

The Relationship between Clinico-biochemical Characteristics and Psychiatric Distress in Young Women with Polycystic Ovary Syndrome

E ADALI¹, R YILDIZHAN¹, M KURDOGLU¹, A KOLUSARI¹, T EDIRNE², HG SAHIN²,
B YILDIZHAN³ AND M KAMACI¹

¹Department of Obstetrics and Gynaecology, and ²Department of Family Medicine, Medical Faculty, Yuzuncu Yil University, Van, Turkey; and ³Department of Obstetrics and Gynaecology, Medical Faculty, Marmara University, Istanbul, Turkey

The relationship between clinico-biochemical characteristics and self-reported psychological parameters in 42 women with polycystic ovary syndrome (PCOS) and 42 age-matched healthy controls was examined. The General Health Questionnaire was used (GHQ-12) to ascertain emotional distress and the Beck Depression Inventory (BDI) to determine depressive symptoms. Emotional distress, depressive symptoms, hirsutism score, body mass index (BMI), waist-to-hip ratio (WHR), luteinizing hormone/follicle-stimulating hormone ratio, serum total testosterone, dehydroepiandrosterone

sulphate levels and the insulin resistance index were significantly greater in women with PCOS than in healthy women. The BDI and GHQ-12 scores of the women with PCOS were significantly higher than those of the control group (BDI, 11.69 ± 9.49 vs 5.80 ± 4.58 ; GHQ-12, 3.38 ± 3.38 vs 1.54 ± 1.97 , respectively), and BMI and WHR were positively correlated with the BDI and GHQ-12 scores. Clinicians should be aware of the increased risk of emotional distress and depression in women with PCOS, especially those who are obese, and of the need to screen these patients for such symptoms.

KEY WORDS: POLYCYSTIC OVARY SYNDROME; DEPRESSIVE SYMPTOMS; EMOTIONAL DISTRESS; PSYCHIATRIC DISTRESS; OBESITY; GENERAL HEALTH QUESTIONNAIRE; MENTAL HEALTH

Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine-metabolic disorders, affecting 5 – 10% of women of reproductive age.¹ Positive diagnosis is based on the patient presenting any two of the following three features: oligo- or

anovulation, clinical and/or biochemical signs of hyperandrogenism, and polycystic ovaries on ultrasound examination.² The primary defect in PCOS appears to be exaggerated androgen synthesis and secretion by the ovaries and adrenal glands.³ Insulin resistance and systemic

hyperinsulinism play a major role in the development of the hyperandrogenism characteristic of the syndrome. Insulin acts synergistically with luteinizing hormone (LH) to stimulate the synthesis of androgens by ovarian theca cells *in vitro*.⁴

Although most studies have shown that the gynaecological and endocrine features of PCOS, including chronic anovulation, hyperandrogenism, difficulty in conceiving, menstrual abnormalities and the metabolic syndrome, can be significantly distressing to patients throughout their lifespan, only a few studies have focused on the impact of PCOS on mental health.

Clinical manifestations of PCOS are painful, uncomfortable and unpredictable, and are associated with characteristics culturally defined as unfeminine and undesirable (for instance hirsutism, obesity, acne and infertility). Many PCOS patients are overweight or obese, and abdominal distribution of body fat is especially characteristic in these women.⁵ Obesity itself increases the risk of insulin resistance, although insulin resistance can also occur in the absence of obesity. PCOS is associated with insulin resistance independent of obesity.⁶ Studies have shown that these patient groups experience increased emotional distress and depression.^{7,8} Augmented levels of androgens in women have been reported to be related to clinical mood disorders in women with and without PCOS.^{9,10}

Rasgon *et al.*⁸ found that elevated levels of insulin resistance and a higher body mass index (BMI) were associated with depression in women with PCOS. Hirsutism, menstrual irregularity and infertility have been shown to be the most distressing symptoms in adults with PCOS, whereas weight difficulties have been identified as the most distressing symptom in adolescents and young women with PCOS.¹¹ In addition, PCOS is one of the

leading causes of infertility and involuntary childlessness, which are major stress factors for many women.¹² Furthermore, the long-term health risks associated with the diagnosis (metabolic syndrome and its sequelae, such as type 2 diabetes mellitus, hypertension, lipid disorders and atherosclerosis) may have a negative impact on psychosocial well-being.⁷

The goals of the present study were to compare the prevalence of emotional distress and depressive symptoms in PCOS patients with those in age-matched healthy women, using self-report measures, and to investigate the relationship between the clinico-biochemical characteristics associated with PCOS and psychiatric distress.

