

Perinatal Outcome of Twin Pregnancies Compared based on Chorionicity and Antenatal Booking Status of Mother

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ABSTRACT

Introduction: Twin pregnancy is considered a high risk pregnancy due to multiple maternal and foetal complications leading to adverse maternal and foetal outcome.

Aim: This study was planned to know foetal outcome of twin pregnancy according to chorionicity and also tried to observe difference in outcome among foetuses born to booked patients at our institute and foetuses those were born to referred patients.

Materials and Methods: A retrospective study of four years pertaining to twin foetuses was carried out at tertiary hospital. Foetal data was collected from the individual mother's file from antenatal period till the time of birth. Foetal outcome was analysed according to chorionicity of placenta and data of whole study population was further stratified into those (298) born to booked patients (minimum 4 antenatal visits) and those (564) referred to our institute. Discrete categorical data were presented as n (%); continuous data were given as mean±SD and range. Means of different parameters for three groups Diamniotic Dichorionic (DADC), Diamniotic Monochorionic (DAMC), Monoamniotic Monochorionic (MAMC) were compared using One-Way ANOVA followed by Post-Hoc Multiple Comparisons test. Proportions were compared between the

referred and booked groups using the chi-square test.

Results: Incidence of twin pregnancies was 22/1000 birth and 65% of them were born to referred patients. Out of 862 twin foetuses, 258 pair (59.8%) were Diamniotic Dichorionic (DADC), 162 (37.5%) were Diamniotic Monochorionic (DAMC) and 11 (2.5%) were Monoamniotic Monochorionic (MAMC) twins. Seventy percent of them were preterm delivered. In relation to chorionicity there was no difference in gestational age (34.9 weeks), however birth weight was significantly different (1.97±0.42 kg, 1.783±0.54 kg, 1.645±0.57 kg in DADC, DAMC and MAMC group respectively, $p<0.001$). Gross foetal malformations were observed in 8/862 (0.9%) of twins. The discordant twins were observed in 8.9% of foetuses. The incidence of intrauterine foetal death was 35/862 (4.0%), (nine in DADC, 20 in MCDA and 6 in MAMC group ($p<0.001$)). There was significant difference in gestational age, birth weight, discordant twin, intrauterine foetal death and Apgar score among referred and booked patients ($p<0.05$).

Conclusion: This study revealed importance of specialised antenatal care in reducing foetal mortality in utero and emphasise us to increase the availability of more number of intensive care units to enhance the survival rate of these premature foetuses after birth to decrease perinatal mortality and morbidity.

Keywords: Acardiac twins, Discordant twins, Multiple pregnancy

INTRODUCTION

Incidence of multiple pregnancies have been increasing following use of fertility enhancing treatments, though it has been correlated with certain race, age and parity of patient [1-5]. In United States, incidence of twin birth has been reported in 3.4/1000 live birth, contributing to more than 96% of multiple births [6]. Indian studies have reported variable incidence of twin pregnancies from 5 per 1000 births to 29/1000 births by Deepthi HR et al., and Tomar SP et al., respectively [7,8]. Dizygotic twins are the consequences of fertilisation of two separate ova from single ovulatory cycle and monozygotic twins develop from division of single fertilised ova.

In twin gestation, chorionicity of placenta can be monochorionic and dichorionic depending upon the number of chorionic membranes. Monozygotic twins can have dichorionic or monochorionic placenta according to the time of division of fertilised ova. Cleavage of dizygotic or monozygotic twins within three days of fertilisation results in two placentas with two amnions and two chorionic membranes. Monozygotic twins will develop with one placenta, one chorion and two amnions when cleavage of zygote occurs from fourth to eighth day following fertilisation and single placenta with one chorion and one amniotic membrane will develop when division occurs from 8th to 12th day after fertilisation.

Sharing of placenta in monochorionic twin pregnancies results in increased risk of perinatal mortality on account of twin-twin transfusion syndrome and discordant twins [9]. Other monochorionic pregnancies related disorders are Twin Reversed Arterial Perfusion (TRAP) sequence, neurologic sequelae from foetal demise of co-twin and anaemia-polycythaemia sequence. Perinatal mortality further increases in monoamniotic twin pregnancies due to risk of conjoined twins and cord entanglements in addition to those associated with monochorionic pregnancies [10,11]. Thus, diagnosis of chorionicity and amniocytosis is required for antenatal management of multiple pregnancies and planning for time of delivery.

