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Original Research Article

A Comparison of Pregnancy-Related Problems in Women with and Without Polycystic Ovarian Syndrome was Conducted (PCOS)

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Abstract

Aim: To comparative study of pregnancy- related complications of women with and without polycystic ovary syndrome (PCOS). **Methods:** The present Prospective study was conducted in the Department of Obstetrics and Gynecology, All India Institute of Medical Science, Patna, Bihar, India for 1 year. The study population consists of two groups Test group (100 Pregnant woman with polycystic ovarian syndrome) and Control group (100 Pregnant woman without polycystic ovarian syndrome). Woman with pre-existing medical conditions like Hypertension, Diabetes Mellitus, Hyperprolactinaemia, Antiphospholipid antibody syndrome, Systemic Lupus Erythematosus, thyroid disorders and those with twin gestation were excluded from the study. **Results:** The participants with overweight/obesity were 35% among the women with PCOS when compared to 25% among the women without PCOS (p=0.47). Proportion of primigravida among women with PCOS was 88% and among women without PCOS was 52%. Mode of conception was spontaneous in 58% and 80% among women with and without PCOS, respectively. IUI/IVF was the method of conception in 24% of women with PCOS, whereas only two women adopted IUI/IVF among the non-PCOS group. Gestational diabetes was reported in 25% women with PCOS as against 15% women without PCOS. the women who are overweight and obese/morbid obesity were found to have increased risk of GDM by 6.90 times and 10.89 times when compared to the normal women and it was found to be statistically significant. Similarly, GDM was found to be 1.35 times higher in Primigravida compared to multigravida women. Similarly, pre-eclampsia was found to be higher among the women with PCOS when compared to the women without PCOS (28% VS 11%). Women with PCOS were having 2.75 (1.12-6.96); p=0.039] times the higher risk of having pre- eclampsia. **Conclusion:** The risk factors for PCOS, Primigravida was significantly associated with the occurrence of PCOS after adjusting for the confounder. On the maternal complications front, PCOS was significantly associated with GDM and pre-eclampsia after adjusting for the confounders.

Keywords: PCOS, GDM, pre-eclampsia.

Introduction

Polycystic ovary syndrome (PCOS) is a common and complicated female endocrinopathy that estimated prevalence varies from 3%–20% depending on the diagnostic criteria used[1]. The most common features of PCOS are abnormal ovulation, clinical or laboratory indices of increased androgen levels, and polycystic ovaries on ultrasonography. Clinical manifestations of PCOS are menstrual irregularity (oligomenorrhea or amenorrhea), hirsutism, persistent acne, androgen dependent alopecia, abdominal obesity, hypertension and infertility[2]. Although the prevalence of PCOS and diversified clinical symptoms are known, the exact pathogenesis of PCOS is not fully recognized yet. It is commonly believed that insulin resistance, hyperandrogenism and obesity play a significant role on the pathophysiologic process of PCOS[3,4]. Insulin resistance is universally accepted as one of the key biochemical features of PCOS supported by complementary hyperinsulinemia, and is associated with ovarian secretion disorder increasing the androgen production by theca cells that lead to hyperandrogenism[5,6]. Obesity, a characteristic of 60–80% of PCOS patients, has a malignant additive effect on features of PCOS such as insulin resistance, hyperandrogenism, infertility, hirsutism and pregnancy complications[7]. However, the definite phenotype of PCOS (different combinations of oligo/anovulation, hyperandrogenism, polycystic ovaries), as well as the extent of obesity in PCOS patients influences the variation of insulin resistance level[8,9]. Furthermore, the interaction of insulin resistance, hyperandrogenism and obesity results in an increased risk of diabetes mellitus type 2 (DM2), metabolic syndrome (MS), cardiovascular diseases (CVD), pregnancy loss and late pregnancy complications (preeclampsia, gestational diabetes). This indicates that PCOS is a chronic disease that impacts women across the lifespan[10].

Nowadays 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 becoming increasingly recognized the problems of gestational diabetes (GDM), pregnancy-induced hypertension, preeclampsia, premature delivery rate, neo-natal birth weight, caesarean section rate, and rate and admission to an NICU, which are all considered to be adverse pregnancy outcomes of PCOS during pregnancy[11-13]. The elevated risk for adverse obstetric complications that was observed in women presenting PCOS varied widely depending on the different phenotypes and features of PCOS[14]. Women with PCOS tend to require ovulation induction or assisted reproductive technology (ART) in order to become pregnant due to oligo-ovulation or anovulation, this treatment for infertility often results in an evaluated rate of multiple births[15,16]. In order to explore the relationship between PCOS and pregnancy outcomes completely, the use of metformin, ovulation induction or ART must be taken into account.

