Cutaneous manifestations in polycystic ovarian syndrome: a clinico-epidemiological study

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Abstract

Objective To document various cutaneous manifestations and associated hormonal abnormalities in patients with polycystic ovarian syndrome (PCOS).

Methods This was a cross-sectional study done which included 50 patients of PCOS. After noting the demographic variables, detailed history with particular reference to menstrual irregularity, infertility, family history etc. was taken. Cutaneous examination was done to note the various cutaneous features of PCOS. Relevant laboratory investigations and hormone assays like follicle stimulating hormone, luteinizing hormone, testosterone (free and total), dehydroepiandrostenedione, sex hormone binding protein, insulin, thyroid stimulating hormone and prolactin were done in patients with PCOS on second day of spontaneous menstruation.

Results Mean age of patients in our study was 22.4±2.5 years. Menstrual disturbances were noted in 38 (76%) patients. The most common cutaneous feature noted in our study was acanthosis nigricans, seen in 31 (62%) cases followed by acne vulgaris noted in 26 cases (52%). Most common hormonal abnormality found in our study was elevated fasting insulin levels seen in 28 cases (56%) followed by elevated luteinizing hormone levels (22 cases, 44%).

Conclusion PCOS is fairly common disorder in women of reproductive age group and is associated with various complications if left unrecognized and untreated. Cutaneous features of PCOS are first to manifest clinically and their screening in suspected cases help in early diagnosis.

Key words
PCOS, acanthosis nigricans, acne vulgaris, insulin resistance.

Introduction

In 1935, Stein and Leventhal first described polycystic ovarian disease in a series of 7 women who presented with bilateral polycystic ovaries, amenorrhea, hirsutism and obesity, hence the eponym "Stein-Leventhal syndrome".[1] Later with the uncovering of its association with metabolic disorders like insulin resistance,

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obesity, type II diabetes and altered lipid profile it was named as polycystic ovarian syndrome.[2,3]

Polycystic ovarian syndrome (PCOS) is one of the most common endocrine disorder affecting 5-10% of the women in the reproductive age group.[4] Common features of PCOS are seborrhea, acne, hirsutism, acanthosis nigricans, alopecia and if left unrecognized or untreated it can lead to metabolic, reproductive, psychological and neoplastic complications.[5] Cutaneous changes are one of the earliest manifestations of PCOS, and as the skin is visible and accessible organ in the body, observation of the former can be of extreme

value to the clinician in diagnosing PCOS. The present study was done to document various cutaneous manifestations and associated hormonal abnormalities in patients with PCOS.

Methods

We conducted a cross-sectional study at out patient department of DVL during the period between august 2014 to June 2016 after institutional ethical committee approval. A total 50 cases of PCOS were included in the study after taking an informed consent.

Inclusion criteria of study were non-pregnant women between 15-35 years of age with history of menstrual irregularities, clinical or biochemical evidence of hyperandrogenism, polycystic ovaries as defined by ultrasonography. Patients with conditions associated with hormonal imbalance like hypothyroidism, virilizing tumours of ovary and adrenal gland, late-onset adrenal hyperplasia, Cushing disease and those who were on hormonal medications etc. were excluded

After noting the demographic variables, detailed history in particular reference to menstrual irregularity, infertility, family history, drug history etc. were taken. A thorough general and systemic examination was carried out. Height and weight of each patient were recorded to calculate the body mass index (BMI). Cutaneous examination was done to note the various common features of PCOS like acne, hirsutism, seborrhea, acanthosis nigricans, acrochordons, loss of hair etc.

Presence of various types of acne lesions like comedones, papules, pustules etc. were noted over the body sites like face, trunk and upper arms and grading was done through acne global assessment scale. Major flexures of the body like neck, axilla, groin etc. were examined for

the presence of thick dark velvety skin (acanthosis nigricans). Hair examination was done to note whether there is diffuse thinning of hair (telogen effluvium) or any patterned hair loss (androgenic alopecia). Modified Ferriman-Gallwey (F-G) score was used to assess the hirsutism, patients with score ≥ 8 were considered to have hirsutism.