Patients and methods

PATIENTS

This prospective study analysed 42 consecutive patients with PCOS and 42 age-matched healthy control women living in the eastern Anatolia region of Turkey and of similar socioeconomic status. They were recruited from the outpatient clinics of the Department of Gynaecology and Obstetrics, Yuzuncu Yil University Medical Faculty (Van, Turkey) over a 7-month period between September 2007 and April 2008. The diagnosis of PCOS was made according to the joint criteria of the European Society of Human Reproduction and Embryology and the American Society of Reproductive Medicine (ESHRE/ASRM).² Patients recruited into the control group were determined to be of good health based on medical history, physical and pelvic examination, blood chemistry and pelvic ultrasonography. None of the control patients exhibited signs or symptoms of the ESHRE/ASRM criteria.

All participants had not taken any medication (oral contraceptives, glucocorticoids, antiandrogens, insulin

sensitizers or psychiatric medications) that could affect their biochemical profile, hormone profile or psychosocial parameters for at least 6 months before entering the study. The exclusion criteria were Cushing's syndrome, congenital adrenal hyperplasia, hyperprolactinaemia, thyroid dysfunction, virilizing tumours, psychiatric disease and a history of infertility.

The study protocol was performed according to the Helsinki Committee requirements and was approved by the Ethics Committee of Yuzuncu Yil University. Written informed consent was obtained from all subjects before participation in the study.

MEASUREMENTS

Clinical and anthropometric variables, including hirsutism score, body mass index (BMI) and waist-to-hip ratio (WHR), were all determined by the same physician. Hirsutism scores were evaluated using the modified Ferriman–Gallwey score, which can range from 1 to 36, with scores ≥ 6 indicating relevant hirsutism.¹³ WHR was used as the measure of central obesity. It was calculated by dividing the minimal waist circumference by the hip circumference at the level of the greater trochanters. The BMI was calculated as weight (kg)/height (m²).

For biochemical analyses, serum and plasma samples were collected between 09.00 and 11.00 h, after an overnight fast of at least 12 h during the follicular phase (between days 3 and 5) of the patients' spontaneous or progestin-induced menstrual cycle. Levels of LH, follicle-stimulating hormone (FSH), total testosterone, dehydroepiandrosterone sulphate (DHEAS) and insulin were determined by chemiluminescent immunoassay using an Immulite® 2000 analyser (Diagnostic Products Corp., Los Angeles, CA, USA). Glucose, total cholesterol, high-density

lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol and triglycerides were measured by enzymatic colourimetric assay using a Roche-Hitachi PP Modular Analyser (Roche-Hitachi, Tokyo, Japan) and its original reagents. Insulin resistance, defined by the homeostasis model assessment insulin resistance index (HOMA-IR), was calculated using the following equation: $\text{HOMA-IR} = \text{fasting insulin } (\mu\text{U/l}) \times \text{fasting glucose (mmol/l)} / 22.5$.¹⁴

Depressive symptoms were assessed using the Turkish version of the Beck Depression Inventory (BDI). This is a 21-item multiple-choice self-report questionnaire that measures severity of depression by asking the person about vegetative, emotional, cognitive and motivational symptoms associated with depression, described in the American Psychiatric Association's publication of the *Diagnostic and Statistical Manual of Mental Disorders*.¹⁵ The scoring methods used in the Turkish BDI are Likert-style (0, 1, 2, 3) ranging from 0 to 63, where a higher total score indicates more severe depressive symptoms. Hisli¹⁶ confirmed the validity and reliability of the Turkish version of BDI among university students. BDI scores ≥ 11 were considered 'depressive' (11 – 16, mild depressive symptoms; ≥ 17 , moderate to severe depressive symptoms).

