

Polycystic ovarian syndrome in women with acne

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Abstract *Background* Acne is a common manifestation of hyperandrogenemia. Polycystic ovarian syndrome (PCOS) is a common endocrine abnormality affecting reproductive aged women. In the female, the most common cause of hyperandrogenemia is PCOS. The purpose of our study was to determine the PCOS in women with acne.

Patients and methods In this observational, cross sectional study, 40 females, aged 15-40 years, with various degree of acne who had not received hormonal treatment, including hormonal contraceptive and antiandrogen therapy, for at least 3 months prior to study and 30 female volunteers (aged 15-40 years) without acne or acne scars were enrolled as controls. The severity of acne was graded as mild, moderate or severe. Clinical data including age, weight, height, body mass index (BMI), menstrual history and androgenic sign (hirsutism, alopecia, acanthosis nigricans) were recorded and hormonal assays and pelvic ultrasonography were done. Clinical parameters (acne with menstrual irregularity) accompanied by other features of hyperandrogenism and/or elevated level of luteinizing hormone (LH) to follicle-stimulating hormone (FSH) ratio and/or ultrasound picture based upon the presence of multiple small subcapsular cysts (diameter 2-8 mm) with dense echogenic stroma, were used to diagnose PCOS.

Results 7.5% patients were obese in case group, which was statistically significant. No statistically significant differences were observed in hormonal profiles (serum LH and serum FSH) but significant differences seen in serum testosterone level and pelvic ultrasound to visualize the polycystic ovary in women with acne. There were 11 (27.5%) women with PCOS among the 40 women with acne; 8 showed PCO picture on ultrasound. 10 cases with elevated LH to FSH ratio. Out of 11 women with PCOS, 1 case was diagnosed only clinically. Control group had also one PCOS (3.3%). Prevalence of PCOS with acne was higher in studied cases than control group, which is statistically significant in our population.

Conclusion All women with acne should be considered for underlying PCOS and asked about their menstrual patterns and examined for other sign of hyperandrogenism. Those who have menstrual disturbances should have hormonal profile determination as well as pelvic ultrasonography for ovarian visualization. Early diagnoses and treatment can avoid the possible complications.

Key words

Acne, hyperandrogenemia, polycystic ovarian syndrome.

Introduction

Acne is a chronic inflammatory disease of pilosebaceous units. Acne vulgaris remains one of the most common conditions affecting adolescents. The pathogenesis of acne is multifactorial and complex.¹ There are four major factors in etiology of acne are seborrhea,

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comedo formation, colonization of sebaceous duct with *Propionibacterium acnes* and inflammation. Seborrhea or increased sebaceous gland activity, dependent on androgenic sex hormone mainly of adrenal or ovarian origin.²

Classic acne vulgaris is usually gradual in onset but an abrupt onset of acne should be further questioned to explore an underlying etiology. Hyperandrogenism should be considered in the female acne patient whose acne is severe, sudden in onset, or associated with hirsutism or irregular menstrual periods. In general laboratory workup is not indicated unless hyperandrogenism is suspected.³ An appropriate, thorough history and physical examination will identify evidence of androgen excess. Laboratory screening for hormonal abnormalities is imperative when clinical signs of hyperandrogenism are present.⁴ Androgen levels in patients with acne are higher than those in controls. Acne is a clinical manifestation of some endocrine diseases.

The polycystic ovary syndrome (PCOS) has the highest prevalence in acne.⁵ The PCOS is a heterogeneous condition which is defined by the presence of two out of the three criteria: oligo- and/or anovulation, hyperandrogenism (clinical and/or biochemical), polycystic ovaries (with the exclusion of other etiology).⁶ The pathogenesis of PCOS is unknown. However it is a complex multigenetic disorder characterized by abnormal gonadotropin release and dysregulation of steroidogenesis. It is a combination of genetic abnormalities combined with environmental factor, such as nutrition and body weight, which then affect the expression of syndrome.⁶ The clinical definition of PCOS changed in recent years and includes one of its cardinal criteria, the dermatological manifestation of hyperandrogenism chiefly acne vulgaris, hirsutism, alopecia and acanthosis. Any one of

these dermatological features may provide early clinical clues to recognition of PCOS. If the condition is unrecognized or untreated, the patient faces increased risk of reproductive, metabolic, cardiovascular, psychological and neoplastic sequelae.⁷ It is one of the most common causes of anovulatory infertility.⁸ Acne is a common manifestation of hyperandrogenemia.⁹ Therefore, acne may not pose only cosmetic concern, but may also be sign of underlying disease. In females, the most common cause of hyperandrogenemia is PCOS. Therefore, all women presenting with acne should be considered for underlying PCOS and asked about their menstrual pattern. Those who have menstrual disturbance should have hormonal profile, pelvic ultrasound which will help early diagnosis of PCOS. However, confirmation of diagnosis and provision of detailed information to the affected women together with the availability of interdisciplinary treatment help to improving PCOS-related symptoms and avoid its possible consequences. It may help in the better management of acne and to reduce their psychological distress.

