

A Study of Various Obstetrics Outcomes and Complications among In-Vitro Fertilization (IVF) Pregnancies

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ABSTRACT

Introduction: Use of In-vitro fertilization (IVF) has raised major concern about the outcome of resulting pregnancies. In-Vitro Fertilization and Embryo Transfer is the most advanced technique of infertility treatment though management of these pregnancies is not that easy as the couples and treating doctors have undue concerns and apprehensions about the outcomes of such pregnancies.

Material and Methods: Obstetrics outcomes in the women conceived through IVF and the neonatal characteristics of the live- born infants at Army Hospital R & R were analyzed in this study between Jan 2017 to Dec 2017.

Results: IVF pregnancies increased the incidence of ectopic pregnancy and multifetal gestation. The rate of cesarean section was also higher in IVF pregnancies. While a large number of cases delivered vaginally, multiple pregnancies and preterm labour were more frequent in the study group. After first trimester they can be managed as a normal pregnancy.

Conclusion: Infertility cases are usually older, and this is one of the reasons for increased complications in pregnancy. Multiple pregnancies are the most prevalent complication in these pregnancies. Risk of ectopic pregnancy has been reported to be at least 2-fold higher in In-vitro fertilization and Embryo- Transfer (IVF-ET) pregnancies.

Keywords: Infertility, In-Vitro Fertilizations, Multiple Pregnancies, Obstetrics Complications

INTRODUCTION

Infertility is defined as a year of unprotected intercourse without pregnancy. This may be primary infertility, in which no previous pregnancies have occurred, and secondary infertility, in which a prior pregnancy, although not necessarily a live birth has occurred. Infertility differs across regions of the world and is estimated to affect 8 to 12 percent of couple worldwide.^{1,2} The World Health Organization (WHO) has made an estimate of 60 to 80 million couples worldwide currently suffer from infertility. The WHO estimates the overall prevalence of primary infertility in India to be between 3.9 and 16.8 percent.³ The leading causes of infertility include male factor, ovulatory disorders, decreased ovarian reserve, tubal injury, blockage, or paratubal adhesions (including endometriosis with evidence of tubal or peritoneal adhesions), uterine factors, cervical and immunological factors, systemic conditions (including infections or chronic diseases such as autoimmune conditions or chronic renal failure), and unexplained factors (including endometriosis and no evidence of tubal or peritoneal adhesions). Treatment options include Intra-uterine insemination (IUI), ovulation induction, IVF, ICSI,

gamete intra-fallopian transfer (GIFT), zygote intra-fallopian transfer (ZIFT), cryopreserved embryo transfers and the use of donor oocytes. IVF involves prevention of premature LH surge, follicle growth, pretreatment, adjunctive medications, oocyte maturation/ovulation triggering, oocyte retrieval, luteal support, fertilization, in vitro embryo culture, transfer of fresh embryos, cryopreservation of fresh embryos, cryopreservation of surplus embryos and first-trimester pregnancy monitoring.

Thus, the aim of the study was to evaluate the obstetric outcomes and complications of pregnancies after IVF in comparison to spontaneous conception (SC). Also, at present, there are no established guidelines; hence, there is need to look into these complications and ascertain if In-vitro fertilization and Embryo-Transfer (IVF-ET) pregnancies can be managed at hospitals other than tertiary care centers.

MATERIAL AND METHODS

The approval from the Ethics Committee of our hospital (Army Hospital R & R) was taken and then this prospective study was performed between 01 Jan 17 to 31 Dec 17. Informed consent was taken. 200 pregnant women who conceived through IVF were recruited to this study. All patients were evaluated by a detailed history, clinical examination, and relevant investigations. After the case was enrolled for the study, the patient was followed up closely throughout pregnancy, labor, and delivery including the condition of the newborn baby. Obstetrics outcomes in the women conceived through IVF and the neonatal characteristics of the live-born infants at this center were analyzed in this study.

STATISTICAL ANALYSIS

Data entry and statistical analysis were performed with the help of Microsoft Excel 2010 and SPSS version 20.0, while categorical variables are presented as absolute numbers and percentages.

