

A Retrospective Study of Perinatal outcome in ART and Spontaneous Pregnancies

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ABSTRACT

Introduction: In today's world, infertility is one of the major emerging health issues which effects about 8-9% of reproductive age group. Infertility due to certain male factors and complete tubal obstruction may require interventional procedure. Increased risk of adverse perinatal outcomes are associated with ART. Study objective was to asses perinatal outcome in pregnant women conceived with inventional techniques.

Material and Methods: A Retrospective study was done at tertiary care hospital from January 2018 to June 2018. and data was collected. The maternal and fetal condition were noted as per records.

Results: Women > 40 years of age had 11.53% of intrauterine death, 65.38% requires NICU admission, 11.53% requires ventilator support and 7.69% had neonatal death. Study also revealed foetal complications like intra uterine death (p value=0.0004), fetal anomalies, IUGR (P value=0.0003) which were atleast four times more in ART group than in spontaneous conception. Study also revealed that out of 167 new born in ART group, there were 28.74% having very low birth weight, 19.76% were having low birth weight and 51.50% had adequate weight, i.e around half of them were having weight less than 2 kgs as compared to spontaneous pregnancy group were only 5.71% i.e 6 babies were born less than 2 kg weight (P value < .0001 highly significant).

Conclusion: Maternal age was significantly associated with perinatal and obstetrical complications. To improve maternal and perinatal outcomes, pre-existing diseases like hypertension, anaemia, diabetes mellitus and hypothyroidism should be treated before conception. Overall aim should be to minimize iatrogenic preterm birth for minor ailments, close supervision of such women can add few more weeks to pregnancy thus improving neonatal outcome.

Keywords: Assisted Reproductive Technology, Spontaneous Conception, Pregnancy, Fetal Anomalies, IUGR

INTRODUCTION

Infertility is one of the major emerging health issues which effects about 8-9% of reproductive age group.¹ Assisted reproductive technologies (ART) are medical procedures used primarily to address infertility. It includes procedures such as in vitro fertilization. It may include intracytoplasmic sperm injection (ICSI), cryopreservation of gametes or embryos, and/or may involve the use of fertility medication. It has been observed that women who went under ART procedure in recent years, majority of them had multiple pregnancies.² Women who undergo ART are at risk of ovarian hyper stimulation syndrome (OHSS). OHSS is a

complication of ovulation induction resulting in enlargement of ovaries and retention of fluids leading to various secondary complications, which normally resolve within two weeks, but can persist if pregnancy occurs. The use of supraphysiological concentrations of hormones during ovarian stimulation has also raised concerns that ART can increase cancer risks linked to hormonal fluctuations. These include breast, ovarian, endometrial, cervical and colon cancers, as well as melanoma. In recent studies there is evidence of an increased risk of Diabetes Mellitus, accidental haemorrhage, preeclampsia, gestational hypertension, placenta previa, and gestational diabetes in ART pregnancies.³

In case of singleton pregnancies, interventional procedure may develop higher chances of adverse perinatal outcomes, such as labour complications and C- section. Studies have shown congenital structural anomalies and chromosomal abnormalities in singleton ART including pregnancy termination.^{4,5}

A "good perinatal outcome" among live births after ART is defined as the live birth of a singleton infant born with normal birth weight (>2,500gm) and completed term (>37 completed weeks of gestation).⁶ However, concern is mounting over the safety of ART and its effect on maternal and fetal well-being. Various studies have shown ART pregnancies have a marked higher risk of multiple pregnancy and adverse perinatal outcome, including preterm delivery, low birth weight, and birth defects, NICU admission requirement, asphyxia, ventilator support and even neonatal death.^{4,7}

Study was done to see the perinatal outcome in pregnancy conceived with assisted reproductive techniques in patients who had delivered at tertiary care hospital from January 2018 to June 2018.

MATERIAL AND METHODS

Medical records department data of pregnant women who conceived through interventional techniques and delivered

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at tertiary care hospital in New Delhi from January 2018 to June 2018 and record of neonate after delivery.

