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New Polycystic Ovary Syndrome in Gynecology

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Abstract

Aims: Polycystic ovarian syndrome is a highly prevalent disorder. The worldwide prevalence of polycystic ovarian syndrome ranges from 4% to 21%. Depression and anxiety are more common and more severe in women with polycystic ovarian syndrome than in women without the disorder. This study aimed to systematically review the literature for polycystic ovarian syndrome.

Information & Methods: A systematic search of EMBASE, Cochrane, PubMed, CINAHL, Google Scholar, Scopus, and International Pharmaceutical Abstracts from inception until January 2019 utilizing the terms polycystic ovarian syndrome was conducted.

Findings: Polycystic ovarian syndrome and insulin resistance share a common genetic background. Metabolic dysfunction can exist among people even when controlling for BMI and body fat distribution. Obesity is common in women with polycystic ovarian syndrome and exacerbates metabolic stress. Infertility was noted by 72% of women reporting polycystic ovarian syndrome. Depression and anxiety are more common and more severe in women with polycystic ovarian syndrome. Cardiovascular disease markers point to a higher risk of Cardiovascular disease in women with polycystic ovarian syndrome. Obstructive sleep apnea is common in clinical samples of women with polycystic ovarian syndrome.

Conclusion: A complication of polycystic ovary syndrome is insulin resistance, metabolic dysfunction, obesity, Infertility, cardiovascular disease, obstructive sleep apnea, Depression, and anxiety.

Keywords

Polycystic Ovary Syndrome [https://www.ncbi.nlm.nih.gov/mesh/68011085];
Midwives [https://www.ncbi.nlm.nih.gov/mesh/68008880];
Gynecologists [Not found]

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Introduction

Definition: Polycystic ovarian syndrome (PCOS) is a highly prevalent disorder [1, 2] affecting multiple aspects of a women's overall health, with long-term effects that transcend well beyond the reproductive age [3, 4].

Prevalence: The worldwide prevalence of PCOS ranges from 4% to 21% [5, 6], depending on the diagnostic criteria used (Table 5). The prevalence of PCOS among different geographic regions ranges from 5% to 10% according to NIH 1990 criteria; from 10% to 15% according to the AE-PCOS 2006 criteria, and from 6% to 21% when the ESHRE/ASRM 2003 criteria were applied (Table 5). Greater estimates of PCOS prevalence with the Rotterdam 2003 and AE-PCOS 2006 criteria are largely attributed to their more expansive definition and inclusion of additional phenotypes, compared with NIH 1990 diagnostic criteria [7].

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in reproductive-aged women, with a prevalence between5%and15%, depending on the diagnostic criteria applied [8, 9].

Symptom: PCOS was first recognized as a clinical entity in the 1930s. At that time it was named Stein–Leventhal syndrome, after the two clinicians who first reported the disorder in seven women who presented with hirsutism, amenorrhea, and enlarged bilateral polycystic ovaries, along with obesity [10, 11].

Risk factor: Zinc is involved in signaling pathways of insulin action, and also its synthesis and storage [12]. The homeostatic model assessment (HOMA)-IR in obese subjects [13, 14]. Other studies reported that circulating zinc levels are lower in women with PCOS [15, 16]. We showed that when detailed analysis is conducted, there is a significant difference between women with PCOS and their healthy counterparts in terms of zinc status. Due to the small number of subjects in previous works, large scale studies are needed before any solid conclusion could be drawn. Familial clustering and the results from twin studies strongly support an underlying genetic basis for PCOS. For example, having a mother or sister with PCOS conveys a 30–50% risk of developing PCOS [17-19]. The Mendelian randomization analyses suggested a causal role of PCOS risk single-nucleotide Polymorphisms for higher BMI, insulin resistance, and lower levels of sex hormone-binding globulin (SHBG) in PCOS. Other previously reported genes, namely, YAP1, THADA, and FSHB, were also replicated [20].

Notably, the loci identified in GWAS so far account for perhaps no more than 10% of the heritability of the disorder [21].

