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Is There a Difference in Anxiety, Body Perception, and Depression Scales According to Subphenotypes of Polycystic Ovary Syndrome?

Polikistik Over Sendrom Fenotipleri Arasında Depresyon, Anksiyete ve Beden Algısı Ölçekleri Açısından Farklılık Var Mıdır?

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Abstract

Objectives: Polycystic ovary syndrome (PCOS) is the most prevalent female reproductive disorder. PCOS is associated with increased mood disorders. We aimed to evaluate the association between PCOS sub-phenotypes and anxiety, body perception, and depression scales in our study.
Materials and Methods: We enrolled 74 patients with PCOS and we assigned them into subphenotypes of PCOS. The Beck depression inventory (BDI-II) was used for depression, the Beck anxiety inventory (BAI) was used for anxiety, and the body esteem scale (BES) was used to assess body perception for all participants.
Results: The BDI-II scores of phenotype A were higher than phenotype D. The BAI scores of phenotype A were higher than phenotype B, C, and D. There was no difference between BES scores through all PCOS phenotypes. There was a difference in modified Ferriman-Gallwey score between phenotypes except between phenotype A and phenotype B (p=0.13). An increase in BMI by 1 kg/m^2 was found to cause a 0.49 increase in depression scores (p=0.01) but there was no association between BMI and BAI and BES scores (p=0.33, p=0.18).
Conclusion: PCOS is associated with mood disorders, especially anxiety and depression. Until now, there was no information about the prevalence of mood disturbances according to subphenotypes of PCOS. The higher prevalence of depression was seen in phenotype A than phenotype D but it was similar among A, B, and C. It has suggested that hyperandrogenism may have a causative effect on pathogenesis of depression in women with PCOS. The higher BAI scores were recorded in phenotype A than phenotype B, C, and D, and BES scores were similar through phenotypes. Although we could not find a close phenotype-mood disorder association, we believe the need for screening for mood disorders, especially anxiety and depression, for patients with PCOS because of the importance of the disease's psychological consequences.
Key Words: PCOS Phenotypes, Depression, Anxiety, Body Perception, Modified Ferriman-Gallwey Score

Öz

Amaç: Polikistik over sendromu (PKOS), en yaygın kadın üreme bozukluğudur. PKOS duygudurum bozuklukları ile ilişkilidir. Çalışmamızda PKOS alt fenotipleri ile anksiyete, beden algısı ve depresyon ölçekleri arasındaki ilişkiyi değerlendirmeyi amaçladık.
Gereç ve Yöntem: Çalışmaya PKOS'li 74 hasta dahil edilmiş ve PKOS'nin alt fenotiplerine ayrılmıştır. Tüm katılımcılara depresyon için Beck depresyon envanteri (BDI-II), anksiyete için Beck anksiyete envanteri (BAE) ve beden algısını değerlendirmek için beden saygısı ölçeği (BES) kullanıldı.
Bulgular: Fenotip A'nın BDI-II skorları, fenotip D'den daha yüksekti. Fenotip A'nın BAI skorları, fenotip B,C ve D'den yüksekti. BES skorları açısından tüm fenotipler açısından fark yoktu. Fenotip A ve fenotip B dışında (p=0,13), fenotipler arasında Ferriman-Gallway skorları açısından fark yoktu.

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BKİ'deki her 1 kg/m^2 artışın, depresyon skorlarında 0,49 artışa neden olduğu, ancak BKİ, BAI ve BES skorları arasında ilişki bulunmadığı tespit edildi (p=0,33, p=0,18).

Sonuç: PKOS duygudurum bozuklukları ile ve özellikle anksiyete ve depresyon ile ilişkilidir. Şimdiye kadar, PKOS alt fenotiplerine göre duygudurum bozukluklarının yaygınlığı hakkında bilgi bulunmamaktadır. Fenotip A'da, fenotip D'ye göre daha yüksek depresyon prevalansı görülmüş, ancak A, B ve C arasında benzerlik görülmüştür. Bu durum, PKOS'li kadınlarda hiperandrojenizmin depresyon patogenezinde nedensel bir etkiye sahip olabileceğini düşündürmüştür. Fenotip A'da, fenotip B, C ve D'ye oranla daha yüksek BAI skorları tespit edilmiş, ancak BES skorları tüm gruplarda benzer bulunmuştur. Fenotip-duygudurum bozukluğu ilişkisi özgül olarak bulunamamış olsa da, hastalığın psikolojik sonuçlarının önemi nedeniyle PKOS'li hastalarda duygudurum bozukluklarının, özellikle anksiyete ve depresyonun taranması gerektiğine inanıyoruz.

