

Gestational age at delivery and neonatal outcome in uncomplicated twin pregnancies: what is the optimal gestational age for delivery according to chorionicity?

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Objective

To investigate the neonatal outcome according to the gestational age at delivery and to determine the optimal timing for delivery in uncomplicated monochorionic and dichorionic twin pregnancies.

Methods

This is a retrospective cohort study of women with uncomplicated twin pregnancies delivered at or beyond 35 weeks of gestation from 1995 to 2013. The primary outcome was neonatal composite morbidity, which was defined as when either one or both twins have one or more of the followings: fetal death after 35 weeks gestation, admission to neonatal intensive care unit, mechanical ventilator requirement, respiratory distress syndrome and neonatal death. To determine the optimal gestational age for delivery according to chorionicity, we compared the neonatal composite morbidity rate between women who delivered and women who remained undelivered at each gestational week in both monochorionic and dichorionic twin pregnancies.

Results

A total of 697 twin pregnancies were included (171 monochorionic and 526 dichorionic twins). The neonatal composite morbidity rate significantly decreased with advancing gestational age at delivery and its nadir was observed at 38 and ≥ 39 weeks of gestation in monochorionic and dichorionic twins, respectively. However, the composite morbidity rate did not differ between women who delivered and women who remained undelivered ≥ 36 and ≥ 37 weeks in monochorionic and dichorionic twins, respectively.

Conclusion

Our data suggest that the optimal gestational age for delivery was at ≥ 36 and ≥ 37 weeks in uncomplicated monochorionic and dichorionic twin pregnancies, respectively.

Keywords: Delivery; Dichorionic; Gestational age; Monochorionic; Twins

Introduction

Recently the number and incidence of multiple pregnancy has been on the rise due to the delayed childbearing age and advancing assisted reproductive technology [1,2]. According to the 2013 Korea Institute for Health and Social Affairs data, the incidence of the multiple pregnancy increased from 2.02% in 2003 to 3.29% by 2013 [3].

Twin pregnancy, in comparison to singletons, is associated with increased complication risks in both mother and neonates

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including perinatal morbidity and mortality. Twin pregnancy itself is attributable to higher rates of preterm delivery, respiratory problem and low birth weight [4-6]. Gestational age at delivery is the single most important factor affecting the neonatal outcome and perinatal mortality in both singleton and twin pregnancies [7,8]. Preterm birth is a leading cause of death and complications in the neonatal period and poor outcomes in childhood [9]. The optimal duration for pregnancy maintenance appears to be shorter in twins, compared with singleton pregnancies [10]. Here the question rises—when is the optimal time to deliver in twin pregnancies? In the absence of significant maternal or fetal complications, it is reasonable to continue the pregnancy for sufficient maturation in order to avoid neonatal complication. In another words, the ideal time for delivery of a pregnancy should be when the risk for neonatal morbidity and mortality is lowest but before the risk for stillbirth begins to substantially rise [11].

Although there have been many studies performed to determine the optimal delivery time for twin pregnancy, the results are controversial and unsatisfying [12,13]. In this study, we analyzed the neonatal outcome according to gestational age at delivery in uncomplicated twin pregnancies based on the Korean data in order to determine the optimal time for delivery in uncomplicated monochorionic and dichorionic twin pregnancies.

Materials and methods

This is a retrospective cohort study of women with twin pregnancies delivered at a tertiary referral hospital in Seoul, Korea from January 1995 to December 2013. The study was approved by institutional review board of Samsung Medical Center. All women with uncomplicated monochorionic and dichorionic twin pregnancies who delivered at our center after 35 weeks of gestation were included. Twin pregnancies complicated by twin-to-twin transfusion syndrome, monoamniotic twins, discordant twins, intrauterine fetal growth restriction, preterm labor, preterm premature rupture of membranes, placenta abruption, placenta previa, hypertension (gestational hypertension, preeclampsia, eclampsia, superimposed preeclampsia, and chronic hypertension), diabetes (gestational diabetes and overt diabetes), presence of other severe maternal medical diseases, fetal death before 35 weeks of gestation or chromosomal anomalies or major congenital malformation

in one or more of twins were excluded. Major fetal congenital malformation was defined as that requires medical or surgical treatment after birth. Discordant twin was defined as inter-twin weight discordance of more than 20%.

