

Birth order, gestational age, and risk of delivery related perinatal death in twins: retrospective cohort study

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Abstract

Objective To determine whether twins born second are at increased risk of perinatal death because of complications during labour and delivery.

Design Retrospective cohort study.

Setting Scotland, 1992 and 1997.

Participants All twin births at or after 24 weeks' gestation, excluding twin pairs in which either twin died before labour or delivery or died during or after labour and delivery because of congenital abnormality, non-immune hydrops, or twin to twin transfusion syndrome.

Main outcome measure Delivery related perinatal deaths (deaths during labour or the neonatal period).

Results Overall, delivery related perinatal deaths were recorded for 23 first twins only and 23 second twins only of 1438 twin pairs born before 36 weeks (preterm) by means other than planned caesarean section ($P > 0.99$). No deaths of first twins and nine deaths of second twins ($P = 0.004$) were recorded among the 2436 twin pairs born at or after 36 weeks (term). Discordance between first and second twins differed significantly in preterm and term births ($P = 0.007$). Seven of nine deaths of second twins at term were due to anoxia during the birth (2.9 (95% confidence interval 1.2 to 5.9) per 1000); five of these deaths were associated with mechanical problems following vaginal delivery of the first twin. No deaths were recorded among 454 second twins delivered at term by planned caesarean section.

Conclusions Second twins born at term are at higher risk than first twins of death due to complications of vaginal delivery. Previous studies may not have shown an increased risk because of inadequate categorisation of deaths, lack of statistical power, inappropriate analyses, and pooling of data about preterm births and term births.

Introduction

Obstetricians recognise that second twins are vulnerable to complications during labour and delivery.¹ Analysis of observational studies in the 1960s seemed to show that second twins were at higher risk of perinatal death than first twins.² These findings were subsequently refuted by a number of large scale studies that failed to show a higher risk³⁻⁶ or that showed only a very slightly higher risk.⁷ Previous large scale studies have generally lacked detailed information on the cause and timing of perinatal death. Consequently, differences in outcomes related to complications during delivery of the second twin may have been masked by other causes of death, such as prematurity, congenital abnormality, and antepartum events. We conducted a large scale, retrospective cohort study of delivery related perinatal deaths in twin pregnancies by linking a national register of data on discharges after childbirth to a national register of perinatal deaths.

Methods

Population

We used the Scottish morbidity record to identify all births between 1992 and 1997 and linked these records to records from the Scottish Stillbirth and Infant Death Enquiry.^{8,9}

Definitions

Stillbirths were defined as babies born at or after 24 weeks' gestation who showed no signs of life after delivery. Neonatal death was defined as death during the first four weeks of life in a liveborn baby.

We defined delivery related perinatal death as intrapartum stillbirth or neonatal death not caused by congenital anomaly, hydrops, or twin to twin transfusion syndrome. The cause of death was subdivided into three paediatric categories: intrapartum anoxia, pulmonary causes, and all other paediatric causes. Deaths due to anoxia were further classified into those with a direct obstetric mechanical cause.

Socioeconomic deprivation, smoking, parity, maternal age, and gestational age were defined as described previously.¹⁰ Term was defined as ≥ 36 weeks' gestation for twin pregnancies.⁶

Results

Between 1992 and 1997, 4545 women delivered twins in Scotland at or after 24 weeks' gestation: 671 (14.8%) were delivered by planned caesarean section and 3874 (85.2%) by other means. On univariate analysis, age, socioeconomic status, height, and parity varied according to gestational age at the time of delivery among women delivered by a means other than planned caesarean section but only parity and maternal height were independent predictors of preterm birth.

The numbers of deaths of first and second twins born before 36 weeks' gestation did not differ significantly (table 1). Among births at or after 36 weeks' gestation, no deaths were recorded among first twins and nine deaths among second twins (3.7 (95% confidence interval 1.7 to 7.0) per 1000 deliveries; $P = 0.004$ for excess of deaths of second twins). Discordance between first and second twins was significantly different in preterm and term births (table 1).

