

Research Article



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COMPLICATIONS OF IN VITRO FERTILISATION PREGNANCIES VISITING DEHRADUN, UTTARAKHAND

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ABSTRACT

Background: With fewer instances of difficulties, assisted reproductive technologies have been extensively embraced in India. Nonetheless, a number of elevated hazards have been observed, such as gestational diabetes, hypertension, and preterm.

Aim: The objective of the current clinical investigation was to examine main problems and risk factors related to in-vitro fertilisation (IVF) pregnancies.

Methods: The procedures, relevant risk factors, and problems connected to IVF were examined in 310 female patients. Following a statistical analysis of the collected data, conclusions were drawn.

Results: The study's findings indicated that utilising two embryos during embryo transfer was linked to a greater risk of twin pregnancies. With $p < 0.05$, no meaningful correlation was seen between any number of pregnancies with either gestational diabetes or gestational hypertension. With $p > 0.05$, the study's findings did not demonstrate a significant correlation between gestational age, gestational diabetes, or gestational hypertension. Additionally, there was no significant association ($p = 0.66$) between the aetiology of infertility and gestational age. Eighteen participants reported having ARDS (acute respiratory distress syndrome) out of 68 preterm newborns.

Conclusion: there is a correlation between the number of embryos and multiple pregnancies. While twin pregnancies are more likely in younger women having in-vitro fertilisation pregnancies, gestational hypertension is more common in older females. With no difference in the age of the females, IVF pregnancies have a greater rate of preterm births.

Keywords: pregnancy problems, perinatal complications, infertility, and in vitro fertilisation (IVF).

INTRODUCTION

The inability to conceive after 12 months of regular sexual activity without the use of contraceptives is known as infertility in the medical world. Infertility is a major problem everywhere, including in India. Approximately 186 million people worldwide are infertile. Eighty-five percent of the afflicted couples know why they are infertile.

Maternal age is thought to be the most important negative prognostic factor for pregnancy. It has been shown that women who are older than 25 to 30 exhibit a decrease in clinical pregnancy.¹

In vitro fertilisation, or IVF, was first used in England in 1978. As the world's need grew, IVF became accessible everywhere. When IVF was first introduced, it was utilised on female patients with bilateral tubal blockage. But infertilities with other aetiologies, such as those with unknown origins, are increasingly included in the indications of IVF. The reason of infertility, the quantity and quality of embryos utilised for transfer, the baseline level of FSH, and the age of the female

undergoing IVF are some of the variables that determine the effectiveness of IVF. An estimated 3% of all births occur through IVF each year.²

Prematurity, gestational diabetes mellitus, hypertension, and/or perinatal problems have all been linked to an increased risk of difficulties in IVF pregnancies. Complications from hypertension are known to affect the mother and the foetus, and can occur in 2% to 33% of pregnancies. These issues fall into three categories: preeclampsia, prenatal hypertension, and persistent hypertension.³

Raised blood pressure before conception, detected during the first 20 weeks of pregnancy, or raised blood pressure that lingered after the 12-week postpartum period are the hallmarks of chronic hypertension. A condition of high blood pressure beyond 20 weeks of pregnancy in a person who had normal blood pressure before to conception and showed no signs of proteinuria or preeclampsia is known as pregnancy-induced hypertension, formerly known as gestational hypertension.⁴

Preeclampsia, which occurs after 20 weeks of pregnancy and indicates a condition affecting numerous organs and maybe proteinuria and high blood pressure, has an uncertain aetiology. When using frozen embryos instead of fresh embryos or natural conception procedures, in vitro fertilisation (IVF) is associated with a higher risk of hypertension throughout pregnancy. On the other hand, compared to fresh embryo transfer, frozen embryo transfer is reported to result in improved obstetric and neonatal outcomes. Complication rates in frozen embryo transfers are 1.5 times greater than in natural embryo transfers and twice as high as in natural conception.⁵

Another pregnancy issue that varies in incidence depending on the diagnostic criteria and the region being evaluated is gestational diabetes mellitus. Gestational diabetes mellitus affects 7% to 25% of women worldwide, and around 14% of women in India have it. A diagnosis of gestational diabetes mellitus indicates the onset of glucose intolerance during pregnancy. Multiple pregnancies, IVF pregnancies, and obesity are among the variables that might contribute to the development of gestational diabetes mellitus and its consequences. In afflicted females, preterm and preeclampsia are also increased risks associated with gestational diabetes mellitus.⁶

A infant classified as preterm or prematurity is one whose gestational age is fewer than 37 weeks. There are other subtypes of prematurity, such as very preterm (28-32 weeks), late preterm (33-36 weeks), and extremely preterm (less than 28 weeks). Prematurity prevalence is estimated by the WHO to be between 5% and 18%. Unknown is the pathophysiology of premature birth.

.. However, a number of risk factors, such as assisted reproduction, have been identified as predisposing factors. Restricting the number of embryos implanted in IVF pregnancies has helped to significantly reduce the risk of premature delivery.⁷. The purpose of the current study was to examine main problems and risk factors related to in-vitro fertilisation (IVF) pregnancies.

