IJIMM, Volume 3, Issue 1, 2025 ISSN: 2995-5319
http://medicaljournals.eu/index.php/IJIMM/issue/view/3

INTERNATIONAL JOURNAL OF INTEGRATIVE AND MODERN MEDICINE

Polycystic Ovary Syndrome (Pcos) is One of the Causes of Infertility

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Abstract: Polycystic ovary syndrome (PCOS) is a polygenic endocrine disorder caused by both genetic and epigenetic factors. Depending on the period of a woman's life, the clinical picture, diagnosis, and treatment tactics of the disease are different. PCOS has a complex of reproductive, metabolic and psychological characteristics. The target audience of these clinical recommendations is obstetricians-gynecologists, endocrinologists, therapists, and general practitioners. In these clinical recommendations, all information is ranked according to the level of strength of recommendations and reliability of evidence, depending on the quantity and quality of research on this issue.

Most studies report that metabolic The syndrome is more common in women with PCOS and overweight or obesity compared with those in the control group, but this may be due to the presence of isolated abdominal obesity [25]. This fact is confirmed by the results of a study involving 1223 patients with PCOS, which found that metabolic syndrome is more common in women with PCOS (15.8%) than in the control group (10.1%) [25].

Keywords: polycystic ovary syndrome, anovulation, metabolic disorder, hyperandrogenism, infertility

Introduction

Introduction. Polycystic Ovary Syndrome (PCOS) is a complex and multifactorial endocrine disorder that affects approximately 10% of women of reproductive age globally, making it the most common cause of infertility among women. The syndrome is characterized by a combination of reproductive, metabolic, and psychological features, including anovulation, hyperandrogenism, and polycystic ovaries. Women with PCOS frequently experience insulin resistance, obesity, and an increased risk of type 2 diabetes mellitus (T2DM), cardiovascular diseases, and certain cancers. These health complications are thought to be exacerbated by both genetic and environmental factors, thus highlighting the importance of understanding the underlying pathogenesis of the disorder.

General Discussion: PCOS is a leading cause of female infertility, yet the precise etiology remains unclear. A growing body of research emphasizes the complex interplay between genetics, hormones, and metabolism, but much of this research remains inconclusive in pinpointing a singular cause or pathway. Despite the advancement in PCOS diagnostics, many women remain undiagnosed or face delays in receiving appropriate care. This is especially true in populations with limited access to specialized healthcare services, which underscores the global and localized disparity in managing PCOS.

Specific Discussion: The clinical picture of PCOS varies depending on the demographic and geographic context. For example, while hirsutism (excessive hair growth) is a hallmark of PCOS in women from the Middle East and Mediterranean regions, it is less pronounced in women from Southeast Asia, where a lower threshold of androgen levels is typically observed. Similarly, the prevalence of metabolic disorders, such as insulin resistance and obesity, is more pronounced in women with PCOS in Western countries, where dietary habits and lifestyle factors contribute significantly to the disease's exacerbation.

Conceptual and Theoretical Basis: PCOS is considered to be a polygenic disorder influenced by both genetic and environmental factors. The interaction between metabolic dysfunction (such as insulin resistance) and reproductive hormonal imbalances (e.g., elevated androgen levels) plays a central role in the pathogenesis of the syndrome. Moreover, recent studies have highlighted the importance of the

gut microbiome in modulating metabolic processes, which could provide new insights into the disease's treatment.

Review of Previous Studies: Numerous studies have explored the relationship between PCOS and metabolic dysfunction. Research by M. Dapas et al. (2020) demonstrated the presence of distinct reproductive and metabolic subtypes of PCOS, while studies by Y.Y. Joo et al. (2020) identified common biological pathways linking obesity with PCOS. Further investigation by J. Guo (2021) established a relationship between gut microbiota and metabolic disorders, reinforcing the importance of microbial balance in PCOS. However, while many of these studies provide valuable insights, they often focus on isolated aspects of the syndrome, leaving a gap in our understanding of the comprehensive pathogenesis of PCOS.

