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DEPICTING THE INCIDENCE OF COMPLICATIONS IN THE IN VITRO FERTILIZATION PREGNANCIES

Dr Vibha Singh Patel,[1] Dr Antarlina Ray[2*]

[1]MBBS, DNB, Senior Resident, Department of Obstetrics and Gynecology, Vardhman Mahavir Medical College And Safdarjung Hospital, New Delhi

[2*]MBBS, DNB, Senior Resident, Department of Obstetrics and Gynecology, Guru Govind Singh Hospital, Raghubir Nagar, West Delhi, Delhi

Address for correspondence

Dr. Antarlina Ray

Email id: antarlina737@gmail.com

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ABSTRACT

Background: Assisted reproductive technologies have been adopted widely in India with fewer incidences of complications. However, various increased risks including gestational diabetes, hypertension, and prematurity have been seen.

Aim: The present clinical study was aimed at analyzing in-vitro fertilization (IVF) pregnancies and associated risk factors and major complications associated with IVF pregnancies.

Methods: In 310 females undergoing IVF, the techniques, associated risk factors, and IVF-related complications were studied. The data gathered were analyzed statistically and results were formulated.

Results: The study results showed that higher chances of twin pregnancy were associated with embryo transfer using 2 embryos. No significant association was seen in several pregnancies and gestational diabetes or gestational hypertension with $p<0.05$. The study results showed no significant association between gestational age gestational diabetes and gestational hypertension with $p>0.05$. 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).

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.

Keywords: infertility, in vitro fertilization, IVF, pregnancy complications, perinatal complications

INTRODUCTION

In a medical context, infertility is defined as an inability to get clinical pregnancy in 12 months of regular sexual intercourse with no contraceptive measures being used. Infertility is highly prevalent globally including India. Globally, approximately 186 million subjects have infertility. In 85% of the affected couples, the cause of infertility is identifiable. The most significant negative predictive factor for pregnancy is considered advanced maternal age. It has been noted that females of age >25-30 years showed a decline in clinical pregnancy.[1]

In England, in 1978, IVF (In vitro fertilization) was used for the first time. With an increase in the demand globally, IVF soon was globally available. In its initial time, IVF was used in females having bilateral tubal occlusion. However, the indications of IVF were extended recently to include infertilities of other etiologies including those of unknown origins. The success of IVF is governed by various factors including the infertility cause, quality and

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number of embryos used for transfer, basal value of FSH, and age of the female undergoing IVF. Nearly 3% of all births every year are from the IVF.[2]

Increased complications risk has been associated with IVF pregnancies including perinatal complications, prematurity, gestational diabetes mellitus, and/or hypertension. The complication associated with hypertension can affect the fetus and female and are reported in nearly 2% to 33% of all pregnancies. These complications can be divided into preeclampsia, gestational hypertension, and chronic hypertension.[3] Chronic hypertension depicts high blood pressure before pregnancy which is diagnosed in the first 20 weeks of gestation or the high blood pressure that did not relieve after 12 weeks postpartum. Gestational hypertension was earlier known as pregnancy-induced hypertension and defines as a condition of high blood pressure after 20 weeks of pregnancy where the subject had normal blood pressure before pregnancy with no signs of proteinuria or preeclampsia.[4]

The etiology of preeclampsia is unknown, and it signifies a disease affecting multiple organs suggesting proteinuria and high blood pressure after 20 weeks of pregnancy. IVF is linked with an increased risk of hypertension during pregnancy with frozen embryo cases compared to fresh embryo and natural conception methods. However, obstetrics and perinatal outcomes in cases of frozen embryo transfer are found to be better compared to fresh embryo transfer. In frozen embryo transfer, complication risks are twice as compared to natural conception and 1.5 times higher than the cases of natural embryo transfer.[5]

Gestational diabetes mellitus is another pregnancy complication whose prevalence can vary based on the diagnostic criteria being used and the geographical area being assessed. Globally, gestational diabetes mellitus is seen in 7% to 25% of females and in nearly 14% of Indian females. Gestational diabetes mellitus depicts glucose intolerance first seen during gestation. Various factors affecting the development of gestational diabetes mellitus include IVF pregnancies, multiple pregnancies, and obesity. Gestational diabetes mellitus also increases the risk of prematurity and preeclampsia in the affected females.[6]

Preterm birth or prematurity defines a newborn as having a gestational age of less than 37 weeks. The prematurity has various subcategories including extremely preterm (<28 weeks), very preterm (28-32 weeks), and late preterm 33-36 weeks. As per WHO, the prematurity prevalence is reported to be 5% to 18%. The pathophysiology of preterm birth remains unknown. However, various predisposing factors like assisted reproduction are identified as risk factors. The incidence of preterm birth has been largely limited by controlling the number of embryos being implanted in the cases of IVF pregnancies.[7] The present study was aimed at analyzing in-vitro fertilization (IVF) pregnancies and associated risk factors and major complications associated with IVF pregnancies.

