TÜBİTAK

Turkish Journal of Medical Sciences

http://journals.tubitak.gov.tr/medical/

Research Article

Turk J Med Sci
(2016) 46: 245-250
© TÜBİTAK
doi:10.3906/sag-1405-72

# Depression, anxiety, and their relation with clinical parameters and androgen levels in hirsute women

**Leyla IRAK[1], Halise ÇINAR YAVUZ[2,*], Berçem AYÇİÇEK DOĞAN[3], Türkan METE[4], Dilek BERKER[3], Serdar GÜLER[3]**

[1]Department of Endocrinology and Metabolism, İstanbul Ok Meydanı Training and Research Hospital, İstanbul, Turkey
[2]Department of Endocrinology and Metabolism, Faculty of Medicine, Turgut Özal University, Ankara, Turkey
[3]Department of Endocrinology and Metabolism, Ankara Numune Training and Research Hospital, Ankara, Turkey
[4]Department of Endocrinology and Metabolism, Samsun Training and Research Hospital, Samsun, Turkey

**Received:** 27.05.2014 • **Accepted/Published Online:** 12.07.2015 • **Final Version:** 17.02.2016

**Background/aim:** The purpose of this study was to assess the prevalence of anxiety and depression among patients with hirsutism and to evaluate the relationships of anxiety and depression with clinical parameters and androgen levels.

**Materials and methods:** One hundred and seven women with hirsutism were enrolled in the study. All participants completed standardized questionnaires to assess depression (Beck Depression Inventory (BDI)) and anxiety (Beck Anxiety Inventory (BAI)). The Ferriman–Gallwey (FG) scores, body mass indexes (BMIs), homeostatic model assessments of insulin resistance (HOMA-IR), and serum androgen levels of all patients were obtained.

**Results:** Seventy-four of the 107 patients (69.15%) had BDI scores indicating depression, and 47 of the 107 patients (43.9%) had BAI scores indicating anxiety disorders. No difference was found between high BAI and normal BAI patients related to BMI, age, FG scores, testosterone levels, and HOMA-IR levels ($P > 0.05$), and no difference was found between high BDI and normal BDI patients related to BMI, age, FG scores, free testosterone levels, and HOMA-IR levels. There was a positive correlation between BDI scores and dehydroepiandrosterone sulphate (DHEA-S) levels ($P < 0.01$).

**Conclusion:** We found considerable amounts of depression, anxiety, and the coexistence of depression and anxiety in patients with hirsutism. Depression and the severity of depressive symptoms were positively correlated with DHEA-S levels.

**Key words:** Anxiety, depression, hirsutism

## 1. Introduction

Hirsutism is defined as the presence of excessive terminal hair in androgen-dependent areas of a woman's body and affects approximately 5%–8% of the population (1,2). It is extremely distressing for patients and has a significant negative impact on their psychosocial development (3). The most common causes of hirsutism are polycystic ovary syndrome (PCOS), idiopathic hirsutism (IH), and nonclassical congenital adrenal hyperplasia (NCAH) (4). Other uncommon causes are ovarian tumors, adrenal tumors, Cushing syndrome, hyperprolactinemia, thyroid diseases, and insulin resistance (IR) syndromes.

Depression is defined as depressed mood or a loss of interest or pleasure in daily activities for more than 2 weeks. Women suffer from depression almost twice as often as men, and depression occurs most frequently between the ages of 20 and 40 (5). Many researchers have found an increased incidence of depression in women with PCOS (6–8), and some researchers have even reported a sevenfold increase in the incidence of suicide among women with PCOS (9).

Generalized anxiety disorder (GAD) is defined as excessive anxiety and worry about a number of events or activities, occurring more days than not for at least 6 months, and out of proportion to the likelihood or impact of the feared events. Anxiety disorders are also common in PCOS (10–13). Based on a questionnaire study, Benson et al. (10) found that 34% of 448 surveyed women with PCOS had anxiety disorders. Anxiety-related symptoms were associated mainly with acne and fertility problems (10). Some studies showed that hirsutism and acne were associated with anxiety and psychotic symptoms, whereas other studies failed to find this association (11–13).