Patients and methods

This was a hospital-based, observational, cross-sectional study which was carried out in the out-patient Department of Dermatology and Venereology of Dhaka Medical College Hospital (DMCH), Dhaka from November 2007 to October 2008 over a period of 12 months. A total of 70 females, 40 female patients with various degree of acne and 30 female volunteers without acne or acne scars aged from 19-40 years were enrolled as controls. Purposive sampling method was done as per inclusion and exclusion criteria. Inclusion criteria included: female acne patients, aged 15-40 years who consented to participate in the study and undergo pelvic USG and blood tests; female acne patients who had not received hormonal treatment,

including hormonal contraceptives and antiandrogen therapy for at least 3 months prior to study; female acne patients with menstrual irregularity; and obese female acne patients. Patients with some co-existing systemic illness or those who were on hormonal, steroid or oral contraceptive therapy were excluded from the study.

The severity of acne was graded as mild, moderate or severe.¹⁰ Clinical data, including age, weight, height, body mass index (BMI), menstrual history and androgenic signs were recorded. Hormonal assays and pelvic ultrasonography were done.

Operational terms and definitions

Acne

Acne is a chronic inflammatory disease of pilosebaceous follicles characterized by comedone, papules, pustules, nodules and often scars.¹¹ Acne was graded as mild: comedone, papules/pustules; moderate: papules, pustules/nodules; and severe: nodulocystic/acne conglobata (severe acne with many abscesses, cysts, marked scarring with sinus).¹⁰

Body mass index (BMI)

The BMI was calculated as weight in kilograms divided by the square of height in meter; thin= BMI<18.5; normal range= BMI 18.5-24.9; overweight= BMI 25-29.9; obese= BMI>30 (according to WHO classification).

Menstrual history

Menstrual factors such as cycle length (minimum/ maximum), cycle irregularities, the duration of menstrual bleeding or the absence of bleeding without being pregnant were examined.

Menstrual irregularity

Fewer than 9 periods a year or periods longer than 40 days apart.¹¹

Ultrasound examination

Pelvic USG were performed in all subjects either transabdominally or transvaginally (in married women). Either a 3.5 MHz transabdominal (full bladder technique) or a 5 MHz transvaginal probe was used. The ovarian morphology was carefully visualized. Polycystic ovary (PCO) diagnosis was based upon the presence of multiple small subcapsular cysts (diameter 2-8 mm) with dense echogenic stroma. PCO was not diagnosed in cases with multiple small cysts scattered throughout the ovary without dense echogenic cores.

Hormonal assays

Blood samples were drawn from all subjects for estimation of serum concentration of testosterone, luteinizing hormone (LH) and follicle-stimulating hormone (FSH). Sera were frozen at -20°C until the time of assay. Measurements of the hormones were performed by radioimmunoassay.

Polycystic ovarian syndrome (PCOS)

The PCOS is a heterogeneous condition which is defined by the presence of two out of the following three criteria: i) Oligo- and/or anovulation; ii) hyperandrogenism (clinically or biochemically); and iii) polycystic ovary, with exclusion of other etiology.⁶

Diagnostic criteria for PCOS

The diagnostic criteria for PCOS was acne with menstrual disturbances accompanied by a clinical feature of hyperandrogenism/ratio of LH to FSH equal to or greater than 2 and/or and by ultrasonic findings of PCO.⁹

Data analysis

Descriptive statistics were calculated, including mean, standard deviation (SD). The chi-square test and unpaired t-test were used to determine the statistical significance. *P* values less than 0.05 were considered statistically significant. All statistical calculations were

done by computer using the program SPSS (Statistical Package for the Social Sciences) version 11.0.

Results

The study included 70 subjects out of which 40 (57.1%) were in case and 30 (42.9%) were in control group. No statistical significant ($p>0.05$) difference was found in menstrual history between case and control in chi square test (**Table 1**). Obesity was found only in case group, in which 3 (7.5%) patients were obese (**Table 1**), $p<0.05$. In USG, polycystic ovary was found in 20.0% and 3.3% in cases and controls, respectively ($p<0.05$), **Table 1**. The mean levels of LH and FSH were not different in two groups, however, serum testosterone levels were significantly lower in controls ($p=0.001$), **Table 2**.

There were 11 females with PCOS among the 40 patients with acne (case group) and 1 (3.3%) PCOS case amongst 30 controls (**Table 3**), ($p<0.05$). Out of 11 PCOS patients in case group, 8 were diagnosed PCOS by acne (A) + menstrual irregularities (MI) + PCO on ultrasound + LH:FSH ($>2:1$), 2 cases by A+MI+LH:FSH with hyperandrogenism (hirsutism, alopecia, acanthosis nigricans) and 1 case diagnosed by A+MI+ hyperandrogenism.

Table 3 compares different characteristics in PCOS cases in two groups. The mean BMI and S. testosterone were statistically significant ($p<0.05$) in chi square, however others were not statistically significant ($p>0.05$).

Discussion

In this study, prevalence of PCOS in acne patients was 27.5%, which was significant. PCOS is a common endocrine disorder. Its etiology remains uncertain, and the diagnostic

Table 1 Menstrual history of the study population (n=70).

