

## Polycystic Ovarian Syndrome and Borderline Personality Disorder: 3 Case Reports and Scientific Review of Literature

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### Abstract

Polycystic ovary syndrome (PCOS) is the most common form of endocrine disorder in premenopausal women. (Polycystic ovary syndrome (PCOS) is also a common endocrine disorder affecting about 6% of women of reproductive age, characterized by gynecologic and endocrine symptoms, including chronic anovulation, infertility, and hyperandrogenism. The clinical spectrum of PCOS encompasses hirsutism, acne and male pattern alopecia, the sequelae of hyperandrogenism, and infertility as a result of ovulatory disturbance. There are many features of PCOS that might predispose to impaired quality of life (QoL), including infertility, cosmetic effects of hyperandrogenism, weight gain and obesity and long-term health implications. It is studied that the clinical features and health implications of PCOS are likely to lead to loss of self-esteem and poor body image, developing into decreased QoL and psychological morbidity. Ching at al. also found that a significantly poorer QoL in women with PCOS compared with age-matched population norms, both in the general and in the overweight and obese Australian female population, particularly in psychological health rather than physical functioning. We present three cases of PCOS with comorbid borderline personality disorder. We also found that they were diagnosed with PCOS many years prior to borderline personality disorder, which resulted into multiple acute psychiatric hospitalizations, poor quality of life and eventually functional disability. If diagnosed early, patient's PCOS can have better quality of life and improved outcome. Clinicians who treat women with PCOS should be mindful of the psychological as well as the physical consequences of the condition. We recommend that patients with PCOS should be routinely screened for borderline personality disorder. With respect to psychosocial support, a positive, respectful and empathic attitude will help to understand the women's worries and needs associated with the diagnosis of PCOS.

**Keywords:** Borderline personality disorder; Polysystic ovarian syndrome; Woman's mental health; Biological psychiatry

### Introduction

Polycystic ovary syndrome (PCOS) is the most common form of endocrine disorder in premenopausal women affecting about 6% of women of reproductive age [1]. Characterized by gynecologic and endocrine symptoms, PCOS is expressed by chronic anovulation, infertility, and hyperandrogenism. The clinical spectrum of PCOS encompasses hirsutism, acne, obesity, male pattern alopecia, and infertility as a result of ovulatory disturbance. It is studied that these clinical features and health implications of PCOS may predispose one to an impaired quality of life (QoL), leading to a loss of self-esteem, poor body image, and psychological morbidity [2]. It was also found that women with PCOS had a significantly poorer QoL when compared with age-matched population norms, both in the general and obese Australian female population, particularly in psychological health rather than physical functioning. This decreased QoL observed in PCOS, combined with poor coping strategies, can result in comorbid psychiatric conditions such as depression and anxiety. Interestingly, these psychiatric comorbidities observed in PCOS are traits often characteristic of individuals with Borderline Personality Disorder (for a complete description of BPD, Table 1). After performing a literature search with 'borderline personality disorder' and 'PCOS', we found no review article reviewing comorbid borderline personality disorder in patients with PCOS. Through retrospective chart review, we found all three patients were diagnosed with polycystic ovarian syndrome by a licensed gynecologist with required laboratory and radiological findings and all of them were diagnosed with borderline personality disorder by a licensed clinician through an unstructured clinical interview. There were comorbid psychiatric diagnoses with PCOS, but BPD was consistently comorbid with PCOS.

### Discussion

#### Polycystic ovarian syndrome and related psychiatric comorbidities

As there are many physical features of PCOS that may predispose one to an impaired QoL, when combined with poor coping skills, these women are at an increased risk for exhibiting depressive episodes and psychiatric problems associated with borderline traits. The side effects of PCOS leading to a decreased QoL include, but are not limited to: infertility, hyperandrogenism, weight gain and obesity, and long-term health implications. Hirsutism (male-pattern hair growth in women) and obesity in particular have been shown to be associated with psychiatric distress and a poorer prognosis. In fact, the impact of hirsutism has been identified with higher anxiety and psychotic symptoms as well as greater social phobia in hirsute women [3]. Due to the debilitating effects this feature of PCOS can have on women, it is crucial for professionals to equip these individuals with adequate coping strategies in order to avoid potential psychiatric distress. Coping, however has thus far not been analyzed in women with PCOS, although the typical symptom constellation of PCOS clearly implies numerous threats and challenges, such as changes in outer appearance, involuntary childless-

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A pervasive pattern of instability of interpersonal relationships, self-image, and affects, and marked impulsivity beginning by early adulthood and present in a variety of contexts, as indicated by five (or more) of the following:

S. No	Contexts
1	Frantic efforts to avoid real or imagined abandonment. Note: Do not include suicidal or self-mutilating behavior, as it is covered in Criterion 5.
2	A pattern of unstable and intense interpersonal relationships characterized by alternating between extremes of idealization and devaluation.
3	Identity disturbance: markedly and persistently unstable self-image or sense of self.
4	Impulsivity in at least two areas that are potentially self-damaging (e.g., spending, sex, substance abuse, reckless driving, binge eating). Note: Do not include suicidal or self-mutilating behavior, which is covered in Criterion 5.
5	Recurrent suicidal behavior, gestures, or threats, or self-mutilating behavior.
6	Affective instability due to a marked reactivity of mood (e.g., intense episodic dysphoria, irritability, or anxiety usually lasting a few hours and only rarely more than a few days).
7	Chronic feelings of emptiness.
8	Inappropriate, intense anger or difficulty controlling anger (e.g., frequent displays of temper, constant anger, recurrent physical fights).
9	Transient, stress-related paranoid ideation or severe dissociative symptoms.

