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Etiology and Pathogenesis of Polycystic Ovary Jennifer E. Gallagher * Syndrome (PCOS)

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Introduction

Polycystic ovary syndrome (PCOS) is the most common endocrine disorders occurring at a frequency of 5 to 15 percent among reproductive aged women. Depending on the diagnostic criteria the prevalence of PCOS may range from 6 to 20 percent. PCOS is a complex condition that involves metabolic, endocrine and psychiatric features. The disease is characterized by chronic anovulation, biochemical or clinical hyper-androgens and polycystic ovary morphology [1,3]. Primarily the oxidative stress and low-grade chronic inflammation were found to be associated with PCOS pathogenesis. Long term metabolic complications and chronic degenerative diseases are also associated with continuous release of the inflammatory markers and such increased inflammation is suggested as having probabilistic initiating influence on PCOS pathogenesis [2]. PCOS is also correlated with higher levels of androgens. There may also be the role of genetic polymorphisms that play a significant role in pathophysiology of PCOS. Apart from these there are also various confounding factors such as pollution, sedentary lifestyle and environmental factors. The uterine hyper inflammatory state under PCOS condition may lead to subfertility, infertility and/or significant pregnancy complications [3].

National Institute of Health and Rotterdam diagnostic criteria for the diagnosis for PCOS provides diverse phenotypic presentation but however it fails to provide the distinct insights and therefore the etiology and the causal factors for PCOS are still not very clear. The biochemical markers that are used to detect PCOS are subject to change and variation owing to several factors such as age, metabolic state, chronic degenerative diseases, the usage of contraceptives and insulin [2,4]. Moreover, these markers cannot be adjudged as either causal or consequence to the disease. Therefore, the genetic factors that are constant and reliable are suitable for accurate diagnosis and determination of the causality of gynecological disorders such as PCOS.

Nutritional and dietary habits play a significant role in the development of gynecological disorders including PCOS. A diet that is rich in the long chain saturated fatty acids can potentially induce inflammation of the hypothalamus. The neurons in the hypothalamus can sense the glucose concentration in the blood and send feed-back for the regulation of the body glucose homeostasis [1,5]. Such studies aid in the development and optimization of effect prevention strategies for PCOS. The hypothalamus plays an important role in the general body

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physiology including the food intake pattern, reproduction and the weight balance. Some studies have focused on the development of diet induced hypothalamic inflammation and its involvement in the pathophysiology of PCOS etiology and the consequent heterogeneity in the clinical, hormonal and the metabolic presentations.

PCOS was found to be highly heritable with a substantial percentage of up to 70%. Genome wide association studies have revealed the susceptibility loci and variants associated with PCOS thus providing novel insights into the physiological pathways that are involved in the manifestation of PCOS. The clustering of the variants that are associated with PCOS was identified based on three etiological pathways involving the adiposity, insulin resistance, and SHBG [4,6]. These studies have suggested the causal role of BMI, SHBG, and insulin resistance on PCOS. Diagnosis based on such approach will also distinguish various subtypes of PCOS and aid in the customized treatment with precise and effective health outcomes.

There is more than one pathophysiological mechanism that is involved in the manifestation of PCOS. The etiological factors could be heterogeneous in nature such as environmental, genetic and epigenetic mechanisms. The potential causal factors that lead to PCOS could include a defect in the GnRH/gonadotropins neuro-endocrine axis. The neurological excitatory and inhibitory signals and the associated regulatory mechanisms and the

metabolic elements interfere with the centers of reproduction in the human brain. Therefore, the insulin resistance, concomitant hyperglycemia and hyperandrogenemia participate simultaneously in the pathogenesis of PCOS.

Some other studies have focused on the role of long non-coding RNAs and micro RNAs and their role in the development of PCOS [3,5]. The molecular mechanisms and the regulatory mechanisms that are involved could provide interesting leads on the molecular mechanism underlying the development of PCOS. The studies have confirmed that high rate of expression of long chain none coding RNA indirectly up regulated the expression of VGEF by down regulating the expression of miR-206 thus promoting the proliferation of KGN cells an inhibiting the apoptosis and promoting the development of PCOS.

Both Endometriosis and PCOS are associated with alteration in the prenatal testosterone levels and abnormal functioning of hypothalamic pituitary gonadal axis. PCOS was found to be mediated with high prenatal testosterone. Some of the new

parameters that are found to be associated with the development of PCOS are gut micro biome composition and the metabolomics of the plasma. These parameters are also indirectly associated with the body physiology.

Prolonged conditions of PCOS predispose the affected women to endometrial and ovarian cancer and therefore precise recommendations need to be implemented at an early stage. There are no effective medications for complete treatment of PCOS and some medications are temporarily effective with undesirable side effects and may lead to reoccurrence after discontinuation. Currently, the prevention of the gynecological disorders is mainly based on hormonal treatment [7]. However, it was observed that diet rich in fruits and vegetables, green tea, vitamins, and other plant derived components help prevent gynecological disorders compared to diet that is rich in animal and dietary fats, red meat and alcohol. Therefore prevention strategies through modification of the diet pattern may help in amelioration of the occurrence of wide range of gynecological disorders including PCOS.

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