Gestational Duration, and Fetal and Infant Mortality for Twins vs Singletons

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The aim of this research was to study fetal and infant mortality in Sweden between 1973 and 1996 in twins vs singletons in relation to gestational duration. Analysis was of fetal and infant mortality based on the number of pregnancies at risk as the denominator rather than the number of deliveries each week. The analysis was based on information stored at the Medical Birth Registry (MBR), the National Board of Health and Welfare, Stockholm. The MBR keeps records on virtually all pregnancies (> 99%) regarding delivery and neonatal information, and for infant mortality up to 1 year of age. During the study period, 2,206,738 singleton and 52,658 twin births were registered. Risk evaluation was made as odds ratio (OR) with a 95% confidence interval. The material was stratified according to parity, maternal age, year of delivery, and delivery unit. Results showed the OR for twin births before 34 weeks gestation was 6 to 8-fold increased compared with singletons. The OR for fetal mortality was increased in all gestational weeks, and like-sexed twins had a consistently poorer prognosis compared to unlike-sexed. Between 1989–96, unlike-sexed twins had a fetal mortality approaching that of singletons. In conclusion, real progress in reduction of infant mortality in twins may be impossible until the high incidence of preterm births can be decreased. Hypothetically, about 100 twin labors would have to be induced to avoid one fetal death in like-sexed twin pregnancies.

Twins have a perinatal mortality 4–8-fold higher than singletons, including increased early neonatal mortality, due primarily to an increased rate of preterm birth (Bleker & Oosting, 1997; Powers & Wampler, 1996). An additional important contributory factor to this difference is the high rate of antenatal death, the major cause being the twin-twin transfusion syndrome (Blickstein, 1990; Rydhstroem, 1996).

A few authors specifically suggest induction of labor to reduce the risk of fetal death (Bleker & Oosting, 1997; Hamilton et al., 1998; Luke, 1996). The two major text books on twin pregnancy and delivery published during recent years, fail to comment on this issue to any great extent (Keith et al., 1995; MacGillivray et al., 1988), although MacGillivray and coworkers advocate induction of labor at 40 weeks' gestation without giving any supporting reference.

The paucity of twin pregnancies in individual maternity units is a major reason that this issue has never been properly addressed. To overcome this difficulty, a national birth register is needed to generate hypotheses. The purpose of this study is to evaluate the difference in fetal and infant mortality between twins and singletons related to gestational duration using the national birth registry of Sweden. A further purpose is to generate hypotheses to support or reject the concept of induction of labor and delivery in twin pregnancy.

Material and Methods

Information regarding the fetal and infant mortality and duration of pregnancy for all women included in the present study was collected from the Medical Birth Registry (MBR) at the National Board of Health and Welfare, Stockholm. The MBR stores prenatal, perinatal and postnatal data on virtually all singleton and twin pregnancies from 1973 to 1996, including gestational duration. Because of missing data for antenatal deaths before 28 gestational weeks, all comparisons concerned only longer gestational duration.

Compared with the official national statistics, less than 1% of all births are unregistered at the MBR (unpublished information). For fetal deaths the drop-out rate is higher, for twins 3–4%. Thus, the analysis included all surviving twins as well as those that died perinatally. The validity of the MBR data was previously verified in a 0.5% random sample of deliveries from 1974 and 1986 (Cnattingius et al., 1990). In the MBR, gestational duration represents the best estimate based on information regarding last menstrual period, expected date of delivery, corrected expected date of delivery (from ultrasound) and the maternity unit's estimate of gestational duration. Only when information was missing for ultrasound examination in the second trimester or regarding the clinical examination late in the first trimester was the last menstrual period used as a basis for determining gestational duration.

The present analysis comprises 2,206,738 singleton pregnancies excluding those with unknown gestational duration as well as those gestations < 28 weeks and > 41 weeks, respectively. In the preliminary analysis, twins were divided into like-sexed (n = 37,562) and unlike-sexed pairs (n = 15,096) in order to ascertain the difference (if any) in gestational duration.

Odds ratio (OR) was used to estimate the differences between twins and singletons; the 95% confidence intervals were calculated according to Miettinen (1976).

