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Polikistik Over Sendromlu Hastalarda Premenstrüel Disforik Bozukluk ve Affektif Mizaç

Premenstrual Dysphoric Disorder and Affective Temperament in Patients with Polycystic Ovary Syndrome

Hülya Ertekin[1], Başak Şahin[1], Halil İbrahim Taş[1], Fatma Beyazıt[2], Mehmet Aşık[4], Yusuf Haydar Ertekin[3]

1Çanakkale Onsekiz Mart Üniversitesi Tıp Fakültesi, Psikiyatri Ana Bilim Dalı, Çanakkale, Türkiye
2Çanakkale Onsekiz Mart Üniversitesi Tıp Fakültesi, Kadın Hastalıkları ve Doğum Ana Bilim Dalı, Çanakkale, Türkiye
3Çanakkale Onsekiz Mart Üniversitesi Tıp Fakültesi, Aile Hekimliği Ana Bilim Dalı, Çanakkale, Türkiye
4Özel Tekden Hastanesi, Endokrinoloji Kliniği, Denizli, Türkiye

ÖZ

GİRİŞ ve AMAÇ: *Bu çalışmada, Polikistik Over Sendromu (PKOS) olan kadınların, afektif mizaç özelliklerini ve Premenstrual Disforik Bozukluk (PMDB) komorbiditesini değerlendirmek ve Sağlıklı Kontrollerle (SK) karşılaştırmayı hedefledik.*

YÖNTEM ve GEREÇLER: *Bu çalışmaya 20 PKOS hastası ve 20 SK dahil edildi. Tüm katılımcılara Hastane Anksiyete ve Depresyon Ölçeği (HADÖ) ve Mizaç Karakter Envanteri (Temperament Evaluation of Memphis, Pisa, Paris and San Diego-Autoquestionnaire version (TEMPS-A)) uygulandı. PMDB ve diğer psikiyatrik bozuklukların tanıları, DSM-5 tanı ölçütlerini kullanarak tüm katılımcılarla bire bir görüşen uzman psikiyatristler tarafından yapıldı.*

BULGULAR: *PKOS'lu hastalarda PMDB'nin eştanısı% 30 (n = 6) iken SK grubunda % 15 (n = 3) idi. PMDB oranları bakımından gruplar arasında anlamlı farklılık gözlenmedi. PKOS'lu hastalarda SK'lere göre daha yüksek oranda majör depresyon (% 25, n = 5) ve anksiyete bozukluğu (% 20, n = 4) olmakla birlikte, sadece anksiyete bozuklukları PKOS'da SK grubuna göre anlamlı derecede yüksekti (p = 0.03).*

TARTIŞMA ve SONUÇ: *PKOS'lu hastalar, DSM-5'e göre duygudurum bozuklukları arasında olan ve adet döngüsü ile ilişkili olan PMDB komorbiditesi açısından risk faktörüne sahip olabilirler. PKOS'lu kadınlarda, PMDB ve diğer psikiyatrik durumları düşünmek ve tedavi etmek, bu hastaların yaşam kalitesini ve işlevselliğini artırabilir.*

Anahtar Kelimeler: *anksiyete bozuklukları, majör depresyon, premenstrüel disforik bozukluk, polikistik over sendromu, psikiyatrik bozukluklar*

ABSTRACT

INTRODUCTION: *This study aimed to evaluate the affective temperaments of women with Polycystic Ovary Syndrome (PCOS), to assess its comorbidity with Premenstrual Dysphoric Disorder (PMDD) and compare with Healthy Controls (HC).*

METHODS: *A total of 20 women with PCOS and 20 HC were included in this study. Hospital Anxiety and Depression Scale (HADS) and Temperament Evaluation of Memphis, Pisa, Paris and San Diego-Autoquestionnaire version (TEMPS-A) were applied to all participants. The Diagnoses of PMDD and other psychiatric disorders were made by staff psychiatrists interviewing all participants using DSM-5 diagnostic criteria.*

RESULTS: *The comorbidity of PMDS in patients with PCOS was 30% (n=6), while it was 15% (n=3) in the HC group. PMDS proportions did not differ significantly between groups. Patients with PCOS had higher major depression (25%, n=5) and anxiety disorders (20%, n=4) compared with HCs, but only anxiety disorders were significantly higher in PCOS than the HC group (p=0.03).*

DISCUSSION and CONCLUSION: *Patients with PCOS may have more comorbidity risk of PMDD, which is a mood disorder according to DSM–5, and associated with menstrual cycles. Considering and treating PMDD and other psychiatric conditions may increase the quality of life and functionality of women with PCOS.*

