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Genetic and epigenetic factors contributing to the development of PCOD

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Abstract

Globally five to ten percent of women who are of reproductive age suffer from Polycystic Ovary Disease, a complicated endocrine disease marked by irregular menstrual periods, hyperandrogenism, and polycystic ovarian morphology. We explore the significance of insulin resistance, metabolic syndrome, and psychosocial comorbidities in addition to talking about the genetic, hormonal, and environmental variables that contribute to PCOD. The most recent diagnostic standards, such as the Rotterdam criteria, are examined, and various forms of treatment including lifestyle changes, medications, and surgery are assessed critical. Emphasis is placed on recent developments in our knowledge of the molecular mechanism behind PCOD and new treatment targets.

Keywords: Polycystic Ovarian Disease; Androgen; Follicular Maturation; Insulin resistance; Diagnostic tools

1. Introduction

Polycystic ovarian disease (PCOD) is a common health problem which is increasing in teenage girls and young women. It is one of the most common endocrine disorders of women in reproductive age group, with prevalence of 15% which occurs in almost all races and nationality and is a leading cause of infertility. In India, the prevalence of PCOD is from 2.2% to 26% [1]. Polycysticovary disease, ultrasonically characterized by commonly enlarged ovaries with increased numbers of small follicles interspersed by abundant stroma [2]. On the basis of so much work and so little yield in the attempt to distinguish ovarian from adrenal factors, one might well begin to wonder if there is not indeed an adrenocortical component in some cases of polycystic ovarian disease [3]. It is the most frequent diagnosis made when patient presents with a syndrome consisting of one or more of the symptoms of hirsutism, acne, oligomenorrhea, or infertility [4].

The presence of increased circulating insulin levels in patients with polycystic ovarian disease (PCOD) has been well documented. We recently reported that hyperinsulinemia, before and during an oral glucose tolerance test (OGTT), occurred in patients with PCOD in the absence of obesity and acanthosis nigricans. Positive correlations of hyperinsulinemia with serum testosterone (T) and androstenedione levels suggested a causal relationship between hyperandrogenism and the exaggerated insulin responses. These findings appeared to be the consequence of insulin resistance, but no direct measurements of insulin sensitivity were performed [5].

A single molecular defect leading to the activation of a serine kinase might explain the two main biochemical disturbances in these patients: hirsutism and insulin resistance [6]. Ovarian wedge resections have been performed on patients with polycystic ovarian disease (PCOD) who either do not ovulate or do not conceive with clomiphene citrate

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[7]. Being a risk factor for the development of cardiometabolic disorders, obesity in women of reproductive age is accompanied by a high frequency of violations of ovulatory function of the ovaries (an ovulation), hyperandrogenism syndrome, menstrual irregularities, infertility, endometrial pathology (hyperplastic processes), an increased risk of developing endometrial and breast cancer, and poor survival rate for ovarian cancer [8]. Some women with ovarian hyperandrogenism exhibit hyperinsulinemia and insulin resistance, and there is an association between serum insulin and androgen levels in patients with polycystic ovarian disease (PCOD) [9]. It is now generally accepted that physiologically effective levels of steroids are reflected by the concentration that is not bound to plasma proteins. It is the "free" steroid which interacts with specific receptors in the target cells to elicit normal or in certain cases abnormal responses [10].

2. Causes of PCOD [11]

2.1. Environmental factors influencing PCOD

- Climatic condition
- Pollution
- Pesticides

2.2. Socio-economic status and lifestyle patterns influencing PCOD

- Education
- Addiction
- Food habits
- Physical activity and sleeping pattern

2.3. Inflammatory mechanisms behind PCOD

- Obesity
- Cardiovascular disease (CVD)
- Type 2 Diabetes mellitus (T2DM)

3. Symptoms of PCOD [12]

- Irregular menstrual cycle
- Increase level of Luteinizing Hormone
- Obesity
- Change in blood pressure
- Increase in androgen level in blood
- High glucose in blood
- Breast enlargement
- Facial hair growth
- Thinning hair on scalp
- Skin darkening
- Acne

4. Etiology of PCOD

Insulin resistance is paramount to the pathophysiology owing to PCOD and can affect as high as 70% of women diagnosed with the disorder [13]. Notably, hyperinsulinemia enhances ovarian androgen production through direct mechanisms and suppresses hepatic sex hormone-binding globulin (SHBG) synthesis, further intensifying the effects of hyperandrogenism [14]. The metabolic impact is systemic, placing individuals. This cascade of hormonal and metabolic imbalances further illuminates the multifaceted nature of PCOD and the detailed of its management. Polycystic ovarian disease is associated with an ovulation, oligomenorrhea, increased circulatory androgens, and elevated insulin levels [15].

