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Original Article

Complications in pregnancies after in vitro fertilization and embryo transfer

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ABSTRACT

Background: Many infertile couples need treatment in different forms including Assisted Reproductive Techniques. In Vitro Fertilization and Embryo Transfer is the most advanced method of infertility treatment. Management of these pregnancies is difficult as the couples and treating doctors have undue concern and apprehension and worry about outcome of such pregnancies. This study was undertaken to find out the complications and mode of delivery and if there is a need to manage them at tertiary care centers.

Methods: 130 cases were included in the study after pregnancy was confirmed in this prospective study. These cases were followed throughout pregnancy and labour. Pregnancy, labour, and neonatal complications were noted.

Results: Incidence of primary infertility was more common. Mean age of patient was more. All the cases were provided standard routine antenatal care. Multiple pregnancies and preterm labour were more frequent in the study group. A large number of cases delivered vaginally.

Conclusion: A large number of pregnancies terminated in vaginal delivery, thereby indicating that these pregnancies though high risk can have vaginal delivery. They can be managed at any hospital once clinical pregnancy is confirmed.

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Introduction

Most of the couples desire to have children and large number of them are able to fulfill their dreams spontaneously within 1–2 years of marriage. Those who are not able to conceive need treatment in different forms including Assisted Reproductive

Techniques (ART). In Vitro Fertilization and Embryo Transfer (IVF–ET) is the most advanced method of infertility treatment. Since the advent of IVF, over a million babies have been born.¹ The treatment of infertile couples has evolved remarkably, especially over the last 20–30 years.² Management of pregnancies after IVF–ET is difficult as the couples and treating doctors have undue concern, apprehension, and worry about outcome

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of such pregnancies. Patients are elderly and there may be other co-morbid conditions; hence, pregnancy after IVF-ET is considered as high risk.

ART in most cases leads to successful delivery of healthy singleton pregnancies. However, there are complications of pregnancy that may develop more frequently in those conceived using IVF-ET. Biochemical pregnancy loss rates following ART vary from as low as 11% to as high as 35%.³ The risk of ectopic pregnancy including heterotopic is increased at least 2-fold in patients who conceive after IVF-ET.⁴ The incidence of late pregnancy loss (after 12 weeks gestation) after ART is typically between 2 and 4% which is higher than that of spontaneously conceived pregnancies (around 1%).⁵ There is higher propensity of multiple pregnancies. The risk of multiple pregnancy is increased substantially in IVF-ET cycles. In 2005, 35.0% of all births in the US resulting from IVF-ET were multiples, a rate 10 times higher than 3% in general population.⁶

Women with IVF-conceived singletons are at increased risk of pre-eclampsia, gestational diabetes, placenta praevia, and perinatal mortality. ART singleton pregnancies also have higher relative risks of having induction of labor and Cesarean section (CS), both emergency and elective.⁷ Various studies have reported that the children born to women who conceived with ART were premature and of low birth weight.⁸ The observations cannot be attributed solely to the higher incidence of multiple pregnancies associated with ART. Many studies of children born after IVF have found a prevalence of congenital malformations similar to that in normal population (2–3%)⁹ but one Australian study observed a 2-fold increased risk of major birth defects among children conceived via conventional IVF or ICSI, compared to that in a matched population of children who were naturally conceived.¹⁰ ART babies also have increased neonatal morbidity.¹¹ The babies born by assisted reproductive technologies showed a 15 times higher risk of NICU admissions. They were mostly for supportive care for initiation of feeding, a few developed complications like neonatal jaundice, neonatal sepsis and respiratory difficulties. A review of long-term developmental outcomes in children conceived by ART has been reassuring, demonstrating that the great majority of children are developing normally.¹²

At present, there are no established guidelines; hence, there is need to look into these complications and ascertain if IVF-ET pregnancies can be managed at hospitals other than tertiary care centers. This prospective study was conducted at one of ART centers of a tertiary care hospital; the aim was to document and analyze complications in IVF-ET pregnancies.