Ultrasonological diagnosis of PCOS was made when ovary showed 12 or more follicles measuring 2-9mm in diameter or if a total ovarian volume $>10cm^3$. In all cases a tentative diagnosis of PCOS was made based on the history and clinical findings and was confirmed by sonological examination.

Relevant laboratory investigations were done like fasting and postprandial blood glucose levels, fasting lipid profile, hormone assays like follicle stimulating hormone (FSH), luteinizing hormone (LH), testosterone free and total, dehydroepiandrostenedione (DHEA-S), sex hormone-binding protein, insulin, thyroid stimulating hormone (TSH) and prolactin were done in patients with PCOS on second day of spontaneous menstruation.

Statistical analysis of the data was done using appropriate statistical methods using the Statistical Package for Social Sciences (SPPS).

Results

The present study comprised of 50 patients with PCOS. Majority of them (23 patients, 46%) were between the age group 21-25 years. The youngest age noted in the study was 13 years and oldest was 33 years with mean age being 22.4±2.5 years.

Mean age of menarche in our patient was 12.8±0.8 years. Menstrual disturbances were noted in 38 (76%) patients and 12 (24%)

patients had normal menstrual cycles. The most common menstrual disturbance noted was oligomenorrhea, seen in 32 (64%) patients and 6 (12%) patients had amenorrhea.

Among the 50 patients, 28 (56%) were married and 22 (44%) were unmarried. Among the married patients, obstetric history was normal in 22 (44%) patients whereas in 8 (16%) patients there was history of infertility. 20 (40%) patients had family history of PCOS. Around 31 (62%) patients were obese and 9 (18%) patients were overweight, remaining patients had normal weight. Type II diabetes was noted in 6 (12%) cases and altered lipid profile in 4 (8%) cases.

The most common cutaneous feature noted in our study was acanthosis nigricans, seen in 31 (62%) cases followed by acne vulgaris noted in 26 (52%) cases. Least common was alopecia noted in 4 (7%) patients, details given in **Table 1**.

Out of the 26 cases of acne vulgaris, majority (12 cases, 24%) had grade II acne vulgaris and grade IV was noted in only 3 cases (6%), details given in **Table 2**.

Among the patients with acanthosis nigricans (31 cases, 62%), neck was the most common site involved (30 cases, 60%) and least common site was intermammary and submammary region (2 cases, 4%), **Table 3**. Among the patients with alopecia (7 cases, 14%), androgenic alopecia was found in 3 (6%) patients and remaining 4 (8%) had telogen effluvium.

Most common hormonal abnormality found in our study was elevated fasting insulin levels, seen in 28 cases (56%) followed by elevated LH levels (22 cases, 44%), details given in **Table 4**.

Table 1 Prevalence of cutaneous manifestations in patients with polycystic ovarian syndrome (n=50).

Cutaneous manifestation	N (%)
Acanthosis nigricans	31 (62)
Acne vulgaris	26 (52)
Hirsutism	21 (42)
Acrochordons	17 (34)
Striae distensae	10 (20)
Androgenetic alopecia	4 (8)

Table 2 Grading of acne vulgaris using Global assessment scale among patients with polycystic ovarian syndrome (n=50).

Grading	N (%)
Grade I	7 (14)
Grade II	12 (24)
Grade III	4 (8)
Grade IV	3 (6)

Table 3 Acanthosis nigricans at different body areas in patients with polycystic ovarian syndrome (n=50).

Sites	N (%)
Neck	30 (60)
Axillae	28 (56)
Intermammary and submammary area	2 (4)
Groins and inner thighs	7 (14)

Table 4 Prevalence of cutaneous manifestations in patients with polycystic ovarian syndrome (n=50).

