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Frequency and correlates of comorbid depression in polycystic ovary syndrome

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Abstract

Women with polycystic ovary syndrome (PCOS) often suffer from psychiatric comorbidities, including depression. Data on the prevalence of depression in Bangladeshi women with PCOS are currently lacking. In this cross-sectional study, conducted in a tertiary hospital of Bangladesh, we evaluated 200 newly diagnosed patients with PCOS aged 18-45 years and 200 otherwise healthy women without PCOS of similar age-group for the presence of depression and its predisposing factors. Depression was assessed by administering the PRIME-MD Patient Health Questionnaire (PHQ-9). PHQ-9 score ≥10 was considered as the threshold for major depression, and a score <5 was labeled as no depression. The frequencies of major depression in PCOS and control groups were 51% and 19%, respectively. The women with PCOS had a 5.12-fold higher risk of major depression in comparison to the non-PCOS controls. PCOS subjects having prediabetes/diabetes had a higher risk of major depression than those with normal glucose tolerance, and those with hyperprolactinemia had a lower risk than those having normal prolactin levels. Age, marital status, obesity, hypertension, menstrual irregularity, hirsutism, acne, dyslipidemia, serum testosterone, and serum TSH levels had no significant influence on the presence of depression. Screening for depression should be done routinely in PCOS patients.

Keywords: pcos, depression, hyperandrogenism, insulin resistance, glucose intolerance

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Introduction

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of reproductive age, with a prevalence of 6-10% in the western world [1]. The reported prevalence of PCOS in the Indian subcontinent is as high as 22.5% [2]. This heterogeneous androgen-excess disorder presents with different degrees of reproductive and metabolic dysfunctions; the wide range of symptoms includes menstrual irregularities, hirsutism, acne, subfertility, fall of scalp hair, weight gain, etc. [1]. These symptoms and metabolic derangements may lead to anxiety, depression, impaired sexual functioning, and marital and social maladjustment [3]. Recently, psychiatric comorbidities in PCOS and their impact on the quality of life have been the research focus. At least one psychiatric disorder among depression, anxiety, and bipolar disorder has been found in 56.9% of women with PCOS [4].

Depression is a common mental disorder and is one of the leading causes of disability worldwide. Globally, more than 300 million people of all ages suffer from depression [5]. Varying prevalence of depression ranging from 11% to 40% has been reported in PCOS women by researchers from different parts of the world [4,6,7,8,9,10]. The prevalence of depression was found higher in PCOS women in comparison to their healthy counterparts in previous researches [4,8,9]. Data on the prevalence of depression in Bangladeshi PCOS women are currently lacking. The current study was conducted to fulfill this gap.

Methods

Following approval of the institutional review board of the hospital, this comparative cross-sectional study was conducted in the Endocrinology outpatient department (OPD) of Mymensingh Medical College Hospital, Bangladesh, from January to December 2018. Assuming the prevalence of PCOS 25%, the confidence level of 95%, and 5% margin of error, the estimated sample size was 289. For financial and resource constraints, 200 newly diagnosed PCOS patients aged 18-45 years diagnosed as per Revised Rotterdam criteria were included in this study [11]. Another 200 otherwise healthy females of the same age group having no clinical features of PCOS recruited from the patients' attendants were included in the comparison group. Samples were collected by a convenient sampling technique. Women who are already diagnosed as having a mental illness and/or taking any psychotropic medications and those having any acute or chronic debilitating illness were excluded. After taking informed written consent, all patients were interviewed and examined for relevant clinical information. Anthropometric measurements were done for all. Obesity status was determined by body mass index (BMI) categories applicable to the Asian Indians [12]. Subjects with waist circumference ≥80 cm were considered to have abdominal obesity; metabolic syndrome was diagnosed by using the International Diabetes Federation (IDF) criteria applicable for South Asian women [13]. Hypertension and pre-hypertension were defined according to the Joint National Committee VII criteria [14].

