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B Ray and M P Ward Platt

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Mortality of twin and singleton livebirths under 30 weeks’ gestation: a population-based study

B Ray,1 M P Ward Platt2

ABSTRACT

Objective: To determine the mortality rates of liveborn twins compared with singletons of less than 30 weeks’ gestation in relation to gestational age, mode of delivery and year of birth in a geographically defined population.


Results: Twins and singletons had similar mortality rates except at the extreme of gestation (23–25 weeks) where twins had higher infant mortality (OR 2.04, 95% CI 1.37 to 3.02). This higher rate was attributable to early and late neonatal deaths (OR 1.86, 95% CI 1.28 to 2.72, and 2.11, 95% CI 1.13–3.94, respectively). When analysed in two epochs, the excess mortality was confined to babies born in 1998–2001. There was no effect of gender or chorionicity.

Conclusions: The excess mortality among twins of less than 30 weeks’ gestation was confined to neonatal deaths in babies of 25 weeks or less, and to the earlier epoch (1998–2001). In the modern era, there appears to be no excess mortality in neonates less than 30 weeks’ gestation when compared with singletons.

The UK Birth Statistics in 2004 showed that the likelihood of women having multiple births was higher at every age in 2004 than 10 years’ previously, and data from our own region are in line with this continuing trend.1 Women aged 40 and over experienced the highest multiple maternity rate (21.6/1000 all maternities).2 It is known that multiple pregnancies are associated with a higher risk of perinatal death than singletons, which may be the result of many factors,3–5 but many of the excess deaths are ultimately due to prematurity.6 7

Some of the existing studies of twinning in relation to gestational age-specific mortality show that extremely premature twins do not suffer more deaths than singletons,8–10 but others have shown an increased mortality compared with singletons.11 12 Furthermore, birth weight does not necessarily account for any twin disadvantage in very preterm babies. Garite et al13 demonstrated that statistically significant differences between mean weights of twins compared with singletons occur only from 32 weeks although Alexander et al14 suggested the difference may start at 28 weeks of gestation.

Most of the deaths in preterm babies now occur at gestational ages of 29 weeks or less, with very low mortality from 30 weeks onwards.15 We therefore focused this study on the mortality outcome in liveborn twins and singletons born at less than 50 completed weeks in a defined geographical area. We wished to ascertain any associations related to mode of delivery, gender and chorionicity. We also investigated any changes in gestation-specific mortality over the time course of the study (1998–2005).

METHODS

To ascertain the twins we used the Multiple Pregnancy Register.1 To ascertain all deaths we used data from the Perinatal Morbidity and Mortality Survey.15 The registers have been approved by ethics committees and have clearance from the Patient Information Advisory Group (PIAG) to hold named patient information without individual consent under section 60 of the Health and Social Care Act (2001).

Denominator data on numbers of singleton livebirths were obtained from the Regional database of neonatal admissions for intensive care held at the neonatal unit of Royal Victoria Infirmary, Newcastle upon Tyne. This database collects audit data for all admissions for neonatal intensive care in the four regional neonatal intensive care units. We also enlisted the help of the special care units in the other peripheral hospitals in the region to ascertain the existence of any babies under 50 weeks who were not transferred to one of the
four intensive care units and who would not have been captured by the routine audit database; however, no patient identifiable data were used nor did we access any health records.

The geographical area is that of North Cumbria, Northumberland, Tyne and Wear, Durham, Darlington and Teesside. We used data from January 1998 to December 2005 and excluded all babies with significant congenital anomalies by cross-checking with the Northern Congenital Abnormality Survey (NORCAS) and using the definitions of the European Surveillance of Congenital Anomalies (EUROCAT) central registry (see http://www.eurocat.ulster.ac.uk/pdf/EUROCAT-Guide-1.3.pdf). We also excluded babies born in this region but resident outside it. Twinning was determined according to the order of delivery. We categorised the timing of death using the standard epidemiological definitions of early, late and post-neonatal death.

For analytical purposes, the babies were grouped by gestational age bands 23–25, 26–27, and 28–29 weeks. Data are presented as absolute numbers and rates per 1000 livebirths or per 1000 survivors where appropriate. Differences in outcome were calculated using the Fisher exact test and are presented as odds ratio and confidence intervals. SPSS V.13.0 and Epi-info statistical software were used to analyse the data.

RESULTS

In the 8-year period from January 1998 to December 2005, 2207 babies were born alive at between 23 weeks and 29 weeks of gestation in the region; 34 higher order multiple births were excluded from the study. In the remaining 2173 liveborn babies, 1674 were singletons and 499 were twins. A total of 156 babies (singletons = 136, twin I = 7 and twin II = 13) were excluded for congenital anomalies. This left a total of 479 twins (twin I = 245 and twin II = 234) who were compared with 1538 singletons (fig 1).

The characteristics of the study population are presented in table 1. The median gestations, birth weights, gestation distribution, gender ratio and rate of caesarean section delivery are comparable between the groups. There was a male preponderance of 56% in twins and 54% in singletons.