\*American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders: DSM-5 (5th ed.). Arlington, VA: American Psychiatric Publishing

**Table 1:** Borderline Personality Disorder: DSM-5 diagnostic criteria\*

ness, and long-term health risks [4]. Obesity, another key feature of PCOS also associated with BPD, shares many of the same psychological disturbances as hirsutism due to health implications and the negative body image experienced by these women. In a study matching women for their body mass index, Jedel et al. found several anxiety symptoms that distinguished women with PCOS from a control group [5]. From this data, it is possible the collective physical symptoms of PCOS can lead to increased psychiatric distress, emulating features of BPD in these women. The clinical implication of these findings 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 [6]. In the medical context, coping processes are induced whenever an acute or chronic condition confronts a patient with threats and challenges that compromise his or her emotional balance [7]. Coping mechanisms constitute an important mediator in the relationship of a stressful situation and the resulting psychological distress. Data, however suggests that faced with the diagnosis of PCOS, passive coping may constitute a maladaptive strategy associated with anxiety and depression symptoms and compromised QoL [8]. Hence, efforts to incorporate psychosocial aspects into counseling and care for women with PCOS should take coping strategies into consideration. Nurses and other health care providers may help to improve coping strategies through education and psychosocial support in women with PCOS [4]. Because PCOS is a gynecological condition with observable physical symptoms and BPD is usually not diagnosed until young adulthood after problematic psychiatric issues arise, it would be beneficial for clinicians to screen women diagnosed with PCOS for borderline traits to avoid future psychiatric distress.

### Possibility of PCOS in borderline personality disorder

Although BPD is usually viewed as a maladaptive personality, diagnosed when one meets the specified criteria for observable traits, there is evidence supporting physiological differences in this population on the neurological level. We now present three hypotheses examining the possible biological mechanisms for the borderline traits observed in both PCOS and BPD.

#### Serotonin hypothesis

Interestingly, the BPD diagnosis was associated with significantly greater cortisol response to ipsapirone, relative to subjects with other personality disorder diagnoses. A similar finding among BPD patients was reported in a study of cortisol response to m-CPP [9]. It is certainly possible that individuals with BPD exhibit relatively increased activity

in the hypothalamic-pituitary-adrenal axis unrelated to the hypothalamic 5-HT1A receptor, which would be consistent with the findings of a recent study reporting higher diurnal salivary cortisol in female BPD patients without major depression, relative to healthy controls [10]. This could result in enhanced cortisol levels in response to similar levels of hypothalamic 5-HT1A receptor activation. In the study, the negative correlation between impulsivity and cortisol response to ipsapirone in the BPD group indicated that this relationship is consistent for the BPD subjects as it is for the sample as a whole. In a sample of individuals characterized by a categorical psychiatric diagnosis such as BPD, exaggerated degrees of traits such as impulsivity may be a more direct correlate of an altered central serotonergic dysfunction [11]. The lack of diagnostic or symptom associations with temperature response to ipsapirone suggests that these disorders may exhibit 5-HT1A receptor dysfunction extrinsic to serotonergic neurons themselves, as there has been no evidence found for cell-body 5-HT1A autoreceptor dysfunction in these individuals [12].

#### HPA axis disturbance hypothesis

As numerous studies have shown a strong correlation between childhood abuse and BPD, it is important to examine the physiological effects of this neglect at a young age. In a recent study by Rinne, et al., it was found that hyper-responsiveness of the hypothalamus-pituitary-adrenal (HPA) axis in chronically abused BPD subjects may be due to the enhanced central drive to pituitary ACTH release. This effect is accounted for by the brain's compensatory mechanisms to stress during periods of sustained childhood abuse. Due to an enhanced efficacy of HPA suppression by dexamethasone, it is possible that the brain's response to abuse attenuates the ACTH response to DEX/CRH [13]. Consistent with the hypothesis that the severity of early life stress is correlated with stress hormone abnormalities in adulthood, Childhood Trauma Questionnaire scores were significantly correlated with CSF CRF levels in individuals with borderline personality disorder [14]. Additionally, Benson et al. found enhanced ACTH and cortisol stress responses were significantly higher in a population of PCOS patients when compared to a group of BMI matched healthy controls [15]. Taken together, this data suggests that in both BPD and PCOS, a hyper-responsiveness of the HPA axis can result in increased cortisol levels in adulthood.

