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Pregnancy Outcome of Monochorionic Twins: Does Amnionicity Matter?

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Objective: To compare the fetal loss rate of monochorionic (MC) twin pregnancies according to their amnionicity. *Methods:* A retrospective review of all MC pregnancy outcomes in a tertiary centre. Pregnancy outcomes were compared for monochorionic monoamniotic (MCMA) versus monochorionic diamniotic (MCDA) pregnancies. *Results:* 29 MCMA and 117 MCDA twin pregnancies were identified. The overall fetal loss rate was significantly higher in MCMA (23/52, 44.2%) compared to MCDA pregnancies (28/233, 12%, Chi squared = 30.03, $p < .001$). Kaplan-Meier analysis showed that fetal survival rate in MCDA twins were significantly higher than in MCMA twins (Log-rank Chi-squared = 27.9, $p < .0005$). Early pregnancy ultrasound identified the causes for these fetal losses in some MCMA twins. After exclusion of identifiable causes, the difference in fetal survival was not significant in the two groups (Log-rank chi-squared = 0.373, $p = .54$). *Conclusion:* The loss rate for MCMA twins is high and occurs mainly due to discordant congenital abnormality, conjoint twins or twin reversed arterial perfusion (TRAP) sequence. Although the fetal loss rate in MCDA is lower than in MCMA pregnancies, the majority of fetal loss in MCDA pregnancies cannot be predicted at the first scan at presentation. The data of this study questions the widespread policy of a difference in the scheduling of elective delivery for MCMA and MCDA twins.

Multiple pregnancies are recognised to be at increased risk of adverse outcome with twin perinatal mortality being 3- to 7-fold higher compared with singleton pregnancies (Chitrit et al., 1999; Powers & Kiely, 1994). Monochorionic diamniotic (MCDA) pregnancies are at higher risk of pregnancy loss compared to dichorionic (DC) twins (Hack et al., 2008; Dias et al., 2010a). The latter difference is thought to be related not only to placental sharing, but also to the presence of inter-twin placental vascular anastomoses. Monochorionic monoamniotic (MCMA) twins account for approximately 1% of monozygotic twins with a reported incidence ranging from 1:1650 to 1:93734 live births (Aisenbrey et al., 1995; D'Alton & Simpson, 1995; Derom et al., 1988; Colburn & Pasquale, 1982; Simonsen, 1966). MCMA pregnancies are also associated with a very high risk of pregnancy loss (Ezra et al., 2005; Roqué et al., 2003). The perinatal mortality rate in MCMA twins was originaly estimated to be 30–70% (Demaria et al., 2004; Raphael, 1961; Timmons & Dealvarez, 1963). This very high loss rate is presumed to be related to umbilical cord accidents, in particular cord entanglement (Allen et al., 2001). However, there are several recent reports documenting a much lower risk of pregnancy loss in monoamniotic pregnancies, with perinatal mortality rates ranging from 10 to 13% of non-anomalous fetuses (Allen et al., 2001; Heyborne et al., 2005). This lower perinatal loss rate was attributed to better pregnancy management and elective early delivery by Caesarean section (Pasquini et al., 2006). The present study aims to compare magnitude of risk and timing of fetal loss in MCMA versus MCDA twin pregnancies.

Materials and Methods

This was a retrospective study of monochorionic (MC) twin pregnancies delivered in a tertiary care university hospital with a regional Fetal Medicine Unit. The ultrasound database of the Fetal Medicine Unit was searched retrospectively for MC pregnancies over a 10-year period from August 1997 to February 2008. All MCMA pregnan-

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cies and only MCDA twins booked for delivery at our centre were included in the study. MCDA pregnancies referred to our unit from other hospitals were excluded. The diagnosis of chorionicity was made on the basis of an ultrasound scan performed before 16 weeks of pregnancy, and confirmed on the histopathology of the placenta. Only twin pregnancies where monochorionicity was confirmed were selected for inclusion in the study. Monoamnionicity was diagnosed when an inter-twin membrane could not be visualised on detailed ultrasound.