Anahtar Kelimeler: PKOS Alt Fenotipleri, Depresyon, Anksiyete, Beden Algısı, Modifiye Ferriman Gallway Skoru

Introduction

Polycystic ovary syndrome (PCOS) is the most prevalent reproductive disorder found in 6-10% of the female population based on race and ethnicity, causing the impairing quality of life and morbidity for women (1). According to a study from our country revealed a prevalence of 6.1% with National Institutes of Health criteria, 15.3% with Androgen Excess Society and PCOS Society, and 19.9% with Rotterdam criteria (2). Besides ovulatory dysfunctions and hyperandrogenism features, PCOS also includes metabolic, cardiovascular, and physics social derangements such as impaired glucose tolerance, type-2 diabetes mellitus, dyslipidemia, coronary heart disease, anxiety, and depression (3-5). There are four phenotypes (A-D) of PCOS according to Rotterdam criteria (6). Phenotype A is composed of hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology (PCOM); phenotype B consists of hyperandrogenism and ovulatory dysfunction. Phenotype C consists of hyperandrogenism, and PCOM and phenotype D consists of ovulatory dysfunction and PCOM. Data derived from population studies showed that phenotype A and B are more associated with metabolic dysfunction, obesity, and menstrual irregularities (4). There are more than thirty cross-sectional designed studies, longitudinal and large population-based studies from different world regions, have examined the association between PCOS and depressive or anxiety symptoms. A recent review reported a 4.18 increased odds of depression and a 5.62 increased odds of anxiety with PCOS than controls (7). The precise mechanism underlying the increased risk of depressive and anxiety symptoms in PCOS is unclear, however potential factors such as obesity, insulin resistance, elevated androgens, infertility, inflammation, and hirsutism may act together.

There are many data about the association of increased risk of psychological consequences for PCOS, but the relation between sub-phenotypes of PCOS and mood disturbances are not evaluated yet. Therefore, we aimed the evaluate the association between PCOS sub-phenotypes and anxiety, body perception, and depression scales.

Materials and Methods

Seventy-four non-pregnant women aged between 17 to 45, having clinical, biochemical, and radiological findings consistent with PCOS, were prospectively enrolled between 2017-2019. The definition of PCOS was determined according to the Rotterdam criteria (8). Rotterdam criteria require two out of three criteria of i) oligo and/or anovulation, ii) clinical and/or biochemical signs of hyperandrogenism, and iii) PCOM diagnosed with either pelvic or transvaginal ultrasonography. Hirsutism was defined according to the modified Ferriman-Gallwey score (mFGS) ($\geq$7) (9). The clinical conditions causing anovulation, hyperandrogenism such as congenital adrenal hyperplasia, prolactinoma, Cushing syndrome/disease, and mood disorders, use of any types of antidepressants were also excluded.

The demographic, clinical, and laboratory data, including body mass index (BMI), were recorded for each participant. Blood samples were obtained from each patient in the morning at an 8 h fasting state to measure biochemistry panel and total testosterone, dehydroepiandrosterone to determine hyperandrogenism. The study was in accordance with the ethical standards of the Ankara University Faculty of Medicine Undergraduate Student Research Ethics Review Board (date: 25.12.2018, decision no: 9530) and with the Helsinki Declaration, and all subjects signed informed consent forms.

Surveys

We administered surveys for depression, anxiety, and body perception to all participants. The Beck depression inventory (BDI-II) (10) was used for depression, the Beck anxiety inventory (BAI) (11) was used for anxiety, and the body esteem scale (BES) (12) was used to assess body perception. Both the BDI and the BAI are 21-item self-report inventories measuring depression and anxiety severity, respectively. Each item is rated on a four-point scale ranging from zero to four in both scales, and the scores range between 0-63. BES has 35 items that is rated on a 5 point scale.

Statistical Analysis

Statistical analysis were performed using the IBM SPSS Statistics for Windows (IBM Corp, Version 22.0. Armonk, NY). The

Kolmogorov-Smirnov test assessed the normality of continuous data. Categorical variables were presented as numbers and percentages (%). Continuous data were displayed as means ± standard deviation for normally distributed variables and median (minimum-maximum) for non-normally distributed variables. The scores of all of the surveys were evaluated according to sub-phenotypes of PCOS. One-Way ANOVA was used to compare the scales among the sub-phenotypes of PCOS groups. Levene's test was used to assess the homogeneity of the variances. When an overall significance was observed, pairwise post-hoc tests were performed using Tukey's test. All tests are two-sided, and statistical significance was set at $p<0.05$.

Results

A total of 74 women with PCOS participated in this study. The mean age of the study group was 27.5±4.9 years. The median BMI, the mean mFGS and the median total testosterone levels of the study group were 26.3 kg/m^2 (18.2-50), 13±7 and 0.5 (0.19-19) ng/mL [normal reference range 0.1-0.9 ng/mL] respectively. When patients were evaluated according to sub-phenotypes of PCOS, the prevalence of type A to D was 43.2% (n=32), 32.4% (n=24), 8% (n=6) and 16% (n=12) and the features (age, mFGS, etc) were given in detail according to the sub-phenotypes (Table 1).

