Original Article

Pregnancy Complications - Consequence of Polycystic Ovary Syndrome or Body Mass Index?

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Abstract

Hyperinsulinemia and hyperandrogenemia are the hormonal changes which are linked to the pregnancy complications seen in women with Polycystic Ovary Syndrome (PCOS).

Aim : This study was done to determine the complications that can occur in pregnant women with polycystic ovary syndrome, and to ascertain whether the complications are related to PCOS per se or the Body Mass Index (BMI) of the women.

Materials and Methods : Data was collected from case records. Study group had women with PCOS, selected according to Rotterdam criteria and control group had women with unexplained infertility, with women in both groups achieving pregnancy either spontaneously, following ovulation induction (OI) with timed intercourse or controlled ovarian hyperstimulation (COH) with Intrauterine insemination (IUI).

Study design : A retrospective study. **Study duration**: Women who attended the clinic between January 2009 – Dec 2014, **Study Setting** : Department of Reproductive Medicine and Andrology, Chettinad Super Speciality Hospital, Chennai.

Results : There were 110 women in the study group and 64 women in the control group. The age and BMI of women in both groups were comparable. The incidence of miscarriage, congenital anomalies, preterm delivery, operative delivery and neonatal complications were similar in both groups. Incidence of Gestational Diabetes mellitus (GDM) was significantly higher in women with PCOS (22.6%), and there was an upward trend with increasing BMI. There was also an increased incidence of Large for gestational age babies in women with PCOS, but there was no statistical significance.

Conclusion : Unlike previous publications, our study revealed no significant increase in pregnancy and neonatal complications in women with PCOS, except for Gestational diabetes, the incidence of which was related to BMI. Therefore, we suggest that PCOS and the pregnancy complications are a consequence of increasing BMI, and that PCOS may not be incriminated as the independent cause for these complications.

Key Words: Polycystic ovary syndrome, PCOS, Hyperinsulinemia, Hyperandrogenemia, Pregnancy complications, Gestational diabetes mellitus, Neonatal complications.

Introduction

Polycystic ovary syndrome (PCOS) is the commonest ovulatory disorder accounting for 60-85% of anovulatory patients[1] and the commonest endocrinopathy in women of reproductive age group[2].

Most women with polycystic ovary syndrome have oligo-ovulation rather than anovulation, ie; they present with irregular cycles and very few have total absence of menstruation. Therefore, the chances of spontaneous conception in women with PCOS is slightly higher when compared to other causes of infertility. Moreover, simpler treatment modalities like ovulation induction provide better success rates in women with just PCOS as the cause for infertility[3]. These have resulted in an increasing prevalence of pregnant women with PCOS.

The altered hormonal milieu of PCOS, like hyperinsulinemia and hyperandrogenemia have been implicated in the pathogenesis of pregnancy complications like gestational diabetes, gestational hypertension and preterm birth. These hormonal changes, followed by development of PCOS are the consequence of excess adipose tissue and not vice versa. Earlier, obesity was being considered as the major cause for PCOS[4], but a retrospective study done in our department showed that, among the women diagnosed with PCOS, 32% had a normal body mass index (BMI)[5]. Obesity has also been proven to be an independent risk factor for pregnancy complications[6].

Aim

To determine the complications that can occur in pregnant women with polycystic ovary syndrome, and to ascertain whether the complications are related to PCOS per se or the BMI of the women.

Materials and methods

Study design : A retrospective study.

Study group : Women who attended the clinic between January 2009 – Dec 2014, and achieved pregnancy either spontaneously, following ovulation induction (OI) with timed intercourse or controlled ovarian hyperstimulation (COH) with Intrauterine insemination (IUI).

Study Setting : Department of Reproductive Medicine and Andrology, Chettinad Super Speciality Hospital, Chennai.

The study group had women with PCOS, who fulfilled the Rotterdam criteria[7] and the control group had women with Unexplained infertility, who were regularly ovulating, had patent fallopian tubes and male partner's sperm parameters were normal.

The case records of the women who attended the clinic and became pregnant either spontaneously, following ovulation induction (OI) with timed intercourse, or Controlled Ovarian Hyperstimulation (COH) with Intrauterine insemination (IUI), were reviewed for treatment details. The department conducts a yearly follow-up programme for the mothers who underwent infertility treatment and for children born after infertility treatment. During this evaluation, a detailed antenatal history is obtained and recorded. Those patients who did not attend the evaluation session were contacted through phone to obtain a detailed antenatal history.

