www.directivepublications.org

World Journal of Eating Disorders

DIRECTIVE PUBLICATIONS

Review Article

Review Of Literature On Polycystic Ovary Syndrome And Eating Disorders.

Ragata Lóral, klaudia Zywot, Wojciech Ualewski, Adam Jagodzi nski and Narek Murawski.

Department of Internal Medicine, Yasmed Medical Center Doha, Qatar.

Abstract

Hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology are the hallmarks of PCOS, a complicated endocrine condition that affects women of reproductive age. Hormonal abnormalities, metabolic dysfunction, and co-occurring mental illnesses, such as eating disorders (EDs), are frequently linked to PCOS. Key hormones, including serotonin, leptin, insulin, ghrelin, kisspeptin, and cortisol, are identified in the review along with their functions in the pathophysiology of PCOS and related mental health issues. Eating and mood issues are linked to serotonin deficit, which is frequently observed in PCOS patients. Variations in the satiety hormone leptin impact the maturation of ovarian follicles and the hypothalamic-pituitary-ovarian axis, raising the risk of infertility.Because of its impact on the limbic system and glucose metabolism, elevated kisspeptin levels in PCOS patients are linked to both hormonal dysregulation and an increased risk of eating disorders like bulimia and binge eating. Insulin resistance and hyperinsulinemia worsen metabolic and reproductive health and encourage eating disorders like bulimia and binge eating. Cortisol and ghrelin also show up as important variables. The analysis highlights the bidirectional association between eating disorders and PCOS, whereby hormonal problems feed a vicious cycle of mental health issues.

Keywords: *eating disorders, hormone imbalances, insulin resistance, hyperandrogenism, serotonin, leptin, ghrelin, cortisol, anxiety, depression, and polycystic ovarian syndrome.*

INTRODUCTION

Ovarian polycystic syndrome is a prevalent condition among women of reproductive age; it is frequently linked to anovulation and is by definition a normo-gonadotropic, normo-estrogenic state [1]. The Rotterdam criteria are used to diagnose it [2]. According to these recommendations, which were developed at an international meeting in Rotterdam in 2023, a patient can be diagnosed with PCOS if at least two of the three symptoms—hyperandrogenism, oligo-/anovulation, and a characteristic sonographic ovary image—are present. Since several of the traits used to diagnose adult women, like acne, irregular menstruation, and polycystic ovary shape, can be typical physiological aspects of puberty, the diagnostic criteria for PCOS, especially during adolescence, are contentious [3].

Although PCOS is caused by about 30 genes, a number of additional factors are also crucial to the development of this complicated illness [4,5]. Many theories about the etiopathogenesis of PCOS have a tendency to support one another. The most widely accepted theory states that insulin resistance and hyperinsulinemia, which in turn cause hyperandrogenism, are the causes of PCOS [6]. Long-term cardiovascular disease, obesity, mental health issues, infertility, sleep disturbances, sexual dysfunction, and metabolic malfunction can all be linked to polycystic ovarian syndrome. those with PCOS are more likely to have eating disorders than those without the condition. Binge eating and bulimia nervosa are the most frequently reported. Anorexia nervosa is seldom diagnosed, but [12]. Episodes of uncontrollably consuming a lot of food in a short length of time are known as binge eating [13]. Contrarily, bulimia nervosa is a disorder in which compensatory behaviors, such as self-induced vomiting, the use of laxatives or diuretics, exhausting physical activity, or fasting, are used after an episode of binge eating in order to avoid gaining weight [14]. Up to 62% of people in this group suffer from eating disorders. Of women, 42% may engage in binge eating, and 12% may

***Corresponding Author:** Ragata Lóral, Department of Internal Medicine, Yasmed Medical Center Doha, Qatar.
Received: 08-Jan-2025, **; Editor Assigned:** 09-Jan-2025 **; Reviewed:** 21-Jan-2025, **; Published:** 29-Jan-2025.
Citation: Ragata Lóral. Review of Literature on Polycystic Ovary Syndrome and Eating Disorders. World Journal of Eating Disorders 2025 January; 1(1).

