CUTANEOUS MANIFESTATIONS OF POLYCYSTIC OVARIAN DISEASE

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ABSTRACT

BACKGROUND

Polycystic ovarian disease (PCOD) is an ill-defined heterogeneous condition with a complex pathophysiology and is one of the commonest endocrine/metabolic disorders, affecting 6 - 10% of women in their reproductive age. Polycystic ovarian disease is the most common endocrine cause of hirsutism, acne and androgenic alopecia.

MATERIALS AND METHODS

Informed oral consent was obtained from all subjects after explanation of the nature and purpose of the study. A special case proforma was prepared to record the demographic data, complaints, history, clinical examination and results of investigations. A detailed history regarding menstrual irregularities, reproductive function, hirsutism, acne, androgenic alopecia, acanthosis nigricans, acrochordons, seborrhoea and other skin changes. Patients were also enquired about use of cosmetics, hoarseness of voice, headache, milky discharge from breast, mass over anterior neck, weight gain, diet, exercise, use of any medications or other forms of treatment, any stress/illness, history of diabetes mellitus, hypertension and coronary artery disease. Family history of polycystic ovarian disease, diabetes mellitus, hypertension, coronary artery disease, metabolic syndrome and cancers was also taken. Menstrual and obstetric history and any medical or surgical illness was recorded. Other causes of acne, hirsutism and alopecia were excluded by appropriate history and examination. All subjects underwent a detailed clinical examination with special reference to the following parameters: Hirsutism scoring was done using modified Ferriman-Gallwey (mFG score) and it was classified as mild (mFG score 9 - 16), moderate (mFG score 17 - 25) and severe (mFG score 26 - 36). Acne was graded as done by Indian authors using a simple grading system, which classifies acne vulgaris into four grades. Androgenic alopecia was looked for and graded as per Sinclair scale. It was also further classified as Ludwig type, Norwood Hamilton type and Olsen type. Acanthosis nigricans was looked for at multiple sites as neck, axilla, submammary area, intermammary areas, groins, elbows, knees, knuckles, dorsum of feet, cubital and popliteal fossa, periumbilical area, face-lips and eyelids. Other causes of the above symptoms and signs were excluded. Entire skin, hair, nails and mucosae were examined for any abnormality. Genitals were checked for any clitoromegaly or vulvar acanthosis. Galactorrhoea and thyroid fullness was looked for.

RESULTS

The peak incidence of polycystic ovarian disease was seen in patients with age group of 21 - 25 years followed by 26 - 30 years. Among the dermatologic and gynaecological complaints, hirsutism, i.e. a cutaneous manifestation was the most common, seen in upto 84% of the women and showed varying severity. The mean Ferriman-Gallwey score was 16.8 +/- 5.39. Hirsutism was most commonly found over the upper lip and lower abdomen followed by thighs, upper abdomen and lower back, chest and upper back, chin and upper arms. Acne was seen in 70% of the patients. Grade II severity acne was the most common presentation followed by Grades III, I and IV respectively. The most common site was face followed by neck, back, upper arms and front of chest. Androgenic alopecia was seen in 32% of the women. The most common clinical type was Ludwig followed by Olsen and Norwood Hamilton type. As per Sinclair scale, grade II severity androgenic alopecia was most common. Acanthosis nigricans was seen in 56% of the patients. The most common site was nape of the neck followed by axilla, groin and submammary areas. The SAHA syndrome, i.e. the combination of seborrhoea, acne, hirsutism and androgenic alopecia was seen in 3 patients. Acrochordons were seen in 32% and seborrhoea was found in 30%. Common gynaecological complaints were oligomenorrhea [62%] and amenorrhea [12%]. Married women commonly presented with infertility [68%]. Significant proportions of our patients had increased BMI and were overweight or obese. Many of them also had central obesity with increased waist circumference and waist-hip ratio. A family history of polycystic ovarian disease was observed in many of the women, either in the mother or siblings, indicating a genetic predisposition to polycystic ovarian disease. Though most of the patients did not have diabetes mellitus, hypertension or coronary artery disease at the time of presentation, many of them had a family history of the same, indicating a predisposition to metabolic syndrome. Among the biochemical assays, though total testosterone was raised in only 6%, free testosterone was raised in 32%, indicating decreased SHBG levels. LH:FSH ratio was raised in 18% and serum prolactin was high in 20% of the women. Ultrasonography detected polycystic ovaries in 96% of the polycystic ovarian disease patients.

