

## A Hospital Based Observational Assessment of the Risk of GDM in Antenatal Mothers with Previous History of PCOS

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### Abstract

**Aim:** The aim of the present study was to evaluate the risk of GDM in antenatal mothers with previous history of PCOS.

**Methods:** The present study was conducted in the Department of Obstetrics and Gynaecology, Sri Krishna Medical college & Hospital. Muzaffarpur, Bihar, India from For one year and including 1950 pregnant women, the medical records of 200 women diagnosed with PCOS were evaluated.

**Results:** A total of 200 women reported a history of PCOS. Women with PCOS before early pregnancy were more likely to be older, had higher prepregnancy BMI, and used assisted reproductive technology compared with women without PCOS. In the adjusted analysis, women with a previous diagnosis of PCOS had a higher risk for GDM than women with no such diagnosis (adjusted OR 1.55, 95% CI: 1.14–2.09). There was also a strong association between PCOS and preterm birth (adjusted OR 1.69, 95% CI: 1.08–2.67). In the stratified analysis using multivariable logistic regression, the adjusted OR for GDM among women with PCOS undergoing assisted reproductive technology was 1.44 (95% CI: 1.03–1.92) and among women with PCOS who conceived spontaneously was 1.60 (1.18–2.15) (Figure 1). Also, the risk of preterm birth was increased in women with PCOS regardless of use of assisted reproductive technology. There was no difference in the incidence of other adverse birth outcomes.

**Conclusion:** Our results suggest that women with PCOS were more likely to develop GDM and experience preterm birth. Future longitudinal studies are needed to better determine the underlying processes of PCOS during gestation and to develop efficient preventive strategies to preclude the adverse effects on both the mother and child.

**Keywords:** Gestational Diabetes Mellitus, Polycystic Ovary Syndrome, antenatal mothers

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### Introduction

Gestational diabetes mellitus (GDM) and polycystic ovary syndrome (PCOS) are the most common endocrine disorders in women of reproductive age. The prevalence of GDM varies from 9% to 25% and the prevalence of PCOS varies from 5% to 15%, depending on the study populations and the diagnostic criteria applied. [1-5] Both disorders are associated with insulin resistance and overweight/obesity. [6,7] Also, genetic factors play a significant role in both conditions. [8,9]

As one of the most common endocrine disorder affecting women during the reproductive years, polycystic ovary syndrome (PCOS) is a syndrome of ovarian dysfunction characterized by chronic

anovulation, hyperandrogenism, and typical morphologic changes of the ovaries based on ultrasonographic examination. [10-12] The prevalence of PCOS is estimated to be 5.00%-14.00% among women during the reproductive years [13-15] and affected patients often present with symptoms and signs of menstrual irregularity, obesity and infertility. [16]

Recent studies [17] have shown that in addition to the above mentioned factors, a history of polycystic ovarian syndrome (PCOS) may be a risk factor for GDM. PCOS is the most common endocrine disorder in women [18] during the reproductive ages

and is often accompanied by insulin resistance and hyperinsulinemia.

Since pregnancy can cause insulin resistance, it seems that patients with PCOS have a greater risk for GDM [19-21] during pregnancy. Nevertheless, in one study [12] no relationship between GDM and PCOS was demonstrated. Because of the high incidence of GDM and the benefits that are associated with early diagnosis and timely intervention, these patients should be followed closely during pregnancy and in the future for the onset of type 2 diabetes mellitus. Knowledge regarding the risk factors of this disease is therefore important so as to diagnose this disorder through early screening. From an economic standpoint it is better to do screening of GDM in patients with risk factors for GDM.

The aim of the present study was to evaluate the risk of GDM in antenatal mothers with previous history of PCOS.

### Materials and Methods

The present study was conducted in the Department of Obstetrics and Gynaecology, Sri Krishna Medical college & Hospital, Muzaffarpur, Bihar, India for one year and including 1950 pregnant women, the medical records of 200 women diagnosed with PCOS were evaluated.