Uncomplicated MCDA and MCMA pregnancies were followed up according to the local protocol of 2-weekly ultrasound scan between 16 and 22 weeks, and 4-weekly scan thereafter. Management and follow-up of pregnancies complicated by liquor discrepancy, polyhydramnios or growth discordance was individualised. Admission to the hospital was only advised for an intervention such as fetoscopic laser or for delivery, but not for monitoring. The diagnosis of monoamnionicity was re-confirmed at the time of delivery or termination on visual inspection of the placenta. MCDA and MCMA pregnancies were electively delivered at 36–37 weeks and at 34 weeks respectively. Pregnancy outcome is routinely entered in the database when it is available. Parents, referring physicians or general practitioners were contacted in case of missing information. Cases for which no outcome was available were excluded.

Twin-to-twin transfusion syndrome (TTTS) was diagnosed when there was polyhydramnios (Deepest pocket > 6 cm before 18 weeks and > 8 cm after 18 weeks) in the recipient and oligohydramnios (deepest pocket < 2 cm) in the donor with or without Doppler flow abnormalities. Severe TTTS was diagnosed when the stage was Quintero stage 2 or higher (Quintero et al., 1999; Senat et al., 2004). Diagnosis of TTTS using liquor discrepancy is not possible in mono-amniotic twins. Identification of TTTS in these cases were based on discrepancy in the size of the urinary bladder and blood flow changes (elevated ductus venosus PI in the recipient, elevated umbilical artery PI in the donor). Fetal growth restriction was diagnosed when the estimated fetal weight was below the 10th centile, with abnormal fetal Dopplers.

Distribution of the data was explored using the Kolmogorov Smirnoff Test and appropriate statistical tests were used to analyse the data. Fetal loss was defined as miscarriage, fetal death or stillbirth of one or both twins. If fetal demise involved one of the two fetuses, the gestational age at the time of diagnosis of the fetal demise was taken to be the time of fetal death. The number of pregnancies with fetal loss was compared between the two groups using chi-squared test. Cumulative survival rate of MCMA and MCDA twins were compared using the log-rank test. We excluded all pregnancies where the cause of the fetal loss was identified at presentation using ultrasound scan and performed the survival curve analysis again. We also performed the survival analysis using number of fetuses rather than pregnancies as the denominator. Ethics approval was not necessary due to the retrospective nature of the study.

Results

A total of 183 monochorionic pregnancies (36 MCMA and 147 MCDA) were seen in the period from August 1997 to February 2008. The outcome was available from 30 MCMA and 117 MCDA twin pregnancies (52 and 233 fetuses respectively). Information of nine fetuses was missing and all of them have been diagnosed as twin reversed arterial perfusion (TRAP) in early scans. One monoamniotic twin pregnancy with normally formed fetuses underwent pregnancy termination for personal reasons. This case was excluded from further analysis. Demographic details of included women are shown in Table 1. TRAP sequence was diagnosed in seven MCMA and one MCDA pregnancy. Table 2 and Table 3 summarise the details of the outcome of monochorionic pregnancies. The overall fetal loss rate was significantly higher in MCMA (23/52, 44.2%) compared to MCDA pregnancies (28/233, 12%, chi-squared = 30.03, $p < .001$).

The overall fetal survival in MCMA and MCDA twins were significantly different (Figure 1, log-rank chi-squared = 27.9, $p < .001$). Most fetal losses in MCMA pregnancies were due to discordant fetal anomalies, conjoint twins or twin reversed arterial perfusion sequence (TRAP) and all these conditions identified at early ultrasound scans. Once these identifiable early pregnancy complications were excluded, the difference in survival of MCMA and MCDA pregnancies was no longer significantly different (Figure 2, log-rank chi-squared = 0.373, $p = .54$). The survival analy-

TABLE 1

Demographics of Women in the Study

	Monoamniotic twin pregnancies n = 30	Diamniotic twin pregnancies n = 117	Significance (p)
Mean age of the mother in years(SD)	31.1 (5.8)	29.5 (5.5)	0.21
Median Parity (IQR)	0 (0 to 1)	0 (0 to 1)	0.47
Median gestational age in weeks at referral (Range)	12 +4 (9 + 3 to 14 + 2)	12 + 4 (9 + 3 to 22 + 3)	0.43
Median gestational age in weeks at loss (Range)	14+1 (9 + 5 to 26 + 4)	19+4 (15 + 2 to 34 + 3)	0.007
Median gestational age in weeks at delivery (Range)	32+2 (13 + 1 to 35 + 2)	36+5 (15 + 2 to 38 + 5)	< .001

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TABLE 2

Outcome of Monochorionic Twin Fetuses Arranged by Amnionicity

	Monoamniotic fetuses (%)	Diamniotic fetuses (%)	Total
Loss	23 (44.2)	28 (12.0)	51
No loss	29 (55.8)	205 (88.0)	234
Total	52	233	285

Note: chi squared = 30.03, p < .001

sis repeated using number of fetuses rather than pregnancies (log-rank chi-squared = 2.12, $p = .15$).

