

Prevalence of Anxiety and Depression among Polycystic Ovarian Syndrome Women-An Review

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ABSTRACT: Polycystic ovarian syndrome (PCOS) is the most common endocrine disorder among women of reproductive age. Symptoms include amenorrhea, hirsutism, infertility, obesity, acne vulgaris, and androgenic alopecia. PCOS is a stigmatizing condition that affects a woman's identity, mental health and quality of life (QOL). Development of anxiety and depression in PCOS is considered as multifactorial. Some researchers have suggested that physical symptoms, such as acne, hirsutism, and obesity, are linked to these psychiatric morbidities. We are still lacking knowledge about many of its aspects, including its etiology, progression throughout life, spectrum of symptoms, and various morbidities. There is inadequacy of research for assessing prevalence of anxiety and depression in PCOS. Our study will aids in recapitulate the most relevant evidence related to anxiety and depression afflicted with PCOS Women.

Keywords: Polycystic Ovarian Syndrome, Anxiety, Depression.

I. INTRODUCTION

A woman is diagnosed with polycystic ovaries, if she has 20 or more follicles in at least 1 ovary measuring 2-9 mm in diameter or a total ovarian volume greater than 10 cm³.^[1] The major features of polycystic ovarian syndrome (PCOS) include menstrual dysfunction, anovulation, and signs of hyperandrogenism.^[2] Although the exact etiology and pathophysiology of this condition is unclear, PCOS can result from abnormal function of the hypothalamic-pituitary-ovarian axis. A key characteristic of PCOS is inappropriate gonadotropin secretion, which is more likely a result of, rather than a cause of, ovarian dysfunction. In addition, one of the most consistent

biochemical features of PCOS is a raised plasma testosterone level.^[3]

In 2003, the European Society for Human Reproduction and Embryology (ESHRE) and the American Society for Reproductive Medicine (ASRM) recommended that at least 2 of the following 3 features are required for PCOS to be diagnosed^[4]:

- Oligo-ovulation or anovulation manifested as oligomenorrhea or amenorrhea
- Hyperandrogenism (clinical evidence of androgen excess) or hyperandrogenaemia (biochemical evidence of androgen excess)
- Polycystic ovaries (as defined on ultrasonography)

The Androgen Excess and PCOS Society (AE-PCOS) published a position statement in 2006^[5] and its criteria in 2009^[6] emphasizing that, in the society's opinion, PCOS should be considered a disorder of androgen excess, as defined by the following:

- Clinical/biochemical evidence of hyperandrogenism
- Evidence of ovarian dysfunction (oligo-ovulation and/or polycystic ovaries)
- Exclusion of related disorders

The Society of Obstetricians and Gynaecologists of Canada (SOGC) indicated that a diagnosis of polycystic ovarian syndrome (PCOS) is made in the presence of at least 2 of the following 3 criteria, when congenital adrenal hyperplasia, androgen-secreting tumors, or Cushing syndrome have been excluded^[7]:

- Oligo-ovulation or anovulation
- Clinical/biochemical evidence of hyper androgenism

- Polycystic ovaries on ultrasonograms (>12 small antral follicles in an ovary)

