Original Article

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Perinatal Outcome of Twin Pregnancies in Relation to Chorionicity at a Tertiary Care Centre in Central Kerala, India: A Prospective Cohort Study

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ABSTRACT

Introduction: In recent years, there has been a significant increase in the incidence of multiple births due to advanced maternal age at conception and the growing use of infertility treatment. Multiple pregnancies are associated with both maternal and perinatal complications. Maternal complications include anaemia, gestational hypertension, gestational diabetes, preterm labour, operative delivery and postpartum haemorrhage. Preterm birth, growth discordance and complications specific to monochorionic twins predispose these babies to adverse perinatal outcomes.

Aim: To assess the perinatal outcomes of twin pregnancies and compare the outcomes of monochorionic and dichorionic pregnancies.

Materials and Methods: The present prospective cohort study was conducted in the Department of Obstetrics and Gynaecology, Government Medical College (Tertiary care centre), Thrissur, Kerala, India, from September 2019 to August 2020. All twins who delivered at a gestational age of ≥28 weeks during the study period were recruited, totaling 76 twin pregnancies. A structured proforma was used to collect demographic and clinical details, including mode of conception, chorionicity, maternal complications, intrapartum events and neonatal outcomes. Data were analysed using Epi Info software.

Results: The mean maternal age of the study participants was 28.39±6.29 years. The incidence of twin pregnancies delivering at ≥28 weeks at Government Medical College, Thrissur, during the study period was 2.8% (76 twins out of 2709 deliveries). Infertility treatment (ovulation induction alone or Assisted Reproductive Techniques (ART) was associated with dichorionic twinning in 19.7% (15 out of 76 twin pregnancies), with a p-value of 0.008. Maternal complications were similar in both dichorionic and monochorionic twins. Preterm Premature Rupture of Membranes (PPROM) occurred in 23 (28.75%) twin pregnancies, 19 (23.75%) had Gestational Diabetes Mellitus while 13 (16.25%) participants had anaemia. Foetal growth restriction, congenital anomalies, and discordant growth were more prevalent in monochorionic twin pregnancies compared to dichorionic twin pregnancies. Although the proportion of babies requiring Neonatal Intensive Care Unit (NICU) admission was higher in monochorionic twins (64% vs 53.9%), the proportion of neonatal deaths was nearly equal between monochorionic and dichorionic twins (10% vs 9.8%).

Conclusion: In the present study, there was no statistical difference in maternal complications between monochorionic and dichorionic twins. However, monochorionic pregnancies had a poorer perinatal outcome compared to dichorionic pregnancies.

Keywords: Dichorionic, Monochorionic, Multiple pregnancies

INTRODUCTION

Multiple pregnancies are associated with a higher risk of developing adverse maternal and perinatal outcomes. Close and more frequent surveillance is required to ensure favorable results [1]. Factors that contribute to multiple pregnancies include racial factors, heredity, rising maternal and paternal age and infertility treatment. Among these, rising maternal age and infertility treatment are found to be the major contributors [1].

According to the secondary analysis of the World Health Organisation Global Survey (WHOGS) conducted on maternal and perinatal health by Vogel JP et al., wherein twin pregnancies in 23 low and middle-income countries were analysed, the prevalence of maternal death and severe adverse maternal outcomes was significantly higher in twin pregnancies compared to singleton pregnancies [2]. Maternal death was 0.3% in twins compared to 0.1% in singletons, and severe adverse maternal outcomes were 9.6% in twins compared to 3.5% in singletons [2]. According to the secondary analysis of the WHO multicountry survey on maternal and newborn health, conducted by Santana DS et al., there was a threefold increased risk of maternal near miss (1.5% vs 0.5%) and severe maternal outcomes (1.9% vs 0.6%), and a fourfold increased risk of maternal death (0.4% vs 0.1%) in twins compared to singletons [3].

