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Original Research Article

A comparative study of spontaneously conceived twin pregnancies vs. twins conceived by assisted reproductive techniques and their maternal and perinatal outcomes: a prospective observational study

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ABSTRACT

Background: The utilization of assisted reproductive techniques has led to a notable increase in the incidence of twin pregnancies. Neonates from multifetal gestations also make up a disproportionate percentage of very-low-birthweight newborns and have increased risks of having congenital malformations and preterm birth. This study was done to compare the maternal and and perinatal outcomes of spontaneously conceived twins and those twins conceived by assisted reproductive techniques.
Methods: The present hospital based observational study was done at Chettinad Hospital and Research Institute, Chennai, India over a period of 36 months between February 2021 to January 2024 among pregnant women with twin gestation attending the outpatient department during the study period. 50 antenatal mothers with twin pregnancy and 50 pairs of twins were studied. Convenient sampling technique was adopted. The subjects were followed up from the booking visit, till the postpartum discharge day. Any adverse maternal, foetal, neonatal outcomes and the treatment given were studied.
Results: The mean birth weight among those with spontaneous conception and assisted reproductive techniques conception was 2.23±0.46 kgs and 2.02±0.51 kgs, respectively. Both the groups were similar with regard to the birth weight. 6.6% babies from the spontaneous conception group and 5% from the assisted reproductive techniques conception group were admitted for respiratory distress and rest from both the groups got admitted for sepsis. The mean duration of hospital stay was 3.58±2.40 days for the spontaneous conception group and 3.75±2.71 days for assisted reproductive techniques conception.
Conclusions: This study concludes that the maternal and fetal outcomes of twin deliveries conceived spontaneously or through assisted reproductive techniques do not differ significantly in their outcome.

Keywords: Assisted reproductive techniques, Placentation, Pre-term, Spontaneous conception

INTRODUCTION

Multiple pregnancies are one of the common outcomes of assisted reproductive techniques procedures. Uniovular twins are derived from the same zygote and are always of the same sex, whereas binovular twins bear only fractional resemblance to each other.[1] Zygosity refers to the type of conception, whereas the chorionicity refers to the placentation, or the number of placentae-monochorionic (one) or dichorionic (two). By nature, approximately 30% of the twins are monozygous and 70% arise from two fertilised ova.[2] The monochorionic placenta can be either diamniotic, or infrequently, monoamniotic. The number of layers of chorion and amnion in monozygotic conception depends on the time of the fertilised ovum. The chorion differentiates on day four and the amnion on day eight after fertilisation. Hence if cleavage occurs before the fourth day, both chorion and amnion split completely giving each

embryo a separate chorion and amnion, resulting in a dichorionic-diamniotic placenta (DCDA)-25% of monozygotic twins. If it occurs between four and eight days after fertilisation, the chorion has already differentiated; therefore, a monochorionic-diamniotic placentation results (MCDA) - 75% of monozygotic twins. In less than 1% of monozygotic conceptions, twinning occurs eight days after fertilisation after both, the chorion and amnion have differentiated-monoamniotic placentation (MCMA).

It has been observed that in vitro fertilization (IVF) leads to 27% more multiple pregnancies than spontaneous conceptions which account for 1%.[3] Twin pregnancies can result in a number of maternal and fetal complications. Several studies have found the incidence of maternal complications such as nutritional anemia, pregnancy-induced hypertension, antepartum hemorrhage, polyhydramnios, preterm, and postpartum hemorrhage to be higher in twin pregnancies than in singletons. Moreover, twin foetuses are found to have lower birth weight and are frequently preterm. They are at a higher risk for prenatal and neonatal morbidity and mortality.[4] Twins may have an early neonatal death rate that is up to seven times higher than that of singletons. The morbidity and mortality rate of the second twin and subsequent foetuses is significantly more in higher order births.[5] When compared to pregnancies that occur spontaneously, there are conflicting reports about whether assisted conception carries any additional risks. While some studies indicate a higher risk of maternal and perinatal complications, other studies show that there is no increased risk to the mother or child as a result of the method of conception. Joy et al in their study concluded that assisted reproductive techniques twins had better or similar perinatal outcomes when compared to twins who were conceived spontaneously.[6]

Hence, our study was conducted to compare the maternal and perinatal outcomes of spontaneously conceived twins and those twins conceived by assisted reproductive techniques (ICSI/ IVF/ ovulation induction/ intrauterine insemination) in terms of maternal and perinatal complications.