Inclusion criteria

- Age - 20-35 years
- Primary and secondary infertility

Exclusion criteria

- Other causes of anovulation like hypothyroidism and hyperprolactinemia
- Other causes for recurrent miscarriages like uterine anomalies, Antiphospholipid antibody syndrome
- Pre-existing Impaired glucose tolerance (IGT) or Diabetes mellitus (DM)
- Concurrent treatment with Metformin
- Recent ovarian surgeries like laparoscopic ovarian drilling
- Multiple gestation
- Ongoing pregnancy
- Associated Male factor
- ART pregnancies
- History could not be elicited

Primary outcome

- Live birth
- Miscarriage
- Termination of pregnancy for anomalies
- Gestational age at delivery (term/preterm)

Secondary outcome

- Mode of delivery (Vaginal delivery/Cesarean section)
- Ectopic pregnancy
- Antenatal morbidities
- Neonatal outcome

Statistical analysis

The association between factors were calculated using Odd's ratio. Significance calculated using Chi square and Student t- test. P value - <0.05 was considered significant.

Results

The number of patients included in each arm is mentioned in Table 1.

Group	Number of women
Study group (PCOS)	110
Control group (Unexplained Infertility)	64

Table 1 - Number of women

Characteristics	PCOS	Unexplained
Mean Age (years)	26.87	27.77
Mean BMI (kg/m^2)	24.94	24.49

Table 2 - Basal characteristics of study participants

The mean age and Body mass index (BMI) of the participants were comparable in both groups, as shown in Table 2, and most of the women in both groups belonged to the category of Normal BMI.

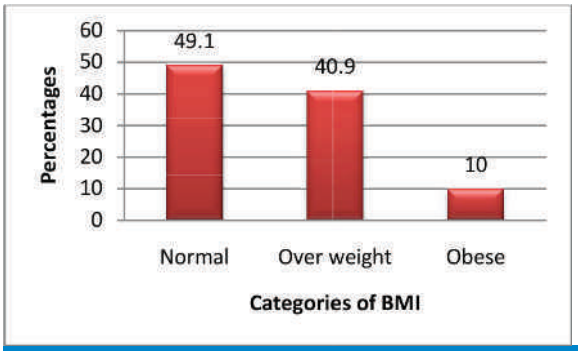

Fig 1 : BMI distribution in PCOS group

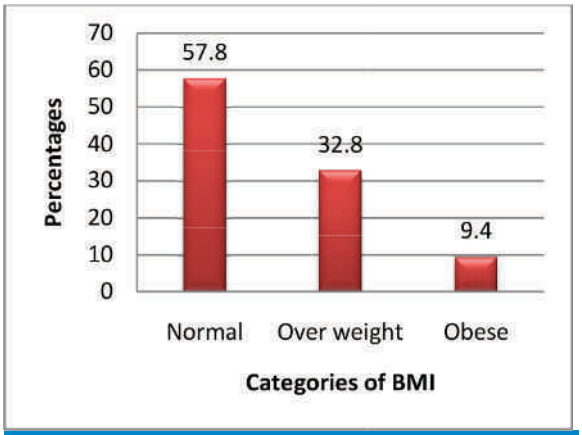

Fig 2 : BMI distribution in Unexplained infertility group

The BMI categorization was done according to the WHO classification of BMI. Normal BMI- 18.5 - 24.9 kg/m2, Overweight - 25 - 29.9 kg/m2, Obese - >30 kg/m2.

	PCOS (n=110)		Unexplained (n=64)		
	Number	Percentage	Number	Percentage	p value
Live birth	84	76.4	48	75.0	0.83
Miscarriage	22	20.0	10	15.6	0.64
Ectopic	2	1.8	5	7.8	0.07
Anomalies	2	1.8	1	1.6	0.9

Table 3 - Outcome of pregnancy

The pregnancy outcome in the groups are shown in Table 3. There was no significant difference in the outcome in both groups. Though there was no statistical significance, the incidence of ectopic pregnancy was higher in the Unexplained infertility group (1.8% vs 7.8%), which could probably be due to a subtle tubal factor in the patients.

Table 4 shows that there is no difference in the mode of delivery among the live births in the two groups.

