Sudden Infant Death Syndrome Among Twins

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Background: Sudden infant death syndrome (SIDS) is a major contributor to infant mortality. Previous studies have suggested that infants born of twin pregnancies are at greater risk for SIDS and that a twin who survives after a co-twin dies is at increased risk for SIDS.

Objective: To attempt to confirm the increased risk of SIDS among and within twin pairs through the use of US vital statistics data.

Methods: We analyzed data from the US-linked birth and infant death certificate tapes for the years 1987 through 1991 to determine the risk of SIDS in twin births compared with singleton births and to describe the characteristics of twin pairs in whom SIDS occurred. The analysis was limited to live births with weights of 500 g or more and gestational ages of 24 weeks or more. We used an algorithm to match co-twins (infants within a twin pair) to measure sex and birth weight concordancy; to identify twin pairs, in which one or both twins died of SIDS; and to examine, when both twins died, whether they died on the same day.

Results: There were 23,464 singleton SIDS deaths and 1,056 twin SIDS deaths during the 5-year period. The crude relative risk for SIDS among twins compared with singleton births was 2.06 (95% confidence interval, 1.94-2.19). The adjusted relative risk independent of birth weight and sociodemographic variables was 1.13 (95% confidence interval, 0.97-1.31). We successfully matched the co-twins of 172,029 twin pregnancies. Of these, 767 were twin pregnancies in which one or both twins died of SIDS. Among the 767 twin pregnancies in which one or both twins experienced SIDS, there were only 7 in which both twins died of SIDS (rate ratio, 4.0 per 100,000 twin pregnancies). In only 1 of these 7 did both twins die on the same day (rate ratio, 0.58 per 100,000 twin pregnancies). The relative risk for a second twin dying of SIDS was 8.17 (90% confidence interval, 1.18-56.67).

Conclusions: Independent of birth weight, twins do not appear to be at greater risk for SIDS compared with singleton births. In addition, the occurrence of both twins dying of SIDS is uncommon, and the occurrence of both twins dying on the same day is extremely uncommon.

Editor’s Note: This simple, eloquent study shows the importance of examining all covariables to determine which is/are (most) important.

Catherine D. DeAngelis, MD

Sudden Infant Death Syndrome (SIDS) was the attributed cause of 3397 infant deaths in 1995 and is the leading cause of death in the postneonatal period.1 The underlying mechanism for SIDS is unknown, but epidemiological studies have pointed to several sociodemographic associations2; associations with environmental conditions, including exposure to cigarette smoke3-5; temperature and seasonal conditions6-8; prone sleeping position and soft bedding9,10; associations with preterm and low-birth-weight births11-13; and an association with twin births.14,15

The study of SIDS among twin births offers a unique opportunity to examine the relationship of the risk of SIDS among temporally related siblings. Although the later death of a surviving co-twin from SIDS is reported as uncommon, it has been suggested16 that the death of both twins on the same day from SIDS may be relatively more frequent. Several other reports17,18 have documented the occurrence of simultaneous SIDS among twins. In addition, the study of SIDS among twins offers the opportunity to evaluate hereditary and environmental interactions. So far, the failure to observe a greater likelihood of sex concordancy among twin pairs in which both twins have died of SIDS points more to the likelihood of environmental factors than hereditary factors being causal in situations in which both twins die of SIDS.15,16

To compare the incidence of SIDS among twin births with the incidence of SIDS among singleton births, to describe the characteristics of twin pairs with SIDS, and to obtain an estimation of the prevalence of simultaneous SIDS in a large population, we carried out an analysis of the...
MATERIALS AND METHODS

We used data from the US-linked birth and infant death certificate tapes obtained from the National Center for Health Statistics, Hyattsville, Md, for the years 1987 through 1991. On these tapes, births are indicated as being part of a twin pregnancy; but there are no twin pair identifiers so that the first and second members of a pair can be linked. To link twin pairs, we used an algorithm developed by Fowler et al. The matching algorithm uses information available on the live birth record and the infant death record that includes state and county of birth; mother’s race, state of birth, level of education, age, marital status, and month of beginning prenatal care; and father’s race, age, and level of education. During the 5-year period, we were able to match 87% of the twins to their respective co-twin using the algorithm described. Among the twins dying of SIDS, the matching rate was 74%.