#### Female Hormone Disturbance Hypothesis

##### Effects of hormonal imbalances

With hormonal imbalance being one of the hallmarks of PCOS, it

should come as no surprise that elevated androgen levels have been associated with a decreased QoL in this population of women [16]. Due to the increased prevalence of masculine traits from hyperandrogenism, women with hyperandrogenic syndromes are at a considerable risk for developing mood disorders [17-19]. Past data also supports the idea that variability and change in estradiol levels may be related to borderline symptoms, whereas absolute levels are not. Importantly, the changes in estrogen levels seem to contribute unique variance to the expression of BPD, attributable to more general factors, as the pattern held when BSI scores for depression, hostility, and anxiety were all statistically controlled [20]. It is thus possible that this variability in estrogen levels in women with borderline traits leads to greater mood instability with the fluctuation of this important hormone. As hormonal imbalances can lead to a greater expression of psychological disturbances, its further study is crucial to advancing the treatment of PCOS and its accompanying borderline traits.

### Treatment of the depressive symptoms and side effects associated with PCOS and BPD

Due to the various hormonal irregularities associated with both PCOS and BPD, it is important to examine treatment options that aim to resolve these imbalances rather than just the side effects of their resulting psychological morbidity. Although literature on the treatment of mood disorders with hormonal agents is not comprehensive, several reports describe resolution of treatment-resistant depression with the use of anti-glucocorticoids. Through investigation of the modulation of HPA activity to treat affective disorders, corticotrophin releasing hormone (CRH) receptor antagonists have been suggested as a possible antidepressant [20]. In a recent study by Rasgon et al., a trial with a CRH receptor antagonist noted a significant decrease in depression and anxiety scores [20]. It is however unknown whether the CRH receptor antagonists are simply treating symptoms of depression rather than the underlying pathophysiology, and whether patients will experience significant withdrawal and possible relapse of the affective disorder after long term administration of the CRH receptor antagonist [20]. As elevated cortisol levels due to hyperactivity of the HPA-axis have been observed in both PCOS and BPD, recent studies suggesting improvement of depressive symptoms with glucocorticoid receptor antagonists offer an interesting solution to this debilitating psychological morbidity. Wolkowitz et al. reported a depression resistant to treatment with monoamine-reuptake inhibitors that improved after treatment with ketoconazole [21]. Based on the presence of abnormal baseline cortisol and resistance to glucocorticoid-mediated negative feedback on cortisol in depressed individuals, the authors suggested that the anti-depressant effect of ketoconazole may be due to cortisol suppression [22-24]. Interestingly, in a recent study Salazar has suggested that alpha lipoic acid (ALA), a drug used to treat type 2 diabetes mellitus by increasing insulin sensitivity, may be useful in treating depression [25]. It is possible that the insulin resistance seen in depressed patients may be caused by increased cortisol, abnormal monoaminergic activity, or other factors [25]. Although the link between insulin resistance and depression is not clearly defined, it is known that insulin contributes to 5-HT synthesis via promotion of tryptophan influx into the brain [26,27]. Since ALA works to increase insulin sensitivity, it is possible that ALA may be useful in treating depression by increasing the availability of tryptophan in the blood [28]. It follows that Metformin, a drug frequently used to treat insulin resistance may be useful in treating depression. In a case described by Fernstrom et al., a woman with PCOS was treated with Metformin and Spironolactone. Metformin (Glucophage) is a biguanide that inhibits hepatic glucose production and increases peripheral

insulin sensitivity, though it does not modify pancreatic insulin secretion. The decrease in insulin resistance may be obtained via decreasing gut absorption of glucose, improving glucose uptake by tissues, and/or increasing the number of insulin receptors [29]. In treating PCOS, Metformin has been shown to decrease insulin resistance, acne, hirsutism, and total and bio-available testosterone [30-32]. A significant decrease in body mass index (BMI) and waist-hip ratio as a result of treatment with metformin has also been observed ) as well as restoration of ovulation [33]. In this specific case, the patient reported weight loss and return of her menstrual cycles, possibly even ovulation as she reported PMS-like symptoms. Spironolactone (Aldactone) is an anti-mineralocorticoid, a diuretic and an anti-androgen. It was originally used to treat hypertension and has also been shown to be a weak inhibitor of testosterone biosynthesis [34]. Having been reported as an effective medication in reducing hirsutism, Spironolactone has also been shown to decrease insulin resistance and fasting insulin levels in PCOS patients along with a recorded decline in testosterone levels [35,36]. Although data supporting the role of these drugs in the treatment of depression does not yet exist, the presented cases suggest that the combination of Metformin and Spironolactone may have a positive effect on the depressed mood and clinical symptoms in women with PCOS.

### Conclusion

Given the high prevalence of PCOS and the debilitating psychological morbidity that can encompass a poor prognosis, the further study of this endocrine disorder is necessary. As many of these psychiatric issues are also evident in borderline traits, we suggest that the screening criteria used to diagnose BPD could be beneficial in identifying women with PCOS who are at risk for future psychiatric hospitalizations or suicide attempts. As the study of PCOS continues, there has clearly been an increased understanding of how hormonal imbalances and regulatory dysfunction can lead to psychological morbidity, but further study is essential to examine more effective treatment options for these irregularities.

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