The study of Karamali *et al.*, indicated that calcium, vitamins D, and K co-supplementation among vitamin D-deficient subjects with PCOS for 8 weeks improved markers of insulin metabolism, serum triglycerides, and VLDL-cholesterol levels compared with the placebo, but did not affect FPG and other lipid profiles [22].

No difference in morning cortisol concentration was found between the two groups, although levels were twice as high as those reported in studies of girls of normal weight [23] Conversely, chronic administration of melatonin to women with PCOS (2 mg per day for six months) significantly decreased testosterone levels and reduced menstrual irregularities [24], suggesting that supraphysiological levels of melatonin can reduce androgen levels.

Thus the presence of increased intraovarian AMH may limit preantral and early antral follicle growth, accounting for higher numbers of these follicles in PCOS compared with normal women [25].

Interestingly, in a subsequent study, it was demonstrated that GDF-9 expression in oocytes of PCOS women undergoing ovulation induction was similar to that observed in oocytes of similarly treated normally women [26].

By mid puberty, the rise in LH secretion stimulates ovarian androgen production. In insulin-resistant states, hyperinsulinemia enhances LH action. In 2012, approximately 17% of girls aged 2–19 years were at_95 percentile ideal body weight [27].

The finding that increased LH pulses and enhanced daytime LH pulse secretion LH hypersecretion is also detrimental to normal follicular growth and might cause premature luteinization of granulosa cells (leading to hypertrophy, lipid accumulation, and other changes in the follicle that normally occur after ovulation [28].

The increased ovarian androgen production observed in PCOS is mainly due to enhanced androgen synthesis by follicular theca cells, which show an increased expression of several genes encoding steroidogenic enzymes [29].

Complication: PCOS and insulin resistance share a common genetic background, as several polymorphisms of genes involved in insulin resistance were found in PCOS women. The most common polymorphisms are those involved in insulin signaling, such as the insulin gene [30]. HemoglobinA_1c above 6.5% has been proposed as the defining criterion for diabetes, but further studies are needed in PCOS women to determine whether this criterion is useful in managing lifestyle interventions and medical management for cardiovascular disease prevention [31]. Metabolic dysfunction can exist among people even when controlling for BMI and body fat distribution, in part because ectopic lipid may accumulate in nonadipose cells through a process called lipotoxicity [32].

Obesity is common in women with PCOS and exacerbates the metabolic stress that we and others view as central to the pathogenesis of the syndrome [33]. PCOS is the primary cause of anovulatory subfertility, with major health and economic costs; however, community-based data are limited on prevalence and treatment trends in infertility in

PCOS. Most infertility and PCOS data are based on selected populations managed in a hospital or infertility clinics, and national funding policies on assisted reproduction vary substantially, making comparisons difficult. In a community-based study, the self-reported prevalence of PCOS was 5.8%. Infertility was noted by 72% of women reporting PCOS compared with 16% of those not reporting PCOS ($P < 0.001$); infertility was 15-fold higher in women reporting PCOS, independent of BMI [34].

Depression and anxiety are more common and more severe in women with PCOS than in women without the disorder [35-37], regardless of the phenotype of PCOS or the presence of obesity [36-38].

Women with PCOS are more likely to have increased oxidative stress, [39] and to experience infertility requiring assisted conception, and when they conceive, there is also an increased risk for pregnancy and delivery complications [40-43].

Cardiovascular disease (CVD) markers (for example, vascular calcification and the thickness of the vascular wall) point to a higher risk of CVD in women with PCOS than in controls, although an increased number of actual cardiovascular events has been difficult to demonstrate [44].

OSA (Obstructive sleep apnea) is common in clinical samples of women with PCOS, affecting 17–75%, substantially higher than in other women of similar age and BMI, and thus is not attributable to the tendency of women with PCOS to be obese [45-49].

Sleep restriction has been demonstrated to result in increased food intake due to increased appetite, exceeding the energy amount needed to meet the requirements of extended wakefulness, and thereby resulting in weight gain [50-52]. Insomnia diagnosis ideally requires assessment by a clinical psychologist [53]. Not unexpectedly, considering the concurrence of hypoestrogenic anovulation and hyperinsulinemia, women with PCOS have an increased risk for endometrial cancer (OR: 2.7). They may also have an increased risk for ovarian cancer, although the OR for this malignancy is unclear. However, no associated increased risk of breast cancer has been shown [54].

