Correlation of Cutaneous Manifestations with Body Mass Index, Blood Glucose, and Hormonal Levels in Patients with Polycystic Ovarian Disease

Abstract

Background: Polycystic ovarian disease (PCOD) is characterized by oligo/anovulation, ultrasonographic evidence of polycystic ovaries and cutaneous features such as hirsutism, acne, acanthosis nigricans, androgentic alopecia, and signs of virilization. **Aim:** Correlation of dermatological manifestations with body mass index (BMI), blood glucose, and levels of free testosterone, dehydroepiandrosterone sulfate (DHEAS), follicle stimulating hormone (FSH), and luteinizing hormone (LH) in patients of PCOD hailing from Pimpri, Pune. **Subjects and Methods:** This observational study was carried out from November 2015–April 2017 on 102 patients (aged 12–45 years, non-pregnant) of PCOD, attending dermatology/gynecology outpatient departments. After recording socio-demographic/menstrual and medical history, BMI was calculated and examination of cutaneous manifestations were done. Participants were then subjected to pelvic ultrasonography and blood sugar/hormonal estimation. **Statistical Analysis:** By using statistical package for the Social Sciences 17.0 software, Chi-square test, and Fisher's exact test. **Results:** Age: 59.80% belonged to the third decade (range,12–40; mean, 26.27 ± 5.05 years); ultrasonography revealed polycystic ovaries in 79.41%. Cutaneous manifestations recorded were – acne (74.50%); acanthosis nigricans (50%); striae (49.02%); hirsutism (40.19%); acrochordons (36.27%); seborrheic dermatitis (32.35%), and androgenetic alopecia (30.39%). Free testosterone (35;34.31%), DHEAS (9;8.82%), LH and FSH (2;1.96% each), and LH: FSH ratio (51;50%) were raised. Statistical association of acanthosis nigricans emerged with free testosterone *(P = 0.034)*, DHEAS *(P = 0.016)*, fasting blood sugar *(P = 0.01)*, and raised BMI *(P = 0.002)* and of hirsutism with raised DHEAS *(P = 0.016)*, free testosterone *(P = 0.012)*, and BMI *(P = 0.022)*. **Conclusion:** Significant correlations demonstrated were acanthosis nigricans with free testosterone, DHEAS, FBS, and BMI and hirsutism with DHEAS, free testosterone, and BMI.

Keywords: *Acanthosis nigricans, acne, hirsutism, obesity, polycystic ovarian disease*

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Introduction

Polycystic ovarian disease (PCOD), a spectral disorder, can commence as early as puberty and affect as many as 4–10% of women of reproductive age,[1] predisposing them to increased risk of infertility, dysfunctional bleeding, endometrial carcinoma, obesity, type II diabetes mellitus, dyslipidemia, hypertension, and, possibly, cardiovascular diseases.[2] Its diagnostic criteria as per the National Institutes of Health (NIH), USA (1990) are hyperandrogenism and/or hyperandrogenemia along with oligo/anovulation and exclusion of disorders such as late onset congenital adrenal hyperplasia, hyperprolactinemia, Cushing syndrome, idiopathic hirsutism, and androgen secreting tumors.[3] The European Society (ESHRE/ASRM) at Rotterdam (2003) mandates– inclusion of two of the following: oligo- or anovulation, clinical and /or biochemical signs of, hyperandrogenism and ultrasonologic evidence of polycystic ovarian morphology as containing ≥12 follicles measuring 2–9 mm and/or an increased ovarian volume of >10 cm³. Hormonal parameters include elevated serum androgens, particularly testosterone and androstenedione, luteinizing hormone (LH), and normal or decreased follicle stimulating hormone (FSH).[3]

We undertook our study – first such from our tertiary care institute – to correlate the prevailing dermatological manifestations

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with body mass index (BMI), blood sugar, and hormonal levels in patients of polycystic ovary syndrome (PCOS) hailing from the area under the Pimpri-Chinchwad Municipal Corporation, Pune, Maharashtra.

