Crimson Publishers
Wings to the Research

Mini Review

Polycystic Ovarian Syndrome - What is New

Deepa Shanmugham[1]* and Ravikumar Sambantham[2]

[1]Department of Obstetrics and Gynaecology, India

[2]Research Scientist and Head, Centre for Biomedical Research, India

ISSN: 2832-4412

***Corresponding author:** Deepa Shanmugham, Department of Obstetrics and Gynaecology, Pondicherry, India

Submission: April 18, 2022
Published: July 05, 2022

Volume 2 - Issue 2

How to cite this article: Deepa Shanmugham, Ravikumar Sambantham. Polycystic Ovarian Syndrome - What is New. COJ Biomed Sci Res. 2(2). COJBSR. 000533. 2022. DOI: 10.31031/COJBSR.2022.02.000533

Keywords: Polycystic ovarian syndrome; Hyperandrogenism; Microbiome; Insulin resistance

Abbreviations: PCOS: Polycystic Ovarian Syndrome; LH: Luteinizing Hormone; FSH: Follicle-Stimulating Hormone; SHBG: Sex Hormone-Binding Globulin; DOGMA: Dysbiosis of Gut Microbiota

Introduction

Polycystic Ovarian Syndrome (PCOS) is a complex metabolic, endocrine and reproductive disorder that results in the overproduction of androgens and is associated with insulin resistance. PCOS is one of the most common endocrine disorders in reproductive-aged women and affects 4-12 % [1]. PCOS is a chronic condition with manifestations that begin most commonly in adolescence with menstrual irregularity and hyperandrogenism, with a transition over time into problems including infertility and metabolic complications.

Diagnosis

The predominantly European definition of PCOS requires an ultrasonically diagnosed typical morphological appearance of the ovary usually according to the criteria of Adams et al. [2]. The Polycystic ovary morphology is defined by ESHRE/ASRM consensus criteria as at least one ovary with >=12 follicles of 2-9mm (between 2-5 days of the cycle) or ovarian volume greater than 10ml in the absence of a cyst or dominant follicle >10mm, established with ultrasound examination of ovaries [3]. The European Society for Human Reproduction and Embryology (ESHRE) and the American Society for Reproductive Medicine, convened in Rotterdam, The N Netherlands, in 2003, concluded that diagnosis of PCOS should be based on at least two of the three major criteria including

a) Oligo/Anovulation

b) Clinical or biochemical signs of hyperandrogenism and

c) Polycystic morphology on ultrasound, after the exclusion of other pathologies with a similar clinical presentation such as congenital adrenal hyperplasia,

Cushing's syndrome and androgen-secreting tumours [4] The 2018 international PCOS guideline updated the Rotterdam criteria and now recommends applying Oligo Anovulation and Hyper Androgeneism while avoiding Polycystic ovarian morphology for PCOS diagnosis in adolescents [5]

Aetiology and Pathogenesis

Although the underlying cause of PCOS is unknown, a genetic basis that is both multifactorial and polygenic is suspected, as there is a well-documented aggregation of the syndrome within families [6]. Clinical and in vitro studies of human ovarian theca cells have suggested dysregulation of the CYP11a gene in patients with PCOS, which encodes the enzyme that performs rate limiting step in steroid biosynthesis [7]. In addition, the insulin

receptor gene in chromosome 19p13.2 may be involved. A recent mathematical review of microarray data in women with PCOS identified 504 protein nodes and 1048 interactions among them and stated that there was a cell cycle protein in this network yet to be identified [8]. Growing evidence supports the concept that PCOS is associated with increased oxidative stress and systemic inflammation. When compared to healthy control subjects, women with PCOS have increased markers of lipid peroxidation, elevated levels of C Reactive proteins, Inflammatory cytokines as well as a higher concentration of blood lymphocytes and monocytes [9].

Pathophysiology

The key elements involved in the pathophysiology are

a) Inappropriate Gonadotropin secretion

b) Insulin resistance

c) Increased circulating androgens

d) Decreased sex hormone-binding globulin

e) Anovulation

Inappropriate gonadotropin secretion

Alteration in the pulsatile GnRH pulsatility leads to preferential production of Luteinizing Hormone (LH) compared with Follicle-Stimulating Hormone (FSH). It is currently unknown whether hypothalamic dysfunction is the primary cause of PCOS or is secondary to abnormal steroid feedback [10].

Insulin resistance

Decreased insulin sensitivity is due to post binding abnormality in insulin-receptor mediated signal transduction [10] .Both lean and obese PCOS patients are found to be more insulin resistant than nonaffected weight-matched controls [11].

Increased androgens

Both insulin and LH stimulate androgen production by theca cells of the ovary [7]. The affected ovaries secret elevated levels of testosterone and androstenedione. Specifically, free testosterone levels are noted in 70 to 80% of women with PCOS and 25 to 65% exhibit elevated levels of DHEAS [12,13].