MATERIALS AND METHODS

The goal of the current observational retrospective study was to examine significant problems and risk factors related to IVF pregnancies as well as IVF pregnancies that were achieved by IVF.

The study was carried out at the Safdarjung Hospital and the Department of Obstetrics and Gynecology at Vardhman Mahavir Medical College in New Delhi with approval from the relevant institutional ethical committee. The Department of Obstetrics and Gynecology at the Institute provided the study's data.

310 female participants who had IVF at the Institute were included in the current research. Females with infertility, patients who donated their oocytes or eggs, and consenting research participants were the study's inclusion criteria. Women who stopped participating in the study midway through and women whose data were incomplete were the study's exclusion criteria.

Following the research subjects' final inclusion, a thorough medical history was documented for each participant, including information on their age, demographics, etiology of infertility, diseases observed during pregnancy, and the maturity and number of embryos being transferred. The Department of Obstetrics and Gynecology's study women files and records provided the data. The research lacked a control group.

The Shapiro-Wilk test and SPSS software version 21.0 were used to statistically analyse the collected data. Based on their distribution, the data were presented as mean, standard deviation, medians, and interquartile ranges. The independent group

quantitative variables were compared using the t-test and the Mann Whitney U test. At $p < 0.05$, the significance threshold was maintained.

RESULTS

The goal of the current observational retrospective study was to examine significant problems and risk factors related to IVF pregnancies as well as IVF pregnancies that were achieved by IVF. The research evaluated 310 infertile patients, whose mean age ranged from 20 to 55 years, with a mean age of 36.55 ± 6.64 years. 10% ($n = 31$), 23.22% ($n = 72$), 32.90% ($n = 102$) and 33.87% ($n = 105$) of the research participants had combination factors, unknown factors, female factors, and male factors as the aetiology of infertility, respectively (Table 1).

Results showed that patients' eggs were used for embryo transfer in 88.06% ($n=273$) of research subjects, artificial insemination was used in 2.90% ($n=9$) of subjects, and egg donation was used in 9.03% ($n=28$) of study subjects. A total of 188 research participants, or 60.64%, utilised two embryos every cycle.

78.06% ($n=242$) of the 310 research participants underwent embryo transfer utilising day 5 embryos. Of the research participants, 18.1% ($n = 56$) had gestational hypertension, while 24.51% ($n = 76$) had gestational diabetes. Subjects with diabetes and gestational hypertension had mean ages of 36.13 ± 5.67 and 37.85 ± 5.21 , respectively. With $p=0.07$, the difference was statistically not significant. However, at 38.84 ± 5.82 and 36.04 ± 5.44 years old, respectively, and with a p -value of 0.02, the individuals with gestational hypertension were considerably older than the females with gestational diabetes mellitus. 274 research participants had their pregnancies terminated at delivery. Of the aborted pregnancies, 66 (24.08%) were twin pregnancies, and 208 (74.91%) were singleton pregnancies.

There was a statistically significant age difference between the mothers of the two types of pregnancies: the mothers of twin pregnancies were found to be younger than the mothers of singleton pregnancies ($p < 0.001$). Table 2 lists the individuals' distribution according to the number of multiple pregnancies and the IVF method employed. Twin and single pregnancies were seen in 28.6% ($n = 8$) and 71.4% ($n = 20$) of the research participants who had donated their eggs, respectively. 50% ($n=4$) of the participants experienced twin and single pregnancies through artificial insemination. Twin and single pregnancies were seen in 0% and 100% ($n=2$) of the individuals who had four embryos transferred, respectively. Twin and single pregnancies were seen in 33.3% ($n = 2$) and 66.7% ($n = 4$) of the individuals who had three embryos transferred, respectively.

Twin and single pregnancies were seen in 63.6% ($n = 42$) and 36.4% ($n = 2$) of the individuals who had two embryos transferred, respectively. Twin and single pregnancies were seen in 6.1% ($n = 10$) and 93.9% ($n = 154$) of participants with a single embryo transfer, respectively (Table 2). With $p < 0.001$, the difference was statistically significant. The findings of the study indicated that the use of two embryos during embryo transfer was linked to an increased risk of twin pregnancy. On the other hand, there was no discernible link found between the use of other methods and repeated pregnancies. Additionally, there was no significant correlation ($p < 0.05$) between the number of pregnancies and either gestational hypertension or diabetes. Preterm births were seen in 26% ($n=68$) of the 262 pregnancies among the research participants.

Compared to full-term neonates, who were 37.16 ± 5.21 years old, preterm babies were 35.3 ± 6.93 years old. Nevertheless, at $p=0.12$, the difference was statistically not significant. With $p > 0.05$, the study's findings did not demonstrate a significant correlation between gestational age, gestational diabetes, or gestational hypertension. Additionally, there was no significant association ($p=0.66$) between the aetiology of infertility and gestational age. Eighteen participants reported having ARDS (acute respiratory distress syndrome) out of 68 preterm newborns.