In the present study we aimed to evaluate the prevalence of anxiety and depression symptoms among patients with PCOS, congenital adrenal hyperplasia, and IH, and

* Correspondence: halisecyavuz@yahoo.com

to assess whether anxiety or depression is related to the degree of hirsutism, IR, or androgen hormone levels.

## 2. Materials and methods

Data were collected from 107 women with hirsutism aged 15–49 years who were patients at the Endocrinology outpatient clinic of Ankara Numune Research and Training Hospital. The patients were divided into three groups based on the diagnosis of PCOS, NCAH, or IH.

Hirsutism was assessed using Ferriman–Gallwey scores in which the patients scored their hair growth on nine different parts of their bodies from 0 (no terminal hair) to 4 (maximal growth) with a maximum score of 36. A score of 8 or more indicated the presence of hirsutism. Patients were tested for the follicle-stimulating hormone, the luteinizing hormone, 17-hydroxyprogesterone (17-OHP), basal prolactin (PRL), total testosterone and free testosterone, dehydroepiandrosterone sulphate (DHEA-S), androstenedione, total cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol, and triglycerides during the follicular phase.

For all patients, blood samples and insulin were obtained after they fasted overnight. Insulin sensitivity was estimated using basal insulin and glucose values to calculate the homeostatic model of IR (HOMA-IR) (14).

The diagnosis of PCOS was performed according to the Rotterdam 2003 criteria and was given to patients with clinical and/or biochemical hyperandrogenism, chronic oligoanovulation, and/or polycystic ovaries on ultrasound. Polycystic ovaries were defined as the presence of ≥12 follicles in each ovary with each follicle measuring 2–9 mm in diameter and/or an increased ovarian volume (>10 mL). To confirm a diagnosis of NCAH, 17-OHP concentrations were examined in the early follicular phase. The patient with a 17-OHP level higher than 2 ng/mL (normal: 0.2–2.6 ng/mL) was subjected to an adrenocorticotropic hormone stimulation test (250 mcg). If the result exceeded 10 ng/mL, a diagnosis of NCAH was confirmed.

The diagnoses of thyroid dysfunction, hyperprolactinemia, and adrenal/ovarian tumors were excluded. The remaining patients with normal serum androgen concentrations and no menstrual irregularity were diagnosed with IH.

All patients completed the Beck Depression Inventory (BDI) and the Beck Anxiety Inventory (BAI) questionnaires. Both the BDI and the BAI are self-report inventories that include 21 multiple choice questions for measuring the severity of depression and anxiety, respectively (15,16). Scores of ≥17 on the BDI indicate severe depression that requires treatment. Each symptom is rated on a 4-point scale ranging from 0 (not at all) to 4 (severely), and the total score can range from 0 to 63, with higher scores corresponding to higher levels of anxiety/depression (16,17).

Data analysis was performed using SPSS for Windows 11.5. Descriptive statistics were expressed as means ± standard deviation for continuous variables and as the number of cases (%) for categorical variables. Pearson's chi-square or Fisher's chi-square tests were used for categorical variables, and $P < 0.05$ was considered significant. For the normally distributed data, a t-test was used to compare the mean values between the two groups.

## 3. Results

Among the 107 patients, 66 patients were diagnosed with PCOS, 10 patients had congenital adrenal hyperplasia, and 31 patients had IH. The demographic data for the 107 hirsute patients are given in Table 1. Patients were between 15 and 47 years of age, with BMI calculations between 16 and 37.9, and 69% of the patients had an HOMA-IR of above 2.8. Sixty-eight percent of the patients had intermediate and high BDI scores, and 45.2% of the patients had high BAI scores. Moreover, 43 of the 107 patients were found to have both anxiety and depression disorders. The DHEA-S level, the total testosterone level, and the free testosterone level were high in 19.4%, 69.8%, and 73.5% of the patients, respectively. The degree of depression was found to be high in patients with a high level of DHEA-S ($P < 0.01$); however, there was no correlation between DHEA-S levels and anxiety ($P = 0.18$). There was no correlation between anxiety or depression and HOMA-IR levels or BMI (Table 2). There were also no correlations between free or total testosterone levels and depression, anxiety ($P = 0.39$), or the coexistence of depression and anxiety ($P = 0.46$) (Table 3). Furthermore, there was no correlation between

