



Polycystic Ovarian Syndrome: An Overview with Special Consideration to Its Oral and Pediatric Clinical Manifestations

Zeba Saleem ¹, Abiha Ahmad Khan ^{*1}, Syeda Aamena Naaz ¹ and Mohd. Javed Naim ²

Abstract

Polycystic ovary syndrome (PCOS) is a complex endocrine disorder affecting women of reproductive age. It is characterized by a combination of symptoms including irregular menstrual cycles, excessive androgen production, and the presence of multiple small cysts on the ovaries. This condition affects approximately 5-10% of women worldwide and is considered one of the most common endocrine disorders in women. The exact cause of PCOS is still unclear, but it is believed to involve a combination of genetic and environmental factors. Insulin resistance and hormonal imbalances play a significant role in the development of this syndrome. High levels of insulin can stimulate the ovaries to produce excess androgens, leading to hormonal dysregulation and subsequent complications such as hirsutism (excessive hair growth), acne, and male pattern baldness. PCOS is associated with a wide range of health problems, ranging from infertility and pregnancy complications to an increased risk of metabolic disorders such as type 2 diabetes and cardiovascular diseases. Furthermore, women with PCOS often experience psychological distress, as the visible symptoms, such as weight gain and fertility issues, can significantly impact their self-esteem

and quality of life. Early diagnosis is crucial to prevent long-term complications and provide appropriate management. This review highlights an overview of PCOS, its clinical features, diagnosis, and treatment strategies involved.

Keywords: PCOS, Polycystic Ovarian Syndrome, Pediatric Manifestations, Oral Manifestations.

1. Introduction

Polycystic Ovary Syndrome is one of the most common endocrine disorders arising in women during their reproductive age. It is heterogeneous with undefined/ indefinite/ unknown etiology but there also exists some solid indications that show PCOS to be due to extensive interactions between various environmental, genetic, and behavioral aspects (Bargiots & Diamanti, 2012). Also, it can be attributed to the increased ratio of luteinizing hormone to follicle-stimulating hormone and increased release of gonadotropin-releasing hormone (Bednarska & Siejka, 2017; Ganie et al., 2019). On following the NIH criteria for diagnosing, PCOS affects nearly 10% of women in their reproductive age whereas as per Rotterdam criteria; PCOS affects 18% of reproductive-age women (March et al., 2010). PCOS is also considered a metabolic disorder with at least 70% undiagnosed cases in the primary healthcare system (Tomlinson et al., 2013). Various signs and symptoms during the initial phases of PCOS are mentioned in Figure 1. Women suffering from PCOS is characterized by the presence of polycystic ovaries, enlarged or dysfunctional ovaries, hyperandrogenism, continuing anovulation for a longer period, gonadotropin abnormalities, resistance to

Significance | Highlighting the oral and pediatric manifestation of PCOS.

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insulin, diabetes, glucose intolerance, dyslipidemia and obesity whereas therapeutic strategy relies on treatment of hirsutism and infertility (Da Silva et al., 2009; Aziz, 2016; Andrade et al., 2016; Hoffman & Ehrmann, 2008; Teede et al., 2010; Diamanti & Dunaif, 2012; Moran et al., 2010; Randeve et al., 2012; Baldani et al., 2015). Due to these chronic outcomes, PCOS further increases the risk of various complications such as cardiovascular diseases, metabolic syndrome, depression, anxiety, etc. (Figure 2) (Glueck & Goldenberg, 2019; Damone et al., 2019). To cope with the situation, losing 5% of the body weight, following a sugar-free & fat-free diet and regular exercise are the most possible recommended procedures with or without some alternative or traditional therapies. Till now, there is no USFDA (United States Food and Drug Administration) approved drug available especially for the treatment of PCOS and most of the drugs are being used off-label but still many approved drugs are available for treating indications of PCOS (medications like Pioglitazone, Empagliflozin, Sitagliptin, Simvastatin, Atorvastatin and N-acetyl cysteine). Furthermore, there is an urgent need for the design and development of newer, effective, and safer drug molecules for the treatment of PCOS and to use the available therapeutic options wisely in the absence of USFDA-approved molecules. This review throws light on PCOS as an alarming condition for women along with its etiology, diagnosis, pathophysiology, and various clinical manifestations.