Our understanding of the natural history of multiple pregnancies has greatly improved over the years as there has been a substantial increase in the number of multiple pregnancies. This has helped to improve the management of multiple pregnancies [4]. Monochorionic pregnancies are found to have poorer perinatal outcomes due to the complications specific to these pregnancies, like twin-to-twin transfusion syndrome and selective foetal growth restriction [5]. Therefore, early determination of chorionicity by ultrasound has become the cornerstone of antenatal care of multiple pregnancies [4]. Practices like selective foetal reduction for higher-order multiple pregnancies and twins discordant for structural or chromosomal anomalies have all evolved over time. The American College of Obstetricians and Gynaecologists (ACOG) now recommends counselling women with higher-order pregnancies about foetal reduction to reduce the complications associated with higher-order pregnancies [6].

Literature on the comparison of perinatal outcomes of dichorionic and monochorionic pregnancies is sparse [7]. The present study was aimed to compare the perinatal outcomes of monochorionic and dichorionic twins. This may help us make appropriate and timely interventions in the management of twin pregnancies.

MATERIALS AND METHODS

The present prospective cohort study was conducted in the Department of Obstetrics and Gynaecology, Government Medical College (Tertiary care centre), Thrissur, Kerala, India, from 1st September 2019 to 31st August 2020. Institutional Ethical Committee approval was obtained under Order No.B6-155/2019/MCTCR(07). Written informed consent was obtained from all the participants. All participants in the study were above 18 years, and consent was obtained from them.

Inclusion criteria: All consecutive mothers with twin pregnancies of ≥28 weeks of gestational age, who were admitted and delivered in the hospital during the study period, were included in the study.

Exclusion criteria: Patients with chronic illnesses such as chronic hypertension, overt diabetes, heart disease, renal disease, or systemic lupus erythematosus were excluded from the study.

Sample size calculation: The proportion of perinatal morbidity in twin pregnancies was 21.8% [8].

q is 1-p

Calculation for single proportion-

Absolute precision (%)=5%

Desired confidence level (%)=95%

$$N=\frac{(Z\alpha/2)^2\times pq}{d^2}$$

$$n=\frac{(1.96)^2\times 21\times 79}{5^2}=254$$

Sample size was calculated using Master sample size calculation software produced by the Department of Biostatistics, Christian Medical College, Vellore, Tamil Nadu, India. The sample size calculated for the present study was 254, but this could not be met as there were only 76 women with twin pregnancies of ≥28 weeks of gestational age during the study period, all of whom consented to be part of the study.

Study Procedure

Chorionicity was determined by ultrasound examination in the first trimester between 10 weeks and 14 weeks of gestational age. The chorionicity was confirmed after delivery by placental examination. Gestational age was calculated using the last menstrual period in spontaneous conceptions, as well as, in ovulation induction pregnancies. The date of embryo transfer was used for In-Vitro Fertilisation (IVF) pregnancies. Preterm was defined as gestational age <37 weeks. Appearance, Pulse, Grimace, Activity and Respiration (APGAR) score <7 at 5 minutes is one of the criteria for neonatal near miss and therefore, was included in analysing neonatal outcomes [9]. A structured proforma was used to collect demographic and clinical details of the participants, including mode of conception, chorionicity, maternal complications, intrapartum events, neonatal outcomes and causes of adverse outcomes wherever they could be identified.

Some of the participants had two or more maternal complications. For example, a patient with gestational diabetes also had gestational hypertension. So, the percentages were calculated out of the total number of complications. There were 54 maternal complications in the dichorionic twins and 26 in monochorionic twins. Pregnancies were considered to have foetal growth restriction if the estimated foetal weight was below the 10th centile for the period of gestation. Growth discordance was defined as a birth weight disparity of more than 20% (ACOG) [10]. Foetal growth restriction, growth discordance, and intrauterine foetal demise were considered pregnancy outcomes and the proportions were calculated out of the number of pregnancies, i.e., 76 total twin pregnancies (51 dichorionic and 25 monochorionic).

Birth weight of the babies, NICU admissions, neonatal deaths and live babies at discharge were considered neonatal outcomes. These were calculated out of the total number of babies, i.e., 152 total babies (102 dichorionic babies and 50 monochorionic babies).

