



Association of Hyperensive Disorders and Diabetes with Pregnancy in Women with Polycystic Ovary Syndrome

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Abstract

Background: Women with PCOS are at an increased risk of metabolic disorders in pregnancy, such as impaired fasting glucose, gestational diabetes and hypertensive disorders of pregnancy. These morbidities, individually or combined, affect pregnancy outcome in these women.

Objective: To evaluate the association of diabetes and hypertensive disorders with pregnancy in women with polycystic ovary syndrome.

Materials and Methods: This is a prospective cohort study conducted over a period of one year. Antenatal women attending the Govt medical college, Trivandrum and diagnosed to have polycystic ovarian syndrome according to Rotterdam criteria were included in the study. For comparison we selected same number of pregnant women without any features of PCOS. Student t- test or Chi-square test were used to test the difference between PCOS and non PCOS group.

Results: Hypertensive disorders in patients with PCOS is statistically significant with $p < 0.015$ and with Relative Risk (95% CI)= 2.0 (1.121-3.567). Significant number of cases with PCOS (69.9%) had diabetes mellitus in pregnancy compared to control group (27.3%).

Conclusion: Hypertensive disorders of pregnancy like gestational hypertension, preeclampsia and chronic hypertension and diabetes (both gestational diabetes and overt diabetes) were significantly increased in women with PCOS compared to the control group.

Keywords: PCOS, Gestational diabetes, Hypertension.

Introduction

The reproductive issues with PCOS are manifold starting with anovulatory cycles leading to subfertility. Today a growing body of evidence points to a high prevalence of pregnancy complications in PCOS women. As a result, PCOS is not only related to metabolic abnormalities, menstrual irregularity or infertility as previously reported, but is becoming increasingly associated with gestational diabetes

(GDM), gestational hypertension, preeclampsia, early pregnancy loss, preterm delivery, fetal growth restriction, low birth weight, increased risk of caesarean section, and rate NICU admission, which are all considered to be adverse pregnancy outcomes of PCOS during pregnancy^[1,2].

The most common endocrine aberrations seen in PCOS are chronically elevated luteinizing hormone (LH) and insulin resistance.. High LH and hyperinsulinemia work synergistically,

causing androgen production and ovarian cyst formation. Obesity which is seen in 50-65% of PCOS patients, may increase the insulin resistance and hyperinsulinemia. The correlation between hyperandrogenism and insulin resistance has been recognized in both obese and non-obese anovulatory women. Thus, it is important to realize that a non-obese patient may also have insulin resistance. However, the insulin levels in obese women are higher than their non-obese counterparts. A recent meta-analysis of pregnancy outcomes in women with PCOS demonstrated a significantly higher chance of developing GDM for PCOS women (odds ratios of about 2.90)^[3]

However, when analyzing the available evidence separately, there were largely conflicting results: While most of the studies demonstrated an increased risk for GDM in PCOS women (odds ratios ranging from 1.15 to 22.15), a few found odds ratios from 0.31 to 0.96.

Hypertensive disorders are common in PCOS. There are several mechanisms for hypertension in PCOS. The potential causes include hyperandrogenism, hyperinsulinemia, obesity and increased sympathetic nervous system activity. The hyperandrogenemia in PCOS women is associated with systolic and diastolic blood pressures in women with PCOS, independent of obesity or insulin resistance.

Effective tackling of metabolic and reproductive issues relating to pregnancy forms the cornerstone of management of PCOS. The current study aims

to assess these adverse outcomes in pregnancy in women with PCOS compare to women without PCOS. Women with PCOS are at increased risk of adverse pregnancy and birth outcomes and may need increased surveillance during pregnancy and parturition.

Materials and Methods

This is a prospective cohort study conducted in the department of Obstetrics and Gynaecology, Government Medical College, Trivandrum. Antenatal women who attended the outpatient department SAT hospital, Government Medical College, Trivandrum soon after pregnancy was confirmed and diagnosed to have polycystic ovarian syndrome according to Rotterdam criteria formed the study group. For comparison we selected the same number of pregnant women who attended our antenatal OP department soon after confirming pregnancy after confirming that they did not have PCOS (had regular cycles and no hyperandrogenism and ultrasound scan showed normal ovaries). Data was collected using a pre-structured questionnaire. T test and Chi square test was used to analyse the data.