In our analysis, we defined SIDS as the death of an infant ascribed an International Classification of Diseases, Ninth Revision (ICD-9) code of 7980, having an autopsy, weighing greater than 500 g, and being 24 weeks’ gestational age or more. All live births weighing less than 500 g or being less than 24 weeks’ gestational age were excluded from the analysis.

Unmatched data are presented to compare SIDS rates between singleton and twin births in the Figure. For the unmatched data, rates are presented as deaths per 1000 live births. Thus, one twin pregnancy contributes 2 live births. Unmatched data for the year 1991 are presented in Table 1 to compare the distribution of selected characteristics between singleton and twin births and to examine SIDS rates by the selected characteristics. Because of the large sample size that 1 year of US vital statistics data provided, we rationalized that the analysis of data from 1 year would be adequate to demonstrate any significant differences between singleton and twin births for the selected characteristics. Matched data are presented to provide characteristics of the twin pairs. For the matched data, rates are presented for twin pregnancies; thus, 2 twins represent one twin pregnancy.

Analyses were accomplished with statistical analysis software. For discrete variable comparisons, \( \chi^2 \) tests for general association and linear trends were used. Student \( t \) tests were used for the comparison of 2 continuous variables. Ninety-five percent confidence intervals (CIs) for rate ratios were calculated using standard methods for proportions. Crude relative risks were calculated using Mantel-Haenszel estimators and test-based 95% CIs. Multivariate logistic regression was used to estimate the relative risk of SIDS among twins compared with singleton births independent of potential confounders. An arbitrary level of statistical significance was set at \( P \leq .05 \). To test the hypothesis that surviving members of a twin pair are at greater risk of SIDS than the risk for either member of the pair at birth, we developed an estimator of the relative risk that reflects the special sample structure of twin pairs (available from the authors).

RESULTS

There were 23,464 singleton SIDS deaths and 19,993,791 singleton live births; 10,56 twin SIDS deaths and 425,941 twin births were available for analysis during the 5-year period. The singleton and twin birth SIDS rates are shown in the Figure. For the 5-year period, the overall singleton SIDS rate was 1.2 deaths per 1000 live births compared with 2.5 deaths per 1000 live births for twins. The crude relative risk for a twin SIDS death compared with a singleton SIDS death was 2.06 (95% CI, 1.94-2.19). During the 5-year period, there was a statistically significant decreasing trend in the SIDS rate for singleton births (\( P < .01 \)), but not for the SIDS rate associated with twin births.

We used data from the year 1991 to examine the distribution of population characteristics between twin births and singleton births and to examine the relative risk of SIDS between twin and singleton births by the population characteristics (Table 1). Although the distribution of population characteristics for race, maternal age, and maternal education level did not appear to differ substantially between twin and singleton births, these small differences did attain statistical significance because of the large sample size. The birth weight and gestational age distribution of twin births, however, differed remarkably from singleton births. Crude relative risks for SIDS between twin and singleton births calculated for each strata of population characteristic demonstrated twin births to be at greater risk for SIDS except for birth weight and the lowest strata of gestational age (Table 1). The multivariate logistic regression relative risk for SIDS among twins compared with singleton births adjusted for birth weight, race, maternal age, and maternal education level was 1.13 (95% CI, 0.97-1.31).

During the 5-year period, there were 171,262 matched twin pregnancies in which both twins survived and 767 matched twin pregnancies in which one or both twins died of SIDS. Twin pregnancies in which one or both twins died of SIDS were more likely to have been associated with a racial distribution that consisted...
of a higher proportion of blacks and a higher proportion of mothers with 12 years of education or less (Table 2). The proportion of twin pregnancies with female-female concordancy was higher among twin pregnancies with a SIDS death compared with that among twin pregnancies in which both twins survived. The mean birth weight for both twins and the gestational age were lower for pregnancies with a SIDS death compared with pregnancies in which both twins survived, while the discordancy in birth weight within twin pairs was greater for the pregnancies with SIDS deaths.

