



MATERNAL AND NEONATAL OUTCOMES AFTER ASSISTED REPRODUCTIVE TECHNOLOGY: A PROSPECTIVE STUDY IN JAIPUR

Obstetrics & Gynaecology

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ABSTRACT

Background- ART encompass all techniques involving direct manipulation of oocytes outside of the body. Forms of ART: IVF, IUI, ICSI, GIFT, ZIFT, TET. ART has completely revolutionized both evaluation and treatment of infertility. These techniques interfere with the process of germ cell proliferation, fertilization, development, and differentiation and may have adverse effects on the embryo. **Method-** This was a hospital based prospective study done to compare between pregnancy, perinatal, neonatal outcomes in pregnant women conceived by assisted reproductive technology v/s spontaneously conceived pregnancy Descriptive type of cross-sectional study conducted in the Department of Obstetrics and Gynecology, SMS Medical College, Jaipur from July 2020 till June 2021. **Result-** Both groups were compared & there is highly significant association between gravidity and reproductive technique. Majority of them i.e., 63.5% who were primigravida had normal delivery, while 40.2% multigravida had delivery via IUI, 30.5% multigravida had spontaneous mode of delivery. Both groups were compared & there is highly significant association between perinatal complication and reproductive technique with p value is <0.005 . Both groups were compared & There is highly significant association between neonatal complication and reproductive technique with <0.005 **Conclusion-** Our study concluded that there is more pregnancy, perinatal & neonatal complications associated with ART conceived women as compared with spontaneously conceived pregnancies. Hence strict control of indications for ART is advised and to strengthen and increase their antenatal visits in ANC clinics. It reduces the complications in ART conceived women and makes the better fetomaternal outcome.

KEYWORDS

ART, IVF, IUI

INTRODUCTION

Infertility is defined as 1 year of regular unprotected intercourse without conception. It affects approximately 10-15% of couples as 85-90% of healthy young couples conceive within 1 year, mostly within 6 months. It is a major issue and a source of social and psychological suffering for many couples.

Fecundability is the probability that a cycle will result in pregnancy and fecundity is the probability that a cycle will result in a live birth. More attention has been paid to the safety of ART worldwide. Although majority of complication with high order > 3 multiples, twins have increased risks of LBW, Preterm & neurological deficits when compared with singletons.^{2,3} 2% rate of ectopic with ART as compared with general population rate⁴

With a view to assess unbiasedly, the truth behind association between perinatal and maternal complications and assisted reproduction, the present study is being undertaken.

MATERIAL AND METHODS

This was a hospital based prospective study done to compare between pregnancy, perinatal, neonatal outcomes in pregnant women conceived by assisted reproductive technology v/s spontaneously conceived pregnancy Descriptive type of cross-sectional study conducted in the Department of Obstetrics and Gynaecology, SMS Medical College, Jaipur from July 2020 till June 2021.

Sample size was calculated as 200 women with spontaneously v/s ART conceived pregnancies at 80% study power and alpha error of 0.05 expecting Pearson correlation coefficient of 0.27 found in seed article (Zhu L, Zhang Y, Liu Y, Zhang r, Wu Y, Huang Y, Liu F, Li M, Sun S, Xing L et al. Maternal and life-birth outcomes of pregnancies following assisted reproductive technology: a retrospective cohort study. Sci Rep. 2016 Oct 20; 6: 35141. doi: 10.1038/srep35141.)

Study universe comprised of women attending the antenatal clinic of the Department of Obstetrics and gynecology, SMS Medical College, Jaipur. The following criteria were used for selecting the cases.

Inclusion Criteria

1. All Pregnant women between 18-40 years of age conceived

spontaneously or following ART.

2. Women giving consent for the study.
3. Women conceived following ART (IVF, IUI, ICSI) will be considered as Group-1 and other will be taken as Group-2.

Exclusion Criteria

1. All women with preexisting medical condition (cardiac disease, chronic hypertension, diabetic) that are diagnosed before 20th week of gestation.
2. Preimplantation genetic diagnosis
3. Surrogacy

The study will be conducted on pregnant women attending Department of Obstetrics and Gynaecology, SMS Medical College and associated groups of hospitals, Jaipur, for antenatal checkup & basic investigations fulfilling the inclusion and exclusion criteria.