The inclusion criteria were singleton pregnancies, <13 weeks of gestation at the first antenatal visit, and history of screening for GDM. Exclusion criteria were multiple gestation pregnancies, history of preexisting diabetes, and missing delivery information. In total, data on 2389 deliveries were obtained from electronic medical records, including demographic data, maternal medical history, and labor and delivery information. We examined outpatient medical records to identify women who were diagnosed at least once with PCOS before early pregnancy (<13 weeks of gestation). PCOS was diagnosed according to the Rotterdam 2003 criteria [11], with presence of at least two of three criteria, including polycystic ovaries, oligomenorrhea, and hyperandrogenism. Polycystic ovaries were detected by ultrasound and defined as 12 or more follicles of 2–9 mm and ovarian volume  $\geq 10$  mL in at least one ovary. Oligomenorrhea was defined by a length of menstrual cycle >35 days or <10 periods/year. Hyperandrogenism was defined based on laboratory and/or clinical symptoms. The only assisted

reproductive technology women underwent was in vitro fertilization.

### GDM and Birth Outcomes

#### Diagnosis of GDM

All pregnant women at the Hospital in underwent a routine 75 g oral glucose tolerance test between 24 and 28 weeks of gestation. GDM was diagnosed according to the modified International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria when one or more of the following glucose levels were elevated: fasting plasma glucose level  $\geq 5.1$  mmol/L, 1 h plasma glucose level  $\geq 10.0$  mmol/L, and 2 h plasma glucose level  $\geq 8.5$  mmol/L.

#### Preterm Birth

Preterm birth was defined as birth at <37 weeks of gestation, classified as moderately (32+0 to 36+6 weeks) and very preterm birth (<32 weeks).

#### Low Birth Weight and Macrosomia

Low birth weight (LBW) was defined as a birth weight <2500 g. Macrosomia was defined as a birth weight  $\geq 4000$  g.

#### Potential Confounders

Potential confounders included characteristics with a possible association with GDM, preterm birth, and fetal growth, including maternal age, maternal education, parity, prepregnancy body mass index (BMI), use of assisted reproductive technology, gestational age at delivery, and newborn sex. Data were obtained from hospital medical records.

#### Statistical Analysis

We compared women with PCOS and those without PCOS group using the chi-squared test for categorical variables and *t*-test for continuous variables. Multivariable logistic regression models were used to examine the association of the risk for GDM and adverse birth outcomes with PCOS after adjusting for confounders. The crude and adjusted odds ratios (ORs) with 95% confidence intervals (95% CIs) were computed to estimate the degree of association.

All *P* values <0.05 were considered statistically significant. Statistical analysis was performed using the statistical package SPSS, version 20 (SPSS Inc., Chicago, IL).

#### Results

**Table 1: Maternal and newborn characteristics according to polycystic ovary syndrome (PCOS) status**

Characteristics	Women with PCOS N=200	Women without PCOS N=1950	P Value
<b>Maternal characteristics</b>			
Age at birth (years)	29.7 ± 3.6	28.6 ± 3.2	<0.001
<25	16	165	<0.001
25–29	90	1150	
30–34	76	545	
≥35	18	90	
<b>Education</b>			
Junior high school or lower	22	181	0.634
High school	58	550	
College	96	980	
Undergraduate or higher	24	239	
<b>Prepregnancy BMI</b>			
≤18.4	20	220	<0.001
18.5–24.9	150	1620	
25.0–29.9	24	88	
≥30.0	6	22	
<b>Parity</b>			
0	192	1760	0.002
≥1	8	190	
<b>Assisted reproductive technology</b>			
Yes	30	60	<0.001
No	170	1890	
<b>Newborn characteristics</b>			
Sex			
Male	110	1050	0.832
Female	90	900	
Mean gestational age (weeks)	39.4 ± 1.5	39.6 ± 1.2	0.105
Mean birth weight (g)	3248 ± 428	3224 ± 408	0.185
<b>Delivery mode</b>			
Vaginal delivery	128	1255	0.654
Cesarean delivery	72	695	

A total of 200 women reported a history of PCOS. Women with PCOS before early pregnancy were more likely to be older, had higher prepregnancy BMI, and used assisted reproductive technology compared with women without PCOS.