Venous blood was collected in the fasting state from each of the participants for biochemical and hormonal analysis. The biochemical analysis included a standard oral glucose tolerance test (OGTT) and interpreted according to the American Diabetes Association guideline [15]. Plasma glucose and serum lipids were measured by fully Automated Biochemistry Analyzer MINDRAY BS-380 (Shenzhen 518057, P. R. China). Serum testosterone, prolactin, and thyroid-stimulating hormone (TSH) were measured by radioimmunoassay (RIA) and interpreted according to the corresponding laboratory's reference ranges.

Depression scoring system:

Depression was assessed in patients and controls by administering the Bangla (local language) version of the PRIME-MD Patient Health Questionnaire (PHQ-9) [16]. The PHQ-9 has been validated in the Indian population and is considered to be a reliable tool for the diagnosis of depression [17]. The PHQ-9 is used to make a provisional diagnosis of depressive disorder as well as it provides a severity score for depressive disorder [16,18]. For the diagnosis of depression, score ≥20 was classified as severe depression, score 15-19 moderately severe depression, score 10-14 moderate depression, score 5-9 mild depression, and a score below 5 (0-4) as no depression. Therefore, a patient obtaining a score of 5 or more was labeled to have depression [16,18]. PHQ-9 score ≥10 is found to have a sensitivity of 88% and a specificity of 88% for major depression [18].

Statistical analysis:

Statistical analysis was done using Statistical Packages for Social Sciences (SPSS), version 23.0 software (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0, Armonk, NY: IBM Corp.). The categorical variables were represented as percentages and measurable variables as mean±SD and/or median. Student's *t*-test, Chi-square test, and non-parametric tests were performed for comparing the variables between different groups as appropriate. Binary logistic regression analysis was performed to find out the odds ratios for the risk factors of depression in the study population. P-value ≤0.05 was considered to be statistically significant.

Results

The demographic and clinical characteristics of the study subjects are shown in Table 1. The mean age and systolic blood pressure (BP) were lower in the PCOS group than controls. Women with PCOS had higher BMI, waist circumference, and PHQ-9 score in comparison to non-PCOS controls. PCOS group had higher proportions of unmarried and abdominally obese subjects. The frequency of depression was 80% and 34% in PCOS and control group, respectively. The major depressive illness that is considered to be clinically significant was present in 51% of PCOS and 19% of the control subjects.

Table 1 General characteristics of the study subjects

Variables	Sub-groups	PCOS (n=200) mean±SD or %	Control (n=200) mean±SD or %	p
Age (years)		22.55 ± 4.89	28.92 ± 3.89	<0.001
Marital status	Married	78 (39%)	187 (93.5%)	<0.001
	Unmarried	122 (61%)	13 (6.5%)	
BMI (Kg/M²)		26.67 ± 5.15	23.98 ± 4.72	<0.001
BMI category	<23	48 (24%)	90 (45%)	<0.001
	≥23	152 (76%)	110 (55%)	
Waist circumference (cm)		88.50 ± 11.75	82.04 ± 8.12	<0.001
Abdominal obesity	Present	157 (78.5%)	106 (53%)	<0.001
	Absent	43 (21.5%)	94 (47%)	
Systolic BP (mmHg)		116 ± 13	124 ± 16	<0.001
Diastolic BP (mmHg)		76 ± 9	77 ± 7	0.849
BP category	Normotensive	138 (69%)	136 (68%)	0.858
	Pre-hypertensive	44 (22%)	48 (24%)	
	Hypertensive	18 (9%)	16 (8%)	
PHQ-9 score (median)		10	2	<0.001
Depression presence	Absent	40 (20%)	132 (66%)	<0.001
	Present	160 (80%)	68 (34%)	
Depression severity	Mild	58 (29%)	30 (15%)	<0.001
	Moderate	58 (29%)	24 (12%)	
	Moderately Severe	29 (14.5%)	13 (6.5%)	
	Severe	15 (7.5%)	1 (0.5%)	

(Within parentheses are percentages over column total)
(p-value by Student's *t*-test, Chi-square test or non-parametric test as applicable)

Table 2 presents the odds ratios of variables for the presence of depression in study subjects (PCOS and controls) obtained by binary logistic regression analysis adjusting for possible confounders. The PCOS patients had a 5.12-fold higher risk of major depression in comparison to their non-PCOS healthy counterparts.

