

Perinatal Outcome in Pregnancies through ART

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Abstract

Introduction: Infertility is nowadays a global problem affecting couples of reproductive condition. Infertility, prevalent among one in every four couples in the developing countries, is a neglected problem. A significant proportion of women postpone their pregnancy due to education and career to late into the fourth and fifth decades. ART includes in vitro fertilization (IVF) with or without intracytoplasmic sperm injection (ICSI), fresh or frozen embryo transfer, IVF with donor oocytes, intrauterine insemination (IUI) either with ovarian stimulation or in unstimulated cycles. As mother having ART treatment is mostly from higher age group, chronic hypertension and diabetes mellitus may be pre-existing leading to further exaggeration during pregnancy. And if not from higher age group then various factors like endometrial, ovarian, PID, endocrinal problem have significant effect on perinatal outcome and complication. **Results:** Total number of 193 patients who have taken ART have been included in our study. 51 (48.57%) out of 105 patients had PIH in singleton ART as obstetrical complication which is most common in our study. 41 (46.59%) out of 88 patients had preterm delivery in multiple gestation ART as a most common obstetrical complication in our study. 16 (15.24%) out of 105 patients had Chronic HTN in singleton ART and 14 (15.91%) out of 88 patients had Chronic HTN in multiple gestation ART as maternal complication which is most common in our study. Out of 283 fetus, 41 (14.48%) were IUGR, 9 (3.18%) were fetal anomaly and 17 (6.01%) were IUD. **Conclusion:** This study helps us to understand that these ART pregnancies are high risk for maternal and fetal complication.

Keywords: Pregnancy; ART; Maternal outcome; Fetal outcome.

Introduction

Infertility is now a days a global problem affecting couples of reproductive condition. Infertility, prevalent among one in every four couples in the developing countries, is a neglected problem.¹ India alone accounts for 30 million couples of infertility of the total 48.5 million globally affected couples.^{2,3} Infertility is a common condition affecting approximately 8-9% of reproductive age.⁴⁻⁶ A significant proportion of women postpone their pregnancy due to education and career to late into the fourth and fifth decade.^{7,8} Various ART procedures have made pregnancy and childbirth possible in all age group scenarion women despite decreasing oocyte quality and quantity, endometrial polyps, uterine fibroids and tubal disease increase with aging which hampers conception and implantation rates.⁸

Assisted reproductive technique (ART) has increasingly grown in last few years. ART includes in vitro fertilization (IVF) with or without intracytoplasmic sperm injection (ICSI), fresh or frozen embryo transfer, IVF with donor oocytes, intrauterine insemination (IUI) either with ovarian stimulation or in unstimulated cycles.

In recent years, an increasingly large proportion of deliveries following ART either multiple pregnancies or single pregnancy. ART associated with increased likelihood of GDM, chronic hypertension and diabetes mellitus leading to further more maternal complication like polyhydromnios, PIH, APH, oligohydromnios, PPRM, pre-eclampsia, etc. As mother having ART treatment is mostly from higher age group, chronic hypertension and diabetes mellitus may be pre-existing leading to further exaggeration during pregnancy.⁹ And if not from higher age group then various factors like endometrial, ovarian, PID, endocrinal problem have significant effect on perinatal outcome and complication. In single pregnancy there is also increased risk of adverse perinatal outcome. A small but significant increase of congenital structural abnormalities and chromosomal abnormalities have also been noted with ART pregnancies resulting in early termination.¹⁰⁻¹² Perinatal outcomes like preterm deliveries, low birth weight and birth defects, NICU admission requirements, asphyxia ventilator support even neonatal deaths are also associated with ART.^{13,14}

Aims and Objectives

To study obstetrical, perinatal and neonatal outcome in pregnancy conceived with Assisted

reproductive techniques in patient's who had delivered at GMCH from January 2013 to till 2018.