Our current understanding of the concepts regarding estrogen biosynthesis and follicular development is based upon the "two-cell theory" of ovarian steroidogenesis. The granulosa cell of the follicle serves as the site of estrogen synthesis, utilizing androgens produced by the interstitial cells as substrate. The aromatase system, a cytochrome P450 mixed

function oxidase enzyme complex, converts the C19 androgen precursors to C18 phenolic steroids. It is activated by follicle-stimulating hormone (FSH) and is essential for follicular estrogen production. Certainly, hyperinsulinism is common but is difficult to interpret clinically, given the fact that it also results from obesity [16].

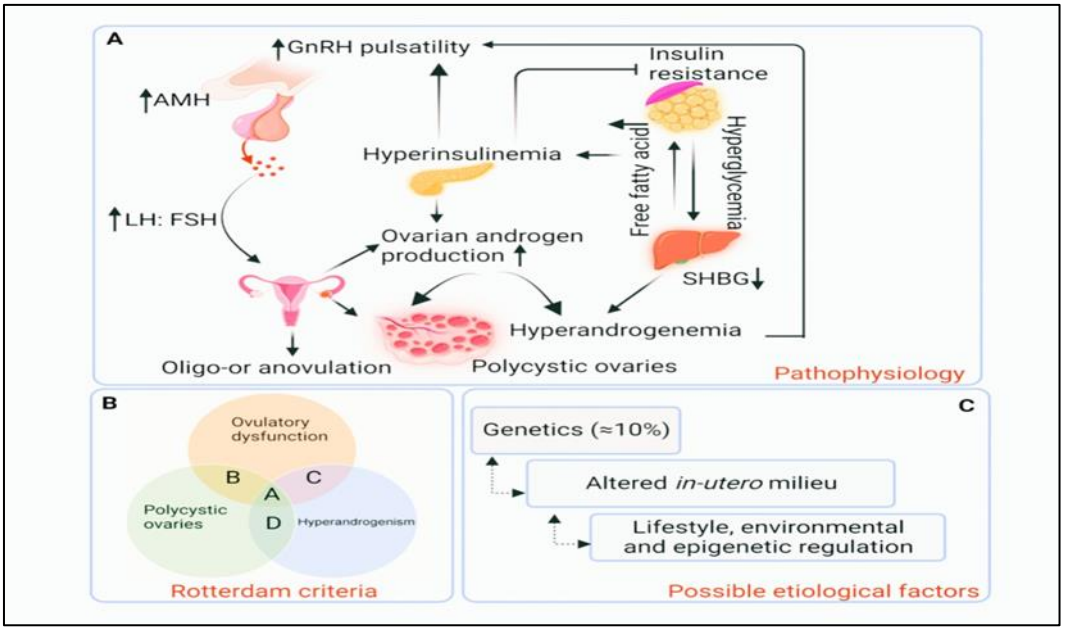

Figure 1 Etiology of PCOD

5. Treatment for PCOD [17]

Allopathic medications such as tamoxifen, metformin, clomiphene citrate, and troglitazone are currently the most popular and effective treatment for PCOD.

5.1. Clomiphene citrate (CC)

It comprises a first-line regimen for inducing ovulatory cycles in individuals with PCOS, imposing fewer adverse effects with cost effective advantage. CC being an estrogen receptor antagonist have a direct effect on negative feedback of the estrogen-signaling pathway, thus elevates FSH. It is a non-steroidal fertility drug. It is witnessed to be efficacious in high doses of 150mg-200mg for ovulation induction in those women who would not conceive with low dosage regimens.

Legro et al witnessed notable deviations in conceiving rates among individuals with a BMI > 30 against having a BMI < 30 individuals. They were provided with Doses of 50–150mg for 5 days, starting on days 3 or 5 of a progestin-induced spontaneous cycle. CC witnessed ovulatory cycles in 75%–80% of PCOS patients, gestation rate was assessed, it was approximately 22% per ovulation cycle. It was observed that clomiphene caused twin pregnancies, and that using letrozole and tamoxifen separately resulted in a single pregnancy. Clomophene miscarriages 10(20%), With tamoxifen 3(6%) and Letrozole 4 (8%) live birth rate: group A:22(44%) Group B:17(34%) Group C:21(42%).