MATERIALS AND METHODS

The present observational retrospective study was aimed at analyzing in-vitro fertilization (IVF) pregnancies and associated risk factors and major complications associated with IVF pregnancies. The study was done at Department of Obstetrics and Gynecology, Vardhman Mahavir Medical College And Safdarjung Hospital, New Delhi after the clearance was given by the concerned Institutional Ethical committee. The data for the study were collected from the Department of Obstetrics and Gynecology of the Institute.

The present study included 310 female subjects that underwent IVF at the Institute. The inclusion criteria for the study were females that were willing to participate in the study, subjects who donated their oocytes or eggs, and females with infertility. The exclusion criteria for the study were females that left the study in between and females with incomplete data.

After the final inclusion of the study subjects, detailed history was recorded for all the subjects along with demographics, pathologies seen during pregnancy, etiology of infertility, maturity of embryos, number of embryos being transferred, and age of the subjects. The data was taken from the records and files of the study females from the Department of Obstetrics and Gynecology. The study had no control group.

The data gathered were analyzed statistically using SPSS software version 21.0 and the Shapiro-Wilk test. The results were expressed as mean and standard deviation and medians and interquartile ranges based on their distribution. Mann Whitney U test and t-test were used for comparing independent group quantitative variables. The level of significance was kept at $p<0.05$.

RESULTS

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The present observational retrospective study was aimed at analyzing in-vitro fertilization (IVF) pregnancies and associated risk factors and major complications associated with IVF pregnancies. The study assessed 310 subjects with infertility with a mean age of 36.55±6.64 years and the mean age of 20-55 years. The etiology of infertility was attributed to combined factors, unknown factors, female factors, and male factors in 10% (n=31), 23.22% (n=72), 32.90% (n=102), and 33.87% (n=105) study subjects respectively (Table 1).

It was seen that in 88.06% (n=273) study subjects embryo transfer was done with the patient's oocyte, in 2.90% (n=9) subjects using artificial insemination, and in 9.03% (n=28) study subjects using egg donation. In 60.64% (n=188) study subjects, 2 embryos per cycle were used. Among 310 study subjects, 78.06% (n=242) subjects had embryo transfer using day 5 embryos. Gestational hypertension was seen in 18.1% (n=56) study subjects and gestational diabetes was reported in 24.51% (n=76) study subjects. The mean age of subjects with gestational hypertension and diabetes was 36.13±5.67 and 37.85±5.21 years respectively. The difference was statistically non-significant with p=0.07. However, subjects with gestational hypertension were significantly older compared to females with gestational diabetes mellitus with respective ages of 38.84±5.82 and 36.04±5.44 years and p=0.02. At birth, pregnancy was terminated in 274 study subjects. In terminated pregnancies 24.08% (n=66) were twins and 75.91% (n=208) were singleton pregnancies.

In the two types of pregnancies, a significant difference was seen in the age of the mothers where females having twin pregnancies were found younger compared to females having singleton pregnancies with p<0.001. The distribution of subjects based on multiple pregnancies occurrence and IVF technique used are listed in Table 2. In subjects with egg donation, twin and single pregnancy was seen in 28.6% (n=8) and 71.4% (n=20) study subjects respectively. In artificial insemination, twin and single pregnancy was seen in 50% (n=4) subjects each. In subjects with 4 embryos transfer, twin and single pregnancy was seen in none and 100% (n=2) subjects respectively. In subjects with 3 embryos transfer, twin and single pregnancy was seen in 33.3% (n=2) subjects and 66.7% (n=4) subjects respectively. In subjects with 2 embryos transfer, twin and single pregnancy was seen in 63.6% (n=42) and 36.4% (n=2) subjects respectively. In subjects with 1 embryo transfer, twin and single pregnancy was seen in 6.1% (n=10) and 93.9% (n=154) subjects respectively (Table 2). The difference was statistically significant with p<0.001.