Approximately 59% of multiple pregnancies inadvertently goes into preterm labour which causes short and long term foetal perinatal morbidity and mortality due to prematurity and low birth weight when compared to singleton pregnancy [1]. Few of the multiple pregnancies patients who get away from preterm labour needs timely delivery to prevent intrauterine deaths and stillbirths especially in monochorionic twin pregnancy. United States's 2010, Infant Mortality Rate (IMR) was 24, 55 and 115 per 1000 live births for twins, triplets, and quadruplets, respectively and 5.5 per 1000 in single births [12]. Thus, recommended gestational age at the time of delivery varied in multiple pregnancies to prevent perinatal mortality. American College of Obstetricians and Gynaecologists (ACOG) recommends planned delivery at 38-38+6 weeks in

normal uncomplicated dichorionic/diamniotic twin pregnancies but the authors of a 2016 systematic review and meta-analysis of cohort studies recommended delivery at 37+0 to 37+6 weeks in uncomplicated dichorionic twin pregnancies as the risk of stillbirth significantly exceeded the risk of neonatal death at 38+0 to 38+6 weeks and later [13,14]. This review recommends delivery of uncomplicated monochorionic diamniotic twin pregnancies at 36+0 to 36+6 weeks due to rising trends of still births over this period whereas ACOG suggests delivery of monochorionic twins at 34+0 to 37+6 weeks of gestation [13,14]. The delivery of monoamniotic pregnancies has been recommended between 32+0 and 34+0 weeks of gestation because of the increasing risk of perinatal mortality in the third trimester [13]. To emphasise the role of specialised care for detection of antenatal complication and timely intervention, this study was planned to compare foetal outcome in twin pregnancy of those who have received antenatal care at our tertiary care hospital (atleast 4 antenatal visits) with those referred from other hospitals.

MATERIALS AND METHODS

A retrospective cohort study was carried out in the Obstetrics Department of Government medical college, Chandigarh from December, 2011 to November 2015 after approval from the Institute's Ethical Committee. The study population included all twin fetuses who delivered after 20 weeks gestation in this institute. Fetuses of patients with chronic disease like chronic hypertension, diabetes mellitus etc., were excluded. Foetal data were obtained from the institute's labour room delivery data entry register along with analysis of individual mother's records. Analysis of foetal data was done according to chorionicity of the placenta and data was also compared among fetuses of patients who were booked at our institute (atleast 4 antenatal visits at our hospital) and with those referred to our institute.

Chorionicity was determined by ultrasound in the antenatal period or in postnatal period by analysis of placenta and sex of the baby was considered whenever there was doubt about the chorionicity. The chorionicity was classified as: Dichorionic (DC) and Monochorionic (MC). Three groups were defined based on chorionicity and amniotic sac: Diamniotic Dichorionic (DADC), Diamniotic Monochorionic (DAMC), Monoamniotic Monochorionic (MAMC).

The foetal parameters that were included: gestational age at birth, mode of delivery, intrauterine death, discordant twin, live birth, and weight of the twins at birth. Other outcomes which were included in the study were Apgar scores and gross congenital malformations which were diagnosed by ultrasound examination during the antenatal period or by clinical examination of the neonate.

The gestational age at birth was defined as extremely preterm <28 weeks, very preterm (28-<32 weeks) and moderate or late preterm (32-<37 completed weeks of gestation). Discordant twin was diagnosed when estimated twin weights differences were greater than 25 percent, based on the weight of the larger twin. Newborns weighing less than 2500 g were classified as low birth weight, those weighing less than 1500 g as very low birth weight and extremely low birth weight when it was less than 1000g. Apgar score less than 7 at 5 minute of birth was the criterion for immediate neonatal morbidity.

STATISTICAL ANALYSIS

Discrete categorical data were presented as n (%); continuous data were given as mean±SD and range. Normality of quantitative data was checked by measures of Kolmogorov-Smirnov tests of normality. As our data was normally distributed data, means of different parameters for three groups (DADC, DAMC, MAMC) were compared using One-Way ANOVA followed by Post-Hoc

Multiple Comparisons test. Proportions were compared between the referred and booked groups using the chi-square test. All statistical tests were two-sided and performed at a significance level of $\alpha=0.05$. Analysis was conducted using IBM SPSS STATISTICS (version 22.0).

RESULTS

During this study period, 862 twin fetuses were born. Out of total, 564/862 (65.2%) twins born to patients who were referred from other hospital and 298/862 (34.5%) were born to patients who were booked at our hospital. Commonest presentation of twins was both vertex in 205/431 (47.5%), 78/431 (18%) were vertex breech, 67/431 (15.5%) were both breech, 61/431 (14%) were breech vertex and 21/431 (4.8%) had transverse lie of first twin. Cesarean section was done in 224/431 (51.9%) and cesarean section for delivery of second twin was done in five cases.