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20-30	112	56.0
30-40	85	42.5
>40	3	1.5
Total	200	100

Table-1: Age Profile

History of ATT	73	34.0
PCOD	27	13.5
Appendectomy	6	3.0
Hypothyroidism	26	13.0
Ectopic	7	3.5
Endometriosis	7	3.5
Tuboplasty	14	7.0
Galactorrhoea	3	1.5
DVT	3	1.5
Hypertension	20	12.5
BOH/ RPL	16	8.0
Down Syndrome	2	1.0

*Many patients had more than one positive history

Table-2: Relevant Past History

Single sac	126	63
Two sac	53	26.5
Three sac	8	4
4 sacs	2	1
Ectopic	7	3.5
No sac	4	2

Table-3: Transvaginal Sonography (day 21)

Threatened Abortion	26	17
Missed Abortion	11	7.1
Hyperemesis	4	2.5
Encirclage	9	5.8
Ectopic	7	4.5
Anemia	5	3.2
Adnexal mass	3	2
Urinary tract infection	5	3.2
Gestational diabetes	16	10.4
Premature rupture of membranes	8	5.2
Preterm premature rupture of membranes	9	5.8
Pre-eclampsia	12	7.8
Pregnancy-induced hypertension	24	15.6
Intrahepatic cholestasis of pregnancy	3	2
Polyhydramnios	1	0.8
Oligohydramnios	2	1.2
Intrauterine growth restriction	3	2
Abruptio	3	2
Placenta previa	1	0.7
Chorioamnionitis	2	1.2

Table-4: Complications in pregnancy

RESULTS

Obstetric outcomes

Since the present study was an observational study; there were no controls. The results were to be compared with the reports

Preterm	42	21
FTND	52	26
LSCS elective	35	17.5
LSCS emergency	44	22
Missed abortion	11	5.5
Vacuum	3	1.5
Forceps	2	1
Ectopic	7	3.5
Biochemical pregnancy	4	2

Table-5: Pregnancy Outcome

Male	119	53.13
Female	112	46.87
Total	231	100

*Number of babies born > the number of cases; due to many sets of multiple pregnancies

Table-6: Gender of the NBB

Less than 1 kg	23 (3 singletons)
1-2 kg	83 (3 singletons)
2-3 kg	100
3-4 kg	25
> 4kg	Nil

Table-7: Birth Weight

in previous studies. Age profile (Table 1) of the patients varied from 23 to 41 years; there were 85 patients whose age varied from 30-40 years. Infertility cases are usually older, and this is one of the reasons for increased complications in pregnancy. There were 90 cases of secondary infertility, and 110 cases were of primary infertility. The relevant past history (Table 2) indicated that the tuberculosis was the commonest positive finding, 34%. Other two common histories were PCOD (13.5%) and hypothyroidism (13%). There were 4 cases of biochemical pregnancy in the series (2.1%). A Transvaginal ultrasound done on day 21 showed 63 cases of multiple pregnancies indicating 33.3% (Table 3). 53 cases were of twin gestation, 8 and 2 of triplet quadruplet sacs respectively. Finally, 51 cases delivered as twins and one case delivered as triplet indicating a large number of vanishing sac/ pregnancy. There were 36 cases of pregnancy-induced hypertension and preeclampsia indicating an incidence of 18%; and 16 cases of Gestational Diabetes Mellitus. There were 11 cases of missed abortion (incidence 7.1%), and seven cases of ectopic pregnancy which were picked up on routine TVS indicating an incidence of 4.5% (Table 4). 79 cases delivered by CS (35 electives and 44 emergency-Table 5) indicated a percentage of 39.5%, but a large number of cases delivered vaginally. There were 42 cases who delivered preterm, a percentage of 21% which is much higher than the normal population, yet there was no case of macrosomia. 231 babies were born to the study group cases (Table 6); 106 babies (45.8%) had weight less than 2kg (Table 7). Most of these were twin pregnancies; there were only six singleton pregnancies where the weight was less than 2 kg.