In the Unani system of medicine, the disease has not been mentioned under the term PCOS but its translation has been done in Arabic as “*Marze ikhyase khusyatur Rahem*”. This disease has been described by Unani physicians under the heading of amenorrhoea, obesity, phlegmatic disease, and liver disorder. Unani concept of PCOD is mainly based on the dominance of Khilte balgham (phlegm). One of the abnormal forms of phlegm is balgham-e-mayi which is thinner in consistency and can accumulate in the sacs to form cysts (Firdose and Shameem, 2016).

1. Diagnosis

Due to the unavailability of any kind of specific/ basic tests (blood test, urine test) for the diagnosis of PCOS, there always exists an issue regarding its conformation. Differential diagnosis is an available criterion but it is still a complicated task as you need to exclude many symptoms and diseases/disorders to diagnose PCOS. Some available recommended investigations are patients' medical history, pelvic examination, change in weight, insulin resistance, assessment of the hormonal level, and transvaginal ultrasound (Differential Diagnosis of PCOS, 2021; Witchel et al., 2019; Polycystic Ovary Syndrome, 2021). As per NHS (National Health Service); irregularity in periods, enhanced androgenic hormone levels, appearance of androgenic symptoms, and radio scans confirming polycystic ovaries are the criteria put forth for

PCOS assessment. In the case of ultrasound analysis, the biochemical hyperandrogenism, ovulatory dysfunction, and polycystic ovaries confirm the diagnosis of PCOS. Important diagnostic criteria that are being employed are NIH criteria (both criteria required), Rotterdam criteria (any two of the three criteria required), and AE-PCOS society criteria (both criteria required) which are as mentioned in Figure 3 along with its various phenotypes as mentioned in Figure 4. Rotterdam criteria is the most widely employed method for the identification of PCOS in adults. (Lizneva et al., 2016; Bulsara et al., 2021; Diagnosis, 2021; European, 2021).

2. Clinical manifestations

Oral manifestations

Khan et al., (2022) in their study on the importance of oral hygiene in PCOS have reported that there exists a lack of awareness involving the association between PCOS and oral hygiene which is supposed to be redressed properly to overcome various mental and physical symptoms related with PCOS.

Rahiminejad et al., (2014) have compared the prevalence of periodontal disease in PCOS subjects and healthy controls and concluded that the incidence of periodontal disease in women with PCOS which may be due to chronic systemic inflammation. Clinical Attachment loss (CAL) and Bleeding on Probing (BOP) sites were found to be higher in women with PCOS ($P < 0.05$) whereas no difference in tooth loss was observed in PCOS and non-PCOS patients ($P = 0.384$).

Tanguturi and Nagarakanti, (2018) have reported that there exists a two-way relationship between PCOS and periodontal disease. Further, he mentioned that PCOS was observed to aggravate/worsen the periodontal condition caused by plaque, low-grade systemic inflammation, insulin resistance, Oxidative stress, and systemic hormonal levels.

Dou et al., (2023) have confirmed the presence of a bidirectional relationship between PCOS and periodontal disease. Various endocrine disorders, low-grade inflammation, and oxidative stress deteriorate periodontal condition whereas periodontal disease increases the risk of PCOS.

Wendland et al., (2021) have reported that there does not exist a significant difference among PCOS patients and healthy control with respect to oral hygiene and periodontal health. Also, he suggested that there exists a weak association between subgingival microflora composition and endocrine and metabolic components of PCOS. As a result, PCOS in young age women was not correlated with higher pathogenicity of subgingival biofilms.