METHODS

The present study was a hospital based observational study done at Chettinad Hospital and Research Institute, Chennai, India over a period of 36 months - between February 2021 to January 2024. The study was carried out among pregnant women with twin gestation attending the outpatient department of Obstetrics and Gynecology during the study period. We studied 50 antenatal mothers with twin pregnancy and 50 pairs of twins. Of these, 30 were spontaneous conceptions and 20 conceived via assisted reproductive techniques. Convenient sampling technique was adopted. Inclusion criteria included all the pregnant women with twin gestation irrespective of the gestational age. The subjects were followed up from the booking visit, till the postpartum discharge day. Any adverse maternal, foetal, neonatal outcomes and the treatment given were studied without bias. Factors such as the maternal age, parity, mode of delivery, gestational age at delivery, comorbid conditions, placentation (both, antenatally on USG and the placenta specimen postnatally), gender of the twin babies, whether babies born alive/ intrauterine foetal demise/ stillbirth, birth weights, APGAR scores (1 and 5 mins) and period of neonatal intensive care unit (NICU) stay were analysed in relation to each other. All patient information was kept anonymous. All data was entered from hospital records. A hospital based observational study was conducted from hospital records. Ethical committee approval for the study was obtained from the institutional ethics committee. All the participants enrolled in the study were duly informed about the study procedure and consent was obtained from all in the language they understand. The collected data was entered into Microsoft Excel 2019 and the master chart created. Statistical analysis was done by SPSS version 26. Quantitative variables were expressed in terms of mean and standard deviation and the qualitative variables using frequency and percentage. To compare the mean between the groups independent t test was used. To compare the distribution of qualitative variables between groups, the chi square test was used.

RESULTS

Out of the 50 participants, 30 (60%) had conceived spontaneously and 20 (40%) conceived following assisted reproductive technique. Among those who received assisted reproductive techniques as intervention for conception, 9 (45%) had Intracytoplasmic sperm Injection (ICSI) and In-vitro fertilization (IVF). 1 (5%) conceived through ovulation induction and intrauterine insemination (Figure 1).

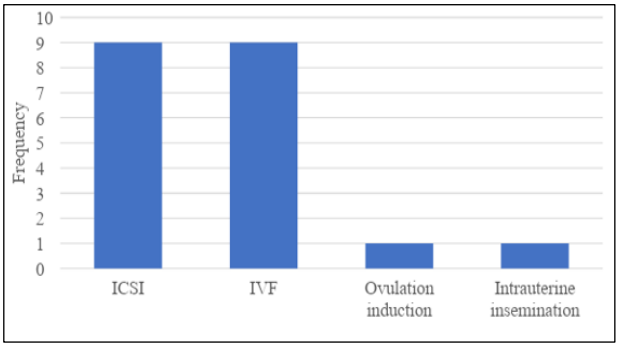

Figure 1: Distribution of reproductive technique undergone among those with Assisted conception.

The mean age among those with spontaneous twin conception was 28.20±3.43 years while that among those conceived using assisted reproductive techniques was 29.55±4.59 years. The mean age was similar between the groups with p value of more than 0.05. The proportion of primigravida pregnancies was significantly more in the assisted reproductive techniques conception group than in

the spontaneous conception group with p value of less than 0.05. The placentation was monochorionic diamniotic (MCDA) for 8 (26.7%) and 1 (5%) in the spontaneous conception and assisted reproductive techniques conception groups, respectively. The distribution was similar between the groups (Table 1).

Table 1: Baseline characteristics between the groups.

Variable		Spontaneous conception (n=30) (%)	Assisted reproductive techniques conception (n=20) (%)	P value
Age (in years)		28.20±3.43	29.55±4.59	0.241
Parity	Primi	12 (40)	16 (80)	0.004
	2	15 (50)	1 (5)	
	3	3 (10)	3 (15)	
Placentation	MCDA	8 (26.7)	1 (5)	0.051
	DCDA	22 (73.3)	19 (95)	

Table 2: Distribution of comorbidities among the mothers between the groups.

Variable		Spontaneous conception (n=30) (%)	Assisted reproductive techniques conception (n=20) (%)	P value
Comorbidities	GDM	12 (40)	11 (55)	0.297
	Hypothyroid	8 (26.6)	7 (35)	0.528
	Short cervix	1 (3.3)	2 (10)	0.330
	Cervical encerclage	0	3 (15)	0.028
	GHTN/preeclampsia	2 (6.6)	3 (15)	0.335
	Anaemia corrected	1 (3.3)	1 (5)	0.768
	Rh negative	1 (3.3)	1 (5)	0.768
	Ventricular septal defect	0	1 (5)	0.216
	Hypotension	0	1 (5)	0.216

With regard to the comorbidities among the pregnant women who had conceived spontaneously, 12 (40%) had gestational diabetes mellitus (GDM) and 8 (26.6%) had hypothyroidism. In the ART conception group, 11 (55%) had GDM, 7 (35%) hypothyroid and 3 (15%) had cervical stitches in situ. None of the spontaneously conceived mothers had cervical stitches in situ. The proportion of participants with cervical encerclage was more in the assisted reproductive techniques group than in the spontaneous conception group (p value <0.05) (Table 2).