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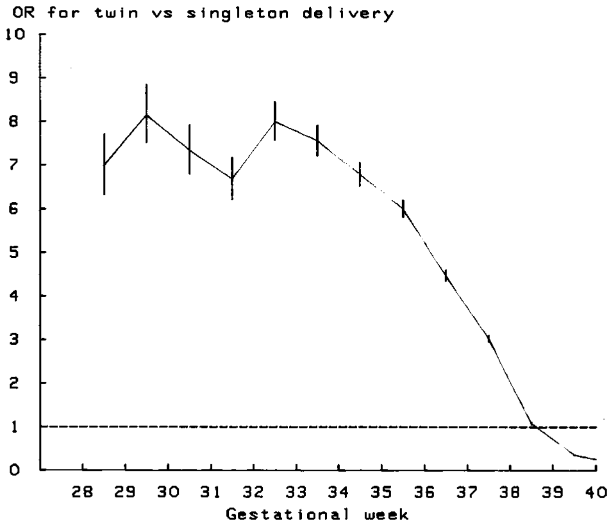

Figure 1

Twin versus singleton birth related to gestational duration in Sweden in 1973–96. OR with 95% confidence intervals.

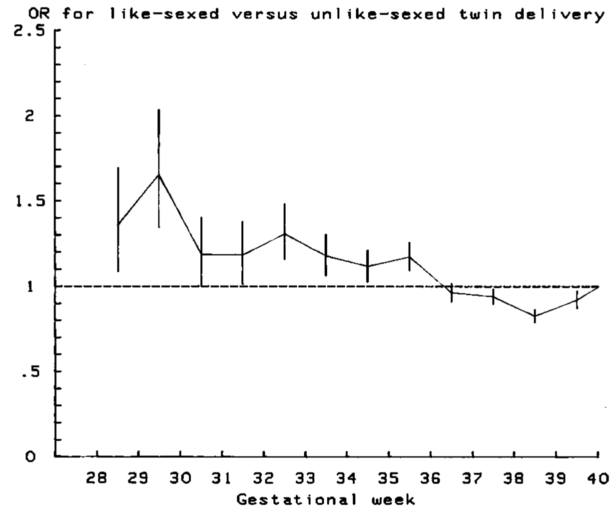

Figure 2

Like-sexed versus unlike-sexed twin birth related to gestational duration in Sweden in 1973–96. OR with 95% confidence intervals.

To control for confounding factors such as parity, maternal age and delivery unit, a stratified analysis was performed according to the Mantel-Haenszel technique (Mantel & Haenszel, 1959).

In most previous studies on fetal death in singleton or twin pregnancy, the number of dead babies was estimated for each week divided by the total number of deliveries that week. As pointed out by Yudkin et al. in 1987 (*vide infra*), this may not be a sound approach. In the present analysis we have used the "at risk" concept, which means that the denominator each week is the number of remaining pregnancies (= not delivered) at risk of fetal death, rather than the number of deliveries that week. The numerator is unchanged. During the study period, no maternity unit in Sweden routinely induced labor in uncomplicated twin pregnancies (unpublished information). Fetal death is defined as a stillborn of at least 28 completed gestational weeks. Infant death (mortality) is defined as an infant dying after birth and up to one year.

Table 1

Numbers of Singleton and Twin Births in Sweden Between 1973 and 1996 Related to Gestational Duration.

Gestational week	Singletons			Twin newborns					
				Same-sexed			Unlike-sexed		
	Total	Fetal death	Infant death	Total	Fetal death	Infant death	Total	Fetal death	Infant death
	n	*n*	*n*	*n*	*n*	*n*	*n*	*n*	*n*
28	2,126	251	500	328	28	96	102	0	24
29	2,661	386	425	446	29	89	112	5	11
30	3,477	471	445	524	36	63	182	4	12
31	4,456	492	406	626	19	53	218	3	9
32	6,197	513	446	1,052	36	46	328	4	15
33	9,167	616	412	1,454	44	37	508	6	12
34	15,142	612	551	2,148	57	43	794	6	16
35	26,447	680	567	3,242	58	36	1,136	10	10
36	52,615	781	688	4,740	43	36	1,988	12	11
37	115,924	804	862	6,986	61	62	2,964	14	16
38	296,501	920	1,236	7,040	52	54	3,284	10	22
39	542,135	923	1,498	4,928	32	22	2,092	12	8
40	678,949	863	1,686	2,972	30	19	1,070	7	6
41	450,941	704	1,209	1,076	11	13	318	2	4
Total	2,206,738	9,016	10,931	37,562	536	669	15,096	95	176