Emotional distress was assessed using the 12-item General Health Questionnaire (GHQ-12). It is a shortened form of GHQ-60, which was developed by Goldberg and Blackwell¹⁷ in order to screen both for the inability to continue normally to carry out the activities of a 'healthy' individual and for new-onset distress in the general population, out-patients and primary care users. It does not indicate severity or the type of disorder; it is a first screening phase for psychiatric distress. Scoring methods used in GHQ-12 are Likert-style (0, 0, 1, 1). On a 0 –

12 point scale, a cut-off score ≥ 3 points was used to indicate a risk of psychiatric distress and is consistent with the use of GHQ-12 in previous studies.¹⁸ Reliability and validity studies of the Turkish version of GHQ-12 at a primary health care level have been carried out by Kilic.¹⁹

STATISTICAL ANALYSIS

All statistical analyses were performed using SPSS® version 10.0 (SPSS Inc., Chicago, IL, USA) for Windows®. Data are presented as mean \pm SD or as percentages. Comparisons between participants with PCOS and controls were analysed by Student's *t*-test. The Z-test was used to analyse the two proportions. Correlations of BDI scores and GHQ-12 scores with clinical and biochemical features in women with PCOS and the controls were examined using Spearman's rank correlation coefficient (r_s). A *P*-value < 0.05 was considered to be statistically significant.

Results

A total of 84 women, aged 19 – 29 years (42 with PCOS and 42 controls), were evaluated. Table 1 shows the sociodemographic, anthropometric and clinical characteristics of the women. The mean ages of women in the PCOS and control groups were not significantly different. There were also no statistically significant differences in education levels, marital status or employment status between the groups.

The mean BMI, WHR, LH/FSH ratios, levels of DHEAS, levels of total testosterone and hirsutism scores of the women in the PCOS group were statistically significantly higher than those in the control group ($P < 0.01$ except for total testosterone which was $P < 0.05$; Table 1).

There were no statistically significant differences in the levels of glucose, total cholesterol, triglycerides, LDL cholesterol, or

HDL cholesterol between the PCOS and control groups ($P > 0.05$). The HOMA-IR levels, indicating insulin resistance, were statistically significantly higher in the PCOS group than in the control group ($P < 0.01$).

The BDI scores of the patients with PCOS were significantly higher than those of the control group ($P < 0.01$). Within the PCOS group, 33.3% of patients were found to be depressed (BDI score ≥ 11) compared with 11.9% of the control group ($P < 0.05$).

The GHQ-12 scores, which evaluate the emotional stress of the subjects, were significantly higher for the PCOS group compared with the control group ($P < 0.01$). Emotional stress (GHQ-12 score ≥ 3) was recorded in 38.1% of the PCOS group and 14.3% of the control group ($P < 0.01$).

Relationships between the BDI and GHQ-12 scores, measured in the PCOS and control groups, and their clinical and biochemical parameters were evaluated using Spearman's correlations analysis (Table 2). In the PCOS group, the BDI scores and the GHQ-12 scores were significantly positively correlated with BMI and with WHR ($P < 0.05$ except for WHR which was $P < 0.01$). No correlations were found between either BDI or GHQ-12 and the clinical and biochemical parameters of the control group.

Discussion

The relationships between the psychological health aspects and the clinical and biochemical characteristics of PCOS are not yet clear. The present study was, therefore, undertaken to clarify the relationship between increased emotional stress, depressive symptoms, and the clinical and biochemical characteristics of PCOS in a group of young patients with PCOS compared with a control group.

PCOS often manifests at an age when finding a partner, sexual activity and

TABLE 1:
Socio-demographic, anthropometric and clinical characteristics of women with polycystic ovary syndrome and healthy controls