5 (16.7%) delivered through labour natural, 10 (33.3%) through elective LSCS and 15 (50%) through emergency LSCS in the spontaneous conception, whereas in the assisted reproductive techniques conception group, 1 (5%) delivered through natural labour, 4 (20%) through elective LSCS and 15 (75%) through emergency LSCS. 44 of the 50 patients had LSCS and 6 mothers had normal deliveries. Thus, the rate of LSCS totally was 88 % (Figure 2). With regard to status of mother after delivery, 1 (3.4%) in the spontaneous conception group died.

19 (63.3%) twins were of the same gender and 11 (36.7%) had different genders in the spontaneous conception group, while in the assisted reproductive techniques group, the proportion was 7 (35%) twins with same sex and 12 (60%) with different sex. 10 (33.3%) patients delivered at term in the spontaneous group and 4 (20%) of the assisted reproductive techniques patients.

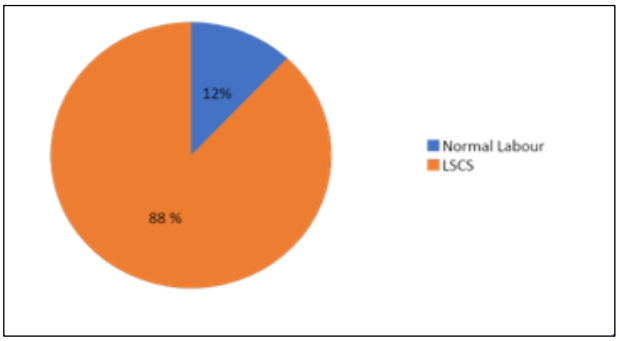

Figure 2: Distribution of mode of delivery across both the group.

The mean birth weight among those with spontaneous conception and assisted reproductive techniques conception was 2.23±0.46 kgs and 2.02±0.51 kgs, respectively. Both the groups were similar with regard to the birth weight. For twin A, the mean APGAR score at 1 minute was 7.73±0.82 among those with spontaneous conception and 7.95±0.39 among those with assisted

reproductive techniques conception. The mean APGAR score at 5 minutes was 8.77±0.77 for spontaneous conception and 9±0.32 for assisted reproductive techniques conception. For twin B, the mean APGAR at 1 minute was 7.67±0.71 and 7.72±0.57 for spontaneous conception and assisted reproductive techniques conception, respectively. At 5 minutes, the mean APGAR was 8.80±0.61 and 9 for spontaneous and assisted reproductive techniques conception, respectively. Both the groups were similar with regard to APGAR scores at 1 and 5 minutes. Among those in the spontaneous conception group, 10% babies were admitted to NICU and the proportion in the assisted reproductive techniques conception group was also 10%. Both the groups were similar with regard to NICU admission. 6.6% babies from the spontaneous conception group and 5% from the assisted reproductive techniques conception group were admitted for respiratory distress and rest from both the groups got admitted for sepsis. The mean duration of hospital stay was 3.58±2.40 days for the spontaneous conception group and 3.75±2.71 days for assisted reproductive techniques conception. The mean was similar between the groups with p value of more than 0.05 (Table 3).

Table 3: Comparison of outcome between the groups.

Variable		Spontaneous conception (n=30) (%)	Assisted reproductive techniques conception (n=20) (%)	P value
Mode of delivery	Normal labour	5 (16.7)	1 (5)	0.185
	Elective LSCS	10 (33.3)	4 (20)	
	Emergency LSCS	15 (50)	15 (75)	
Gender of the baby	Same	19 (63.3)	7 (35)	0.091
	Different	11 (36.7)	12 (60)	
	Not known	0	1 (5)	
Status of mother	Alive	29 (96.6)	20 (100)	0.409
	Dead	1 (3.4)	0	
Term/preterm	Term	10 (33.3)	4 (20)	0.519
	Moderate preterm	2 (6.7)	4 (20)	
	Late preterm	15 (50)	10 (50)	
	Very preterm	3 (10)	2 (10)	
Birth weight	Twin A	2.23±0.46	2.02±0.51	0.153
	Twin B	2.07±0.48	1.99±0.51	0.559
APGAR 1 min	Twin A	7.73±0.82	7.95±0.39	0.282
	Twin B	7.67±0.71	7.72±0.57	0.780
APGAR 5 min	Twin A	8.77±0.77	9±0.32	0.209
	Twin B	8.80±0.61	9	0.144
NICU admission	Yes	3 (10)	2 (10)	0.741
	No	37 (90)	18 (90)	
Causes of NICU admission	Respiratory distress	2 (6.6)	1 (5)	0.807
	Sepsis	1 (3.3)	1 (5)	0.768
Duration of hospital stay		3.58±2.40	3.75±2.71	0.816