**Table 1.** Demographic and clinical data of the studied hirsute patients.

| Variables | N = 111 |
|---|---|
| Age | 24.06 ± 5.9 |
| Body mass index | 24.8 ± 4.8 |
| Age at first menarche | 13.43 ± 1.2 |
| Diagnosis | |
| *Polycystic ovary syndrome* | 66 (61.7%) |
| *Nonclassical congenital adrenal hyperplasia* | 10 (10%) |
| *Idiopathic Hirsutism* | 31 (29%) |
| Ferriman–Gallwey score | 12 (8–28) |
| HOMA-IR* | 2.06 ± 1.4 |

*HOMA-IR: the homeostasis model assessment of insulin resistance.

**Table 2.** Depression, anxiety, and correlations with clinical features of hirsute patients.

| Variables | Depressed group | | | Anxiety group | | | Depressed and anxious group | | |
|---|---|---|---|---|---|---|---|---|---|
| | No (35) | Yes (72) | P-value | No (57) | Yes (47) | P-value | No (64) | Yes (43) | P-value |
| Ferriman–Gallwey score | | | 0.755 | | | 0.709 | | | 0.403 |
| *> 12* | 13 | 29 | | 21 | 19 | | 27 | 20 | |
| *< 12* | 22 | 43 | | 36 | 28 | | 37 | 23 | |
| Irregular menses | | | 0.304 | | | 0.272 | | | 0.270 |
| *Yes* | 16 | 41 | | 28 | 28 | | 33 | 25 | |
| *No* | 18 | 30 | | 28 | 18 | | 31 | 17 | |
| Body mass index | | | 0.512 | | | 0.331 | | | 0.168 |
| *< 30* | 30 | 58 | | 49 | 37 | | 55 | 33 | |
| *> 30* | 5 | 14 | | 8 | 10 | | 9 | 10 | |
| HOMA–IR* | | | 0.48 | | | 0.052 | | | 0.280 |
| *< 2.8* | 22 | 47 | | 40 | 27 | | 42 | 25 | |
| *> 2.8* | 5 | 16 | | 7 | 13 | | 22 | 18 | |

*HOMA-IR: the homeostasis model assessment of insulin resistance.

**Table 3.** Depression, anxiety, and correlations with androgen hormone levels.

| Variables | Depressed group | | | Anxiety group | | | Depressed and anxious group | | |
|---|---|---|---|---|---|---|---|---|---|
| | No (32) | Yes (63) | P-value | No (52) | Yes (43) | P-value | No (59) | Yes (39) | P-value |
| DHEA-S** | | | 0.009 | | | 0.18 | | | 0.141 |
| *High* | 11 | 8 | | 13 | 6 | | 14 | 5 | |
| *Normal* | 21 | 58 | | 39 | 37 | | 45 | 34 | |
| Androstenedione | | | 1.000 | | | 1.000 | | | 0.633 |
| *High* | 28 | 55 | | 44 | 36 | | 49 | 33 | |
| *Normal* | 3 | 5 | | 4 | 4 | | 6 | 4 | |
| Total testosterone | | | 0.564 | | | 0.077 | | | 0.127 |
| *High* | 21 | 40 | | 36 | 23 | | 43 | 23 | |
| *Normal* | 7 | 18 | | 10 | 15 | | 14 | 14 | |
| Free testosterone | | | 0.6 | | | 0.6 | | | |
| *High* | 8 | 19 | | 16 | 11 | | 44 | 30 | |
| *Normal* | 26 | 48 | | 38 | 33 | | 17 | 10 | |

**DHEA-S: dehydroepiandrosterone sulphate.

the severity of hirsutism and depression, anxiety, or the coexistence of depression and anxiety.