After subdividing into the gestation bands 23–25, 26–27, and 28–29 weeks, the mortality outcome was computed for 0–7 days, 7–28 days, and 29–365 days (table 2). Twins had an overall higher mortality rate compared with singletons only in the 23–25 weeks band (OR 2.04), with the statistically significant excess mortality confined to the early and late neonatal periods.

Table 3 shows the effect on mortality rates by mode of delivery for twins and singletons. Only among the 23–25 weeks babies was there any relationship with mode of delivery.
born vaginally having a mortality odds ratio of 4.06 (CI 2.46 to 6.70) relative to caesarean section.

We did not find any effect of gender either for all gestations or among babies of 23–25 weeks. There was no effect of choriopticity. Figure 2 illustrates the gestational age-specific mortality for twins and singletons from 1998 to 2001 and 2002 to 2005. There is noticeable improvement in both the twins and singleton mortality outcome between the two epochs, with convergence of outcomes at a gestation of 27 weeks.

**DISCUSSION**

We have demonstrated that any disadvantage to being a twin, in this population of very premature babies, is confined to the extreme of viability and to the epoch of 1998 to 2001, rather than in more recent years. Indeed, inspection of fig 2 suggests that in the earlier epoch, the disadvantage to being a twin persisted up to 26 weeks of gestation, and the impression given by table 2, that the higher mortality is confined to 23–25 weeks, is an artefact of the pre-study choice of gestational age bands for the analysis. The figure also suggests that any disadvantage from being a twin has now disappeared.

While it is true that in general twins have more congenital anomaly than singletons, our data showed an opposite trend. This might have been because we have focused on a highly selected set of births, those occurring very preterm. We are not aware of any other data in this highly selected group to suggest whether the ratio of congenital anomaly in twins-singletons is similar to or different from that when all babies are considered. Alternatively, perhaps the twins with congenital anomalies had more antenatal or early pregnancy loss, or that the reasons why singletons and twins go into preterm labour may themselves be different, which may also help to account for the unexpectedly different rates of malformation in the two groups. Monochorionic twins are known to be at higher risk during the pregnancy, and it has been suggested (from unit-based data) that they suffer more postnatal deaths compared with dichorionic twins, but our observations, confined to liveborn twins, have failed to confirm this.

The strength of our study is that it presents population-based data in a society where high-quality medical facilities are readily accessible to all. The neonatal service of the whole region is provided by a single neonatal network, which assures a degree of uniformity of management. The use of data from reliable regional databases, together with cross-checking at the level of individual units, means that we can be confident about the quality of the data.

Our study has a number of limitations. We may have missed a very small number of babies born outside the region to mothers resident in the region who received all their neonatal care outside the region, which may affect our denominator numbers. Although when considering the whole group we compared 479 twins with 1538 singletons over an 8-year period, the numbers are quite small when they are subdivided into groups. Hence some of our results need cautious interpretation. Also some data were missing such as birth weight (singletons 4%), mode of delivery (singleton 16% and twins 7%) and choriopticity (17%). Furthermore our data do not allow us to correct for other confounders, but in any case this does not matter for those more mature babies in whom being a twin or singleton had no impact on mortality. It is only of importance when trying to explain the difference between twins and singletons in the least mature babies, where there are too few subjects to allow for a meaningful multivariable analysis even if we had access to the relevant obstetric data.

We would be particularly cautious about reading too much into the findings for mode of delivery. In the first place the numbers are small, and in the second, the decision-making for choosing a particular mode of delivery is complex, so the factors giving rise to the apparent association probably have more to do with the reasons for choosing the mode of delivery than the delivery itself.

Our data are compatible with both the view that twins are at a disadvantage and the view that they are not. It all depends which period of time is chosen for study. However, we do not feel that we can confirm the notion that twins actually do better than singletons. An analysis of birth registry data in Sweden11 in 1992 showed similar findings to ours, although this must be interpreted with caution because we defined our cohort in terms of gestational age, not birth weight. On the other hand, studies by Shinwell et al14 and Donovan et al15 using babies <1500 g showed no significant difference in the mortality outcome between singletons and twins. However, analysing our own data by birth weight, with a cut-off at 700 g, gave a similar result for the infant mortality rate among twins to that of singletons in the least mature babies, where there are too few numbers. Although when considering the whole group we compared 479 twins with 1538 singletons over an 8-year period, the numbers are quite small when they are subdivided into groups. Hence some of our results need cautious interpretation. Also some data were missing such as birth weight (singletons 4%), mode of delivery (singleton 16% and twins 7%) and choriopticity (17%). Furthermore our data do not allow us to correct for other confounders, but in any case this does not matter for those more mature babies in whom being a twin or singleton had no impact on mortality. It is only of importance when trying to explain the difference between twins and singletons in the least mature babies, where there are too few subjects to allow for a meaningful multivariable analysis even if we had access to the relevant obstetric data.

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Finally, it is encouraging to note that the number of deaths in extreme preterm gestation appears to have fallen in twins as well as singletons, and that the apparent disadvantage of very preterm twins was greatly reduced in the more recent epoch (2002–5).
REFERENCES


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