CONCLUSION

Polycystic ovarian disease is the most common chronic debilitating endocrinopathy of women in the reproductive age group with long-term health consequences. Dermatological problems like hirsutism, acne, androgenic alopecia, acanthosis nigricans and seborrhoea may serve as markers for identifying the polycystic ovarian disease syndrome, which may otherwise be resistant to routine treatments. Further studies are required to assess the grading of severity of these symptoms in PCOS patients, which may help to establish the severity of the syndrome. Also, these may serve as markers for patients at risk of developing metabolic syndrome. Early recognition of this disorder gives a chance to reverse the symptoms and signs associated with the disease, while correcting the metabolic abnormalities that may pose a significant health risk for untreated individuals and improving the physical, social and mental well-being of the patient. Early recognition also provides a chance for lifestyle modification [i.e. a comprehensive program of diet, exercise and behavioural therapy] that improves insulin resistance, dermatological complaints, menstrual

irregularities, fertility and also decreases long-term health risks. However, more research in the genetic and environmental factors is needed to underscore preventive strategies in future in families with polycystic ovarian disease.

KEY WORDS
Polycystic Ovarian Disease, Acne, Hirsutism, Androgenic Alopecia.

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BACKGROUND

Polycystic ovarian disease (PCOD) is one of the commonest endocrine metabolic disorders affecting 6 - 10% of women in their reproductive age.[1] Polycystic ovarian disease is characterised by anovulation and hyperandrogenism. Genetic predisposition coupled with lifestyle changes in the modern era play the key role to result in hyperinsulinaemia, polycystic ovarian disease and hyperandrogenism.[2] In PCOD, basic defect is androgen excess and ovary is the primary site for androgen production.[3] Polycystic ovarian disease is the most common endocrine cause of hirsutism, acne and androgenic alopecia.[4] Since an initial report in 1980, progress in characterising the relationship between insulin resistance and polycystic ovarian disease has been substantial.[5] Women with polycystic ovarian disease are both insulin resistant and hyperinsulinaemic in relation to weight matched controls.[6] Insulin resistance is defined as reduced glucose response to a given amount of insulin,[7] while chronic hyperinsulinaemia represents a compensatory response to target tissue problem.[8] Insulin resistance is implicated in the pathophysiology of polycystic ovarian disease leading to hyperandrogenism and anovulation.[9] Insulin resistance has genetic predisposition with complex heritage. Mechanism is mainly post-receptor failure.[10] Insulin resistance is responsible for gynaecological and dermatological symptoms as well as metabolic manifestations like hypertension, dyslipidaemia, obesity and type II diabetes mellitus.[11] Treatment of polycystic ovarian disease varies widely according to symptoms.[12] South Asian women with polycystic ovarian disease are more likely to suffer from insulin resistance compared to Caucasians and have lower sex hormone binding globulin [SHBG] levels.[13] It is important to recognise girls and young women at risk for polycystic ovarian disease, as early intervention may prevent long-term sequelae and improve quality of life.[14]

Objective of Study

To study the incidence of cutaneous manifestations like hirsutism, acne vulgaris, androgenic alopecia, acanthosis nigricans and other dermatological disorders in patients with PCOD.

MATERIALS AND METHODS

Study Centre

This study was undertaken in the Department of Dermatology, Venereology and Leprosy at Gandhi Hospital, Secunderabad.

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Study Period

This study was conducted from December 2014 to June 2016.

Sample Size

Fifty cases of polycystic ovarian disease.

Inclusion Criteria

Patients in reproductive age group, both married and unmarried, who were diagnosed to have polycystic ovarian disease.

Exclusion Criteria

Patients with the following conditions are excluded from our study-

- Hypothyroidism.
- Prolactinoma.
- Cushing's syndrome.
- Congenital adrenal hyperplasia.
- Adrenal tumours.
- Hypothalamic amenorrhoea.
- Premature ovarian failure.
- Pregnant women.