Prevalence of anxiety in women with PCOS ranges from 34% to 57%.^[8,9] Prevalence of depression in PCOS varies from 28% to 64%.^[10,11] This wide range of prevalence rates might be due to different ethnicities, different sociocultural characteristics of the study populations, or use of different methodologies to assess psychiatric morbidity. Development of anxiety and depression in PCOS is considered as multifactorial. Some researchers have suggested that physical symptoms, such as acne, hirsutism, and obesity, are linked to these psychiatric morbidities.^[12] Recently, in a systematic review and meta-analysis, they found that women with PCOS had a fourfold greater odds of depressive symptoms compared with age-matched control women.^[13] Further sub analysis of body mass index (BMI)-matched subjects also demonstrated greater odds of depressive symptoms in women with PCOS. They previously examined the risk of depression in PCOS and found a persistent high prevalence of depression after 12–18 months.^[14] Mood disorders are commonly associated with anxiety disorders, especially generalized anxiety disorder.^[15] The estimated prevalence of anxiety disorders is 5%–8% in women seen in the primary care setting. They previously reported that more women with PCOS (14%) compared with control women (1%) had anxiety symptoms.^[16] Abnormal or inappropriate anxiety can become a problem when it occurs without any recognizable stimulus or when the stimulus does not warrant such a reaction. Often, anxiety gets generalized to other situations, and can then become overwhelming or associated with life in general. Typically, GAD develops over a period of time and may not be noticed until it is significant enough to cause problems with functioning. In the National Comorbidity Survey, patients with GAD had a high prevalence of social phobia, specific phobia, panic disorder, and major depression.^[17, 18]

There is inadequacy of research for assessing prevalence of anxiety and depression in PCOS. Our review will aid in recapitulating the most relevant evidence related to anxiety and depression afflicted with PCOS Women.

II. ANXIETY AND DEPRESSION PREVALENCE IN POLYCYSTIC OVARIAN SYNDROME

Hollinrake E et al., performed a cohort study and their goal was to estimate the

prevalence of depressive disorders in women with PCOS compared with controls and to evaluate the correlation between depression, hyperandrogenism, and other metabolic markers. Women with PCOS (Rotterdam criteria; n = 103). Women without PCOS seen during the same time period for an annual exam were used as control subjects (n = 103). Primary Care Evaluation of Mental Disorders Patient Health Questionnaire (PRIME-MD PHQ) and the Beck Depression Inventory were used.

PCOS women were at an increased risk for depressive disorders (new cases) compared with controls. The overall risk of depressive disorders in women with PCOS was 4.23 (95% CI 1.49-11.98; P<.01) independent of obesity and infertility. Compared with the non-depressed PCOS subjects, the depressed PCOS subjects had a higher body mass index (BMI) and evidence of insulin resistance (P<.02). They report a significantly increased risk of depressive disorders (as defined by the Diagnostic and Statistical Manual IV) in women with PCOS and recommended routine screening in this population.^[16]

Depression and QoL were assessed in women with PCOS and healthy controls (n = 1359) by Barnard L et al., The polycystic ovary syndrome health-related QoL questionnaire (PCOSQ) was modified to include an acne subscale. Seventy-one percentage of women with PCOS who were taking anti-androgen (AA) medication and 67% not taking AA medication were classified as depressed. Women with PCOS had lower QoL on all seven factors of the modified PCOSQ (emotional disturbance, weight, infertility, acne, menstrual symptoms, menstrual predictability and hirsutism). Weight was the largest contributor to poor QoL for women taking and not taking AA medication. Women taking AA medications, independent of diagnosis, generally had better QoL than women not taking them. This large study refines our understanding of depression and QoL in PCOS and demonstrates the need to regularly review the psychological health of women with PCOS.^[19]

Mansson M et al., included women with PCOS (n = 49) meeting the Rotterdam criteria for PCOS, and 49 age matched controls identified from the population registry, were recruited. Serum-testosterone and sex hormone binding globulin were analyzed. Women with PCOS had higher lifetime incidence of depressive episodes, social phobia, and eating disorders than controls. Suicide attempts were seven times more common in the PCOS group than in the controls. Current as well as lifetime use of antidepressants and anxiolytic drugs

were more common in the PCOS group. Their study demonstrates that PCOS is also linked to psychiatric syndromes as verified by structured clinical assessments. The clinical implication of this study is that clinicians treating women with PCOS should be aware that these women are a high risk group for common affective and anxiety disorders as well as suicide attempts.^[20]

