

## Case Report

# The Role of Polycystic Ovarian Syndrome in Chronic Inflammation, Psychological Health, and the Gut Microbiota State: A Case Report

**Davis CC and Popp JK\***

Athletic Training Program, Purdue University, USA

**\*Corresponding author:** Jennifer K Popp, Athletic Training Program, Purdue University, 800 West Stadium Avenue, West Lafayette, IN 47907, USA**Received:** December 18, 2021; **Accepted:** January 13, 2022; **Published:** January 20, 2022**Abstract**

Polycystic Ovarian Syndrome (PCOS) is endocrine and gynecological disorder that affects women of reproductive age. This is a case report of a patient with PCOS who was misdiagnosed and presented with several endocrine and gynecological symptoms. This case emphasizes the need for a holistic healthcare approach to treat the underlying organ dysfunction in women with PCOS. It highlights the interconnectedness between endocrine and reproductive dysfunction. This case report examines the chronic inflammatory state, risk of developing psychological disorders, and gut microbiota diversity in women with PCOS.

**Keywords:** Polycystic Ovarian Syndrome; Endocrinology; Gynecology; Psychology; Primary Care

**Abbreviations**

CBT: Cognitive-Behavioral Therapy; CNS: Central Nervous System; CRP: C-reactive Protein; GI: Gastrointestinal; GM: Gut Microbiota; HPA Axis: Hypothalamus-Pituitary-Adrenal Axis; IR: Insulin Resistance; PCOS: Polycystic Ovarian Syndrome

**Case Presentation**

Patient is a 22-year-old female who was diagnosed with polycystic ovarian syndrome (PCOS) at 14 years of age. At the age of 13, the patient experienced menarche, followed by amenorrhea for 6 months. During this period of amenorrhea, she presented with unexplained extreme fatigue, headaches, muscular weakness, decreased immunity, and concentration impairment, and was diagnosed with mononucleosis. However, her symptoms lasted 9 months, rather than 2-4 weeks, which is typical with a mononucleosis diagnosis. During these 9 months, the patient was evaluated by many specialists, and underwent a battery of diagnostic tests. At the age of 14, the patient resumed menses; however, the resumption of menses brought the following symptoms: abnormal menstrual cycles, mood swings, cystic acne, anxiety, sharp pelvic pain, abdominal weight gain, and gastrointestinal dysfunction. An internal medicine physician diagnosed the patient with PCOS at the age of 14 years based on chronic fatigue and results of blood work, which revealed the following: elevated insulin levels, decreased thyroid stimulating hormone, and elevated estrogen and androgen levels, along with nutritional deficiencies that included decreased magnesium, and vitamins B12 and D levels. A transvaginal ultrasound performed at age of 20 resulted in additional diagnoses of cystic ovaries and endometriosis.

Immediately following her PCOS diagnosis, the patient began a holistic lifestyle change consisting of healthy foods, regulation of macromolecule input, exercise regimen conducive with her hormonal levels, vitamin supplementation, and stress management techniques.

After three months of these lifestyle changes, the patient experienced a significantly improved quality of life. Continued interventions include a complete blood count and comprehensive metabolic panel 2-3 times per year to ensure the interventions are appropriate. The patient is able to function normally; however, her symptoms are cyclical based on menstrual cycle. During periods of stress, the patient becomes fatigued, and struggles to maintain normal insulin levels, which causes an increase in inflammatory markers, leading to gastrointestinal upset and nutrient malabsorption.

**Discussion**

PCOS is a multifaceted endocrine and gynecological disorder which effects 15-20% of women of reproductive age [1]. This disorder effects every part of the endocrine system [3-13]. The diversity of PCOS symptoms leads to prolonged diagnosis and misguided treatment plans [2]. Diagnosis of PCOS is made by utilizing the Rotterdam Diagnostic Criteria, presented in Table 1 [2]. Symptoms occur as a result of endocrine organs (Table 2) and body systems (Table 3) affected by PCOS [3-13].