Keywords: *anxiety disorders, major depression, premenstrual dysphoric disorder, polycystic ovary syndrome, psychiatric disorders*

İletişim / Correspondence:

Dr. Hülya Ertekin
Çanakkale Onsekiz Mart Üniversitesi Tıp Fakültesi, Psikiyatri Ana Bilim Dalı, Çanakkale, Türkiye
E-mail: tashalilibrahim@gmail.com
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INTRODUCTION

Polycystic Ovary Syndrome (PCOS) is one of the most common endocrine disorders in women of reproductive-age and the most common cause of chronic anovulation associated with androgen excess. It is estimated that the prevalence of PCOS is 5-10% (1). PCOS is defined as menstrual disturbances like amenorrhea or oligomenorrhea, hirsutism or acne, hyperandrogenism, and frequently obesity. Patients with PCOS have more common chronic anovulation and infertility than healthy controls (HCs) (2-3).

Depression, impaired sexual functioning, and marital and social maladjustment, bipolar disorder, anxiety disorders, and binge eating disorder are more frequently in women with PCOS than HCs (4-6). Many reasons have been proposed for these relationships, such as negative body image associated with obesity, hyperandrogenism, higher infertility rates, hirsutism, acne, and vitamin D deficiency (7-9).

Premenstrual Dysphoric Disorder (PMDD) is categorized under Depressive Disorders in the DSM-5 and occurs in 1.8-5.8% of menstruating women (10). The etiology of PMDD has not been defined clearly. The theory is that premenstrual symptoms may occur owing to differential sensitivity to mood disturbing effects of gonadal steroid fluctuations in vulnerable women (11). Gonadal steroid fluctuations may modulate serotonergic transmission, and dysregulation of the serotonin system in women with PMDD has been demonstrated in many studies (12).

Affective temperament features are subclinical manifestations of classical mood disorders, which have been identified in the last decade by several studies (13-15). The affective temperament has been described as the biological and genetic tendency of the personality, which provides an automatic emotional response to events, establishing an individual's activity level, rhythms, mood, and related cognitions (13, 16). Affective temperament features may help to predict the risk of depression (15, 17).

We hypothesized that PMDD may have higher comorbidity in women with PCOS than healthy females. This study aimed to evaluate the affective temperaments of women with PCOS, to assess its comorbidity with PMDD, and compare with HCs.

METHODS

Study Design and Subjects

A total of 20 women with PCOS and 20 HCs were included in this study. Each participant signed an informed consent form per the Declaration of Helsinki. The approval of this study was given by the local ethics committee of Çanakkale Onsekiz Mart University. Twenty-five of the 91 recently diagnosed (January-June 2016) patients with PCOS in the Çanakkale Onsekiz Mart University Hospital Endocrinology outpatient unit agreed to participate.

Inclusion criteria of the study were meeting the Rotterdam criteria to diagnose PCOS (18). Five patients were excluded because of having thyroid disease, Cushing's syndrome, non-classical congenital adrenal hyperplasia, drug-associated PCOS, or abnormal prolactin (19).

Age-matched with the patients, the healthy controls were selected from females who had no systemic disorder after physical examinations, had no diagnosed psychiatric disorders, and had no history of menstrual irregularities, hyperandrogenism, infertility, or physical signs of hirsutism. Hormone levels of the HCs were not analyzed.

Both groups were evaluated for menstrual cycles, body mass index (BMI). Amenorrhea was defined as absent menstrual cycles in the last 90 days, and oligomenorrhea was defined as more than 35 days between periods with fewer than eight cycles in the previous year. The degree of hirsutism was scored by an endocrinologist according to the Ferriman Gallwey scoring system (20). FSH, LH, estradiol (E2), and total testosterone (tT) levels were analyzed in women with PCOS.

Demographic form, Temperament Evaluation of Memphis, Pisa, Paris and San Diego-Autoquestionnaire version (TEMPS-A), and Hospital Anxiety and Depression Scale (HADS) were applied to all participants. The Diagnoses of PMDD and other psychiatric disorders were made by staff psychiatrists interviewing all participants using DSM-5 diagnostic criteria. The diagnosis of

PMDD was made by interview and the participants were not reevaluated longitudinally.