Method and Collection of Data

A Retrospective study was conducted and data was compiled of pregnant women who conceived through interventional techniques and delivered. The maternal and fetal condition were noted as per records.

Study Area: Department of Obst and Gynae.

Study Design: Retrospective study.

Study Duration: January 2018 to June 2018.

Sample Size: All cases from January 2018 to June 2018.

Inclusion Criteria

Pregnant women delivered at tertiary care hospital who conceived after ART and IUI.

Exclusion Criteria

Pregnant women delivered at tertiary care hospital without interventional techniques.

Methodology

Medical records department data of pregnant women who

conceived through interventional techniques were taken into account and various tools were used for statistical analysis.

STATISTICAL ANALYSIS

Percentage and number were presented as Categorical variables. Mean \pm SD and median were presented as continuous variable. Data normality was tested using Kolmogorov-Simrnov test. In case of normality was rejected then non parametric test was used.

Various Statistical test was applied as follows-

1. Quantitative variables were compared using unpaired t-test/Mann-Whitney Test between the two groups.
2. Quantitative variables were correlated using Chi-Square test/Fishers exact test.

A p value of <0.05 was considered statistically significant.

The data was entered in MS EXCEL spreadsheet and analysis was done using SPSS version 21.0

RESULT

Table 1 shows thatneonatal complications like IUD, low birth, prematurity, asphyxia, hypoglycaemia, NICU admission, intubation, ventilator support and even neonatal death were observed more in age group >40 year than other age groups.

Maternal Age No. of New born	<30yrs (n=62)	31-40 yrs (n=79)	>40 yrs (n=26)	Total (n=167)	p-value
IUD	5(8.06%)	8(10.12%)	3(11.53%)	16(9.58%)	0.156
Low birth	19(30.64%)	21(26.58%)	9(34.61%)	49(29.34%)	0.005
Prematurity	19(30.64%)	27(34.17%)	20(76.92%)	66(39.52%)	0.001
Asphyxia	27(43.54%)	32(40.50%)	18(69.30%)	77(46.10%)	0.001
Chest retraction	18(29.03%)	22(27.84%)	11(42.30%)	51(30.53%)	0.005
Delayed cry	15(24.19%)	18(22.78%)	8(30.76%)	41(24.55%)	0.002
Decreased tone	2(3.22%)	3(3.79%)	2(7.69%)	7(4.19%)	0.136
Bradycardia	1(1.61%)	3(3.79%)	1(3.84%)	5(2.99%)	0.05
Hypoglycaemia	2(3.22%)	2(2.53%)	1(3.84%)	5(2.99%)	0.126
Intubation	16(25.80%)	20(25.30%)	9(34.61%)	45(26.94%)	0.05
NICU admission	34(54.83%)	42(53.16%)	17(65.38%)	93(55.68%)	0.001
C-pap required	10(16.12%)	12(15.18%)	6(23.07%)	28(16.76%)	0.05
Ventilator support	5(8.06%)	7(8.86%)	3(11.53%)	15(8.98%)	0.05
Neonatal death	12(19.35%)	15(18.98%)	2(7.69%)	29(17.36%)	0.001

Table-1: Comparison of Maternal age in relation to Perinatal Outcomes in pregnancythrough ART.

	Group		Total	P Value
	Art (n=167)	Spontaneous conceptio (n=105)		
IUD	16(9.58%)	0(0.00%)	16(5.88%)	0.0004
Fetal Anomaly	5(2.99%)	0(0.00%)	5(1.84%)	0.160
IUGR	37(22.16%)	6(5.71%)	43(15.81%)	0.0003
Total	167(100.00%)	105(100.00%)	272(100.00%)	

Table-2: Distribution of women according to Fetal Complications.