**The Role of chronic inflammation in polycystic ovarian syndrome**

Women with PCOS experience a chronic inflammatory state due a disproportionate ratio of inflammatory markers to anti-inflammatory metabolites [14]. PCOS is characterized by increased levels of inflammatory markers including C-reactive protein (CRP) and Alpha(1)-acid glycoprotein [1,14]. Elevated levels of pro-inflammatory markers are due to hyperandrogenism, and increased adipose tissue forms as a result of insulin resistance (IR) in women with PCOS [1,14]. Albumin and adiponectin are anti-inflammatory agents that are lower in women with PCOS [14]. As a result, there is increased CRP/albumin ratio due to hyperandrogenism's positive impact on liver synthesis of CRP [14]. Long term health effects due to the unequal ratio of inflammatory and anti-inflammatory markers are obesity, insulin resistance, type 2 diabetes, cardiovascular disease,

**Table 1:** Rotterdam Diagnostic Criteria 2003 for diagnosing women with polycystic ovarian syndrome [2].

Hyperandrogenism	Anovulation/Oligo-ovulation	Polycystic ovaries via transvaginal ultrasound
Hirsutism	Bleeding Interval <21 days	Presence of 12 or more follicles 2-9mm in diameter in either ovary AND/OR
Cystic hormonal acne	Bleeding Interval >35 days <8 menses per year	Increased ovarian volume > 10mL (without cyst or dominant follicle in either ovary)
Male-pattern alopecia	Infertility No menstruation for 3 consecutive months in last 12 months	

**Table 2:** Endocrine organs affected by polycystic ovarian syndrome [3-6].

Endocrine Organs	Pancreas [3,4]	Liver [3]	Adrenal glands [5]	Thyroid gland [6]
Symptoms/Side Effects	<ul style="list-style-type: none"> <li>Insulin resistance</li> <li>Excess insulin production: abnormal production of androgens by ovaries and adrenals</li> <li>Hypoglycemia</li> <li>Increased risk of type 2 diabetes/metabolic disorder</li> <li>Central obesity</li> <li>Chronic inflammation</li> </ul>	<ul style="list-style-type: none"> <li>Elevated blood lipid levels</li> <li>Risk of cardiovascular disorders</li> <li>Increased demand on liver</li> <li>Elevated estrogen levels: need to be detoxified/eliminated by liver</li> <li>Fatty liver</li> </ul>	<ul style="list-style-type: none"> <li>Adrenal hyperplasia</li> <li>Hypothalamic-Pituitary-Adrenal axis (HPA axis) dysregulation</li> <li>Chronic elevated cortisol production</li> <li>Chronic sympathetic nervous system response</li> <li>Anxiety</li> <li>Insomnia</li> <li>Fatigue</li> <li>Produce excess androgens due to insulin resistance</li> <li>Weight gain</li> <li>Increased risk of heart disease and stroke</li> </ul>	<ul style="list-style-type: none"> <li>Hypothyroidism</li> <li>Fatigue</li> <li>Increased Thyroid Stimulating Hormone and prolactin production</li> <li>Prolactin causes anovulation and abdominal obesity</li> <li>Decreased circulation to distal extremities: disruption in temperature regulation</li> <li>Dysregulation of basal metabolic rate: changes in heart rate, blood pressure, respiratory rate</li> </ul>

and metabolic dysfunction [1,14].

Interventions to reduce inflammation in PCOS patients include reducing hyperandrogenism and insulin resistance [1,14]. Insulin sensitizers including Metformin and Myo-inositol have been shown to improve insulin sensitivity [15,16]. When comparing Metformin and Myo-inositol, Metformin has several gastrointestinal side effects. In addition, Myo-inositol has regulatory reproductive effects including normalizing menstrual cycles and ovulation in women with PCOS [16]. Oral contraceptives used to treat PCOS further exacerbate insulin resistance and hyperandrogenism, as well as disrupts normal reproductive system functioning [7].