have bulimia nervosa [15]. This study will examine polycystic ovarian syndrome, emphasizing the role that hormone and neurotransmitter abnormalities play in the emergence of eating disorders. Since serotonin levels have been found to differ between healthy and PCOS-afflicted women, it will be the primary neurotransmitter discussed. We have chosen to highlight a few of the many hormones that are crucial to the mechanism of PCOS and related eating disorders: insulin, since hyperinsulinemia is linked to PCOS; ghrelin (because of its effect on hunger and the development of obesity, which is one of the main causes of PCOS and related eating disorders); and leptin and its pathological fluctuations, which disrupt follicle maturation.

APPROACH

Using searches in the PubMed, Web of Science, and Scopus databases, we conducted a review of the literature on eating disorders in women with PCOS. "Polycystic ovary syndrome" or "PCOS," "eating disorders," "eating disorders in PCOS," "psychiatric disorders in PCOS," "hormonal changes," "binge eating," and "bulimia nervosa" were among the search terms used to find publications. The examined publications focused on research that were no more than five years old and were published between 1993 and 2024. Works lacking open access, case reports, and articles written in languages other than English were not included. The nations in which the investigations were carried out were not subject to any limitations. Results from duplicate searches were eliminated. In order to find any other articles that might be able to offer insightful commentary on the current paper, we also manually reviewed the reference lists from the many studies that were part of this review.

DIAGNOSTIC STANDARDS

Stein and Leventhal initially identified PCOS as an endocrinological metabolic condition with an unclear cause in 1935. The causes of PCOS are now much better understood, and diagnostic standards have evolved over time.The National Institute of Child Health and Human Development (NIH) finished the first set of criteria, referred to as the "classic," in 1990. The PCOS criteria at the time included oligomenorrhea or amenorrhea and the presence of clinical and/or laboratory indicators of hyperandrogenism. Ultrasonography did not play as significant a part as it does now in diagnosis. Although they were suggested, ultrasound tests to look for signs of PCOS in the ovaries were not required for diagnosis.

The well-known "Rotterdam criteria," which were expanded with ultrasonography but devoid of hyperandrogenism, were the result of a 2003 discussion that was carried out in Rotterdam [16]. According to the criteria, one or both ovaries must have 12 or more follicles with a diameter between 2 and 9 mm and/or an increased ovarian volume greater than 10 cm3 in order for ultrasonography to detect PCOS. The third to fifth days of the menstrual cycle is when this examination should be conducted; however, the timing of examination is irrelevant for individuals who are amenorrheic or have irregular periods. But the main Rotterdam criteria lacked specificity: once transvaginal ultrasonography became more widely available.Prior to 2006, hyperandrogenism—once the primary criterion for diagnosing PCOS—was not required for women to be diagnosed with the condition. In 2006, hirsutism and/or biochemical hyperandrogenism were established as required PCOS criteria by the Androgen Excess Society (AES), which once more made hyperandrogenism a prerequisite. The NIH began working on harmonizing PCOS criteria in 2012 because there were three distinct classifications. The Rotterdam criteria were expanded to include hyperandrogenism as a consequence of collaboration among PCOS specialists. Gynecologists still employ the broader Rotterdam criteria nowadays.

These days, a patient is diagnosed with PCOS if two of the three criteria—polycystic-appearing ovarian morphology (PCOM), oligo-/anovulation, and clinical or biochemical hyperandrogenism—are met. Elevated total or free testosterone is known as biochemical hyperandrogenism.

One accurate indicator of estimated free testosterone is the free androgen index (FAI), which is computed by dividing total testosterone by the level of sex hormone binding globulin (SHBD) and then multiplying the result by 100. Hyperandrogenism can also be diagnosed using bioavailable testosterone, which is made up of both free and albumin-bound testosterone [16].