A nation-wide, internet-based survey, anxiety and depression (Hospital Anxiety and Depression Scale, HADS) and quality of life (SF-12) were assessed together with sociodemographic information and clinical PCOS symptoms in 448 PCOS women by Benson et al., Finally, 34% showed clinically relevant HADS anxiety scores and 21% had clinically relevant HADS depression scores. Quality of life was significantly impaired in PCOS women with anxiety (P, 0.001), in particular, in women with comorbid anxiety and depression (P, 0.001). They concluded that PCOS women may be at an increased risk for clinically relevant anxiety, and comorbid anxiety and depression is also very common. Anxiety contributes to impaired quality of life in PCOS. Given the high prevalence and the serious implications, and the availability of effective treatment options given proper diagnosis, clinicians should be more aware of anxiety disorders in women with PCOS.^[21]

In this study, the author was to determine the conversion risk and predictors for depression in women with polycystic ovary syndrome. So, Kerchner A et al., conducted a prospective longitudinal study. The Primary Care Evaluation of Mental Disorders Patient Health Questionnaire was used to diagnose major depressive disorder and other depressive syndromes, anxiety syndromes, and binge eating disorder. Subjects completed a questionnaire on knowledge about polycystic ovary syndrome and treatment satisfaction.

A total of 60 of 103 subjects responded to the second survey. Mean time between the two surveys was 22 months (range 12-26 months). The overall prevalence of depression was 40% (24/60). Of these, 10 women screened positive for major depressive disorder or other depressive syndromes and 14 were receiving antidepressant medications. Total subjects with mood disorders in this study were 34/60 (56.6%), including 11.6% with anxiety syndromes and 23.3% with binge eating disorder.

They concluded that there is a significant risk for mood disorders (defined by the Diagnostic and Statistical Manual of Mental Disorders-IV) in women with polycystic ovary syndrome. This

finding together with a high conversion risk for depression over a 1- to 2-year period underscores the importance of routine screening and aggressive treatment of mental health disorders in this population.^[14]

Jedel E et al., conducted a study in women with PCOS (n = 30) and controls (n = 30) were recruited from the community. Persons with ongoing psychotropic medication were excluded. All potential participants underwent gynecological examination to confirm case-control status. Participants completed the self-reported versions of the Brief Scale for Anxiety (BSA-S) and Montgomery Asberg Depression Rating Scale (MADRS-S). Women with PCOS had a higher BSA-S score compared with controls and they scored higher on the following four individual symptoms: reduced sleep (P < 0.001), worry (P = 0.004), phobias (P < 0.001), and pain (P < 0.001). No statistical difference was demonstrated regarding MADRS-S scores (P = 0.053). Finally, concluded that several anxiety symptoms distinguished women with PCOS from a control group matched on BMI. A better understanding of the symptoms is needed to identify and alleviate anxiety symptoms in this vulnerable group.^[22]

Polycystic ovary syndrome (PCOS) is associated with high levels of depression, which impact quality of life and limit self-efficacy, yet less is known about prevalence of anxiety. Deeks AA et al., performed a cross-sectional, observational study of community-based women with PCOS comprehensively examined mood and found that anxiety existed at higher levels than depression, anxiety was under diagnosed, and more women with PCOS who reported infertility were depressed.^[8]

Thomson RL et al., carried out a study to assess the impact of adding exercise to dietary restriction on depressive symptoms and health-related quality of life (HRQOL) in women with polycystic ovary syndrome (PCOS). They included 104 overweight/obese PCOS women (aged 29.3 ± 0.7 years; body mass index [BMI] 36.1 ± 0.5 kg/m²). Forty-nine women completed the intervention (diet only = 14, diet and aerobic exercise = 15, diet and combined aerobic-resistance exercise = 20). By week 20 all groups achieved weight loss and had improvements in depression and PCOS-specific HRQOL scores, except for body hair domain score. There was no difference between treatments for all outcomes. This study demonstrated that dietary restriction alone and combined with exercise had similar benefits for

improving depression and HRQOL scores in overweight and obese women with PCOS.^[23]

