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Original Research Article

Pregnancy outcomes in the *in vitro* fertilization conceived polycystic ovary syndrome patients: a prospective study

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ABSTRACT

Background: *In vitro* fertilization (IVF) is the need of modern era which was first developed to overcome the infertility resulting from irreparable tubal disease but now is applied more broadly for treatment of all causes of infertility including polycystic ovary syndrome (PCOS) and is associated with obstetric complications as well. This study aimed to whether pregnancy-related outcomes and complications are differed between patients with polycystic ovary syndrome (PCOS) and those with other causes of infertility who had undergone IVF. Objective were to compare maternal and fetal outcome in IVF conceived women with PCOS v/s without PCOS. Prospective comparative study at a tertiary care hospital.

Methods: After getting approval from institutional ethical and scientific research committee, 108 IVF conceived women are studied, where IVF is done using controlled ovarian stimulation with GnRH antagonist protocol followed by freeze all strategy and preparation of endometrial lining. Frozen embryo transfer done in subsequent cycle over a period of one year. Study group includes women with PCOS and control group includes women without PCOS. The entire data is statistically analysed using statistical package for social sciences (SPSS ver 22.0, IBM Corporation, USA) for MS Windows.

Results: Out of 108 IVF conceived pregnant women studied, 50% were PCOS (study group) and 50% non PCOS (control group). We have compared maternal and neonatal outcome in both the groups which shows patient in PCOS group has higher incidence of GDM, severe pre-eclampsia, preterm labour, LBW babies, SGA babies and babies admitted to NICU.

Conclusions: Women with PCOS should be given notice of additional adverse pregnancy outcomes as well receiving early diagnosis and treatment for these complications during pregnancy and postpartum period.

Keywords: PCOS, IVF, COS, Maternal outcome, Fetal outcome

INTRODUCTION

In vitro fertilization (IVF) has completely changed the treatment of infertility since last 4 decades and has been increasingly used worldwide. The risks of obstetric complications are much higher in IVF conceived pregnancy as compared to spontaneously conceived pregnancies.^{1,2}

PCOS is an important cause of infertility in women of reproductive age because of the associated anovulation.³

Although anovulation is to be the primary defect responsible for failure to achieve the pregnancy in this disorder, other potential consideration may hamper fertility including insulin resistance, hyperandrogenism and obesity, which requires ovulation induction using clomiphene citrate, gonadotropins or even IVF. These treatment methods are known to increase the incidence of multiple pregnancies, gestational diabetes mellitus, pre-eclampsia, etc., Furthermore, pregnancies established after IVF carry an increased risk for maternal complications and fetal complications in itself.⁴

PCOS has a negative effect on women's health across the lifespan like anxiety, depression, insulin resistance, abdominal obesity, hypertension and dyslipidemia.⁵ Depending on the particular criteria used for diagnosis and the population studied, the prevalence of PCOS has been reported to range from 8% to 13% in women of reproductive age. amongst which 70% of affected women remaining undiagnosed.^{6,7}

Many studies have been performed to study the effect of PCOS on pregnancy and the effect of pregnancy on PCOS. The hormonal milieu that is exaggerated in PCOS women is quite well understood at the biochemical and genetic levels. The maternal and neonatal outcomes of PCOS women who have undergone IVF-embryo transfer (IVF-ET) have not been widely studied.⁸

pregnancies established after IVF carry an increased risk for maternal complications. However, the increased risk of developing adverse obstetric complications has been suggested to occur independently of obesity as well as in populations without assisted reproductive techniques.⁷ The rationale of this study is to find out whether the adverse obstetric outcomes are increased in IVF conceived women in general, or particularly in those PCOS women who are undergoing IVF-ET. It is also important to analyses via a literature review whether the increased adverse outcomes are due to infertility in general or PCOS.

METHODS

After getting approval from institutional ethical and scientific research committee, this study was conducted after satisfying inclusion criteria.

Study design

The study design was systematic literature review, prospective and comparative study.

Study place

The study carried out at obstetrics and gynecology department, in collaboration with Ruby hall IVF and endoscopy centre, Ruby hall clinic, Pune, Maharashtra.

Study period

The study conducted from September 2020 to August 2021.

The 108 pregnant women conceived successfully by IVF, done using controlled ovarian stimulation with GnRH antagonist protocol followed by freeze all strategy and preparation of endometrial lining. Frozen embryo transfer done in subsequent cycle over a period of one year. Study group includes women with PCOS and control group includes women without PCOS. Study has been conducted on pregnant women attending to IVF Antenatal clinic in our hospital, who conceived with IVF and ET, keeping

follow up till delivery and getting delivered in the same set up.