Maternal demographic characteristics included parity, use of assisted reproductive technology and chorionicity. Chorionicity was determined by early sonographic findings such as gestational sac number, placental number, the presence of either “twin-peak” or “T” sign and fetal gender and this was later confirmed through pathologic examination of the placenta. All patients established an accurate gestational age through first trimester ultrasound. Pregnancy outcome included gestational age at delivery, mode of delivery, and indications for cesarean section.

Neonatal outcome measures were collected and analyzed, which included gender, birth weight, Apgar scores, fetal death in utero (FDIU), admission to neonatal intensive care unit (NICU), mechanical ventilator support, respiratory distress syndrome (RDS) and neonatal mortality. RDS was defined as the presence of respiratory grunting and retracting, an increased oxygen requirement (FiO₂ >0.4) combined with ground-glass appearance and air bronchograms on chest X-ray. Neonatal composite morbidity was defined as having one or more of the following: FDIU, NICU admission, RDS and neonatal mortality.

The unit of analysis for neonatal outcomes was the twin pair when either one or both twins have the outcome. The outcome was analyzed and compared according to gestational

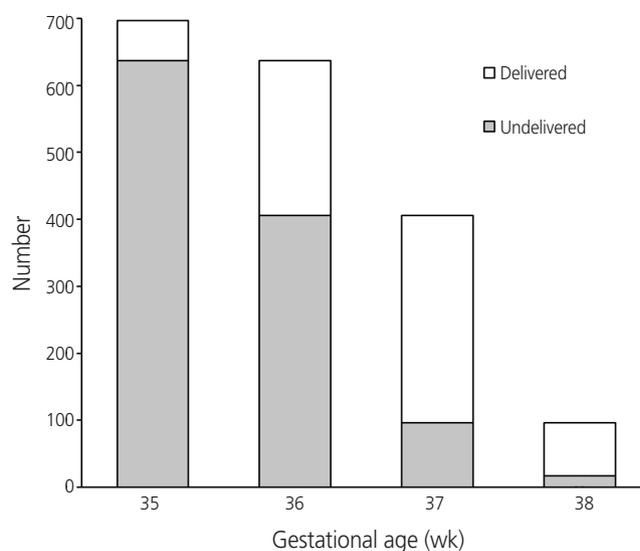


Fig. 1. Numbers of patients with uncomplicated twin pregnancies: delivered and undelivered at each gestational week.

age at delivery (35, 36, 37, 38, and ≥ 39 weeks) and chorionicity. The analysis of variance was used to compare continuous variables and the Jonckheere-Terpstra test was used to identify the trends. Proportions were compared using the chi-square test and linear-by-linear association was used to identify trends. To determine the optimal gestational age for delivery, we compared the neonatal composite morbidity rate between women who delivered and women who remained undelivered at each gestational weeks (Fig. 1). For example, the comparison was done between 60 women who delivered at 35 weeks of gestation and 637 women who remained undelivered at 35 weeks and delivered at or beyond 36 weeks of gestation. The comparison was repeated at each advancing gestational week. The results were considered statistically significant for P -value < 0.05 . Statistical analyses were conducted using IBM SPSS ver. 20 (IBM Corp., Armonk, NY, USA).

Results

A total of 1,695 women with twin pregnancies were recorded during the 19 years of study period. Among them, 998

(58.9%) pregnancies were excluded by the aforementioned criteria and 697 (41.1%) uncomplicated twin pregnancies were included in the final study population. Among them, 171 (24.5%) were monochorionic and 526 (75.4%) were dichorionic twins.

Among the 697 women with uncomplicated twin pregnancy, 60 (20 monochorionic and 40 dichorionic) delivered at 35 weeks of gestation, 231 (61 monochorionic and 170 dichorionic) delivered at 36 weeks of gestation, 310 (68 monochorionic and 242 dichorionic) delivered at 37 weeks of gestation, 79 (16 monochorionic and 63 dichorionic) delivered at 38 weeks and remaining 17 (6 monochorionic and 11 dichorionic) delivered at ≥ 39 weeks of gestation.