Variable	PCOS (<i>n</i> = 42)	Control (<i>n</i> = 42)	Statistical significance ^a
Age (year)	23.54 ± 3.13	24.45 ± 2.47	NS
Education			
High school or less, <i>n</i> (%)	32 (76.2%)	34 (81.0%)	NS
College or postgraduate, <i>n</i> (%)	10 (23.8%)	8 (19.0%)	NS
Marital status			
Married, <i>n</i> (%)	31 (73.8%)	35 (83.3%)	NS
Single, <i>n</i> (%)	11 (26.2%)	7 (16.7%)	NS
Employment status			
Employed, <i>n</i> (%)	11 (26.2%)	8 (19.0%)	NS
Student, <i>n</i> (%)	8 (19.0%)	6 (14.3%)	NS
Unemployed, <i>n</i> (%)	23 (54.8%)	28 (66.7%)	NS
BMI (kg/m ²)	28.42 ± 4.30	24.11 ± 4.14	<i>P</i> < 0.01
BMI < 25 kg/m ² , <i>n</i> (%)	14 (33.3%)	27 (64.3%)	<i>P</i> < 0.01
BMI ≥ 25 kg/m ² , <i>n</i> (%)	28 (66.7%)	15 (35.7%)	<i>P</i> < 0.01
WHR	0.82 ± 0.04	0.74 ± 0.02	<i>P</i> < 0.01
LH/FSH	2.05 ± 0.37	1.26 ± 0.26	<i>P</i> < 0.01
DHEAS (µg/dl)	223.64 ± 68.73	127.00 ± 51.21	<i>P</i> < 0.01
Total testosterone (ng/dl)	61.21 ± 36.03	46.28 ± 15.78	<i>P</i> < 0.05
Glucose (mg/dl)	86.34 ± 12.25	88.06 ± 6.83	NS
Total cholesterol (mg/dl)	166.26 ± 23.04	153.22 ± 31.71	NS
LDL cholesterol (mg/dl)	92.04 ± 24.32	89.95 ± 19.10	NS
HDL cholesterol (mg/dl)	54.3 ± 19.22	56 ± 21.53	NS
Triglycerides (mg/dl)	99.78 ± 66.93	98.83 ± 58.52	NS
Hirsutism score	12.42 ± 3.40	4.50 ± 1.15	<i>P</i> < 0.01
HOMA-IR	3.21 ± 0.71	2.39 ± 0.24	<i>P</i> < 0.01
BDI score	11.69 ± 9.49	5.80 ± 4.58	<i>P</i> < 0.01
BDI score ≥ 11, <i>n</i> (%)	14 (33.3%)	5 (11.9%)	<i>P</i> < 0.05
GHQ-12 scores	3.38 ± 3.38	1.54 ± 1.97	<i>P</i> < 0.01
GHQ-12 score ≥ 3, <i>n</i> (%)	16 (38.1%)	6 (14.3%)	<i>P</i> < 0.01

Data are presented as mean ± SD unless stated otherwise.

^aStudent's *t*-test and the Z-test.

NS, not statistically significant (*P* > 0.05); BMI, body mass index; WHR, waist-to-hip ratio; LH, luteinizing hormone; FSH, follicle-stimulating hormone; DHEAS, dehydroepiandrosterone sulphate; LDL, low-density lipoprotein; HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment of insulin resistance; BDI, Beck Depression Inventory; GHQ, General Health Questionnaire.

marriage are important. The associated cosmetic and psychosexual implications are thought to cause profound emotional distress in affected women. Several aspects of the disorder can potentially cause considerable emotional stress.²⁰

Obesity and, specifically, central obesity, is

a common feature of PCOS that worsens the phenotype.²¹ Depressive symptoms and mood disorders are common in most obese patients.²² However, there is varying information about the effects of obesity on the risk of depression. In the present study, BMI and WHR were significantly greater in

TABLE 2:
 Spearman's rank correlations (r_s) of BDI scores and GHQ-12 scores with the clinico-biochemical features of women with polycystic ovary syndrome (PCOS) and healthy controls

Clinico-biochemical feature	PCOS ($n = 42$)		Controls ($n = 42$)	
	BDI scores (r_s)	GHQ-12 scores (r_s)	BDI scores (r_s)	GHQ-12 scores (r_s)
BMI (kg/m ²)	0.334*	0.346*	0.096	0.028
WHR	0.325*	0.425**	0.054	0.122
HOMA-IR	0.104	0.192	0.094	0.088
LH/FSH	0.115	0.227	0.080	0.040
DHEAS (µg/dl)	0.105	0.009	0.149	0.119
Total testosterone (ng/dl)	0.102	0.059	0.005	0.229
LDL cholesterol (mg/dl)	0.217	0.097	0.073	0.232
HDL cholesterol (mg/dl)	0.031	0.008	0.252	0.109
Triglycerides (mg/dl)	0.086	0.157	0.221	0.200
Hirsutism score	0.093	0.009	0.225	0.079

* $p < 0.05$, ** $p < 0.01$.