Material and methods

The present Prospective study was conducted in the Department of Obstetrics and Gynecology, All India Institute of Medical Science, Patna, Bihar, India, for 1 year. The study population consists of two groups Test group (100 pregnant women with polycystic ovarian syndrome) and Control group (100 pregnant women without polycystic ovarian syndrome). Woman with pre-existing medical conditions like Hypertension, Diabetes Mellitus, Hyperprolactinaemia, Antiphospholipid antibody syndrome, Systemic Lupus Erythematosus, thyroid disorders and those with twin gestation were excluded from the study. On obtaining the informed consent, the interview was conducted by the investigator herself. The data was collected using the standardized

pretested structured interview schedule. Complete history and examination were done. Regular follow up of the participants up to delivery and pregnancy outcome in both test and control groups was carried out.

Results

The mean age of the participants was 27.5 years with a minimum of 18 years and a maximum of 35 years. The participants with overweight/obesity were 35% among the women with PCOS when compared to 25% among the women without PCOS (p=0.47). Proportion of primigravida among women with PCOS was 88% and among women without PCOS was 52%. Primigravida were having 3 times higher chance of presenting with PCOS when compared to the multigravida and it was found to be statistically significant (Table-1). Mode of conception was spontaneous in 58% and 80% among women with and without PCOS, respectively. IUI/IVF was the method of conception in 24% of women with PCOS, whereas only two women adopted IUI/IVF among the non-PCOS group. It can be noted that spontaneous abortion occurred in three and two women with PCOS and without PCOS respectively. Gestational diabetes was reported in 25% women with PCOS as against 15% women without PCOS.

Table 2 shows that the women who are overweight and obese/morbid obesity were found to have increased risk of GDM by 6.90 times and 10.89 times when compared to the normal women and it was found to be statistically significant. Similarly, GDM was found to be 1.35 times higher in Primigravida compared to multigravida women.

Similarly, pre-eclampsia was found to be higher among the women with PCOS when compared to the women without PCOS (28% VS 11%). Women with PCOS were having 2.75 (1.12-6.96); p=0.039] times the higher risk of having pre- eclampsia. Even after adjusting for confounders like age, BMI and parity, there was 2.51 times higher risk among women with PCOS to have pre-eclampsia. Similarly, as the age increases, the risk of pre-eclampsia also increases (Table-3).

Table 1: Univariate and multivariable logistic regression analysis of risk factors and its association with PCOS (N=100)

Characteristics	Unadjusted PR (95% CI)	p value	Adjusted PR (95% CI)	p value
Age in years	0.95 (0.91-1.14)	0.59	1.10 (0.95-1.01)	0.77
Socio-economic status				
Lower*				
Middle	1.11 (0.52-1.81)	0.17	1.24 (0.91-1.51)	0.26
Upper	-----	0.88	-----	0.97
BMI category				
Normal	1.11 (0.52-1.83)	0.89	0.97(0.52-1.63)	0.77
Overweight	1.41 (0.72-2.76)	0.31	1.45 (0.58-2.04)	0.21
Obesity/ Morbid* obesity				
Parity				
Primi	2.81 (1.42-5.71)	0.003	2.97(1.40-5.91)	0.004
Multi*				
Mode of conception				
Spontaneous*				
Ovulation induction/assisted	8.17 (0.96-70.80)	0.052	9.3 (0.3-267.6)	0.22

Table 2: Univariate and multivariable logistic regression analysis of gestational diabetes mellitus and its association with PCOS and other riskfactors (N=100)

Characteristics	Unadjusted PR (95% CI)	p value	Adjusted PR (95% CI)	p value
PCOS				
Yes	1.61 (0.68-3.78)	0.26	1.37 (1.22-1.50)	0.006
No*				
BMI category				
Obesity/ Morbid obesity	10.33 (4.14-31.72)	<0.001	17.21 (6.61-44.07)	<0.001
Overweight	6.88 (2.11-21.17)	0.001	6.11 (1.92-19.17)	0.003
Normal*				
Parity				
Primi	1.42 (0.53-3.38)	0.58	2.65 (1.21-5.03)	0.008
Multi*				

Table 3: Univariate and multivariable logistic regression analysis of pre-eclampsia and its association with PCOS and other risk factors (N=100)

Characteristics	Unadjusted PR (95% CI)	p value	Adjusted PR (95% CI)	p value
PCOS				
Yes	2.75 (1.12-6.96)	0.039	2.47 (1.23-5.17)	0.021
No*				
Age in years	1.11 (1.01-1.22)	0.044	1.15 (1.08-1.06)	<0.001
BMI category				
Obesity/ Morbid obesity	7.83 (3.01-20.92)	<0.001	10.10 (4.27-23.39)	<0.001
Overweight	5.47 (1.98-15.42)	0.003	3.87 (1.32-10.54)	0.013
Normal*				
Parity				
Primi	1.33 (0.55-3.31)	0.29	1.87 (1,76-1.72)	<0.001
Multi*				

*Variables used in the model: PCOS, age, BMI and parity

Discussion

This study showed that the mean age was comparable between both the groups. However, those with 32 years and above were significantly higher in PCOS group when compared to the pregnant women without PCOS. In addition to that, it is noteworthy to mention that 10 out of 15 women aged 32 years and above in PCOS group were primigravida and all the women either adopted IUI/IVF for getting pregnant, which explains the reason behind the age distribution and the higher proportion of primigravida above 32 years of age in the PCOS group. Infertility was invariably present in all the women who conceived after 32 years of age. The increased number of primigravida above 32 years of age could also be explained by the theory that androgen production in women may decrease as a result of ovarian ageing and decreased production of adrenal androgens, which in turn could result in the increasing number of mature follicles and thus more conception. However, there are no evidence supporting this plausibility and research done over this have resulted in inconsistent results.