STATISTICAL ANALYSIS

The data was coded and entered into Microsoft Excel software and then analysed separately for dichorionic and monochorionic pregnancies using Epi Info software. Quantitative data was analysed using Fisher's-exact test, while qualitative data was analysed using proportions and the Chi-square test. A p-value of ≤0.05 was considered statistically significant.

RESULTS

During the study period, there were a total of 2709 deliveries. 76 twin deliveries met the inclusion and exclusion criteria, making the incidence of twin deliveries 2.8%. Among the 76 twins, 51 (67.1%) were dichorionic diamniotic, 21 (28%) were monochorionic diamniotic, and 4 (5%) were monochorionic monoamniotic. The mean age of the participants was 28.39±6.29 years. Maternal age was higher in women with dichorionic twins (29.14±6.74 years) compared to those with monochorionic twins (26.88±5.06 years) [Table/Fig-1]. A positive family history of multiple pregnancies was observed in 11 out of 76 (14.5%) participants, which was not statistically significant (p-value=1.000). Among those with a family history of twins, 63.6% (7 out of 11) were dichorionic [Table/Fig-1]. Out of 51 dichorionic twins, 11 (21.6%) were conceived through IVF, showing a significant association between ART and dichorionic twinning (p-value=0.008). All monochorionic twin pregnancies were spontaneous conceptions [Table/Fig-1]. The most frequent maternal complication in the study was PPROM, affecting 15 (27.8%) dichorionic twins and 8 (30.7%) of monochorionic twins. Some twin pregnancies had multiple

Variables	DCDA		MCDA+MCMA		p-value
	Number (n)	Percentage# (%)	Number (n)	Percentage$ (%)	
Age (years)					
≤20	3	5.9	2	8	0.488, Fisher's-exact test
21-24	10	19.6	7	28	
25-29	22	43.1	11	44	
30-34	4	7.8	3	12	
≥35	12	23.5	2	8	
Gravidity					
Primigravida	24	47.05	11	44	0.474, Fisher's-exact test
Second gravida	18	35.3	11	44	
Third gravida	6	11.7	1	4	
Fourth gravida	1	1.9	2	8	
Fifth gravida and more	2	3.9	0	0	

Booking status					
Booked in	24	43.1	12	48	0.938, Chi-square test
Referred	27	52.9	13	52	
Family history					
Yes	7	13.7	4	16	1.000, Fisher's-exact test
No	44	86.323	21	84	
Mode of conception					
Spontaneous	36	70.5	25	100	**0.008**, Fisher's-exact test
Ovulation induction	4	7.8	0	0	
IVF	11	21.6	0	0	

[Table/Fig-1]: Maternal characteristics according to chorionicity.
DCDA: Dichorionic diamniotic; MCDA: Monochorionic diamniotic; MCMA: Monochorionic monoamniotic; #calculated out of number of DCDA twin pregnancies; $calculated out of number of MCDA+MCMA twin pregnancies; The p-value in bold font indicates statistically significant values

co-morbid conditions. Gestational diabetes was present in 13 (24%) Dichorionic Diamniotic (DCDA) twins and 6 (23.1%) of monochorionic twins [Table/Fig-2]. In one case, a second gravida with DCDA twin pregnancy developed peripartum cardiomyopathy at 34 weeks, necessitating immediate termination of pregnancy by caesarean section [Table/Fig-2]. Out of 76, 67 (88%) twins were delivered before 37 weeks of gestational age. Only one (4%) monochorionic twin crossed 37 weeks as she did not receive regular antenatal care [Table/Fig-3]. Out of 51, 30 (58.8%) dichorionic and out of 25, 18 (72%) monochorionic twins underwent caesarean section [Table/Fig-3]. There was no significant difference in maternal risk factors between dichorionic and monochorionic pregnancies, and there were no maternal mortalities in the present study.