Bhattacharya SM and Jha A conducted a comparative cross-sectional study found that women with polycystic ovary syndrome are at a significantly higher risk of depression compared with non-PCOS women. The study fails to find enough evidence to explain the high prevalence of depression among PCOS patients by the selected socio-demographic, clinical, and biochemical parameters.^[10]

Pastore LM et al., used Cross-sectional analysis of questionnaires (Quick Inventory of Depressive Symptomatology-Self-Report, Body Esteem Scale) with (n=94) and without (n=96) PCOS, matched by BMI category. Non-parametric tests, Spearman correlations, and negative binomial regression models were analyzed. In both the PCOS and non-PCOS cohorts, depression symptom severity was positively correlated with dissatisfaction with physical appearance and physical conditioning.

Most of the obese PCOS cohort had low body satisfaction and depression symptoms, therefore individual differences in the body dissatisfaction scores were not helpful in identifying depression symptom severity. Neither testosterone nor free testosterone was associated with depression symptom severity in PCOS women after controlling for body dissatisfaction and age.^[24]

Dokras A done a study in polycystic ovary syndrome women has gynecologic, reproductive and metabolic co-morbidities that span their entire lifespan. More recently a higher risk of mood and anxiety disorders has been reported in women with PCOS. Women with PCOS have higher depression scores and a higher risk of depression independent of BMI. Although clinical features of hyperandrogenism affect health related quality of life, the association between hirsutism, acne, body image and depression is currently unclear. Similarly there is limited data on the association between variables such as biochemical hyperandrogenism or infertility and depression. Women with PCOS are also at risk for symptoms of generalized anxiety disorder.

Because the peak incidence of depression is during the reproductive years, gynecologists are front line professionals in the effort to identify and treat women with PCOS who have depression. Unfortunately women with depression may describe their presenting problems are “sleep

disturbances” or “fatigue” and hence the diagnosis may be missed. The exact etiology for increased risk of depressive and anxiety symptoms in women with PCOS remains unclear.

The effectiveness of weight loss strategies or decreasing serum androgens on depression or anxiety scores needs to be evaluated in PCOS. Data from the National Comorbidity Survey application found that only 41.1% of individuals diagnosed with mood disorders received some form of treatment.^[26]

It is known that with adequate treatment, 50–70% of patients with depression recover completely. Although the optimum treatment strategies in women with PCOS have not been evaluated, current data underscores that these women should be routinely screened for mood and anxiety disorders and adequately treated using established therapies. These data underscore the need to screen all women with PCOS for mood and anxiety disorders and adequately treat women who are diagnosed with these conditions.^[25]

Moran LJ et al., aimed to assess the psychological features in women with different polycystic ovary syndrome (PCOS) phenotypes [National Institute of Health (NIH) and non-NIH diagnostic criteria] and women without PCOS. An observational, cross-sectional study compared overweight (BMI ≥ 25 kg/m²) premenopausal women with PCOS (n = 29 NIH and n = 25 non-NIH) and controls (n = 27). Anxiety and depression were compared between women with NIH or non-NIH PCOS and women without PCOS. Health-related quality of life (HRQoL) domains related to emotions, body hair, weight, infertility and menstrual problems were compared between women with NIH and non-NIH PCOS.

Results was found to be women with PCOS had worse anxiety (P = 0.007) and depression (P = 0.048) compared with women without PCOS. Both women with NIH PCOS and non-NIH PCOS presented more often with moderate anxiety (P = 0.005 and P = 0.01, respectively) compared with women without PCOS. Women with NIH PCOS had worse HRQoL related to infertility (P = 0.012), emotions (P = 0.02) and weight (P = 0.016).

