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RESEARCH ARTICLE

RISK OF ADVERSE PREGNANCY OUTCOMES IN WOMEN WITH POLYCYSTIC OVARY SYNDROME

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Abstract

Objective: To study the risk of adverse pregnancy outcomes in women with polycystic ovary syndrome
Design: Population based cohort study.
Participants: patient attending OPD in ChalmedaAnand Rao institute of medical sciences 100 births among women with a diagnosis of polycystic ovary syndrome and 100 births among women without such a diagnosis.
Main outcome measures: Risk of adverse pregnancy outcomes (gestational diabetes, pre-eclampsia, preterm birth, stillbirth, neonatal death, low Apgar score (<7 at five minutes), meconium aspiration, large for gestational age, macrosomia, small for gestational age), adjusted for maternal characteristics (body mass index, age), socioeconomic factors
Results: Women with polycystic ovary syndrome were more often obese. Polycystic ovary syndrome was strongly associated with pre-eclampsia and very preterm birth and the risk of gestational diabetes was more than doubled . Infants born to mothers with polycystic ovary syndrome were more prone to be large for gestational age and were at increased risk of meconium aspiration and having a low Apgar score (<7) at five minutes
Conclusions: Women with polycystic ovary syndrome are at increased risk of adverse pregnancy and birth outcomes These women may need increased surveillance during pregnancy and parturition.

Introduction:-

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder of reproductive-aged women[1,2]. Polycystic ovary syndrome is one of the most common endocrine disorders, affecting about 5-15% of women of reproductive age[3].The condition is characterised by oligo-ovulation or anovulation, biochemical or clinical hyperandrogenism, and polycystic ovaries.According to the Rotterdam criteria polycystic ovarian syndrome (PCOS) is defined by the presence of two of three of the following criteria: oligo-anovulation, hyperandrogenism and polycystic ovaries (≥ 12 follicles measuring 2-9 mm in diameter and/or an ovarian volume > 10 mL in at least one ovary)[4].The cause of polycystic ovary syndrome is not fully understood, but evidence of a genetic component has been recognised in family and twin studies[5].Oligo-ovulation or anovulation in women with polycystic ovary syndrome is a major cause of infertility, and such women might require ovulation induction or assisted reproductive

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technology to become pregnant[6]. The insulin resistance in at least 50% of PCOS women appears to be related to excessive serine phosphorylation of the insulin receptor. A factor extrinsic to the insulin receptor, presumably a serine/threonine kinase, causes this abnormality and is an example of an important new mechanism for human insulin resistance related to factors controlling insulin receptor signaling. Serine phosphorylation appears to modulate the activity of the key regulatory enzyme of androgen biosynthesis, P450c17. It is thus possible that a single defect produces both the insulin resistance and the hyperandrogenism in some PCOS women .In total, 80% of women affected by anovulatory infertility have PCOS, which is further adversely affected by excess weight[8,9,10]

Lifestyle modifications can change the metabolic and endocrine consequences of having polycystic ovary syndrome, thus possibly improving infertility caused by anovulation[7].

Studies suggests that polycystic ovary syndrome has a negative impact on pregnancy outcomes, with an increased risk of gestational diabetes, hypertensive disease during pregnancy. Rates of preterm delivery (PTD) in women with PCOS are increased, particularly for those with hyperandrogemia[9]

Consequently the extent to which the risk of adverse pregnancy outcomes in women with polycystic ovary syndrome is attributed to the underlying disorder or infertility treatment is uncertain.

Methods:-

From the OPD patient of ChalmedaAnand Rao institute of medical sciences birth register we created a cohort among women with singleton pregnancies giving birth between 2021and 2022. Because twin and multiple pregnancies differ in fetal growth and duration of gestation and have a higher occurrence of complications during pregnancy we excluded such pregnancies from the study population.Using the unique personal identification number assigned to each patient. We recorded the date of the first diagnosis of polycystic ovary syndrome

Data from the medical birth register includes information on the mother as well as the pregnancy, delivery, and neonatal period. Data are prospectively collected, starting at the woman's first antenatal visit.