Hormone Assays

Fasting blood samples of women with PCOS were collected in the early follicular phase. E2, FSH, LH, and tT levels were measured using an electrochemiluminescence immunoassay on a Roche Cobas e-601 analyzer (Roche Diagnostics GmbH, Mannheim, Germany).

Statistical analysis

The PASW Statistics 19 statistical program was used for data analysis, and P values of <0.05 were considered statistically significant. Mann–Whitney U tests were used to compare differences between groups for non-parametric numerical variables. Fisher's Exact Test was used to compare differences between groups for non-parametric categorical variables.

RESULTS

Data of 20 women with PCOS and 20 HC females were analyzed. The mean age of patients with PCOS was 27.40±5.45 years, while the mean age of HC subjects was 28.35±5.44 years. There was no statistically significant difference between groups concerning age. However, body weight and BMI were significantly higher in the patient group (Table 1).

When we compared the mean TEMPS-A and HADS scores between groups, we found that all temperament subtype scores, as well as HADS depression, anxiety and total scores, were higher among patients with PCOS compared with HCs. However, these differences were not statistically significant except TEMPS-hyperthymic total scores. TEMPS-hyperthymic total scores were statistically higher among patinets with PCOS compared with HC's (p=0.01) (Table 1).

The comorbidity of PMDS in patients with PCOS was 30% (n=6), while it was 15% in HC group. PMDS rate did not differ significantly between groups (Table 1).

Compared with HCs, patients with PCOS had higher major depression (5%, n=1 vs. 25%, n=5) and anxiety disorders (0% vs. 20%, n=4), but the difference was only significant for anxiety disorders group (p=0.03) (Table 1).

Table 1: Comparison of women with PCOS and HC subjects

	PCOS (n=20)	HC (n=20)	p
Age (years)*	27(18-42)	26(23-40)	NS
Height (m) *	1.62(1.50-1.72)	1.66(1.55-1.78)	NS
Body weight (kg) *	84.78(48-118)	61.42(49-87)	<0.001
BMI(kg/m²)*	31.64(19.47-41.81)	22.38(16.96-31.20)	<0.001
Oligo/amenorrhea*	30%	0%	<0.001
Infertility history (n; %)	20%	0%	NS
LH *	8.75(2.10-24.40)	-	-
FSH *	4.9(2.6-8)	-	-
Estradiol*	50.45(25-193)	-	-
Total testosterone*	0.47(0.04-0.80)	-	-
HADS-anxiety *	8.28(0-20)	6.15(2-11)	NS
HADS-depression*	6.39(0-17)	3.85(0-13)	NS
HADS-total *	14.67(2-32)	10.0(2-24)	NS
TEMPS- depression*	7(3-15)	5(1-14)	NS
TEMPS-cyclothymic*	10(3-19)	5.5(0-14)	NS
TEMPS-hyperthymic *	9(3-15)	6(1-17)	<0.005
TEMPS-irritable *	4(0-15)	2(0-7)	NS
TEMPS-anxious *	7(3-20)	5.5(0-14)	NS
PMDS			NS
Yes (n; %)	6 (30%)	3 (15%)	
No (n; %)	14(70%)	17 (85%)	
Depression(HADS)**			NS
Yes (n; %)	7 (35%)	6 (30%)	
No (n; %)	13 (65%)	14 (70%)	
Anxiety (HADS)*			0.01
Yes (n; %)	7 (35%)	1 (5%)	
No (n; %)	13 (65%)	19 (95%)	
Major depression			NS
Yes (n; %)	5 (25%)	1 (5%)	
No (n; %)	15 (75%)	19 (95%)	
Anxiety disorder			0.03
Yes (n; %)	4 (20%)	0 (0%)	
No (n; %)	16 (80%)	100 (100%)	

BMI: Body Mass Index, HADS: Hospital Anxiety Depression Scale, PCOS: polycystic ovary syndrome, HC: healthy controls, NS: Not Significant
**Median values, **According to HADS cut-off score*

DISCUSSION

In this study, we compared demographic characteristics, PMDS, affective temperament, psychiatric disorders, levels of depression, and anxiety between patients with PCOS and healthy women. Comparisons showed that the body weight, BMI, HADS anxiety, and anxiety disorders were

significantly higher in patients with PCOS than HCs. Also, PMDS comorbidity, all temperament subtype scores, HADS depression scores, HADS total scores, and major depression were higher in patients with PCOS compared with HCs.