The maternal characteristics and pregnancy outcome of twin pregnancies delivered at each gestational week are shown in Table 1. The five groups were similar in terms of maternal age, parity, and assisted reproductive technology performance. However, the cesarean delivery rate decreased significantly as gestational age advanced, which was significantly less common after 38 weeks of gestation. The rate of cesarean section due to previous cesarean section or uterine surgery decreased significantly with advancing gestational age at delivery, which

Table 1. Maternal characteristics and pregnancy outcome according to GA at delivery

	35 wk (n=60)	36 wk (n=231)	37 wk (n=310)	38 wk (n=79)	≥ 39 wk (n=17)	P -value ^{a)}	P -value ^{b)}
Age (yr)	32.8 \pm 4.7	31.8 \pm 3.8	31.9 \pm 3.4	31.8 \pm 3.9	30.1 \pm 3.2	0.113	0.237
Multiparity	23 (38.3)	59 (25.5)	79 (25.5)	16 (20.3)	5 (29.4)	0.181	0.098
ART	25 (41.7)	104 (45.0)	155 (50.0)	40 (50.6)	8 (47.1)	0.650	0.184
Chorionicity						0.205	0.143
Monochorionic	20 (33.3)	61 (26.4)	68 (21.9)	16 (20.3)	6 (35.3)		
Dichorionic	40 (66.7)	170 (73.6)	242 (78.1)	63 (79.7)	11 (64.7)		
GA at delivery (wk)	35.6 \pm 1.8	36.5 \pm 1.9	37.3 \pm 1.9	38.3 \pm 1.7	39.4 \pm 3.6	< 0.001	< 0.001
CS	59 (98.3)	227 (98.3)	289 (93.2)	62 (78.5)	9 (52.9)	< 0.001	< 0.001
Indications for CS						< 0.001	< 0.001
Previous CS or uterine surgery	8 (13.6)	25 (11.0)	36 (12.5)	1 (1.6)	0 (0)		
Elective ^{c)}	24 (40.7)	89 (39.2)	72 (24.9)	21 (33.9)	3 (33.3)		
Malpresentation ^{d)}	23 (39.0)	110 (48.5)	172 (59.5)	27 (43.5)	1 (11.1)		
Failure to progress	1 (1.7)	2 (0.9)	8 (2.8)	13 (21.0)	4 (44.4)		
Nonreassuring fetal status	3 (5.1)	1 (0.4)	1 (0.3)	0 (0)	1 (11.1)		

Data are presented as mean \pm standard deviation or number (%).

GA, gestational age; ART, assisted reproduction techniques; CS, cesarean section.

^{a)}Analysis of variance for continuous variables and chi-square test for categorical variables; ^{b)}Jonckheere-Terpstra test for continuous variables and linear-by-linear regression for categorical variables; ^{c)}When both twins had vertex presentation; ^{d)}When one or both twins had non-vertex presentation.

