

Original Article**CO-RELATION OF IVF PREGNANCY TO MATERNAL HEALTH AND PREGNANCY OUTCOME AT TERTIARY HEALTH CARE CENTER, GOA MEDICAL COLLEGE**Disha Modi¹, Manjusha Jindal², Guruprasad Pednecar³¹Junior resident, ²Associate professor, ³Head of Department,

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ABSTRACT:

Introduction: Infertility is a worldwide issue with 8-12% couples suffering from lifetime infertility. In vitro fertilization (IVF) has been a ray of hope for infertile couples especially in the elderly women. IVF conception increases the obstetric complications and adverse pregnancy outcomes as per literature. The present study was undertaken to find co-relation of IVF pregnancy to maternal health and pregnancy outcome in the state of Goa. **Methods:** This is a retrospective case control study done in Goa Medical College, from May 2018 to April 2019. A total of 54 patients who had conceived after In Vitro Fertilization by donor/self oocyte / sperm were included in the study. Various demographic factors, gestational age, singleton /twin pregnancy, medical and obstetrical complications in pregnancy were noted. Further Pregnancy outcomes were noted in terms of gestational age at abortion/delivery, mode of delivery, birth weight, perinatal outcome, need for Intensive Care for mother and baby and neonatal and maternal mortality. **Results:** Mean age of subjects in study group was 38.5 years compared to controls (26.2 years). There was increased risk of GDM by five folds (p value <0.001) and pre-eclampsia by four folds (p value <0.001). Multifetal gestations were noted in 40.7% subjects (p value <0.01). 31.4% pregnancies aborted due to various obstetrical complications compared to none in control group. 22% subjects delivered prior to 34 weeks (p value 0.04). 75% patients delivered by LSCS (p value <0.001). Risk of low birth weight of neonates was two times more than control group. **Conclusions:** In view of increased complications seen with IVF pregnancies, it is important to follow stringent guidelines for these techniques in the interest of these couples and society at large.

Keywords: IVF pregnancies, maternal health, pregnancy outcome

INTRODUCTION

Infertility is a worldwide issue with 50 to 80 million couples in the reproductive age (8-12% couples)

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and 34 million in the developing countries suffering from lifetime infertility according to WHO 2010 census¹. In India, primary infertility ranges between 3.9 to 16.8%, prevalence varying in various states.²

Considering the marital rate in 2020, similar to the current rate, the number of infertile couples could increase from 220 million in 2015 to 244 million by 2020. Infertility in the reproductive age group is ranked 5th most serious global disability³. In vitro fertilization (IVF) has been a ray of hope for infertile couples especially in the elderly women.

One lakh couples underwent IVF in 2015 for the treatment of primary infertility which is expected to rise exponentially in coming years as much as touching to 2.6 lacs in 2020³.

IVF conception increases the obstetric complications and adverse pregnancy outcomes as per literature⁴. There are no such studies done in our geographical area, hence, present study was undertaken to find co-relation of IVF pregnancy to maternal health and pregnancy outcome in the state of Goa.

METHODS

This is a retrospective case control study done in Goa Medical College, from May

2018 to April 2019. Ethical approval was obtained from institutional Ethics Committee.

Sample size: 54 patients (All patients presenting from May 2018 to April 2019)

Sampling Method: Census method

All the patients presenting to GMC who had conceived after In Vitro Fertilization by donor/self oocyte/sperm were included in the study. Various demographic factors, maternal age, gestational age at delivery, singleton/multi fetal pregnancy, medical and obstetrical complications in pregnancy were noted from records. Pregnancy outcomes were noted in terms of gestational age at abortion/delivery, mode of delivery, birth weight, perinatal outcome, need for Intensive Care for mother and baby and neonatal and maternal mortality. The outcome was compared with equal number of controls who had conceived spontaneously. The data was analyzed using SPSS version 22. Categorical variables were expressed in percentages and proportions and quantitative variables in mean \pm SD. Significance was checked using Student t test and $p < 0.05$ was taken as significant.

RESULTS

During the present study, total of 54 patients were studied and compared with the same number of

patients as controls who had conceived spontaneously.