DISCUSSION

Infertility was evaluated in 310 participants with a mean age of 36.55 ± 6.64 years and a mean age range of 20–55 years in this retrospective investigation. Of the research individuals, 10% ($n = 31$), 23.22% ($n = 72$), 32.90% ($n = 102$), and 33.87% ($n = 105$) had combination factors, unknown factors, female factors, and male factors as the aetiology of infertility, respectively.

These results were in line with research conducted in 2017 by Eskew AM et al. and in 2021 by Wang J et al., where participants were evaluated using demographic information similar to that of the current study. According to research data, patients' eggs were used for embryo transfer in 88.06% ($n=273$) of study subjects, artificial insemination was used in 2.90% ($n=9$) of study subjects, and egg donation was used in 9.03% ($n=28$) of study subjects. A total of 188 research participants,

or 60.64%, utilised two embryos every cycle. 78.06% (n=242) of the 310 research participants underwent embryo transfer utilising day 5 embryos. Of the research participants, 18.1% (n = 56) had gestational hypertension, while 24.51% (n = 76) had gestational diabetes. The mean age of the participants with diabetes and gestational hypertension was 37.85±5.21 years and 36.13±5.67 years, respectively.

With p=0.07, the difference was statistically not significant. However, at 38.84±5.82 and 36.04±5.44 years old, respectively, and with a p-value of 0.02, the individuals with gestational hypertension were considerably older than the females with gestational diabetes mellitus. 274 research participants had their pregnancies terminated at delivery. Of the aborted pregnancies, 66 (24.08%) were twin pregnancies, and 208 (74.91%) were singleton pregnancies. These results were in line with studies by Fechner AJ et al. (2015) and Eichelberger KY10 (2017), who found that the prevalence of gestational hypertension and diabetes in their study participants was similar and that the subjects' age was higher for females with gestational hypertension than for controls.

It was observed that there was a significant age difference between the moms (p<0.001) between the mothers of twin pregnancies and the mothers of singleton pregnancies. Twin and single pregnancies were seen in 28.6% (n = 8) and 71.4% (n = 20) of the research participants who had donated their eggs, respectively. 50% (n=4) of the participants experienced twin and single pregnancies through artificial insemination. Twin and single pregnancies were seen in 0% and 100% (n=2) of the individuals who had four embryos transferred, respectively. Twin and single pregnancies were seen in 33.3% (n = 2) and 66.7% (n = 4) of the individuals who had three embryos transferred, respectively. Twin and single pregnancies were seen in 63.6% (n = 42) and 36.4% (n = 2) of the individuals who had two embryos transferred, respectively.

Twin and single pregnancies were seen in 6.1% (n = 10) and 93.9% (n = 154) of the individuals who underwent a single embryo transfer, respectively. With p<0.001, the difference was statistically significant. These findings corroborated those of Vogel JP et al. (2018) and Sanders JN et al. (2022), whose authors proposed that younger females who received two embryo transfers, like in our study, had a greater risk of twin pregnancies.

It was shown that the use of two embryos during embryo transfer was linked to increased odds of twin pregnancy. On the other hand, there was no discernible link found between the use of other methods and repeated pregnancies. Additionally, there was no significant correlation (p<0.05) between the number of pregnancies and either gestational hypertension or diabetes. Preterm births were observed in 26% (n=68) of the research individuals out of 262 pregnancies. Compared to full-term neonates, who were 37.16±5.21 years old, preterm babies were 35.3±6.93 years old. Nevertheless, at p=0.12, the difference was statistically not significant. These findings were consistent with research by McLennan AS et al.(2018) and Luke B et al.(2007), who found that preterm newborns had lower gestational ages than full-term infants. The study's findings indicated that there was no significant correlation (p>0.05) between gestational age, gestational diabetes, and gestational hypertension.

Also, no significant correlation was seen in the gestational age and etiology of infertility with p=0.66. Among 68 preterm infants, 18 subjects reported ARDS (acute respiratory distress syndrome). These results were comparable to the findings of Dietl A et al¹⁶ in 2015 and Uzunov AV et al¹⁷ in 2022 where authors suggested no association of gestational age to gestational diabetes or gestational hypertension.

CONCLUSION

Considering its limitations, the present study concludes that embryo numbers are correlated with multiple pregnancies. In older females, gestational hypertension is commonly seen, whereas, twin pregnancies are more common in younger females undergoing in-vitro fertilization pregnancies. A higher incidence of premature deliveries is seen in IVF pregnancies with no difference in the age of the females.

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TABLES

Characteristics	N	%
Mean age (years)	36.55±6.64	
Age range (years)	20-55	
Etiology of infertility		
Combined	31	10
Unknown	72	23.22
Female	102	32.90
Male	105	33.87

Table 1: Demographic data of study subjects

Pregnancy type/ IVF technique	Twin pregnancy		Single pregnancy		p
	N	%	N	%	
Egg donation	8	28.6	20	71.4	<0.001
Artificial insemination	4	50	4	50	
Embryo transfer with 4 embryos	0	0	2	100	
Embryo transfer with 3 embryos	2	33.3	4	66.7	
Embryo transfer with 2 embryos	42	63.6	2	36.4	
Embryo transfer with 1 embryo	10	6.1	154	93.9	

Table 2: Pregnancy distribution based on IVF technique in study subjects