Materials and Methods

We have collected the data from 2013 to 2018 and prospective data of the year 2018, all patients admitted in GMCH, Udaipur who are conceived after assisted reproductive technique and divided then into singleton and multiple pregnancy and compared then with control of same and also classified in donor and self conception.

Results

The present study was conducted analyze the data from Department of Obstetrics and Gynaecology at GMCH, Udaipur where pregnancies as a result of assisted or artificial reproductive techniques admitted in GMCH and there perinatal outcomes were noted.

Table 1 shows the association of age with donor and self. 55 out of 86 women who were >35 years of age had IVF by Ovum Donor (63.95%) while 69 (64.48%) out of 107 women who were <35 years of age had IVF by self and 19 (17.75%) out of 107 had IUI by self.

Table 1: Test of Association of Age with Donor and Self

Age (in Years)	Donor		Total	Self		Total	χ^2 Value	p-value
	IVF	IUI		IVF	IUI			
≤35	31	0	31	69	19	88	41.11	<0.001
>35	55	0	55	18	1	19		
Total	86	0	86	87	20	107		

Table 2 shows incidence of multifetal pregnancy more in ART. Various maternal medical outcomes have been described in Table 3(a). Various obstetrical complications like PIH, oligo, PPRM, GDM and preterm delivery significant in more

ART. Amongst 193 women who underwent ART conception and were admitted at our hospital there was no instrumental delivery, 157 (81.35%) had cesarean section. Out of 193 women 109 (56.5%) had high BMI.

Table 2: Incidence of multifetal pregnancy in ART

Pregnancy	Cases (%)	Control (%)
Single	105 (54.40)	179 (92.75)
Twins	86 (44.56)	14 (7.25)
Triplets	2 (1.04)	0
Total	193 (100)	193 (100)

Table 3(a): Maternal Outcomes

Category	Cases (%) N = 193	Control (%) N = 193	p-value
Obstetrical complications			
Polyhydramnios	10 (5.18)	3 (1.55)	>0.05
Placenta previa	11 (5.7)	5 (2.59)	>0.05
PIH	88 (45.6)	11 (5.69)	<0.01
Oligo	52 (26.94)	12 (6.22)	<0.01
PPROM	40 (20.73)	7 (3.63)	<0.01
GDM	39 (20.21)	12 (6.22)	<0.01
Preterm delivery	72 (37.31)	20 (10.36)	<0.01
Antepartum hemorrhage	6 (3.11)	1 (0.52)	>0.05
Medical complications			
Hypothyroid	74 (38.34)	12 (6.22)	<0.01
Anemia	28 (14.51)	26 (13.47)	>0.05
Chronic hypertension	30 (15.54)	14 (7.25)	<0.05
DM 2	11 (5.7)	1 (0.52)	<0.01
Mode of delivery			
Vaginal delivery	36 (18.65)	83 (43.01)	<0.01
ISCS	157 (81.35)	110 (22.28)	
Ob/H			
Primi	125 (64.77)	160 (82.90)	<0.01
Multi	68 (35.23)	33 (17.10)	
BMI			
Normal	84 (43.52)	152 (78.76)	
Overweight	80 (41.45)	40 (20.72)	<0.01
Obese	29 (15.02)	1 (0.52)	
Intra and postpartum complication			
PPH	14 (7.25)	7 (3.63)	>0.05
Obstetric hysterectomy	7 (3.63)	1 (0.52)	>0.05
Pulmonary edema	1 (0.52)	0	>0.05
Heart disease	1 (0.52)	0	>0.05

Various medical outcomes of singleton and multiple gestation have been described in Table 3(b). 51 (48.57%) out of 105 patients had PIH in singleton ART as obstetrical complication which is most common in our study. 41 (46.59%) out of 88 patients had pre-term delivery in multiple gestation ART as a most common obstetrical complication in our study. 16 (15.24%) out of 105 patients had Chronic HTN in singleton ART and 14 (15.91%) out of 88

patients had Chronic HTN in multiple gestation ART as maternal complication which is most common in our study. Out of 105 patients who had IVF 68 (64.76%) were having primary infertility. Out of 105 singleton pregnancies 5 (4.76%) patient had PPH and out of 88 multiple pregnancies 9 (10.93%) had PPH as maternal complication which shows increased incidence of PPH in multiple pregnancy.

