GYNECOLOGY

Association among depression, symptom experience, and quality of life in polycystic ovary syndrome

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BACKGROUND: Clinical stigmata of polycystic ovary syndrome include hirsutism, obesity, menstrual disturbances, and infertility. These symptoms impair health-related quality of life. Depression is also common. The relationship among depression, symptom self-perception, and quality of life in polycystic ovary syndrome is poorly understood.

OBJECTIVE: We sought to investigate the relationship between health-related quality of life and depression in women with polycystic ovary syndrome.

STUDY DESIGN: We conducted a secondary analysis of a multicenter, randomized clinical trial (Pregnancy in Polycystic Ovary Syndrome II, NCT00719186) comparing clomiphene citrate vs letrozole in the treatment of infertility. Subjects included 732 women ages 18–40 years with polycystic ovary syndrome by modified Rotterdam criteria. The validated Polycystic Ovary Syndrome Health-Related Quality of Life survey was self-administered, assessing the following domains: emotions, body hair, body weight, menstrual problems, and infertility; scores range from 1–7, with lower numbers indicating poorer quality of life. Depression was evaluated via the Primary Care Evaluation of Mental Disorders Patient Health Questionnaire. Quality-of-life scores were compared between depressed and nondepressed women. Multivariate linear regression models analyzed the association between depression and quality-of-life scores, controlling for age, body mass index, hirsutism score, and duration of infertility.

RESULTS: In all, 64 women (8.4%) met criteria for depression. Depressed women reported reduced quality of life in all domains compared to nondepressed women: mood (3.1 vs 4.6, $P < .001$), body hair (3.5 vs 4.2, $P = .002$), weight (2.0 vs 3.5, $P < .001$), menstrual problems (3.3 vs 4.1, $P < .001$), and infertility (1.9 vs 3.0, $P < .001$). Global quality-of-life score was reduced in depressed women (2.8 vs 3.9, $P < .001$). Impairments in quality of life in depressed women persisted in all domains after controlling for objective parameters including age, body mass index, hirsutism score, and infertility duration.

CONCLUSION: Depression is associated with reduced quality of life related to polycystic ovary syndrome symptoms. Disturbances in health-related quality of life in depressed women are not explained by objective measures including body mass index, hirsutism scores, and duration of infertility. Depression may color the experience of polycystic ovary syndrome symptoms and should be considered when there is significant discordance between subjective and objective measures in women with polycystic ovary syndrome.

Key words: depression, health-related quality of life, polycystic ovary syndrome, quality of life

Introduction

Up to 15% of reproductive-age women are affected by polycystic ovary syndrome (PCOS).[1,2] The diagnostic triad for PCOS comprises ovulatory dysfunction, hyperandrogenism, and polycystic ovarian morphology on ultrasound.[3] Hyperandrogenism may manifest biochemically (ie, in the serum) or clinically in the form of hirsutism and acne. Metabolic dysfunction is common in PCOS,[4,5] related to insulin resistance,[6] and embodied in increased rates of obesity. An estimated 1 in 2 women with PCOS is obese.[7] Additionally, women with PCOS face an estimated 3–8 times increased risk of depression.[8–10] The pathophysiology explaining the elevated prevalence of depression in PCOS is unknown.

Health-related quality of life (HRQOL) is "the extent to which one's usual or expected physical, emotional and social well-being are affected by a medical condition"[11] and is an increasingly emphasized patient-reported outcome.[12] Women with PCOS have been shown to have decreased HRQOL.[13,14] Symptoms inherent in the disorder, including emotional disturbances, growth of body hair, increased body weight, menstrual problems, and infertility are frequently cited as reasons for the perturbed HRQOL.[13,15–17] Depression is also common in PCOS.[8] It has been suggested that PCOS somatic symptoms such as obesity and hirsutism are linked to depression risk;[18,19] however, the causal direction of this association is poorly understood. Indeed, while PCOS symptoms may reduce HRQOL and contribute to depression risk, it is possible that depression itself might modulate how women perceive their symptoms and thereby HRQOL.

Understanding the connections between depression and HRQOL is a critical step toward identifying opportunities to enhance overall well-being in the PCOS population. The objective of our study was to test the hypotheses that: (1) depressed women perceive their PCOS symptoms more negatively or severely compared to nondepressed women, and (2) that differences in symptom self-perception are not explained by differences in objective clinical measures.

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AJOG at a Glance

Why was this study conducted?

To examine the association between depression and health-related quality of life (QOL) in polycystic ovary syndrome (PCOS).