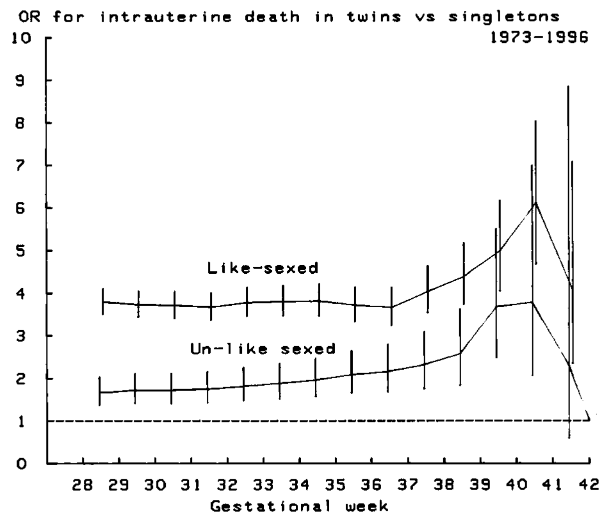

Figure 3

Intra-uterine fetal death in like-sexed and unlike-sexed twin birth vs singleton birth related to gestational duration in Sweden in 1973–96. OR with 95% confidence intervals.

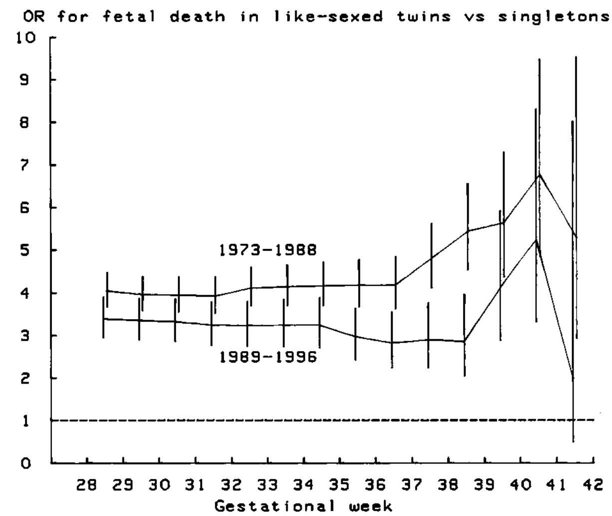

Figure 4

Intra-uterine fetal death in like-sexed twin birth vs singleton birth related to gestational duration in Sweden in 1973–88 and in 1989–96. OR with 95% confidence intervals.

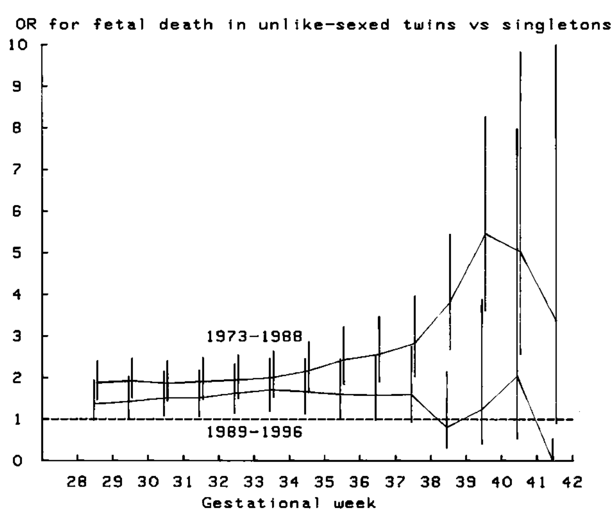

Figure 5

Intra-uterine fetal death in unlike-sexed twin birth vs singleton birth related to gestational duration in Sweden in 1973–88 and in 1989–96. OR with 95% confidence intervals.