Table 3(b): Maternal Outcomes

Category	Singleton		p-value	Multiple		p-value
	Cases (%) N = 105	Control (%) N = 179		Cases (%) N = 88	Control (%) N = 14	
Obstetrical complications						
Polyhydramnios	6 (5.71)	2 (1.12)	<0.05	4 (4.54)	1 (7.14)	>0.05
Placenta previa	7 (6.67)	2 (1.12)	<0.01	4 (4.54)	3 (21.43)	>0.05
PIH	51 (48.57)	5 (2.79)	<0.01	37 (42.04)	6 (42.86)	>0.05
Oligo	34 (32.38)	7 (3.91)	<0.01	18 (20.45)	4 (28.57)	>0.05

Category	Singleton		p-value	Multiple		p-value
	Cases (%) N = 105	Control (%) N = 179		Cases (%) N = 88	Control (%) N = 14	
PPROM	26 (24.76)	4 (2.23)	<0.01	14 (15.91)	3 (21.43)	>0.05
GDM	23 (21.90)	8 (4.47)	<0.01	16 (18.18)	4 (28.57)	>0.05
Preterm delivery	31 (29.52)	12 (6.70)	<0.01	41 (46.59)	8 (57.14)	>0.05
Antepartum hemorrhage	2 (1.90)	0	>0.05	4 (4.54)	1 (7.14)	>0.05
Medical complications						
Hypothyroid	30 (28.57)	9 (5.03)	<0.01	34 (38.64)	3 (21.43)	>0.05
Anemia	17 (16.19)	16 (8.94)	>0.05	11 (12.5)	10 (71.43)	<0.01
Chronic hypertension	16 (15.24)	6 (3.35)	<0.01	14 (15.91)	8 (57.14)	<0.01
DM 2	6 (5.71)	0	<0.01	5 (5.68)	1 (76.14)	>0.05
Mode of delivery						
Vaginal delivery	32 (30.48)	81 (45.25)	0.01	4 (4.54)	2 (14.28)	>0.05
ISCS	73 (69.52)	98 (54.67)		84 (95.45)	12 (85.71)	
Ob/H						
Primi	68 (64.76)	152 (84.92)	<0.01	57 (64.77)	8 (57.14)	>0.05
Multi	37 (35.24)	27 (15.08)		31 (35.23)	6 (42.86)	
BMI						
Normal	38 (36.19)	143 (79.89)	<0.01	46 (52.27)	9 (64.28)	>0.05
Overweight	35 (33.33)	36 (20.11)		45 (51.14)	4 (28.57)	
Obese	11 (10.48)	0		18 (20.45)	1 (7.14)	
Intra-and postpartum complication						
PPH	5 (4.76)	2 (1.12)	<0.01	9 (10.93)	5 (35.71)	<0.05
Obstetric hysterectomy	2 (1.90)	0	>0.05	5 (5.68)	1 (7.14)	<0.01
Pulmonary edema	0	0	-	1 (1.14)	0	>0.05
Heart disease	1 (0.95)	0	>0.05	0	0	-

Fetal outcomes are described in Table 4(a). Out of 283 fetus, 41 (14.48%) were IUGR, 9 (3.18%) were fetal anomaly and 17 (6.01%) were IUD.

Fetal outcomes are described in Table 4(b). Out of 105 fetus, 13 (12.38%) were IUGR, 4 (3.81) were fetal anomaly and 5 (4.76%) were IUD among

singleton which is significant as compared to control singleton. Whereas incidence of IUGR, fetal anomaly, IUD and live birth were almost similar in IVF multiple gestation and spontaneous multiple gestation or no such difference found in multiple group.