Maternal complications	DCDA		MCDA+MCMA	
	Number (n)	Percentage# (%)	Number (n)	Percentage$ (%)
Anaemia	9	16.7	4	15.4
Gestational hypertension	5	9.2	3	11.5
Non severe preeclampsia	4	7.4	2	7.7
Severe preeclampsia	2	3.7	0	0
HELLP syndrome (Haemolysis, Elevated Liver Enzymes, Low platelet)	2	3.7	1	3.8
Gestational diabetes	13	24	6	23.1
Preterm Premature Rupture of Membranes (PPROM)	15	27.8	8	30.7
Abruption	1	1.8	0	0
Postpartum haemorrhage	2	3.7	2	7.7
Peripartum cardiomyopathy	1	1.8	0	0

[Table/Fig-2]: Distribution of twins according to chorionicity and maternal complications.
#Calculated out of number of maternal complications in DCDA twin pregnancies; $Calculated out of number of maternal complications in MCDA+MCMA twin pregnancies

Variables	DCDA		MCDA+MCMA		p-value*
	Number (n)	Percentage# (%)	Number (n)	Percentage$ (%)	
Mode of delivery					
LSCS	27	52.9	17	68	0.700
Vaginal	20	39.2	7	28	
Vaginal delivery for first twin/ LSCS for second twin	3	5.9	1	4	
Forceps	1	1.96	0	0	

Gestational age at delivery (weeks)					
>28-30	9	17.6	1	4	0.124
>30-33	7	13.7	6	24	
>33-37	27	52.9	17	68	
>37	8	15.6	1	4	
Foetal growth restriction					
Twin A	2	3.9	2	8	0.805
Twin B	6	1.2	4	16	
Both	6	1.2	2	8	
Discordant twins	8	15.7	6	24	0.530
Intrauterine foetal demise					
Twin A	1	1.96	0	0	1.000
Twin B	4	7.84	2	8	
Both	1	1.96	1	4	

[Table/Fig-3]: Distribution of twin pregnancies according to gestational age at delivery, mode of delivery, foetal growth restriction, discordant twins and intrauterine foetal demise.
*Fisher's-exact test; #Calculated out of number of DCDA twin pregnancies; $calculated out of number of MCDA+MCMA twin pregnancies

The proportion of pregnancies with foetal growth restriction were 8 (32%), out of 25 monochorionic and 14 (27.45%), out of 51 dichorionic twin pregnancies [Table/Fig-3]. Discordant growth was higher among monochorionic pregnancies, with a proportion of 8 (15.7%), out of 51 dichorionic twins compared to 6 (24%), out of 25 monochorionic [Table/Fig-3]. The rate of intrauterine foetal demise of one or both foetuses was similar among dichorionic, 6/51 (11.76%) and monochorionic, 3/25 (12%) pregnancies. Single foetal demise was also similar among dichorionic, 5/51 (9.8%) and monochorionic, 2/25 (8%) twin pregnancies [Table/Fig-3].

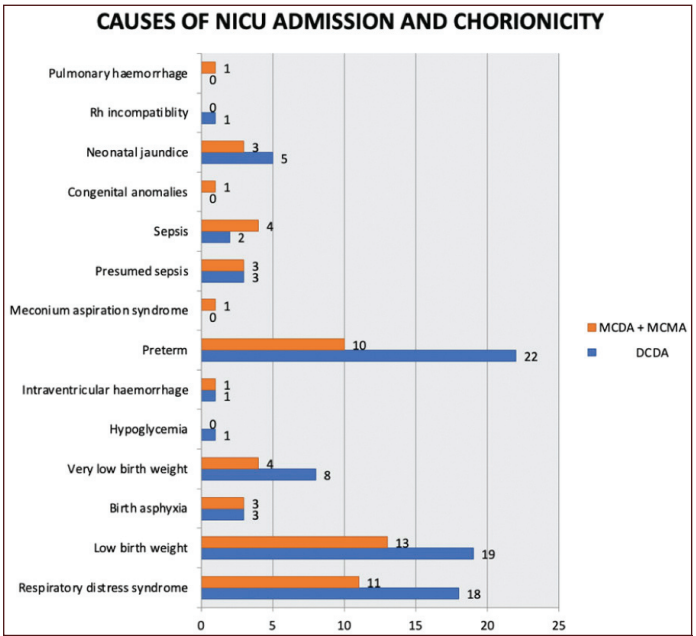
Among the 152 babies, 102 were from dichorionic pregnancies, while 50 were from monochorionic pregnancies. Most babies weighed between 2.5 kg and 1.5 kg. Sixty four (62.7%) out of 102 dichorionic babies and 34 (68%) out of 50 monochorionic babies weighed between 2.5 kg and 1.5 kg. Among dichorionic babies, 3/102 (2.94%) had congenital anomalies, While 6/50 (3%) of monochorionic babies had congenital anomalies. The association of chorionicity with congenital anomalies was statistically significant (p-value=0.033) [Table/Fig-4]. The number of babies alive at discharge was consistent between both monochorionic and dichorionic twin pregnancies, with a survival rate of 80% [Table/Fig-4].