Materials and methods

It was proposed to study IVF-ET pregnancies for the period of 2 years. The study population comprised of the patients registered and followed up at ART center of a tertiary care hospital. All patients who underwent IVF-ET were evaluated by a detailed history, clinical examination, and relevant investigations. 130 cases were enrolled for the study, the objective being to follow up all the cases with positive β hCG test on day 18 of IVF-ET. Transvaginal sonography (TVS) was

performed on day 21 to find out if it was a clinical or biochemical pregnancy. After the case was enrolled for the study, the patient was followed up closely throughout pregnancy, labor, and delivery including the condition of newborn baby. Normal standard antenatal care was provided, except the hormonal support initially.

Results were recorded in the form of outcome of pregnancy like abortion (early and late), ectopic pregnancy, multiple pregnancy, antepartum hemorrhage, congenital malformation, intrauterine growth restriction (IUGR), induction of labor, type of delivery – term or preterm, vaginal delivery or CS, and condition of newborn baby including NICU admission.

Results and discussion

Since this was only an observational study, there were no controls; the results were to be compared with the reports in literature. Age profile (Table 1) of the patients varied from 23 to 41 years; there were 56 patients whose age varied from 30 to 40 years. Infertility cases are usually older and this is one of the reasons for increased complications in pregnancy. There were 55 cases of secondary infertility whereas 75 cases were of primary infertility. The relevant past history (Table 2) indicated that tuberculosis was the commonest positive finding, almost 30%. The study by Sharma et al. too revealed that genital tuberculosis was common in their series of infertility cases.¹³ Other two common positive histories were PCOD and hypothyroidism. Biochemical pregnancy is the one where β hCG is positive which indicates pregnancy but subsequently no pregnancy is demonstrable on TVS probably due to very early pregnancy loss. There were 4 cases of biochemical pregnancy in this series (3.7%). Very early pregnancy losses

Table 1 – Age profile.

Age	Number	Percentage
20–30	72	55.4
30–40	56	43.1
>40	2	1.5
Total	130	100

Table 2 – Relevant past history.

History	Number	Percentage
History of ATT	39	30
PCOD	08	6.1
Appendectomy	02	0.15
Hypothyroidism	10	0.76
Ectopic	04	3.0
Endometriosis	04	3.0
Tuboplasty	06	4.5
Galactorrhoea	01	0.07
DVT	01	0.07
Hypertension	08	0.6.1
BOH/RPL	11	8.4
Down syndrome	01	0.07

Many patients had more than one positive history.

Table 3 – Complications in pregnancy.

Complication	Number	Percentage
Threatened abortion	25	19.2
Missed abortion	6	4.6
Hyperemesis	4	3.07
Encirclage	7	5.4
Ectopic	4	3.07
Anemia	2	1.54
Adnexal mass	3	2.3
Urinary tract infection	2	1.54
Gestational diabetes	8	6.1
Premature rupture of membranes	4	3.07
Preterm premature rupture of membranes	5	3.8
Pre-eclampsia	6	4.6
Pregnancy induced hypertension	11	8.5
Intra hepatic cholestasis of pregnancy	2	1.54
Polyhydramnios	1	0.7
Oligohydramnios	1	0.7
Intra uterine growth restriction	2	1.54
Abruptio	2	1.54
Placenta previa	1	0.7
Chorioamnionitis	1	0.7

may occur without realization even during spontaneous pregnancies. The incidence in this study was lower³ probably due to small sample size. There were six cases of missed abortion (incidence 4.6%) which were picked up on routine sonography (Table 3). Four cases of ectopic pregnancy were picked up on routine TVS indicating an incidence of 3%. Risk of ectopic pregnancy has been reported to be at least 2-fold higher in IVF-ET pregnancies.¹⁴ The cause of increased chances of ectopic pregnancy is presumed to be the migration of embryos or direct transfer into fallopian tubes.

Heterotopic pregnancies are extremely rare in spontaneous pregnancies but far more common in infertile women who conceive after ovulation induction or IVF. In this study, no case of heterotopic pregnancy was detected. There was no case of mid trimester pregnancy loss, whether spontaneous or induced. Incidence of late pregnancy loss that is after 12 weeks after ART is typically between 2 and 4%⁵ which is higher than that of spontaneously conceived pregnancies. The cause of mid trimester pregnancy loss may be fetal death or termination of pregnancy due to chromosomal and other abnormality. There was no case of congenital or chromosomal abnormality. Further reason for late pregnancy loss is the increased incidence of multiple pregnancies.