DISCUSSION

The study was conducted to assess the association of applications of ART with various perinatal outcomes. We present occurrence of various perinatal outcomes among women who conceived with ART at the Army Hospital (Research and Referral), New Delhi; an apex hospital in the Armed Forces with a highly specialized ART center. 200 cases were enrolled for the present study; there were no controls in this study as it was an observational study. The findings were compared with those available in the literature. The commonest complication was multiple pregnancies along with another sequel. The incidence of twins was the highest. A large number of pregnancies had a vaginal delivery, thereby indicating that these IVF-ET pregnancies can have a normal delivery. They should be treated as high-risk labor cases.

There has been an increasing trend of use of ART globally, including India as an ever-increasing number of infertile couples is seeking treatment.^{4,5} While ART has helped infertile couples, these techniques have been associated with adverse pregnancy outcomes. There has been an increased risk of LBW, preterm babies, and multiple pregnancies. The study conducted by Narayan et al.⁶ corroborated the findings of an earlier study carried out in the hospital which showed an excess prevalence of multiple births, LBW, and preterm babies among ART conceived women. However, that study was descriptive in nature and did not use a comparison group. The results of our study are consistent with the findings of mentioned studies. The present study is reliable and has reasonable internal validity.

Since this was only an observational study, the results were to be compared with the reports in the literature. Age profile of the patients varied from 23 to 41 years. Infertility cases are usually older, and this is one of the reasons for increased complications in pregnancy. There were 75 cases of secondary infertility whereas 125 cases were of primary infertility. The relevant past history (Table 2) indicated that tuberculosis was the commonest positive finding, almost 34%. The study by Sharma et al.⁷ too revealed that genital tuberculosis was common in their series of infertility cases. Other two common positive histories were PCOD and hypothyroidism. There were 4 cases of biochemical pregnancy in this series. Biochemical pregnancy is one where β hCG is positive which indicates pregnancy but subsequently no pregnancy is demonstrable on TVS probably due to very early pregnancy loss. Very early pregnancy losses may occur without realization even during spontaneous pregnancies. The incidence in this study was lower probably due to small sample size.⁸

There were 36 cases of pregnancy-induced hypertension and preeclampsia and 16 cases of Gestational Diabetes Mellitus which was higher than the normal population.⁹ There may be other factors like increased maternal age, infertility, or treatment of infertility-causing increased complications. An increased risk for the development of pregnancy-induced hypertension (PIH) and gestational diabetes has been

documented in women with singleton babies¹⁰ and higher probability of vaginal bleeding in twin pregnancies.^{11,12}

There were 11 cases of missed abortion (incidence 7.1%) which were picked up on routine sonography (Table 4). Seven cases of ectopic pregnancy were picked up on routine TVS indication an incidence of 4.5%. Risk of ectopic pregnancy has been reported to be at least 2-fold higher in IVF-ET pregnancies.¹³ 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% which is higher than that of spontaneously conceived pregnancies.¹⁴ 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. A further reason for late pregnancy loss is the increased incidence of multiple pregnancies.

Further, 79 cases delivered by CS (35 elective and 44 emergency- Table 5) indicated a percentage of 39.5% 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 through CS. According to previous researches, with increasing experience of IVF cases, the cesarean section rate has been shown to fall.¹⁵ It has been assumed that the high rate of cesarean sections among IVF patients reflects, in part, the increased anxiety surrounding the management of these premium pregnancies.¹⁶ Reports by Doyle et al.¹⁷ and Wang et al.¹⁸ have suggested that assisted conception poses an added risk in ongoing singleton pregnancies with a higher rate of intrauterine growth retardation and perinatal loss and an increased risk for pregnancy-induced hypertension.¹⁰ Data shows that cesarean section is more common, though not statistically significant, in women with twin pregnancies after assisted reproduction compared to spontaneous conception (69% versus 55%; $p=0.07$). Studies without matched controls showed an increased incidence of cesarean sections.^{1,19,20}