## 4. Discussion

Hirsutism had a significant negative impact on health-related quality of life (HRQoL) measures in women and

was associated with higher prevalence of anxiety in several studies (13,17). Oral contraceptive treatment improved the HRQoL measures in PCOS patients, but had no effect on their symptoms of depression and anxiety (18). There are a few studies showing correlations between the degree of hirsutism and depression or anxiety. Ekbäck et al. (19) recently found that higher levels of hair growth correlated significantly with a lower HRQoL and with symptoms of both anxiety and depression. In the present study, there was no correlation between the degree of hirsutism and depression or anxiety.

The relationship between androgen levels and mood and behavior parameters in women is controversial. High androgen levels may contribute to a higher risk of psychiatric disorders in pediatric patients with genetic causes of androgen excess. Mueller et al. (20) showed increased rates of anxiety disorders, disruptive behavioral disorders, and attention deficit hyperactivity disorder in children (8–18 years) with the diagnosis of classic congenital adrenal hyperplasia or familial male precocious puberty. Morotti et al. (21) found that moderate hirsutism and hyperandrogenism did not impact body image and self-esteem as a consequence on sexual function. However, Månsson et al. (22) found a correlation between greater free androgen index (FAI) values and greater levels of anxiety. In the present study, we did not find any correlation between total testosterone or free testosterone and depression or anxiety.

Platt et al. (23) showed that more than 50% of adolescents diagnosed with IR and obesity reported elevated symptoms of depression. In a cross-sectional study, Zhao et al. (24) found that waist circumference or abdominal obesity was significantly associated with an increased likelihood of developing major symptoms of depression or moderate-to-severe symptoms of depression among overweight and obese adults in the United States. In the present study, we did not find any association between BMI and depression or anxiety.

The association between IR and IH is not clear. Bonakdaran et al. (25) did not find significant differences between the levels of serum insulin and the prevalence of IR in PCOS, IH, and healthy subjects, but Unlühizarci et al. (26) found an association between IR and IH. In the present study, we did not find any association between IR and IH.

It has been shown that PCOS-diagnosed women with high anxiety scores have significantly elevated HOMA-IR and FAI values in comparison with PCOS-diagnosed women with low anxiety scores, independently of BMI (22). In the present study we did not find any correlation between HOMA-IR levels and depression or anxiety. Similarly, in other studies, there was no significant difference between the hormonal and metabolic profiles of PCOS patients and depression in those patients (27,28).

In our study there was a 40.1% coexistence of anxiety and depression in hirsute patients. Benson et al. (29) and Bazarganipour et al. (30) also showed the coexistence of anxiety and depression in patients diagnosed with PCOS.

It has been suggested that hypothalamic-pituitary-adrenal (HPA) system dysregulation has an important role in the pathophysiology of depression; hyperactivity of the HPA-system in major depression is reflected by an increased secretion of adrenal hormones, especially cortisol and dehydroepiandrosterone (31). Morrison et al. (32) reported that the association between serum DHEA-S levels and symptoms of depression during the menopausal transition varied with age. In younger women symptoms of depression were positively associated with DHEA-S levels, but in older women they were negatively associated with DHEA-S levels (32). Bromberger et al. (33) failed to find any association between DHEA-S levels and symptoms of depression. Annagür et al. (34) found significant association of DHEA-S levels with depression and GAD, and significant association of 17-OHP levels with depression. In the present study we showed positive correlations of depression and the severity of depressive symptoms with DHEA-S levels. In studying a group of patients composed of young female subjects with an average age of 24, we found that younger patients with hirsutism and with high DHEA-S levels tended to have more symptoms of depression.