After explaining and obtaining written informed consent from all the women and attendants, they will be recruited in this study.

Institute Review Board And Ethical Committee Approval Will Be Taken.

A detailed history (obstetric, menstrual, personal, past, and family history) and clinical examination.

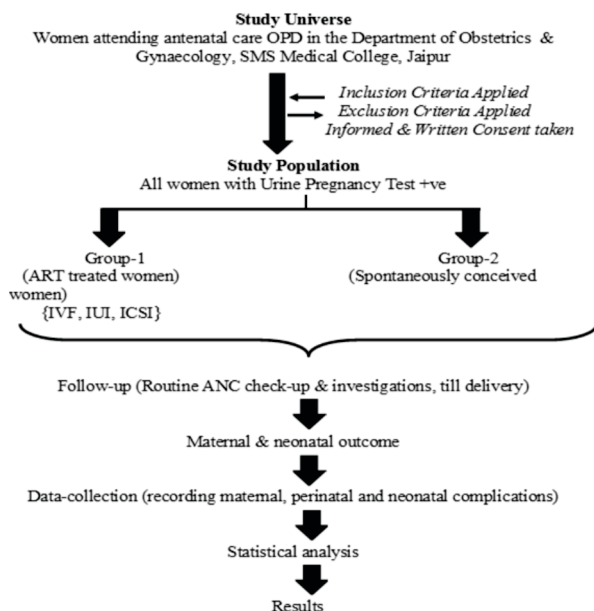
All women will be investigated with necessary laboratory investigations including CBC, ABORh, HbsAg, HIV, VDRL, S.TSH, DIPSI, Urine complete & microscopy.

USG will be done for fetal well-being.

Then, Women will be categorized as Group-1 & Group-2 based upon their method of conception (either spontaneously / ART) & they will be followed up further till their outcomes of pregnancy (any abortions/ any maternal or neonatal complication/IUDs/ NICU admission).

Statistical Analysis

Continuous variables will be summarized as mean and will be analyzed by using unpaired 't' test. Nominal / categorical variables will be summarized as proportions and will be analyzed by using chi square/ Fischer exact test. P-value <0.05 will be taken as significant.

FLOW CHART**RESULTS**

A total of 200 women with ART treated and spontaneously conceived women were recruited for the study between 2020 and June 2021. All the observations were tabulated and analyzed

Table no. 1: Distribution of patients according to age

Age group (years)	Spontaneous		ART				No. of patients
	No.	%	No.	%	No.	%	
21-25	30	55	13	24	11	20.3	54
26-30	55	52.3	29	27.6	21	20	105
31-35	8	26.7	6	20	16	53.3	30
36-40	7	63.6	1	9	3	27.2	11
TOTAL	100		49		51		200

In our study age distribution of patients shows that majority of patients i.e. 50% belonged to 26-30 year age group, followed by 28% who belonged to 21-25 year age group, then 22% belonged to 31-35 year age group, and minimum no of patients i.e. 4% belonged to 36-40 year age group.

Table no 2: Distribution of patients according to mode of delivery

Mode of delivery	Spontaneous		ART				No. of patients
	No.	%	No.	%	No.	%	
LSCS	37	39.3	20	21.2	37	39.3	94
NVD	63	59.4	22	20.7	21	19.8	106
TOTAL	100		49		51		200

Our study also explains the mode of delivery in patients, which states that 57% of them had LSCS and 43% had normal vaginal delivery.

Table no. 3: Distribution of population according to presence of pregnancy complication

Pregnancy complication	Spontaneous	Art		No. of patients
		IUI	IVF	
GDM	22	20	10	52
HDP	37	13	9	59
Pre eclampsia	15	6	10	31
IHCP	3	8	4	15
Infection	5	4	2	11
Total	82	51	35	168

Chi square statistic is 13.7, and p value is 0.008 The chi-square statistic is 3.8961. The p-value is .420251. The result is not significant at $p < 0.005$. There is no significant association between pregnancy complication and reproductive technique.