Mean age of the patients who had IVF conception was 38.5 years in this study as compared to 26.2 years in the control group. (p value 0.01) (Table 1)

**TABLE 1:
AGE OF PATIENT AT CONCEPTION**

| Age at conception | Study Group (IVF conception) | Control Group (spontaneous conception) |
|-------------------|------------------------------|--|
| <35years | 6 (11.1%) | 52(96.2%) |
| 36-40years | 16 (29.6%) | 2(3.7%) |
| 41-45years | 18 (14.8%) | 0(0%) |
| >46years | 14(25.9%) | 0(0%) |

Donor oocyte was used in 80% cases while donor sperm in 40% for conception.

31 patients in the study group had undergone various surgical procedures prior to IVF. 13 subjects had hysteroscopic metroplasty with cavity enhancement (24%), six had myomectomy (11%), 15 patients had hysteroscopic adhesiolysis (27%), 22 had undergone diagnostic laparoscopy (42%). one patient had previous LSCS. 23 patients didn't undergo any prior surgeries in the study group (p value 0.01). However, in the control group, none of the patients underwent any surgery prior to the conception.

*Total number of surgeries are exceeding the study subject as some patients had more than one surgeries

Medical Complications:

Medical complications were noted in the patients of both the groups. In study group, 30 patients (55%) had overt diabetes mellitus, one of them had non proliferative diabetic retinopathy, nine patients (16%) had hypertension. 22 patients (40%) were detected to have hypothyroidism. Two patients developed peripartum cardiomyopathy

with global dyskinesia of left ventricle with ejection fraction of <35%. These medical conditions were compared with the control group (19.1%). The results are statistically significant (p value <0.001) (Table 2)

**TABLE2:
MEDICAL COMPLICATIONS**

| Medical Complications | Study Group (IVF conception) | Control Group (spontaneous Conception) |
|-----------------------|------------------------------|--|
| ODM | 30 (55.5%) | 1(1.9%) |
| Chronic hypertension | 9 (16.6%) | 1(1.9%) |
| Heart disease | 2 (4%) | 1(1.9%) |
| Hypothyroidism | 22(40.8%) | 7(13.4%) |

*Total number of complications exceed the number of subjects as some subjects had more than one complications

Obstetrical complications:

Obstetrical complications like gestational diabetes mellitus, gestational hypertension, pre-eclampsia, multi fetal gestation, placenta Previa were noted. Compared to the control group, IVF patients had four times more risk of GDM, (P value <0.001), five times more risk of pre-eclampsia (p value <0.001). One patient had status eclampticus at 20.5weeks. Seven patients (12%) had placenta Previa, one patient had abruptio placentae, (p <0.001). Among placenta previa cases, two patients had adherent placenta for whom, obstetric hysterectomy was performed. Two patients (3%) in control group had placenta Previa. 22 patients (40%) of study group had multi fetal gestation, one being triplets while others twin gestation (p value <0.01). Control group had three (5.5%) multi fetal gestation. (Table 3)

**Table 3:
OBSTETRICAL COMPLICATIONS**

| Obstetrical Complications | Study Group (IVF conception) | Control Group |
|---------------------------|------------------------------|---------------|
| GDM | 17 (31.5%) | 4(7.4%) |
| Gestational hypertension | 16 (30.6%) | 11(20.3%) |
| Pre-Eclampsia | 12 (22.2%) | 3(5.5%) |
| Multi fetal gestation | 22(40.7%) | 3(5.5%) |
| Praevia | 7(12%) | 2(3.7%) |

In this study, among the IVF conception patients, 12 patients (31%) had spontaneous or induced abortion as a result of obstetrical complications (p value 0.04).

Two patients in the study group were reported to have ectopic pregnancy. One, ruptured ectopic, laparotomy followed by salpingectomy was performed and other unruptured ectopic pregnancy managed conservatively.

Gestational Age at Outcome:

Abortion- 12

Ectopic- 2

Deliveries- 40

Live Birth- 61 (20 single, 19 twins, 1 triplet)

Still Birth- none

Neonatal Death- 10

12 patients (22%) delivered prior to 34 weeks. In Control group, only 4 patients (7%) delivered before 34 weeks. (p value 0.04). 23 patients (42%) continued pregnancy beyond 34 weeks but didn't complete 37 weeks. (Table 4).

Table 4:**GESTATIONAL AGE AT DELIVERY**

| GESTATIONAL AGE AT DELIVERY | Study Group (IVF conception) | Control Group |
|------------------------------------|-------------------------------------|----------------------|
| <28 weeks(including abortions) | 17 (31.4%) | 0(0%) |
| 28-34 weeks | 12(22.2%) | 4(7.4%) |
| 34-37 weeks | 23 (42.5%) | 27(50%) |
| >37 weeks | 0(0%) | 23(42.5%) |
| Ectopic Pregnancy | 2(3%) | 0(0%) |

Neonatal Outcome:

Out of 40 patients delivering live births in the IVF group, 30 patients delivered by cesarean section as compared to 17 LSCS done in the control group (p <0.001).