Of the nine deaths of second twins at term, five were intrapartum stillbirths and four were neonatal deaths. Seven of the nine deaths were attributed to intrapartum anoxia (2.9 (1.2 to 5.9) per 1000 deliveries). The cause of death was classified as mechanical in five of the seven anoxic deaths at term; this equated to 2.1 (0.7 to 4.8) per 1000 deliveries. Both twins were delivered vaginally in six out of the seven deliveries at term in which the second twin died from anoxia and in all five of the deliveries at term in which anoxia had an obstetric mechanical cause.

No differences in any maternal characteristics for twins delivered at term by a means other than planned

Table 1 Delivery related perinatal deaths of first and second twins delivered by a means other than planned caesarean section in relation to gestational age and cause of death

Cause of death	Preterm births (n=1438)*					Term births (n=2436)				P value for preterm v term§
	First twin	Second twin	Both twins	P value†	Odds ratio (95% CI) for second twin	First twin	Second twin‡	Both twins	P value†	
All	23	23	42	>0.99	1.0 (0.6 to 1.8)	0	9	0	0.004	0.007
Intrapartum anoxia	5	5	2	>0.99	1.0 (0.3 to 3.5)	0	7	0	0.02	0.04
Pulmonary causes	18	19	25	>0.99	1.1 (0.6 to 2.0)	0	0	0		
All other paediatric causes	11	10	4	>0.99	0.9 (0.4 to 2.1)	0	2	0	0.5	0.48

*In 11 of the preterm births, both twins died but because of different causes.

†McNemar's exact test for discordance between first twins and second twins.

‡Odds ratio for death of the second twin could not be calculated because the odds of death among first twins at term were zero in all categories.

§Fisher's exact test of discordant twin pairs, preterm versus term.

caesarean section were seen according to whether the second twin died (table 2). When twins' characteristics were compared, no difference was seen in the proportion that were discordant for sex, but the percentage discrepancy in birth weight was significantly higher for pairs of twins in which the second twin died than for pairs in which both twins survived. When the actual weights for the nine pregnancies in which the second twin died during delivery at term were analysed, four of the second twins were larger than the first twins and five were smaller; the median birth weight did not differ between the first and second twins.

Multivariate conditional logistic regression confirmed that the interaction between birth order and gestational age was independent of maternal age, parity, smoking, height, and socioeconomic deprivation. When outcomes for the 454 twin pairs delivered at term by planned caesarean section were analysed, no delivery related perinatal deaths of either first or second twins were seen.

Discussion

We observed an excess of delivery related perinatal deaths of second twins born at term compared with their cotwins. The absolute risk of perinatal death for second twins born at term was approximately 1 in 270 for all causes, 1 in 350 for death due to intrapartum anoxia, and 1 in 500 for anoxic death due to a mechanical cause. These absolute risks are high in comparison with similar data for singleton term births in Scotland over the same period: delivery related perinatal death occurred in about 1 in 1000 births among nulliparous women and 1 in 2000 births among multiparous women; death due to a mechanical obstetric cause occurred in only 1 in 20 000 births.¹¹

Methodological issues

Previous studies have compared the outcome of second twins born vaginally either with vaginally delivered cotwins^{2 3 5-7} or with second twins delivered by caesarean section.^{4 12-14} They failed to show a significant association between birth order and the risk of delivery related perinatal death. We were able to make both comparisons in our study and also addressed several limitations in methods that were apparent in previous studies.

Firstly, this study examined the outcomes of over 4500 twin pairs. Many previous studies that examined perinatal mortality in relation to birth order had fewer than 1000 twin pairs and many had fewer than 500 twin pairs.¹⁵ Given the relative rarity of delivery related perinatal death caused by intrapartum anoxia,¹¹ such studies are clearly underpowered and would inevitably yield negative findings.

