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A Review on Endocrine disorder and an Overview of Polycystic Ovarian Syndrome

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ABSTRACT
Polycystic ovary syndrome (PCOS) is a complex endocrine and metabolic disordercharacterized by anovulation, infertility, obesity, insulin resistance, and polycystic ovaries. Lifestyle or diet, environmental pollutants, genetics, intestinal dysbiosis, neuroendocrine changes and obesity are risk factors that predispose women to PCOS. These factors can contribute to the development of metabolic syndrome by causing hyperinsulinemia, oxidative stress, hyperandrogenism, folliculogenesis disorders and irregular menstrual cycles. Dysbiosis of the gut microbiota may play a pathogenic role in the development of PCOS. Restoration of gut microbiota with probiotics, prebiotics, or faecal microbiota transfer (FMT) can be an innovative, effective, and non-invasive way to prevent and alleviate PCOS. This review discusses various risk factors that may contribute to the etiology, incidence, and modulation of PCOS in addition to plausible therapeutic interventions, including miRNA therapy and eubiosis of the gut microbiota, that may contribute to the treatment and management of PCOS.

KEY WORDS: PCOs, FMT, Hyperinsulinemia, Irregular Menstrual Cycle

I. INTRODUCTION

Polycystic ovary syndrome (PCOS) is a complex condition characterized by high androgen levels, menstrual irregularities and/or small cysts in one or both ovaries. The disorder can be morphological (polycystic ovary syndrome) or mainly biochemical (hyperandrogenemia). Hyperandrogenism, a clinical feature of PCOS, can interfere with follicular development, ovarian microcysts, anovulation, and menstrual changes. One of the most prevalent endocrine system conditions affecting women of reproductive age is polycystic ovary syndrome (PCOS), also known as hyperandrogenic anovulation (HA) or Stein–Leventhal syndrome. This chronic and heterogeneous disorder manifests itself as menstrual dysfunction, infertility, hirsutism, acne, and obesity. It describes a condition where at least one ovary has an ovarian volume greater than 10 mL and at least one ovary has an estimated ten small cysts, with diameters ranging from 2 to 9 mm, develop [1]

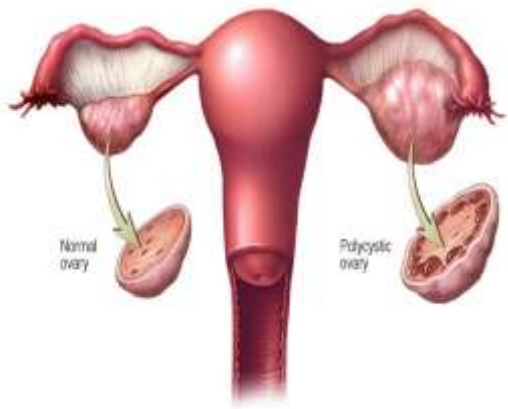

FIG. 1 : Diagrammatic Representation of PCOs[2]

EPIDEMOLOGY

PCOS is a heterogeneous disease that affects at least 7 percent of adult women.3 According to the National Institutes of Health Office of Disease Prevention, PCOS affects approximately 5 million women of reproductive age in the United States. The cost to the US health care system to detect and manage PCOS is approximately $4 billion annually. The age-standardized incidence rate of PCOS in women of reproductive age was 82.44 per 100,000 in 2017, 1.45% higher than in 2007 [3]

ETIOLOGY

PCOS can be described as an oligogenic disorder in which the interaction of multiple

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genetic and environmental factors determines a heterogeneous clinical and biochemical phenotype. Although the genetic etiology of PCOS remains unknown, a family history of PCOS is relatively common; However, familial associations with PCOS are unclear. The lack of phenotypic information prevents formal discriminant analysis. However, the current literature suggests that PCOS clusters in families like autosomal dominant. Environmental factors associated with PCO (e.g., obesity) may be exacerbated by poor dietary choices and physical inactivity; infectious agents and toxins may also play a role. The reproductive and metabolic features of PCOS are sometimes reversible with lifestyle changes such as diet and exercise.[4]

