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Original Article

Complications and Outcome of Pregnancy in Infertile PCOS Patients

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Abstract

BACKGROUND: Polycystic ovarian syndrome (PCOS) is a complex hormonal disturbance that has numerous implications for general health and fertility. It is the most common cause of ovulatory disturbance, leading to infertility and probably, pregnancy loss. This study evaluated the complications and outcome of pregnancy in women with polycystic ovarian syndrome (PCOS).

METHODS: The course and outcome of 47 singleton pregnancy in women with well-documented PCOS were compared with those in 100 healthy controls.

RESULTS: The incidence of an abnormal glucose-challenge test, gestational diabetes mellitus and pregnancy induced hypertension were significantly increased in pregnant women with PCOS ($P<0.05$)

CONCLUSION: Women with PCOS were at increased risk of gestational diabetes and pregnancy induced hypertension.

KEY WORDS: polycystic ovarian syndrome, infertility, Pregnancy Complications.

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Polycystic ovary syndrome (PCOS) is an enigmatic disorder with different clinical and biochemical features. The hallmark of PCOS is excess androgen production by the ovaries and to a lesser extent by the adrenal gland. Obesity is a common feature of PCOS, however the disease may also manifest in lean subjects [1].

It has been shown that 21-23% of the normal female population has PCO on ultrasound scan [2]. PCOS prevalence was estimated at 4.6% with a possible range of 3.5% To 11.2% by Knochenhauer and co-workers, also preliminary data from a cross-sectional study in Greece indicated a 9% prevalence of PCOS on rely of both oligomenorrhea a hyperandrogenism [3]. Women with PCOS have a greater frequency and degree of both hyperinsulinemia and insulin resistance when compared with weight – matched controls [4]. Obesity is a risk factor for pregnancy–induced hypertension including both preeclampsia and gestational hypertension. Glucose intolerance and insulin resistance have also been linked to pregnancy-induced hypertension. These observations suggest that PCOS might be associated with an increased risk for this pregnancy complication [5].

Paradisi and co-workers reported that mean diastolic blood pressure throughout pregnancy was significantly higher among women with PCOS throughout pregnancy was significantly higher among women with PCOS as compared with normal controls [6].

Lanzone and co-workers evaluated preconceptional andgestational of insulin in patients with polycystic ovary syndrome and concluded

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that the PCOS population was at higher risk of developing carbohydrate abnormalities than the normal population of a similar reproductive age [7].

Radon et al. believed that because up to 80% of obese and 30% of lean women with PCOS demonstrate insulin resistance before conception and as many as 50% are affected by impaired glucose tolerance later in life, women with PCOS may be at an increased risk for glucose intolerance during pregnancy [8]. In this regard, Urman et al. evaluated complications and outcome of pregnancy and reported that women with PCOS were at increased risk of gestational diabetes mellitus (GDM) and pregnancy induced hypertention (PIH) and this risk appeared to be independent of body mass index (BMI) [9].

PCOS is one of the most common reproductive endocrinological disorders of women and the most common cause of anovulation infertility. So the high prevalence of PCOS, multiple and serious complications attributed to it were main factors to us for evaluation of Iranian women with PCOS.

The aim of this study was to assay the pregnancy complications (preeclampsia, GDM, preterm labor) and outcome of pregnancy in women with PCOS.

Methods

This research is a analytic, perspective cohort study with two groups (PCOS and control). Independent variable was previous history of PCOS and dependent variables were GDM, preeclampsia and preterm labor.

Inclusion criteria were GA<28 weeks of pregnancy, Iranian race, agreeable to research, distinctive address and phone.

Exclusion criteria were diagnosis of mole hydatiforme, multiple pregnancy, oligohydramnious, polyhydramnious, Rh incompatibility hydropsFetalis, placenta previa, PROM, cervical incompetence, abnormalities of uterus, fetal anomalies, previous history of chronic hypertension, diabetes, kidney, heart, infectious disease, severe anemia and history of operation in recent pregnancy.

147 eligible pregnant women referring to infertility clinics and hospitals of Isfahan for prenatal care were selected.

