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Comparative study of pregnancy- related complications of women with and without polycystic ovary syndrome (PCOS)

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Abstract

Background: Polycystic ovarian syndrome (PCOS) is a multifactorial metabolic condition, characterised by infertility, anovulation, hyperandrogenism and increased risk for many metabolic diseases like Diabetes mellitus.

Materials & Methods: A prospective cohort study of 100 pregnant women (50 women with PCOS and 50 women without PCOS) aged 20-35 years attending the gynaecology outpatient department of VMKV Medical college and hospital was conducted from over a period of 18 months to determine the maternal complications associated with PCOS.

Results: Mean age of the participants is 26.5. The participants with overweight/obesity are 34.0% among the women with PCOS when compared to 26.0% among the women without PCOS ($p=0.375$). Gestational diabetes is reported in 23.4% women with PCOS as against 14.6% women without PCOS. Women with PCOS are having 2.65 times the higher risk of having pre-eclampsia. Primigravida are having 2.89 times higher chance of presenting with PCOS.

Conclusion: Among the women with PCOS, GDM and pre-eclampsia are the common pregnancy related complications. Obesity is independently associated with GDM, pre-eclampsia and spontaneous abortion.

Keywords: Polycystic ovarian syndrome, gestational diabetes, pre-eclampsia, obesity

Introduction

Polycystic ovarian syndrome (PCOS) is a multifactorial metabolic condition primarily affecting women ^[1]. Being an endocrinopathy, PCOS is characterised by infertility, anovulation, hyperandrogenism and increased risk for many metabolic diseases like Diabetes mellitus. Etiology of PCOS is not clearly known and still many speculations revolve around it. Studies from all around the world conclude that the disease is caused due to the interplay of various genetic, environmental and metabolic factors ^[2]. Clinical manifestations include irregular or absence of menstruation, abnormal growth of hair over the face (hirsutism), acne, obesity and alopecia. Acne is a prime problem in an adolescent girl ^[3].

PCOS adversely affects the health status of a women of reproductive age group by increasing the chance of many chronic morbidities. Increased chance of glucose intolerance, obesity, type 2 Diabetes mellitus, psychiatric problems, cardiovascular diseases and sleep disorders are common in PCOS women. Women with PCOS are having more chance of having anovulatory infertility and weight gain also adversely affects it.

Only limited researches are undertaken in India to assess the problem and previously no cohort study was conducted in Tamil Nadu among PCOS women. In order to bridge this gap and do an in-depth analysis into this topic this prospective cohort study was planned to study the pregnancy- related complications of women with and without PCOS in a tertiary care hospital in Salem.

Materials and methods

A prospective cohort study of pregnant women aged 20-35 years attending the gynaecology outpatient department of Vinayaka Mission's Kirupananda Variyar Medical College and Hospital, Salem district, Tamil Nadu was conducted.

The study population consists of two groups Test group (Pregnant woman with Polycystic ovarian syndrome) and Control group (Pregnant woman without Polycystic ovarian syndrome).

The sample size for the study was calculated to be 100 (50 in each group), using the software N Master version 2.0 based on the study by Yunhui Wang *et al.* 119 considering the incidence of GDM among PCOS women as 55% and the incidence of GDM among non PCOS women as 15% in order to observe a minimum difference of 25% in the proportion of GDM between PCOS and non PCOS pregnant mothers, with 80% power and 5% level of significance.

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 upto delivery and pregnancy outcome in both test and control groups was carried out

Results

The mean age of the participants was 26.5 years with a

minimum of 20 years and a maximum of 34 years. The participants with overweight/obesity were 34.0% among the women with PCOS when compared to 26.0% among the women without PCOS ($p=0.375$). Proportion of primigravida among women with PCOS was 86.0% and among women without PCOS was 50.0%. Primigravida were having 2.89 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 56.0% and 78.0% among women with and without PCOS, respectively. IUI/IVF was the method of conception in 22.0% 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 23.4% women with PCOS as against 14.6% 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 6.80 times and 11.33 times when compared to the normal women and it was found to be statistically significant. Similarly, GDM was found to be 1.32 times higher in Primigravida compared to multigravida women.