Transvaginal ultrasound done on day 21 showed 42 cases of multiple pregnancies indicating an incidence of 34.3% (Table 4). 35 cases were of twin gestation, 6 and 1 of triplet and

Table 4 – TVS (day 21).

Finding	Number	Percentage
Single sac	80	60
Two sacs	35	27
Three sacs	6	0.46
4 sacs	1	0.23
Ectopic	4	0.31
No sac	4	0.31

Table 5 – Pregnancy outcome.

Outcome	Number	Percentage
Preterm	28	21.5
FTND	19	10.4
LSCS elective	19	10.4
LSCS emergency	24	18.4
Missed abortion	15	11.5
Mid trimester abortion	2	1.7
Vacuum	7	0.53
Forceps	2	1.7
Ectopic	4	3.7
Biochemical pregnancy	4	3.7

quadruplet sacs respectively. Finally, 35 cases delivered as twins, indicating a large number of vanishing sac/pregnancy. One case underwent fetal reduction. There were 17 cases of pregnancy-induced hypertension and pre-eclampsia indicating an incidence of 11%. There were 8 cases of Gestational Diabetes Mellitus which was higher than the normal population.⁷ There may be many other factors like increased maternal age, infertility, or treatment of infertility causing increased complications.

43 cases delivered by CS (19 elective and 24 emergency – Table 5) indicated a percentage of 33.8% slightly higher than the normal population, but a large number of cases delivered vaginally, contrary to the belief of many that all IVF pregnancies should be delivered by CS. Various studies have reported higher incidence of IUGR and prematurity in pregnancies following IVF-ET.¹¹ Though multiple pregnancies may be responsible for this but it cannot be solely attributed to multiple pregnancies. There were 28 cases who delivered preterm, a percentage of 21% which is much higher than normal population. Though the incidence of GDM was higher, yet there was no case of macrosomia.

149 babies were born to the study group cases (Table 6); there were 45 (36%) babies whose birth weight was less than 2 kg (Table 7). Most of these were twin pregnancies; there were only six singleton pregnancies where the weight was less than 2 kg. This too indicates that multiple pregnancies is the commonest complication in these pregnancies as reported by Brosil et al.¹¹ There was one case of congenital heart disease who died during neonatal period. Initial studies comparing babies born following IVF or ICSI with spontaneously conceived controls suggested no increase in the incidence of congenital abnormalities although the magnitude of these was in the hundreds rather than the thousands or tens of thousands that is needed in order to determine any genuine difference.¹⁰

There were eight cases of perinatal deaths which included still birth and neonatal deaths. This works out to be 54 perinatal deaths per 1000 which is higher than pregnancies conceived spontaneously. A large number (25%) of babies (38 out of 149) were shifted to NICU either for observation or treatment. This incidence is much higher. It has been shown that ART babies have increased neonatal morbidity.¹⁵ Many other studies have suggested an increase in neonatal morbidity and mortality but do not sufficiently address the effect of confounders such as birth weight and gestational age.

Table 6 – Gender of the NBB.

Gender	Number	Percentage
Male	80	53
Female	69	47
Total	149	100

Number of babies born is more than the number of cases due to many sets of multiple pregnancies.

Table 7 – Birth weight.

Birth weight	Number
Less than 1 kg	15 (3 singleton)
1–2 kg	30 (singleton 3)
2–3 kg	66
3–4 kg	38
>4 kg	Nil

Conclusion

130 cases were enrolled for the study; there were no controls in this study as it was an observational study. The findings were compared with those available in literature. The commonest complication was multiple pregnancies along with other sequel. Incidence of twins was the highest. A large number of pregnancies had vaginal delivery, thereby indicating that these IVF–ET pregnancies can have normal delivery. They should be treated as high-risk labor cases.

There is a need for further large sample, multicentric studies along with the controls to compare the results with pregnancies conceived spontaneously. It is difficult to get comparable controls, as the factors in IVF–ET pregnancies are different. Doctors and patients both are concerned and fearful but these cases require routine antenatal care except hormonal support initially. These cases can go for normal vaginal birth; CS should be performed for obstetrical indications only.

Conflicts of interest

The authors have none to declare.

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