A healthy diet and supplementation of essential macro and micronutrients in women with PCOS is vital to the reduction of this chronic inflammatory state [17]. High fiber diets contain inositol, which is utilized to reduce IR and the risk of developing metabolic abnormalities [17]. Diets that include unrefined complex carbohydrates and low amounts of simple sugars improve pancreatic insulin sensitivity, regulate menstrual cycles, as well as reduce the production of pro-inflammatory markers, hyperandrogenism, and increase gut microbiome diversity [8,17]. Diets with elevated levels of saturated fats, such as red meats, do fail to promote normal levels of insulin and glucose [17].

As far as supplementation, curcumin reduces inflammation and the prevalence of IR when used in conjunction with Metformin [17]. Chromium also reduces IR, and promotes normal ovulation [17]. Vitamin D, B12, and folate reduce IR [18]. Zinc, magnesium, and selenium improve serum glucose levels [17].

Exercise reduces the risk of developing IR and hyperandrogenism in women with PCOS [18]. There is minimal evidence related to exercise standards for women with PCOS; therefore, it is recommended that women with PCOS achieve 150 min of moderate physical activity

per week [2]. However, this guideline does not consider the cyclic hormonal changes women experience, and how to best align exercise with optimal endocrine and reproductive function [19]. In follicular and ovulatory phases, women experience fewer hormonal symptoms and higher levels of estrogen, which makes them better suited to participate in high-intensity exercise [19,20]. This is due to estrogen’s positive impact on glucose availability and nerve conduction [20]. During the luteal phase, high levels of progesterone have the opposite effect of estrogen [20]. During the end of the luteal phase and menstrual phase, women experience more hormonal symptoms and less energy to perform high-intensity exercise [19]. More research is needed to identify the most beneficial types of physical activity during different phases of the menstrual cycle [2].

**The role of hypothalamic pituitary axis dysregulation and psychological disorders in the chronic inflammatory state of women with polycystic ovarian syndrome**

Women with PCOS have an increased risk of developing depression and anxiety [21,22]. Chronic hyperandrogenism causes a negative body image, which contributes to the development of these psychological disorders [11,21,22]. Elevated serum cortisol levels due to hypothalamic-pituitary-adrenal (HPA) axis dysregulation and adrenal gland overstimulation in women with PCOS leads to hyperandrogenism and psychological disorders [21,22].

Additionally, chronic stress causes sympathetic nervous system activation and an overactive HPA axis [5,23]. Women with PCOS are unable to inhibit this chronic sympathetic response; therefore, adrenal fatigue, anxiety, depression, and exacerbated chronic disease symptoms ensue [5,23]. Inflammation also increases in response to chronic stress [23,24]. Abdominal obesity in women with PCOS is in response to HPA axis dysregulation, which increases inflammatory markers [23,24]. This contributes to the unequal ratio between inflammatory makers and anti-inflammatory agents [23,24].