DISCUSSION

About 50 antenatal mothers with twin pregnancies consulting at Chettinad Hospital and Research Institute, Kelambakkam, Tamil Nadu either from the first trimester, or at any time in the antenatal period (including first visit in labour) were followed up at the Department of Obstetrics and Gynaecology. 20 of these patients had conceived by assisted reproductive techniques at outside hospitals, 18 of whom were by ICSI (IVF), 1 by ovulation induction and 1 by intrauterine insemination. 30 of the twin pregnancies were by spontaneous conception. The pregnant mothers were followed up from the booking visit, till the postpartum discharge day. The mean age was similar between the groups: 28.20±3.43 years in the spontaneous conception and 29.55±4.59 years in the assisted reproductive techniques groups. This was in contrast to the study done by Anbazhagan et al which showed that patients who underwent assisted conception were considerably older than those who conceived spontaneously.[3] Giesler et al also reported a similar result where the age of the mothers in the assisted conception group was higher than that of spontaneous conception group.[7] The difference can be attributed to the differences in sample size. The proportion of primigravida was significantly more in the assisted reproductive techniques conception group than in the spontaneous conception group. Among those spontaneously conceived, 12 (40%)

were primigravida and among those in the assisted reproductive techniques conception group, 16 (80%) were primigravida. This is consistent with the finding of Caserta et al which showed that the women who conceived via assisted reproductive techniques were more often nulliparous than the women who conceived spontaneously.[8] With regards to comorbidities, the majority of the women in both groups had GDM. Among the pregnant women who had conceived spontaneously, 12 (40%) had GDM and among those in the assisted reproductive techniques conception group, 11 (55%) had GDM. This observation is similar to the study by Gao et al which showed that the major obstetric complication is GDM but the incidence is somewhat lesser which is 13.5% in spontaneous conception and 19.4% in assisted reproduction group.[9] However, Giesler et al in their study observed that hypertension disorders of pregnancy were more frequent than other complications.[7] With regard to the mode of delivery, there was no significant difference between both the groups, emergency LSCS being the commonest in both the groups. 15 (50%) mothers delivered through emergency LSCS in the spontaneous group whereas in the assisted reproductive techniques conception group 15 (75%) delivered through emergency LSCS. There are studies indicating that the twins in ART conception were delivered more commonly through emergency LSCS. Giesler et al observed that emergency LSCS was more frequent in assisted reproductive techniques group than in spontaneous conception group[7]. Pourali et al also observed that incidence of LSCS deliveries were more common in the assisted reproductive techniques group than among spontaneously conceived twin gestations.[10] This can be attributed to the fact that LSCS was the preferred procedure for the obstetrician due to the poor obstetric histories and precious nature of the babies conceived through the assisted reproductive techniques methods which shortens the wait period even in cases of slightest intrapartum complications. There is no significant difference in birthweight among both the groups. The mean birth weight among those with spontaneous conception and assisted reproductive techniques conception was 2.23±0.46 kgs and 2.02±0.51 kgs, respectively. This observation is consistent with findings of Pourali et al which observed that the birthweights between both the groups were not significantly different.[10] Anbazhagan et al and Geisler et al also observed a similar finding in which the birth weights across both the groups were similar.[3,7] Both the groups were similar with regard to the APGAR score at 1 and 5 minutes. This result was consistent with the observations of Pourali et al.[10] Regarding NICU admission, there is no significant difference between the two groups. This result was comparable to the observations of Geisler et al which reported that there was no significant difference in NICU admissions between the groups.[7] Anbazhagan et al also observed a similar result with regards to NICU admissions.[3] The main strength of the study is that as the study included twin pregnancies irrespective of the placentation, the effect of it on fetal outcomes can be studied on further steps. The main limitation is that the study involves a smaller sample size and the convenient sampling technique. An extensive multicentric study with a larger sample can provide further insights into the subject.

CONCLUSION

This study concludes that the maternal and fetal outcomes of twin deliveries conceived spontaneously or through assisted reproductive techniques do not differ significantly in their outcome. This study can help fertility specialists and obstetricians counsel couples about treatment and pregnancy outcomes following conception with twins.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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