Sudden infant death syndrome: seasonality and a biphasic model of pathogenesis

Anne-Louise Ponsonby, Terence Dwyer, Michael Edwin Jones

Abstract

Study objective—This paper examines the relationship between season, age, and the sudden infant death syndrome (SIDS). It provides a theoretical model for the pathogenesis of SIDS and uses it as a framework to consider risk factor mechanisms.

Design—A case series analysis was used to examine season and age in relation to SIDS and seasonal pattern and age at death distribution of perinatal risk factors.

Setting—The source population for the SIDS cases in this study was all live births in the state of Tasmania, Australia, 1975 to 1987 inclusive.

Subjects—Cases were all infants born 1975 to 1987 who died of SIDS on whom birth notification information was available (n = 348). The live birth cohort 1980–87 (n = 55 944) was used as the control population for risk factor identification.

Measurements and main results—The median ages of death for spring, summer, autumn, and winter born infants were 115, 103–5, 91 and 78 days. Spring and summer born infants died at a significantly older median age than winter born infants. The month of birth distribution of SIDS cases did not alter significantly from a uniform, non-seasonal distribution (P > 0.25) but month of death was seasonally distributed (P < 0.01). Premature and low birthweight infants died at an older median age (P < 0.05) than term and non-low-birthweight infants. An excess of male infant deaths and infant deaths to older mothers occurred during winter (P < 0.05).

Conclusions—The pathogenesis of SIDS can be represented as a biphasic model with three pathways of risk factor operation. In this study, season influenced the age at death of SIDS infants. We propose that risk factors with a strong seasonal distribution are likely to be operating in the postnatal period.

Although the pathogenesis of the sudden infant death syndrome (SIDS) remains unclear many researchers believe it to be a biphasic event. Antenatal factors may cause the infant to be physiologically vulnerable.1 Such a vulnerable infant may then require environmental loading factors to trigger a SIDS event during the postnatal period.2 The age at death distribution of SIDS is unusual, with low risk during the neonatal period, a marked increase from the second until the fourth postnatal month, and a decline thereafter. The age at death distribution is thought to reflect a development physiological process which places the infant at risk of SIDS, although this has been disputed.3 4 Seasonal variation in the incidence of SIDS has been well documented, with an increase in cases during the winter months. Recent work in Sweden and England has concluded that the seasonal pattern of SIDS death is predominantly associated with variation in month of death rather than in month of birth.5 6 Different hypotheses to explain the winter SIDS excess have been proposed. These include an association with viral illness, hypothermia, and hyperthermia.7 A winter excess of SIDS cases in Tasmania has previously been described.8 9 This paper outlines a study of relationships between season, age, and perinatal risk factors for SIDS. A theoretical model of SIDS pathogenesis is proposed.

Methods

MATERIALS

This study examined all resident SIDS deaths among infants born in Tasmania during the years 1975 to 1987 inclusive. It was conducted retrospectively by a review of infant records, in particular the database of the Tasmanian obstetric and perinatal audit.10

A SIDS case was defined as the sudden death of an infant or young child which is unexpected by history and in which a thorough necropsy examination fails to demonstrate an adequate cause of death.11 Among infants born in 1975–1987 inclusive we identified 353 resident SIDS deaths. All infants dying suddenly and unexpectedly had received a necropsy examination. The SIDS incidence was 3.64 per 1000 live births.

A statutory notification of birth form has been collected on all deliveries since 1974. It contains sociodemographic, obstetric, and perinatal information. The birth notification database is managed by the Department of Obstetrics and Gynaecology, University of Tasmania and the Tasmanian Department of Health Services. For the time period 1975 to 1987, birth notification data were obtained on over 99% of the 96 880 live births in the State. Birth notification data were also available on 348 of the 353 infants who later died of SIDS, representing 98.6% of such infants.

ANALYSIS OF THE DISTRIBUTION OF SIDS CASES BY MONTH OF DEATH

Infant date of birth, date of death, and sex were obtained for the SIDS cases. Frequency tables of adjusted month of birth and adjusted month of
The effect of season of birth and season of death on the age at death distribution of SIDS

The adjusted months of birth were grouped into seasons. For example, the adjusted months 1, 2, and 12, corresponding to January, February, and December, were grouped as summer. The age at death distribution was examined for each season of birth. As the age at death distribution is not normally distributed, the median rather than mean age at death was used to describe the average age at death. The rank transformation was used and a conventional analysis of variance conducted to assess the overall significance of any variation in average ranked age at death for the four seasons of births. The differences between the four groups of infants born in the different seasons with regard to median age at death were examined using the Bonferroni multiple comparison test. Age at death was also grouped by season of death and analysed in the same way.

Figure 1 SIDS cases by month of birth, Tasmania 1975–1987

Table 1 Birth notification factors associated with an increased risk of SIDS in Tasmania

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Reference group</th>
<th>Significance level</th>
<th>Unadjusted odds ratio (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>Female</td>
<td><em>p &lt; 0.001</em></td>
<td>1.48 (1.20–1.83)</td>
</tr>
<tr>
<td>Birthweight &lt; 2500 g</td>
<td>Birthweight ≥ 2500 g</td>
<td><em>p &lt; 0.001</em></td>
<td>3.02 (1.75–5.22)</td>
</tr>
<tr>
<td>Gestation ≥ 36 weeks</td>
<td>Gestation &gt; 36 weeks</td>
<td><em>p &lt; 0.001</em></td>
<td>2.79 (2.07–3.76)</td>
</tr>
<tr>
<td>Multiple birth</td>
<td>Single birth</td>
<td><em>p &lt; 0.001</em></td>
<td>2.30 (1.40–3.80)</td>
</tr>
<tr>
<td>Multiparity</td>
<td>Primiparity</td>
<td><em>p &lt; 0.05</em></td>
<td>1.27 (1.01–1.59)</td>
</tr>
<tr>
<td>Maternal age &lt; 20 years</td>
<td>Maternal age ≥ 20 years</td>
<td><em>p &lt; 0.001</em></td>
<td>2.53 (1.97–3.26)</td>
</tr>
</tbody>
</table>

Figure 2 SIDS cases by month of death, Tasmania 1975–1987

The relationship of perinatal risk factors for SIDS to season of death and age at death

Birth notification details were obtained for the cases (n = 348) and a large set of control infants (n = 55 944). The control group were all infants born live 1980–1987 inclusive. Control infants for earlier years were not selected because their birth notification data were not on the computerised database.