Clinical hyperandrogenism is assessed using the modified Ferriman-Gallwey scale, the gold standard for hirsutism diagnosis. Since total and free testosterone levels in adolescents are similar to those in adults 1 to 2 years following menarche, hyperandrogenism ought to be one of the primary diagnostic criteria for teenage women [23, 24]. The adjusted Ferriman-Gallwey hirsutism scores should resemble those of an adult by the age of 18. The modified Ferriman–Gallwey score was found to be unrelated to age in a sample of 633 unselected women, primarily between the ages of 18 and 45, who were presenting for a pre-employment physical examination [25].

Adolescents who are two years past menarche may therefore be eligible to employ adult criteria for hyperandrogenism and ovarian volume, but not follicular count [26]. There are two sets of proposed criteria for PCOS in adolescents.

An ESHRE/ASRM working group suggested one that calls for the patient to exhibit polycystic ovarian morpholology (ovarian volume >10 cm3), oligo-/anovulation (oligo-/amenorrhea for at least two years, or primary amenorrhea by

the age of 16), and clinical or biochemical hyperandrogenism (increased serum androgens and/or progressive hirsutism). Other etiologies must be excluded in order to satisfy all three requirements [27].The other set was created by the Endocrine Society's clinical practice guidelines committee [28] and states that the patient must exhibit polycystic ovarian morphology (ovarian volume >10 cm3), persistent oligo-/anovulation (oligo-/amenorrhea for at least two years, or primary amenorrhea by the age of 16), and clinical or biochemical hyperandrogenism (increased serum androgens and/or progressive hirsutism). Other etiologies must be excluded in order to meet two of the three requirements. Girls should receive symptomatic treatment if they don't meet all of the diagnostic requirements. It has been determined that most teenage females who exhibit the syndrome's early symptoms will manifest PCOS by the time they are eighteen.

SEROTONIN

A neurotransmitter called serotonin (5-HT) influences mood, behavior, memory, and a host of other brain functions. Serotonin is mostly linked to neurological and mental conditions such eating disorders, anxiety, and sadness. The production of serotonin requires the amino acid tryptophan. Tryptophan hydroxylase hydroxylates it, while 5-hydroxytryptophan decarboxylase decarboxylates it [35].

Luteinizing hormone (LH), which is controlled by gonadotropin-releasing hormone (GnRH), is one of the increased parameters in women with PCOS. Serotonin is one of the numerous variables that can control the body's pulsatile release of GnRH/LH, as it can prevent the pituitary from secreting LH [36].The coexistence of psychiatric diseases in this patient population is caused by dysregulated neurotransmitter levels. Women with PCOS are more likely than women without PCOS to experience clinically significant anxiety and sadness, according to a study that used the Hospital Anxiety and sadness Scale. 41% of PCOS patients who took part in the study had anxiety problems, and 12% of the same participants had depressive symptoms [40].

In addition to hormonal changes, PCOS can result in changes in appearance, including weight gain, acne, seborrhea, androgenetic alopecia, and hirsutism [41]. These symptoms are quite unattractive in women based on beauty standards. PCOS patients have decreased self-esteem and weight-related anxiety [8,42]. Eating disorders and body dissatisfaction can result from both hirsutism and a high BMI [43–45]. It was discovered that 36.3% of women with hirsutism also had eating issues [46].

THE HORMONE LEPTIN

Adipocytes create the satiety hormone leptin. Its concentration is proportional to the white fat tissue's triacylglycerol quantity. Leptin inhibits follicle formation and causes infertility via affecting NLPR3 receptors in the ovary, which are linked to ovulation, as well as LEPR receptors in the hypothalamus, which cross the blood–brain barrier.

In addition to lowering food intake and raising thermogenesis, hypothalamic stimulation also has an impact on the hypothalamic–pituitary–ovarian axis, which triggers the release of the chemicals GnRH and LH. The maturation of oocytes is significantly influenced by these two hormones.