Table no. 4: Distribution of patients according to perinatal complication

Perinatal complication	Spontaneous	ART		No. of patients
		IUI	IVF	
Multiple pregnancy	9	5	23	37
Abortion	12	4	1	17
Ectopic pregnancy	0	4	0	4
Polyhydramnios	3	8	4	15
Oligohydramnios	5	11	13	29
PPH	6	5	2	13
Placenta previa	1	11	7	19
Total	36	48	50	114

Chi square statistic is 13.7, and p value is 0.008 There is highly significant association between perinatal complication and reproductive technique. In present study perinatal outcomes were also analysed in which 5% had abortion.

Several previous studies have compared the risk of spontaneous abortion following assisted reproductive technology with that in natural pregnancies. Typically, these studies have not clearly stated the definitions of pregnancy and spontaneous abortion.

Table no. 5: Distribution of patients according to neonatal complication

Neonatal complication	Spontaneous		ART				No. of patients
	No.	%	No.	%	No.	%	
Pre term	10	28.5	12	34.2	13	37.1	35
LBW	16	38.02	13	30.9	13	30.9	42
Macrosomia	7	21.8	12	37.5	13	40.6	32
Small for date babies	46	64.8	12	17	13	18.3	71
TOTAL	100		49		51		200

Chi square statistic 41.5, and p value is 0.0001 There is highly significant association between neonatal complication and reproductive technique.

DISCUSSION

Our study also explains the mode of delivery in patients, which states that 57% of them had LSCS and 43% had normal vaginal delivery.

Similarly in study of Sullivan EA et al⁵ crude rate of caesarean section was 50.1 percent versus 28.9 percent for all other births.

Similarly Previous studies Reubinoff BE et al⁶ also provide reliable evidence that women who become pregnant through assisted reproductive technology are more likely to choose caesarean section delivery, which increases the caesarean section rate.

Distribution of patients according to complication during pregnancy transferred that 30% of them had gestational diabetes mellitus. Above table stated that 22% of patient had HDP, while 78% of them had not. Complication in pregnancy also revealed that 16% patients had pre-eclampsia.

Previous studies conducted by Harlev A et al⁷, Wennberg AL et al, Martin AS et al, Qin JB et al have reported that ART has an increased incidence of hypertension during pregnancy, GDM, IHCP, postpartum haemorrhage, premature delivery, and low birth weight, which is consistent with our present results.

Kelley et al⁸ have suggested that in pregnancy, PCOS women experience increased risk of miscarriage, gestational diabetes, pre-eclampsia, and extremes of fetal birth weight.

The study cannot distinguish whether the increased risk of spontaneous abortion in assisted reproductive technology pregnancies is due to the treatment they received, or to unmeasured patient characteristics. Population differences, such as maternal age and previous spontaneous abortion, certainly accounted for part of the increased risk. Women with a history of infertility have been reported to have higher rates of spontaneous abortion.

Indeed, Gray and Wu (2000)⁹ have reported a significantly higher risk of spontaneous abortion in women with a history of subfertility. Our study states that 4% of patients had ectopic pregnancy. Similar findings are shown in study of Chang HJ et al¹⁰ in which it was found that data on the risk factors for developing ectopic pregnancy after IVF are still inconsistent. Between fresh nondonor IVF and embryo transfer cycles,

the significant risk factor for ectopic pregnancy was tubal factor infertility, and endometriosis, rather than male factor infertility.

Higher ectopic pregnancy rate could be associated with zygote intrafallopian transfer, assisted hatching, large embryo transfer volume, deep fundal transfer, and frozen embryo transfer. The supraphysiologic progesterone level may decrease uterine contractility and enhance implantation in the uterine cavity in fresh embryo transfer compared with frozen embryo transfer cycles.

Although recent results suggest reassurance in risk of ectopic pregnancy with frozen transfer, clinicians should be remembering this possibility while performing a frozen embryo transfer. Higher implantation potential per embryo at the blastocyst stage may increase the risk of ectopic pregnancy than cleavage stage. Especially, according to numbers of embryos transferred, different risk of ectopic pregnancy after IVF was noted.

Distribution of patients according to perinatal outcomes in our study transferred that 28% of total patients had multiple pregnancy.