6. Artificial intelligence in PCOD diagnosis

Reasoning, learning, problem-solving, perception, language comprehension, and other skills are all components of artificial intelligence (AI). A lot of researchers use AI to automatically categorize ultrasound pictures. AI may identify illnesses by "learning" characteristics from vast amounts of data through clinical experience. AI is able to eliminate undesirable and useless data from its operation and produce results with fewer or no errors. Using ultrasound waves, AI is used to determine the stage of PCOS as well as the health of the uterus and fallopian tube. Additionally, it measures the size of the follicle and the quantity of ovarian cysts [18].

Laparoscopic ovarian electrocautery and ovarian laser vaporization or photocoagulation have been employed as alternative surgical treatments to ovarian wedge resection in the management of polycystic ovarian disease (PCOD) failing to respond to medical induction of ovulation [19].

Since PCOS is a common hormonal disorder that is difficult to identify, computer-assisted blood tests, symptoms, and other characteristics can create a novel and simple way to diagnose it. By collecting clinical data and building a model by writing algorithms, Machine Learning has shown its efficiency in the health sector when it comes to diagnosing diseases accurately [20].

Normal ovary	Polycystic ovary

Figure 2 Normal ovary versus polycystic ovary

7. Conclusion

PCOD is associated with multivariate symptoms and a single biochemical diagnostic criterion is not sufficient for clinical diagnosis. A complete convincing animal model which characterizes all the symptoms of PCOD similar to human PCOD was not well established PCOS is a very challenging endocrine-metabolic disorder, since various aspects need to be considered to frame and manage its clinical features, as in the case of other multifactorial diseases

As there is currently no cure, the management of PCOS is directed toward improving the patient's health related conditions using symptomatic alleviation and prevention of long-term complications (including the development of the metabolic syndrome and associated diseases ,i.e., cardiovascular disease and type II diabetes mellitus) It can be concluded that ovarian electrocautery, done during a planned diagnostic laparoscopy, may be a better alternative to the more expensive LH-RH for induction of ovulation in PCOD patients who do not conceive after gonadotropin therapy

Several recent studies I-a have demonstrated that the endorphins, a group of endogenous opioids, may play an important role in the regulation of the normal menstrual cycle

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] Archana Shirsath, Neela Aundhakar , Prathmesh Kamble. Study of oxidative stress and antioxidant levels in polycystic ovarian disease. International J. of Healthcare and Biomedical Research. July 2015; 03(04): 16-24.

[2] Fatma A. Aleem, M.D., Ph.D. Mladen Predanic, M.D., M.sc.Transvaginal color Doppler determination of the ovarian and uterine blood flow characteristics in polycystic ovary disease. Fertility and Sterility. March 1996; 65(3): 510-516.

[3] Joseph W. Goldzieher, M.D., and Leonard R. Axelrod, ph.D. Clinical and biochemical features of Polycystic ovarian disease. Fertility and Sterility. 1963; 14(6): 631-653.

[4] Fred Benjamin, M.D. t Stanley Deutsch, Ph.D. Hildy Saperstein, M.D. Vickie L. Seltzer, M.D. Prevalence of and markers for the attenuated form of congenital adrenal hyperplasia and hyperprolactinemia masquerading as polycystic ovarian disease. Fertility and Sterility. August 1986; 46(2): 215-221

[5] Mitchell E. Geffner, M.D., Solomon A. Kaplan, M.D., Noelle Bersch, B.A., David W. Golde, M.D., Elliot M. Landaw, M.D., ph.D., R. Jeffrey Chang, M.D. Persistance of insulin resistance in Polycystic ovarian disease after inhibition ofovarian steroid secretion. Fertility and sterility. March 1986; 45(3): 327-333.15-221.

[6] P.GCrosignani and A.E.Nicolosi. Polycystic ovarian disease: heritability and heterogeneity. European society of Human Reproduction and Embryology. 2001; 7(1): 3-7.

[7] Chun Fu Wang, M.D., Carl Gemzell, M.D. The use of human gonadotropins for the induction of ovulation in women with polycystic ovarian disease. Fertility and Sterility. May 1980; 33(5): 479-486.

[8] Halimovae'zozamirzohidovna. Obesity as a risk factor for recurrent polycystic ovary disease.

[9] Asian journal of Pharmaceutical and biological research. Sept-Dec 2021; 10(3): 96-114.