With respect to chorionicity, 258 (59.8%) pairs were DADC, 162 (37.5%) were DAMC and 11 (2.5%) were Monoamniotic Monochorionic (MAMC) twins. Out of 862 pairs, 608/862 (70.5%) were premature born. There were 62/422 (14.6%) vs 02/186 (1.07%), $p<0.001$ indicated premature born twins in referred and booked patients.

Foetal parameters according to chorionicity are presented in [Table/Fig-1]. Foetal data among referred and booked patients are given in [Table/Fig-2].

Foetal Parameter	Total birth	DADC	DAMC	MAMC	P-value
Foetuses/ neonates	862	516 (59.9%)	324 (37.5%)	22 (2.5%)	
Average gestational age at birth (weeks)	34.9±2.6	35.0±2.3	34.7±3.2	34.45±3.1	0.309
Average birth weight (kg)	1.89±0.48	1.97±0.42	1.78±0.54	1.64±0.57	<0.001
≤1 Kg	36 (4.2%)	8 (1.6%)	27 (8.3%)	1 (4.5%)	<0.001
>1-1.5 kg	153 (17.7%)	70 (13.6%)	73 (22.5%)	10 (45.5%)	
1.6- <2.4 Kg	572 (66.4%)	376 (72.9%)	187 (57.7%)	09 (40.9%)	
≥2.5 KG	101 (11.7%)	62 (12%)	37 (11.4%)	02 (9.1%)	
Foetuses with discordant twins ≥25%	77 (8.9%)	29 (5.6%)	43 (13.3%)	05 (22.7%)	<0.001
Live birth	827 (96%)	507 (98.2%)	304 (93.8%)	16 (73%)	0.32
Intrauterine deaths	35 (4.15%)	09 (1.7%)	20 (6.2%)	06 (27.3%)	<0.003
5 minute Apgar score at birth <7	29 (3.4%)	14 (2.7%)	14 (4.3%)	1 (4.5%)	0.37

[Table/Fig-1]: Perinatal outcome in 862 twin fetuses according to chorionicity. DADC-Dichorionic diamniotic; DAMC-Monochorionic Diamniotic; MAMC-Monochorionic diamniotic

Foetal parameter	Total (862)	Unbooked (564)	Booked (298)	p-value
Average gestational age	34.9 weeks	34.6±2.97	35.42±2.01	0.002
Birth weight (kg)	1.97±0.42	1.82±0.50	2.03±0.41	0.002
IUFD	35 (4.0%)	30 (5.3%)	05 (1.7%)	0.010
Discordant twins	77 (8.9%)	59 (10%)	18 (6.0%)	0.03
Apgar score <7 min	29 (3.4%)	24 (4.2%)	05 (1.7%)	0.047

[Table/Fig-2]: Foetal parameter according to antenatal care. IUFD-Intrauterine Foetal Death

Intrauterine foetal deaths were 35 (both twins in 6 pregnancies and one twin in 23 pregnancies). Congenital malformations were hydrocephalus in 1, one case of ambiguous genitalia 1 and one case of occipital encephalocele in dichorionic pregnancy. Monochorionic group have 2 cases of bilateral club foot, anencephaly in 1, 1 case

of exomphalos, absent limbs and absent umbilical cord and one case was of acardiac twin.

DISCUSSION

The prevalence of twins in this study was 22/1000 of birth that is on higher side when compared to other studies by Deepthi HR et al., and Tomer SP et al., [7,8]. This is explained by referral of patient's with multiple pregnancies from near by health care centre to our Institute. In this study 86.6% fetuses were born through spontaneous conception that co-relates with Assuncao RA et al., who had reported only 3.8% rate of twins conception by assisted reproduction and Behávková K et al., reported 80% rate of spontaneous conception in twin pregnancy [15,16].

As per a WHO fact sheet (2012), India is amongst the top most country contributing to world's premature deliveries and rising incidence of multiple pregnancies is one of the contributing factor [17]. In present study, out of 70% prematurely delivered twins, 10% of twins baby were born at very preterm gestation (<before 32 weeks of gestation) and 60% were delivered at late preterm gestation (>32 to <37 weeks). Martin JA et al., has reported 60.4% rate of preterm birth in twins and 12.2% of them were born at very preterm (<32 weeks) gestation in United States population [6].

The mean gestational age at birth was 34.9±2.6 weeks in this study whereas, it was reported as 35.2 weeks, 34.6 weeks (SD: 3.9, range: 21.3 to 40.3), and 33.48 weeks±3.32 weeks in a study by Martin JA et al., Assuncao RA et al., and Singh and Trivedi respectively [6,15,18]. According to chorionicity there were no differences in mean gestational age in present study but Assuncao RA et al., did find significant difference in gestational age among three group and it was lesser in MCMA and MCDA twins as compared to Dichorionic group [15], 32.9 weeks, 33.6 weeks and 35.4 weeks respectively. Although, mean gestational age at birth was significantly different in referred and booked patients in this study that may be due to higher percentage of induced preterm delivery in referred patients.