**Table 3:** Systems affected by polycystic ovarian syndrome [7-13].

Systems	Gastrointestinal System [7-10]	Lymphatic System/Skin [7,8]	Reproductive System [11-13]
<b>Symptoms/ Side Effects</b>	<ul style="list-style-type: none"> <li>Decreased diversity of gut microbiota</li> <li>Increased non-beneficial gut bacteria</li> <li>Chronic inflammation damages intestinal lining</li> <li>Decreased nutritional absorbance</li> <li>Decreased immunity</li> <li>Increased risk of metabolic diseases</li> <li>Gastrointestinal hormone dysfunction</li> <li>Gas, bloating, Gastrointestinal (GI) upset</li> <li>Irritable bowel syndrome</li> <li>Abnormal Central Nervous System (CNS)-gut axis</li> <li>Decreased serotonin production by intestinal enterochromaffin cells: increased psychological disorders</li> <li>Eating disorders</li> </ul>	<ul style="list-style-type: none"> <li>Elimination dysfunction</li> <li>Cystic acne</li> <li>Eczema</li> <li>Skin bacterial infections</li> </ul>	<ul style="list-style-type: none"> <li>Hyperandrogenism and Hypoestrogenism</li> <li>Androgenic alopecia</li> <li>Hirsutism</li> <li>Anovulation</li> <li>Oligomenorrhea/Amenorrhea</li> <li>Polycystic ovaries</li> <li>Central obesity</li> <li>Decreased sex drive</li> <li>Infertility</li> <li>Pregnancy issues: preterm delivery, miscarriages, pre-eclampsia, gestational diabetes</li> <li>Ovulatory disorders</li> <li>Autoimmune disorders due to hypoestrogenic state</li> <li>Endometriosis/endometrial cancer</li> <li>Elevated luteinizing hormone production: compromises oocyte development and pancreatic function</li> </ul>

Interventions to reduce the prevalence of psychological disorders in women with PCOS include cognitive-behavioral therapy (CBT) [25]. CBT in conjunction with a nutritious diet and adequate physical activity have been proven to increase quality of life and psychological health in women with PCOS [25,26]. Yoga is one example of a form of exercise that, in conjunction with a holistic medical approach, improves emotional well-being and endocrine function [27]. Overall, routine psychological well-being assessments and services are recommended for women with PCOS [2].

### The role of chronic inflammation in polycystic ovarian syndrome's gut microbiota state

The gut microbiome (GM) contains a diverse group of bacteria that support digestive system processes as well as regulation of other endocrine organs [8]. A healthy GM is responsible for nutritional absorption through the small intestine and improving immunity against pathogens [8]. Women with PCOS lack a diverse GM, making them more susceptible to nutritional deficiencies, contracting harmful pathogens, and abnormal production of androgens [7,8]. Additionally, there are more non-beneficial types of GM bacteria, leading to an immunocompromised and chronic inflammatory state in women with PCOS [7]. An increase in non-beneficial types of GM bacteria also causes a decrease in insulin sensitivity, which in turn leads to abdominal obesity [7].

Due to the chronic inflammatory state in women with PCOS, the gastrointestinal lining becomes damaged and is more susceptible to diffusion of substances across its barrier [8]. As a result of this damage of the lining, toxins are released into the bloodstream [7]. This continual damage to the beneficial intestinal lining intensifies PCOS symptoms [7].

A normal Central Nervous System (CNS)-gut axis is essential in decreasing the risk of developing psychological disorders in women with PCOS [7,8]. Women with PCOS have an abnormal CNS-gut axis due to less diversity of their GM and chronic damage to their intestinal lining [7,8]. Damage to the intestinal lining decreases the amount of intestinal enterochromaffin cells that produce serotonin [7,8]. Decreased levels of serotonin cause dysfunction of psycho-endocrinological processes associated with HPA axis regulation and cognitive development [7,8].

Due to the significant impact an abnormal GM has on digestive and other endocrine processes, gut health intervention is an essential part of the holistic treatment of PCOS [17]. Diets high in fiber content protect the intestinal lining from damage and inflammation, reduce the abnormal production of androgens, increases nutritional absorption, and improves overall immunity [7,8,17]. In addition, supplementation of probiotics and prebiotics aids in regulation of the GM in women with PCOS [4,7]. Probiotics decrease inflammation as well as increase immunity [7]. Probiotics and prebiotics have regulatory reproductive effects, including regulating ovulation and decreasing hyperandrogenism [4].

### Conclusion

Polycysticovariansyndromeisacomplexandhighlyinterconnected endocrine and gynecological disorder. A holistic healthcare approach should be taken to treat the underlying organ dysfunction associated with PCOS symptoms. This includes interprofessional collaboration between primary care physicians, endocrinologists, gynecologists, and psychologists. Lifestyle modifications including proper diet and supplementation, medications, stress management, and exercise are needed to reduce chronic inflammation and the risk of developing psychological disorders, as well as improving gut microbiota diversity. Women with PCOS can achieve a high quality of life and a decreased risk of developing comorbidities if diagnosed early and provided proper treatment.