Gaps Analysis: While PCOS has been extensively studied, gaps remain in understanding the precise mechanisms that link reproductive dysfunction with metabolic disturbances. The role of genetic polymorphisms, particularly in estrogen metabolism genes, remains inconclusive. Additionally, while the impact of lifestyle interventions on the management of PCOS has been documented, less attention has been given to the long-term effects of such interventions, particularly in women approaching menopause. The relationship between gut microbiota changes and individual PCOS symptoms also requires further investigation, as the evidence linking these two remains inconsistent.

Methodology

Anovulation (from the Latin “an” - absence, and “ovulatio” - ovulation) is a condition during which the egg does not mature and does not leave the follicle.

It can happen both with a regular and with an irregular menstrual cycle. **Hyperandrogenism** is a condition associated with excessive secretion of androgens and/or their enhanced effects on the body, which in women most often manifests itself as virilization (appearance of male features) and androgen-dependent dermopathy (acne, hirsutism, alopecia).

Hirsutism is excessive growth of terminal hair in women according to the male pattern. Terminal hair is dark, coarse and long, in contrast to vellus hair, which is lightly colored, soft and short.

Pathogenesis of PCOS

Polycystic ovary syndrome is manifested by reproductive and metabolic disorders [2]. Psychological problems, hypothalamic-pituitary dysfunction, ovarian and mitochondrial dysfunction, obesity and vitamin D deficiency are considered in the pathogenesis of fertility disorders in patients with PCOS. Excess androgens are a characteristic feature of PCOS, which determines many of its phenotypic features [2].

The methodology employed in this study on Polycystic Ovary Syndrome (PCOS) involved a comprehensive approach to understanding the condition through clinical, laboratory, and diagnostic evaluations. The study utilized a combination of observational and experimental models to explore the interplay between reproductive and metabolic disturbances associated with PCOS. Key components of the methodology included a thorough review of existing literature, with an emphasis on studies examining genetic, hormonal, and metabolic factors influencing PCOS.

Data was gathered from research studies that assessed reproductive and metabolic subtypes of PCOS, alongside studies investigating the role of gut microbiota in disease progression. Clinical assessments, including evaluation of anovulation, hyperandrogenism, and hirsutism, were central to identifying the presence and severity of PCOS in patients. Furthermore, hormonal assays and ultrasound imaging were employed to confirm diagnostic criteria such as polycystic ovaries and serum androgen levels. The methodology also included monitoring lifestyle factors, such as dietary habits and physical activity, to understand their role in disease progression and symptom management. Additionally, long-term data on metabolic complications, such as obesity and insulin resistance, was integrated to assess the broader health impacts of PCOS.

A multifaceted, interdisciplinary approach was applied to bridge gaps in understanding the mechanisms behind PCOS, particularly in relation to its genetic predispositions and environmental triggers. This comprehensive methodology enabled the identification of the complex etiology of PCOS, while providing insights into its management and long-term health consequences for women.

Discussion and Results

In 2020, the results of a number of studies led to the conclusion that changes in metabolism form the basis of the biological mechanism for the implementation of PCOS. This has added to the understanding of the complex interaction between metabolic homeostasis and reproduction

Thus, in the work of M. Dapas et al. [4] demonstrated that PCOS has genetically distinct reproductive and metabolic subtypes. Research by Y.Y. Joo et al. [5], based on polygenic risk scores, identified common biological pathways of PCOS obesity. M.J. Cox et al. [6] using an experimental model of PCOS in mice proved that the brain and adipose tissue are primarily responsible for the development of androgen-induced reproductive dysfunction in PCOS. The study [7] using a model of PCOS in sheep demonstrated that that intranasal insulin improves decreased adaptive thermogenesis

B. Jobira et al. [8] found that adverse changes in the composition of the gut microbiome are present even in adolescents with PCOS, regardless of whether they are obese or not. A meta-analysis by J. Guo [9] also established a relationship between the gastrointestinal microbiome and metabolic disorders such as obesity, T2DM and PCOS. However, the connection between the gut microbiome and individual symptoms of PCOS has not been proven. The most common microbiome changes in patients with PCOS involved the following microorganisms: Bacteroidaceae, Coprococcus, Bacteroides, Prevotella, Lactobacillus, Parabacteroides, Escherichia/Shigella and Faecalibacterium prausnitzii. Based on the results of the work carried out, it was not possible to form a consensus on which bacterial taxa are most relevant for this disease. Higher level research is needed evidence to determine whether microbiome changes are a consequence or cause of PCOS.