Baby weight(kg)	Group		Total	P value
	ART (n=167)	Spont. Conception (n=105)		
1) \leq 1.5	48(28.74%)	0(0.00%)	48(17.65%)	<0.0001
2)1.51-2	33(19.76%)	6(5.71%)	39(14.34%)	
3) $>$ 2	86(51.50%)	99(94.29%)	185(68.01%)	
Total	167(100.00%)	105(100.00%)	272(100.00%)	

Table-3: Distribution of women according to baby weight.

	Group		Total	P value
	ART(n=167)	Spont. Conception (n=105)		
Healthy New Born	65(38.92%)	77(73.33%)	142(52.21%)	<0.0001
Low birth	49(29.34%)	7(6.67%)	56(20.59%)	<0.0001
Very low birth	47(28.14%)	0(0.00%)	47(17.28%)	<0.0001
Prematurity	62(37.13%)	7(6.67%)	69(25.37%)	<0.0001
Asphyxia	77(46.11%)	13(12.38%)	90(33.09%)	<0.0001
Chest retraction	51(30.54%)	9(8.57%)	60(22.06%)	<0.0001
Delayed cry	41(24.55%)	4(3.81%)	45(16.54%)	<0.0001
Decreased tone	7(4.19%)	1(0.95%)	8(2.94%)	0.157
Bradycardia	5(2.99%)	0(0.00%)	5(1.84%)	0.160
Hypoglycemia	5(2.99%)	4(3.81%)	9(3.31%)	0.737
Intubation	45(26.95%)	1(0.95%)	46(16.91%)	<0.0001
NICU admission	93(56%)	3(2.86%)	3(1.10%)	0.057
Neonatal Mortality	29(17.37%)	0(0.00%)	29(10.66%)	<0.0001

Table-4: Distribution of women according to Neonatal Complications.

Table 2 shows that various fetal complications like IUD, fetal anomalies and IUGR were seen more frequent in ART group.

Table 3 shows that out of 167 new born in ART group, there were 28.74% having very low birth weight, 19.76% were having low birth weight and 51.50% had adequate weight, i.e. around half of them were having weight less than 2 kgs as compared to spontaneous pregnancy group were only 5.71% i.e. 6 babies born were less than 2 kg weight (P value<0.0001, highly significant).

Table 4 shows that out of various neonatal complications seen in ART and spontaneous conception were low birth, very low birth weight, neonatal Mortality, prematurity, bradycardia, asphyxia, chest retractions, delayed cry, decreased tone, NICU admission, hypoglycaemia.

DISCUSSION

In our study it was observed that as the age increases there was increasing number of obstetrical complications and adverse perinatal outcomes in pregnancy conceived after assisted reproductive technique (table 1). In group > 40 years of age we had 11.53% of intrauterine death, 65.38% requires NICU admission, 11.53% requires ventilator support and 7.69% had neonatal death. So maternal age is one of the risk factor for poor maternal and neonatal outcome, also other studies says that maternal age is the single most important prognostic factor for ART success.^{8,9}

It is conceivable that the effect of older age on the risk of adverse birth outcome, such as caesarean delivery and preeclampsia, may significantly differ by the method of conception and parity because women who conceived by ART have a higher risk of number of adverse perinatal outcome,^{10,11}

In our study fetal complications like intrauterine death (p value=0.0004), fetal anomalies, IUGR (P value=0.0003) are also noted atleast four times more in ART group than in spontaneous conception, these complications are more or less associated with other complications and also age factor of ART group.

The mean birth weight in ART group was 1.99 kg and in spontaneous group was 2.85kg, there were 28.74% of babies