The study results showed that higher chances of twin pregnancy were associated with embryo transfer using 2 embryos. However, no significant correlation was seen between the use of other techniques and multiple pregnancies. Also, no significant association was seen in the number of pregnancies and gestational diabetes or gestational hypertension with p<0.05.

Among 262 pregnancies, preterm births were seen in 26% (n=68) of study subjects. It was seen that preterm birth babies were ones of 35.3±6.93 years compared to full-term newborns at 37.16±5.21 years. However, the difference was statistically non-significant with p=0.12.

The study results showed no significant association between gestational age gestational diabetes and gestational hypertension with p>0.05. 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).

DISCUSSION

The present retrospective study assessed 310 subjects with infertility with a mean age of 36.55±6.64 years and the mean age of 20-55 years. The etiology of infertility was attributed to combined factors, unknown factors, female factors, and male factors in 10% (n=31), 23.22% (n=72), 32.90% (n=102), and 33.87% (n=105) study subjects respectively. These findings were similar to the studies of Eskew AM et al[8] in 2017 and Wang J et al[9] in 2021 where authors assessed subjects with demographic data comparable to the present study.

The study results showed that in 88.06% (n=273) study subjects embryo transfer was done with the patient's oocyte, in 2.90% (n=9) subjects using artificial insemination, and in 9.03% (n=28) study subjects using egg donation. In 60.64% (n=188) study subjects, 2 embryos per cycle were used. Among 310 study subjects, 78.06% (n=242) subjects had embryo transfer using day 5 embryos. Gestational hypertension was seen in 18.1% (n=56) study subjects and gestational diabetes was reported in 24.51% (n=76) study subjects. The mean age of subjects with gestational hypertension and diabetes was 36.13±5.67 and 37.85±5.21 years respectively. The difference was statistically non-significant with p=0.07. However, subjects with gestational hypertension were significantly older

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compared to females with gestational diabetes mellitus with respective ages of 38.84±5.82 and 36.04±5.44 years and p=0.02. At birth, pregnancy was terminated in 274 study subjects. In terminated pregnancies 24.08% (n=66) were twins and 75.91% (n=208) were singleton pregnancies. These findings were consistent with the studies of Eichelberger KY[10] in 2017 and Fechner AJ et al[11] in 2015 where authors reported a similar prevalence of gestational diabetes and hypertension in their study subjects and reported females with gestational hypertension to be older compared to the controls.

It was seen that a significant difference was seen in the age of the mothers where females having twin pregnancies were found younger compared to females having singleton pregnancies with p<0.001. In subjects with egg donation, twin and single pregnancy was seen in 28.6% (n=8) and 71.4% (n=20) study subjects respectively. In artificial insemination, twin and single pregnancy was seen in 50% (n=4) subjects each. In subjects with 4 embryos transfer, twin and single pregnancy was seen in none and 100% (n=2) subjects respectively. In subjects with 3 embryos transfer, twin and single pregnancy was seen in 33.3% (n=2) subjects and 66.7% (n=4) subjects respectively. In subjects with 2 embryos transfer, twin and single pregnancy was seen in 63.6% (n=42) and 36.4% (n=2) subjects respectively. In subjects with 1 embryo transfer, twin and single pregnancy was seen in 6.1% (n=10) and 93.9% (n=154) subjects respectively. The difference was statistically significant with p<0.001. These results were in agreement with the findings of Vogel JP et al[12] in 2018 and Sanders JN et al[13] in 2022 where authors suggested higher chances of twin pregnancies in younger females with 2 embryo transfers as in the present study.

It was seen that higher chances of twin pregnancy were associated with embryo transfer using 2 embryos. However, no significant correlation was seen between the use of other techniques and multiple pregnancies. Also, no significant association was seen in the number of pregnancies and gestational diabetes or gestational hypertension with p<0.05. Among 262 pregnancies, preterm births were seen in 26% (n=68) of study subjects. It was seen that preterm birth babies were ones of 35.3±6.93 years compared to full-term newborns at 37.16±5.21 years. However, the difference was statistically non-significant with p=0.12. These results were in line with the studies of McLennan AS et al[14] in 2018 and Luke B et al[15] in 2007 where authors reported lesser gestational age of preterm- infants compared to full-term infants.

The study results showed no significant association between gestational age gestational diabetes and gestational hypertension with p>0.05. 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 al[16] in 2015 and Uzunov AV et al[17] 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**		**Singe 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