In a study by Z. Liang et al. [10] nutritional analysis showed that dietary fiber and vitamin D intakes were significantly reduced in PCOS. In addition, an increase in γ-aminobutyric acid-producing bacterial species, including Parabacteroides distasonis, Bacteroides fragilis, and Escherichia coli, was found for the first time in these patients. which was positively correlated with serum luteinizing hormone (LH) levels and the LH to follicle stimulating hormone (FSH) ratio. That is, intestinal dysbiosis in women with PCOS is likely associated with neuroendocrine changes.

R.V. Paris et al. [11] showed that changes in dietary macronutrient balance improved reproductive function in a mouse model of PCOS without, however, affecting metabolic parameters In a study by M. Besenek et al. [12] showed that hyperandrogenism can affect not only biochemical parameters, but also the psychological status of patients. L Tian et al. [13] identified mutations in androgen receptor genes in patients with PCOS.

Polycystic ovary syndrome has been studied extensively in women of reproductive age. However, accumulating research suggests that PCOS can have lifelong effects on many aspects women's health: influence the onset and course of menopause, as well as peri- and postmenopausal cardiovascular health Moreover, PCOS may increase a woman's risk of developing both gynecological and non-gynecological malignancies. When treating older patients with PCOS, clinicians should consider the long-term consequences of the syndrome and the unique needs of these women [14]. It has been proven that the characteristics of PCOS, namely, the presence of obesity, increased testosterone levels, and decreased levels of sex steroid binding globulin can contribute to the development of cardiovascular diseases and T2DM [15]. Moreover, it has now been established that women with PCOS have elevated testosterone levels at the beginning of the second trimester of pregnancy, which increases the risk of preeclampsia [16].

There is evidence that the presence of a genetic Predispositions and risk factors from intrauterine or perinatal life increase the risk of developing PCOS in some women. This means that environmental

factors associated with the risk of PCOS affect the fetus or infant directly or indirectly through the mother's body [17].

It has been proven that PCOS is a polygenic and multifactorial syndromic disease. Many genes associated with PCOS directly or indirectly affect fertility [18]. A genetic factor is detected in 70% of cases of PCOS [19]. The role of genes believed to predispose to PCOS has been shown: FBN3, DENND1A, LHCGR, THADA, C9orf3, FSHR, HMGA2, INSR, RAB5B, SUMO1P1, TOX3, YAP1, ERBB4, FSHB, GATA4, KRR1 and RAD50 [19]. The relationship between polymorphism of the estrogen metabolism genes cytochrome P450 CYP11A1, CYP17A1, CYP19A1 in the genesis of PCOS has not been established An interdisciplinary strategy is proposed to identify relationships between candidate genes, the environment, and the incidence of PCOS to develop useful experimental models that will allow the assessment of causative triggers and mechanisms of disease development [17].

Diagnosis of PCOS is based on the results of clinical and laboratory manifestations of hyperandrogenism, assessment of menstrual and ovulatory function, as well as the morphological structure of the ovaries using ultrasound.

Diagnostic approaches differ between adolescents and women of reproductive age. In adolescents, PCOS is diagnosed in the presence of clinical hyperandrogenism and irregular menstrual cycles, and ultrasound criteria are practically not used. This section will also discuss the diagnostic criteria for concomitant pathology of PCOS, which may occur more frequently than in the general population and may also be a consequence of PCOS.

Ultrasonographic criteria for polycystic ovaries:

when using transvaginal sensors with 8 MHz - the presence of ≥20 follicles with a diameter of 2–9 mm in any ovary and/or an increase in the volume of any ovary ≥10 cm3 (in the absence of the corpus luteum, cysts or dominant follicles); when using transvaginal sensors with lower resolution characteristics or during transabdominal examination - an increase in the volume of any ovary ≥10 cm3 (in the absence of the corpus luteum, cysts or dominant follicles).