Discussion

The present study demonstrates that MCMA twins have a significantly higher rate of pregnancy loss as compared to MCDA twins. Many MCMA pregnancies are complicated by abnormalities diagnosable on early pregnancy ultrasound assessment, making the pregnancy loss predictable. The commonest problems were discordant fetal abnormality, conjoint twins and twin reversed arterial perfusion (TRAP) sequence. Fetal loss in MCDA pregnancies occurred less often and was not predictable. However, once pregnancy abnormalities were excluded, the fetal loss rates in MCMA and MCDA pregnancies were not significantly different.

It is accepted that the rate of fetal loss in MCMA twins is increased many-fold as compared to singleton pregnancies, with a perinatal mortality rate of 30–70% (Chitrit et al., 1999; Demaria et al., 2004; Powers & Kiely, 1994; Raphael, 1961; Timmons & Dealvarez, 1963). Since the loss rate of MC twins is also high, it is unclear whether the main reason for the high loss rate in MCMA twins is due to sharing the placenta and/or amniotic cavity. In order to distinguish the possible etiology of perinatal loss in MCMA pregnancies, the appropriate comparator is MCDA pregnancies with a shared placenta, rather than singleton pregnancy or twin pregnancy in general. The high loss rate in MCMA twins was initially thought to be mainly due to cord entanglement and subsequent strangulation. However, cord entanglement can be seen in the majority of MCMA twins on prenatal ultrasound (Dias et al., 2010b; Hamilton and Byrd 2009; Pasquini et al., 2006; Rodis et al. 1997). It is therefore probable that the cord entanglement in MCMA twins with pregnancy loss is due to a reporting bias.

Apart from cord entanglement, other complications such as fetal abnormalities, twin-to-twin transfusion syndromes and selective IUGR are possible reasons for the high loss rate in MCMA twins (Acosta-Rojas et al., 2007; Fick et al., 2006; Gratacós et al., 2008). The latter two complications are more likely to develop if inter-twin anastomoses are fewer and if the placental cord insertions are far apart (Denbow et al., 2000). In contrast, placental

TABLE 3

Details of Fetal Losses in the Study

Amnionicity	GA at loss (Weeks +days)	GA at delivery (Weeks +days)	Fetal outcome	Details
MCDA	15+2	15+2	2 IUD	Unexplained
MCDA	15+3	40+5	1 live birth	TRAP-Interstitial laser at 15+4 weeks
MCDA	15+4	38+5	1 live birth	Unexplained
MCDA	17+2	38+3	1 live birth	Unexplained
MCDA	17+3	17+3	2 IUD	TTTS (Quintero stage V) at 13 weeks
MCDA	18+1	18+1	Miscarriage	Unexplained
MCDA	18+4	18+4	2 IUD	Unexplained
MCDA	18+4	18+4	2 IUD	Unexplained
MCDA	19+3	37+4	1 IUD	TTTS, (Quintero stage III), Donor died just after the laser
MCDA	19+4	19+4	2 IUD	Severe TTTS (Quintero stage V)
MCDA	20+4	20+4	2 IUD	PPROM
MCDA	21+5	21+5	2 IUD	Unexplained
MCDA	21+6	37+5	1 IUD	Severe TTTS (Quintero stage V)
MCDA	22+5	22+5	2 IUD	Unexplained
MCDA	22+6	26+4	I IUD	Unexplained
MCDA	24+1	24+1	1 IUD	Anencephaly
MCDA	26+4	27	1 IUD	Severe IUGR
MCDA	31	31	1 IUD	Severe TTTS (Quintero stage V)
MCDA	34+3	34+3	1 IUD	Severe IUGR
MCMA	9+6	9+5	Termination	Conjoined twins
MCMA	11+4	11+4	Missed miscarriage	TRAP
MCMA	12+5	-	Termination	Conjoined twins
MCMA	12+6	12+6	Termination	Body stalk anomaly
MCMA	13+1	13+1	2 IUD	Unexplained
MCMA	14	14	Termination	Body stalk anomaly
MCMA	14+1	14+1	2 IUD	TRAP
MCMA	15	38+6	1 Interstitial laser at 15 weeks	TRAP
MCMA	15+5	38+1	1 Interstitial laser at 16 weeks	TRAP
MCMA	19+2	19+2	2 IUD	Unexplained
MCMA	19+4	33+6	1 Interstitial laser at 19 weeks	TRAP
MCMA	22+0	22+1	2 IUD	Unexplained
MCMA	22+1	22+1	Termination	TRAP
MCMA	26+4	34+3	1 Interstitial laser	TRAP
MCMA	33+4	34+2	1 IUD	Unexplained