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	0.98 (0.92-1.04)	0.564	1.00 (0.96-1.01)	0.851
Socio-economic status				
Lower	Reference		Reference	
Middle	1.01 (0.56-1.83)	0.165	1.14 (0.91-1.41)	0.241
Upper	-----	0.991	-----	0.998
BMI category				
Normal	1.01 (0.56-1.83)	0.973	0.93 (0.55-1.59)	0.802
Overweight	1.43 (0.75-2.73)	0.281	1.41 (0.48-2.34)	0.186
Obesity/ Morbid obesity	Reference		Reference	
Parity				
Primi	2.89 (1.46-5.70)	0.002	2.90 (1.45-5.99)	0.003
Multi	Reference		Reference	
Mode of conception				
Spontaneous	Reference		Reference	
Ovulation induction/assisted	8.12 (0.94-69.80)	0.056	9.1 (0.3-287.6)	0.211

Table 2: Univariate and multivariable logistic regression analysis of gestational diabetes mellitus and its association with PCOS and other risk factors (N=95)

Characteristics	Unadjusted PR (95% CI)	p value	Adjusted PR (95% CI)	p value
PCOS				
Yes	1.60 (0.68-3.78)	0.280	1.35 (1.28-1.51)	0.007
No	Reference		Reference	
BMI category				
Obesity/ Morbid obesity	11.33 (4.04-31.79)	<0.001	17.18 (6.61-44.67)	<0.001
Overweight	6.80 (2.18-21.15)	0.001	6.18 (1.98-19.27)	0.002
Normal	Reference		Reference	
Parity				
Primi	1.32 (0.52-3.38)	0.562	2.55 (1.29-5.03)	0.007
Multi	Reference		Reference	

Similarly, pre-eclampsia was found to be higher among the women with PCOS when compared to the women without PCOS (27.7% VS 10.4%). Women with PCOS were having 2.65 [(1.02-6.86); $p=0.044$] times the higher risk of having pre-eclampsia. Even after adjusting for confounders like age, BMI and parity, there was 2.48 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). Preterm delivery and LSCS was more among women without PCOS. Foetal

distress was the most common indication of LSCS (29.4%) followed by previous LSCS (19.0%) among the women who underwent LSCS. Short stature was the indication of LSCS only in 5.9% of women who underwent LSCS. Obese/morbid obese women were having 1.09 times higher risk of undergoing LSCS when compared to the normal women and it was found to be significant even after adjusting for confounders. Similarly, primigravida had higher risk of undergoing LSCS after adjusting for confounders.

Table 3: Univariate and multivariable logistic regression analysis of pre-eclampsia and its association with PCOS and other risk factors (N=95)

Characteristics	Unadjusted PR (95% CI)	p value	Adjusted PR (95% CI)	p value
PCOS				
Yes	2.65 (1.02-6.86)	0.044	2.48 (1.13-5.47)	0.024
No	Reference		Reference	
Age in years	1.13 (1.01-1.28)	0.047	1.05 (1.05-1.06)	<0.001
BMI category				
Obesity/ Morbid obesity	7.93 (3.01-20.92)	<0.001	10.00 (4.27-23.39)	<0.001
Overweight	5.44 (1.91-15.49)	0.002	3.79 (1.38-10.44)	0.010
Normal	Reference		Reference	
Parity				
Primi	1.32 (0.52-3.38)	0.272	1.77 (1.76-1.77)	<0.001
Multi	Reference		Reference	

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



Fig 1: Distribution of the study participants by body mass index (BMI) (N=100)

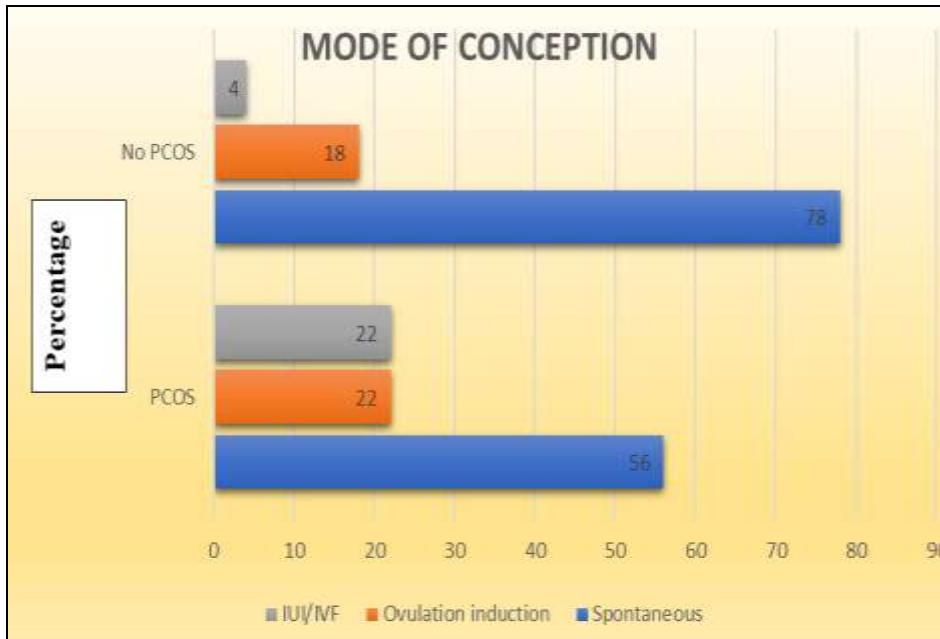


Fig 2: Distribution of the study participants by obstetric characteristics (Mode of conception) (N=100)