There is also research on how leptin affects ovarian receptors [48]. Research on mice has demonstrated that whereas low levels of leptin promote the shift from primary to secondary follicles, high levels of leptin, through its action on NLPR3 receptors, hinder this process. Overeating caused by bulimia nervosa and binge eating disorder lowers the amounts of triacylglycerols in adipose tissue, which in turn stimulates leptin, which lowers levels of LH and GnRH. and prevents follicles with ovarian leptin receptors from maturing. However, in cases of extremely low leptin levels, anorexia nervosa, fast weight loss, and starvation also result in decreased levels of LH and GnRH and handinhibition at the primary follicle stage.

INSULIN

A condition known as insulin resistance (IR) occurs when cells lose their sensitivity to insulin. Hyperinsulinemia is the primary factor influencing the causes of IR. A patient with a high insulin level is frequently associated with a nutrient-poor diet, particularly one that is heavy in high-glycemic index goods, and little physical exercise.

As a result, women with bulimia nervosa will frequently have elevated insulin levels due to binge eating, which is defined as consuming large amounts of typically unhealthy, processed food. A high level of insulin is maintained in the bloodstream despite compensatory measures like vomiting.When the insulin receptor is activated, mTORC1kinase and S6K kinase initiate a biochemical reaction pathway that causes the insulin receptor to internalize from the cell membrane. In conclusion, insulin has no effect even at high concentrations [51]. An investigation into the relationship between insulin resistance and temporary overeating was conducted in 2009. For four weeks, 18 young individuals participated in the study and experienced binge eating. Following the study period, each participant had an adipose tissue sample, which was analyzed and studied in vitro. It was discovered that there were almost 40% less insulin receptors [52].Burghen identified the link between insulin resistance and PCOS in 1980. It is impacted by a number of outcomes brought on by elevated blood insulin levels. The hypothalamic-pituitary-ovarian axis contains a large number of insulin receptors, and when these receptors bind to insulin, several factors

contribute to PCOS. First, insulin causes the adrenal glands and ovaries to oversecrete androgens. Consequently, there is an increase in the blood's content of testosterone. Additionally, hyperinsulinemia increases the production of LH by ovarian theca cells, which in turn triggers the release of GnRH and an excess of androgens [53]. Insulin has a direct impact on oocyte maturation as well. While hyperinsulinemia impairs the oocytes' capacity to develop, physiological levels of insulin have a stimulating effect on the maturing oocytes.

KISSPEPTIN

The arcuate nucleus and anteroventral periventricular nucleus of the hypothalamus produce kisspeptin, a hormone crucial to the reproductive system and glucose homeostasis [58]. More than 90% of neurons that release gonadotropin have the kisspeptin receptor KISS1R, which promotes the release of pulsate GnRH [59]. Research revealed that the GnRH and kisspeptin concentration maxima overlap, further demonstrating that kisspeptin influences GnRH secretion. Follicle-stimulating hormone (FSH) and luteinizing hormone (LH), which are essential for menstruation and fertility, are released in response to GnRH. Even though most KISS1Rs are located in hypothalamus, they have also been found in the limbic system, specifically the amygdala, thalamus, hippocampus and cingulate cortex [60]. The limbic system is an anatomical area of brain which is responsible for emotion, memory, ambitions and behavior. Studies have shown that kisspeptin has an anxiogenic, but antidepressive effect on rats. Localization of those receptors in the limbic system may be interesting in context of this publications. Both bulimia nervosa and anorexia nervosa's neural roots are related to a dysfunctional limbic system. Some studies have shown that kisspeptin serum levels are increased in women with PCOS. The pancreas has also been shown to contain kisspeptin receptors, the majority of which are located in the endocrine portion and a small number in the exocrine portion [63]. Studies conducted both in vitro and in vivo have demonstrated that high levels of kisspeptin enhance the release of insulin in response to glucose [64,65]. Kisspeptin, however, requires a sufficient concentration of glucose in order to enhance insulin secretion. Women who suffer from binge eating or bulimia nervosa have high blood glucose levels because of compulsive eating. If they also have PCOS and high serum kisspeptin levels, these conditions work together to cause insulin resistance, which is a contributing factor in the pathophysiology of PCOS.