Subjects and Methods

An observational study with 102 women, aged 12–45 years, attending the departments of dermatology/obstetrics and gynecology was conducted.

Inclusion criteria: Patients of reproductive age group who fulfilled the Rotterdam criteria were included in the study. These include:
1. Oligo/anovulation (oligo-ovulation was defined as fewer than nine menstrual periods per year or a cycle duration of at least 45 days; anovulation, as absence of menstruation for three consecutive months during the previous year)
2. Hyperandrogenism (clinical/biochemical):The clinical parameters indicative of hyperandrogenism were acne, hirsutism, androgenic alopecia, and biochemical-raised free testosterone or dehydroepiandrosterone sulfate (DHEAS) levels
3. Policystic ovaries as defined by ultrasonography (containing ≥12 follicles measuring 2–9 mm and/or an increased ovarian volume of >10 cm^3).

Exclusion criteria: Pregnancy or presence of any other endocrinopathy.

Informed consent, sociodemographic information, past medical history, and any previous investigations for the diagnosis of PCOS were recorded. Special emphasis was given to recording menstrual history and dermatological manifestations– such as hirsutism, acne, seborrhea, androgenetic alopecia (AGA), acanthosis nigricans (AN), striae, skin tags, and BMI.

All the patients underwent pelvic ultrasonography and estimation of free testosterone, DHEAS, FSH, LH, thyroid stimulating hormone (TSH), and fasting glucose levels.

Data entered in proforma were analyzed using the Statistical Package for Social Sciences (SPSS) 17.0 software. Chi-square and Fisher's exact tests were used for significance testing in the cross tabulation tables. Statistical significance was determined at P value <0.05.

Results

Majority (61; 59.80%) of our patients belonged to the third decade of life; 20 (19.61%) being from the first half of the fourth (31–35 years) decade.

Polycystic ovaries were detected on ultrasonography in 81 (79.41%) of the cases. Cutaneous manifestations, in descending order, were acne (76; 74.50%), AN (51; 50%), striae (50; 49.02%), hirsutism (41; 40.19%), acrochordons (37; 36.27%), seborrheic dermatitis (33; 32.35%), and AGA (31; 30.39%).

Levels of free testosterone were raised in 35 (34.31%); DHEAS in 9 (8.82%); LH and FSH in 2 (1.96%) each. Exactly half (51) of our study patients had raised LH:FSH ratio.Correlation of cutaneous features and biochemical parameters are enlisted in Table 1.

Acne was most common during the third decade of life (45; 59.21%) and was most commonly (34; 44.74%) of grade II. Raised LH:FSH (40; 52.63%) and free testosterone levels (27; 35.53%) of the study participants were not statistically significant.

Levels of free testosterone in 24 (47.06%; p=0.034) and of DHEAS in 7 (13.73%; p=0.016) among 51 of our study participants with AN were found significantly elevated as was the fasting blood sugar in 10 (19.6%; p=0.01) of the AN patients. Raised BMI (>22.9) present in 43 (84.3%) --32(62.74%) overweight and 11 (21.57%) obese -- of these AN patients was also statistically significant (p=0.002).

Twenty (48.78%) of our 41 patients with hirsutism had raised free testosterone as well as LH:FSH ratio; 7 (17.07%) DHEAS and 29 (70.73%) BMI. Statistically significant associations between hirsutism and levels of DHEAS ($P = 0.016$), free testosterone ($P = 0.012$), and raised BMI ($P = 0.022$) were found.

AGA seen in 31 (30.39%) of our study patients was of the Ludwig grade I in 17 (54.84%) and grade II/III in 7 (22.58%) each. Among them, LH:FSH ratio was found elevated in 13 (41.93%);DHEAS 11 (35.48%), and free testosterone 2 (1.96%) none was, statistically significant. However, statistically significant ($P = 0.043$) rise in TSH levels emerged.