No significant differences were observed between the two PCOS phenotypes for HRQoL domains related to body hair or menstrual problems. Both NIH (P = 0.024) and non-NIH (P = 0.016) PCOS status predicted anxiety, whereas age (P = 0.008) and free androgen index (P = 0.027)

predicted depression. They concluded that PCOS is associated with anxiety and depression.^[27]

Acmaaz G et al., aimed to determine which symptoms increased such problems as depression, anxiety, low self-esteem, and social worry by classifying PCOS according to symptoms. The study was carried out with two groups. The first group consisted of 86 patients who were diagnosed with PCOS and the second group consisted of 47 healthy volunteers. Liebowitz' Social Anxiety Scale, Rosenberg' Self-Esteem Scale, Short-Form 36, Quality of Life Scale, Beck Anxiety Inventory, and Beck Depression Inventory were administered to each volunteer. Depression scores of infertile group were higher while anxiety scores of the obese group were bigger than other groups. The most affected group was oligomenorrhea-hirsutism group in terms of physical functioning, physical role function, pain, social functioning, emotional role function, and emotional well-being. So, they suggested not only gynecologist but also a multidisciplinary team may examine these PCOS patients.^[28]

Banting et al., carried out a research included women aged between 18-50 years with (n = 153) and without PCOS (n = 64) completed a Hospital Anxiety and Depression Scale questionnaire at one time point. Final report came out like women with PCOS displayed higher severity of depression (p = 0.004) and anxiety (p < 0.001) symptoms compared to controls. Overall, for physically active women, depression was significantly less severe than in their inactive counterparts (p < 0.001). There were no differences in anxiety by physical activity status and no interaction effects between PCOS and activity status for depression or anxiety.

They concluded that physical activity is associated with lower depression in women with PCOS compared to controls. Being more active may offer mental health benefits in managing PCOS.^[29]

Scaruffi E et al., performed a research study included sixty PCOS subjects were evaluated by anthropometric, metabolic, hormonal, clinical, and psychological parameters. Results were found to be psychiatric disorders: 10.2% anxiety and 16.3% major depressive disorder. Rorschach test's results shows 55.1% depression of their patients had chronic stress. PCOS women have relevant psychiatric disorders, when compared with normal subjects.^[30]

Upadhyaya SK, Sharma A and Agrawal A noticed that patients of polycystic ovarian syndrome (PCOS) often suffer from psychiatric co morbidities, such as anxiety and depression. Indian literature regarding prevalence of these disorders in PCOS patients is scanty. So, they want to assess prevalence of anxiety and depression in patients of PCOS. They conducted a cross-sectional observational study, which was done in obstetrics and gynecology department of tertiary care centre. Patients of PCOS were assessed on hospital anxiety depression scale and sociodemographic and clinical information was gathered using semi-structured questionnaire. Data are expressed as proportions. The results were found to be prevalence of anxiety of 28% and depression 11% among PCOS Patients.^[12]

Tan J et al., enrolled 120 outpatients with PCOS and 100 healthy controls in this study. Standardized questionnaires were administered to assess general MH conditions (General Health Questionnaire-12-item version), anxiety (State-Trait Anxiety Inventory), depression (Beck Depression Inventory), as well as health-related quality of life (HRQoL) measured using the 36-item short-form health survey. The independent samples t-test was conducted for continuous study variables. For categorical variables, the Pearson Chi-square test, Fisher's exact test, and logistic regression were performed.

The prevalence of anxiety (13.3% vs. 2.0%) and depression (27.5% vs. 3.0%) was higher in patients with PCOS when compared to controls (both P < 0.05). Patients with PCOS had decreased HRQoL. Patients with PCOS who had fertility requirements were more likely to be anxious and depressed than those without fertility requirements (anxiety: 22.6% [12/53] vs. 5.9% [4/67], P = 0.008; depression: 37.7% (20/53) vs. 19.4% (13/67), P = 0.026).