Secondly, to our knowledge, this study is the only large scale analysis to include data on both intrapartum stillbirths and neonatal deaths but to exclude antepartum deaths. Given that most delivery related perinatal deaths in second twins at term were intrapartum stillbirths, previous large scale studies that excluded stillbirths probably underestimated the risk to the second twin.^{3-5 7} The only large scale study that included stillbirths was unable to distinguish between antepartum and intrapartum stillbirths.⁶

Thirdly, most studies have compared first and second twins across the whole range of gestational ages rather than stratified by gestational age.^{3 5 7} The former method is legitimate only if the relative risk is homogeneous across the range of gestational ages. A statistical interaction between birth order and gestational age, however, is predictable. Eighty per cent of twins delivered at 24 weeks die compared with less than 1% at term.⁶ The principal determinant of the risk of death

Table 2 Maternal and obstetric characteristics of pregnancies at term according to death of second twin among women not delivered by planned caesarean section. Values are numbers (%) unless otherwise specified

Characteristics	Both twins survived (n=2427)	Second twin died (n=9)	P value*
Mother			
Median (interquartile range) maternal age (years)	30 (26-33)	29 (26-32)	0.99
Median (interquartile range) height (cm)	163 (159-167)	162 (158-165)	0.72
Nulliparous	900 (37.1)†	4 (44.4)	0.73
Smoker	660 (30.6)†	2 (22.2)	>0.99
In upper two fifths of deprivation category	1000 (41.9)†	5 (55.6)	0.50
Twin			
Discordant for sex	808 (34.0)	2 (22.2)	0.73
Median (interquartile range) % discrepancy in birth weight	9.5 (4.5-15.9)	15.1 (12.1-21.0)	0.02

*Percentage estimated after records with missing values were excluded.

†Fisher's exact test or Mann-Whitney U test, as appropriate.

What is already known on this topic

It is difficult to assess the wellbeing of second twins during labour

Deliveries of second twins are at increased risk of mechanical problems, such as cord prolapse and malpresentation, after vaginal delivery of first twins

Increased risks of perinatal death in second twins have not been shown, but the methods of these studies were flawed

What this study adds

Second twins delivered at term are at increased risk of delivery related perinatal deaths

Intrapartum anoxia caused 75% of these deaths in second twins, and most of these resulted from mechanical problems after vaginal delivery of first twins

Planned caesarean section of twins at term may prevent perinatal deaths

is prematurity, which clearly is the same for both twins. The potential for birth order to increase the baseline risk due to complications during labour and delivery, therefore, would be expected to increase with advancing gestational age. Our study confirmed a positive interaction between being a second twin and gestational age and thus confirms that the assumption of homogeneity implicit in previous analyses was invalid.

Finally, our statistical analysis took into account the paired nature of the data. Many previous studies, including previous large scale analyses,³⁻⁷ compared data on first and second twins by using statistical techniques that assume independence of observations. The use of unpaired tests for paired data is inappropriate. If we had used the same analytical approach as some previous studies (failed to stratify by gestational age and used a statistical test for unpaired data), we would have observed, overall, 67 deaths among all first twins and 75 among second twins; this would have failed to reach significance (χ^2 test, $P=0.49$).

The excess of deaths due to intrapartum anoxia was significant only for twins born at term. Although no significant difference was seen between the risks of death for first and second twins born preterm, the confidence intervals for the odds ratio of death of the preterm second twin (relative to the first twin) due to intrapartum anoxia were 0.3 to 3.5. Our data cannot exclude an excess risk of anoxic death for preterm second twins; further larger analyses are required.

Caesarean deliveries

Since the excess of deaths of second twins at term seems to be attributable to labour, current data suggest that planned caesarean delivery may be protective against perinatal death among twins. Although there were no deaths of second twins following planned caesarean delivery at term, the numbers were too small to confirm a protective effect of planned caesarean

section. Sample size calculations show that it will be difficult to obtain randomised controlled trial data to test the hypothesis that planned caesarean section would be protective against perinatal death in twin pregnancies. With a rate of three deaths of second twins due to intrapartum anoxia per 1000 deliveries, allowing 80% power for a one sided test, and assuming that the rate of perinatal death in the planned caesarean group is zero, a randomised controlled trial would need to recruit about 6500 women with twin pregnancies. We propose that women with twin should be counselled about the risk to the second twin and the theoretical possibility of a protective effect of planned caesarean section when considering mode of delivery at term.

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Correction

Gabapentin induced cholestasis

In the Drug Point by Charles E Richardson and colleagues (21 September, p 635), gabapentin was reported to be an unlicensed indication for the management of diabetic neuropathy. The authors have now clarified, however, that gabapentin has in fact been licensed for the treatment of neuropathic pain for over two years.