Methods

This is a descriptive study. Informed oral consent was obtained from all subjects after explanation of the nature and purpose of the study. A detailed history regarding menstrual irregularities, reproductive function, hirsutism, acne, androgenic alopecia, acanthosis nigricans, acrochordons, seborrhoea and other skin changes. Patients were also enquired about use of cosmetics, hoarseness of voice, headache, milky discharge from breast, mass over anterior neck, weight gain, diet, exercise, use of any medications or other forms of treatment, any stress/ illness, history of diabetes mellitus, hypertension and coronary artery disease. Family history of polycystic ovarian disease, diabetes mellitus, hypertension, coronary artery disease, metabolic syndrome and cancers was also taken. Menstrual and obstetric history and any medical or surgical illness was recorded. Other causes of acne, hirsutism and alopecia were excluded by appropriate history and examination.

Vitals

(Pulse, blood pressure, temperature, respiratory rate) were recorded.

Routine Investigations

Included complete blood picture, complete urine examination, erythrocyte sedimentation rate, blood urea, serum creatinine and serum bilirubin.

Biochemical and Hormonal Assays

Included oral GTT, total and free testosterone, LH, FSH, TSH and prolactin.

Ultrasonography
Done to diagnose polycystic ovaries.

RESULTS
The study was carried from December 2014 to June 2016. The study was carried out on patients who were diagnosed as polycystic ovarian disease. A total of 50 polycystic ovarian disease cases were studied.

Age Distribution	Number of Patients	Percentage
15-20	**12**	**24%**
21-25	**18**	**36%**
26-30	**17**	**34%**
31-35	**2**	**4%**
36-40	**1**	**2%**
Table 1. Age distribution of Patients		

Secondary	9	22%

Dermatological Manifestations

	No. of Patients	Percentage
Nil or ≤ 7	8	16%
8-16 [mild]	23	46%
17-25 [moderate]	14	28%
≥ 26 [severe]	5	10%
Table 2. Hirsutism Score		

	No. of Patients	Percentage
Normal	15	30%
Acne	35	70%
Table 3. Prevalence of Acne Vulgaris in PCOD		

	No. of Patients	Percentage
Present	16	32%
Absent	34	68%
Table 4. Prevalence of Androgenic Alopecia in PCOD		

	No. of Patients	Percentage
Present	28	56%
Absent	22	44%
Table 5. Prevalence of Acanthosis Nigricans in PCOD		

	No. of Patients	Percentage
SAHA syndrome	3	6%
Acrochordons	16	32%
Seborrhoea	15	30%
Pityriasis capitis	17	34%
Telogen effluvium	12	24%
Table 6. Other Dermatological Findings		

	No. of Patients	Percentage
None	29	58%
Sibling	12	24%
Maternal	9	18%
Table 7. Family History of PCOD		

Condition	No. of Patients	Percentage
Impaired glucose tolerance	5	10%
Diabetes	0	0%
Hypertension	2	4%
Coronary artery disease	0	0%
Cancers	0	0%
Table 8. Associated Medical Conditions		

Biochemical Abnormalities

	No. of Patients showing Elevated Levels	Percentage
Free testosterone	16	32%
Total testosterone	3	6%
Table 9. Elevated Levels of Testosterone in Patients		

	No. of Patients	Percentage
≥ 3	9	18%
< 3	41	82%
Table 10. LH/FSH Ratio		

	No. of Patients	Percentage
≥ 24	10	20%
<24	40	80%
Table 11. Serum Prolactin (ng/mL)		

	No. of Patients	Percentage
Present	48	96%
Absent	2	4%
Table 12. Ultrasound Features of PCOD		

DISCUSSION
Polycystic ovarian disease is the most common reproductive disorder in women of child bearing age and has a prevalence of 6 to 10%.[1] There are ethnic and racial differences in clinical and biochemical features of polycystic ovarian disease.[2]