GHRELIN

During famine, the stomach's enteroendocrine cells A generate the peptide hormone ghrelin. Among its duties are appetite control and growth hormone secretion. Furthermore, ghrelin controls ovarian function, intestinal motility, endocrine and exocrine pancreatic secretion, and stomach acid secretion [66,67]. Studies have indicated that ghrelin levels are lower in women with PCOS [68–70].

Similarly, those with obesity and binge eating had lower ghrelin levels, whereas those with anorexia nervosa have higher ghrelin levels [71–73]. Studies have also shown that PCOS patients' ghrelin levels do not differ from those of non-PCOS individuals [74]. On the other hand, a study found that ghrelin levels were considerably lower in non-obese women with PCOS and without PCOS than in obese women with PCOS. According to the same study, ghrelin levels in non-obese PCOS patients were comparable to those in non-obese people without PCOS [75]. This may indicate that being overweight has a greater correlation with a group of PCOS patients' lower ghrelin levels than the actual polycystic ovarian syndrome. Ghrelin can contribute to increased hunger and overeating, which increases body fat and is a risk factor for PCOS, even if its direct impact on regulating the reproductive system's function has rarely been studied [68].

CORTISOL

Cortisol, often known as the stress hormone, is a steroid hormone that belongs to the glucocorticoid family. It is produced in smaller quantities by various tissues as well as by the zona fasciculata of the adrenal gland's cortex. Elevated levels of cortisol in the blood are seen in many PCOS-affected women [76]. The immunological system, the metabolism of fats and carbohydrates, and the reproductive system are all significantly impacted by this hormone. Either the ovary itself or the hypothalamus-pituitary-ovary axis have demonstrated its suppressive impact.Elevated levels of CRH (corticotropin-releasing hormone) reduce the ovaries' capacity to produce the right amount of hormones required for oogenesis by increasing prolactin production and inhibiting GnRH secretion [1]. Research on mice has demonstrated that people who experience ongoing stress have poor oogenesis, which in turn leads to higher cortisol levels. Researchers found that the expression of growth and differentiation factor 9 (GDF 9) was inhibited, which may be the cause of the increased ovarian follicle atresia and the inhibition of both secondary and antral ovarian follicle development. Further research further shown that antral follicles express less brain-derived neurotrophic factor (BDNF). The most prevalent eating disorder among women with PCOS is binge eating, which is known to be significantly triggered by stress [78]. This eating pattern might be a coping strategy used to manage the psychological strains brought on by PCOS. Stress is another factor that has a detrimental impact on self-esteem and body image satisfaction [79].

REFERENCES

1. Steegers-Theunissen, R.P.M.; Wiegel, R.E.; Jansen, P.W.; Laven, J.S.E.; Sinclair, K.D. Polycystic Ovary Syndrome: A Brain Disorder Characterized by Eating Problems Originating during Puberty and Adolescence. Int. J. Mol. Sci. 2020, 21, 8211. [CrossRef]

2. Shirin Dason, E.; Koshkina, O.; Chan, C.; Sobel, M. Diagnosis and Management of Polycystic Ovarian Syndrome. CMAJ Can. Med. Assoc. J. 2024, 196, E85. [CrossRef]

3. Infertility Problems with Ovulation—Women's Health Issues—MSD Manual Consumer Version.

4. Gorsic, L.K.; Dapas, M.; Legro, R.S.; Hayes, M.G.; Urbanek, M. Functional Genetic Variation in the Anti-Müllerian Hormone Pathway in Women With Polycystic Ovary Syndrome. J. Clin. Endocrinol. Metab. 2019, 104, 2855–2874. [CrossRef] [PubMed]

5. Hiam, D.; Moreno-Asso, A.; Teede, H.J.; Laven, J.S.E.; Stepto, N.K.; Moran, L.J.; Gibson-Helm, M. The Genetics of Polycystic Ovary Syndrome: An Overview of Candidate Gene Systematic Reviews and Genome-Wide Association Studies. J. Clin. Med. 2019, 8, 1606. [CrossRef]