Table 2 Binary logistic regression for the predictors of major depression (PHQ-9 score ≥10) in study subjects (N=400)

Variables	Sub-groups	No. of subjects in subgroup (n)	Odds Ratio (95% CI)	p
Subject category	Controls	200	Referent	
	PCOS	200	5.12 (2.62-9.98)	<0.001
Age Group	<25 years	142	Referent	
	≥25 years	258	1.19 (0.61-2.36)	0.606

Marital Status	Unmarried	135	Referent	
	Married	265	1.14 (0.63-2-.06)	0.670
BMI	<23	138	Referent	
	≥23	262	0.78 (0.38-1.60)	0.502
Abdominal obesity	Absent	137	Referent	
	Present	263	1.69 (0.81-3.51)	0.162
BP category	Normal	274	Referent	
	Pre HTN / HTN	126	1.39 (0.86-2.25)	0.176

Table 3 Binary logistic regression for the predictors of major depression (PHQ-9 score ≥10) in PCOS women (n=200)

Variables	Subgroups	No. of subjects in subgroup (n)	Odds Ratio (95% CI)	p
Menstrual cycle	Regular	13	Referent	
	Irregular	187	1.29 (0.37-4.52)	0.684
Hirsutism	Absent	50	Referent	
	Present	150	1.00 (0.49-2.04)	0.996
Acne	Absent	157	Referent	
	Present	43	0.94 (0.46-1.93)	0.870
H/O weight gain	Absent	73	Referent	
	Present	127	1.22 (0.62-2.41)	0.567
Subfertility (n=78*)	Absent	48	Referent	
	Present	30	1.46 (0.57-3.72)	0.426
Acanthosis nigricans	Absent	48	Referent	
	Present	152	0.92 (0.42-2.04)	0.838
Glycemic status	NGT	157	Referent	
	AGT	43	2.73 (1.08-5.21)	0.031
Dyslipidemia	Absent	24	Referent	
	Present	176	2.14 (0.80-5.70)	0.128
Metabolic syndrome	Absent	110	Referent	
	Present	90	1.36 (0.71-2.62)	0.354
S. Testosterone	Normal	145	Referent	
	Elevated	55	1.36 (0.69-2.66)	0.376
S. Prolactin	Normal	173	Referent	
	Elevated	27	0.38 (0.15-0.97)	0.043
S. TSH	≤5.0 μIU/mL	167	Referent	
	>5.0 μIU/mL	33	0.93 (0.41-2.11)	0.859

*in married subjects only; NGT= Normal glucose tolerance; AGT= Abnormal glucose tolerance

Table 3 presents the odds ratios of the factors related to PCOS for the presence of depression in PCOS women obtained by binary logistic regression analysis adjusting for possible confounders. PCOS subjects with abnormal

glucose tolerance (prediabetes/diabetes) had a 2.73-fold higher risk of major depression than those with normal glucose tolerance, and those with hyperprolactinemia had a 0.38-fold lower risk than those having normal prolactin levels.

Discussion

The current study evaluated 200 PCOS women and another 200 healthy controls for the presence, severity, and contributing factors of depression. The frequency of depression among PCOS women very high (80%), and this was higher than that observed in non-PCOS controls (34%). More than half (51%) of the PCOS women were found to have major depression (PHQ-9 score ≥10). The PCOS women had a 5.12-fold higher risk of major depression in comparison to the controls. PCOS women having prediabetes/diabetes had a higher risk of major depression than those with NGT, and those with hyperprolactinemia had a lower risk than those having normal prolactin levels.