Results

Out of 118 PCOS patients 57.6% conceived after treatment for infertility and 42.4% spontaneously. In the study group 8.5% had past history diabetes which is statistically significant with p value 0.001.

Table 1 Past history of diabetes

			Past h/o DM		Total
			Yes	No	
Category	PCOS	N	10	108	118
		%	8.5	91.5	100.0
	No PCOS	N	0	118	118
		%	0.0	100.0	100.0

$$\chi^2=9.424$$

$$df=1$$

$$p=.001$$

In pregnant women with PCOS 3% had past history of hypertension which is not statistically significant with p value 0.081. In pregnant women with PCOS 22.9% were overweight and 10.2% were obese, Hence high BMI is statistically significant in PCOS with $p < 0.001$.

In the PCOS group 34.9% had hypertensive complications which includes gestational hypertension, preeclampsia and chronic hypertension. Hypertensive complications in patients with PCOS was statistically significant with $p < 0.005$ and with relative risk (95% CI)= 2.261 (1.335-3.828).

Table 2 Hypertensive disorders of pregnancy

			Hypertensive Disorders of pregnancy		Total
			Yes	No	
Category	PCOS	N	29	54	83
		%	34.9	65.1	100.0
	No PCOS	N	17	93	110
		%	15.5	84.5	100.0

$$\chi^2 = 9.894$$

$$df=1$$

$$p=0.002$$

Relative Risk (95% CI)= 2.261 (1.335-3.828)

Out of 29 cases of hypertension in the PCOS group, 62.1% had gestational hypertension, 27.6%

had preeclampsia and 10.3% had chronic hypertension.

Table 3. Types of hypertensive disorders in the PCOS group

			Type of Hypertensive disorder			Total
			GHTN	Pre eclampsia	Chronic HTN	
Category	PCOS	N	18	8	3	29
		%	62.1	27.6	10.3	100.0
	No PCOS	N	14	2	1	17
		%	82.4	11.8	5.9	100.0

The study shows that diabetes in PCOS pregnancy is statistically significant with relative risk of 2.562 and $p < 0.001$. Relative Risk (95% CI)= 2.562(1.831-3.586). Out of 58 diabetes PCOS

patients 87.9% cases was gestational diabetes, 12.1% cases was overt diabetic. In control group no overt diabetes was there.

Table 4 Diabetes in PCOS

			Diabetes		Total
			Yes	No	
Category	PCOS	N	58	25	83
		%	69.9	30.1	100.0
	No PCOS	N	30	80	110
		%	27.3	72.7	100.0

$\chi^2=34.619$ $df=1$ $p<0.00$

Out of 58 diabetes PCOS patients 87.9% cases had gestational diabetes, 12.1% cases had overt

diabetic. In control group no overt diabetes was there.

Table 5 Types of diabetes

			Type of DM		Total
			GDM	Overt DM	
Category	PCOS	N	51	7	58
		%	87.9	12.1	100.0
	No PCOS	N	30	0	30
		%	100.0	0.0	100.0

$\chi^2=3.934$ $df=1$ $p=0.041$

Out of 58 diabetic PCOS patients 53.4% were on medical nutritional therapy, 36.2% were on insulin and 10.3% were on insulin along with oral hypoglycemic agents. In non PCOS group of 30 patients with diabetes, 76.7% were on medical nutritional therapy, 13.3% were on insulin and 10% were on insulin along with oral hypoglycemic agents.