Decreased Sex Hormone-Binding Globulin (SHBG)

The synthesis of SHBG is suppressed by insulin and androgens in PCOS patients. This leads to increased free testosterone to develop hyperandrogenism [14].

Anovulation

Although the precise mechanism is unclear, hypersecretion of LH and insulin resistance lead to anovulation and a substantial number of patients resume ovulatory cycles when treated with metformin.

PCOS and Gut Microbiota

In recent years, the relationship between PCOS and gut microbiota has been the interest in the studies involving the pathogenesis of PCOS. Studies have shown that there is an alteration in the general composition of gut microbiome in patients with PCOS and changes in and diversity of microbiota [15,16]. The Dysbiosis of Gut Microbiota (DOGMA) hypothesis suggested that an imbalance of intestinal flora with increased intestinal permeability results in activation of immune system with inflammatory response, which leads to insulin resistance [17]. Further studies are being done to explore the role of the gut microbiome in PCOS.

Management of Polycystic Ovarian Syndrome

The clinical management of women with PCOS should be focussed on her individual problems. Diet and exercise are key to symptom control. Even a modest amount (5% of body weight) of weight loss (diet & exercise) can result in restoration of normal ovulatory cycles. It has been shown that metformin ameliorates hyperandrogenism and abnormalities of gonadotropin secretion in women with PCOS and can restore menstrual cyclicity and fertility [17] Pharmacological ovulation induction can be used to induce ovulation, but it is generally second line after intensive lifestyle therapy in overweight or obese women with PCOS. Clomiphene Citrate (CC), an oral ovulation induction agent in use for over 40 years, is generally considered to be the first-line pharmacological therapy to improve fertility outcomes in anovulatory women with PCOS.

References

1. Asuncion M, Calvo RM, San Milan JL (2000) A prospective study of polycystic ovary syndrome in unselected caucasian women from Spain. J Clin Endocrinol Metab 85(7): 2434-2438.
2. Adams J, Polson DW, Franks S (1986) Prevalence of polycystic ovaries in women with anovulation and idiopathic hirsutism. Br Med J 293(6543): 355-359.
3. ESHRE Capri Workshop Group (1995) Anovulatory infertility. Hum Repro 10(6): 1549-1553.
4. The Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group (2004) Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertil Steril 81(1): 19-25.
5. Franks S, Gharani N, Waterworth D (1997) The genetic basis of polycystic ovary syndrome. Hum Reprod 12(12): 2641.
6. Franks S (2006) Candidate genes in women with polycystic ovary syndrome. Fertil Steril 86(1): 15.
7. Mohamed HZA, Harun S (2009) Construction of a polycystic ovarian syndrome pathway based on the interaction of PCOS related protein retrieved from bibliomic data. Theoretical Biology and Medical modelling 6: 1-7.
8. Sabunsu T, Vural H, Harima M (2001) Oxidative stress in polycystic ovarian syndrome and its contribution to the risk of cardiovascular disease. Clinical Biochemistry 34(5): 407-413.
9. Hayes FJ, Taylor AE, Martin KA (1998) Use of gonadotropin-releasing hormone antagonist as a physiologic probe in polycystic ovary syndrome: Assessment of neuroendocrine and androgen dynamics. J Clin Endocrinol Metab 83(7): 2243-2249.
10. Dunaif A (1997) Insulin resistance and polycystic ovary syndrome: Mechanisms and implication for pathogenesis. Endocrine Rev 18(6): 774-800.

11. Dunaif A, Segal KR, Shelly DR (1992) Evidence for distinctive and intrinsic defects in insulin action in polycystic ovary syndrome. Diabetes 41(10): 1257-1266.

12. Moron C, Knochenhauer E, Boots LR (1999) Adrenal androgen excess in hyperandrogenism: Relation to age and body mass. Fertil Steril 71(4): 671-674.

13. O'Driscoll JB, Mamtora H, Higginson J (1994) A prospective study of prevalence of clear cut endocrine disorders and polycystic ovaries in 350 patients presenting with hirsutism or androgenic alopecia. Clin Endocrinol 41(2): 231-236.

14. Berg C, Carlsson B, Olsson JH (1993) Regulation of androgen production in cultured human thecal cells by insulin-like growth factor1 and insulin. Fertil Steril 59(2): 323-331.

15. Torres PJ, Siakowska M, Banaszewska B, Pawelczyk L, Duleba AJ, et al. (2018) Gut microbial diversity in women with polycystic ovary syndrome correlates with hyperandrogenism. J Clin Endocrinol Metab 103(4): 1502-1511.

16. Tremellen K, Pearce K (2012) Dysbiosis of Gut Microbiota (DOGMA)-A novel theory for the development of polycystic ovarian syndrome. Med Hypotheses 79(1): 104-112.

17. Nestler JE, Jakubowicz DJ, Evans WS (1998) Effects of metformin on spontaneous and clomiphene-induced ovulation in the polycystic ovary syndrome. N Engl J Med 338(26): 1876-1880.