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Inter-twin delivery interval, short-term perinatal outcomes and risk of caesarean for the second twin

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Abstract

Objective: To examine the association between inter-twin delivery interval and short-term perinatal outcomes of the second twin after vaginal delivery of the first twin.

Methods: Retrospective cohort study including twin pregnancies with a vaginal delivery of the first twin between January 2011 and September 2017 in a tertiary hospital in Melbourne, Australia. The main outcome measure was a composite of adverse neonatal outcome (at least one of perinatal death, admission to neonatal intensive care unit [NICU], endotracheal intubation, Apgar < 7 at 5 minutes and cord lactate > 4.0). Proportions of adverse outcomes for the second twin were compared between groups of interval < or > 10 and ≤ or > 30 minutes.

Results: The composite adverse neonatal outcome occurred in 201 (58.2%) and a caesarean section occurred in 7 cases (2%) of the 345 pregnancies included. Delivery interval was associated with higher cord lactate. Low Apgar scores were more frequent with interval > 30 minutes (17.9% versus 6.6%, $p = 0.03$), as well as caesarean section for the second twin (10.7% versus 1.3%, $p = 0.01$). Composite adverse outcome and admission to NICU were not significantly influenced by the delivery interval. Predictors of adverse outcome were gestational age, abnormal cardiotocography and breech delivery of the second twin.

Conclusion: The inter-twin delivery interval is associated with higher rates of low Apgar score and higher cord lactate for the second twin. These associations do not translate into higher rates of admission to NICU and their long-term clinical implications are uncertain.

Introduction

The rate of twin birth in Australia has increased in the last few decades from 2.7% in 1991 to a peak of 3.4% in 2002 reflecting the advent and development of assisted reproductive techniques (ART).^{1,2}

Despite a paucity of evidence, increasing inter-twin delivery interval has been thought to be associated with adverse outcomes in the delivery of vaginal twins.³ The introduction of widespread electronic fetal monitoring during labour has called into question the traditional limit of 30 minutes.³⁻⁵ Setting a “benchmark time frame” has profound clinical implications and may contribute to the rate of emergency caesareans in the second twin.^{3,6,7}

Although vaginal delivery seems to be a safe option in twins both from a short and long-term perspective, the second twin is at a greater risk of adverse neonatal outcomes, independent of the planned mode of delivery.^{8,9} Whether this risk results from a longer delivery interval in the setting of vaginal birth is unclear. Some studies have demonstrated a pH decline for the second twin with increasing inter-twin delivery interval,^{3,10,11} while other studies found no difference.¹² These contradictory findings may be due to the use of different methodologies used and the lack of adjustment for confounders in some studies. The clinical significance of these associations, particularly in the setting of a reassuring CTG, is uncertain.

A retrospective Cohort study of 4,110 twin pregnancies in Germany demonstrated a decline in mean umbilical arterial pH with increasing time interval, however no association with admission of the second twin to neonatal intensive care unit (NICU) or perinatal death.¹³ NICU admission rates and adverse neonatal outcomes based on time interval were also unchanged in other studies.¹⁴

Regarding caesarean section rates, the evidence suggests an increasing time interval and specifically a time frame of above 30 minutes is associated with a higher rate of caesarean of the second twin^{13,15}. However, establishing an upper time limit in practice would involve more active management of the second twin, potentially increasing internal podalic version with breech extractions or instrumental deliveries, with unknown clinical impact and risk¹⁵. Furthermore, it is hard to establish causality, as it is difficult to determine if the lack of active management of the second twin leads to caesarean section or if the prolonged inter-twin delivery interval reflects labour dystocia necessitating a caesarean section.

This study aims to examine a possible association between the delivery interval for the second twin and short-term adverse perinatal outcomes after vaginal delivery of the first twin, as well as risk of caesarean section for the second twin.

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Methods

Study population and data collection

Retrospective data were retrieved using a pre-specified query of the Birthing Outcomes System[®] (BOS, version 6.03.05, Management Consultants and Technology Services, Caulfield, Victoria, Australia). Twin pregnancies delivering between January 2011 and September 2017 in a tertiary hospital in Melbourne, Australia, were captured and the records were de-identified. Twin pregnancies with a vaginal delivery of the first twin after 24 weeks' gestation were included. Those that underwent an elective caesarean section or caesarean section of the first twin were excluded. Cases of major congenital abnormalities in either twin were also excluded. Medical records were checked for inconsistencies and missing data.