Hirsutism was noted in 84% cases in our study. Overall, the presence of hirsutism is a strong indicator of androgen excess (e.g. polycystic ovarian disease) with over 85% of hirsute women demonstrating some form of hyperandrogenism.[11]

In our study, the mean hirsutism score calculated using the modified Ferriman-Gallwey score was 16.81 +/- 5.39. This is comparable and slightly higher than other studies by Espinos et al and Panadis et al,[15,16] wherein the mean scoring of the hirsutism in the patients with polycystic ovarian disease was 12.0 +/- 4.4 and 8.2 +/- 4.6. In our study, acne vulgaris was present in 70% of the patients. This was comparable with Balen et al and Rosenfield's study who reported an incidence of acne as 66.2% and 70% respectively.[6,17] Our value was slightly higher than the studies by Sivayoganathan et al and Ozdemir S et al, wherein both these studies showed the prevalence of acne to be 53% among polycystic ovarian disease patients.[18,19]

Most of the patients in our study had grade 2 acne [54%] followed by grade 3 [20%], grade 1 [17%] and grade 4 [8.57%]. Polycystic ovarian disease is an important contributing factor in females with resistant acne vulgaris.[20] Androgenic alopecia was present in 32% of the

cases in our study. This lies in between the prevalence values of Sivayoganathan et al (16%), Kala K et al (17%) and Ozdemir S et al (34.8%).[5,18,19]

In the study by Cela E et al 67% of women with androgenic alopecia had polycystic ovarian disease, while only 27% women among the control group had polycystic ovarian disease. They also reported that the prevalence of polycystic ovarian disease was significantly higher in women with alopecia than in the control population.[21]

Acanthosis nigricans was found in 56% in our study with predominance in the neck region. This was higher compared to other studies done by Sivayoganathan et al (23%) and Ozdemir S et al (5.2%).[18,19] Hud et al reported a prevalence of acanthosis nigricans in adult obese patients has been estimated to be 74%.

Seborrhea was present in 30% of the cases. This is similar to the findings in Ozdemir S et al who found seborrhea in 34.8% of the polycystic ovarian disease patients.[19]

Acrochordons were noted in 32% of the patients in our study. As per Kala K et al, acrochordons were noted in 16% of the patients.[5]

SAHA syndrome is characterised by the tetrad: seborrhea, acne, hirsutism and androgenic alopecia. In our study, the SAHA syndrome was seen in 6% of the patients. In contrast in the study done by Dalamaga et al, it was reported to be found in 17% of the patients.[22]

In our study, 42% had family history of polycystic ovarian disease in mother or siblings. Based on the clustering of cases in families, polycystic ovarian disease is considered to be a heritable disorder.[23,24]

Impaired glucose tolerance was found in 10% of the women in our study. This finding is slightly lower than the study by Carmina E, wherein it was observed that the prevalence of altered glucose tolerance ranges between 20 and 35% in young women with polycystic ovary syndrome and this predisposes the patients to an increased risk for type II diabetes and cardiovascular diseases later in life.[25]

Moving from the young fertile age to the menopausal age, the prevalence of type II diabetes continues to increase and may reach 10 - 16% of polycystic ovarian disease women.[8]

Our study had shown 4% incidence of hypertension in study subjects, which signifies early onset of metabolic syndrome in polycystic ovarian disease group.[26]

In our study, 32% of study population had increased free testosterone levels. This signifies decreased SHBG levels, which can be considered as a surrogate marker of insulin resistance. Livadas S et al in their study reported elevated free testosterone in 17.2% of the patients with polycystic ovarian disease.[27]

About 20% of study subjects had LH/FSH ≥ 3. An increase in LH pulse frequency explains this increase in the LH/FSH ratio.[28]

In our study 20% of our study population had raised serum prolactin levels, which is comparable to other studies.[29] Patients with polycystic ovarian disease, administration of bromocriptine has reduced LH levels and restored ovulatory function.[30]

CONCLUSION

Dermatological problems like hirsutism, acne, androgenic alopecia, acanthosis nigricans and seborrhoea may serve as markers for identifying the polycystic ovarian diseases.

However, more research in genetic and environmental factors is needed to underscore preventive strategies in future in families with polycystic ovarian disease.

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