We classified maternal age (years) at birth into four groups: 13-24, 25-29, 30-34, and ≥35. Body mass index was calculated (weight (kg)/(height $(m)^2$) and the women categorised as lean (body mass index ≤19.9), normal weight (20.0-24.9), overweight (25.0-29.9), or obese (≥30.0). Parity was classified into nulliparous or parous women. Through linkage with the education register we obtained information on the number of years of formal education completed categorised as 11 or fewer or 12 or more. The medical birth register also contains information on concurrent diseases such as diabetes mellitus and essential hypertension . Pre-eclampsia was defined as a blood pressure reading of 140/90 mm Hg or more with proteinuria of more than 0.3 g over 24 hours. Gestational diabetes was, according to clinical practice, defined as plasma glucose levels of 12.2 mmol/L or more after oral glucose tolerance test (75 g glucose orally administered and plasma glucose measured after two hours) or fasting blood glucose levels of 7.0 mmol/L or more. Infants born small for gestational age were defined as having birth weights of less than 2 standard deviations below the mean for gestational age and sex of the infant. Similarly, large for gestational age was defined as a birth weight of more than 2 standard deviations above the mean for gestational age. Macrosomia was defined as a birth weight of 4500 g or more. Post-term pregnancy was defined as delivery at 42 weeks or more of gestation and preterm birth as delivery at less than 37 weeks of gestation, classified as moderately (32+0 to 36+6 weeks) and very preterm birth (<32 weeks). Stillbirth was defined as intrauterine fetal death after 28 weeks of gestation. A low Apgar score was defined as less than 7 at five minutes. Neonatal death was defined as death of the infant from 0 to 27 days after birth. The presence of meconium aspiration was obtained by diagnosis at discharge.

Outcome:

The main outcome measures were gestational diabetes, pre-eclampsia, preterm birth, stillbirth, neonatal death, low Apgar score, meconium aspiration, large for gestational age, macrosomia, and small for gestational age. We compared women with a diagnosis of polycystic ovary syndrome with women with no PCOS, taking into account possible confounders, such as maternal age, body mass index, parity, years of formal educationandyear of delivery. Absolute rates were standardised for difference in characteristics between women with and without polycystic ovary syndrome.

Results:-

A total of 200 singleton births between 2021 and 2022 were included in the cohort, with 100 births among mothers with a diagnosis of polycystic ovary syndrome. Women with polycystic ovary syndrome were more likely to be

nulliparous than women with no PCOS (P<0.001). Women with polycystic ovary syndrome had an almost doubled prevalence of a body mass index greater than 25.0 (P<0.001). Giving birth at advanced maternal age (>35 years) was more common in women with than without polycystic ovary syndrome (P<0.001). Women with polycystic ovary syndrome were more likely to have hypertensive disease and diabetes mellitus than women without polycystic ovary syndrome

Table 1:- Characteristics of women with and without polycystic ovary syndrome (PCOS) giving birth to singleton pregnancies (200 total births).

Maternal characteristics	No of births (rate %)		P value*
	Women with PCOS (n=100)	Women without PCOS (n=100)	
Age (years):			
13-24	8 (8.95)	15 (15.85)	<0.001
25-29	30 (31.16)	32 (32.74)	
30-34	40 (40.01)	33 (33.85)	
≥35	19 (19.88)	17 (17.55)	
Body mass index:			
≤19.9	4 (4.53)	9 (9.91)	<0.001
20.0-24.9	34 (34.88)	55 (55.33)	
25.0-29.9	28 (28.52)	24 (24.51)	
≥30.0	32 (32.07)	10 (10.25)	
Parity:			
0	50 (52.55)	42 (43.66)	<0.001
≥1	47 (47.45)	56 (56.34)	
Education level (years):			
≤11	56 (56.69)	56 (56.11)	0.47
≥12	43 (43.31)	43 (43.89)	
Essential hypertension:			
Yes	1 (0.69)	1 (0.28)	<0.001
No	99 (99.31)	99 (99.72)	
Diabetes mellitus:			
Yes	3 (2.01)	1 (0.38)	<0.001

Table 2:- Pregnancy outcomes in women with and without polycystic ovary syndrome (PCOS) giving birth to singleton pregnancies (200 total births).