Note: MCDA = Monochorionic diamniotic twins, MCMA = Monochorionic monoamniotic twins, TRA*P*=Twin Reversed Arterial Perfusion sequence, IUD = Intrauterine death PPROM = Preterm Prelabour Rupture of Membranes

The term 'Unexplained' is used when neither ultrasound nor autopsy (when accepted by parents) could ascertain the cause of death.

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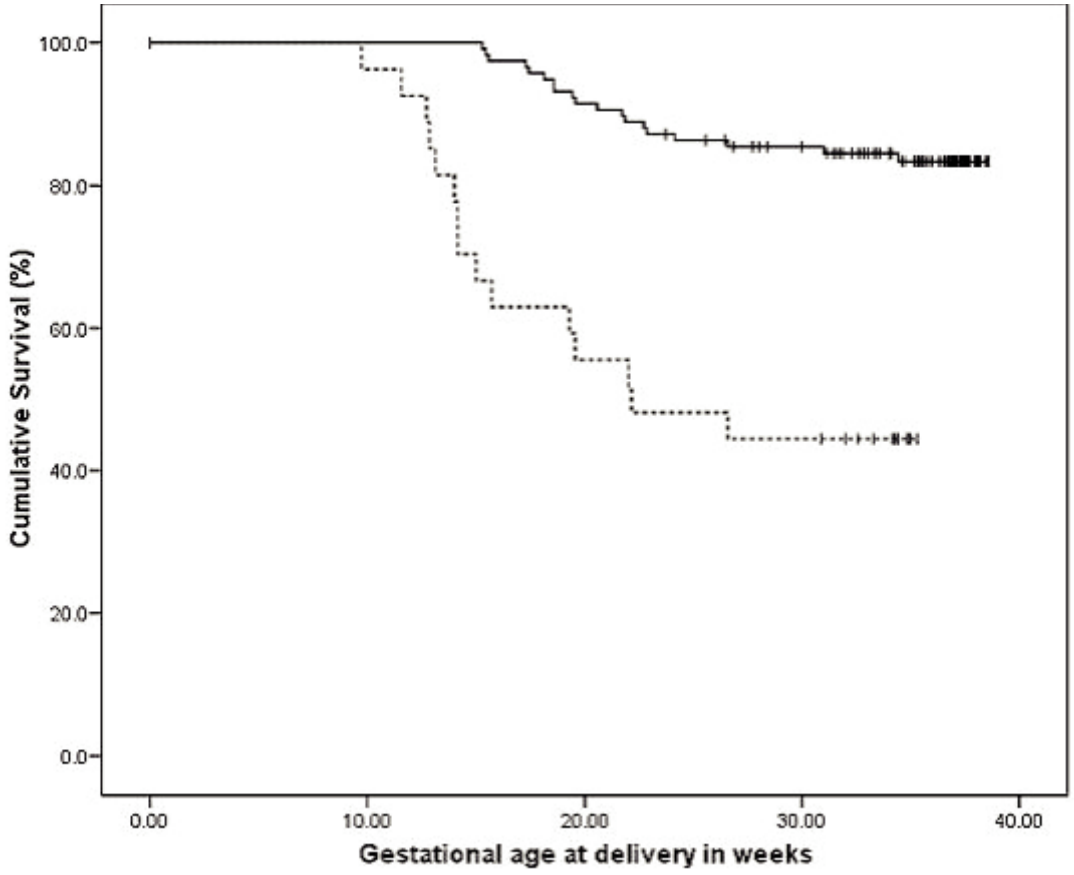