125 In our community-based sample, among women with PCOS (the majority of whom had not previously been diagnosed), 50% had symptoms consistent with clinical depression (Center for Epidemiologic Studies Depression Scale) compared with 30% of their peers [55].This is the first study to our knowledge in the UK examining the association of PCOS and autism, as well as the first population-based study examining the prevalence of PCOS in women with autism [54].

Diagnosis:These newer Rotterdam criteria for PCOS are currently recommended for clinical use and include all patients defined by 1990 NIH criteria (i.e., classic PCOS) along with women with either (1) clinical/ biochemical hyperandrogenism and polycystic ovaries (i.e., ovulatory PCOS) or (2) polycystic ovaries with ovulatory dysfunction [56, 57].

Prolonged heavy bleeding should raise consideration of abnormal endometrial hyperplasia and even endometrial adenocarcinoma. About 10% of women with PCOS will exhibit regular ovulatory cycles [58].

However, with the advent of newer equipment and advanced technology, the precision of counting follicles has improved. A recent task force report recommended that the threshold for polycystic ovary morphology based on follicle count should be increased to greater than 25 follicles per ovary to avoid overinterpretation of polycystic ovary morphology and misdiagnosis of PCOS [59].

Hyperandrogenism is likely the best indicator of PCOS in adolescence. Persistent irregular bleeding beyond 2 years after menarche is consistent with PCOS.

Treatment: A recent systematic review and meta-analysis suggest that the combination of lifestyle modification with metformin reduced BMI in women with PCOS to a greater degree than lifestyle modification alone [60].

Fertility treatment should start with counseling about success rates, discontinuation of harmful habits (especially smoking), screening for medical comorbidities, and treating excess weight. Pursuing 'low-tech' therapies, such as lifestyle modification and/or dose escalation of oral medications (for example, clomifene or letrozole; see below) to achieve ovulation, often requires the patience of both the clinician and the patient. The chance of conceiving is only 5–10% per ovulatory cycle in women with PCOS (versus 10–15% per cycle in women without PCOS) [61, 62].

Several studies have been conducted on the use of vitamin D in PCOS, but data from a recent meta-analysis does not support the suggestion that vitamin D supplementation improves insulin sensitivity in the disorder [63].

Besides, OCP use considerably reduces the risk of endometrial hyperplasia and endometrial cancer [53], while providing effective contraception when anti-androgen therapy is also used.

Consequently, hormonal therapy should be combined with counseling regarding the use of cosmetic treatments for hirsutism (for example, shaving, depilation, laser epilation, and electrology) acne (for example, topical antibacterials, and topical or oral retinoids), and androgenic alopecia (for example, minoxidil and hair transplantation) [64].

Finally, OCP use improves hirsutism and menstrual disturbances along with PCOSQ scores, but without any significant change in depression or anxiety symptoms [65].

The prevalence of outcomes did not significantly change the exclusion of studies using metformin during pregnancy, which is consistent with prior literature on miscarriage, GDM, and PE [66-68].

Bariatric surgery. For those women who fail to control their weight on diet alone, bariatric surgery is an important option but should be reserved for women with PCOS with severe obesity (a BMI of >40)

or with moderate obesity (a BMI of >35) who also have additional health issues. A meta-analysis of 13 primary studies has shown that bariatric surgery decreased the incidence of PCOS symptoms from 45.6% to 7.1%, with a mean weight loss of 57.2% [69].

Instrument and Methods

A systematic search of EMBASE, Cochrane, PubMed, CINAHL, Google Scholar, Scopus, and International Pharmaceutical Abstracts from inception until January 2019 utilizing the terms PCOS was conducted.

The data used in the study are available upon request to the corresponding author.