Pregnancy outcomes	No of births (rate %)	P value

	Women with PCOS (n=100)	Women without PCOS (n=100)	
Gestational diabetes:			
Yes	4 (3.30)	1 (0.90)	<0.001
No	96 (96.70)	99 (99.10)	
Pre-eclampsia:			
Yes	6 (5.84)	3 (2.95)	
No	94 (94.16)	97 (97.05)	<0.001
Antepartum bleeding or placental complications:			
Yes	2 (1.56)	2 (1.22)	
No	98 (98.44)	98 (98.78)	0.37
Caesarean section:			
Yes	23 (22.44)	15 (14.68)	
No	77 (77.56)	85 (85.32)	0.001
Data missing	0	30	
Very preterm birth (<31+6 weeks)			
Yes	2 (1.73)	1 (0.67)	
No	98 (98.27)	99 (99.33)	<0.001
Moderately preterm birth (32+0 to 36+6 weeks)			
Yes	6 (6.11)	4 (4.27)	

Table 3:- Perinatal outcomes in women with and without polycystic ovary syndrome (PCOS) giving birth to singleton pregnancies 200 total births).

Perinatal outcomes	No of births (rate %)		P Value
	Women with PCOS (n=100)	Women without PCOS (n=100)	
Stillbirth:			
Yes	1 (0.45)	1 (0.33)	
No	99 (99.55)	9 (99.67)	0.73
Apgar score <7 at 5 minutes:			
Yes	2 (1.89)	1 (1.10)	0.0095
No	98 (98.11)	99 (98.90)	

Discussion:-

In the present population based study a diagnosis of polycystic ovary syndrome was associated with increased risks of adverse pregnancy outcomes that could not be attributed to maternal characteristics such as advanced age or being overweight or obese.

Maternal obesity is associated with increased birth weight in offspringswell as glucose intolerance and gestational diabetes.Women with polycystic ovary syndrome are in general more overweight than women without the condition. The estimates in the present study were, however, adjusted for body mass index, suggesting that polycystic ovary syndrome may increase the rate of fetal growth independently. Women with polycystic ovary syndrome are, regardless of body mass index, at increased risk of developing gestational diabetes. Infants born to mothers with polycystic ovary syndrome were more likely to have low Apgar scores at five minutes and experience meconium aspiration. These infants may be more susceptible to fetal distress during labour. However, there was no association with stillbirth, and the increased risk for neonatal death was not statistically significant.

Women with polycystic ovary syndrome can conceive spontaneously but with a delayed fertile window since there is a tendency of regular menstrual cycles with advancing age. In the present study we found that women with polycystic ovary syndrome were slightly older than women without polycystic ovary syndrome. Advanced maternal age is strongly correlated with many of the adverse pregnancy outcomes in this study however, although we adjusted for maternal age in the multivariate analysis, a residual effect could still be possible.

Strengths and limitations of the study:

A major strength of this study was the sample size, making it possible to study rare pregnancy outcomes such as stillbirth, meconium aspiration, low Apgar scores at five minutes, and neonatal death. Women with polycystic ovary syndrome according to the Rotterdam criteria,and not seeking medical assistance for irregular menstrual periods or infertility problems, might have been incorrectly classified as not having the disease. Such misclassification would lead to an underestimation of the association between polycystic ovary syndrome and adverse pregnancy outcomes. When the National Institutes of Health and Rotterdam criteria for polycystic ovary syndrome were compared, the prevalence was doubled. Furthermore, it is likely that we included women with more severe disease as exposed, and the findings may consequently not be generalisable to all women with polycystic ovary syndrome.

Possible pathophysiological mechanisms

The pathophysiological mechanisms behind the increased risk of adverse pregnancy outcomes among women with polycystic ovary syndrome are not fully known. In this study, polycystic ovary syndrome was associated with being overweight and obese, with an increased risk of macrosomia and large for gestational age infants, even after adjustments for body mass index. A higher prevalence of pre-eclampsia and gestational diabetes may account for increased fetal stress leading to preterm birth, low Apgar scores at five minutes, and meconium aspiration. Women with polycystic ovary syndrome have increased levels of androgens, which have been associated with the development of pre-eclampsia. Metformin treatment during pregnancy does not seem to lower maternal androgen levels but has been shown to decrease severe pregnancy and post-partum complications, which may be mediated by reduced uterine artery impedance.

Conclusion:-

These women may need increased surveillance during pregnancy and parturition. Future research would benefit from focusing on glucose control, medical treatment, and hormonal status among women with polycystic ovary syndrome during pregnancy.

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