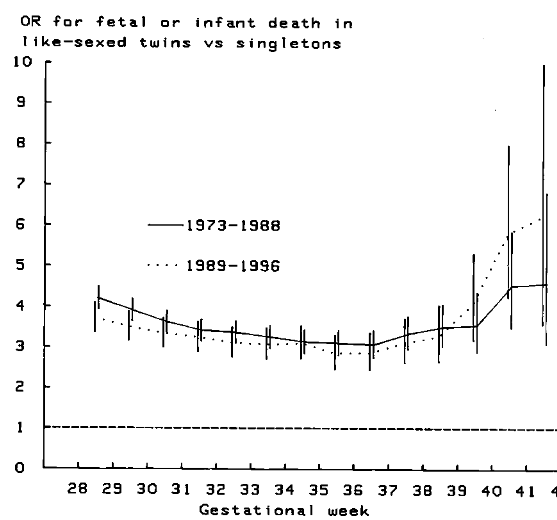

Figure 6

Intra-uterine fetal or infant death in like-sexed twin birth vs singleton birth related to gestational duration in Sweden in 1973–88 and in 1989–96. OR with 95% confidence intervals.

Results

The crude figures used in the analysis are shown in Table 1. Altogether, 2,206,738 singleton and 52,658 twin births were included. For low gestational weeks the OR for twin vs singleton birth was consistently above 6.0 (Figure 1). Only after 38 weeks' gestation was the OR below unity. Like-sexed twins consistently had a significantly increased risk of preterm delivery compared with unlike-sexed twins (Figure 2).

Like-sexed twins had a significantly higher OR for fetal death than unlike-sexed twins when both groups were compared with singletons (Figure 3). The OR for liked-sexed twins was consistently above 3–4, whereas the corresponding figure for unlike-sexed twins reached this high level only at term.

To analyse the effect of year of delivery in greater detail, the material of like-sexed twins was divided into two groups, those deliveries before 1989 and deliveries after 1988, respectively. A considerable reduction in OR for fetal death was observed during the latter period; between 35 and 38 weeks gestation, the reduction was even more pronounced. For unlike-sexed twins, a similar graph emerged but with lower OR (Figure 5), indicating that unlike-sexed twins had a prognosis similar to that of singletons.

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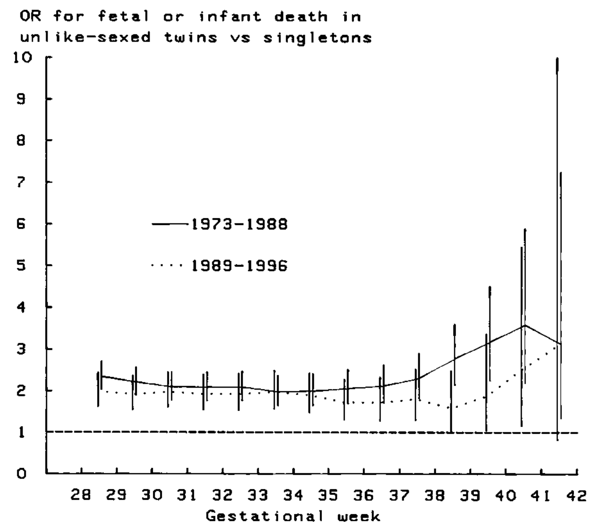

Figure 7

Intra-uterine fetal or infant death in unlike-sexed twin vs singleton birth, related to gestational duration in Sweden in 1973–88 and in 1989–96. OR with 95% confidence intervals.

In terms of combined fetal or infant mortality, no improvement was seen for like-sexed twins in the second compared with the first period (Figure 6). After 39 weeks a higher OR is even evident in the later period. For unlike-sexed twins the prognosis seems to be improved during the second period, irrespective of gestational duration, though without any real significant difference (Figure 7).

Discussion

This paper sought to compare fetal and infant mortality for twins vs singletons and to generate hypotheses to improve prognosis for twins. The significantly increased incidence of preterm delivery for twins compared to singletons prior to 34 weeks in all likelihood explains the significantly increased infant mortality seen in this and all previous studies. The factors responsible for this significant increase in preterm twin delivery are not understood with certainty although Blickstein et al. (2000) recently stressed the concept of an upper limit to uterine volume. In the absence of more exact knowledge explaining why and how preterm labor begins, the reason why twins are born on average 3–4 weeks earlier than singletons is speculative. At present, no form of treatment is able to improve prognosis to any great extent (Gyetvai et al., 1999; MacLennan et al., 1990).