Similarly, a study conducted by Aniket D. Kulkarni et al¹¹ from 1998 to 2011, the estimated proportion of twin births that were attributable to IVF increased from 10% to 17% (a 70% increase, $P < 0.001$ for trend). Similar results are shown in S R Murray et al¹² in which the association between assisted reproduction technologies (ART) and multiple pregnancy is well-established, with a multiple birth rate of 24% in ART pregnancies. Multiple pregnancy is associated with significantly increased maternal and perinatal morbidity and mortality, as well as increased costs to the National Health Service.

Similarly, many authors have found that ART twins to be at a disadvantage at terms of prematurity, low birth weight, higher caesarean section rate, length of stay in the neonatal intensive care unit, and perinatal mortality. In our study, 17% of patients had PPH and 18% of patients had placenta previa.

To date there are existing reviews of Helmerhorst FM et al¹³ and Qin JB et al which had outcomes for created by IVF and/or ICSI. Our findings are generally consistent with previous reviews. According to them the ART singleton pregnancies had a significantly increased risk of placenta previa (RR 3.71, 95% CI 2.67-5.16; $I(2) = 72\%$), placental abruption (RR 1.83, 95% CI 1.49-2.24; $I(2) = 22\%$), antepartum hemorrhage (RR 2.11, 95% CI 1.86-2.38; $I(2) = 47\%$), postpartum hemorrhage (RR 1.29, 95% CI 1.06-1.57; $I(2) = 65\%$), polyhydramnios (RR 1.74, 95% CI 1.24-2.45; $I(2) = 0\%$), oligohydramnios (RR 2.14, 95% CI 1.53-3.01; $I(2) = 0\%$), cesarean sections (RR 1.58, 95% CI 1.48-1.70; $I(2) = 92\%$).

Perinatal outcomes according to above table transferred that 25% of patients had preterm labour. Distribution of patients according to neonatal outcomes are being shown in above table which states that 25% of total patients had preterm labour.

In support of above data, there is study done by Jin Liang Zhu¹⁴, -. The elevated risk of SGA among infertile couples persisted after adjustment for maternal age, parity and smoking. In our study 12% of total patients had macrosomic babies. Similarly, in other study Castillo et al¹⁵ observed in a multicenter cohort study a trend of increasing birth weight of newborns from pregnancies obtained through IVF. In their study, the authors observed an increase in birth weight by 13.4 grams per year during the study period.

Simultaneously, it was observed that newborns obtained after ART were at risk of large for gestational age and macrosomia, especially if cryopreservation techniques were used. Large for gestational age and macrosomia in singletons born after frozen/thawed embryo transfer (FET) in assisted reproductive technology (ART).

Similarly in the other study of Mohamad Eid HAMMADEH et al¹⁶, the outcome of pregnancies following assisted conception have revealed adverse results compared to natural conception such as a higher rate of preterm deliveries, low birth weight and small for gestational age (SGA) in live born singleton and twin babies, SGA, extremely low birthweight (LBW < 0.001).

A meta-analysis of 15 studies comprising 12,283 singleton infants of women who underwent IVF and 1.9 million singleton infants of

women who had naturally occurring pregnancies showed higher odds of perinatal mortality (odds ratio [OR], 2.2; 95% confidence interval [CI], 1.6-3.0), preterm delivery (OR, 2.0; 95% CI, 1.7-2.2), low birth weight (OR, 1.8; 95% CI, 1.4-2.2), very low birth weight (OR, 2.7; 95% CI, 2.3-3.1), and small-for-gestational-age status (OR, 1.6; 95% CI, 1.3-2.0) in IVF pregnancies, after adjusting for maternal age and parity.

CONCLUSION

Our study concluded that there is more pregnancy, perinatal & neonatal complications associated with ART conceived women as compared with spontaneously conceived pregnancies. Hence strict control of indications for ART is advised and to strengthen and increase their antenatal visits in ANC clinics. It reduces the complications in ART conceived women and makes the better fetomaternal outcome.

Limitation Of The Study

1. This study will be performed in a single center which is a tertiary referral center.
2. Small sample size.

Conflict Of Interest: The authors declare no conflict of interest

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