Assessment Of The Prevalence Of Polycystic Ovary Syndrome Among Egyptian Patients With Pre -Eclampsia

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Presented by

Amal Shawky Ali
M.B.,B.Ch, Suez Canal University, (2000)
Resident of Obstetrics and Gynecology,
Boulak El Dakror Hospital

Under supervision of

Prof. Abdel Mageed Ismail
Professor of Obstetrics and Gynecology
Faculty of Medicine, Ain Shams University

Dr. Mohammed Alsherbeeny
Assistant Professor of Obstetrics and Gynecology
Faculty of Medicine, Ain Shams University

Faculty of Medicine
Ain Shams University
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تحت إشراف

الأستاذ الدكتور/ عبد المجيد إسماعيل

أستاذ أمراض النساء والتوليد

كلية الطب - جامعة عين شمس

الدكتور/ محمد الشربيني

أستاذ مساعد أمراض النساء والتوليد

كلية الطب - جامعة عين شمس

كلية الطب

جامعة عين شمس

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most common endocrinopathies affecting 5-10% of women in reproductive age *(Lakhani et al., 2002)*.

Insulin resistance and compensatory hyper-insulinemia are the major causes of the metabolic syndrome (MS) and are also the main pathophysiology of PCOS. According to the International Diabetes Federation criteria, one-third of the PCOS women had MS *(Weerakiet et al., 2007)*.

MS is a cluster of metabolic abnormalities including abdominal obesity, glucose intolerance, hypertension, and dyslipidaemia and is associated with an increased risk of vascular events *(Daskalopoulou et al., 2006)*.

Pre-eclampsia (PE) is a common obstetric syndrome affecting about 7-10% of pregnant women *(Gorzelak et al., 2000)*.

Pre-eclampsia is a major cause of maternal mortality (15-20%) and morbidities (acute and long term), perinatal deaths, preterm birth, and intrauterine growth restriction *(Sibai et al., 2005)*.

Although the pathophysiology of pre-eclampsia has not yet been fully elucidated certain theories have been put forward including: endothelial cell damage, decreased placental perfusion, changed vascular reactivity, instability between prostacyclin and thromboxane and genetic factors *(Higgins et al., 1998)*.

Diamant et al. (1982) found that pregnancies after induction of ovulation accompanied with a higher incidence of PE. Overproduction of steroid hormones, especially androgens was suggested as the main factor for the appearance of PE in PCOS patients.

In 1998, a study by Dekker, et al., found that the incidence of pre-eclampsia was higher in patients with PCOS than in controls. This higher incidence could not be explained by body mass index (BMI), endocrine profile before pregnancy, induction of ovulation or treatment regimens *(Dekker et al., 1998)*.

In 2000, Kashyap, et al., found that pregnant PCOS patients had a high incidence of PE (31.8%), versus non-PCOS patients, who had lower PE incidence (3.7% *(Kashyap et al., 2000)*.

AIM OF THE WORK

The aim of this study is to assess the prevalence of Polycystic ovary syndrome (PCOS) among Egyptian patients with pre-eclampsia (PE).

DEFINITION OF PCOS

The definition of polycystic ovary syndrome (PCOS) varies markedly among investigators; some use clinical criteria that may include anovulation, obesity, hirsutism, insulin resistance and sonographic visualization of polycystic ovaries *(El-Tabbakh et al.. 1986)*, while others use laboratory criteria that may include elevated serum LH levels. Elevated circulating androgens and increased LH: FSH ratio *(Yen, 1980)*.

The Rotterdam Consensus Workshop, (2003) concluded that PCOS is a syndrome of ovarian dysfunction along with the cardinal features of hyperandrogenism and polycystic ovary morphology (PCO) PCOS remains a syndrome and, as such, no single diagnostic criterion (such as hyperandrogenism or PCO) is sufficient for clinical diagnosis. Its clinical manifestation may include menstrual irregularities, signs of androgen excess and obesity, insulin resistance and elevated serum LH. Levels are also common features in PCOS. PCOS is associated with increased risk of type II diabetes and cardiovascular events.

1- Epidemiology of PCOS:

Polycystic ovary syndrome (PCOS) is one of the most common endocrinopathies affecting 5-10% of women in reproductive age *(Lakhani et al., 2002)*.

A good estimate of PCOS prevalence comes from a population. Based study by *Knochenhauer et al., (1998a)*. Menstrual cycle characteristics and clinical androgen excess were assessed among 277 women undergoing a routine pre-employment history and physical examination in Alabama and serum androgen levels were measured in 198 of these women not on hormonal therapy. Among this cohort, PCOS prevalence was estimated at 4.6% with a possible range of 3.5% to 11.2%.