Maternal characteristics were recorded, as were chorionicity, gestational age at birth and delivery details (inter-twin delivery interval in minutes, mode of delivery, abnormal cardiotocography and need for intrauterine manipulation with internal podalic version and breech extraction of the second twin).

The perinatal outcomes analysed included birthweight, Apgar scores, arterial cord lactate, need for respiratory support, admission to NICU, length of stay in NICU, and a composite of adverse neonatal outcomes (at least one of perinatal death, admission to NICU, endotracheal intubation, Apgar < 7 at 5 minutes of life and cord lactate > 4.0).

Abnormal cardiotocography was defined as per The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) guidelines.¹⁶

Ethical approval

The study complied with the National Health and Medical Research Council (NHMRC) 2014 Ethical Considerations in Quality Assurance and Evaluation Activities¹⁷ and was approved by Monash Health Human Ethics Committee (NMH HREC Reference Number: HREC/17/MonH/572, Monash Health Ref: RES-17-0000-655L).

Statistical analysis

Categorical variables were expressed in absolute values and percentages and continuous variables in medians and interquartile ranges (IQR).

The primary outcome measure was the relationship between inter-twin delivery interval and the occurrence of the composite adverse neonatal outcome. The groups were

divided into an inter-twin interval $\leq$ or $>$ 10 minutes and $\leq$ or $>$ 30 minutes. The individual perinatal outcomes and caesarean section for the second twin were compared between the groups with Chi-square or Fisher's exact test for categorical variables and t-test or Mann-Whitney U test for continuous variables depending on the distribution of the data.

Logistic regression was used to identify predictors of adverse neonatal outcomes and to adjust the analysis for confounders. Statistical analysis was performed using SPSS 25.0[®] (IBM SPSS Inc., Chicago, IL, USA).

Results

A total of 345 twin pregnancies were included. Of those included, 243 (70.4%) were dichorionic and 102 (29.6%) monochorionic. Baseline characteristics of the study population are shown in Table 1. The median inter-twin interval was 11 minutes, ranging from one to 178 minutes.

Maternal characteristics were similar between different interval groups. Monochorionicity and breech extraction of the second twin were associated with a shorter delivery interval. Delivery of the second twin by instrumental techniques and emergency caesarean section were significantly more common in the groups with interval > 10 and > 30 minutes when compared to interval ≤ 10 and ≤ 30 minutes. The mean birthweight of the second twin was significantly higher when the interval was > 10 and > 30 minutes.

Composite adverse neonatal outcome occurred in 201 (58.2%) neonates. The delivery interval did not significantly influence the occurrence of the composite neonatal adverse outcome. Significant independent predictors of composite adverse neonatal outcome were lower gestational age, abnormal CTG and breech delivery (p values < 0.001 , 0.005 and 0.03 , respectively – Table 3).

Delivery interval > 30 minutes was independently associated with higher rates of low Apgar score (17.9% versus 6.6%, $p = 0.03$, R^2 0.23), and the occurrence of Apgar score < 7 at 5 minutes was 3.8 times more likely when the inter-twin delivery interval was more than 30 minutes (adjusted OR 3.83, 95% CI 1.24-11.82, Table 3) after adjustment for gestational age at birth, maternal age, birthweight, the occurrence of abnormal CTG and mode of delivery. Only interval > 30 minutes and gestational age at birth were predictive of Apgar score at 5 minutes < 7 ($p=0.03$ and $p=0.005$, respectively). There was no significant association between mode of delivery and low Apgar score.

Breech delivery of the second twin (adjusted odds ratio 2.0, 95% CI 1.15–3.78) and delivery interval were independent predictors of cord lactate > 4.0 , with an increase in 0.04 units of lactate per minute. However, this did not translate into significantly different proportions of admission to NICU or high lactate in the groups with interval ≤ 30 minutes and > 30 minutes. For admission to NICU, only gestational age at birth and abnormal CTG provided significant independent prediction (Table 3).

Although chorionicity and birthweight of the second twin were significantly different between the study groups, neither of these variables or difference in birthweight between the

first or the second twin were significant predictors of adverse neonatal outcomes in the regression analysis.

Caesarean section for the second twin occurred in 7 cases (2%). The only significant independent predictor of caesarean section for the second twin was the delivery interval ($p=0.003$) after adjustment for possible confounders in the logistic regression analysis (gestational age at birth, birthweight, birthweight discrepancy, the occurrence of abnormal cardiotocography and breech presentation). Delivery interval > 30 minutes had an adjusted odds ratio of 9.39 (95% CI 2.0-44.3) for an emergency caesarean section of the second twin after vaginal delivery of the first twin.