During the 5-year period, of the 767 pregnancies with SIDS deaths, there were only 7 in which both twins died of SIDS (Table 3). Of these 7 pregnancies in which both twins died of SIDS, there was only 1 in which both twins died on the same day. Thus, the probability of both twins dying of SIDS is 4.0 per 100 000 twin pregnancies (95% CI, 3.9-4.1), and the probability of both twins dying of SIDS on the same day is 0.58 per 100 000 twin pregnancies (95% CI, 0-1.72). These figures would be equivalent to rate ratios of 0.004 per 1000 twin births and 0.00058 per 1000 twin births, respectively. Using a special estimator to account for the trinomial conditional probabilities in twin pregnancies, we also calculated the relative risk of a second twin dying given that one twin had already died of SIDS. The relative risk that we estimated was 8.17, with 95% CIs of 1.18 to 56.67.
Table 4. Characteristics of Twin Pregnancies in Which Both Twins Died of SIDS*

<table>
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<tr>
<th>Pair</th>
<th>Race</th>
<th>Birth Order</th>
<th>Sex</th>
<th>Gestational Age, wk</th>
<th>Birth Weight, g</th>
<th>Age at Death, wk</th>
<th>Difference in Age at Death, wk</th>
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<td>3</td>
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</table>

* SIDS indicates sudden infant death syndrome. The mean ± SD gestational age was 37.6 ± 1.6 weeks; birth weight, 1882 ± 389 g; age at death, 13.4 ± 5.8 weeks; and difference in age at death, 6.0 ± 5.4 weeks.

We examined several characteristics of twin pregnancies in which both twins died of SIDS (Table 4). All but 1 of the 7 twin pregnancies were concordant for sex; the mean weights of the twins appeared to be less than the mean weight of twin pregnancies in which only one twin had died of SIDS, and the mean gestational age appeared higher than that of twin pregnancies in which only one twin died of SIDS. Based on a standard reference for fetal growth, these twins were all small for gestational age.2 The mean postnatal age at death was 13.4 weeks, and the deaths of the twin pairs were separated by a mean of 6 weeks.

Among the 7 twin pregnancies in which both twins died but only one died of SIDS, the other causes of death included a perinatal cause (1 twin), injury (1 twin), pneumonia (2 twins), acute renal failure (1 twin), sickle cell anemia (1 twin), and an unknown or unspecified cause (1 twin). None of these other causes of death occurred on the same day as the SIDS death, and the deaths were separated by a mean of 14 weeks (SD, 11 weeks).

We report an unadjusted 2-fold higher rate of SIDS among twins compared with singleton births. These results are compatible with other studies in the literature and point to the generally high risk that twins have for all forms of infant mortality. Froggatt et al speculated that the increased frequency of SIDS among twins may be related to the higher prevalence of low birth weight and prematurity in the twin population. Malloy and Hoffman, using a portion of the data set reported herein (1987 US-linked tapes), demonstrated that, following adjustment for birth weight, race, sex, maternal age, marital status, maternal education level, and gravidity, infants of multiple pregnancies were at no greater risk for SIDS than infants born of singleton pregnancies (odds ratio, 0.91; 95% CI, 0.78-1.06). Data from the year 1991 presented in this report again demonstrate that when birth weight is controlled, the risk for SIDS does not appear to be greater for the twin population of live births.

Compared with twin pregnancies in which both twins survived, pregnancies in which one or both twins died of SIDS were noted to occur more frequently in the black population and to be more prevalent among mothers with 12 years of education or less. These sociodemographic variables have been previously reported as risk factors for SIDS among singleton births. Compared with twin pregnancies in which both twins survived, twin pregnancies in which one or both twins died of SIDS had lower birth weights, greater discordancy in weights, and lower gestational ages. Beal also observed the more frequent occurrence of birth weight discordancy in twin pairs in which there was one SIDS death. Owen et al reported a lower birth weight, greater discordancy in the birth weight, and shorter gestations in those with SIDS vs their siblings. The small mean differences in birth weight (266 g) and gestational age (5 days) between surviving twin pairs and twin pairs that incurred at least one SIDS death are not intended to be interpreted at a clinical level, but rather point out how these 2 groups differ and provide information for further hypothesis generation about the meaning of birth weight and gestational age differences in the pathophysiological characteristics of SIDS.