Findings

PCOS and insulin resistance share a common genetic background. Metabolic dysfunction can exist among people even when controlling for BMI and body fat distribution. Obesity is common in women with PCOS and exacerbates metabolic stress. Infertility was noted by 72% of women reporting PCOS. Depression and anxiety are more common and more severe in women with PCOS. Cardiovascular disease (CVD) markers point to a higher risk of CVD in women with PCOS. Obstructive sleep apnea (OSA) is common in clinical samples of women with PCOS. Prolonged heavy bleeding should raise consideration of abnormal endometrial hyperplasia and even endometrial adenocarcinoma. In insulin-resistant states, hyperinsulinemia enhances LH action. In 2012, approximately 17% of girls aged 2–19 years were at_95 percentile ideal body weight.

Fertility treatment should start with counseling about success rates, discontinuation of harmful habits (especially smoking), screening for medical comorbidities, and treating excess weight. Pursuing 'low-tech' therapies, such as lifestyle modification and/or dose escalation of oral medications (for example, clomifene or letrozole; see below) to achieve ovulation, often requires the patience of both the clinician and the patient.

Discussion

To the best of our knowledge, present study is the systematic review evaluated patients with PCOS compared with healthy subjects.

PCOS is the most common obesity-related endocrine syndrome in females. Two studies suggest that the Polycystic ovarian morphology of PCOS is inherited in an autosomal dominant fashion [1, 2]. The prevalence of obesity in PCOS case series is influenced by ethnicity and by referral patterns [3, 4].

Polycystic ovary syndrome is a common (4% to 21%) disorder among reproductive age women. Depending on diagnostic criteria, PCOS's prevalence was approximately 4%–6.6% in accordance with NIH 1990 criteria and approximately 4%–21% when Rotterdam 2003 criteria were applied [5].

PCOS has been described as a state of chronic inflammation mainly defined as an increased serum CRP compared to the weight matched controls [6]. Furthermore, PCOS patients are more likely to have increased visceral fat mass and higher waist to hip ratio [7]. Visceral fat may be a key factor describing components of metabolic syndrome and of low grade chronic inflammation

through producing various cytokines and also adipokines [7, 8].

lower zinc concentrations inside immune cells heightened inflammatory procedures and cytokine expression [9]. Therefore, zinc deficiency may act as an initiator or promoter of the underlying mechanisms and metabolic features of PCOS [10], which could be different in obese subjects.

A number of hereditary and environmental factors contribute to ovarian hyperandrogenism and/or insulin resistance.Increased LH relative to FSH was the first laboratory abnormality identified in classic PCOS. Mean LH levels correlate positively with LH pulse frequency [11, 12].

Maternal PCOS is a risk factor for PCOS in daughters. One set of studies compared the singleton daughters, about two-thirds of whom were pubertal, of 99 Chilean women with PCOS (defined by NIH criteria) with those of 88 control women [13, 14].

higher prevalence of miscarriage in PCOS was maintained in hyperandrogenic phenotypes [15, 16]. This likely aggravates sex hormone imbalances that contribute to adverse pregnancy and birth outcomes through endometrial abnormalities like thickening the [17, 18] Endometrium dysregulating angiogenesis and inducing a state endometrium [19-22] of inflammation in and consequently impacting [18, 23, 24] on implantation and placentation.

PCOS is a polygenic, multifaceted disease with a frequent metabolic component (overweight/obesity, increased serum levels of triglycerides, fasting insulin and decreased insulin sensitivity) [25].

Researchers reported higher TSH and TPO antibodies in infertile patients with PCOS than in controls (14.8 % vs. 4.0 %; and 19.3 % vs. 3.9 %) [26]. Also, they reported that out of 168 young Brazilian PCOS women with a mean age of 24 years, 149 (88.7 %) had normal thyroid function and 19 (11.3 %) subclinical hypothyroidism with TSH levels between 4.5 and 10 mIU/l, representing a higher prevalence of subclinical hypothyroidism in PCOS than in the general population [27].

Conclusion

A complication of polycystic ovary syndrome is insulin resistance, metabolic dysfunction, Obesity, Infertility, Cardiovascular disease, OSA, Depression, and anxiety.

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