Our study included Study group 1 containing IVF conceived pregnant women with PCOS, which was defined by 2003 Rotterdam criteria i.e., evidence of oligo or anovulation, clinical and/or biochemical signs of hyperandrogenism and polycystic ovaries on Ultrasound : one ovary fitting the description is sufficient to define PCO (more than 12 follicles in each ovary measuring 2-9mm in diameter , and/or increased ovarian volume>10 ml) and Study group 2 includes IVF conceived pregnant women without PCOS. We included patients of age group 18-40 years in our study we have excluded Spontaneously conceived pregnant women, women with pre-existing medical illness like DM/HTN, women with anovulation not due to PCOS, women <18 years and >40 years, women with obesity not due to PCOS, women with hirsutism due to adrenal or other causes from our study.

Detailed history was taken of all 108 women including age, gravida status, socioeconomic status, menstrual history, obstetric history, past history, family history. Examination finding including BMI, facial hair, acne. Spontaneous miscarriage is diagnosed as pregnancy that failed to reach up to 20 weeks of gestation, not including ectopic and induced abortions. Pre-eclampsia is diagnosed as BP> 140/90 mmHg after 20 weeks of gestational age associated with proteinuria >300 mg/24 hours. Gestational diabetes mellitus diagnosed by giving a 75-gm oral glucose load, regardless of fasting status. Venous blood sample is collected at 2 hours for estimating plasma glucose by GOD-POD method. GDM is diagnosed if 2-hour plasma glucose is >140 mg/dl. Antepartum Haemorrhage defined as bleeding from or into the genital tract after 28 weeks of gestational age but before the birth of the baby.

Multiple pregnancy is diagnosed when more than one fetus simultaneously develops in the uterus, it is called as multiple pregnancy. Labour starts before 37 completed weeks of gestational age considered as preterm labour. When birth weight of baby was less than 2500 gm termed as low birth weight. Baby born with birth weight less than 10th percentile of the average for the gestational age termed as small for gestational age baby. Baby born with gestational age more than 90th centile of the average for the gestational age termed as large for gestational age baby.

Statistical analysis

The entire data was statistically analysed using statistical package for social sciences (SPSS ver 22.0, IBM Corporation, USA) for MS windows. P<0.05 was considered to be statistically significant.

RESULTS

We found in our study that PCOS patients who are IVF conceived are overweight with irregular menstrual history in past (Table 1).

Table 1: Demographic details of patients.

Parameters	PCOS women	Non PCOS women	P value
Age (Years)			
<20			
21-30	17	09	0.072
31-40	37	45	
Gravida status			
Primigravida	37	37	
Multi with pre abortion	12	14	
Multi with prev IUFD	03	02	0.999
Multi with prev ectopic	02	01	
BMI (Kg/m²)			
Normal weight	14	34	
Over weight	25	13	0.001
Obese	15	07	
Menstrual history			
Regular	21	08	
Irregular	33	46	0.005
Socioeconomic status			
Upper class	23	20	
Middle class	28	32	0.713
Lower class	03	02	

Table 2: Comparison of maternal outcome in IVF conceived women with PCOS and without PCOS.

Maternal outcome	Women with PCOS	Women without PCOS	P value
Spontaneous miscarriage	05	04	0.999
Gestational diabetes	21	10	0.019
Pre-eclampsia	22	10	0.047
Antepartum haemorrhage	04	01	0.363
Preterm labour	10	05	0.007
Multiple pregnancy	09	08	0.676

Table 3: Comparison of fetal outcome in IVF conceived with PCOS and without PCOS.

Fetal outcome	Women with PCOS	Women without PCOS	P value
Low birth weight baby	14	04	0.018
Small for gestational age	12	01	0.002
Large for gestational age	04	01	0.118
NICU admission	13	02	0.001

In case of maternal outcomes incidence of GDM, pre-eclampsia and preterm labour is more in IVF conceived PCOS women (Table 2).

In case of fetal outcome incidence of LBW babies, SGA babies and need of NICU admission of babies is more in IVF conceived women with PCOS (Table 3).