According to the sub-phenotypes of PCOS, the mean/median scores of BDI-II, BAI, and BES, and the mean scores of mFGS and the differences between sub-phenotypes for BDI-II, BAI, BES, and mFGS were summarized in Table 2. The BDI-II scores of phenotype A were higher than phenotype D. The BAI scores of phenotype A were higher than phenotype B, C, and D. There was no difference between BES scores through all phenotypes. There was a difference in mFGS between phenotypes except between phenotype A and phenotype B (p=0.13).

There was a correlation between BMI and BDI-II scores ($p<0.01$, $r=0.46$) (Figure 1). An increase in BMI by 1 kg/m^2 was found to a 0.49 increment in depression scores (p=0.01). On the other hand, there was no correlation between BMI and BAI and BES scores (p=0.33, p=0.18, respectively).

There were also significant positive correlations among these four factors between mFGS and BDI-II, BAI, and BES scores ($r=0.41$, $p<0.01$, $r=0.35$, $p=0.02$, $r=0.36$, $p=0.02$, respectively).

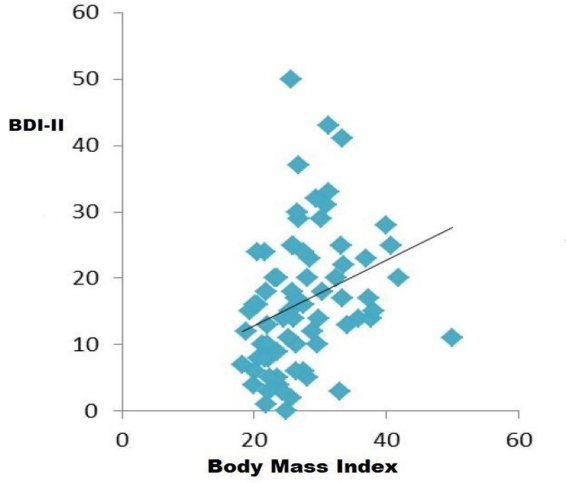

Figure 1: Correlation analysis between BDI-II and body mass index
BDI-II: Beck depression inventory-II

Table 1: The characteristics of the participants according to the subgroups

	Phenotype A	Phenotype B	Phenotype C	Phenotype D	p
Number of patients	32	24	6	12	0.39
Age (years)	25.5±4	25.3±3.5	21.5±1.8	25.8±4.4	0.11
Body mass index (kg/m^2)	27.1±5.8	27.7 (20-34)	34.2±4.7	28.2±5.5	0.01
mFGS	13.1±3.9	13.9±3.7	17.8±1.9	8.3±1.3	<0.01
Total testosterone (ng/mL)	0.5 (0.19-15)	2.5 (0.28-19)	3.6±2.3	0.24 (0.2-0.5)	<0.01

mFGS: Modified Ferriman-Gallway score

Table 2: The median/mean scores of BDI, BAI, BES and mFGS and the differences for BDI-II, BAI, BES and mFGS aacording to the sub-phenotypes of PCOS

	Phenotype A	Phenotype B	Phenotype C	Phenotype D	p A-B	p A-C	p A-D	p B-C	p B-D	p C-D
BDI-II	21±12	15±9	6 (2-25)	12±6	0.07	0.07	0.03*	0.76	0.85	0.99
BAI	17 (6-49)	11 (2-50)	10±12	12±7	0.04*	0.02*	0.01*	0.21	0.88	0.33
BES	100±29	88±27	89±20	86±22	0.35	0.80	0.39	1	0.99	0.99
mFGS	17±7	15±5	9±3	14±3	0.13	<0.01*	<0.01*	0.01*	<0.01*	<0.01*

BDI-II: Beck depression inventory-II, BAI: Beck anxiety inventory, BES: Body esteem scale, mFGS: Modified Ferriman-Gallway score, PCOS: Polycystic ovary syndrome
*: Statistically significant

Discussion

Women with PCOS are more likely to suffer from mood disorders such as anxiety and depression. Obesity or weight gain and hyperandrogenism associated symptoms such as hirsutism, acne, and infertility are possible contributing factors for these mood disorders. In our study, we aimed to evaluate these mood disorders according to subphenotypes of PCOS to find out which components of the disease display important effects on these mood disorders. In our study, we found i) higher prevalence of phenotype A, ii) phenotype A has higher BDI scores than phenotype D, iii) phenotype A has higher BAI scores than phenotype B, C, D iv) BES scores were not different through phenotypes.