Zia et al., (2022) studied the effect of chronic periodontitis on bone mineral density in females with PCOS and observed lower bone mass, enhanced C-terminal telopeptides of type I collagen, reduced alkaline phosphatase, increased hydroxy vitamin D levels

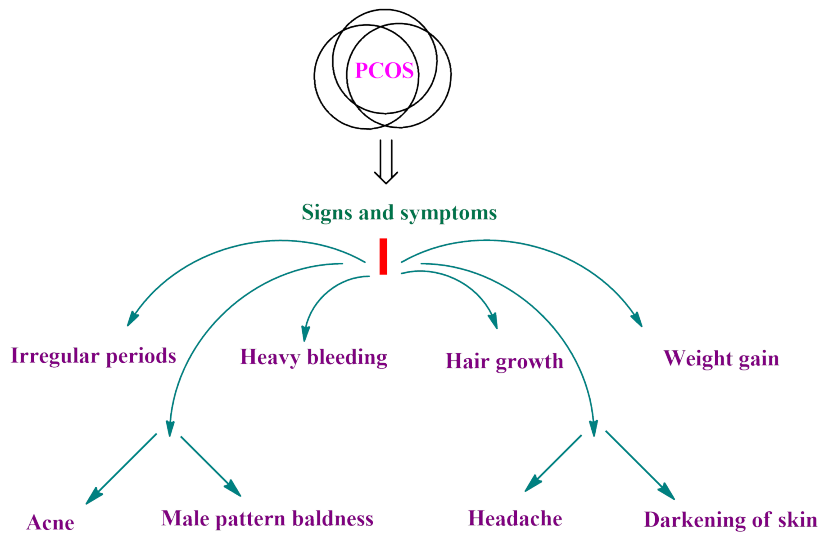


Figure 1. Signs and symptoms of PCOS. PCOS causes fewer than eight periods annually. Obese women with PCOS bleed considerably. Over 70% of women with this illness have hair on their bodies and faces. A condition known as hyperinsulinemia significantly boosts sebum production and enhances androgen stimulation. PCOS women may be fat 80% of the time. In middle-aged women, excessive levels of androgen may cause alopecia, characterized by receding hair growth on top of the head or hair recession, which may be progressively worse. Hair on the scalp thins and falls off. Dark spots may appear in the contours of the body such as the neck, crotch, and breasts. Hormone fluctuations may cause headaches in some women.

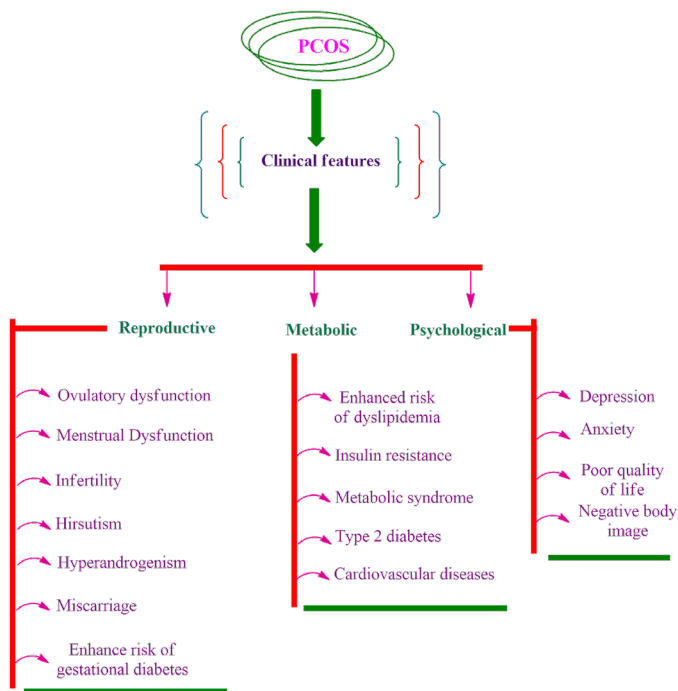


Figure 2. The clinical features of polycystic ovary syndrome (PCOS) may be classified into reproductive, metabolic, and psychological. More than 50% percent of women who have polycystic ovary syndrome (PCOS) seek therapy for infertility, and 70-80% of them suffer from either oligomenorrhea or amenorrhea.