We found considerable rates of depression, anxiety, and comorbidity of depression and anxiety (68%, 45.2%, and 40.1% respectively) in patients with hirsutism. Additionally, depression and the severity of depressive symptoms positively correlated with DHEA-S levels. Therefore, patients with hirsutism should be screened for accompanying depression and anxiety and more attention should be paid to patients with high levels of DHEA-S.

## References


1. Azziz R, Sanchez LA, Knochenhauer ES, Moran C, Lazenby J, Stephens KC, Taylor K, Boots LR. Androgen excess in women: experience with over 1000 consecutive patients. J Clin Endocr Metab 2004; 89: 453-462.
2. Yildiz BO, Bolour S, Woods K, Moore A, Azziz R. Visually scoring hirsutism. Hum Reprod Update 2010; 16: 51-64.
3. Barth JH, Catalan J, Cherry CA, Day A. Psychological morbidity in women referred for treatment of hirsutism. J Psychosom Res 1993; 37: 615-619.
4. Somani N, Harrison S, Berkfeld WF. Clinical evaluation of hirsutism. Dermatol Ther 2008; 21: 376-392.

5. Accortt EE, Freeman MP, Allen JJ. Women and major depressive disorder: clinical perspectives on causal pathways. J Womens Health (Larchmt) 2008; 17: 1583-1590.

6. Castelo-Branco C, Cancelo MJ. Comprehensive clinical management of hirsutism. Gynecol Endocrinol 2010; 26: 484-493.

7. Kerchner A, Lester W, Stuart SP, Dokras A. Risk of depression and other mental health disorders in women with polycystic ovary syndrome: a longitudinal study. Fertil Steril 2009; 91: 207-212.

8. Hollinrake E, Abreu A, Maifeld M, Van Voorhis BJ, Dokras A. Increased risk of depressive disorders in women with polycystic ovary syndrome. Fertil Steril 2007; 87: 1369-1376.

9. Månsson M, Holte J, Landin-Wilhelmsen K, Dahlgren E, Johansson A, Landén M. Women with polycystic ovary syndrome are often depressed or anxious-a case control study. Psychoneuroendocrinology 2008; 33: 1132-1138.

10. Benson S, Arck PC, Tan S, Hahn S, Mann K, Rifaie N, Janssen OE, Schedlowski M, Elsenbruch S. Disturbed stress responses in women with polycystic ovary syndrome. Psychoneuroendocrinology 2009; 34: 727-735.

11. Mallon E, Newton JN, Klassen A, Stewart-Brown SL, Ryan TJ, Finlay AY. The quality of life in acne: a comparison with general medical conditions using generic questionnaires. Brit J Dermatol 1999; 140: 672-676.

12. Ozcan Dag Z, Oguzturk O, Isik Y, Turkel Y, Bulcun E. Personality profile in patients with polycystic ovary syndrome. Gynecol Endocrinol 2015; 17: 1-3.

13. Cinar N, Kizilarslanoglu MC, Harmanci A, Aksoy DY, Bozdag G, Demir B, Yildiz BO. Depression, anxiety and cardiometabolic risk in polycystic ovary syndrome. Hum Reprod 2011; 26: 3339-3345.

14. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and cell function from fasting plasma glucose and insulin in man. Diabetologia 1985; 28: 412-419.

15. Beck AT, Brown G, Epstein N, Steer RA. An inventory for measuring clinical anxiety: psychometric properties. J Consult Clin Psych 1988; 56: 893-897.

16. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch Gen Psychiat 1961; 4: 53-63.

17. Drosdzol A, Skrzypulec V, Plinta R. Quality of life, mental health and self-esteem in hirsute adolescent females. J Psychosom Obst Gyn 2010; 31: 168-175.

18. Cinar N, Harmanci A, Demir B, Yildiz BO. Effect of an oral contraceptive on emotional distress, anxiety and depression of women with polycystic ovary syndrome: a prospective study. Hum Reprod 2012; 27: 1840-1845.

19. Ekbäck MP, Lindberg M, Benzein E, Arestedt K. Health-related quality of life, depression, and anxiety correlate with degree of hirsutism. Dermatology 2013; 227: 278-284.