Babies born to the IVF pregnancies were found to have low birth weights. 38 babies (61%) had birth weight in range of 1-2.5kg, 16 babies (27%) had weight of <1kg weight. 7 babies (12%) had >2.5kg birth weight. While in the control group, 33 babies (58%) had >2.5kg of birth weight. (p value 0.001) (Table 5)

**TABLE 5:
BIRTH WEIGHT OF NEONATES**

| BIRTH WEIGHT OF NEONATE | Study Group (IVF conception) n=61 | Control Group (spontaneous) n=57 |
|--------------------------------|--|---|
| <1kg | 16 (27%) | 4(7%) |
| 1-2.5kg | 38 (61%) | 20(35%) |
| >2.5kg | 7 (12%) | 33(58%) |

Out of 61 live births to the IVF pregnancies, 10 babies (16.4%) died in the neonatal period including 1 twin who developed cerebral abscess, expired due to meningitis. Out of the multifetal conceptions, two twin gestation patients presented with twin1 intra uterine fetal demise, both delivered twin2 after 34 weeks, however one baby expired within 10 days. 51 babies (80%) in study group survived the neonatal period. In the spontaneous conception group, one baby expired due to complex congenital heart disease in the baby (p value 0.01).

In the study group, 19 babies (31%) required NICU care. In the control group, three babies required NICU care (p value 0.04).

Six subjects in the IVF group required ICU admission, however none required ventilator support.

Two maternal deaths (2.7%) were reported in the IVF group, both due to amniotic fluid embolism (3703 deaths in 1 lakh live births). However, no maternal deaths were reported in the control group (p value 0.01).

DISCUSSION:

Use of assisted reproductive technologies are increasing over the years and it is expected to increase in future years due to rising trends of infertility because of multiple causes.

The mean age of the patients with IVF conception in present study was 38.5 years similar to that reported by Tan et al⁵ (36.2 years), Bergh et al⁶ in Sweden (36.5years). The probable cause of increased maternal age in the IVF group may be due to lifestyle changes including late marriages and career pressures. In study by Tan et al⁵, the percentage of women with age >35years and >40 years were 42% and 5% respectively. In present study, percentage was 29.6% and 14.8% respectively. Increased maternal age in this study is due to restricted knowledge of availability of infertility treatment options.

In present study, 80% of the patients were conceived on donor oocyte. However, in Laura et al⁷, 37% IVF conceptions were with donor oocyte.

57% subjects in the study group, prior to IVF, had undergone various surgical procedures like hysteroscopic metroplasty with cavity enhancement, myomectomy, hysteroscopic adhesiolysis, diagnostic laparoscopy. None of the subjects in the control group underwent any prior procedures (p value 0.01). These procedures were believed to improve the success rate of the IVF conception, however no study is reported in literature for the association of above surgeries and the successful conception rate.

Our study had 4 times increase in the risk of gestational diabetes mellitus as compared to the control group (31.5% in study group and 7.5% in control group, p value <0.001). Jackson et al⁸ reported 5 times increase in the risk (16% GDM in IVF group and 3% in control group). Maman et al⁹ demonstrated 45% risk of GDM in study group. In their study, the increase in incidence is due to polycystic ovary syndrome (PCOS) requiring ART.

Present study had 5 times increased risk of pre eclampsia in IVF pregnancies (22% cases as compared to 5% in the control group, p value <0.001). According to Tan et al⁵, the rate of hospitalization due to hypertension was 14%, 17%, 28% in singleton, twins and triplet pregnancies, risk was twice more than control group (p value <0.001). Maman et al⁹ showed 14% cases of pre-eclampsia compared to 4% in control group (p value <0.002).

Our study had 40.7% of multiple pregnancies, all twin gestation with one triplets as compared to 5.5% in control group (p value <0.01). Tan et al⁵ presented 25% multiple pregnancy in IVF and 1% in natural conception group. Schieve et al¹⁰ in Atlanta had 43% twins, 12% triplets and 1% quadruplet. According to Bergh et al⁶ 26.9% had multiple birth in IVF group (23.9% twins and 2.8% triplets) compared to 1% in control group.