In the present study, no case of heterotopic pregnancy was detected. There was no case of mid-trimester pregnancy loss, whether spontaneous or induced. Heterotopic pregnancies are extremely rare in spontaneous pregnancies but far more common in infertile women who conceive after ovulation induction or IVF. The incidence of late pregnancy loss that is after 12 weeks after ART is typically between 2 and 4% which is higher than that of spontaneously conceived pregnancies. The cause of mid-trimester pregnancy loss may be foetal 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. Various studies have indicated the higher incidence of intrauterine growth restricted fetuses (IUGR) and prematurity in pregnancies following IVF- ET.²¹ Though multiple pregnancies may be responsible for this, it cannot be solely attributed to multiple pregnancies.

Further, there were 42 cases who delivered preterm, a percentage much higher than normal population. Though the incidence of GDM was higher, yet there was no case of macrosomia. Since multiple pregnancies was common among ART conceived women, the risk of preterm birth was increased. It has been reported that the preterm delivery rates were 10% among singletons; however, the rates for twins were nearly 50%, and those for triplets were > 95%.²² The women were delivered if there was an onset of labor and risk of neonatal complications. Consequently, significantly higher number of babies was preterm with the greater tendency for LBW. Apart from this, LBW could also be due to multiple pregnancies and maternal malnutrition among pregnant women due to lower educational and socio-economic status. In a study conducted by Reubinoff (1997)¹⁶, preterm labor was a common complication in both groups without significant differences in accordance with another controlled study with 260 singleton IVF pregnancies. Pregnancy-induced hypertension, vaginal bleeding, preterm labor, and amnion infection syndrome can, isolate or in combination, led to spontaneous preterm delivery or urge immediate cesarean section.

The higher preterm birth rate of twin pregnancies after assisted reproduction seems to be one of the major factors having a significant impact on the caesarean section rate. The anxiety of ART patients and their physicians with regard to safeguarding pregnancy and delivery have been postulated to increase the rate of cesarean sections.²³ It has been reported that preterm labor occurs in near half of twin pregnancies and likely to occur four times greater among multiple than singleton gestations.²⁴ Our findings supported the results reported by Tan et al.²⁵ in which preterm labor occurred in 58% of the ART group compared with 52% in the control group. In contrast, Zaib-un-Nisa et al.²⁶ found preterm labor in 42% of ART twin deliveries compared with 51% spontaneous twin deliveries.

Finally, 231 babies were born to the study group cases; out of which there were 106 (45.8%) babies whose weight was less than 2kg. There were only six singleton pregnancies where the weight was less than 2 kg while most of these were twin pregnancies. This too indicates that multiple pregnancies are the commonest complication in these pregnancies as reported by Brosil et al.²¹ Studies show a lower mean birth weight after assisted conception; however when controlled for confounding variables only pregnancy-induced hypertension remains as significant parameter leading to a decrease in birth weight, at least in singleton pregnancies. Pregnancy-induced hypertension was more often observed among the ART group and, therefore leads to reduced birth weight. No other factors such as gestational diabetes or smoking were associated with the reduced birth weight. Gestational and maternal ages were essentially the same between the study

groups.²⁷

CONCLUSION

Total 200 IVF pregnancy cases were enrolled for the study, and there were no controls as it was an observational study. The findings were compared with those available in literature. The commonest complication was multiple pregnancies along with another sequel. The incidence of twins was the highest. There were 42 cases who delivered preterm, though multiple pregnancies may be responsible for this, it cannot be solely attributed to this factor. A large number of pregnancies had vaginal delivery, thereby indicating that these IVF-ET pregnancies can have a normal delivery. They should be treated as high-risk labor cases. These cases can go for normal vaginal birth; CS should be performed for obstetrical indications only. Doctors and patients both are concerned and fearful, but these cases require routine antenatal care except hormonal support initially.

Furthermore, there is a need for a large sample, multi-centric studies along with the controls to compare the results with pregnancies conceived spontaneously.

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