Table 2. Neonatal outcome according to gestational age at delivery

	35 wk	36 wk	37 wk	38 wk	≥39 wk	P-value ^{a)}	P-value ^{b)}
All neonates	(n=60)	(n=231)	(n=310)	(n=79)	(n=17)		
Fetal death in utero	2 (3.3)	0 (0)	2 (0.6)	0 (0)	0 (0)	0.042	0.133
1-Minute Apgar score <4	0 (0)	4 (1.7)	4 (1.3)	0 (0)	1 (5.9)	0.290	0.681
5-Minute Apgar score <7	0 (0)	1 (0.4)	3 (1.0)	0 (0)	1 (5.9)	0.095	0.166
NICU admission	25 (43.1)	40 (17.3)	28 (9.1)	4 (5.1)	1 (5.9)	<0.001	<0.001
Mechanical ventilator support	7 (11.7)	6 (2.6)	3 (1.0)	0 (0)	1 (5.9)	<0.001	0.001
Respiratory distress syndrome	6 (10.0)	1 (0.4)	0 (0)	0 (0)	0 (0)	<0.001	<0.001
Neonatal mortality	0 (0)	1 (0.4)	0 (0)	0 (0)	1 (5.9)	<0.001	0.175
Perinatal mortality	2 (3.3)	1 (0.4)	2 (0.6)	0 (0)	1 (5.9)	0.031	0.657
Composite morbidity ^{c)}	29 (48.3)	39 (16.9)	31 (10.0)	4 (5.1)	1 (5.9)	<0.001	<0.001
Monochorionic	(n=20)	(n=61)	(n=68)	(n=16)	(n=6)		
Fetal death in utero	1 (5.0)	0 (0)	0 (0)	0 (0)	0 (0)	0.108	0.093
1-Minute Apgar score <4	0 (0)	1 (1.6)	0 (0)	0 (0)	1 (16.7)	0.008	0.160
5-Minute Apgar score <7	0 (0)	1 (1.6)	1 (1.5)	0 (0)	1 (16.7)	0.077	0.157
NICU admission	7 (36.8)	15 (24.6)	9 (13.2)	2 (12.5)	1 (16.7)	0.151	0.027
Mechanical ventilator support	2 (10.0)	2 (3.3)	1 (1.5)	0 (0)	1 (16.7)	0.137	0.524
Respiratory distress syndrome	2 (10.0)	0 (0)	0 (0)	0 (0)	0 (0)	0.004	0.017
Neonatal mortality	0 (0)	1 (1.6)	0 (0)	0 (0)	1 (16.7)	0.008	0.160
Perinatal mortality	1 (5.0)	1 (1.6)	0 (0)	0 (0)	1 (16.7)	0.033	0.862
Composite morbidity ^{c)}	9 (45.0)	15 (24.6)	9 (13.2)	2 (12.5)	1 (16.7)	0.031	0.006
Dichorionic	(n=40)	(n=170)	(n=242)	(n=63)	(n=11)		
Fetal death in utero	1 (2.5)	0 (0)	2 (0.8)	0 (0)	0 (0)	0.366	0.474
1-Minute Apgar score <4	0 (0)	3 (1.8)	4 (1.7)	0 (0)	0 (0)	0.740	0.723
5-Minute Apgar score <7	0 (0)	0 (0)	2 (0.8)	0 (0)	0 (0)	0.669	0.603
NICU admission	18 (46.2)	25 (14.7)	19 (7.9)	2 (3.2)	0 (0)	<0.001	<0.001
Mechanical ventilator support	5 (12.5)	4 (2.4)	2 (0.8)	0 (0)	0 (0)	<0.001	<0.001
Respiratory distress syndrome	4 (10.0)	1 (0.6)	0 (0)	0 (0)	0 (0)	<0.001	<0.001
Neonatal mortality	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	-	-
Perinatal mortality	1 (2.5)	0 (0)	2 (0.8)	0 (0)	0 (0)	0.366	0.474
Composite morbidity ^{c)}	20 (50.0)	24 (14.1)	22 (9.1)	2 (3.2)	0 (0)	<0.001	<0.001

Data are presented as number (%).

NICU, neonatal intensive care unit.

^{a)}Analysis of variance or chi-square test; ^{b)}Jonckheere-Terpstra test for continuous variables and linear-by-linear regression for categorical variables; ^{c)}Defined as having one or more of the following: NICU admission, mechanical ventilator support, respiratory distress syndrome, neonatal mortality and fetal death in utero.

was significantly less common after 38 weeks of gestation. The rate of elective cesarean section for co-vertex twins (when both twins had vertex presentation) was not significantly different among the groups, but the rate of cesarean section for malpresentation twins (when one or both twins had non-vertex presentation) was significantly less common after 39

weeks of gestation. The rate of cesarean section due to failure to progress and nonreassuring fetal status significantly increased after 38 and 39 weeks of gestation, respectively.

The neonatal outcomes according to gestational age at delivery are described in Table 2. There were no differences in 1 minute Apgar score less than 4- and 5-minute Apgar score

Table 3. Neonatal composite morbidity of twins delivered versus undelivered at each gestational week

	GA (wk)	Delivered	Undelivered	OR (95% CI)	P-value
All	35	29/60 (48.3)	75/637 (11.8)	7.010 (4.001–12.281)	<0.001
	36	39/231 (16.9)	36/406 (8.9)	2.088 (1.285–3.392)	0.003
	37	31/310 (10.0)	5/96 (5.2)	2.022 (0.764–5.355)	0.149
	38	4/79 (5.1)	1/17 (5.9)	0.853 (0.089–8.151)	1.000
Monochorionic	35	9/20 (45.0)	27/151 (17.9)	3.758 (1.418–9.554)	0.005
	36	15/61 (24.6)	12/90 (13.3)	2.120 (0.913–4.920)	0.077
	37	9/68 (13.2)	3/22 (13.6)	0.966 (0.237–3.938)	1.000
	38	2/16 (12.5)	1/6 (16.7)	0.714 (0.053–9.700)	1.000
Dichorionic	35	20/40 (50.0)	48/486 (9.9)	9.125 (4.587–18.151)	<0.001
	36	24/170 (14.1)	24/316 (7.6)	2.000 (1.098–3.643)	0.022
	37	20/242 (9.1)	2/74 (2.7)	3.600 (0.826–15.685)	0.069
	38	2/63 (3.2)	0/11 (0)	Not available	1.000

Values are presented as number (%).