Variables	DCDA		MCDA+MCMA		p-value*
	Number (n)	Percentage# (%)	Number (n)	Percentage$ (%)	
Birth weight (kg)					
>2.5	7	6.9	1	2	1.000
2.5-1.5	64	62.7	34	68	
<1.5	31	30.4	15	30	
Congenital anomalies					
Twin A	1	0.98	0	0	**0.033**
Twin B	0	0	3	6	
Both	1 (=2 babies)	1.96	0	0	

APGAR score <7 at 5 minutes					
Twin A	1	0.98	2	4	0.591
Twin B	5	4.9	3	6	
Both	10 (=20 babies)	19.6	5 (=10 babies)	20	
NICU admission					
Twin A	3	2.9	3	6	0.740
Twin B	4	3.9	3	6	
Both	24 (=48 babies)	47.05	13 (=26 babies)	52	
Neonatal death					
Twin A	2	1.96	1	2	1.000
Twin B	2	1.96	2	4	
Both	3 (=6 babies)	5.9	1 (=2 babies)	4	
Live baby at discharge					
Both babies live	41	80	20	80	1.000
One baby live	5	9.8	3	12	
No babies live	5	9.8	2	8	

[Table/Fig-4]: Neonatal outcomes according to chorionicity.
*Fisher's-exact test; #Calculated out of number of DCDA babies; $Calculated out of number of MCDA+MCMA babies

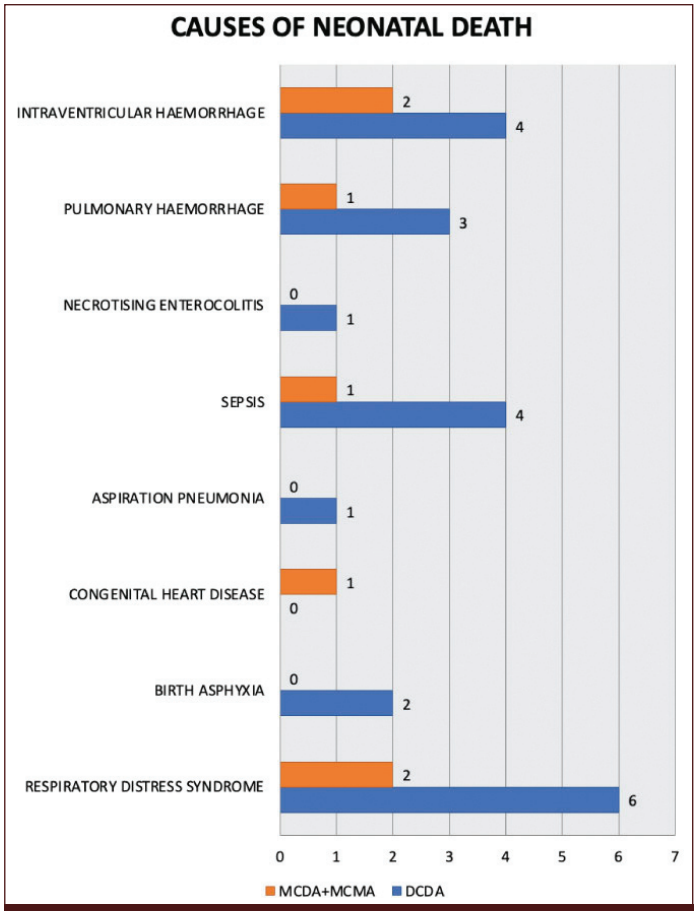
The primary cause for admission to the NICU was prematurity, observed in both dichorionic (22 out of 102) and monochorionic twins (10 out of 50) [Table/Fig-5]. Most twins had multiple complications requiring admission to the NICU. The most common cause of neonatal mortality was respiratory distress syndrome, affecting six dichorionic infants and two monochorionic infants who succumbed during the immediate neonatal period [Table/Fig-6].