BDI, Beck Depression Inventory; GHQ-12, General Health Questionnaire; BMI, body mass index; WHR, waist-to-hip ratio; HOMA-IR, homeostasis model assessment of insulin resistance; LH, luteinizing hormone; FSH, follicle-stimulating hormone; DHEAS, dehydroepiandrosterone sulphate; LDL, low-density lipoprotein; HDL, high-density lipoprotein.

patients with PCOS, for whom results also showed highly elevated emotional distress and depression compared to the control group. These findings support previous studies indicating that obesity may be a risk factor for psychological distress and depression in patients with PCOS.^{7,8,23} The results of the present study are contradictory to data presented by Benson *et al.*²⁴ that did not support a connection between obesity and depression in patients with PCOS. It is unclear how much of the clinical overlap between mood disorders and obesity is due to iatrogenic factors, co-occurrence of two common disorders, or inherited pathogenic factors.²⁵ It is possible that depression may be independently associated with BMI, as both weight gain and obesity are distressing symptoms that are associated with depression.²⁶

Insulin resistance is a cardinal finding in the pathophysiology of PCOS.²⁷ The present study demonstrated insulin resistance in

women with PCOS. The relationship between insulin resistance and depression has been investigated in a few studies, with contradictory results.²⁸⁻³⁰ Whilst the specific mechanism has not yet been determined, there is evidence indicating that insulin has a role in neuro-cognitive functions and of some overlapping pathophysiological relationships between altered insulin sensitivity and mood changes.³¹ Depression has been associated with increased cortisol levels, increased sympathetic activity and decreased central nervous system serotonin levels, features also associated with insulin resistance.²⁵ Depression is about twice as common in people with diabetes compared with those without it and the treatment of depression can improve glucose control, although this is not a consistent finding.³² If depression modulates insulin sensitivity, then populations with underlying insulin resistance (including women with PCOS) and concomitant depression might demonstrate

a more rapid deterioration in metabolic status from insulin resistance to type 2 diabetes mellitus. Aggressive treatment of depression might be a strategy for preventing or slowing the progression from insulin resistance.^{29,32} In the present study, however, self-related symptoms of depression and emotional stress were found not to be related to insulin resistance among young women with PCOS. Similar findings were reported by Roos *et al.*³³ Determining the relationship between insulin resistance and psychiatric distress in PCOS will require further investigation.

Women with PCOS have clinical and/or biochemical signs of hyperandrogenism. Several studies have shown a correlation between depression scores and the levels of serum androgen.^{34,35} It has been suggested that women with PCOS have a lower self-esteem and a more negative self-image, and have higher levels of depression and psychological distress owing to the physical appearance of hyperandrogenism, including obesity, hirsutism, cystic acne, seborrhoea and hair loss, possibly by influencing feminine identity.^{7,9,22,25} Other studies, however, have demonstrated no association between depressive symptoms, the physical appearance of hyperandrogenism and levels of serum androgen.^{8,24,36} In the present study, analysis of young women with PCOS showed that GHQ-12 and BDI scores bear no relationship to the levels of total testosterone and DHEAS or to the hirsutism score.

PCOS is most closely associated with depression and emotional distress, and this has important implications for the diagnosis and treatment of disorders. The therapy of PCOS should tackle both physical and

psychological complaints. This is because depression reduces motivation, and yet good motivation is key to compliance with medication and the dietary management of PCOS.^{8,11}

It has, so far, not been possible to forecast the extent or nature of psychological distress by evaluating the severity of physical symptoms of patients with PCOS. Clinicians should routinely evaluate each patient with PCOS from a mental health perspective and be aware of the impact of PCOS on mental well-being. Patient evaluation by brief questionnaires can be easily applied in the polyclinic, however the most effective way to determine the nature, severity and appropriate therapy for PCOS patients is through consultation with an expert psychologist or psychiatrist. The present study examined the relationship between psychiatric distress as measured by GHQ-12, depression as measured by the BDI score, and the clinico-biochemical characteristics of women with PCOS. Scores of GHQ-12 and BDI in the PCOS group were higher than those in the control group and showed a close relationship between emotional stress, depression and obesity. In order to achieve psychosocial health, patients with PCOS require a multi-disciplinary approach (involving gynaecologists, endocrinologists dermatologists and psychiatrists). Psychological symptoms should be evaluated as well as clinical symptoms and this should be a routine part of their examinations.

Conflicts of interest

The authors had no conflicts of interest to declare in relation to this article.

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Author's address for correspondence

Assistant Professor Ertan Adali

Yuzuncu Yil Universitesi, Arastirma Hastanesi, Kadin Hastaliklari ve Dogum Anabilim Dalı,
Van, Turkey.

E-mail: ertanadali@yahoo.com