Key findings

Reduced QOL was reported by depressed women for all PCOS-specific symptom domains, including: body hair, weight, infertility, menstrual disturbances, and emotions, and, in depressed women, differences in symptom distress were not accounted for by objective measures of body mass index, hirsutism scores, and infertility duration.

What does this add to what is known?

These findings suggest that depression may color how women experience PCOS symptoms and correspond to reduced QOL.

Materials and Methods

We conducted a secondary analysis of data from a multicenter, double-blind, randomized clinical trial comparing clomiphene citrate vs letrozole in the treatment of infertility in 750 women with PCOS (Pregnancy in Polycystic Ovary Syndrome II).[20] Subjects provided written, informed consent to participate in the clinical trial. This secondary analysis utilized only deidentified data, and was exempt from institutional review board approval accordingly.

Subjects

The study cohort included 732 female patients, ages 18−40 years, enrolled in the Pregnancy in Polycystic Ovary Syndrome II clinical trial at 1 of 11 centers. PCOS was diagnosed by modified Rotterdam criteria,[21] requiring chronic ovulatory dysfunction in addition to hyperandrogenism, or polycystic appearing ovaries, or both. Ovulatory dysfunction was defined as oligomenorrhea (ie $\leq$8 menses annually), a spontaneous intermenstrual interval of $\geq$45 days, or chronic anovulatory bleeding with midluteal serum progesterone of $<$3 ng/dL. Hyperandrogenism included hirsutism (modified Ferriman-Gallwey [mFG] score $>$8), or elevated serum testosterone or free androgen index. Polycystic morphology was defined per Rotterdam criteria as $\geq$12 antral follicles 2−9 mm in diameter, or increased ovarian volume $>$10 cm^3 in at least 1 ovary on transvaginal ultrasound. Related disorders were screened out by thyroid-stimulating hormone, prolactin, and 17-hydroxyprogesterone. Additional details regarding eligibility criteria are available publicly.[22] Subjects who completed both the PCOS Questionnaire (PCOSQ) and Primary Care Evaluation of Mental Disorders (PRIME-MD) Patient Health Questionnaire (PHQ) at the screening visit were included in this analysis.

At the screening visit, thorough history and physical examination, including calculation of body mass index (BMI), was performed. The mFG scoring system[23] was utilized to assess hirsutism.

Health-related quality of life

Validated instruments were self-administered at the screening visit. HRQOL was assessed using the PCOSQ survey.[24] PCOSQ is a validated, Likert-type 26-item questionnaire, which examines 5 domains specifically targeted to quality of life (QOL) in PCOS: emotional disturbance, body hair, weight, menstrual problems, and infertility. Items query the severity and frequency of symptomatic distress related to PCOS. Reponses are coded from 1−7. Scoring of PCOSQ provides separate domain scores for each of the 5 domains, as the numeric mean of items in that domain, as well as a global score, as the mean of the 5 domain scores. Scores range from 1−7, with 1 indicating poorest function and highest distress, and 7 indicating optimal function and minimal distress.

Depression

The PRIME-MD PHQ[25] was used to assess depression. The PRIME-MD PHQ is a validated, self-administered questionnaire designed to diagnose specific mental disorders in the primary care setting, in accordance with the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*.[26] The sensitivity and specificity (73% and 94%, respectively) for diagnosing depressive disorders are considered excellent compared to the gold standard structured clinical interview.[25] The survey assesses the frequency of 9 symptoms of clinical depression over the preceding 2 weeks. "Depression" is indicated by experiencing at least 3 of 9 symptoms on at least "more than half the days." One of these symptoms must be "little interest or pleasure in doing things" or "feeling down, depressed, or hopeless" or both, in accordance with *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*.

Statistical analysis

Descriptive statistics were provided. Baseline characteristics of depressed vs nondepressed women were compared using 2-sided *t* tests or χ^2 as indicated; PCOSQ scores were compared using *t* tests. Univariate and multivariate linear regression models assessed the association between depression and PCOSQ domain and global scores. The multivariate model was adjusted for age, BMI, mFG score, and duration of infertility. To determine whether the relationship between a woman's BMI and her body weight PCOSQ score varied on the basis of whether or not she was depressed, a linear regression model incorporating an interaction term between depression and BMI was examined (outcome: body weight domain PCOSQ score). This analysis was repeated to evaluate potential interactions between depression and hirsutism score as predictors of body hair domain PCOSQ score, and between depression and duration of infertility as predictors of infertility domain PCOSQ