Table 1: Correlation of cutaneous manifestations with raised hormonal levels							
Cutaneous features	No. of patients	FSH	LH	LH:FSH	Free testosterone	DHEAS	BMI
Acne	76	2	2	40	27	6	42
Acanthosis nigricans	51	2	2	22	24	7	43
Striae distensae	50	2	2	23	22	6	40
Hirsutism	41	2	2	20	20	7	29
Acrochordons	37	1	1	19	10	4	24
Seborrheic dermatitis	33	1	1	14	9	4	23
Androgenetic alopecia	31	0	0	13	2	11	17

FSH=Follicle stimulating hormone; LH=Luteinizing hormone; DHEAS=Dehydroepiandrosterone sulfate; BMI=Body mass index

Among the 33 (32.35%) participants with seborrheic dermatitis, 9 (27.27%) had raised free testosterone; 4 (12.12%) each raised DHEAS and TSH; 1 (3.03%) each raised LH and FSH and 14 (42.42%) raised LH:FSH.

Participants with acrochordons (37; 36.27%) revealed raised free testosterone (10, 27.03%); DHEAS (4,10.81%); TSH (2, 5.4%); LH/FSH (1 each, 2.7%), and LH:FSH (19, 51.35%).

Striae distensae were seen in 50 (49.02%) participants, 40 (80%) of whom were obese; however, no correlation with BMI accrued.

Discussion

PCOS, one of the most common endocrine disorders affecting women of reproductive age, is characterized by three fundamental features –hyperandrogenism, chronic anovulation, and ultrasonographic evidence of polycystic ovaries. The main pathophysiology appears to be excess of androgens of ovarian origin, probably due to abnormal regulation of steroidogenesis and disturbed insulin metabolism.[3]

Most (61; 59.80%) of the participants in the relevant studies[4–10]–conducted during the last decade in our country [Table 2], including ours, belonged to the third decade of life. 18.6–55% participants thereof, revealed elevated free testosterone 10.2–65% DHEAS; 6.8–35% LH; 1.7–12.5% FSH, and 8.5–38% LH:FSH [Table 3];[4,7–10] the incidence of raised LH being the lowest and that of LH:FSH, the highest in our study.

The ultrasonographic evidence of polycystic ovaries recorded by Jayaram *et al*.[8] from India (92%) and Liou *et al*.[10] from Taiwan (93%) were higher and that in an Iranian meta-analysis by Jalilian *et al*.[11] (52%), lower than that in our study.

Incidence of menstrual disturbances among the participants of Indian studies has varied widely (33.33–100%);[6,8] ours approximating the intermediate values.[4,9]

Prevalence of obesity among the participants of Indian studies ranged from 32.5[7] to 80%.[9] Majumdar and Singh[5] reported menstrual irregularities among 67.56% (79.2% obese; 44% non-obese) of their study patients. In a large (*n*, 1741) study from London, Balen *et al*.[12] reported prevalence of obesity to be 38.4%; Goldzieher and Axelrod[13] from USA reported it to be a slightly higher (41%) among 600 participants.

Acne the most common cutaneous manifestation in our study, revealed no statistically significant association with any of the hormonal parameters. Among the participants of the previous Indian studies, prevalence of acne has ranged from 20[6] to 67.5%,[7] being higher among the obese than the non-obese participants in one[5] and having a significant association with raised LH levels (*P* = 0.036) in another.[8]

AN was the second most common cutaneous manifestation in our study and it had statistically significant correlation with four parameters i.e., raised free testosterone (*P* = 0.034), fasting blood sugar (*P* = 0.01), raised BMI (*P* = 0.002), and DHEAS (*P* = 0.002), more than any of the earlier Indian studies. Previous studies did report positive correlation of AN with obesity[6,8] and with increased free testosterone and DHEAS.[7]

In our study hirsutism showed statistically significant correlation with three parameters i.e., BMI (*P* = 0.022), raised free testosterone (*P* = 0.012), and raised