[10] Leena Anttila, M.D., Ying-Qing Ding, M.B., Kristiina Ruutiainen, M.D., Risto Erkkola, M.D., Kerttu Irjala, M.D., Ilpo Huhtaniemi, M.D. Clinical features and circulating gonadotropin, insulin, and androgen interactions in women with polycystic ovarian disease. Fertility and Sterility. June 1991; 55(6): 1057- 1061.

[11] Roy G. Smith, Ph.D., Palige K. Besch, Ph.D. Buena Dill, M.T. (A.S.C.P.) Veasy C. Buttram, Jr., M.D. Saliva as a Matrix for Measuring Free Androgens: Comparison with Serum Androgens in Polycystic Ovarian Disease. Fertility and Sterility. May 1979; 31(5): 513-517.

[12] Sunandini Ghosh1,Shrinjana Dhar, Sandip Bhattacharjee, Pritha Bhattacharjee.Contribution of environmental, genetic and epigenetic factors to obesity-related metabolic syndrome. Nucleus. 11 April 2023; https://doi.org/10.1007/s13237-023-00420-y

[13] Rashmi Wardhan. Polycystic Ovarian Cyst Disorder (PCOD): Causes and Control. International Journal of Biotechnology and Biomedical Sciences. January-June 2016; 2(1): 32-33. http://www.krishisanskriti.org.

[14] PonJola Coney, M.D.Polycystic ovarian disease: current concepts of pathophysiology and therapy.Fertility and Sterility. November 1984; 42(5): 667-682.

[15] Sharvi, Shweta Gupta , Umang. Etiology of Polycystic Ovarian Disease (PCOD): Systematic Review.International Journal of Toxicological and Pharmacological Research. 2025; 15(1): 82-87.t: https://www.researchgate.net/publication/388494657

[16] Fredrika Pekonen, M.D., Timo Laatikainen, M.D., Richard Buyalos, M.D., Eeva-Marja Rutanen, M.D.

[17] Decreased 34K insulin-like growth factor binding protein in polycystic ovarian disease. Fertility and Sterility. June 1989; 51(6): 972-975.

[18] Robert J Norman, Ruijin Wu and Marcin T Stankiewicz. Polycystic ovary syndrome. Medical Journal of Australia, 2004; 180 (3):132-137.

[19] Aasiya Bashir, Lahanya Guha and Ishfaq Ahmad Bhat. Comprehension, Management, and Treatment of Polycystic Ovarian Syndrome via Allopathic, Unani and Ayurvedic Perspectives. Journal of Gynecology and Women's Health. March 2021; 21(1): 001-009. DOI: 10.19080/JGWH.2021.21.556055.

[20] Anushka Agrawal, Ranjit Ambad1, Radhika Lahoti2, Parikshit Muley3, P.S. Pande. Role of Artificial Intelligence in PCOS Detection. Journal of Datta Meghe Institute of Medical Sciences University. 27-Sep-2022; 17:491-494. DOI:10.4103/jdmimsu.jdmimsu_278_22.

[21] Timur Giirgan, M.D.Hiisnii M.D. Hakan Yarali, M.D. Osman Develioglu, M.D. Hulusi Zeyneloglu, M.D. Tarik Aksu, M.D. Evaluation of adhesion formation after laparoscopic treatment of polycystic ovarian disease. Fertility and Sterility. December 1991; 56(6): 1176-1178.

[22] Dana Hdaib, Noor Almajali, Hiam Alquran, Wan Azani Mustafa, Waleed Al-Azzawi, Ahmed Alkhayyat. Detection of Polycystic Ovary Syndrome (PCOS) Using Machine Learning Algorithms. 5th International Conference on Engineering Technology and its Applications 2022- (5thIICETA2022). September 2022; 532-536.

[23] Soumya V, Venkatesh P and Sharfudeen. Polycystic Ovary Disease (PCOD)- An Insight into Rodent Models, Diagnosis and Treatments. Journal of Clinical and Medical Images. 06 July 2021; 5(11): 1-13.

[24] Vincenzina Bruni1 & Anna Capozzi & Stefano Lello. The Role of Genetics, Epigenetics and Lifestyle in Polycystic Ovary Syndrome Development: the State of the Art. Reproductive Sciences. 11 March 2021.https://doi.org/10.1007/s43032-021-00515-4

[25] Aparna Prathap, T. P. Subhalakshmi, P. Joseph Varghese. A Cross-sectional Study on the Proportion of Anxiety and Depression and Determinants of Quality of Life in Polycystic Ovarian Disease. Indian Journal of Psychological Medicine. May-June 2018; 40(3): 257-262.