Discussion

PCOS is characterised by oligoovulation or anovulation, hyperandrogenism and polycystic

ovarian morphology associated with insulin resistance and obesity. C.M. Boomsma et al metaanalysis about PCOS shows that women with PCOS are at increased risk of developing serious complication during pregnancy (1). Maternal complications are GDM, PIH and preeclampsia, and increased chance of caesarean section. Fetal complications includes premature delivery, SGA, LGA, admission to NICU and increased perinatal mortality. The metaanalysis published by Boomsma al in 2006 included 15 studies with a total of 720 women in PCOS and 4505 controls.

According to this study the risk of PIH, preeclampsia, GDM, preterm delivery, SGA, macrosomia is high compared to non PCOS.(odds ratio – PIH = 3.67 (1.96-6.81), Preeclampsia = 3.47 (1.95-6.17), GDM=2.94 (1.70-5.08), preterm delivery =1.75(1.16-2.62), SGA=1.16(0.31-5.12), Marcosomia =1.13(0.73-1.75) .According to Boomsma et al 2006 (1) metaanalysis GDM is about 3 times higher in women with PCOS compared to those without PCOS.

In a study by Mikola M (2) GDM developed in 20% of the PCOS patients and in 8.9% of the controls (P < 0.001). After logistic regression analysis, BMI >25 seemed to be the greatest predictor for GDM (adjusted OR 5.1; CI 3.2-8.3), while PCOS remained as another independent predictor (adjusted OR 1.9; CI 1.0-3.5).

A metaanalysis by Constantin A (3) evaluated the risk of GDM in women with PCOS and included 15 studies. Women with PCOS demonstrated significantly higher risk for development of GDM, yet with significant between-study heterogeneity. In the subgroup of cohort studies, this finding remained robust (7.11, 95% CI 2.95–17.12), whereas in the subgroup of case-control studies, it did not (0.89, 95% CI 0.38–2.06).

More recently Joham et al 2014 (4) conducted a large community based cohort study of reproductive aged women, and found that PCOS prevalence was 5.8% (95% confidence interval (CI): 5.3%–6.4%). Hypertension prevalence was 5.5% (95% CI: 3.3–7.7) in women reporting PCOS and 2.0% (95% CI: 1.6–2.3) in women not reporting PCOS. In this large community based cohort of reproductive-aged women, PCOS was independently associated with a higher risk of GDM and T2DM, independent of body mass index. In women aged 28-33 years, PCOS prevalence was 5.8% [95% confidence interval (CI) 5.3%-6.4%]. The prevalence of GDM (in women reporting prior pregnancy) and T2DM was 11.2% and 5.1% in women with PCOS and 3.8% and 0.3% in women without PCOS, respectively (P for both < .001). PCOS was associated with an increased odds of GDM and T2DM. After

adjusting for age, body mass index, hypertension, smoking, and demographic factors, the odds of GDM (odds ratio 2.1, 95% CI 1.1-3.9, P = .02) and T2DM (odds ratio 8.8, 95% CI 3.9-20.1, P < .001) remained increased in women reporting PCOS (5).

Another study by Turhan NO et al showed that a family history of diabetes mellitus, pre-pregnancy body mass index (BMI) and gestational weight gain was significantly higher in PCOS patients than controls. The prevalence of gestational diabetes mellitus (GDM) was similar in both groups. Impaired glucose tolerance (IGT) was observed in 18.4% of PCOS patients vs. 5.1% of controls. The main predictor of GDM was found pre-pregnancy BMI >25 while main predictor of IGT was found as PCOS (6).

A systematic review and metaanalysis of a total of 27 studies, involving 4982 women with PCOS and 119692 controls was done (7). Women with PCOS demonstrated a significantly higher risk of developing GDM (OR3.43; 95% CI: 2.49-4.74), PIH (OR3.43; 95% CI: 2.49-4.74), preeclampsia (OR2.17; 95% CI: 1.91-2.46), preterm birth (OR1.93; 95%CI: 1.45-2.57), caesarean section (OR 1.74; 95% CI: 1.38-2.11) compared to controls.

Conclusion

Hypertension disorders in pregnancy like gestational hypertension, preeclampsia, chronic hypertension and diabetes (both gestational diabetes and overt diabetes) rate were significantly increased in pregnant women with PCOS.

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