Depression is one of the common psychiatric disorders in patients with PCOS. Kercher et al. showed that the overall prevalence of depression was 40% in women with PCOS (21). In a recent study, Tan et al. found the frequency of depression as 27.5% in PCOS, which was higher than HCs (22). Anxiety disorders and depression were the most common psychiatric disorders in PCOS in Turkey (23, 24). Annagür et al. (23) showed the prevalence of depression as 33%, while Aşık et al. (24) found the prevalence of depression 42.3% in patients with PCOS. In this study, consistent with the study of Tan et al. we found higher clinical major depression (not statistically significant) prevalences in patients with PCOS compared to HC subjects. The lower prevalence of depression in our study may be explained by method differences from other studies. Having interviewed all participants against the DSM-5 diagnostic criteria can be regarded as a strength of our research. PMDD is categorized under Depressive Disorders according to the DSM-5 (10). Sex hormone fluctuations at the end of the luteal phase are implicated in the etiology of PMDD (25). Despite normal levels of sex hormones, recent evidence suggests that women with PMDD have altered sensitivity to ovarian-hormone dynamics (26). According to the PMDD diagnostic criteria, at least 5 of 11 symptoms must be present in the premenstrual phase (10).

The prevalence of PMDD is 1.8-5.8 according to DSM-5 (10). 3-9% of women have PMDD in studies utilizing DSM–IV criteria (27, 28). In this study, we found the prevalence of PMDD 30% in patients with PCOS while it was 15% in HC subjects. Menstrual irregularity, infertility, hirsutism, acne, and obesity are the most common manifestations of PCOS, which is one of the most frequent endocrine disorders among premenopausal women. Studies have shown that diseases such as irregular menstrual cycles, hormonal changes, infertility, insulin dysregulation, obesity, and acne can be significant factors in the development of psychiatric disorders in patients with PCOS. Although it is not possible to fully elucidate the etiology why PMDD is higher in patients with PCOS compared to healthy controls, the hormonal changes present in these patients and the psychological responses to these hormonal changes may be accused. Besides, the presence of PMDD together with some depressive disorders makes it essential to evaluate PMDD in future studies, especially when patients with PCOS are being evaluated.

In this study, we found higher depression, hyperthymia, cyclothymia, irritability, and anxiety temperament scores in patients with PCOS than HC subjects. Consistent with our work, Asik et al. (24) found higher depression, cyclothymia, irritability, and anxiety temperament scores in patients with PCOS. Akiskal et al. (13) and Kesebir et al. (15) demonstrated higher irritable, anxious, depressive, and cyclothymic temperament scores in depressive patients compared to healthy controls. These results suggest that premorbid affective temperament can be a predictor of depression.

Increased frequency of psychiatric disorders in patients with PCOS has been shown in many studies. 14% of women with PCOS had anxiety symptoms in a recent study (29). In a systematic recent review and meta-analysis of the literature, increased prevalence of generalized anxiety and mean anxiety scores in women with PCOS compared to controls was demonstrated (30). Asik et al. (24) found higher anxiety scores in women with PCOS. Our study confirmed higher anxiety scores and anxiety disorders in patients with PCOS. 20% of women with PCOS had anxiety disorders in our study. Although some risk factors have been related to depression and anxiety in women with PCOS, the etiology of psychiatric symptoms (particularly depressive and anxiety symptoms) in women with PCOS remains unclear.

Some limitations of this study can be mentioned as follows: First, the relatively small sample size limits the generalizability of our findings. This study is preliminary work on this subject. We plan a study which shall include more participants. The second limitation was the PMDD diagnosis having done only with one interview. Longitudinal follow-up of patients with PMDD diagnosis may increase

the validity of the PMDD diagnosis. The control group was not matched with for BMI with patients with PCOS. Obesity may have affectes on the higher rates of psychiatric disorders in the patient group.

CONCLUSIONS

This is the first study to evaluate women with PCOS for PMDD prevalence. We interviewed all participants, and all psychiatric diagnoses were made by staff psychiatrists. Women with PCOS are more likely to have higher frequencies of mood and anxiety disorders as shown in many studies. Patients with PCOS may have more significant risk comorbidity for PMDD. PMDD may be a common psychiatric disorder in PCOS which is associated with menstruel cycles. Also, affective temperament is one of the critical elements of the etiology of psychiatric conditions in women with PCOS. These patients should be evaluated about affective temperament, PMDD, and other psychiatric disorders. Evaluating affective temperament of patients with PCOS may help to investigate patients with PCOS under risks for mood and anxiety disorders. Considering and treating these psychiatric conditions may increase the quality of life and functionality of women with PCOS.

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