Mode of delivery	Groups		Odds ratio	Chi square	P-value	95% CI	
	PCOS (n=84)	Unexplained (n=48)				Lower	Upper
LSCS	54 (64.3%)	29 (60.4%)	1.179	0.196	0.658	0.568	2.449
Vaginal	30 (35.7%)	19 (39.6%)					

Table 4 - Comparison between mode of delivery

Though the number of preterm deliveries were higher in the PCOS group, as shown in Fig 3, there was no significant difference. [OR 1.83 (95% CI 0.5565-6.0392), p value – 0.3190].

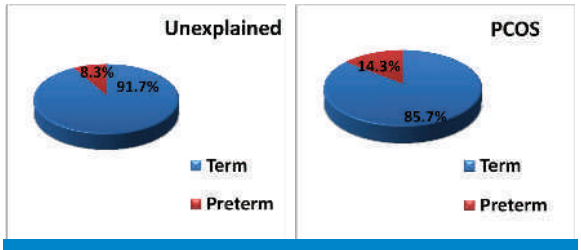

Fig 3 : Gestational age at delivery

The pregnancy morbidities as shown in Table 5, were calculated only in women whose pregnancies resulted in live birth. Except for the incidence of gestational diabetes, the other pregnancy morbidities were not significantly higher in women with PCOS. Among the pregnancies that crossed viability, 22.6% of the women had developed gestational diabetes (GDM) and were started on Insulin therapy at around 5 months of gestation. In women with unexplained infertility, none developed GDM. In the PCOS group, 2 women had gestational hypertension (GHTN), whereas none had GHTN in the unexplained infertility group. Due to small numbers, the significance of GHTN cannot be explained in this study. The other antenatal complications like prelabour rupture of membranes (PROM), polyhydramnios, oligohydramnios and Fetal growth restriction (FGR), were similar in both the groups.

	PCOS (live birth, n = 84)		Unexplained (live birth, n= 48)		
	Number	Percentage	Number	Percentage	p value
GDM	19	22.6	0	0	0.02
GHTN	2	2.4	0	0	0.49
PROM	7	8.3	2	4.2	0.37
FGR	1	1.2	1	2.1	0.69
Oligohydramnios	4	4.8	3	6.2	0.71
Polyhydramnios	1	1.2	0	0	0.73

Table 5 - Antenatal complications

As per the study objective, in order to ascertain whether it is PCOS or obesity which is responsible for the increased incidence of GDM in the PCOS group, the women were classified according to the WHO classification for BMI. The distribution of BMI in women with GDM is shown in Fig 4.

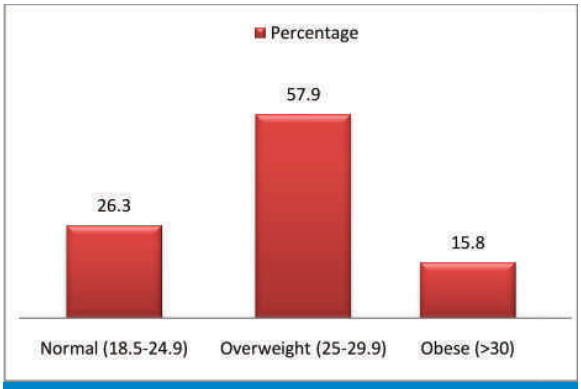

Fig 4 : Pre-pregnancy BMI distribution of women with GDM

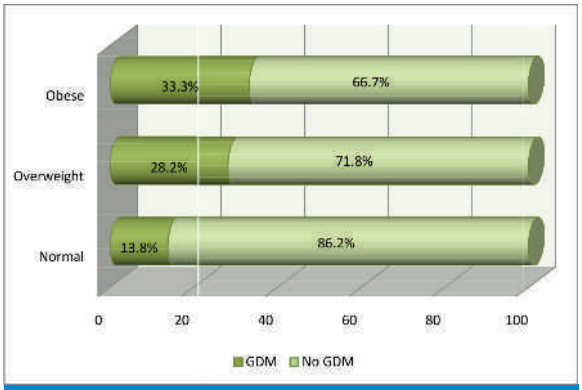

Fig 5 : Incidence of GDM in relation to pre-pregnancy BMI in women with PCOS

Among the women with GDM, 26.3% had normal BMI, 57.9% were overweight and 15.8% were obese, thereby interpreting that the number of obese patients were comparatively lesser. As seen in Fig 5, when the incidence of GDM was calculated in all women with PCOS, in relation to the pre-pregnancy BMI, 13.8% of women with normal BMI, 28.2% of overweight women and 33.3% of obese women had developed GDM. Therefore it is obvious that there was an increasing tendency for developing GDM as the pre-pregnancy BMI increased.

