sim 80$$

where:

$k = 1.96$ – reliability coefficient based on the level of confidence

$P = 0.10$ – According to Ndefo *et al.* (2013),^[16] PCOS affects 5-10% of reproductive age women

$$q = 1 - P$$

d^2 = maximum amount of deviation from true frequency.

However, due to the finite and limited source of population, we can use this formula to reduce the number of sample size:

$$n = \frac{N_0}{1 + \frac{(N_0 - 1)}{N}} = \frac{80}{1 + \frac{(79)}{92}} = 40$$

where:

N_0 = computed sample size

N = diagnosed case of PCOS in UERM outpatient department from 2014 to 2016

Using this formula, the adjusted number of samples needed in this study is 40.

Data collection methods

All diagnosed PCOS patients who satisfied the inclusion criteria were examined. All of them were brought to the OBGYN consultation room to be examined. All patients signed a consent form prior to examination. Age, height, weight, body mass index (BMI), and OB score were also noted for each patient. Visual scoring for hirsutism using the mFG scoring system was performed with 1 senior OBGYN resident present for comparison of results. Each body area was visually scored on a scale of 0–4; 0 indicates no terminal hair growth while a score of 4 indicates full male pattern terminal hair growth. These individuals had their blood extracted. Centrifugation of blood samples and separation of blood serum were done at UERM Laboratory. Serum was then brought to MRL Cybertec Corp. where testosterone and sex hormone-binding globulin (SHBG) tests were done using DRG testosterone enzyme-linked immunosorbent assay (ELISA) and DRG SHBG ELISA kits. Stat Fax 4200 reader, Stat Fax 2600 microplate washer, and Stat Fax 2200 incubator shaker were the machines used during the running of samples. The Stat Fax 4200 reader was calibrated prior to running of samples. FAI was then computed using the formula: tT (nmol/L)/SHBG (nmol/L) \times 100.^[4,17] Values of >4.94 were interpreted as hyperandrogenemia. FAI was used in defining hyperandrogenism because it is the nonprotein-bound fraction which represents the biologically active fraction of testosterone.^[4]

Data processing and analysis

Data were analyzed using Stata version 13 software (Lakeway Drive College Station, Texas, USA). Frequency tables were generated to display the distribution of PCOS

patients by age, BMI, gravidity, parity, mFG scores, level of tT, and SHBG with its corresponding FAI.

To determine the correlation between visual (mFG scores) and biochemical (FAI) evaluations in PCOS patients, Spearman rank-order correlation was used. This method was also applied to assess the correlation between mFG scores and tT levels, as well as between mFG scores and BMI. Pearson product-moment correlation was employed to evaluate the relationship between BMI and tT levels with FAI. $P < 0.05$ was considered statistically significant.

The effectiveness of using the mFG score to correctly identify PCOS patients with and without hirsutism was assessed through measures of validity, including sensitivity, specificity, and likelihood ratios (positive and negative). The optimal mFG cutoff score for this sample of Filipino PCOS patients was determined using the receiver operating characteristic (ROC) curve.

Results

A total of 52 PCOS patients were identified. The mean age was 28 (standard deviation ± 5 years), with ages ranging from 18 to 40 years. Twenty-five percent were overweight, and 42% were obese. The majority were nulligravid and nulliparous. Most had mFG scores below 8. tT levels were >1.9 nmol/L in 69% of cases, while SHBG was <122 nmol/L in 81% of cases. FAI was <4.94 in slightly over 50% of patients [Table 1].

mFG scores were predominantly <8 in all weight categories. FAI was predominantly >4.94 among normal and obese and ≤ 4.94 among underweight and overweight [Table 2].

As mFG scores increased, FAI also increased, but the correlation was very low ($r = 0.0488$) and statistically insignificant ($P = 0.7311$). Similarly, as testosterone levels increased, mFG scores also increased, but the correlation was very low ($r = 0.1124$) and not statistically significant ($P = 0.4276$). The correlation between mFG scores and BMI was negative, indicating that as BMI increased, mFG scores decreased. However, this correlation was also very low ($r = -0.0230$) and not statistically significant ($P = 0.8713$) [Table 3].

As BMI increased, FAI also increased. The correlation, although low ($r = 0.3230$), was statistically significant ($P = 0.0195$) [Table 4]. Testosterone levels also increased with increasing BMI, and the correlation, though low ($r = 0.3502$), was significant ($P = 0.0109$) [Table 4].

Based on Table 5, an mFG score ≥ 4 gave acceptable sensitivity and specificity values. An mFG ≥ 4 identified

44% of PCOS patients to have hirsutism, while an mFG score of <4 identified 74% of patients as not having hirsutism. The cutoff mFG value of 4 correctly classified PCOS patients as having hirsutism or not 59.6% of the time.