FIGURE 1

Kaplan Meier Survival curve of MCMA (dotted line) and MCDA twins (solid line).

cord insertions in MCMA twins are usually very close (Hack et al., 2009; Umur et al., 2000) and associated with the presence of a large AA-anastomosis. The presence of these arterio-arterial anastomoses protects against hemodynamic disequilibrium by allowing inter-twin blood flow. This explains why development of twin–twin transfusion syndrome is uncommon in mono-amniotic twin pregnancies. Most fetal losses in the current series of MCMA twins were due to the presence of major congenital abnormalities or TRAP sequence, rather than TTTS or selective IUGR.

Several reports have recently documented a lower risk of pregnancy loss in MCMA pregnancies and attributed this achievement to close fetal monitoring in pregnancy and elective early delivery by cesarean section (Allen et al., 2001; Dias et al., 2010b; Heyborne et al., 2005). However, an alternative explanation is that improved pregnancy outcome is a consequence of the exclusion of early pregnancy losses, discordant anomalies and TRAP sequence or conjoined twins or due to exclusion of cases before 20 weeks (Allen et al., 2001; Hack et al., 2009; Roqué et al., 2003). Many units electively deliver monoamniotic pregnancies at 32 to 34 weeks due to the assumed increasing risk of stillbirth. This is based on previous publications suggesting a rise in the rate of stillbirth after 32 to 34 weeks (Ezra et al., 2005; Roqué et al., 2003). Roque et al. (2003) undertook a review of published outcomes in 133 non-conjoined MCMA twin pregnancies reported between 1990 and 2002. They reported a relatively constant perinatal loss rate of 2–4% per 2-week interval from 15 to 32 weeks. They also reported a significantly increased loss rate of 11% and 21.9% at 33–35 weeks and 36–38 weeks, respectively. This report prompted the commonly practiced elective early delivery of monoamniotic twins at 32 to 34 weeks. However, the conclusions of this study may be seriously flawed. Out of the five intrauterine deaths after 33 weeks, three were anomalous and one fetus was macerated. Moreover, six out of the ten infants delivered after 33 weeks suffered from a serious congenital malformation (two lethal). Therefore it is not surprising that the loss rate increased after 33 weeks by virtue of the fact that this was when they were delivered rather than as a consequence of increasing risk.

Hack et al. (2009) recently reported on perinatal outcome in 98 MCMA twin pregnancies. Again, only pregnancies reaching 19 weeks were included. Two pregnancies (2/98, 2.04%) were complicated by intrauterine

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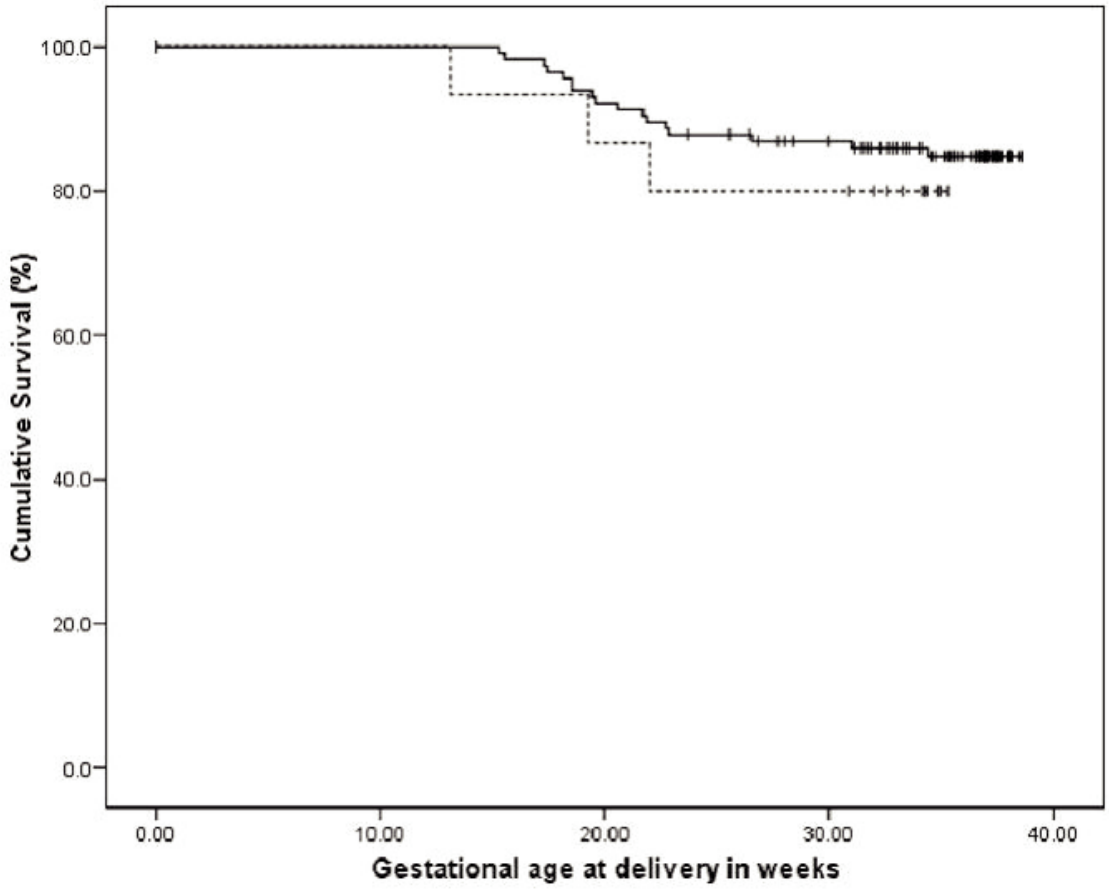