Table 2: Prevalence of clinical features in PCOS among Indian studies

Name of the study-year (*n*)	Menstrual irregularities	Obesity	Acne	Acanthosis nigricans	Hirsutism	Androgenetic alopecia	Seborrheic dermatitis
Rajashekar *et al*.[4]- 2008 (1057)	58.94%(623)	48.72%(515)	-	-	-	-	-
Majumdar and Singh[5]- 2009 (450)	67.56%(304)	66.67%(300)	34.67% (156)	-	31.77% (143)	-	-
Ramanand *et al*.[6]- 2013 (120)	100%(120)	75%(90)	20% (24)	44.16% (53)	44.16% (53)	6.66% (8)	-
Gowri *et al*.[7]- 2013 (40)	-	32.5%(13)	67.5% (27)	22.5% (9)	62.5% (25)	30% (12)	52.5% (21)
Jayaram *et al*.[8]- 2016 (87)	33.33%(29)	72.41%(63)	64.3% (56)	47.1% (41)	41.4% (36)	6.9% (6)	1.1% (1)
Keen *et al*.[9]- 2017 (100)	65%(65)	80% (80)	48% (48)	30% (30)	78% (78)	31% (31)	29% (29)
Present study (102)	66.67%(68)	59.8%(61)	74.5% (76)	50% (51)	40.19% (41)	30.38% (31)	32.35% (33)

PCOS=Polycystic ovary syndrome

Table 3: Comparison of hormone levels in Indian studies

Name of the study -year (*n*)	Free testosterone	DHEAS	LH	FSH	LH:FSH
Rajashekar *et al*.[4]- 2008 (1057)	44.64%	65%	17.18%	5.25%	-
Gowri *et al*.[7]-2013 (40)	55% (22)	45% (18)	35% (14)	12.5% (5)	-
Jayaram *et al*.[8]- 2016 (87)	18.6% (11)	10.2% (6)	6.8% (4)	1.7% (1)	8.5% (5)
Keen *et al*.[9]- 2017 (100)	28% (28)	-	16% (16)	3% (3)	38% (38)
Present study (102)	34.31% (35)	8.82% (9)	1.96% (2)	1.96% (2)	50% (51)

FSH=Follicle stimulating hormone; LH=Luteinizing hormone; DHEAS=Dehydroepiandrosterone sulfate; BMI=Body mass index

DHEAS (*P* = 0.016).Among two of the previous Indian studies, prevalence of hirsutism was 78%[9] and 31.77%,[5] of which latter showed association with obesity (obese, 22.44%; non-obese, 9.33%).

Regarding striae, only one previous Indian study reported its prevalence (13%);[9] none mentioning its location and hormone levels in the participants. We recorded these over abdomen in 47 (94%); thighs, 37 (74%); arms, 33 (66%) and raised free testosterone in 22 (44%) and DHEAS in 6 (12%), none of which was statistically significant.

Levels neither of any of the androgens nor LH:FSH were found to be statistically significant. Gowri *et al*.[7] reported increased free testosterone in 12 (30%) of their patientsand Jayaram *et al*.,[8] a significant association *(P* = 0.047) with raised LH levels. Interestingly, in these cases in our study, levels of TSH were found significantly raised.

Among Indian studies the prevalence of seborrheic dermatitis ranged from 1.1–52.5%;[7–9] ours being 32.5%. There was no significant association with hormones, blood glucose, and BMI. Gowri *et al*[7] had reported 21 (52.5%) of their patients with seborrhea associated with raised fasting insulin, free testosterone, and DHEAS.

None of the studies to date, including ours, reveal acrochordons to have a statistical correlation with androgen levels.

Conclusion

The most common cutaneous manifestation in our study was acne and significant correlations were acanthosis nigricans with free testosterone, DHEAS, FBS, and BMI and hirsutism with DHEAS, free testosterone, and BMI.

Limitations

Small size, lack of screening due to financial constraints for fasting free insulin levels, and components of metabolic syndrome are some of the limitations of the present study.

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Conflicts of interest

There are no conflicts of interest.

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