### References

1. Aboeldalyl S, James C, Seyam E, Ibrahim EM, Shawki HE-D, Amer S. The Role of Chronic Inflammation in Polycystic Ovarian Syndrome-A Systematic Review and Meta-Analysis. *International journal of molecular sciences*. 2021; 22.
2. Al Wattar BH, Fisher M, Bevington L, et al. Clinical Practice Guidelines on the Diagnosis and Management of Polycystic Ovary Syndrome: A Systematic Review and Quality Assessment Study. *Journal of Clinical Endocrinology & Metabolism*. 2021; 106: 2436-2446.
3. Ahmadi M, Faramarzi M, Basirat Z, Kheirkhah F, Chehrizi M, Ashabi F. Mental and personality disorders in infertile women with polycystic ovary: a case-control study. *African health sciences*. 2020; 20: 1241-1249.
4. Shamasbi SG, Ghanbari-Homayi S, Mirghafourvand M. The effect of probiotics, prebiotics, and synbiotics on hormonal and inflammatory indices in women with polycystic ovary syndrome: a systematic review and meta-analysis. *European Journal of Nutrition*. 2020; 59: 433-450.

5. Gourgari E, et al. "Bilateral adrenal hyperplasia as a mechanism for hyperandrogenism in women with polycystic ovary syndrome." *Journal of Clinical Endocrinology and Metabolism*. 2021; Jc20154019.
6. Singla R, Gupta Y, Khemani M, Aggarwal S. Thyroid disorders and polycystic ovary syndrome: An emerging relationship. *Indian Journal of Endocrinology and Metabolism*. 2015; 19: 25-29.
7. Yurtdaş G, Akdevelioğlu Y. A New Approach to Polycystic Ovary Syndrome: The Gut Microbiota. *Journal of the American College of Nutrition*. 2020; 39: 371-382.
8. Zhao X, Jiang Y, Xi H, Chen L, Feng X. Exploration of the Relationship Between Gut Microbiota and Polycystic Ovary Syndrome (PCOS): a Review. *Geburtshilfe Frauenheilkd*. 2020; 80: 161-171.
9. Mathur R, Ko A, Hwang LJ, Low K, Azziz R, Pimentel M. Polycystic ovary syndrome is associated with an increased prevalence of irritable bowel syndrome. *Digestive diseases and sciences*. 2010; 55: 1085-1089.
10. Almís H, Orhon FŞ, Bolu S, Almís BH. Self-Concept, Depression, and Anxiety Levels of Adolescents with Polycystic Ovary Syndrome. *Journal of pediatric and adolescent gynecology*. 2021; 34: 311-316.
11. Ahmadi M, Faramarzi M, Basirat Z, Kheirkhah F, Chehrizi M, Ashabi F. Mental and personality disorders in infertile women with polycystic ovary: a case-control study. *African health sciences*. 2020; 20: 1241-1249.
12. Gholizadeh Shamasbi S, Dehgan P, Mohammad-Alizadeh Charandabi S, Aliasgarzadeh A, Mirghafourvand M. The effect of resistant dextrin as a prebiotic on metabolic parameters and androgen level in women with polycystic ovarian syndrome: a randomized, triple-blind, controlled, clinical trial. *European Journal of Nutrition*. 2019; 58: 629-640.
13. Papadakis G, Kandaraki EA, Tseniklidi E, Papalou O, Diamanti-Kandarakis E. Polycystic Ovary Syndrome and NC-CAH: Distinct Characteristics and Common Findings. A Systematic Review. *Frontiers in endocrinology*. 2019; 10: 388.
14. de Medeiros SF, de Medeiros MAS, Barbosa BB, Yamamoto AKLW, Yamamoto MMW. The connection of alpha-1 acid glycoprotein inflammatory marker with anthropometric, hormonal, and metabolic characteristic of women with polycystic ovary syndrome. *Journal of Obstetrics & Gynaecology Research*. 2021; 47: 3571-3582.