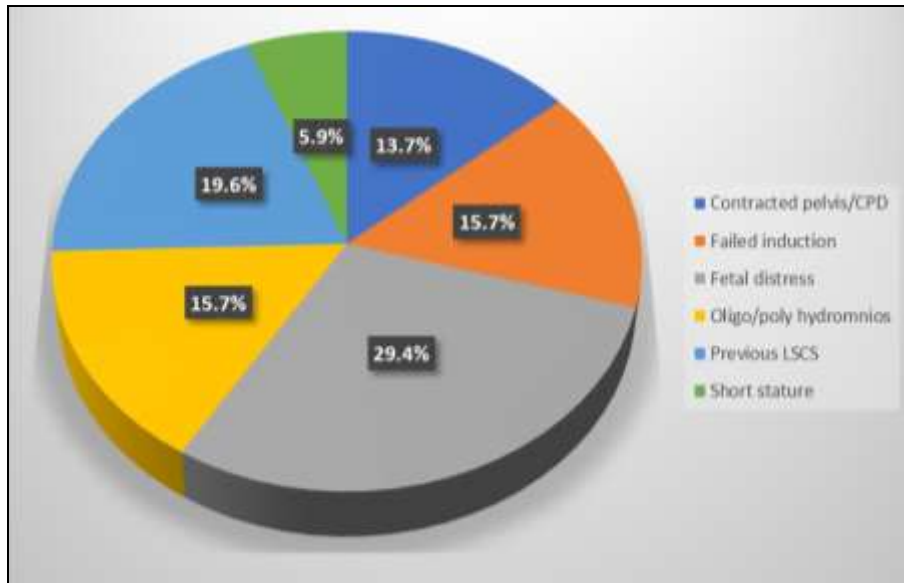


Fig 3: Indications of LSCS among the study participants (N=51)

Discussion

There had been lots of studies deciphering the association of PCOS with the adverse pregnancy outcomes. However, there is paucity of cohort studies in this particular part of the country and this study could well serve as a preliminary step for understanding the magnitude of the problem prospectively.

This study showed that the mean age was comparable between both the groups. However, those with 30 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 14 women aged 30 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 30 years of age in the PCOS group. Infertility was invariably present in all the women who conceived after 30 years of age. The increased number of primigravida above 30 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 evidences supporting this plausibility and researches done over this have resulted in inconsistent results. A study conducted by Sterling L *et al.* [4] 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 86% in our study population as against 50% 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 (20% overweight & 14% obesity) compared to women without PCOS. Alvarez-Blasco F *et al*⁵ 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 increased hepatic de

novo lipogenesis and hyperlipidaemia which in turn can lead on 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 [6]. Also, many studies [7-9] 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.* [10], Jakubowicz DJ [11] and Gray RH *et al.* [12] 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.* [10]. 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 [4, 13, 14]. Similar to our study findings many other studies [15, 16] 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 [17]. 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 2.5 times the higher risk of developing pre-eclampsia and these findings were similar as reported by many studies across the globe [4, 7, 13, 14]. However some studies had reported that there is no association between these two factors [18]. The possible mechanism could be impaired vascular adaptation to pregnancy or hyper-androgenemia. 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.

Surprisingly, there was no association of PCOS with the pre-term delivery in our study. Even there was no association of other factors with preterm delivery. Numerous other studies have shown association for the same [4, 9, 20, 21, 22]. One of the well-known risk factor for pre-term delivery is pre-eclampsia which is common in women with PCOS. That might well explain the plausibility of pre-term babies in PCOS women, apart from numerous other causes. Our study shows that women with PCOS were having lesser risk for cesarian delivery, which is contrary to the available literature [21, 22]. However the exact reason for the same should be explored more. There was a significant association between obesity, primipara and age with the cesarian delivery.

Conclusion

The study population was similar in their age, BMI and socio-economic status. Primigravida women and assisted mode of conception was more in women with PCOS. Among the women with PCOS, pre-eclampsia was the common pregnancy related complication (27.7%) followed by gestational diabetes mellitus (23.4%). Foetal distress was the most common indication of LSCS (29.4%) followed by previous LSCS (19.0%) among the women who underwent LSCS. Short stature was the indication of LSCS only in 5.9% of women who underwent LSCS. Amongst 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. Hence a multi-centre study with a considerably larger sample size and different study characteristics is the need of the hour, to understand the complications more deeply, which could help a long way in preventing the occurrence of complications and improve the quality of life among the PCOS patients.

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