

A Hospital Based Observational Study to Evaluate the Risk of GDM in Antenatal Mothers with Previous History of PCOS

Tanu Sharma¹, Abhishek Ranjan², Minu Sharan³

¹Senior Resident, Department of Obstetrics and Gynaecology, Patna Medical College and Hospital, Patna, Bihar, India

²Assistant Professor, Department of General Surgeon, Katihar medical college and Hospital, Katihar, Bihar, India

³Professor, Department of Obstetrics and Gynaecology, Patna Medical College and Hospital, Patna, Bihar, India

Received: 08-12-2023 / Revised: 10-01-2024 / Accepted: 23-02-2024

Corresponding Author: Dr. Abhishek Ranjan

Conflict of interest: Nil

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, Patna Medical College and Hospital, Patna, Bihar, India 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

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

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, Patna Medical College and Hospital, Patna, Bihar, India for 12 months 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 ≥ 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 antenatal clinic 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 ≥ 5.1 mmol/L, 1 h plasma glucose level ≥ 10.0 mmol/L, and 2 h plasma glucose level ≥ 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 ≥ 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
Maternal characteristics			
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	
Education			
Junior high school or lower	22	181	0.634
High school	58	550	
College	96	980	
Undergraduate or higher	24	239	
Prepregnancy BMI			
≤18.4	20	220	<0.001
18.5–24.9	150	1620	
25.0–29.9	24	88	
≥30.0	6	22	
Parity			
0	192	1760	0.002
≥1	8	190	
Assisted reproductive technology			
Yes	30	60	<0.001
No	170	1890	
Newborn characteristics			
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
Delivery mode			
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	188	1848	Reference	Reference
Macrosomia				
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.

References

1. Norman RJ, Dewailly D, Legro RS, Hickey TE. Polycystic ovary syndrome. *Lancet*. 2007 Aug 25;370(9588):685-97.
2. Roos N, Kieler H, Sahlin L, Ekman-Ordeberg G, Falconer H, Stephansson O. Risk of adverse pregnancy outcomes in women with polycystic ovary syndrome: population based cohort study. *BMJ*. 2011 Oct 13;343:d6309.
3. Sacks DA, Hadden DR, Maresh M, Deerochanawong C, Dyer AR, Metzger BE, Lowe LP, Coustan DR, Hod M, Oats JJ, Persson B, Trimble ER; HAPO Study Cooperative Research Group. Frequency of gestational diabetes mellitus at collaborating centers based on IADPSG consensus panel-recommended criteria: the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study. *Diabetes Care*. 2012 Mar;35(3):526-8.
4. Helseth R, Vanky E, Salvesen O, Carlsen SM. Gestational diabetes mellitus among Norwegian