Table 1 : four Major Clinical Phenotypes of PCOs

Feature	Phenotype A	Phenotype B	Phenotype C	Phenotype D
Biochemical/clinical hyperandrogenism	+	+	+	–
Chronic anovulation	+	+	–	+
Polycystic ovaries	+	–	+	+

CLINICAL PRESENTATION[5]

* Enlarged ovaries with numerous small cysts
* Irregular menstrual cycles
* Pelvic pain
* Hirsutism
* Alopecia
* Acne
* Acanthosis
* Nigricans
* Skin tags

PATHOPHYSIOLOGY

The pathophysiology of PCOS involves primary defects in the hypothalamic-pituitary axis, insulin secretion and function, and ovarian function. Although the cause of PCOS is unknown, PCOS has been associated with insulin resistance and obesity. An association with insulin action is expected; insulin helps regulate ovarian function, and the ovaries respond to excess insulin by producing androgens, which can lead to anovulation. Stopping follicle maturation is a sign of ovarian abnormalities.Clinical symptoms of PCOS include luteinizing hormone (LH) and gonadotropin. - releasing hormone (GnRH) levels, while follicle stimulating hormone (FSH) levels are low or unchanged. As a result of increased GnRH, stimulation of ovarian follicles in turn produces more androgens. Follicular arrest can be corrected by increasing endogenous FSH levels or by administering exogenous FSH. [6]

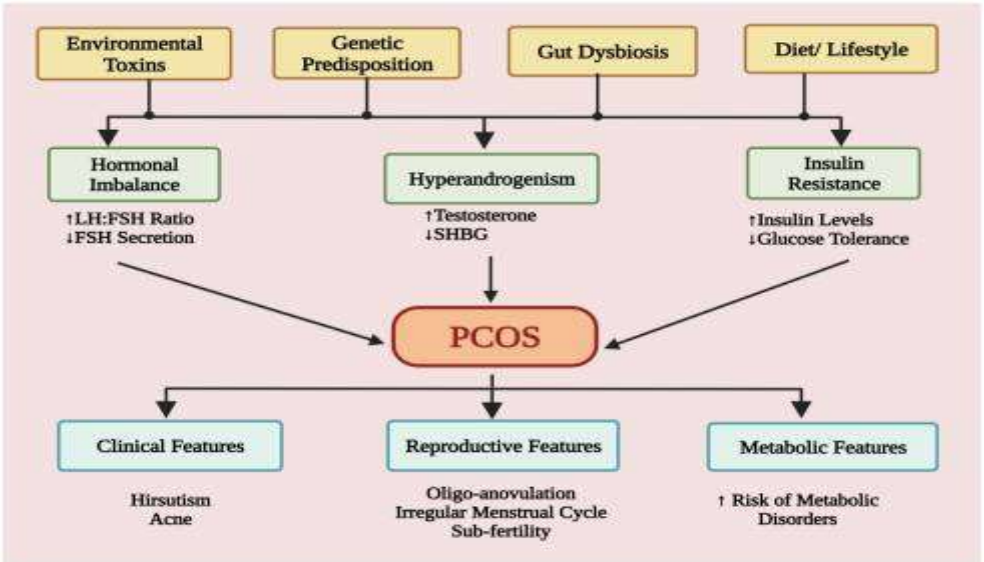

FIG.1 : pathophysiology of PCOs[7]

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DIAGNOSIS

There is no single test to diagnose polycystic ovary syndrome (PCOS). A physical exam includes checking for signs of excess hair, insulin resistance, and acne.

* **Pelvic Exam:** During a pelvic exam, your provider may check your genitals for masses, growths, or other changes.
* **Blood test:** Hormone levels can be measured through blood tests. This test can rule out possible causes of menstrual cycle problems or androgen excess that mimic PCOS. You may have other blood tests, such as fasting cholesterol and triglyceride levels. A glucose tolerance test can measure your body's response to sugar (glucose).
* **Ultrasound:** Ultrasound can check the appearance of your ovaries and the thickness of your endometrium. A rod-like device (sensor) is inserted into the vagina. The sensor emits sound waves that are converted into images on a computer screen. [8]

Algorithm 1: Diagnostic algorithm for polycystic ovary syndrome (PCOS)