In our cohort, we found the prevalence of PCOS subphenotypes from type A to D as 43.2% (n=32), 32.4% (n=24), 8% (n=6) and 16% (n=12) respectively. It was reported that more than half of PCOS patients constitute of phenotype A, whereas the other three phenotypes have a similar prevalence (4). Another systematic review and meta-analysis showed a pooled estimates of detected PCOS phenotype prevalence as phenotype A, 50% [95% confidence interval (CI), 46%-54%] phenotype B, 13% (95% CI, 11%-17%), phenotype C, 14% (95% CI, 12%-16%) and phenotype D, 17% (95% CI, 13%-22%) (13). Our findings were similar to the literature showing domination for the classic form of PCOS (phenotype A and B), which constitutes approximately two-thirds of PCOS patients' total.

PCOS phenotypes A and B are associated with menstrual irregularities, higher insulin levels, insulin resistance, higher BMI, and prevalence of obesity as compared with PCOS phenotypes C and D. Phenotype C is generally associated with mildly elevated serum androgens, insulin levels, hirsutism scores, and metabolic syndrome when compared to classic PCOS or phenotype D (14). Phenotype D, also known as non-hyperandrogenic PCOS, is not associated with increased endocrine and metabolic dysfunction and lower prevalence of metabolic syndrome (4). These observational data show that hyperandrogenism is a crucial factor in the development of metabolic disturbances associated with PCOS. The effects of hyperandrogenism for metabolic syndrome are the distribution of white adipose tissue, increased adipocyte size and differentiation, reduced lipolysis and adipokine secretion, reduction of insulin-stimulated glucose uptake, liver fat accumulation, and β cell dysfunction. Androgen excess also promotes metabolic dysfunction through specific brain centers (15). A question arises whether there may be some differences in terms of mood disturbances according to subphenotypes of PCOS.

Previously published meta-analyses in women with PCOS have shown that depression and anxiety are more prevalent in women with PCOS than controls. A comprehensive review representing 3.050 subjects with PCOS and 3858 controls reported women with PCOS to have over three times the odds of depressive symptoms and over five times the odds of anxiety symptoms than controls. Women with PCOS and depression were reported to have higher mean values of insulin resistance, BMI, hirsutism, and infertility (16). Depression is also more prominent in patients with impaired quality of life from body esteem and associated fatigue, sleep disturbances, phobia, appetite changes, and binge eating (17). There is not any published data about the prevalence of mood disturbances according to subphenotypes of PCOS. In our cohort, we found a higher prevalence of depression in phenotype A than phenotype D but similar between A, B, and C. This pointed out lower depression scores in the non-hyperandrogenic phenotype. Although the causes of depression in women with PCOS remain unknown, this can be hypothesized due to the effect of hyperandrogenism (18,19). Nevertheless, both animal models and comprehensive human studies provide more valuable information to better understand hyperandrogenism for depression in PCOS patients.

Data derived from clinical observational studies also suggest an association between BMI and depression. Depressed women with PCOS with similar hyperandrogenism levels have higher BMI than non-depressed women with PCOS (17,20). However, other observational studies showed an increased risk of depression in women with PCOS persisted after adjustment for BMI (6). In our study, we found that an increase in BMI by 1 kg/m^2 was found to a 0.49 increment in depression scores (p=0.01). It is a chicken or the egg paradox, and it is still unknown that obesity is a risk factor for depression in PCOS, or depression is a risk factor for obesity in PCOS.

Besides the depression findings, we only observed higher BAI scores in phenotype A than phenotype B, C, D, and BES scores were similar through phenotypes. We also did not find a correlation between BMI and BAI and BES scores (p=0.33, p=0,18, respectively). It was a surprising finding with the general belief of that women who were obese had a negative appreciation of body image, regardless of a PCOS diagnosis (21).

Our study's strength was that it was the first study evaluating depression, anxiety, and body perception in a group of patients according to the subphenotypes of PCOS. The limitations were the lack of a healthy control group and the small size of the participants.

Conclusion

There is a need for screening for mood disorders, especially anxiety and depression, for patients with PCOS because of the importance of the disease's psychological consequences. Moreover, if a specific relationship between mood changes and

PCOS phenotypes is found, likewise depression and pphenotype A in our study, specific scales can be determined and used for each subphenotype for cost and time saving before referral to the specialists.

Ethics

Ethics Committee Approval: This study was approved by Ankara University Faculty of Medicine Undergraduate Student Research Ethics Review Board (date: 25.12.2018, decision no: 9530).

Informed Consent: All subjects signed informed consent forms.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: T.A.E., Concept: D.Ç., Design: Ö.D., Data Collection or Processing: M.S.S., B.Y., Z.T., Ş.N.Y., E.O., E.G., H.H.Ş., Analysis or Interpretation: M.S.S., B.Y., Z.T., Ş.N.Y., E.O., E.G., H.H.Ş., Literature Search: A.G.C., Writing: A.G.C.

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