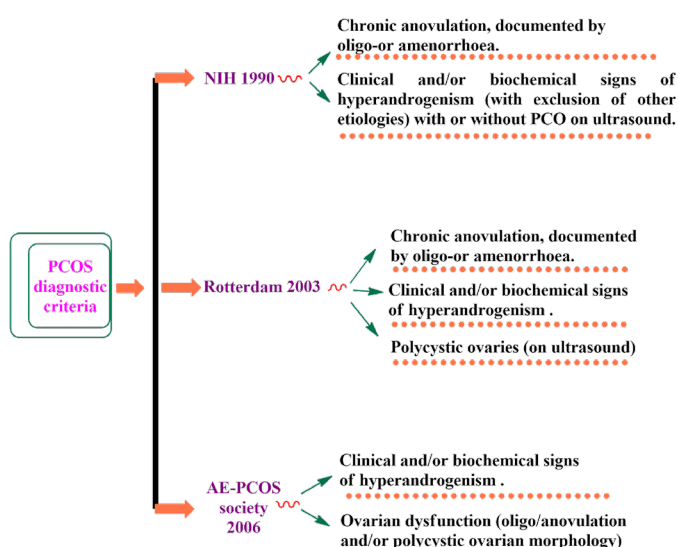


Figure 3. Diagnostic criteria for PCOS. (Abbreviations: AE-PCOS stands for Androgen Excess and PCOS society.)

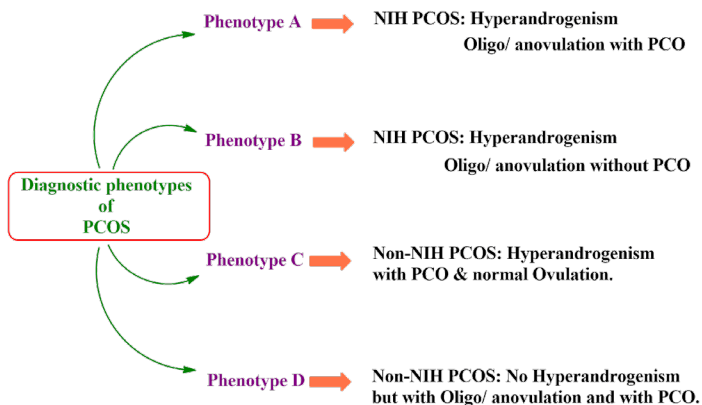


Figure 4. Diagnostic phenotypes of PCOS.