**Table 2: Risk of gestational diabetes mellitus (GDM) and adverse birth outcomes in women with polycystic ovary syndrome (PCOS) versus women without PCOS**

Characteristics	Women with PCOS (n= 200)	Women without PCOS (n = 1950)	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)*
GDM				
Yes	36	224	1.52 (1.13, 2.03)	1.55 (1.14, 2.09)
No	164	1726	Reference	Reference
Preterm birth				
Yes	18	85	1.93 (1.26, 2.95)	1.69 (1.08, 2.67)
No	182	1865	Reference	Reference
Small for gestational age				
Yes	16	185	0.92 (0.62, 1.37)	0.79 (0.51, 1.23)
No	184	1765	Reference	Reference
Large for gestational age				
Yes	25	176	1.43 (1.00, 2.03)	1.39 (0.98, 1.99)
No	175	1774	Reference	Reference
Low birth weight				
Yes	12	102	1.13 (0.70, 1.84)	1.20 (0.74, 1.95)

No Macrosomia	188	1848	Reference	Reference
Yes	14	80	1.56 (0.98, 2.52)	1.21 (0.94, 2.01)
No	186	1870	Reference	Reference

In the adjusted analysis, women with a previous diagnosis of PCOS had a higher risk for GDM than women with no such diagnosis (adjusted OR 1.55, 95% CI: 1.14–2.09). There was also a strong association between PCOS and preterm birth (adjusted OR 1.69, 95% CI: 1.08–2.67). In the stratified analysis using multivariable logistic regression, the adjusted OR for GDM among women with PCOS undergoing assisted reproductive technology was 1.44 (95% CI: 1.03–1.92) and among women with PCOS who conceived spontaneously was 1.60 (1.18–2.15) (Figure 1). Also, the risk of preterm birth was increased in women with PCOS regardless of use of assisted reproductive technology. There was no difference in the incidence of other adverse birth outcomes.

### Discussion

Polycystic ovary syndrome (PCOS), one of the most common endocrine disorders occurring during reproductive age, is characterized by ovulatory dysfunction, biochemical or clinical hyperandrogenism, and polycystic ovaries. [23] Its prevalence ranges from 5% to 20% depending on the diagnostic criteria used. [24,25] PCOS is currently considered a syndrome with metabolic consequences that could affect women's health during different stages of reproductive age. [26]

A total of 200 women reported a history of PCOS. Women with PCOS before early pregnancy were more likely to be older, had higher prepregnancy BMI, and used assisted reproductive technology compared with women without PCOS. There are three possible explanations: (1) PCOS has different characteristics and clinical impact in different ethnic groups, (2) increased insulin resistance in PCOS has different clinical effects depending on the insulin metabolism characteristic of different ethnicities and environments, and (3) the prevalence of GDM in women with PCOS is affected by the different diagnosis criteria (the WHO or the modified IADPSG criteria). [27] In addition, PCOS is a major cause of infertility in women, and these women might require assisted reproductive technology to become pregnant. [28] Some studies have suggested that assisted reproductive technology is associated with an increased risk of GDM [29-31] which indicated that women with pregnancies that were conceived while undergoing assisted reproductive technology have impaired glucose tolerance compared with those who conceived spontaneously.

In the adjusted analysis, women with a previous diagnosis of PCOS had a higher risk for GDM than

women with no such diagnosis (adjusted OR 1.55, 95% CI: 1.14–2.09). There was also a strong association between PCOS and preterm birth (adjusted OR 1.69, 95% CI: 1.08–2.67). In the stratified analysis using multivariable logistic regression, the adjusted OR for GDM among women with PCOS undergoing assisted reproductive technology was 1.44 (95% CI: 1.03–1.92) and among women with PCOS who conceived spontaneously was 1.60 (1.18–2.15). Also, the risk of preterm birth was increased in women with PCOS regardless of use of assisted reproductive technology. There was no difference in the incidence of other adverse birth outcomes. In previous reports, women with PCOS often required assisted reproductive technology to become pregnant, increasing the risk of multiple births and hypertensive disease, which are associated with preterm birth. [32-34] The association between PCOS and preterm birth may thus be an interaction with assisted reproductive technology. In our stratified analysis, the results did not support the statement that adverse pregnancy outcomes among women with PCOS were mediated by assisted reproductive technology. There was no significant association between the interaction of PCOS with assisted reproductive technology and preterm birth. This indicates that PCOS is also an independent risk factor of preterm birth. This finding is supported by two studies from Northern Europe [35], which reported that preterm birth associated with assisted reproductive technology could be explained by factors that lead to infertility, rather than the assisted reproductive technology.

### Conclusion

Our results suggest that women with PCOS were more likely to develop GDM and experience preterm birth. Future longitudinal studies are needed to better determine the underlying processes of PCOS during gestation and to develop efficient preventive strategies to preclude the adverse effects on both the mother and child.

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