Using ultrasound scan criteria only, 20-33% of apparently healthy women in the child bearing period have been found to have polycystic ovaries in population studies whereas a prevalence of 4-10% in women of reproductive age is commonly quoted when the diagnosis is based on clinical, biochemical and ultrasound scan features *(Polson et al., 1998)*.

For the clinical definition used here, chronic anovulation plus androgen excess the prevalence is

probably in the 55% range *(De Wailly et al., 1997)*. Incidence date has not been reported.

Adopting the new consensus ESHRE/ASRM definition of PCOS as the gold standard over the next few years could-potentially overcome this challenge; however, as the new ESHRE/ASRM consensus definition does not incorporate indices of insulin resistance, this will not be easy *(Sharma et al., 2005)*.

Etiology of PCOS

Theories of etiology of PCOS:

Although the etiology of PCOS remains unknown, we can expect a polygenic background with involvement of both genetic and environmental factors. Several factors may contribute to development of PCOS (Jacobs et al., 1999).

1- Hereditary factors in PCOS:

Studies of large families suggested inheritance in an autosomal dominant fashion with premature balding as the phenotype in males. The strong link between hyperinsulinemia and hyperandrogenism also suggests that the stimulatory effect of insulin on ovarian androgen production is influenced by a

genetic predisposition or susceptibility *(Govind et al., 1999)*.

Several studies suggested a familial or hereditary cause of PCOS. Either as a single gene mutation or an evolving set of symptoms. Further researches for genes that are associated with a susceptibility to polycystic ovaries have implicated a locus on the insulin gene and the gene encoding P_{450}= (Cyp_{11a} or P_{450} cytochrome enzyme) but not the gene encoding P_{450} C_{17} (Cyp_{17} or 17 alpha hydroxylase and 17.20 lyase enzymes). P_{450}SCO and $P_{450}C_{17}$ enzymes dysregulation and abnormal hyperactivity would account for the altered steroidogenesis in both ovaries and adrenal gland. These studies also imply an autosomal dominant mode of inheritance directing clinicians to counsel families because theoretically 50% of mothers and sisters within the family can manifest this disorder. The actual expression is however less (perhaps 40%) due to modification by both genetic and environmental factors *(Speroff, 2005)*.

2- Endocrinological cause of PCOS:

A- Hypothalamic pituitary abnormality:-

Yen et al. (1976) described the classic derangement in the hypothalamus-pituitary secretion as a

relative increase in LH and relative decrease in FSH levels in PCOS, and found that possibilities of primary hypothalamic pituitary abnormality are:

1- Abnormal hypothalamic regulation of gonadotropins.

2- Abnormal feed back at pituitary level, leading to increased sensitivity.

3- A combination of the two factors.

The altered pattern of GnRH secretion can contribute to this characteristic LH: FSH ratio, and the increases pituitary and hypothalamic sensitivity can be attributed to the increased estrogen levels.

Franks, (1995) examined the possible role of the lack of cyclic exposure to progesterone in the development of gonadotropins and androgen abnormalities in PCOS, stated that when PCOS patients were treated with medroxy progesterone acetate (MPA) for 5 days. There were significant decreases of gonadotropins and androgen to values no longer different from normal.

They concluded that these results are consistent with the concept that ovulation failure and progesterone deficiency play a facilitatory role in the development of

the hypothalamic-pituitary abnormality giving rise to disordered LH secretion in PCOS.

The gonadotrophin pattern (high LH and low FSH) can also be due to increased frequency of GnRH pulsatile secretions *(Hayes et al., 1998)*.

B- Ovarian endocrinal abnormalities:

McNatty and Baird, (1978) found higher levels of androstenedione than oestradiol in follicles with no FSH, and higher levels of oestradiol than androsteendione in follicles containing FSH. Through-out the menstrual cycle it is thought that theca cells under the stimulation of LH provide androstenedione substrate for oestrogen synthesis by granulosa cells *(Tsang et al., 1979)*.

Erickson et al. (1979) showed that ability to aromatize is related to follicle size. Granulosa cells from small follicles (4-6mm diameter) from both normal and polycystic ovaries where unable to aromatize whereas cells from larger follicles (8-15mm) can aromatize added androstenedione. Addition of FSH and androstendedione to cultured granulosa cells from both polycystic and normal ovaries resulted in a marked increase in oestrogen production not seen