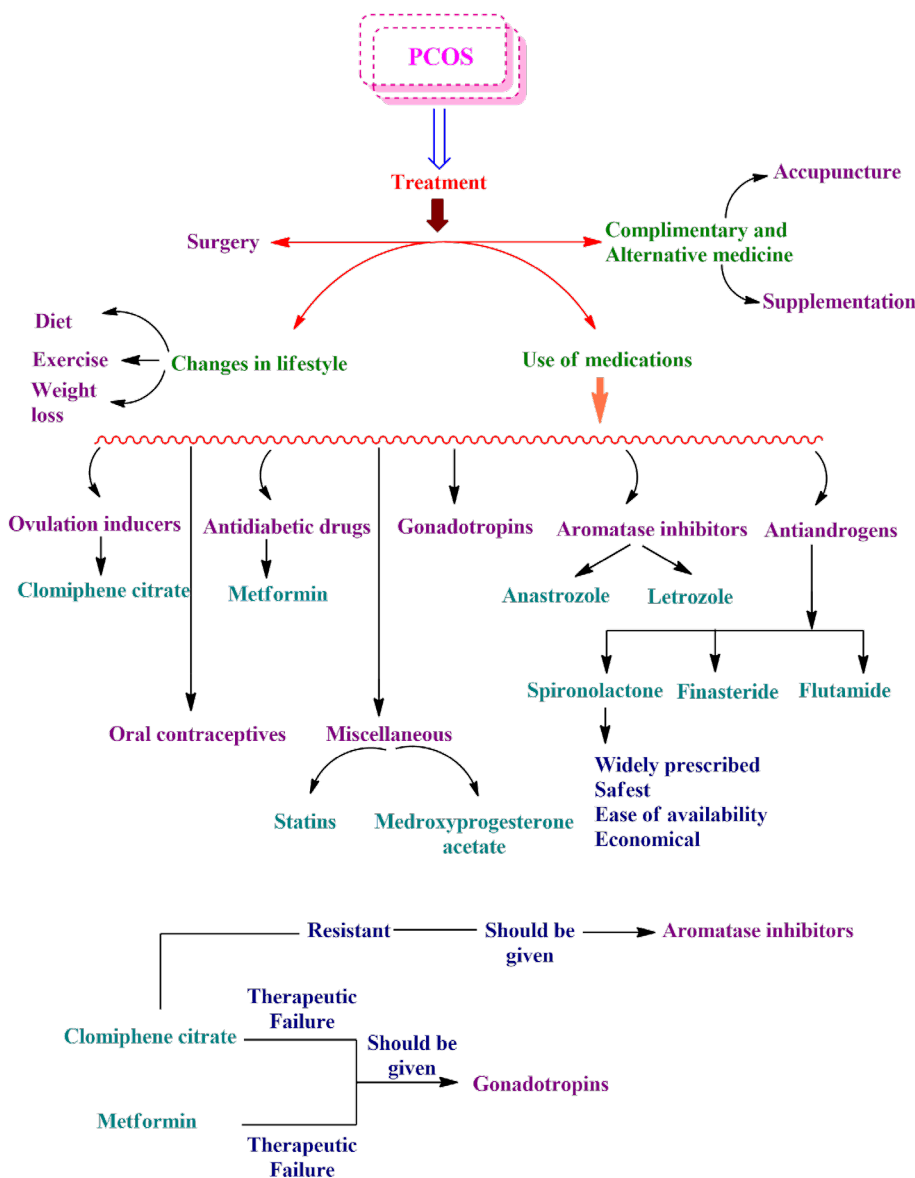


Figure 5: Treatment of Polycystic Ovarian Syndrome.

and unacceptable clinical periodontal findings in patients suffering from chronic periodontitis with PCOS in comparison to healthy group.

Saljoughi et al., (2020) have assessed the levels of Visfatin in gingival crevicular fluid in patients suffering from chronic periodontitis with PCOS. The results revealed that the levels of Visfatin were found to be elevated in the PCOS group in comparison to the healthy control group. Also, Patients with PCOS and periodontitis had higher levels of Visfatin than healthy control. This revealed the role of Visfatin as a correlating link between PCOS and chronic periodontitis.

Pediatric manifestations

Akamine et al., (2019) analyzed the presence of ovarian cysts in 16 neonates and reported that patients with cyst sizes less than 40 mm (simple cyst) can be managed under observation whereas patients with cyst sizes more than 40 mm (complex cyst) can be managed through ovarian cystectomy. Furthermore; he reported that transumbilical ovarian cystectomy should be preferred over other surgical procedures.

Anderson et al., (2014) have compared the ovarian biopsies of girls and adult women and reported that follicles in girls of all age groups can be grown in *in-vitro* conditions (helpful to those who may have malignant contamination of ovarian tissue). Also; the reduction in the growth of isolated follicles revealed that there exist intrafollicular differences and local environmental differences. Furthermore; the maturation process of the ovarian follicles enhances follicular developmental competence and the loss of abnormal follicles.