GA, gestational age; OR, odds ratio; CI, confidence interval.

less than 7 among all five groups. None of twins delivered at ≥ 37 weeks of gestation had RDS. There were 4 cases of FDIU, and 2 cases of neonatal mortality. The rate of FDIU, neonatal mortality and perinatal mortality was significantly different among five groups, but there was no statistically significant correlation with its rate and advancing gestational age.

In monochorionic twins, the rate of NICU admission, RDS and neonatal composite morbidity significantly decreased with advancing gestational age at delivery. The nadir of composite morbidity rate was observed at 38 weeks of gestation. There was one neonatal mortality case in a woman with monochorionic twin pregnancy who delivered at 40 weeks and 5 days by emergency cesarean section due fetal distress during spontaneous labor. The first twin was healthy at birth and survived, but the second twin expired due to hypoxic encephalopathy.

In dichorionic twins, the rate of NICU admission, mechanical ventilator support, RDS and neonatal composite morbidity significantly decreased with advancing gestational age at delivery. The nadir of composite morbidity rate was observed at ≥ 39 weeks of gestation, where there was no NICU admission, neonatal morbidity or mortality.

The results of the neonatal composite morbidity rate comparison between women who delivered and women who remained undelivered at each gestational week are shown in Table 3. In monochorionic twins, the neonatal composite morbidity rate was significantly higher among twins delivered at 35 weeks' gestation compared to those undelivered and were

born after 35 weeks. However, the neonatal composite morbidity rates were similar between delivered and undelivered cases at 36, 37, and 38 weeks of gestation. In dichorionic twins, the neonatal composite morbidity rate of twins delivered at 35 and 36 weeks of gestation was higher than that of twins compared to those undelivered at this gestational week. This composite morbidity difference became insignificant between delivered and undelivered groups at or beyond 37 weeks of gestation.

Discussion

In this study, we have reviewed the 697 cases of uncomplicated twin pregnancies and investigated maternal and neonatal outcomes to determine the optimal delivery time in uncomplicated twin pregnancies. Our results suggest that the optimal delivery time may be at or beyond 36 weeks for monochorionic twins, and at or beyond 37 weeks for dichorionic twins, considering the similar neonatal composite morbidity after this period regardless of delivery.

Currently the optimal timing of delivery of twin pregnancy is still controversial, with some experts suggesting preterm or early-term delivery to avoid late stillbirth risk, while others support maintaining pregnancy to decrease the prematurity related neonatal morbidities [14]. Some studies have suggested that twins mature faster than singletons, and, therefore, may

be better equipped for earlier delivery thus the lowest perinatal mortality rate for twins occurs at an earlier gestational age than singletons [15]. A population-based study from the US National Center for Health Statistics suggested that the nadir in perinatal mortality occurs between 37 to 39 weeks in twins versus 39 to 41 weeks of gestation in singletons [16]. A review based on the Swedish Medical Birth Registry including 32,942 twins showed that perinatal mortality was lowest at 37 to 38 weeks [8]. Another study from Japan reported the mean duration of pregnancy on 88,936 infants of multiple gestations (96% twins) and 6,020,542 infants born of singleton pregnancies to be 37.0 and 39.6 weeks of gestation, respectively [17]. In their study, the incidence of stillbirth and early neonatal death reached nadir at 37 to 38 weeks of gestation in all twins. In our study, the perinatal mortality was lowest (none out of 79 twin pregnancies) at 38 weeks of gestation. However, we were not able to find an optimal gestational age for delivery at which the perinatal mortality is significantly lower than the other gestational week, because there were only 6 cases of perinatal death among all 697 twin pregnancies. The fact that only uncomplicated twin pregnancies included in the study population, may have attributed to low perinatal mortality in this study. Aforementioned population-based studies included the complicated pregnancies therefore their optimal delivery time may be unreasonable to apply in uncomplicated twin pregnancies. Therefore we sought to determine the optimal gestational week at delivery for twins when the risk of composite morbidity is significantly lower than other gestational weeks.

