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# Depression in relation to biochemical parameters and age in women with polycystic ovary syndrome

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ABSTRACT

*Objective:* The phenotype of women with PCOS changes with age. The study was aimed to address whether changes in biochemical parameters associated with age of the patients correlate with depression severity measured with the use of screening tools.

*Study design:* This was a single center observational study. Women with PCOS meeting the Rotterdam criteria for PCOS were recruited. Hormonal and clinical parameters including symptoms of hyperandrogenism, age, BMI, androgen and blood lipids were analyzed in 60 patients (median age 27, median BMI 23 kg/m$^2$) together with evaluation of depressive symptoms with the use Beck Depression Inventory, Patient Health Questionnaire-Nine Item (PHQ-9), Quick Inventory of Depressive Symptomatology-Self Report 16 Item (QIDS-SR16).

*Results:* The prevalence of depression was equal 22–33% depending on the questionnaire. The older women tended to present significantly higher BMI, SBP, waist circumference and lower androstenedione and DHEAS values than the younger group of patients. The prevalence of depression was higher in the group of older patients, however without statistical significance. Among the cohort of older patients (age $\geq$ 27 years, $n$ = 29) significant correlates of depression included: nonHDL, LDL, HDL, total cholesterol ($p < 0.05$), even after controlling for BMI. In the younger study cohort (age $<$ 27, $n$ = 28) the only significant correlates included BMI and waist circumference.

*Conclusion:* Women with PCOS reporting depressive symptoms present higher levels of androgens and blood lipids. Clinicians treating women with PCOS should be aware that this group of patients is at increased risk of depression irrespectively of age and phenotype.



## Introduction

Main features of polycystic ovary syndrome include ovulatory dysfunction, androgen excess, and polycystic ovaries. Main factors in pathophysiology of PCOS are hyperandrogenism and insulin resistance. Prior studies report the 6–12% prevalence of PCOS among women [1–7]. PCOS is associated with a number of medical comorbidities including diabetes, cardiovascular disease, obesity, endometrial cancer and up to the recent findings – depression, which is reported to be present in up to 50% of women with PCOS. Several studies of affective disorders have been conducted to assess the biochemical correlates of affective disorders in women with PCOS [8,9]. However, their results regarding the biochemical determinants of depression are still inconclusive. A series of recent studies (both cross sectional and longitudinal) indicate that the phenotype of PCOS changes with age [10,11]. Therefore, we attempted to evaluate the older and younger subgroups of patients separately, in order to not to miss the tendencies present within these groups.

The aim of our study was the assessment of severity and biological correlates of depressive symptoms among women with PCOS using screening tools such as Patient Health Questionnaire-Nine Item (PHQ-9), Quick Inventory of Depressive Symptomatology-Self Report 16 Item (QIDS-SR16) with respect to age and, thus, various phenotypes of a patient.

## Materials and methods

### Subjects

This was a single-center cross-sectional study. All subjects were women referred to the Department of Gynecological Endocrinology of the Medical University of Warsaw between October 2012 and

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February 2013 for diagnose of PCOS. The diagnosis of PCOS was based on the revised Rotterdam criteria (2 out of 3) [12]: oligo- and/or anovulation, clinical and/or biochemical signs of hyperandrogenism, polycystic ovaries, as defined by Endocrine Society Clinical Practice Guideline [13]. The criteria require exclusion of other etiologies of hyperandrogenism such as congenital adrenal hyperplasias, androgen-secreting tumors and Cushing's syndrome.

Exclusion criteria are as follows: other causes of hyperandrogenism (mentioned above), diabetes mellitus, hypogonadotropic hypogonadism, dietary restrictions, hormonal therapy and psychiatric drugs.

All women gave their oral and written consent and the study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee, Medical University of Warsaw, Poland.

### *Study protocol*

Case history and gynecological examination including transvaginal ultrasound were carried out in all the women included into the study.

The study protocol involved completing three questionnaires: Patient Health Questionnaire-Nine Item (PHQ-9), Quick Inventory of Depressive Symptomatology-Self Report 16 Item (QIDS-SR16), Beck Depression Inventory (BDI) and a demographic questionnaire including obstetric history, education, marital status and place of residence.

Patient Health Questionnaire-Nine Item (PHQ9) consists of 9 items that correspond to the nine DSM-IV-TR criteria [14,15]. Quick Inventory of Depressive Symptomatology-Self Report 16 Item (QIDS16) which cover the symptoms of DSM-IV-TR unipolar major depression [16]. Beck Depression Inventory (BDI) is a scale of good internal consistency, sensitive to change, consisting of 21 multiple choice items, with 4 statements per item [17].