[Table/Fig-5]: Causes of Neonatal Intensive Care Unit (NICU) admission.

DISCUSSION

In the present study, the incidence of twin deliveries was 2.8%. All pregnancies conceived following ART in the study were dichorionic, 11/51 (21.6%). There were no monochorionic pregnancies following IVF, likely due to lower survival rates and higher risk of second trimester loss for monochorionic twins conceived after IVF [11]. Participants included in the study were only those who had reached ≥ 28 weeks of pregnancy.



[Table/Fig-6]: Causes of neonatal death.

Among the 76 pairs of twins, 51 (67.10%) were dichorionic diamniotic, 21 (28%) were Monochorionic Diamniotic (MCDA) and 4 (5%) were Monochorionic Monoamniotic (MCMA). This distribution is similar to the findings in the study by Assunção RA et al., where 60% were DCDA, 30.8% were MCDA, and 6.6% were MCMA [12]. Total of 47% of dichorionic pregnancies and 44% of monochorionic pregnancies were primigravidas. The mean maternal age in the present study was 28.39±6.29 years, consistent with other studies [8,12-16].

When maternal complications were analysed, hypertensive disorders accounted for 20% of the complications. A similar incidence of medical complications in twins was reported by Chowdhury S and Hussain MA, with hypertension seen in 22.6% [15]. GDM was present in 23.75% of the participants in the present study, a higher proportion compared to similar studies [15,16]. This could be due to the high prevalence of diabetes in the population and the strict screening protocol for gestational diabetes followed. In a similar study conducted by Alsam S and Rashid Y in Pakistan, a much higher prevalence (36.2%) of diabetes in pregnancy was reported [Table/Fig-7] [8,12-16].

The most common complication found in the present study was PPROM, present in 23 (28.75%) of the study subjects, which is much higher compared to similar studies. In the study by Mercer BM et al., PPROM was found to complicate 7% to 8% of twin pregnancies [17].

In the present study, 67/76 (88%) twins were delivered before 37 weeks of gestational age. Preterm birth among twins was higher compared to other studies [Table/Fig-8] [12-14,18].

The mode of delivery was analysed and was found to be similar to other studies [14,18]. In the present study, 48/76 (63%) participants were delivered by caesarean section, including those done for the second of twins. This comprised 30/51 (58.8%) of dichorionic twins and 18/25 (72%) of monochorionic twins.

Name of author	Place of study	Number of subjects	Incidence of twins	Mean maternal age	Pregnancy following ART	GDM	HTN	APH	PPH
Present study	Kerala	76	2.8%	28.4	14.5%	23.75%	20%	1.25%	5%
Sarojini et al., [8]	Bengaluru	117	1.1%	25.4	-	-	-	1.3%	5.2%
Assunção RA et al., [12]	Brazil	289	3.4%	29.1	3.8%	-	-	-	-
Upreti P [13]	Nainital	218	1.9%	25.4			17.9%	5.9%	4.1%
Alsam S and Rashid Y [14]	Pakistan	70	0.97%	26.1	-	36.2%	37.8%		
Chowdhury S and Hussain MA [15]	Bangladesh	53	1.4%		-	5.7%	22.6%	5.7%	18.9%
Sultana R et al., [16]	Ujjain	147	1.85%	24.08	-	5.4%	14.3%	6.1%	2.7%

[Table/Fig-7]: Comparison of the present study and similar studies in relation to few of the maternal characteristics and complications [8,12-16].
GDM: Gestational diabetes mellitus; HTN: Hypertension; APH: Antepartum haemorrhage; PPH: Postpartum haemorrhage