Lastly, conclusion was found to be PCOS and related symptoms may be risk factors for depression and anxiety. Professionals should be concerned with the MH of women with PCOS, and psychological therapy should be considered.^[31]

Laura GC and Dokras A conducted a research study and their findings women with PCOS have increased odds of depressive symptoms and anxiety symptoms. Obesity, insulin resistance, and elevated androgens may partly contribute to this association. Summary Screening for anxiety and depression is recommended in women with PCOS at the time of diagnosis. Some of the PCOS-

related treatments including lifestyle modification, OCPs, laser treatment, and pioglitazone have shown favorable effects on depression or anxiety symptoms. Future studies should focus on understanding the mechanisms that lead to the increased risk of depression and anxiety in women with PCOS and the best interventions in this population which is already at risk for several comorbidities.^[32]

Greenwood EA et al., sought to investigate the relationship between healths related quality of life and depression in women with polycystic ovary syndrome. Subjects included 732 women ages 18-40 years with polycystic ovary syndrome by modified Rotterdam criteria. Depression was evaluated via the Primary Care Evaluation of Mental Disorders Patient Health Questionnaire. 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.

Depressed women reported reduced quality of life in all domains compared to non-depressed women: mood ($P < .001$), body hair ($P = .002$), weight ($P < .001$), menstrual problems ($P < .001$), and infertility ($P < .001$). 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. 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.^[33]

Hamdi et al., conducted a study included 80 PCOS adolescents. All participants completed standardized questionnaires assessing anxiety and depression. A multiple linear regression model was used to analyze the impact of potential variables on anxiety and depression scores of the adolescents with PCOS. Results were found to be significantly higher levels of anxiety, specifically generalized and social anxieties, as well as depression were found in adolescents with PCOS when compared to controls. Higher BMI was found to be associated with higher levels of depression and generalized anxiety, and higher modified Ferriman–Gallwey score with higher level of panic disorder in adolescents affected by PCOS. They concluded that PCOS adults were experience significantly more

emotional distress compared to adolescents without PCOS. This emotional distress may be related, at least in part, to certain clinical features of PCOS including obesity and hirsutism. PCOS in adolescents should be assessed not only for the gynecological and metabolic aspects but also for the emotional aspects of the disease.^[34]

Chaudhari et al., performed a research to study the prevalence of anxiety and depression among women suffering from PCOS and to determine if symptoms of PCOS were associated with psychiatric morbidity, impact of psychiatric morbidity on the QOL. Seventy females in the reproductive age group (18–45 years) diagnosed with PCOS as per Rotterdam criteria and without any preexisting psychiatric illness were clinically interviewed for anxiety and depressive disorders which were then rated according to the Hamilton scales. Binary logistic regression was performed to study the association of the symptoms with the psychiatric morbidity. QOL scores of patients with and without psychiatric morbidity were compared using Mann–Whitney U-test. They found prevalence of anxiety and depression in sample was 38.6% and 25.7%, respectively. Infertility and alopecia were associated with anxiety, while acne was associated with depression. Hirsutism was associated with a lower psychological QOL. Patients with psychiatric morbidity had a significantly lower QOL than those without PCOS.^[35]

III. CONCLUSION

An extended amount of knowledge has been learned about PCOS since it was initially described by Stein and Leventhal (1935). Yet, we are still lacking knowledge about many of its aspects, including its etiology, progression throughout life, spectrum of symptoms, and various morbidities. Supplementary studies are needed to bridge between the various susceptibility factors that might contribute to PCOS. The current diagnostic guidelines are still vague and might not detect patients with less severe non-classic phenotypes. Since proper diagnosis is a crucial step to initiate treatment and prevent future morbidities, further clinical research should seek not only to update and unify guidelines but also to provide an appropriate rationale for diagnostic tools that can detect all PCOS phenotypes. Early detection of long-term morbidities through appropriate screening tests constitutes an essential part of the management of this condition. Guidelines strongly

recommend lifestyle modifications as a critical part of the management.^[36]

In conclusion, we hope this review provided an updated summary that sheds light over the complex nature of PCOS. Future research has to focus on the missing blocks in our growing knowledge about this condition, for that physicians will be able to provide the finest care for patients.

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