Maternal and neonatal complications that require prompt preterm delivery occur more frequently in twin pregnancies than singleton pregnancies [9]. The delivery time of the twin pregnancy with complication is decided according to the condition of the complication and obstetrical indications. For this reason, we have excluded the complicated twin pregnancy. In our study population of uncomplicated twin pregnancies, the neonatal composite morbidity rate significantly decreased with advancing gestational age at delivery which reached nadir at 38 weeks of gestation. However, the pattern of neonatal outcome in relation to gestational age at delivery was considerably different between the monochorionic and dichorionic twin pregnancies.

Optimal delivery time should be considered differently for monochorionic and dichorionic twins, taking in the fact that monochorionicity is associated with increased adverse peri-

natal outcomes when compared with dichorionicity [18,19]. The 2011 United Kingdom National Institute for Health and Clinical Excellence Guidelines for multiple gestations suggested that women with uncomplicated monochorionic twin pregnancies should deliver electively after 36 weeks 0 days, and women with the uncomplicated dichorionic pregnancies should deliver electively after 37 weeks 0 days [20]. There is another recommendation that stems from a joint National Institute of Child Health and Human Development/Society for Maternal Fetal Medicine workshop states that a delivering between range of 34 to 37 weeks of gestation for monochorionic twins and 38 weeks of gestation for dichorionic twins are acceptable [21]. Robinson et al. [22] designed analytic model to compare different timing of delivery in uncomplicated monochorionic diamniotic twin and demonstrated that delivery between 36 and 38 weeks' gestation is preferred. Majority of expert opinion is that it is reasonable to consider deliver uncomplicated dichorionic twins after 37 or 38 weeks of gestation but no later than 39 weeks of gestation [4,11]. In our result, the nadir of neonatal composite morbidity was observed at 38 weeks in monochorionic twins and at or beyond 39 weeks of gestation in dichorionic twins. Nevertheless, neonatal composite morbidity did not significantly decrease after 36 and 37 weeks of gestation in monochorionic and dichorionic twin, respectively, when they were analyzed and compared in two divided groups: delivered versus undelivered groups at each gestational week. This method of comparison, rather than comparing the outcome in each gestational age by multiple comparison method, may be more reasonable for determining the optimal gestational age for delivery for it allows us to weigh between the merit and disappointing outcome that is followed by delivery at a specific gestational period. And our results showed that the optimal gestational age for delivery was at ≥ 36 and ≥ 37 weeks in uncomplicated monochorionic and dichorionic twin pregnancies, respectively.

Earlier optimal gestational age at delivery in monochorionic twins, compared to dichorionic twins, is not well understood. The higher risk of adverse neonatal outcome in monochorionic twins is considered to be the possible predisposing factor, requiring early delivery [23]. In monochorionic twins, a single placenta is shared by each twin, which may result in imbalanced vascular anastomosis followed by an ischemic injury and hypovolemia [24]. Because the degree of vascular anastomosis vary greatly, the imbalance of blood flow level also has variation, which can cause minor complications that are diffi-

cult to evaluate by using prenatal or antenatal surveillance [25]. This minor complication in monochorionic twins is considered to cause earlier worsening of neonatal outcome, thus resulting in an earlier optimal gestational age for delivery between monochorionic twins and dichorionic twins.

The composite morbidity increased in twins born at ≥ 39 weeks of gestation, which is due to one neonatal death occurred in monochorionic twin pregnancy delivered at 40 weeks and 5 days. However, the number of patients delivered at ≥ 39 weeks of gestation was not adequate enough to show the statistical significance, where there were only 17 cases delivered at ≥ 39 weeks of gestation and among these 3 cases delivered at ≥ 40 weeks of gestation. Therefore, we were not able to set the upper limit of optimal gestational age for delivery from our study population and this is one of the main limitations of this study.

This study is further limited by its inherent disadvantage of a retrospective study design that limits ability to control potential confounding factor and information bias. In addition, because our data has been accumulated for 19 years, treatments and management on twin pregnancy may not have been consistent.

In conclusion, our data suggest that in the absence of complication, delivery should be delayed up until at least 36 weeks in monochorionic twin pregnancies and at least 37 weeks in dichorionic twin pregnancies. However, prospective studies with adequate sample size and control of potential confounding biases are needed to further confirm our findings and to determine the optimal gestational age for delivery in uncomplicated twin pregnancies.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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