6. Rodriguez-Paris, D.; Remlinger-Molenda, A.; Kurzawa, R.; Głowi´nska, A.; Spaczy´nski, R.; Rybakowski, F.; Pawelczyk, L.; Banaszewska, B. Psychiatric Disorders in Women with Polycystic Ovary Syndrome. Psychiatr. Pol. 2019, 53, 955–966. [CrossRef]

7. Thannickal, A.; Brutocao, C.; Alsawas, M.; Morrow, A.; Zaiem, F.; Murad, M.H.; Javed Chattha, A. Eating, Sleeping and Sexual Function Disorders in WomenwithPolycystic OvarySyndrome(PCOS):ASystematicReviewandMeta-Analysis. Clin. Endocrinol. 2020, 92, 338–349. [CrossRef]

8. Ba¸sar Gökcen, B.; Akdevelio˘glu, Y.; Canan, S.; Bozkurt, N. Increased Risk of Eating Disorders in Women with Polycystic Ovary Syndrome: A Case-Control Study. Gynecol. Endocrinol. 2020, 36, 764–767. [CrossRef]

9. Burnatowska, E.; Wikarek, A.; Oboza, P.; Ogarek, N.; Glinianowicz, M.; Kocelak, P.; Olszanecka-Glinianowicz, M. Emotional Eating and Binge Eating Disorders and Night Eating Syndrome in Polycystic Ovary Syndrome—A Vicious Circle of Disease: A Systematic Review. Nutrients 2023, 15, 295. [CrossRef] [PubMed]

10. Ollila, M.M.; Arffman, R.K.; Korhonen, E.; Morin-Papunen, L.; Franks, S.; Junttila, J.; Piltonen, T.T. Women with PCOS Have an Increased Risk for Cardiovascular Disease Regardless of Diagnostic Criteria—A Prospective Population-Based Cohort Study. Eur. J. Endocrinol. 2023, 189, 96–105. [CrossRef]

11. Purwar, A.; Nagpure, S. Insulin Resistance in Polycystic Ovarian Syndrome. Cureus 2022, 14, e30351. [CrossRef] [PubMed]

12. Cooney, L.G.; Gyorfi, K.; Sanneh, A.; Bui, L.M.; Mousa, A.; Tay, C.T.; Teede, H.; Stener-Victorin, E.; Brennan, L. Increased Prevalence of Binge Eating Disorder and Bulimia Nervosa in Women with Polycystic Ovary Syndrome: A Systematic Review and Meta-Analysis. J. Clin. Endocrinol. Metab. 2024, 109, 3293–3305. [CrossRef]

13. Lalonde-Bester, S.; Malik, M.; Masoumi, R.; Ng, K.; Sidhu, S.; Ghosh, M.; Vine, D. Prevalence and Etiology of Eating Disorders in Polycystic Ovary Syndrome: A Scoping Review. Adv. Nutr. 2024, 15, 100193. [CrossRef] [PubMed]

14. Christ, J.P.; Cedars, M.I. Current Guidelines for Diagnosing PCOS. Diagnostics 2023, 13, 1113. [CrossRef] [PubMed]

15. Smet, M.-E.; McLennan, A. Rotterdam Criteria, the End. Australas. J. Ultrasound Med. 2018, 21, 59–60. [CrossRef]

16. Kahraman, F.C.; Erdo˘gan, S.S. Grading of Hirsutism A Practical Approach to the Modified Ferriman-Gallwey Scoring System. Adv. Dermatol. Allergol./Poste¸py Dermatol. I Alergol. 2021, 39, 744. [CrossRef] [PubMed]

17. Kanbour, S.A.; Dobs, A.S. Hyperandrogenism in Women with Polycystic Ovarian Syndrome: Pathophysiology and Controversies. Androgens 2022, 3, 22–30. [CrossRef]