There were a minimal increase (1.70) in the likelihood of having hirsutism when the mFG ≥ 4 and a minimal decrease (0.88) in the likelihood of having hirsutism when the mFG <4 [Table 5].

The probability that mFG score would correctly identify hirsutism among PCOS patients was 58%, as shown by the area under the curve. Based on the ROC curve, which follows an almost diagonal path, the mFG score as a measure for correctly identifying hirsutism among PCOS patients may have low discriminatory power [Figure 1].

Discussion

The general objective of this study was to identify the correlation between visual scoring (mFG scoring system) and biochemical evaluation of hirsutism in PCOS patients. Among the 52 identified PCOS patients, only 5 (9.6%) were classified as hirsute using the visual

Table 1: Profile of polycystic ovarian syndrome patients

Characteristics	n (%)
Demographic	
Age (years), mean \pm SD	28.4 \pm 5.1
Median (minimum–maximum)	28 (18–40)
Clinical	
BMI	
Underweight	3 (5.8)
Normal	14 (26.9)
Overweight	13 (25.0)
Obese	22 (42.3)
Gravidity	
0	41 (78.8)
≥ 1	11 (21.2)
Parity	
0	42 (80.8)
≥ 1	10 (19.2)
mFG scores	
<8	47 (90.4)
≥ 8	5 (9.6)
Laboratory	
Total testosterone (nmol/L)	
≤ 1.90	16 (30.8)
>1.90	36 (69.2)
Sex hormone-binding globulin (nmol/L)	
≤ 122	42 (80.8)
>122	10 (19.2)
FAI	
≤ 4.94	27 (51.9)
>4.94	25 (48.1)

FAI: Free androgen index, BMI: Body mass index, SD: Standard deviation, mFG: Modified Ferriman–Gallwey

Table 2: Visual and biochemical evaluation of polycystic ovarian syndrome patients according to body mass index

BMI classification	Visual		Biochemical	
	mFG <8, n (%)	mFG ≥8, n (%)	FAI ≤4.94, n (%)	FAI >4.94, n (%)
Underweight	3 (100)	0	3 (100)	0
Normal	9 (64.3)	5 (35.7)	6 (42.9)	8 (57.1)
Overweight	9 (69.2)	4 (30.8)	8 (61.5)	5 (38.5)
Obese	13 (59.1)	9 (40.9)	10 (45.5)	12 (54.5)

BMI: Body mass index, mFG: Modified Ferriman–Gallwey, FAI: Free androgen index

Table 3: Correlation between modified Ferriman–Gallwey with free androgen index, total testosterone, and body mass index

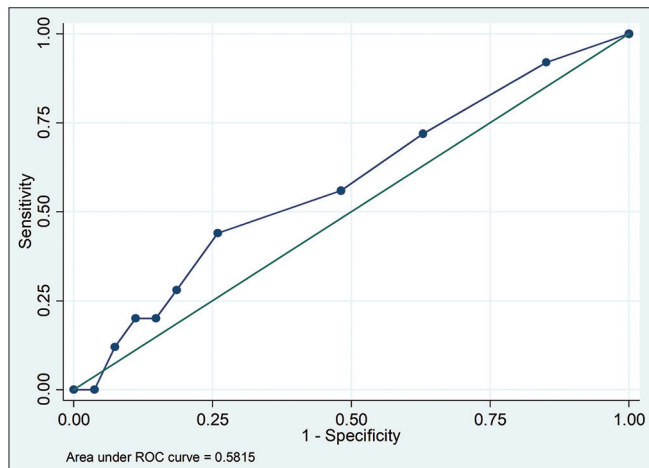
mFG	FAI	Total testosterone	BMI
Correlation coefficient	0.0488	0.1124	−0.0230
P*	0.7311	0.4276	0.8713

*Spearman rank-order correlation. BMI: Body mass index, mFG: Modified Ferriman–Gallwey, FAI: Free androgen index

Table 4: Correlation between body mass index with free androgen index and testosterone

BMI	FAI	Testosterone
Correlation coefficient	0.3230	0.3502
P*	0.0195	0.0109

*Pearson product-moment correlation. BMI: Body mass index, FAI: Free androgen index

**Figure 1:** Receiver operating characteristic curve of mFG score. ROC: Receiver operating characteristic

scoring (mFG scoring system) with a cutoff of 8, in contrast to 25 patients (48.1%) identified as hirsute by FAI and 36 patients (69.2%) by testosterone levels. Positive correlations were observed between FAI and mFG scores, as well as between testosterone levels and mFG scores, but both correlations were statistically insignificant. Similarly, a study by Karimah and Hestiantoro^[10] on 30 Indonesian women with PCOS also showed positive correlations between mFG scores with FAI and testosterone.