In PCOS group (n=47) the diagnosis of PCOS was based on a combination of clinical and biochemical criteria: 1) ovulatory dysfunction (oligomenorrhea, amenorrhea) 2) clinical evidence of hyperandrogenism (hirstism, acne) 3) hyperandrogensim (elevated Testosterone, androstendione or dehydroepiandrosterone sulphate) 4) luteinizing hormone/ follicle- stimulating hormone ratio>2. Age and weight before pregnancy were recorded.

The control group (n=100) were selected randomly from pregnant women who attended for prenatal care at the same hospitals and had no history of PCOS and infertility. These women matched for age and weight with case group (ratio was 2:1).

A glucose challenge test (GCT) for screening GDM was performed on all patients between the 24th and 28th weeks of gestation.

The women ingested 50g of glucose and plasma glucose was measured 60 minutes later. A plasma glucose value ≥140 mg/dl was accepted as an indication for performing a standard three-hour l00g oral glucose tolerance test (GTT). National diabetes Data Group criteria were used for diagnosis of GDM. Briefly, two or more elevated values other than the fasting plasma glucose were considered sufficient to make the diagnosis of GDM. PIH was defined as blood pressure ≥$^{140}/_{90}$mm Hg after 20 weeks of gestation and associated with proteinuria and/or pathologic edema. Proteinuria was defined as 100 mg/dl or 2+ in at least two random urine specimens collected six or more hours apart or >300 mg in 24 hours.

PIH was classified as mild unless one or more of the signs or symptoms defined for severe disease were present. A combination of the following criteria was used for diagnosis of preterm labor:

1) Gestational age of more than 20 weeks but less than 37 weeks.

2) Persistent uterine contractions (2 every 10 minutes during 30 minutes observation).

3) Progressives cervical dilatation and effacement

4) Rull out of placenta previa and abruption of placenta

5) Intact amnion and chorion membranes.

These subjects followed up continuously to delivery Time and data using a questionnaire was collected. Statistical analysis was performed by the chi-square and t-student Tests using SPSS software. Statistical significance was considered when P was <0.05.

Results

Patient characteristics were presented in Table 1.

The duration of infertility was 2-4 years in PCOS group. All these women had been treated with either clomiphene citrate and exogenous gonadotropins or invitro fertilization and embryo transfer.

The average body mass index and BMI>25 kg/m^2 in PCOS patients was greater than the control group.

(Mean BMI was 25.1±4.4 in PCOS versus 23.4±3.3 in control and BMI>25 kg/m^2 was 42.6% in PCOS versus 32% in control).

Table 1. Patient characteristics

Characteristic	PCOS (n=47)	Control (n=100)
Age (years)	27.8±5.2	28±4.9
Mean BMI (kg/m^2)	25.1±4.4	23.4±3.3
Mean weight gain (kg)	11.7±3.7	13.1±4.3
Age> 35 yr	10.6%	14%
BMI> 25 kg/m^2	42.6%	32%
Primigravidity	53.2%	45%
Primiparity	74.5%	70%

Pregnancy complications were shown in Table 2.

Mild and severe preeclampsias were encountered more commonly in PCOS patients (42.5% versus 10%).

Significantly more pregnant women with PCOS as compared to the controls demonstrated an abnormal response to a 50g glucose challenge Test (31.9 % versus 8%). Moreover, the incidence of gestational diabetes in the two groups was 12.8% versus 2% that was statistically significant. The rate of preterm labor was 19.1% in PCOS and 10% in control group, which was not a significant difference. Table 2.

Table 2. Pregnancy complications in PCOS and control

Complication	PCOS (n=47)	Control (n=100)	P
Mild PIH	15 (31.9) %	8 (8) %	_< %5
Sever PIH	5 (10.6) %	2(2) %	< 0.05
GCT>140 mg/dl	15(31.9) %	8(8) %	< 0.05
GDM	6(12.8) %	2(2) %	< 0.05
Preterm Labor	9(19.1) %	10(10) %	NS

Neonatal characteristics were presented in Table 3.