Step 1: Irregular cycles + clinical hyperandrogenism
(exclude other causes)* = diagnosis
Step 2: If no clinical hyperandrogenism
Test for biochemical hyperandrogenism (exclude other causes)* = diagnosis
Step 3: If ONLY irregular cycles OR hyperandrogenism
Adolescents ultrasound is not indicated = consider at risk of PCOS and reassess later Adults - **request ultrasound for PCOM***, if positive (exclude other causes)* = diagnosis

* Exclusion of other causes = TSH, prolactin, 17-OH progesterone, FSH or if clinically indicated exclude other causes (e.g. Cushing's Syndrome, adrenal tumours). For hypogonadotrophic hypogonadism, usually due to low body fat or intensive exercise, exclude clinically and with LH/ FSH.
PCOM = polycystic ovarian morphology on ultrasound

FIG.3 : Diagnostic Algorithm for PCOs[9]

MANAGEMENT

Drug	dosage	Adverse effects
Oral contraceptives	One tablet po daily	Breast tenderness, increased risk of thromboembolism
Clomiphene	50-150 mg Po daily days 5 – 9 of cycle	Hot flashes, nausea, headache, multiple gestation
Gonadotropins	Dosage and duration depend on product and patient response	Abdominal pain, breast tenderness, injection site reaction, multiple pregnancy
Glucophage, Glucophage XR	500mg po BID to 850mg po tid	Lactic acidosis, anorexia
Spironolactone (Aldactone)	100-200mg Po daily	Intermenstrual bleeding, hypokalemia, hypotension

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Pioglitazone(Actos) Rosiglitazone (Avandia)	30-45 mg PO daily 4mg PO daily to bid	Increased LDL with rosiglitazone, weight gain and edema

Table.2 : Treatment plan of PCOs

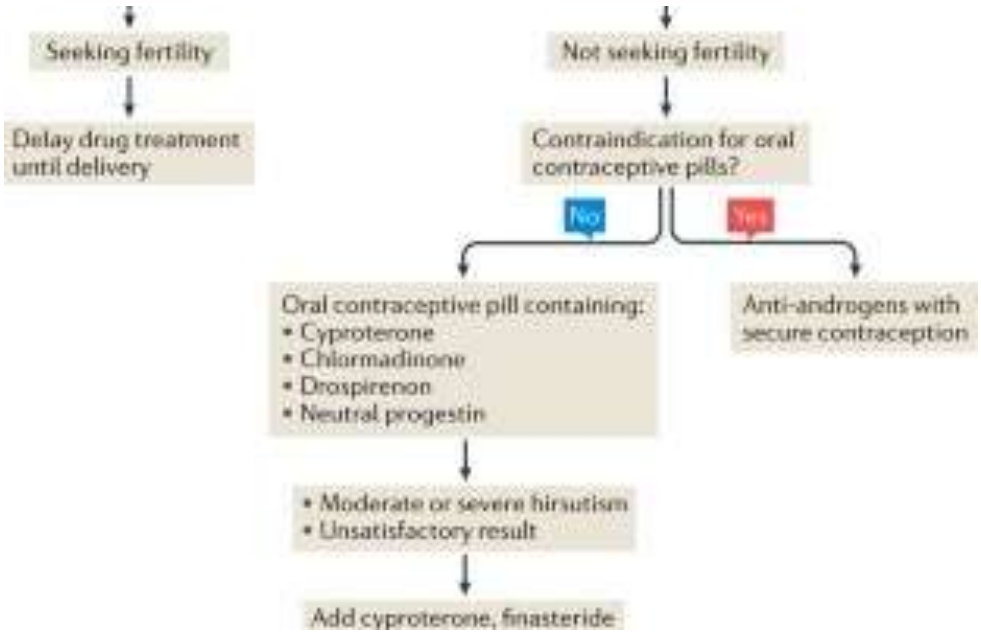

FIG. 4 : Treatment algorithm for PCOs

II. CONCLUSION

Polycystic ovary disease is a complex disease that requires multiple treatments, depending on why the patient is seeking treatment. Clomiphene has shown the best results in the treatment of infertility, while little is known about the pharmacological treatment of androgenic symptoms. Long-term effects of PCOS, including type 2 diabetes and cardiovascular disease, can be treated with antidiabetic drugs and statins.

Conflict of Interest: Nill

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