### *Laboratory data*

Clinical (including depression assessment) and laboratory data were collected during the same hospitalization. Clinical data included age, height, weight, waist circumference, blood pressure, menstrual interval, presence of hyperandrogenism symptoms (hirsutism, acne, male-pattern hair loss). Body mass index (BMI) was calculated as weight (kg)/height $(m)^2$. Insulin resistance was determined using the homeostatic model assessment (HOMA) calculation [fasting insulin × fasting glucose/22.5]. Laboratory data included 17 alpha hydroxyl P, DHEAS, total testosterone, androstenedione, SHBG FSH, LH, TSH, free T4, anti-TPO, anti-TG, leptine, glucose at 0′, 60′,120′ and insulin at 0′, 60′, 120′ of OGTT, cortisol 6, 8, 21, 22, ASPAT, ALAT, PRL 22, 2, 6, overnight 1 mg dexamethasone test; II phase: progesterone, prolactin, E2; fasting laboratory data: glucose, total cholesterol, low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), triglycerides. The ovarian morphology was assessed by ultrasound according to ASRM/ESHRE consensus [18]. The measurement was carried out with the Enzyme Linked Fluorescent Assay technique by BioMerieux.

### *Statistical analysis*

Mann–Whitney test was used to test for differences in continuous variables. Categorical variables were evaluated using Fisher exact test. Results are reported as median/mean ± SD. Statistical significance was defined as $p < 0.05$. Statistical analysis was performed using the SAS v 9.3 (SAS Institute, Cary, NC, USA). The following scores denoted depression: PHQ9 score ≥10; BDI ≥ 10; QIDS score ≥11. Univariate associations between depression scores and hormonal and metabolic parameters were evaluated using Spearman rank correlation coefficients. The analysis included age as potential confounder.

## Results

Out of the final group of 60 patients, the percentage numbers of patients with scores indicative on depression are as follows: 27% patients – PHQ9 score ≥10, 33% patients – BDI score ≥10, 22% patients – QIDS score ≥11.

The median age was equal 27 years (Q1–Q3: 24–32 years), with a minimum of 19 and maximum 46. We have divided the study group into 2 subgroups: (A) subjects aged <27 years, (B) subjects aged ≥27 years.

Median BMI was equal 23 $kg/m^2$ (Q1–Q3 = 20–30), 40% of patients presented BMI > 25 $kg/m^2$; median systolic blood pressure (SBP) was 120 mmHg and median diastolic blood pressure (DBP) was 70 mmHg.

The prevalence of the hyperandrogenism symptoms was as follows: hirsutism 73%, acne 29%, alopecia 13%. Only 14% of women were menstruating regularly. Polycystic ovary morphology in the ultrasound examination was identified in 93% of patients. 31% patients had history of pregnancy. Median androgen levels (Q1–Q3): DHEAS 7.99 μmol/L (6.03–9.20), testosterone 0.56 ng/ml (0.33–0.77), androstenedione 4.40 ng/ml (3.40–5.60), free androgen index, FAI 4.5 (2.9–7.8). Prolactin level above the upper reference limit of 35 ng/ml was found in 50% of women in our study group. Impaired glucose tolerance was diagnosed in 16% patients, and impaired fasting glucose in 5% pts. Median HOMA-IR was 1.22 (0.88–2.07).

The older women tended to present significantly higher BMI, SBP and waist circumference values than the younger group of patients (Table 1). Among the hormonal parameters, the levels of androstenedione and DHEAS were significantly higher in the group of younger patients. There was no significant difference between the age groups neither in the prevalence of the following symptoms: hirsutism, acne, alopecia, oligoovulation nor the hormonal and metabolic parameters: SHBG, TSH, E2, fasting glucose, HOMA, total cholesterol, LDL, HDL, TG, nonHDL. The prevalence of depression was higher in the group of older patients: 33% vs. 22% assessed with PHQ9, 27% vs. 19% assessed with QIDS, 40% vs. 30% assessed with BDI, however without statistical significance ($p > 0.05$ in all cases). Nor were the score of depression significantly different between the two cohorts.

### *Comparison of depressed and non-depressed patients*

While we consider the total of patients, only few of the parameters differed significantly between the groups of depressed and non-depressed patients, depending on the inventory used. Depressed patients with PHQ9 score ≥10 demonstrated higher levels of nonHDL (median values 141 vs. 100 mg/dl, $p = 0.0034$), LDL (117 vs. 86 mg/dl, $p = 0.0069$), total cholesterol (188 vs. 163 mg/dl, $p = 0.0166$) and triglycerides (TG; 104.5 vs. 68.5 mg/dl, $p = 0.0115$). The same significant tendency was observed when BDI or QIDS were used to assess depression (BDI ≥ 10; QIDS score ≥11), $p < 0.05$. Additionally, depressed patients tended to present greater waist circumference and lower HDL (while assessed with the use of PHQ9 and BDI), greater progesterone (QIDS), prolactin (PHQ9) and greater BMI (BDI), $p < 0.05$. Tables 2 and 3 present the evaluated data.

In the whole study group we have observed a significant positive correlation between depression scores and the following parameters: BMI, waist circumference, total testosterone, free