PCOS is not only one of the most common endocrine problems among reproductive-aged women but is also highly associated with metabolic problems such as obesity, diabetes mellitus, and metabolic syndrome.^[4,15] Increased body weight is a prevalent feature in PCOS, affecting 50% of patients.^[4] In our sample of 52 patients, 35 (67.31%) were noted to have increased BMI. Although the reasons for the high prevalence of obesity in PCOS patients remain unclear, androgen excess and insulin resistance are considered independent factors contributing to its development.^[4] Obesity can lead to elevated production of insulin-related growth factors due to insulin resistance.^[4] This, in turn, stimulates theca cells to produce larger amounts of androgens and decreases the production of SHBG by the liver.^[4] Lower SHBG levels in circulation result in increased free testosterone, which contributes to hyperandrogenic symptoms and arrested maturation of ovarian follicles, as seen in ultrasounds. This is supported by our data, which revealed a statistically significant positive correlation between BMI with FAI ($r = 0.3230$, $P = 0.0195$) and testosterone levels ($r = 0.3502$, $P = 0.0109$). Hence, caloric restriction, lifestyle modification, and metformin can help restore ovarian function.^[4]

It would be logical to expect that as BMI increases, mFG scores would also increase, given that higher BMI is associated with higher FAIs due to increased tT and lower SHBG. However, our data showed otherwise. We observed a negative correlation between mFG scores and BMI, indicating that as BMI increases, mFG scores decrease. A study by Liou *et al.*^[18] reported that the percentage of hirsutism and/or acne in obese women with PCOS was significantly lower than in nonobese women (odds ratio, 0.6; 95% confidence interval, 0.4–0.9). Few studies have compared the prevalence of hirsutism and/or acne in obese versus nonobese women with PCOS, and results have been inconsistent.^[18] The increased androgen production in obesity might be balanced by an increased androgen clearance rate, leading to less pronounced androgen effects.^[18]

One of the main issues with using the mFG scoring system is the cutoff value, as race, genetics, and other population factors significantly affect hair growth.^[12] Several studies have sought to identify appropriate cutoffs for different races. For instance, a study by Cheewadhanaraks *et al.*^[13] found that 97.8% of Thai women had an mFG score of 2 or less. Another study by Zhao *et al.*^[14] reported that an mFG score >2 was observed in 48% of PCOS patients in China. Karimah and Hestiantoro^[10] found that the cutoff value for Indonesian women was >5. In this study, a lower cutoff mFG value of >4 was found to be acceptable for Filipinos in diagnosing hirsutism, with a sensitivity of 44% and a specificity of 74%. A larger sample size

Table 5: Measures of validity of modified Ferriman–Gallwey score for identifying hirsutism

mFG cutoff scores	Sensitivity (%)	Specificity (%)	Likelihood ratio (+)	Likelihood ratio (–)	Correctly classified (%)
≥ 0	100	0	1.00	0.54	48.1
≥ 1	92	14.8	1.08	0.76	51.9
≥ 2	72	37.0	1.14	0.85	53.9
≥ 3	56	51.9	1.16	0.76	53.9
≥ 4	44	74.0	1.70	0.88	59.6
≥ 5	28	81.5	1.51	0.94	55.8
≥ 6	20	85.2	1.35	0.90	53.9
≥ 7	20	88.9	1.80	0.95	55.8
≥ 9	12	92.6	1.62	1.04	53.9
≥ 11	0	96.3	0	1.0	50.0
>11	0	100			51.9

mFG: Modified Ferriman–Gallwey

could improve the correlation and significance of these findings. Nevertheless, this study contributes to predicting hirsutism and assessing the possibility of elevated testosterone and FAI, leading to better and earlier management.

Conclusion

The study demonstrated a positive correlation between mFG scores and both FAI and tT levels, indicating that as mFG scores increase, FAI and tT levels also increase. In addition, a positive correlation was observed between BMI and both FAI and tT levels, consistent with findings from other studies. This underscores the importance of weight management, lifestyle modifications, and medications like metformin in managing PCOS and restoring ovarian function.

The study also concluded that Filipinos tend to have less body hair compared to other races, such as Caucasians, for whom the universal mFG cutoff of >8 was established. Consequently, an mFG cutoff value of <4 may be more appropriate for predicting hirsutism in Filipinos.

Recommendations

A larger sample size is needed in order to increase the correlation and significance of the study. A multicenter study as well as a regional comparative study can help in validating our results.

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Authorship contributions

Marth Louie Z. Tarroza, MD - Involved in the conceptualization, methodology, resources, data

collection, analysis, interpretation of data, writing of the original draft, review and editing, visualization.

Debby F. Pacquing-Songco, MD - Involved in the conceptualization, methodology, review and editing, supervision, visualization.

Brenda Bernadette B. Zamora, MD - Involved in the conceptualization, methodology, review and editing, visualization.

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Conflicts of interest

There are no conflicts of interest.

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