Author of study	Place of study	Number of subjects	Preterm birth		CS		Foetal demise		Low birth weight (<2.5 kg)		APGAR <7	
			DC	MC	DC	MC	DC	MC	DC	MC	DC	MC
Assunção RA et al., [12]	Brazil	289	54.3%	83.1%	84.8%		5.1%	24.1%	64.8%	85.5%	3.4%	9.7%
Upreti P [13]	Nainital	218	58.3%	51.2%	11%		-					
Alsam S and Rashid Y, [14]	Lahore	70	30.75%	30.75%	43.6%	45.1%	17.9%	16.13%	-	-	17.9%	16.13%
Domingues AP et al., [18]	Portugal	826	65%	80.2%	56.9%	52.6%	2.2%	3.8%	64%	77.5%	1%	2.6%
Present study	Kerala, India	76	84.3%	96%	58.8%	72%	9.8%	8%	93.1%	98%	25.4%	30%

[Table/Fig-8]: Comparison of the present study with similar studies in relation to preterm birth, CS rate, foetal demise, low birth weight and low APGAR score [12-14,18].

Author of study	Place of study	Number of subjects	Congenital anomalies		NICU admission		Neonatal death	
			DC	MC	DC	MC	DC	MC
Domingues AP et al., [18]	Portugal	826	3.7%	3.7%	38.9%	50%	2.4%	0.6%
Glinianaia SV et al., [20]	United Kingdom	2175	3.43%	6.33%	58.1%	75%	-	-
Present study	Kerala, India	76	2.94%	6%	53.9%	64%	9.8%	10%

[Table/Fig-9]: Comparison of the present study and similar studies in relation to few of the perinatal complications [18,20].

The proportion of pregnancies with foetal growth restriction was higher in monochorionic compared to dichorionic twins, 8 (32%) vs 14 (27.45%). This included pregnancies with either one or both babies with foetal growth restriction. This finding was similar to the study by Fox NS et al., where 27% of women with twin pregnancies delivered at least one twin with a birth weight <5th percentile. In our study, 18% (14 out of 76) of twins had growth discordance whereas in the study by Fox NS et al., 16% of patients had birth-weight discordance of ≥20% [19].

It was found that an APGAR score <7 at 5 minutes was observed in 15/50 (30%) monochorionic twins compared to 26/102 (25.4%) dichorionic twins. Compared to other similar studies, the present study had a larger number of babies with an APGAR score of <7 at five minutes [12,14,18].

A total of 3/102 (2.94%) dichorionic babies had congenital anomalies, while 3/50 (6%) monochorionic babies in the present study had congenital anomalies. The association of monochorionicity with congenital anomalies was found to be statistically significant in the current study (p-value=0.033). This finding was similar to the results of the study by Glinianaia SV et al., [20].

The most common cause for neonatal intensive care admission was prematurity in both dichorionic, 22/102 (21.6%) and monochorionic twins, 13/50 (26%) babies. Respiratory distress syndrome was more common among monochorionic babies (22% vs 17.6%). This is similar to the study by Domingues AP et al., where admission to the NICU was higher among monochorionic babies [18]. Neonatal death occurred in 10/102 (9.8%) babies of dichorionic babies, while 5/50 (10%) babies of monochorionic babies died in the neonatal period. The most important cause of neonatal death was respiratory distress syndrome, similar to the study by Domingues AP et al., [18]. Similar studies related to some perinatal complications have been tabulated in [Table/Fig-9] [18,20].

Limitation(s)

The study duration was only for a one-year period, and the sample size was small. The present study was conducted in a single tertiary centre, which included only women attending a publicly-run healthcare facility. Therefore, the present study cannot be considered representative of twin pregnancies in the general population.

CONCLUSION(S)

Twin pregnancies were associated with a higher risk of PPROM, GDM, and preeclampsia in the present study. Foetal growth restriction, congenital anomalies, and the need for NICU admissions were found to be higher among monochorionic babies. Therefore, twin pregnancies require early diagnosis, determination of chorionicity and focused antenatal care to improve both maternal and perinatal outcomes. Further studies are required to improve foetomaternal outcomes of monochorionic and dichorionic pregnancies.

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