Table 3. Neonatal characteristics Characteristic

	PCOS	Control
Median gestational age (wk)	39 (32-43)	39 (34-41)
Median birth weight (g)	3300 (650-4200)	3200(1600-4750)
Low birth weight a.	10(21.3%)	6 (6%)
Macrosomia b	4 (8.5%)	4(4%)
Neonatal intensive care Unit admission	10(21.3%)	11(11%)
Perinatal death	1(2.1%)	1(1%)

a. Birth weight <2500 gr
b. Birth weight > 4000 gr

Discussion

In this study, results showed that incidence of abnormal glucose challenge test, GDM and PIH in pregnant women with PCOS were higher than the control group. It may be correlated with obesity in these women, as 42.6% of PCOS patients had BMI>25 kg/m^2 versus 32% in control group. The typical obesity of PCOS characterized by centripetal distribution of fat in the center of the body as opposed to the thighs and hips is associated with greater risk of hypertension, diabetes and dyslipidemias [10]. As it is emphasized before, hyperinsulinemia is one of the various metabolic abnormalities commonly found in conjunction with PCOS relatively independent of obesity. Insulin is a hormone with hemodynamic actions. Insulin resistance and huper insulinemia have been proposed as permissive factors in the development of future serious vascular disease. There is evidence to suggest that insulin is a

vasodilator of skeletal muscle vasculature with this effect impaired in states of insulin resistance such as obesity and non-insulin dependent diabetes mellitus. Insulin–mediated vasodilatation may play a role in the regulation of vascular Tone since a pressor response to systemic norepinephrine infusions is increased leading to hypertension in insulin-resistant subjects. Finally insulin has been shown to interact in an unknown manner with the endothelium to increase nitric oxide synthesis and release. States of insulin resistance may be associated with a defect in insulin's action in modulating the nitric oxide system. Inhibition of the nitric oxide system during pregnancy has been shown to cause hypertension, proteinuria and fetal growth retardation in pregnant rats. All the above experimental data suggest that the insulin resistance and hyperinsulinism associated with PCOS may be responsible in part for some of the pregnancy complications such as PIH and gestational carbohydrate intolerance [9].

In a research, Kashyap and Claman (2000) investigated PCOS patients who were pregnant following gonadotrophin therapy and found that PCOS is an important risk factor for the development of PIH [11].

Also, Mikola and Hiilesmaa (2001) followed obstetric outcome of women with PCOS and reported that PCOS slightly increased the risk for GDM but didn't have an important effect on the rate of premature delivery and preeclampsia [12].

In contrast, in another study by Vollenhoven and Clark (2000) no difference was seen in the prevalence of GDM and pregnancy outcomes between the PCOS patients pregnant after ovulation induction with gonadotrophins and the controls [13].

Anttila and Karjala (1998) studied the polycystic ovaries in women with gestational diabetes and observed that polycystic ovaries were a common finding among women with GDM and suggested that women with PCO are at risk for developing GDM and should be screened accordingly [14]. Conn and Jacobs (2000) also reported that women with type 2 diabetes mellitus had a higher prevalence of PCOS than that reported in the general population [15].

In another research, Radon and Mcmahon (1999) evaluated impaired glucose tolerance in pregnant women with polycystic ovary syndrome and noted that women with PCOS are at increased risk of glucose intolerance and preeclampsia during pregnancy [8].

Juff and Esterlitz (1998) investigated relationship between abnormal glucose tolerance and hypertensive disorders of pregnancy in healthy nulliparous women. They observed that level plasma glucose 1 hour after a 50g glucose challenge was positively correlated with the likelihood of preeclampsia and thus women with GDM were at increased risk for hypertensive disorders during pregnancy [16].

Findings of our study also showed that incidence of LBW (21.3% in PCOS versus 6% in control), Macrosomia (8.5% in PCOS versus 4% in control), and admission to neonatal care unit (21.3% versus 11%) were higher in PCOS group, which indicated a high risk pregnancy in these women. In conclusion, pregnant PCOS patients should be followed carefully for the occurrence of various pregnancy complications including GDM and hypertension and LBW using GCT, GTT, and control of BP, edema, proteinuria, weight gain and fetal growth.

Further study regarding to approaches for prevention and decline of pregnancy complications associated with PCOS are recommended.

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