- women with polycystic ovary syndrome: prevalence and risk factors according to the WHO and the modified IADPSG criteria. *Eur J Endocrinol*. 2013 Jun 7;169(1):65-72.
5. Koivunen S, Kajantie E, Torkki A, Bloigu A, Gissler M, Pouta A, Väärasmäki M. The changing face of gestational diabetes: the effect of the shift from risk factor-based to comprehensive screening. *Eur J Endocrinol*. 2015 Nov;173(5):623-32.
 6. Bhatena RK. Insulin resistance and the long-term consequences of polycystic ovary syndrome. *J Obstet Gynaecol*. 2011;31(2):105-10.
 7. Hildén K, Hanson U, Persson M, Fadl H. Overweight and obesity: a remaining problem in women treated for severe gestational diabetes. *Diabet Med*. 2016 Aug;33(8):1045-51.
 8. Vink JM, Sadrzadeh S, Lambalk CB, Boomsma DI. Heritability of polycystic ovary syndrome in a Dutch twin-family study. *J Clin Endocrinol Metab*. 2006 Jun;91(6):2100-4.
 9. Lowe WL Jr, Scholtens DM, Sandler V, Hayes MG. Genetics of Gestational Diabetes Mellitus and Maternal Metabolism. *Curr Diab Rep*. 2016 Feb;16(2):15.
 10. Hart R. Polycystic ovarian syndrome—prognosis and treatment outcomes. *Curr Opin Obstet Gynecol*. 2007;19(6):529–535.
 11. Dunaif A. Insulin resistance and the polycystic ovary syndrome: mechanism and implications for pathogenesis. *Endocr Rev*. 1997;18(6):774–800.
 12. Rotterdam EA-SPcwg. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS) *Hum Reprod*. 2004;19 (1): 41–47.
 13. Asuncion M, Calvo RM, San Millan JL, Sancho J, Avila S, Escobar-Morreale HF. A prospective study of the prevalence of the polycystic ovary syndrome in unselected Caucasian women from Spain. *J Clin Endocrinol Metab*. 2000;85(7):2434–2438.
 14. Eilertsen TB, Vanky E, Carlsen SM. Increased prevalence of diabetes and polycystic ovary syndrome in women with a history of preterm birth: a case-control study. *BJOG*. 2012;119(3):266–275.
 15. Khorshidi A, Azami M, Tardeh S, Tardeh Z. The prevalence of metabolic syndrome in patients with polycystic ovary syndrome: A systematic review and meta-analysis. *Diabetes Metab Syndr*. 2019;13(4):2747–2753.
 16. Eroglu D, Zeyneloglu HB. Metabolic disorders in patients with recent gestational diabetes mellitus. *J Obstet Gynaecol Res*. 2006;32(4): 408–415.
 17. Holte J, Gennarelli G, Wide L, Lithell H, Berne C. High prevalence of polycystic ovaries and associated clinical, endocrine, and metabolic features in women with previous gestational diabetes mellitus. *The Journal of Clinical Endocrinology & Metabolism*. 1998 Apr 1;83(4):1143-50.
 18. Speroff L, Fritz MA, editors. *Clinical gynecologic endocrinology and infertility*. lippincott Williams & wilkins; 2005.
 19. Radon PA, McMahon MJ, Meyer WR. Impaired glucose tolerance in pregnant women with polycystic ovary syndrome. *Obstetrics & Gynecology*. 1999 Aug 1;94(2):194-7.
 20. Anttila L, Karjala K, Penttilä TA, Ruutiainen K, Ekblad U. Polycystic ovaries in women with gestational diabetes. *Obstetrics & Gynecology*. 1998 Jul 1;92(1):13-6.
 21. Mikola M, Hiilesmaa V, Halttunen M, Suhonen L, Tiitinen A. Obstetric outcome in women with polycystic ovarian syndrome. *Human reproduction*. 2001 Feb 1;16(2):226-9.
 22. Haakova L, Cibula D, Rezabek K, Hill M, Fanta M, Zivny J. Pregnancy outcome in women with PCOS and in controls matched by age and weight. *Human Reproduction*. 2003 Jul 1;18(7):1438-41.
 23. Goodarzi MO, Dumesic DA, Chazenbalk G, Azziz R. Polycystic ovary syndrome: etiology, pathogenesis and diagnosis. *Nature reviews endocrinology*. 2011 Apr;7(4):219-31.
 24. Roos N, Kieler H, Sahlin L, Ekman-Ordeberg G, Falconer H, Stephansson O. Risk of adverse pregnancy outcomes in women with polycystic ovary syndrome: population based cohort study. *Bmj*. 2011 Oct 13;343.
 25. Reyes-Muñoz E, Castellanos-Barroso G, Ramírez-Eugenio BY, Ortega-González C, Parra A, Castillo-Mora A, Julio F. The risk of gestational diabetes mellitus among Mexican women with a history of infertility and polycystic ovary syndrome. *Fertility and sterility*. 2012 Jun 1;97(6):1467-71.
 26. Palomba S, De Wilde MA, Falbo A, Koster MP, La Sala GB, Fauser BC. Pregnancy complications in women with polycystic ovary syndrome. *Human reproduction update*. 2015 Sep 1;21(5):575-92.
 27. Helseth R, Vanky E, Salvesen Ø, Carlsen SM. Gestational diabetes mellitus among Norwegian women with polycystic ovary syndrome: prevalence and risk factors according to the WHO and the modified IADPSG criteria. *European journal of endocrinology*. 2013 Jul;169(1):65-72.
 28. Rajashekar L, Krishna D, Patil M. Polycystic ovaries and infertility: our experience. *Journal of human reproductive sciences*. 2008 Jul 1;1 (2):65-72.
 29. Wang YA, Nikravan R, Smith HC, Sullivan EA. Higher prevalence of gestational diabetes mellitus following assisted reproduction

- technology treatment. *Human Reproduction*. 2013 Sep 1;28(9):2554-61.
30. Jones BJ, Zöllner J, Haynes S, Cheng F, Dornhorst A. In vitro fertilization treatment influences glucose tolerance in multiple pregnancy. *Diabetic Medicine*. 2013 Feb;30(2):252-4.
31. Ashrafi M, Gosili R, Hosseini R, Arabipoor A, Ahmadi J, Chehrazai M. Risk of gestational diabetes mellitus in patients undergoing assisted reproductive techniques. *European Journal of Obstetrics & Gynecology and Reproductive Biology*. 2014 May 1;176:149-52.
32. Boomsma CM, Eijkemans MJ, Hughes EG, Visser GH, Fauser BC, Macklon NS. A meta-analysis of pregnancy outcomes in women with polycystic ovary syndrome. *Human reproduction update*. 2006 Nov;12(6):673-83.
33. Eilertsen TB, Vanky E, Carlsen SM. Increased prevalence of diabetes and polycystic ovary syndrome in women with a history of preterm birth: a case-control study. *BJOG: An International Journal of Obstetrics & Gynaecology*. 2012 Feb;119(3):266-75.
34. Sterling L, Liu J, Okun N, Sakhujia A, Sierra S, Greenblatt E. Pregnancy outcomes in women with polycystic ovary syndrome undergoing in vitro fertilization. *Fertility and sterility*. 2016 Mar 1;105(3):791-7.
35. Romundstad LB, Romundstad PR, Sunde A, von Düring V, Skjærven R, Gunnell D, Vatten LJ. Effects of technology or maternal factors on perinatal outcome after assisted fertilisation: a population-based cohort study. *The Lancet*. 2008 Aug 30;372(9640):737-43.