A study conducted by Sterling L et al.[17] had reported a slightly higher mean age of the PCOS pregnant women. As supported by other well accepted theories, the number

of Primigravida among PCOS group was 88% in our study population as against 52% in the non PCOS women and it was statistically significant.

Among the risk factors for PCOS, our study showed that Primigravida was strongly associated with PCOS and PCOS women had higher BMI values (22% overweight & 15% obesity) compared to women without PCOS. Alvarez-Blasco F et al.[18], in his study in Spain has reported that the risk of PCOS was 5 times higher in obese women when compared to the normal women (28.3% vs 5.5%, respectively). The study demonstrated the prevalence of PCOS may be markedly increased in overweight and obese women. This supports the widely accepted hypothesis that overweight, and obesity are common among adolescent girls and adult women with PCOS. Insulin resistance which is present in PCOS suppresses adipocyte lipolysis, resulting in increased serum free fatty acids and triglycerides, ultimately leading to obesity. However, there are studies showing different results too. In a study, girls related to women with PCOS showed higher 17-hydroxyprogesterone concentrations, increased insulin resistance and decreased insulin induced suppression of fatty acid concentrations compared with healthy controls[19]. Also, many studies[20-22] have supported the hypothesis that obesity is a potential risk factor for PCOS similar to our study.

Our study doesn't show any association of PCOS with early pregnancy loss. Studies by Joham AE et al.[23], Jakubowicz DJ[24] and Gray RH et al.[25], have reported that women with PCOS have higher risk of early pregnant loss when compared to the women without PCOS. One possible association for the spontaneous abortion could be treatment with ovulation- inducing agents. However, the association for those who conceive naturally could not be established. Our study didn't establish any association for ovulation inducing drugs and spontaneous abortion. Other possible explanation could be obesity can be an indirect predictor by increasing insulin resistance which in turn can cause miscarriage on its own or by increasing adrenal secretion, which could be explained from the study conducted by Joham AE et al.[23], Our study findings also supported these findings where obesity/morbid obesity was independently associated with spontaneous abortion, even after adjusting for other confounders.

In regard to GDM, the women with PCOS had significant association when compared to the controls after adjusting for confounders. Numerous studies and meta-analysis have conferred association between PCOS and GDM[26,27]. Similar to our study findings many other studies[28,29] reported obesity as an independent predictor of GDM. Most studies and meta- analysis had concluded that there is 2.5 to 4 times higher risk of GDM with PCOS mothers. The pathophysiological process underlying the PCOS phenotype is complex and remains poorly understood. However, central to the process is an increased level of IR and the accompanying compensatory hyperinsulinemia (HI). Surprisingly, the association could have been because of obesity which could be an independent risk factor, but that has been controlled in our study through multivariable logistic regression. However, there are some theories which explains that visceral fat rather than the central obesity which plays an important role in IR and thus GDM. This assumption is supported by the fact that there is resumption of ovulation after weight loss is correlated with a greater degree of visceral fat loss rather than subcutaneous fat loss[30]. These are the supporting yet confusing plausible explanations which could link PCOS, obesity, IR and GDM. However, the exact mechanism is still a question for debate.

Our study showed that PCOS women had 2.51 times the higher risk of developing pre-eclampsia and these findings were similar as reported by many studies across the globe[20,26,27]. However some studies

had reported that there is no association between these two factors[31]. The possible mechanism could be impaired vascular adaptation to pregnancy or hyperandrogenemia. The underlying relationship between PCOS and pre-eclampsia remains relatively elusive but is thought to be related to the similar pathophysiological processes that predispose PCOS women to higher rates of metabolic syndrome, such as central obesity and increased IR. Not surprisingly, Obesity/morbid obesity was associated with increased risk of pre-eclampsia. It is noteworthy to describe that age and Primigravida were also having higher risk of pre-eclampsia.

Conclusion

The present study concluded that the risk factors for PCOS, primigravida was significantly associated with the occurrence of PCOS after adjusting for the confounder. On the maternal complications front, PCOS was significantly associated with GDM and pre-eclampsia after adjusting for the confounders. Obesity was independently associated with GDM, pre-eclampsia and spontaneous abortion. Primigravida was significantly associated with GDM and pre-eclampsia. Even though there is a possible clinical significance between PCOS and other pregnancy outcomes, the association could be seen only for PCOS with GDM and pre-eclampsia, due to less sample size and thereby, less power of the study.

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