Table 4(a): Fetal Outcomes

Category	Cases (%)	Control (%)	p-value
IUGR	41 (14.48)	2 (0.97)	<0.001
Fetal anomaly	9 (3.18)	1 (0.48)	
IUD	17 (6.01)	2 (0.97)	
Live birth	216 (76.33)	202 (97.58)	
Total	283 (100)	207 (100)	

Table 4(b): Fetal Outcomes

Category	Singletons		p-value	Multiple		p-value
	Cases (%)	Control (%)		Cases (%)	Control (%)	
IUGR	13 (12.38)	1 (0.56)	<0.001	28 (15.73)	1 (3.57)	>0.05
Fetal anomaly	4 (3.81)	0		5 (2.81)	1 (3.57)	
IUD	5 (4.76)	1 (0.56)		12 (6.74)	1 (3.57)	
Live birth	83 (79.05)	177 (98.88)		133 (74.72)	25 (89.28)	
Total	105 (100)	179 (100)		178 (100)	28 (100)	

Table 5(a) shows various neonatal outcomes. Out of 216 newborns of ART, healthy newborn were 72 (33.33%), APGAR score (>7) were 199 (92.13%),

NICU admission were 145 (67.13%), Prematurity were 56 (25.93%), LBW were 71 (32.87%), VLBW were 71 (32.87%).

Table 5(a): Neonatal Outcomes

Category	Cases (%) N = 216	Control (%) N = 202	p-value
Healthy newborn	72 (33.33)	180 (89.11)	<0.001
APGAR score (≥ 7)	199 (92.13)	201 (99.50)	<0.01
NICU admission	145 (67.13)	10 (4.95)	<0.001
Prematurity	56 (25.93)	10 (4.95)	<0.001
Very low birth weight	71 (32.87)	4 (1.98)	<0.001
Chest retraction	60 (27.78)	1 (0.49)	<0.001
Low birth weight	73 (33.80)	10 (4.95)	<0.001
Asphyxia	61 (28.24)	0	<0.001

Table 5(b) shows various neonatal outcomes. Out of 83 neonates, healthy newborns were 64 (77.71%), APGAR score (>7) were 75 (90.36%), NICU admission were 51 (61.45%), Prematurity were 10 (12.05%), LBW were 15 (18.07%), VLBW

were 8 (9.64%) seen in singleton ART. Out of 133 neonates APGAR score (>7) were 124 (93.23%), NICU admission were 94 (70.68%), VLBW were 63 (47.37%) and LBW were 58 (43.61%) seen in multiple gestation ART.

Table 5(b): Neonatal Outcomes

Category	Singletons		p-value	Multiple		p-value
	Cases (%) N = 83	Control (%) N = 177		Cases (%) N = 133	Control (%) N = 25	
Healthy newborn	64 (77.71)	175 (98.87)	<0.001	8 (6.01)	5 (20.0)	0.05
APGAR score (≥ 7)	75 (90.36)	177 (100)	<0.01	124 (93.23)	24 (96.0)	<0.01
NICU admission	51 (61.45)	1 (0.56)	<0.001	94 (70.68)	9 (36.0)	<0.01
Prematurity	10 (12.05)	2 (1.13)	<0.01	46 (34.59)	8 (32.0)	>0.05
Very low birth weight	8 (9.64)	0	<0.01	63 (47.37)	4 (16.0)	<0.01
Chest retraction	14 (16.87)	0	<0.01	46 (34.59)	1 (4.0)	<0.01
Low birth weight	15 (18.07)	6 (3.39)	<0.01	58 (43.61)	4 (16.0)	0.01
Asphyxia	15 (18.07)	0	<0.01	46 (34.59)	0	<0.001

Discussion

This study is not only to assess pregnancy outcomes in ART but also incidence of IVF/IUI technique by using self/donor oocytes and their relationship with the age. In our study (Table 1), out of 193 cases 86 (44.55%) patients had undergone IVF treatment by donor oocytes. Out of which 55 (63.95%) women were over 35 years of age. 107 (55.44%) cases had undergone IVF/IUI treatment by self oocytes, out of which 88 (45.95%) cases were below 35 years of age. These data show that with increasing age there is increase incidence of treatment with donor oocytes while age effects quality of oocyte. Our data was also supported by Yadav *et al.* in which there was increased incidence of donor oocyte treatment

with increasing age.¹⁵ Our study there was also increased incidence of twin pregnancy compared to control group (Table 2).