15. Facchinetti F, Orrù B, Grandi G, Unfer V. Short-term effects of metformin and myo-inositol in women with polycystic ovarian syndrome (PCOS): a meta-analysis of randomized clinical trials. *Gynecological endocrinology : the official journal of the International Society of Gynecological Endocrinology*. 2019; 35: 198-206.
16. Fruzzetti F, Capozzi A, Canu A, Lello S. Treatment with d-chiro-inositol and alpha lipoic acid in the management of polycystic ovary syndrome. *Gynecological endocrinology : the official journal of the International Society of Gynecological Endocrinology*. 2019; 35: 506-510.
17. Calcaterra V, Verduci E, Cena H, et al. Polycystic Ovary Syndrome in Insulin-Resistant Adolescents with Obesity: The Role of Nutrition Therapy and Food Supplements as a Strategy to Protect Fertility. *Nutrients*. 2021; 13.
18. Amirjani S, Asemi Z, Bazarganipour F, et al. Dietary intake and lifestyle behaviour in different phenotypes of polycystic ovarian syndrome: a case-control study. *Journal of Human Nutrition & Dietetics*. 2019; 32: 413-421.
19. Solli GS, Sandbakk SB, Noordhof DA, Ihalainen JK, Sandbakk Ø. Changes in Self-Reported Physical Fitness, Performance, and Side Effects Across the Phases of the Menstrual Cycle Among Competitive Endurance Athletes. *International Journal of Sports Physiology and Performance*. 2020; 15: 1324-1333.
20. McNulty KL, Elliot-Sale KJ, Dolan E, et al. The Effects of Menstrual Cycle Phase on Exercise Performance in Eumenorrheic Women: A Systemic Review and Meta-Analysis. *Sports Medicine*. 2020; 50: 1813-1827.
21. Blay SL, Aguiar JVA, Passos IC. Polycystic ovary syndrome and mental disorders: a systematic review and exploratory meta-analysis. *Neuropsychiatric disease and treatment*. 2016; 12: 2895-2903.
22. Dokras A, Stener-Victorin E, Yildiz BO, et al. Androgen Excess- Polycystic Ovary Syndrome Society: position statement on depression, anxiety, quality of life, and eating disorders in polycystic ovary syndrome. *Fertility and sterility*. 2018; 109: 888-899.
23. Chen X, Gianferante D, Hanlin L, et al. HPA-axis and inflammatory reactivity to acute stress is related with basal HPA-axis activity. *Psychoneuroendocrinology*. 2017; 78: 168-176.
24. Martocchia A, Gallucci M, Noale M, et al. The cortisol burden in elderly subjects with metabolic syndrome and its association with low-grade inflammation. *Aging Clinical & Experimental Research*. 2020; 32: 1309-1315.
25. Abdollahi L, Mirghafourvand M, Babapour JK, Mohammadi M. Effectiveness of cognitive-behavioral therapy (CBT) in improving the quality of life and psychological fatigue in women with polycystic ovarian syndrome: a randomized controlled clinical trial. *Journal of Psychosomatic Obstetrics & Gynecology*. 2019; 40: 283-293.
26. Jiskoot G, Dietz de Loos A, Beerthuis A, Timman R, Busschbach J, Laven J. Long-term effects of a three-component lifestyle intervention on emotional well-being in women with Polycystic Ovary Syndrome (PCOS): A secondary analysis of a randomized controlled trial. *PLoS one*. 2020; 15: e0233876.
27. Thakur D, Saurabh Singh DS, Tripathi DM, Lufang D. Effect of yoga on polycystic ovarian syndrome: A systematic review. *Journal of bodywork and movement therapies*. 2021; 27: 281-286.