The twin-twin-transfusion syndrome represents a major unique risk factor facing the monochorionic twin pregnancy. It also explains the increased fetal death rate associated with this condition (Blickstein, 1990). As no information exists in the MBR regarding chorionicity, we could only divide the material into like-sexed and unlike-sexed pregnancies. A previous population based study has shown that monozygotic and dizygotic dichorionic pregnancies have similar perinatal mortality (Derom et al., 1995). The pregnancy at risk for the twin-twin-transfusion is the diamniotic (and monoamniotic) monochorionic twin pregnancy, constituting in our population 40–45% of all like-sexed pregnancies. These high-risk pregnancies are invariably monozygotic, as opposed to (proven) dizygotic pregnancies which, at least during the second period, had an only marginally increased fetal death rate in most gestational weeks, compared with singletons (Figure 5).

No real progress has been made in our understanding of this "vascular malformation" since the publication of Schatz (1882) in the late 19th century. The larger, hydropic twin is transfused by the smaller, anemic, growth-retarded twin via deep arterio-venous placental anastomoses connecting the two circulations (Blickstein, 1990). It is claimed that intra-uterine laser coagulation of the placental anastomoses is more effective than amniocentesis for preventing labor in early preterm pregnancy (Hecher et al., 1999).

At term or near term, a more appropriate treatment may be labor induction (Manor et al., 1999). The present figures make it possible to estimate the number of labor induction in pregnancies needed in order to avoid fetal death (Table 1). These calculations are based on the belief that virtually every fetal death is caused by the twin-twin-transfusion syndrome. Ninety-eight labors would have to be induced (2972+1076/30+11) to avoid one fetal death at 40 weeks' gestation (hypothetically on the first day of that week). The corresponding number of inductions at 38 weeks would be 128, and at 36 weeks 121. Obviously, other risk factors for fetal death than like-sex pregnancy (identified with ultrasound) must be involved to reduce the number of inductions. A dissimilarity in birthweight exceeding 4–500 g, or 25%, might be a reasonable limit (Rydhström, 1994). Only twin pregnancies identified in the first or early second trimester as being monochorionic would need to be induced (Blickstein, 1990). One can only speculate that these restrictions might reduce the number of inductions to 20% of the above figures, indicating that at 36 weeks 20–30 twin pregnancies would need to be induced to avoid one fetal death. A truly randomised study testing the effects of labor induction with the aim of reducing perinatal mortality from 2% to 1% (power 0.80, alpha 0.05) would require 4,000 twin pregnancies. Such a study not only would be impracticable, but it would be hazardous to the mother.

Several confounders were taken into consideration in the present study. The dropout rate was less than 1% of all singletons but slightly higher for twins. The dropout rate for pregnancies with fetal death (unpublished information) was higher than 1%, especially regarding twins (3–4%). It is unlikely that misclassification occurred, as the figures for fetal or infant mortality were continually cross-checked with national vital statistics. Another problem is the validity of information on gestational duration held at the MBR. This might represent a problem regarding twins as well as singletons up to the early 1980s before second trimester ultrasound screening was introduced. Presently, > 98% of all pregnancies are examined with ultrasound (Rydhström & Grennert, 1995).

In the present analysis we used the "at risk" concept (Yudkin et al., 1987). Fetuses at risk of fetal death at a specific gestational age must include all live fetuses at that gestational age. Rates of fetal death at each gestational week represents the probability of fetal death among babies born at each gestational age and fail to include all fetuses actually at risk of death in utero. Minakami and Sato (1996) using the total number of deliveries each week as the denominator found twins at 38 weeks gestation to have a perinatal mortality similar to singletons at 43 weeks gestation. Their conclusion was that an appropriate date of delivery might be 37 to 38 weeks' gestation. In this analysis no separation was made of like-sexed vs unlike-sexed twins. Neither was the confounding effects of parity, maternal age, delivery unit or year of birth on perinatal mortality controlled for. For these reasons our results are difficult to compare.

In conclusion, the present study has shown that twins have a significantly higher fetal and infant mortality than singletons in most gestational weeks. This is due to an increased rate of preterm birth and a significantly increased risk of fetal death. At present, the only way to reduce fetal mortality at term may be to induce labor and delivery. However, to achieve a significant reduction, a large number of twin pregnancies would require induction.

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