DISCUSSION

Present study conducted on total of 108 IVF conceived women, among these 54 women had history of PCOS (according to Rotterdams criteria 2003) and 54 women were without PCOS. Age, gravida status, menstrual history, socioeconomic status and BMI were comparable in both the groups. Out of 54 women without PCOS 11.27% had antenatal complications where as 21.9% women with PCOS landed with antenatal complications.

The age of patients in our study had no significant difference between both the groups like in consensus with a study conducted by Roos et al that giving birth at an advanced maternal age (>35 years) was more common in women with PCOS than non PCOS women.⁹

Insulin resistance, hyperinsulinemia and obesity are the common clinical features with women in PCOS. Women with PCOS were found to have increased risk of carbohydrate metabolism impairment. In our study there was significant difference of BMI between both the groups like in consensus with a study conducted by Haakooa et al where the weight difference was significantly different among both the groups.¹⁰

Maternal complication in the form of spontaneous abortion in our both the groups was not found to be statistically significant, $p > 0.05$ which was opposed to study conducted by Wang et al and Bagegni et al who concluded that risk of spontaneous miscarriage is higher in IVF conceived women with PCOS.^{11,12} Our study observation is supported by Palomba et al in their study which suggested that the rate of miscarriages was similar in PCOS and non PCOS women.¹³

In our study there was considerable difference in prevalence of pre-eclampsia in PCOS women as compared to normal IVF conceived women which was statistically significant, in contrast to results obtained by Mikola et al, Haakova et al and Han et al in their studies did not show any association of PCOS and development of hypertensive disease of pregnancy.^{10,14} Our study results are supported by Bjercke et al, Boomsma et al, Bagegni et al, Qin et al and Sha et al in their studies which concluded that there was strong association between risk of pre-eclampsia and PCOS.^{7,12,15-17}

In our study the risk of GDM is high in women having PCOS and there was statistically significant difference between the two groups which was supported by studies conducted by Qin et al, Yunhui et al, Palomba et al and

Sha et al which concluded that gestational diabetes mellitus is higher in women with PCOS even after eliminating confounding factors like obesity.^{7,11,13,17} In contrast to our study Haakova et al and Bagegni et al concluded that there was no increased risk of glucose intolerance in women with PCOS during pregnancy.^{10,12}

Prevalence of preterm labour is significantly higher in PCOS women in contrast to studies conducted by Bagegni et al and Han et al they found no significant association between PCOS and preterm delivery.^{12,18} They attributed the incidence of preterm deliveries in their study population to higher rate of multiple pregnancies from the use of assisted reproductive technologies to achieve pregnancy.¹⁸ Similar results like our study was concluded by Yamamoto et al and Yunhi et al showed a significant association between PCOS and preterm delivery even after eliminating confounding factor of multiple gestation, as twin pregnancy itself is a risk factor for preterm delivery.^{11,19}

In our study we found that prevalence of multiple pregnancies was not significantly higher in women having PCOS which was supported by many other studies like Mulders et al, Kuivasaari-Pirinen et al, Swanton et al, Han et al and Zhang et al which concluded no significant difference in multiple pregnancy rate between IVF conceived PCOS and non PCOS group.²⁰⁻²³

Risk of antepartum haemorrhage was not significantly higher in women having PCOS. Azizia et al has reported in a study that antepartum haemorrhage is more common in women with PCOS although the sequence of events leading up to this is unclear. These women also have a higher rate of interventions due to complicated IVF conceived pregnancies.²⁴

The fetal outcome in terms of low birth weight (LBW) babies, small for gestational age (SGA) babies and babies requiring NICU admission was significantly higher in babies born to mother having PCOS with $p < 0.05$. Though the prevalence of large for gestational age babies was higher in women having PCOS, there was no significant difference between the two groups.

Limitations

As our study sample is less, according to the sample size collection method used, we cannot assess the comparative outcome on large scale basis. Also, in our study we have studied IVF conceived women only by frozen embryo transfer after using GnRH antagonist protocol stimulation. We have not studied fresh embryo transfer results and other stimulation protocols.

CONCLUSION

Notwithstanding the limitations of heterogeneity, the current study demonstrates that women undergoing IVF having PCOS are at increased risk of adverse maternal and

fetal complications, which may be vital in clinical practice. Women with PCOS should be given notice of additional adverse pregnancy outcomes as well receiving early diagnosis and treatment for these complications during pregnancy and postpartum period. In order to manage pregnancy in women with PCOS more effectively, investigations and screening tests should be done along with lifestyle modification and metformin therapy in these women.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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