We observed a much lower probability of both twins dying of SIDS than reported in previous studies. Beal, in an extensive review of the literature on the subject of SIDS among twins, observed that among 625 twins whose co-twin had died of SIDS, 6 subsequently died of SIDS (rate ratio, 9.6 per 1000 twin births). She also reported that among 637 twin infants whose co-twins died of SIDS, there were 12 twins who died of SIDS on the same day as their co-twin (rate ratio, 18.8 per 1000 twin births). This compares with rate ratios of 0.004 per 1000 twin live births and 0.00058 per 1000 twin live births for both twins dying and simultaneous SIDS, respectively, reported in our analysis. We speculate that because these earlier studies were based on case series and small regional samples, selection biases account for the appearance of a much higher prevalence of both twins dying of SIDS and simultaneous SIDS than exists when an entire birth cohort is analyzed.
Twins provide a unique opportunity to study the occurrence of SIDS among siblings that are temporally related. We calculated a relative risk of 8.17 for a second twin dying of SIDS given that the first twin had died. We acknowledge that this point estimate may be imprecise as suggested by the wide CIs. These wide CIs are a function of the small number of twin pairs in which both twins died of SIDS. However, given the lack of information on this subject, the point estimate we have derived provides the most reliable estimate of risk for subsequent SIDS with a twin pair currently available in the literature. The relative risk of 8.17 appears to be compatible with the risks associated with subsequent sibling deaths from SIDS currently reported in the literature. Studies25,26 have estimated the risk of recurrence of SIDS in siblings to vary from less than 2-fold to a 10-fold increase in risk. More recent studies27,28 suggest a risk of recurrence of about 6.0. Thus, the occurrence of a second twin dying of SIDS does not appear to be any greater than what has been reported for non-twin siblings.

Among twin pregnancies in which both twins died, we observed a high sex concordancy rate, with a female predominance; these infants had much lower birth weights than among twin pairs in which only one infant died of SIDS; and all were growth retarded or small for gestational age. Other reports of SIDS among twins have failed to show sex concordancy either in pairs in which both twins died of SIDS or among pairs in which only one of the pair died of SIDS.15,16 Given our small sample size of SIDS in which both twins died, it is difficult to draw any inferences about the likelihood that the observation of concordancy among the twin pregnancies in which both twins died implies a hereditary component to the disease process.

A limitation of this study is that with the use of vital statistics data we cannot guarantee that the cause of death has been accurately ascribed. We have attempted to be more critical in our definition of SIDS by using only those cases in which an autopsy was performed. Nonetheless, we cannot assure that all the deaths reported as caused by SIDS had death scene investigations and reviews of the medical records of those with SIDS as a means of attaining a most correct ascertainment of SIDS.26 Only 4 states (California, Minnesota, Missouri, and New Mexico) have detailed written protocols for a SIDS scene investigation.29 The strength of the use of vital statistics data, however, lies in the broad spectrum of the US population that the information is drawn from and the large sample size that it provides to more accurately estimate the prevalence of rare events.

In summary, we observed that, although the incidence of SIDS in the twin population is higher than that in the population of singleton births, this increased risk is a function of the increased prevalence of low-birth-weight infants in the twin population. The probability that both twins may die of SIDS is extremely small, and the probability of both twins dying of SIDS simultaneously is even smaller. The risk of a second twin dying of SIDS given that a first twin has already done so does not appear to be any greater than the risk of a temporally unrelated sibling dying of SIDS. We speculate that environmental factors may play a larger role in SIDS deaths among twins than hereditary factors and that attention to the same precautions for SIDS prevention among infants of single pregnancies, such as infant supine sleep position, are appropriate for infants of twin pregnancies.

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