The exposure disease associations of birth notification variables were examined by 2 × 2 contingency tables. Unadjusted odds ratios with 95% Cornfield confidence intervals were calculated for each risk factor. This screening process identified variables which discriminated significantly between cases and controls (table I). For each of the two levels of the identified exposure, seasonal homogeneity of SIDS cases was examined using the X² test. Median age at death was also examined using the Kruskal-Wallis test.

Results

The seasonal distribution of SIDS analysed by month of birth and month of death

Figure 1 shows that the month of birth distribution for SIDS cases did not differ significantly from a uniform, non-seasonal distribution (X² = 12.7, p > 0.1). Further analysis fitted a generalised linear model, specifically looking for sinusoidal seasonality, and detected no significant effect (X² = 5.2, p > 0.05). However, the month of death distribution (figure 2) of SIDS cases did display seasonality with a winter peak (X² = 27.7, p < 0.01). The test for seasonality following a sinusoidal pattern was also significant (X² = 24.8, p < 0.001).

The age at death distribution differed by season of birth (fig 3). Thirty per cent of SIDS infants born in...
Seasonality and pathogenesis of SIDS

Spring and 17% of sids born in summer died at an age greater than six months. This compares with 9% and 6% of sids infants born in autumn and winter respectively. The median ages of death for spring, summer, autumn, and winter born infants were 115, 103-5, 91 and 78 days respectively. The multiple comparison test concluded that spring and summer born infants died at a significantly older age than winter born infants (table II). However, the age at death distribution did not differ by season of death. None of the differences between the median ages of death for each pairwise comparison of seasons of death were significant at the 5% level. The median age at death did not differ significantly by season of death when the overall variation was considered [F test: F value (3,344) = 1; p > 0.4].

The relationship of perinatal risk factors for SIDS to season of death and age at death

The seasonal patterns of the perinatal characteristics of the sids infants are outlined in table III. The seasonal distribution of each risk factor is compared to the seasonal pattern of the corresponding reference group. The risk factor “male sex” showed a stronger seasonal pattern ($\chi^2 = 22.90$, $p < 0.001$) and higher winter: summer ratio ($\chi^2 = 4.62$, $p < 0.05$) than the reference group of female infants. Female infants did not show a seasonal pattern ($\chi^2 = 3.60$, $p > 0.05$). Sids infants born to young mothers (<20 years) showed no seasonal pattern ($\chi^2 = 1.71$, $p > 0.05$) and a lower winter:summer ratio ($\chi^2 = 5.1$, $p < 0.05$) than the sids infants born to older mothers. The median age at death was calculated for each of the risk factors. Premature infants (<36 weeks) died at an older median age (112 days) than non-premature infants (92 days). Low birthweight infants (<2500 g) died at an older median age (114-5 days) than heavier infants (91 days). The difference in median age at death was significant at the 5% level for these two groups. No significant difference was found between the median age at death for the following variables when compared to their reference groups: maternal age <20 years, male infant sex, multiple birth, multiparity.

Discussion

This study found the month of death distribution of the sids cases to be seasonally distributed but the month of birth distribution not to differ significantly from a uniform, non-seasonal distribution.
Image of a page from a document discussing the pathogenesis of sudden infant death syndrome (SIDS). The text highlights factors influencing SIDS, including environmental and biological factors. It mentions a study by Helweg-Larsen et al. that found a higher risk in infants born during certain months, and discusses the implications of these findings for understanding SIDS. The text also references the importance of considering postnatal factors and the role of maternal smoking and anaemia. A diagram illustrates the factors contributing to SIDS, with a focus on the seasonal distribution of deaths.
Seasonality and pathogenesis of SIDS

A risk factor for SIDS could act by more than one path. Maternal cigarette smoking has been associated with an increased risk of SIDS. This risk factor may operate by all three pathways in the model (fig 4). The effect may be mediated antenatally through the association between maternal smoking and intrauterine growth retardation. Infants of mothers who smoke have higher admission rates for lower respiratory tract infection, particularly during winter. In addition, maternal smoking could have a direct postnatal toxic effect. Maternal smoking is particularly associated with SIDS infants who are under 12 weeks of age. Nicholl and O’Cathain also found that comparatively few babies had any necropsy evidence of lower respiratory tract disease, suggesting that antenatal smoking rather than postnatal smoking may be more important in these infants.

With regard to infant age, this study found premature infants died of SIDS at a significantly older age than non-premature infants, confirming the work of previous studies, although this relationship has not always been demonstrated. This finding suggests that the SIDS age at death curve reflects postconceptional rather than postnatal age. Our finding of an older age at death in low birthweight infants probably reflects the close correlation of low birthweight and prematurity.

In conclusion, the pathogenesis of SIDS can be represented by a biphasic model with three pathways of risk factor operation. Seasonality has been considered in relation to risk factor mechanism. In Tasmania, SIDS cases displayed a uniform season of birth distribution and a seasonal month of death distribution. As a consequence the median age at death varied by season of birth. We propose that risk factors with a strong seasonal component are likely to be operating in the postnatal period.

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