FIGURE 2

Kaplan Meier Survival curve of MCMA and MCDA after exclusion of cases with TRAP sequence, major structural abnormality seen on the first scan and conjoined twins

death after 32 weeks. This is very similar to 7/198 (3.53%) experiencing an IUD after 32 weeks in MCDA pregnancies reported earlier by the same group (Hack et al., 2008). Baxi and Walsh (2010) reported on 25 monoamniotic twins and no fetal deaths were recorded after 32 weeks. Prospective risk of stillbirths in monochorionic twins is a subject of interest in many recent publications and after 32 weeks of gestation it is thought to be around 0.8–1.6% (Lewi et al., 2008; Smith et al., 2010). Stillbirth risks for MCMA and MCDA twins show a small difference if at all. As there is no established policy for timing of delivery in MCDA twins, most centres would elect to deliver them at 36–37 weeks. It is true that unexpected intrauterine deaths can take place at any time, but the data of this study demonstrates that this can happen in both MCMA and MCDA pregnancies. Therefore, the existence of differing policy for MCDA and MCMA pregnancies is not justified from the current available evidence. Moreover, delivery at 32 to 34 weeks may be associated with both short and long term adverse outcomes for the offspring. There is no statistically significant difference in pregnancy loss rates in MCDA and MCMA twin pregnancies once the already recognised abnormalities are accounted for. Therefore, the policy of a difference in the scheduling of elective delivery for MCMA and MCDA twins should be reconsidered. Since monoamniotic pregnancies in this series were electively delivered at 34 weeks, it is not possible to comment if continuing the monoamniotic pregnancies beyond 34 weeks is safe. The risk of fetal loss in diamniotic and monoamniotic monochorionic pregnancy is not significantly different at least till 34 weeks according to the findings of this study.

The strength of the current study is the methodology. The patient records over the period of ten years were reviewed. The amnionicity and chorionicity were assigned early in pregnancy and were confirmed after birth by histologically aided with visual inspection when possible. Some limitations in this study should be acknowledged. It is a retrospective study. Vast majority of losses in MCMA group were attributable to the presence of congenital abnormalities or TRAP sequence which was apparent on the first scan. Exclusion of these cases resulted in limited number of MCMA but not MCDA pregnancies. The finding of lack of difference in the loss rate between these two groups could be also due to the study being underpowered.

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Conclusion

This study has shown that MCMA pregnancies are at increased risk of early pregnancy loss as compared to their MCDA counterparts, and this is due to associated congenital malformations. For those MCMA pregnancies where both fetuses were normally formed, the outcome was no different compared to MCDA pregnancies.

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Disclosure of Interests

The authors declare no conflicts of interest.

Details of Ethics Approval

The retrospective nature of this observational study did not require ethics approval.

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