The findings reported in literature are similar to the present study. The main determinant of multiple pregnancies is the number of embryos transferred. Campbell et al¹¹ in their study had significant increase in the number of babies born per delivery from 1 to 1.36 as the embryos transferred increased from 1 to 4 or more (p value 0.0001).

In present study 12% placenta praevia cases and one case of abruptio placentae was noted as compared to 3.7% in the controls (p value <0.01). Tan et al⁵ reported 33% placenta praevia cases and 8% abruptio placenta cases compared with 1.4% in the controls (p value <0.05). Jackson et al⁸ showed 20% placenta praevia cases. The increase is due to difference in the nature of the placental development during chorion formation in vitro which predisposes the patient to various utero placental insufficiencies. Abnormality in the location and function of the placenta and blood flow through the umbilical artery leads to pregnancy induced hypertension, pre-eclampsia, intra uterine growth restriction, placenta previa, placental abruption⁸.

There were 22% abortions, both spontaneous and induced in IVF group as a result of obstetrical complications (p value 0.04) in our study. FASTER trial¹² conducted in 2005 demonstrated 2.1 times more fetal loss prior to 24 weeks due to associated fetal anomalies in ART group.

22% subjects in our study, delivered prior to 34 weeks, comparable to 25% in Tan et al⁵, 11.5% in Jackson et al⁸, 11.2% in Bergh et al⁶. More number of preterm deliveries were due to associated obstetrical complications and patients and relatives bias towards the valued pregnancy.

This study compared the mode of delivery in both the study groups. 75% patients delivered by cesarean section as compared to 3% in control group. Study by Tan et al⁵ had 51% LSCS rate compared to 12% in control group. Jackson et al⁸ reported 26% rate of LSCS in IVF group compared to 19% in control group. The increase in

the LSCS rate in present study is probably due to other associated obstetrical complications and biased decision in view of precious pregnancy and anxious parents regarding neonatal outcome.

Risk of low birth weight in the neonate was two times in our study (88% in study group and 42% in the spontaneous conception group). A report from the Center for Disease Control and Prevention of IVF pregnancies¹³ demonstrated 1.8fold increased risk (45% in IVF group and 20% in control group). Similarly, Tan et al⁵ showed two fold increase in the risk (32% in IVF group and 15% in control group). The increase in low birth weight is due to the high incidence of multiplicity and preterm deliveries.

Present study didn't have any still births in the study group as well as the control group. However, 0.5% pregnancies had still birth in study by Tan et al⁵. Bergh et al⁶ reported 4% still births in the study group compared to 1.1% in the control group. In their study, the increased incidence is due to more congenital anomalies.

In our study group, 31% babies required NICU care. In the control group, three babies required NICU care (p value 0.04). results were similar to that demonstrated by Tan et al⁵ where 29% babies required NICU care (41% twins and 85% triplets) compared to 3% in control group. 27% in Jackson et al⁸ required NICU care as compared to 2% in the spontaneous group.

16.4% neonatal deaths were noted in the present study compared to controls (1.75%, p value 0.01). The result is similar to Jackson et al report⁸ (19.6% in study group and none in control group). Attributable cause to perinatal mortality is extreme prematurity, very low birth weight and associated congenital malformations.

There was increased maternal morbidity and mortality in the present study. Six subjects required high dependency care compared to none in controls. Two maternal deaths were noted in the IVF group, both due to amniotic fluid embolism (3703 deaths / lakh). However, no maternal deaths were seen in the control group (p value 0.01).

There was alarming high rate of maternal mortality in our study. On literature search, we could not find a study reporting maternal mortality in women undergoing IVF conceptions.

CONCLUSIONS

Patients who undergo IVF present at higher mean age and may have associated medical conditions. In addition they may have to undergo various surgeries to enhance conception and successful pregnancy rates; thus predisposing to obstetrical complications. The obstetrical and medical complications were very significant in the present study. The maternal mortality in study subjects was alarmingly high (3703/ lakh live births). In view of increased complications seen with IVF pregnancies, it is important to follow stringent guidelines for these techniques in the interest of these couples and society at large. Pre conception counselling of the couple is mandatory prior to the ART and all the consequences and expected outcomes should be discussed in detail.

Further studies are required to study the association of preconception surgeries and conception and pregnancy outcome and the maternal mortality in these subjects with larger sample size.

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