There was no significant difference in the neonatal outcome in both groups(Table 7). Neonatal intensive care unit (NICU) admission rates were higher in neonates of women with PCOS , but the numbers were not statistically significant. NICU admission was primarily for preterm care or for observation of the neonate in view of GDM in the mother. Among the babies born to women with PCOS and gestational diabetes, 3 babies developed hypoglycemia for which they required NICU admission and glucose infusion.

Though not statistically significant, there was an increased incidence of large for gestational age (LGA) babies in the PCOS group. Among the mothers who gave birth to LGA babies, only one mother had GDM. It was assessed if there is a correlation between the mother's BMI and the increased birth weight of babies. As seen in the Fig 6, all mothers with LGA babies were non-obese, and more than half of them were of normal built, suggesting that it could be due to the metabolic and hormonal changes in mothers with PCOS. We may not be able to arrive at a conclusion in view of numbers.

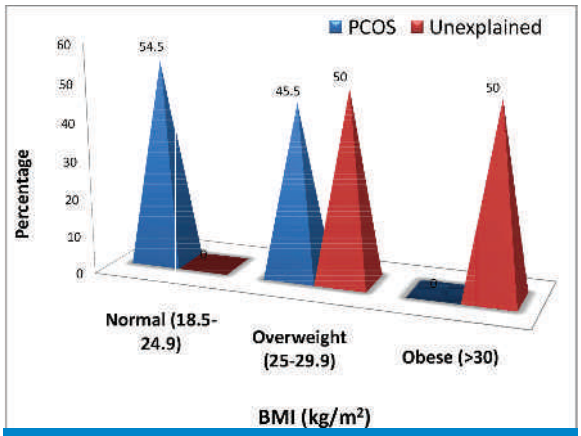

Fig 6 : BMI distribution of mothers of LGA babies

Discussion

Boomsma et al (2006) conducted a meta-analysis of the pregnancy outcome with PCOS, and found a higher risk of developing GDM, pre-eclampsia and preterm birth[8]. There was also a significantly higher perinatal mortality and NICU admissions in these patients. Most of the studies included in the meta-analysis did not take into account the BMI of the patients, which would be a direct confounding factor. In this study, the study and the control group were age- and BMI-matched.

	PCOS (live birth = 84)		Unexplained (n=48)		
	Number	Percentage	Number	Percentage	p value
NICU	21	25	7	14.6	0.16
Physiological jaundice	4	4.8	3	6.2	0.71
Preterm care	5	5.9	2	4.2	0.97
Respiratory distress	3	3.6	1	2.1	0.63
Hypoglycemia	3	3.6	0	0	0.34
Infection	1	1.2	0	0	0.45
Single umbilical artery	1	1.2	0	0	0.45
Observation	5	5.9	1	2.1	0.55
Large for gestational age	11	13.1	2	4.2	0.17

Table 6 - Neonatal outcome

The live birth rate, miscarriage rate and the incidence of preterm delivery, operative delivery and congenital anomalies was similar in both groups. Incidence of GDM was significantly higher in women with PCOS (22.6%), and it was also seen that among all women with PCOS, higher the BMI, higher was the probability of developing GDM. With this observation, we comprehend that, PCOS may not be the cause for GDM, but both PCOS and GDM are the consequence of increasing BMI. A study done in Jammu and Kashmir, India, showed similar results, but the number of PCOS women included were lesser than our study[9].

Studies have quoted a threefold increase in the incidence of neonatal hypoglycemia is babies born to women with PCOS[10]. In our study, the neonatal outcome was similar in both the groups, except for the incidence of hypoglycemia. Among the 19 babies born to GDM mothers, 3 babies developed neonatal hypoglycemia for which they required intravenous glucose infusion. Preterm babies and babies born to GDM mothers required neonatal intensive care monitoring.

Conclusion

Women with PCOS are generally said to have a greater tendency to develop pregnancy and long term health complications[8]. This conclusion was derived from studies, in which the comparison was not done with age and BMI matched controls. PCOS was thus thought to be 'the cause' for these complications. According to our study, in women with similar BMI, there was no difference in the incidence of any pregnancy complication in PCOS women. The incidence of gestational diabetes also increased with increasing BMI. Therefore, we suggest that PCOS may not be the independent or primary cause for the pregnancy complications or metabolic diseases like coronary artery disease, cerebrovascular disease and uterine malignancies. There may be a common factor like the BMI or weight gain which is involved in the pathogenesis of all these events.

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