Though the underlying mechanisms of the relationship between PCOS and depression remain poorly understood, numerous possible explanations have been provided for the result regarding the increased risk of depressive disorder in PCOS patients. Visible features of PCOS, such as hirsutism, acne, alopecia, as well as potential reproductive consequences such as menstrual irregularity, and subfertility can be deeply stigmatizing to women [19]. In a study, the PCOS women described the subjective experience of the disease as feeling robbed of their self-concept, the essence of being feminine and attractive, thus making PCOS, as the "thief of womanhood" [20]. A link between hyperandrogenism and depression among women with PCOS also has been proposed [21]. Insulin resistance and obesity are common in patients with PCOS. Insulin-resistance related comorbidities, including hypertension, type 2 diabetes, and dyslipidemia, have been noted to be related to depressive symptoms [4,21,22].

Several studies have confirmed that depression is a common comorbidity in patients with PCOS through the reported prevalence varied greatly [4,6,7,8,9,10]. Kerchner et al. found 40% of PCOS women to have depression, whereas the frequency was 18.9% in the study done by Sayyah-Melli et al. [6,8]. The prevalence of depression in PCOS women was 11-50% in the studies done in India [7,9,10]. In a follow-up study, the incidence of the new diagnosis of depression diagnosed by psychiatrists was higher in PCOS women (2.93%) than non-PCOS controls (2.26%) [4]. These studies also revealed a higher prevalence of depression among PCOS women than non-PCOS controls. The variable frequencies of depression observed among the PCOS worldwide can be explained by the fact that different methods and tools used for screening and diagnosing and the influence of culture on the epidemiology of depression [23]. Though the overall frequency of depression was higher in the current study, the frequency of major depression was almost similar to previous studies.

This study identified dysglycemia as an independent risk for depression in PCOS women [odds ratio 2.73 (CI: 1.08-5.21)]. Compared with the nondepressed subjects with PCOS, the depressed subjects with PCOS had greater evidence of insulin resistance in previous studies [6]. Glucose intolerance, dyslipidemia, and metabolic syndrome, all of which are the results of insulin resistance may contribute to depression in PCOS [4]. PCOS subjects with hyperprolactinemia had lower risks of depression in the current study [odds ratio 0.38 (CI: 0.15-0.97)]. No previous studies evaluated the role of serum prolactin levels on depression.

The contributing factors of depression in PCOS have been investigated by many researchers. Barry et al. observed that younger women with PCOS were less depressed than older women with PCOS [24]. Being unmarried is an independent predictor of depression, according to a previous study [26]. Some studies found depression to be associated with higher BMI, and waist-to-hip ratio in women with PCOS through others did not found such associations [3,6,24,25]. The presence of HTN was also a risk factor of depression in the Bangladeshi population[26]. Some studies identified menstrual irregularities as a contributing factor to depression in PCOS [24]. According to the findings of Açmaz et al., the actual determinants of depression were infertility and hirsutism [27]. Among PCOS women, Chaudhari et al. found higher risks of depression in PCOS subjects with acne than those without acne [7]. There is conflicting evidence on the effect of serum androgen levels with depression in PCOS [6,24]. Though the effect of serum TSH level on presence and severity of depression in PCOS patients is not evaluated yet, Bauer et al. showed that TSH levels in hypothyroidism correlated with the severity of depression [28].

The present study found no significant differences in the risk of depression among lower and higher age groups, married and unmarried women, normal-weight and overweight/obese women, and among normotensive and hypertensive women.

This study has some limitations. The sample size was small, and it was a single-center study; the sample may not represent the whole country. The Bangla version of the

PHQ-9 Questionnaire was not validated in the study population. The healthy comparison group was not matched for age, marital status, and obesity status. Nevertheless, this one is the first study in Bangladesh investigating depression in PCOS and may serve as the basis for further large-scale, multi-center study in this subject.

Conclusion

A very high frequency of depression was observed in PCOS subjects, and they had a higher risk of depression than non-PCOS controls. Glucose intolerance and a normal prolactin level were found to be the independent predictors of depression in PCOS. Screening for depression should be done routinely in PCOS patients.

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Conflict of interest

None

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