Akin et al., (2010) conducted a study on fetal-neonatal ovarian cysts on 20 subjects with mean age of diagnosis to be 34 gestational weeks. The ovarian cyst was observed in the right ovary in 75% of the cases with a mean size of 53 ± 15 mm which was considered as a large cyst in 16 of the total cases. 25% of the cases exhibited torsion in the ovary and that can be treated surgically to protect the ovary and ensure fertility. USG is to be carried out at regular intervals till the disappearance of the ovarian cyst.

3. Treatment

Due to the unavailability of any specific therapeutic approach for the treatment of polycystic ovarian syndrome; there are no FDA-approved drugs available currently to deal with the syndrome. The treatment is most probably symptom-directed and might not be required in milder cases of PCOS that need only follow-up. Also, the treatment must be individualized, dynamic, adjustable to changing circumstances, and accepted as per the patient's requirements. The treatment strategies are categorized under 4 headings which are changes in lifestyle, use of medications, surgery, and complimentary & alternative medicine (can be used

alone or in combination with various therapies) (Figure 5). The selection of the therapy should be based on the condition of the patient and the symptoms that appeared. A therapeutic regimen along with lifestyle changes will help in ameliorating the patient's condition. The outcome of the therapy may lead to enhanced fertility, well-regulated menstrual cycle, reduced weight, and decreased hyperandrogenic symptoms like acne and hirsutism (Bednarska and Seijka, 2017; Escobar, 2018; Zeind et al., 2023; Liu et al., 2015; Sadeghi et al., 2022; Conway et al., 2014).

4. Discussion

Several health issues, including obesity, insulin resistance, belly fat, metabolic diseases, and cardiovascular risk factors, are prevalent in women with polycystic ovary syndrome (PCOS) and little is known about the origins of polycystic ovary syndrome (PCOS), although there is growing evidence that it may be a multigenic condition influenced by environmental variables including nutrition and lifestyle choices as well as epigenetic factors. This is a long-lasting illness that may affect a person throughout their whole life and has significant impacts on both their well-being and their financial future. Both hyperandrogenism and insulin resistance have a role in PCOS advancement. Most PCOS-afflicted women exhibit insulin resistance, particularly those who are overweight, and these women are at a higher risk of developing metabolic syndrome, prediabetes, and Type 2 diabetes mellitus. Rehabilitation ought to emphasize offering assistance, instruction, and treating psychological issues, while aggressively emphasizing the need of a healthy way of life. Additionally, focused medical care should be implemented as necessary. The main course of action for a large percentage of individuals is centered on lifestyle modifications. In most circumstances, a proactive and comprehensive strategy that emphasizes lifestyle changes is the most efficient way to address the symptoms of PCOS and minimize the risk of long-term issues. Even though most women stay clinically in the unhealthy overweight or obese spectrum, modest, attainable targets of 5% total body weight reduction lead to considerable clinical enhancement. It is medically essential to combat hyperandrogenism and to closely track and control potential long-term metabolic consequences such as dyslipidemia, impaired glucose tolerance (IGT), type 2 diabetes mellitus (DM2), and risk factors for cardiovascular disease. It is important to assess family members who are at a higher risk for metabolic disorders as well.

5. Conclusion

PCOS is a common and complex endocrine and reproductive disorder affecting women worldwide and shows its close association with insulin resistance, obesity, and various metabolic disorders. It presents with a variety of symptoms (may be due to

diet or lifestyle factors) and can lead to significant health complications. Early diagnosis and appropriate management are essential to improve the quality of life for affected individuals. Further research is needed to better understand the underlying mechanisms and develop more effective treatment options for this condition.

Author contribution

Z.S developed the idea, study design, wrote, A.A.K, S.A.N., M.J.N. wrote, reviewed, edited the paper.

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Competing financial interests

The authors have no conflict of interest.

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