Discussion

Main findings and clinical implications

This study demonstrated that the inter-twin delivery interval did not influence the rates of composite adverse neonatal outcomes and the rates of admission to NICU. These outcomes seem to be mainly related to prematurity or the occurrence of fetal distress. Two previous cohort studies have reported similar results^{13, 14}.

While there was a significant positive association between increasing inter-twin delivery interval and cord lactate, consistent with previous literature findings^{13, 15}, this incremental difference in lactate values is of doubtful clinical significance and the more concerning high lactates were not different between groups based on the cut off of 30 minutes. Of note, the composite adverse neonatal outcome was not different between the respective groups. A lower Apgar score at 5 minutes was associated with an interval > 30 minutes, even when adjusted for confounders including gestational age at birth, with an adjusted odds ratio of 3.8. However, the long-term clinical significance of this finding is unknown, given there was no difference in other individual neonatal outcomes and the composite adverse neonatal outcome. Rather, the progressive increase in cord lactate as interval increases and the higher proportion of low Apgar score with prolonged delivery interval (> 30 minutes) may be due to an acute injury from which the infant recovers with neonatal resuscitation and with no other apparent clinical consequences in the short-term. An awareness of the potential impact of the time interval, and lack of clear evidence of harm with increasing time, should be taken in account by clinician together with the full clinical picture.

As expected, the main factors associated with adverse neonatal outcome and admission to NICU are mainly a result of signs of fetal distress and lower gestational age at birth.

The theoretical risk of the cervix and the lower segment reforming has not been evaluated in this study. Concerning the potential impact on mode of delivery, there was a statistically significant and independent association between an inter-twin delivery interval greater than 30 minutes and caesarean section after adjustment for possible confounders. Since the causality and the nature of this association in our study and previous studies cannot be determined, an imposed time limit in clinical practice may not affect this rate. Our study demonstrated a caesarean rate of 2% in the second twin, which is lower than the 4 to 10% rate sighted in the literature^{13, 18, 19}. This may reflect institutional factors, including the

availability of senior clinicians experienced in vaginal twin delivery, instrumental delivery and breech extraction.

Ultimately, an appreciation of the many clinical factors, including progression of labour, fetal heart rate monitoring of the second twin, level of experience of staff present, the lie of the second twin, and patient preference, that form the overall picture, may hold more significance than a defined time limit. Although some guidelines recommend an upper time limit, there is currently lack of evidence to support this and caution is recommended when interpreting it as an absolute indication for expediting delivery.

Limitations of the study

The retrospective nature of this study and its inherent possibility of bias are the main limitations of this study. However, a less biased approach would only be possible through a multicentre randomised clinical trial, which may be difficult to perform given the frequency of twins undergoing vaginal delivery and the likely substantial attrition rate that would be inevitable in order to avoid compromising safety. Additionally, the large number of pregnancies included in this study and the consistency of the results with the majority of the previously published data strengthen the findings of this study.

Conclusion

An increased inter-twin delivery interval is associated with higher rates of low Apgar score and an increase in cord lactate. However, these associations do not translate into higher rates of admission to neonatal intensive care unit and their long-term clinical implications are uncertain.

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Table 1. Baseline and delivery characteristics of the study population.

	TOTAL (N=345)	Interval		p	Interval		p
		≤ 10 minutes (n=164)	> 10 minutes (n=181)		≤ 30 minutes (n =317)	> 30 minutes (n=28)	
Maternal age, years, mean (SD)	30.9 (5.2)	31.1 (4.8)	30.8 (5.5)	0.58	30.9 (5.2)	31.2 (5.4)	0.78
Weight, Kg, median (IQR)	68.0 (60.0-82.0)	69.0 (58.2-80.7)	67.0 (60.0-83.5)	0.91	68.5 (60.0-82.2)	67.5 (57.7-80.7)	0.63
Height, cm, mean (SD)	164.7 (7.1)	164.7 (6.6)	164.7 (7.6)	0.95	164.7 (6.9)	164.9 (9.8)	0.88
Body mass index, Kg/m², median (IQR)	25.1 (22.2-29.4)	25.4 (22.0-29.7)	25.1 (22.6-29.4)	0.85	25.1 (22.2-29.4)	25.5 (21.4-30.4)	0.65
Chorionicity							
Monochorionic, n (%)	102 (41.6)	59 (36.0)	43 (23.8)	0.01	99 (31.2)	3 (10.7)	0.02
Dichorionic, n (%)	243 (58.4)	105 (64.0)	138 (76.2)		218 (68.8)	25 (89.3)	
Gestational age, weeks, median (IQR)	36.1 (34.2-37.0)	36.2 (33.9-37.0)	36.2 (34.3-37.1)	0.19	36.1 (34.2-37.0)	36.8 (34.3-37.5)	0.09
Onset of labour							
Spontaneous, n (%)	138 (40.0)	66 (40.2)	72 (39.8)	0.93	127 (40.1)	11 (39.3)	0.93
Induction, n (%)	207 (60.0)	98 (59.8)	39 (60.2)		190 (59.9)	17 (60.7)	
Mode of delivery twin 2							
Spontaneous vertex, n (%)	104 (30.2)	42 (25.6)	62 (34.3)	0.09	95 (30.0)	9 (32.1)	0.83
Instrumental (forceps or vacuum), n (%)	66 (19.1)	10 (6.1)	56 (30.9)	<0.01	55 (17.4)	11 (39.3)	<0.01
Breech, n (%)	168 (48.7)	112 (68.3)	56 (30.9)	<0.01	163 (51.4)	5 (17.9)	<0.01