There was also increased incidence of maternal obstetrical and medical complications in cases rather than in controls. Out of 193 cases 72 (37.31%) patients had preterm delivery which was more than controls (10.36%). There was also increased incidence of PIH in cases, which was 45.6%. So, in our study, there was threefold increased incidence of preterm labor and eightfold increased incidence of PIH. Study conducted by Desari P *et al.* in 2009 there is increased incidence of obstetrical complication in ART pregnancies especially PIH and preterm labor and GDM and PPROM which supports our study. The association between PIH

and ART has also been noted by other authors, including Jackson *et al.*¹⁶ in 2004 and Wang *et al.*¹⁷ in 2002 (Table 3a). We have also shown increased incidence of abnormal placentation with IVF use which is around twofold increased incidence.

Postpartum hemorrhage in ART group were 7.25% compared to control group which was 3.6%. There was also increased rate of obstetric hysterectomy in ART treated cases which was 7 (3.62%) out of 193 cases compared to 1 (0.5%) out of 193 spontaneous pregnancies which again proves ART conception as high risk, leading to poor maternal and perinatal outcome. A recent study by Francois *et al.*¹⁹ in 2015 has shown that multiple pregnancy had a sixfold increased risk of emergency postpartum hysterectomy compared to singleton pregnancies. So, it seems logical to conclude that increased multiple pregnancy rates with ART provides a further contribution to the rising peripartum hysterectomy rates (Table 3b).

In our study, out of 283, 41 (14.48%) fetuses were IUGR which was higher than control group. In IUGR cases, more rates seen with multiple pregnancies rather than singleton pregnancies, (Table 4a and 4b). The Apgar score >7 in ART group was in 199 babies (92.13%) while in spontaneous group was 201 (99.50%). So, Apgar of the babies that born after ART were lower than spontaneous conception, comparing with study by Dooley W *et al.* in 2016 in UK found that babies conceived through ART were born at significantly low Apgar than conceived spontaneously.²⁰

In our study 73 (33.80%) babies were of low birth weight in ART group compared to spontaneous group where 10 (4.95%) babies were low birth weight. Out of 286 babies 71 (32.87%) were very low birth weight compared to 4 (1.98%) in spontaneous pregnancies. This shows significant difference in birth weight of babies of ART patients and spontaneous pregnancies. It is probably due to increased incidence of preterm deliveries and multiple pregnancies related to ART. Such poor outcome with ART has mainly a contributing factor like multiple pregnancies and increased age of mother. An Australian study similarly reported that 12.3% NICU admission in between 1994 to 2005 resulted from assisted reproduction, out of those 5% were singletons, 27% were twins, and 65% were triplets. ART multiple pregnancies pose more risk than spontaneous multiple pregnancies for perinatal adverse outcome is less clear. There was also increased rate of NICU admission with ART babies which was 67.13% compared to spontaneous group which was 4.95%. Out of which 36% babies

required intubation and 26.39% babies required C pap. In our study various neonatal complications like chest retractions, asphyxia, delayed cry, decreased tone, bradycardia, hypoglycemia were almost 2–3 folds more noted in ART compared to spontaneous group (Table 5a and 5b).

Conclusion

This study helps us to understand that this ART pregnancies are high risk for maternal and fetal complication. So, more emphasis should be given on methods preventable which can be like reduce BMI before transfer control blood pressure. Single embryo transfer and more over dealing this patient in tertiary health center with multidisciplinary approach with ICU and NICU facility.

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