	Case (n=40) N (%)	Control (n=30) N (%)
<i>Menstrual history</i>		
Irregular	12 (30)	13 (43.3) ^{NS}
Regular	28 (70)	17 (56.7) ^{NS}
<i>Body mass index</i>		
Normal	18 (45.0)	16 (53.3) ^{NS}
Overweight	19 (47.5)	14 (46.7) ^{NS}
Obese	3 (7.5)	0 (0.0) ^S
<i>USG of uterus with adnexal</i>		
Polycystic ovary	8 (20.0)	1 (3.3) ^S
Normal ovary	32 (80.0)	29 (96.7) ^{NS}

NS=not significant ($p>0.05$), S=significant ($p<0.05$).

Table 2 Mean distribution of biochemical parameters of the study population (n=70).

Biochemical parameters	Case (n=40) Mean±SD	Control (n=30) Mean±SD
LH (nmol/l)	13.4 ±13.0 (2.72-83.77)	11.3±9.2 ^{NS} (1.75-42.68)
FSH (nmol/l)	8.9±6.4 (1.26-30.06)	8.9±5.9 ^{NS} (1.89-26.6)
Serum testosterone (nmol/l)	81.0±38.0 (3.2-183)	46.7±25.3 ^S (0.20-106.2)

NS=not significant ($p>0.05$), S=significant ($p < 0.05$) with unpaired t test.

FSH=serum follicle-stimulating hormone, LH=serum luteinizing hormone.

Table 5 Characteristics in PCOS patients in case and control groups.

Mean values	Cases (n=11)	Controls (n=1)
Age (years)	21.5±4.8	24.7±5.9
Weight (kg)	63.0±8.8	58.2±6.5
BMI (kg/m ²)	27.5±3.6	24.4±3.1 ^S
LH (nmol/l)	15.8±7.0	12.5±14.7
FSH (nmol/l)	7.8±3.0	9.3±7.3
Testosterone (nmol/l)	115.5±7.3	67.5±30.3 ^S

S=significant ($p < 0.05$), BMI=body mass index, FSH=serum follicle-stimulating hormone, LH=serum luteinizing hormone.

criteria are still debated. This syndrome has a wide spectrum of clinical, biochemical and ovarian morphological features.⁹ The clinical definition of PCOS has changed in recent years and includes as one of its cardinal criteria the dermatological manifestation of hyperandrogenism, chiefly acne vulgaris,

hirsutism and androgenic alopecia.⁷ In this study, the mean age of respondent was 23.8±5.7 years. The result of the observation was similar with the study done in Italy,¹² where mean age of respondents were 23.6±6.06 years.¹² In our study, 47.5% patients were overweight and 7.5% acne patients were obese according to WHO criteria. The mean BMI status of PCOS with acne was 27.5±3.6 kg/m² and without PCOS was 24±3.1 kg/m². BMI status in PCOS with acne was significantly higher than acne without PCOS in our study. This finding was similar with the previous data.⁹ Patient with PCOS typically have menstrual disorder, obesity, hirsutism and often acne. This study found that almost 30% female acne patient had menstrual irregularities. 40% female acne patient had also menstrual irregularity in previous study.⁹ While assessing an individual patient of acne, a detailed history of menstrual disorder especially oligo- and amenorrhea is mandatory.¹³ Hirsutism and alopecia may also be seen in women with acne due to hyperandrogenemia.¹³ No statistically significant differences were observed in hormonal profiles (serum LH and FSH) between case and control groups in our study. However, serum testosterone level significantly tends to be higher in patient with PCOS with acne. The limitations of the hormone assays are also due to differences and variation in the assay techniques. Even in typical PCOS cases, the LH to FSH ratio might not be higher than usual.⁹ In the present study, the LH to FSH ratio was also not higher in PCOS cases. These are consistent with the results by Timpatanapong and Rojanasakul study.⁹

PCO was visualized by ultrasonography in about 20% of case group and 3.3% of control group in our study, which was significant. However, Timpatanapong and Rojanasakul found PCO only in cases, not in control group.⁹ There is substantial heterogeneity of

symptoms and signs among women with PCOS. In addition to different diagnostic criteria used, the ethnic background of women with PCOS may affect the clinical and hormonal condition.¹⁴

Clinical parameters (acne with menstrual irregularity) accompanied by other features of hyperandrogenism (hirsutism/acanthosis nigricans/alopecia) with or without elevated level of LH to FSH ratio (equal to or greater than 2) and/or ultrasound picture were used in this study to diagnose PCOS. PCOS found higher in case (n=11) than control group (n=1) among the study subjects. However, the prevalence of PCOS in women with acne in our study is lower than other studies. Other researcher found 37.3% and 45.37% acne patient had PCOS in their studies,^{9,12} except for the a study¹⁵ which found that only 19% acne patient had PCOS.

We conclude that all female patients with acne should be screened for PCOS by history and examination and if necessary, pelvic ultrasound and hormonal assays should be done.

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