Cesarean section, n (%)	7 (2.0)	0 (0)	7 (3.9)	0.01	4 (1.2)	3 (10.7)	0.01
Birthweight twin 1, g, mean (SD)	2290 (555)	2258 (582)	2319 (528)	0.31	2281 (555)	2393 (555)	0.30
Birthweight twin 2, g, mean (SD)	2268 (560)	2204 (583)	2327 (533)	0.04	2246 (557)	2528 (534)	0.01
Epidural, n (%)	312 (90.4)	150 (91.5)	89 (89.5)	0.53	289 (91.2)	23 (82.1)	0.17

Table 2. Neonatal outcomes according to different groups of inter-twin delivery interval

	TOTAL (N=345)	Interval		p	Interval		p
		< 10 minutes (n=164)	> 10 minutes (n=181)		< 30 minutes (n =317)	> 30 minutes (n=28)	
Emergency caesarean section, n (%)	7 (2.0)	0 (0.0)	7 (3.9)	0.01	4 (1.3)	3 (10.7)	0.01
Composite adverse outcome, n (%)	201 (58.2)	98 (59.8)	103 (56.9)	0.59	186 (58.7)	15 (53.6)	0.60
Admission to NICU, n (%)	81 (23.5)	39 (23.8)	42 (23.2)	0.90	75 (23.7)	6 (21.4)	0.79
Apgar score 5< 7, n (%)	26 (7.5)	11 (6.7)	15 (8.3)	0.58	21 (6.6)	5 (17.9)	0.03
Cord lactate > 4.0, n (%)	152 (44.1)	70 (57.9)	82 (68.9)	0.08	140 (62.2)	12 (80.0)	0.17
CPAP use, n (%)	155 (44.9)	77 (47.0)	78 (43.1)	0.47	145 (45.7)	10 (35.7)	0.30
Intubation, n (%)	53 (15.4)	26 (15.9)	27 (14.9)	0.81	51 (16.1)	2 (7.1)	0.28
Oxygen therapy, n (%)	112 (32.5)	54 (32.9)	58 (32.0)	0.86	103 (32.5)	9 (32.1)	0.97
Jaundice, n (%)	189 (54.8)	92 (56.1)	97 (53.6)	0.64	171 (53.9)	18 (64.3)	0.29
Sepsis, n (%)	36 (10.4)	18 (11.0)	18 (9.9)	0.75	35 (11.0)	1 (3.6)	0.33
Length of stay in NICU, days, median (IQR)	6.0 (4.0-14.0)	7.5 (4.0–17.7)	6.0 (4.0-12.0)	0.56	6.0 (4.0–15.0)	6.5 (4.0–10.5)	0.21

Table 3. Adjusted odds ratios and 95% confidence intervals for adverse neonatal outcomes for the second twin in multivariable logistic regression analysis

	COMPOSITE (R² 0.19)	NICU admission (R² 0.61)	Apgar < 7 at 5 minutes (R² 0.23)	Cord lactate > 4.0 (R² 0.06)
Gestational age (weeks)	0.73 (0.65-0.82)	0.40 (0.32-0.50)	0.80 (0.72-0.90)	NS
Abnormal CTG	1.75 (1.10-2.80)	2.16 (1.01-4.63)	NS	NS
Breech delivery	1.73 (1.09-2.75)	NS	NS	1.78 (1.01-3.17)
Interval (minutes)	NS	NS	NS	1.04 (1.01-1.08)
Interval > 30 minutes	NS	NS	3.83 (1.24-11.82)	NS

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