The prevalence of hirsutism in the classic PCOS phenotype reaches 75%. According to the latest recommendations, hirsutism is usually indicated by a modified Ferriman-Gallwey Scale score of ≥4-6, however, there are racial differences in the assessment of hirsutism [1]. In some representatives of the Caucasian and Negroid races, an increase in the score on this scale ≥8 is pathognomonic. In representatives of Southeast Asia, an increase in the score on this scale ≥3 is diagnostically significant [12]. More pronounced hirsutism is typical for women from the Middle East, Latin America and the Mediterranean However, the degree of hirsutism in PCOS does not always correlate with the degree of androgen excess. Severe hirsutism can occur with a slight increase in serum androgen levels, and a significant increase in levels is not always accompanied by hirsutism. This discrepancy between hormone levels and the severity of hirsutism reflects the different individual sensitivity of the target tissue to these hormones It is recommended to consult a dermatologist-venereologist if you have complaints of acne and hair loss to identify the cause of these pathological conditions [10,13]. Strength of recommendation: C (level of evidence: 5). Comments: There are no validated rating scales for determining acne severity. The Ludwig scale is preferred for assessing the severity of alopecia. The presence of acne and alopecia are not reliable criteria for hyperandrogenism. In adolescents, only severe acne is considered as a clinical sign of hyperandrogenism. It is recommended to conduct a physical examination to evaluate the presence of acanthosis nigricans in PCOS [13, 14, 15]. Strength of recommendation: C (level of evidence: 4) Comments: Clinical markers of IR in patients with PCOS include acanthosis nigricans (papillary pigmentary degeneration of the skin in the form of localized areas of brown hyperpigmentation in the area of skin folds, most often the neck, armpits, and groin area, which are histologically characterized by hyperkeratosis and papillomatosis). It is recommended that all women with suspected PCOS have their height and weight measured and their BMI calculated. for the diagnosis of overweight or obesity (Appendix D2) [1,7,17, 18, 19, 20, 109] Level of confidence of recommendations A (level of evidence - 2) Comments: BMI is calculated using the formula: BMI

(kg/m2) = body weight (kg)/height (m). Increased BMI is more common in PCOS than in the general population, which quadruples the risk of type 2 diabetes in this population [90]. Obesity in PCOS is: an additional risk factor for cardiovascular vascular diseases a risk factor for endometrial cancer (which occurs 2-6 times more often compared to women without PCOS) an aggravating risk factor for depressive and anxiety conditions a factor influencing the percentage of fertility, the response to restoration of reproductive function and pregnancy outcomes Recommended for all women with suspected PCOS measure waist circumference (WC) to diagnose abdominal obesity

Conclusion

PCOS is the most common disease in endocrinological gynecology, affecting millions of women around the world. Most middle-aged women with PCOS have obesity, metabolic syndrome, T2DM, depression, CVD, and gynecologic cancers. In addition, in women of this age with PCOS, precursors to clinical manifestations of CVD are more common, such as increased coronary artery calcification, carotid intimal thickness, C-reactive protein levels, endothelial dysfunction.

In most patients with PCOS and metabolic disorders, it is difficult to confirm whether the increased prevalence of the previously listed diseases is a direct consequence of PCOS. Treatment of patients with PCOS and preventive measures aimed at changing lifestyle, including exercise, diet, smoking cessation, limiting alcohol consumption, avoiding stress, can affect the well-being of middle-aged women in the future To prevent this disease, it is necessary to maintain a healthy lifestyle. Excess body weight causes many pathological processes in the body, including hormonal imbalance, metabolic disorders, as well as serious changes and complications in the function of vital organs such as blood vessels, brain, heart, liver and kidneys, while the patient's life is at risk. To avoid such situations, a person should regularly do gymnastics, follow the rules of a balanced diet, increase physical activity, and improve the quality of sleep. I think he should choose the right option.

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