Overall 88% of babies were low birth weight (<2.5 kg) in this study and this incidence was higher than reported by Martin JA et al., Behavkova K et al., and Bangal VB et al., in 57.5%, 78.67%, and 82% of twins respectively that may be explained by poor nutritional status and low BMI in our population [6,16,19]. Mean birth weight of twins was 1.89±0.48 kg in this study whereas it was 2.33 kg by Martin JA et al., and 1.95 kg in a study by Singh and Trivedi [6,18]. Birth weights were significantly different among DADC, DAMC, MAMC group and also in referred and booked patients due to higher percentage of discordant twin and intrauterine foetal death in monochorionic group and in referred patients.

Growth discordancy was observed in 8.9% of twins in this study lower than reported by Assuncao RA et al., (12.8%) and Puccio G et al., (19.35%). This may be due to difference in definition of discordant twins that was taken as twin weight difference of 20%, whereas, it was taken as 25% twin weight difference in this study [15,20]. Although, no definitive causes of discordant twin have been determined but it has been co-related with conception with ovulation induction, multiple pregnancy reduction and foetal malformation by Audibert F et al., [21]. In this study, discordant twins were more commonly associated with monochorionic pregnancy that co-relates with increased perinatal morbidity and mortality in monochorionic pregnancy.

In this study, 35 (4.5%) of twins had intrauterine death and maximum rate of intrauterine death were in monochorionic monoamniotic twins 06 (27.3%), followed by monochorionic diamniotic 20 (6.2%) and was lowest in dichorionic diamniotic twins 09 (1.7%). Assuncao

RA et al., reported 38 (6.6%) rate of intrauterine foetal deaths in twin pregnancy and 26/216 (12%) were from monochorionic group and 9/350 (2.5%) from dichorionic group, and three were from unknown group [15]. Hillman SC et al., has reported intrauterine foetal demise in monochorionic and dichorionic twins in 15 and 3% of twins whereas in this study it was 7.5% and 1.7% in monochorionic and dichorionic fetuses respectively [22].

Growth discordancy was observed in 43% of intrauterine death whereas pregnancy induced hypertension and antepartum haemorrhage were seen in 31% and 20% of intrauterine death respectively. Mahony R et al., reported twin-twin transfusion syndrome as the most common cause of intrauterine death before 30 weeks gestation whereas only 1 case of intrauterine death with twin-twin transfusion syndrome was noticed in this study as most of the intrauterine demise were after 31 weeks in this study except three were at 21, 25 and 28 weeks of gestation, all were from monochorionic group with two presented with antepartum haemorrhage and 1 with TTTS [23].

Most important is the role of antenatal care, out of 35 (4.0 %) IUFD, 30 (5.3%) were in unbooked patients and 05 (1.7%) intrauterine death were in booked patients which were observed in monochorionic group only. There were intrauterine death of both fetuses in 6 twins and foetal distress was observed in another twin in 10/23 (43%) twins who had one intrauterine death in utero that suggest increase risk of neonatal morbidity in second twin also.

This study revealed intrauterine death in all normally grown foetus at around 38±1.7 weeks in dichorionic group and in monochorionic group at 31.9±6.29 weeks. This observation was conflicting to that reported by Mahony R et al., who had reported low risk of intrauterine death in normally grown foetus after 34 weeks [23].

Twin pregnancy always presumed to be a risk factor of increased foetal malformations but in this study only 8/862 (0.9%) had some foetal malformations. Other studies had reported foetal malformations in 12.8% and 6.6% of twin fetuses by Assuncao RA et al., and Puccio G et al., respectively [15,20]. None of the congenital malformations were associated with growth discordancy in this study except acardiac twin. Low incidence of foetal malformations may be due to earlier termination of pregnancy by better availability of sonography nowadays.

There was no significant difference in 5-minute Apgar score of ≤ 7 among all the three groups but it was significantly different when compared between referred and booked patient 24 (4.2%) vs 05 (1.7%), (p, 0.04) respectively that may be explained by more number of referred patients with complications.

LIMITATION

Major drawback of this study is being a retrospective study and non-availability of neonatal data regarding survival rate after birth. Reason being limited availability of intensive care unit at our hospital as compared to number of premature delivery that may have given variable results in those neonates who were not able to get intensive care.

CONCLUSION

Monochorionic pregnancy needs more frequent antenatal sonography from early gestation because of association with discordant twins and subsequent risk of intrauterine deaths. Normally grown foetus in dichorionic pregnancy seeks frequent follow-ups in later gestation and delivery should be conducted at optimum time to prevent intrauterine deaths at advanced gestation.

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