were below 1.5 kg weight in ART group and none below 1.5 kg weight in spontaneous group, there was 19.76% babies between 1.5 to 2 kg weight in ART group and 5.71% of babies were between 1.5-2 kg weight in spontaneous group, that comes to 94.29% of babies were above 2kg in spontaneous group where only 51.50% babies were above 2 kg weight in ART group (p value<0.0001 highly significant), almost half of the babies in ART population were below 2 kg and among the low birth also half were below 1.5 kg weight compared to spontaneously conceived group almost all babies were adequate to their weight, comparing to study by Dhalwani NN et al compare risk of adverse perinatal outcomes among ART of a total of 32,762 (0.8%) of 3,896,242 singleton live births in the three states were conceived via ART noted the odds of low birth weight were 33% higher (adjusted odds ratio [aOR]=1.33; 95% CI, 1.13, 1.56) and 20% higher for preterm birth (aOR=1.20; 95% CI, 1.07, 1.34). The odds of SGA and low apgar score were not significantly different in both group (Aor=1.22; 95% CI, 0.88, 1.68; and Aor=0.75%; 95% CI, 0.54, 1.05, respectively).¹²

Comparing neonatal outcome we observe that only 38.92% babies in ART group were healthy comparing to spontaneous group where 73.33% babies were healthy (p value <0.0001 highly significant). The neonatal outcome in our study shows poor in ART group comparing to spontaneous group (table 4), the rate of low birth was almost 5 times higher in ART group, that of prematurity 9 fold more in ART group, including various neonatal complications such as chest retraction, asphyxia etc. Multiple pregnancies are associated with four to ten times greater perinatal mortality compared to singleton gestations. A total of 12.2% of all preterm infants, 15.4% of all neonatal deaths, and 9.5% of fetal deaths have been related to twin deliveries.¹³ Filicori et al. suggested that low and very low birth weights were more likely to increase in infants conceived with ART than spontaneous conceptions. It has been proposed that infertility itself increases risk of preterm birth and low birth weight due to investigation of worse prenatal and obstetric complications of singleton pregnancies after ART^{14,15} higher rate of chromosomal abnormalities, preterm birth, growth retardation, cerebral

palsy, NICU admission and death in one year are neonatal complications attributed to ART induced pregnancies^{16,17}, all these neonatal complications is a challenge which we routinely noted in ART group compared to spontaneously conceived group which were negligible here.

Such poor neonatal outcome with ART has many contributing factors like multiple pregnancies and increased age of mother. A recent two year study at one Quebec hospital showed that 17% of all NICU admission were from multiple pregnancies in women undergoing ART. Of these, 91% resulted from IVF, with 2 to 6 embryos transferred, and 9% from pregnancies conceived after OS¹⁸. An Australian study similarly reported that 12.3% of NICU admission between 1994 and 2005 resulted from assisted reproduction. Of those, 5% were singletons, 27% were twins, and 65% were triplets.¹⁹ There is no doubt that the increasing use of ART has led to increased perinatal morbidity and mortality secondary to an increase in the incidence of multiple pregnancy. Whether ART multiples pose more risk than spontaneous multiples for perinatal adverse outcomes is less clear. Controlled studies of perinatal outcomes comparing twin pregnancies conceived after ART with those of spontaneously conceived twins (as well as 2 systematic reviews²⁰ reveal data that are somewhat conflicting.)

CONCLUSION

To conclude we observe that women in ART group had higher age group and BMI. There was a significant association between obstetrical and perinatal complications with age. Obesity can be addressed in pre-conception period. To improve perinatal outcome and prevent premature births, maternal pre-existing disease like anaemia, chronic hypertension, hypothyroidism and diabetes mellitus should be treated before conception.

IUGR, prematurity, fetal anomaly and IUD were fetal complications which were more common in ART group. Premature babies had more of neonatal complications which required intubation, NICU admission and ventilator support. Neonatal mortality was also significantly seen in 17.37% of patient.

Our aim should be to minimize iatrogenic preterm birth for minor ailments, close supervision of such women can add few more weeks to pregnancy thus improving neonatal outcome. To conclude significantly increased obstetrical and neonatal complications may be attributable to increased maternal age, multiple pregnancies, pre-existing medical diseases and morbidities related to sub fertility itself rather than ART pregnancies per se.

Limitations

The study was conducted for a period of 6 months to evaluate perinatal outcome and the results may not be absolute owing to small number of study subjects.

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