20. Mueller SC, Ng P, Sinaii N, Leschek EW, Green-Golan L, VanRyzin C, Ernst M, Merke DP. Psychiatric characterization of children with genetic causes of hyperandrogenism. Eur J Endocrinol 2010; 163: 801-810.

21. Morotti E, Persico N, Battaglia B, Fabbri R, Meriggiola MC, Venturoli S, Battaglia C. Body imaging and sexual behavior in lean women with polycystic ovary syndrome. J Sex Med 2013; 10: 2756-2760.

22. Månsson M, Holte J, Landin-Wilhelmsen K, Dahlgren E, Johansson A, Landén M. Women with polycystic ovary syndrome are often depressed or anxious: a case control study. Psychoneuroendocrinology 2008; 33: 1132-1138.

23. Platt AM, Egan AM, Berquist MJ, Dreyer ML, Babar G, Ugrasbul F. Health-related quality of life, depression, and metabolic parameters in overweight insulin-resistant adolescents. J Pediatr Health Car 2013; 27: 120-126.

24. Zhao G, Ford ES, Li C, Tsai J, Dhingra S, Balluz LS. Waist circumference, abdominal obesity, and depression among overweight and obese U.S. adults: National Health and Nutrition Examination Survey 2005-2006. BMC Psychiatry 2011; 11: 130.

25. Bonakdaran S, Kiafar B, Barazandeh Ahmadabadi F. Evaluation of insulin resistance in idiopathic hirsutism compared with polycystic ovary syndrome patients and healthy individuals. Australias J Dermatol 2014; Dec 13.

26. Unlühizarci K, Karababa Y, Bayram F, Kelestimur F. The investigation of insulin resistance in patients with idiopathic hirsutism. J Clin Endocr Metab 2004; 89: 2741-2744.

27. Livadas S, Chaskou S, Kandaraki AA, Skourletos G, Economou F, Christou M, Boutzios G, Karachalios A, Zerva A, Xyrafis X et al. Anxiety is associated with hormonal and metabolic profile in women with polycystic ovarian syndrome. Clin Endocrinol 2011; 75: 698-703.

28. Sadat Hosseini M, Ramezani Tehrani F, Azizi F. The lack of association between idiopathic hirsutism and metabolic disturbances: Iranian PCOS Prevalence Study. Gynecol Endocrinol 2013; 29: 821-825.

29. Benson S, Hahn S, Tan S, Mann K, Janssen OE, Schedlowski M, Elsenbruch S. Prevalence and implications of anxiety in polycystic ovary syndrome: results of an internet-based survey in Germany. Hum Reprod 2009; 11: 1446-1451.

30. Bazarganipour F, Ziaei S, Montazeri A, Foroozanfard F, Kazemnejad A, Faghihzadeh S. Psychological investigation in patients with polycystic ovary syndrome. Health Qual Life Outcomes 2013; 11: 141.

31. B Weber B, Lewicka S, Deuschle M, Colla M, Heuser I. Testosterone, androstenedione and dihydrotestosterone concentrations are elevated in female patients with major depression. Psychoneuroendocrinology 2000; 25: 765-771.

32. Morrison MF, Ten Have T, Freeman EW, Sammel MD, Grisso JA. DHEA-S levels and depressive symptoms in a cohort of African American and Caucasian women in the late reproductive years. Biol Psychiat 2001; 50: 705-711.

33. Bromberger JT, Schott LL, Kravitz HM, Sowers M, Avis NE, Gold EB, Randolph JF Jr, Matthews KA. Longitudinal change in reproductive hormones and depressive symptoms across the menopausal transition: Results from the Study of Women's Health Across the Nation (SWAN). Arch Gen Psychiat 2010; 67: 598-607.

34. Annagür BB, Tazegül A, Uguz F, Kerimoglu ÖS, Tekinarslan E, Celik Ç. Biological correlates of major depression and generalized anxiety disorder in women with polycystic ovary syndrome. J Psychosom Res 2013; 74: 244-247.