Increased hormonal levels	N (%)
Fasting insulin level	28 (56)
Luteinizing hormone	22 (44)
Testosterone	18 (36)
Dehydroepiandrostenedione	12 (24)
Thyroid stimulating hormone	4 (8)
Follicle stimulating hormone	2 (4)
Prolactin	2 (4)

Discussion

PCOS is an anovulatory disorder with diverse manifestations. It can be completely asymptomatic on one hand and on the other hand it can be associated with severe manifestations like infertility, metabolic disorder, myocardial infarction and even neoplasia. Several factors have been identified to play a role in the etiopathogenesis of PCOS, among them genetic, androgen excess and insulin metabolism play a key role.[6] Women

with PCOS have raised LH levels which may be due to increased pulse frequency of hypothalamic gonadotropic hormone (GnRH) or low levels of progesterone resulting from oligo- or anovulation.[7,8] Altered FSH to LH ratio stimulate the ovarian theca cells to produce androstenedione. Insulin also plays key role in hyperandrogenemia by stimulating the theca cell androgen production and also by decreasing the sex hormone binding globulin production by the liver.[9-11]

The resulting hyperandrogenemia clinically manifests as acne, hirsutism, seborrhea etc. Both PCOS and metabolic syndrome share pathophysiological spectrum like insulin resistance and androgen excess which can explain obesity, type II diabetes, lipid abnormalities seen in patients with PCOS.[12-14] PCOS is characterized by oligo- or anovulation which is responsible for infertility. Continuous stimulation of endometrium by estrogen results in endometrial hyperplasia and eventually endometrial carcinoma.[15]

The mean age of the patients in our study was was comparable with the studies carried out by Sharma *et al*.[16] Majumdar and Singh.[17]

Acne in patients with PCOS is often refractory to the treatment and even if they respond, recurrence is quiet common soon after stopping the therapy. In the present study acne vulgaris was observed in 52% of the patients which was similar to the study by Keen*et al*.[18] (48%), whereas in Conway *et al*.[19] reported lower prevalence (24%).

Acanthosis nigricans is defined as the presence of thick dark velvety skin in the major flexures of the body like neck, axilla, groin and other frictional areas. High levels of insulin acting through insulin-like growth factor receptors in the epidermis are responsible for this cutaneous change. In the present study, 61% of the patients showed acanthosis nigricans and most common site was neck followed by axillae. Prevalence of acanthosis nigricans was higher in the study by Sharquie *et al*.[20] (68%) and lower in that by Curth[21] (55%) compared to our study. This difference in prevalence can be due to association of acanthosis nigricans with multiple genetic variants, diabetes, obesity etc.

Prevalence of hirsutism in our study was 42%. Studies by Conway and Jacobs[19] and Saxena *et al*.[22] reported higher prevalence of hirsutism among PCOS patients (61% and 89%, respectively) than our study. This difference can be due to variation in race and ethnicity of study population and also difference in criteria used for defining the hirsutism.

Prevalence of seborrhea in our study was 53%, whereas Keen *et al*.[18] reported a lower figure (29%). This difference may be due to evaluation in a parametric manner, ideally sebometer should be employed for the metric measurement.

In our study alopecia was observed in 14% of the patients, with female pattern baldness accounting for 6%. Keen *et al*.[18] reported somewhat higher prevalence (39%).

Most common hormonal abnormality found in our study was elevated fasting insulin levels seen in 28 (56%) cases. Most common hormonal abnormality noted in Gowris *et al*.[23] study was also elevated insulin level but percentage was higher than our study (67.5%).

Conclusion

Most common cutaneous feature noted in our study was acanthosis nigricans and most common hormonal abnormality noted was elevated fasting insulin levels. PCOS is fairly common disorder in women of reproductive age

group and is associated with various complications if left unrecognized and untreated. Cutaneous features of PCOS are first to manifest clinically and their screening in suspected cases help in early diagnosis.

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