A prospective study of smoking during pregnancy and SIDS

Kirsten Wisborg, Ulrik Kesmodel, Tine Brink Henriksen, Sjurdur Frodi Olsen, Niels Jørgen Secher

Abstract

Aims—To study the association between smoking during pregnancy and sudden infant death syndrome (SIDS) using prospectively collected data, making it possible to account for a number of potential confounders.

Design—Prospective follow up study (n = 24 986).

Results—The overall rate of SIDS was 0.80 per 1000 live births (n = 20). Children of smokers had more than three times the risk of SIDS compared with children of non-smokers (OR = 3.5; 95% CI 1.4–8.7), and the risk of SIDS increased with the number of cigarettes smoked per day (p < 0.05). Adjustment for parity, alcohol, and caffeine intake during pregnancy, maternal height and weight before pregnancy, years of school, occupational status, marital status, and number of antenatal care visits did not change the results. Adjustment for mother's age marginally reduced the risk of SIDS associated with smoking (OR = 3.0; 95% CI 1.2–7.3).

Conclusions—Given the prospective nature of the study, the number of deaths is small; however, if our results reflect a true association between smoking during pregnancy and SIDS, approximately 30–40% of all cases of SIDS could be avoided if all pregnant women stopped smoking in a population with 30% pregnant smokers. Our study adds to earlier evidence for an association between smoking during pregnancy and SIDS. The strengths of the study are the possibility to adjust for a number of potential confounders and the fact that information about smoking habits during pregnancy was prospectively collected.

(Arch Dis Child 2000;83:203–206)

Keywords: smoking; pregnancy; SIDS

In industrialised countries, sudden infant death syndrome (SIDS) may account for 40% of all deaths from 1 month to 1 year of age.1 The sleeping position of the infant2 and the smoking habits of the mother3–6 have been identified as possible causal factors of SIDS. Since the beginning of the 1990s, the medical communities in Australia and several northern European countries have advocated a non-prone sleeping position of infants. This was followed by notable decreases in SIDS occurrences, thus substantiating the infant’s sleeping position as a causal factor.7

Epidemiological evidence linking SIDS with smoking derives from case control studies8–11 and register based studies.12 While results from case control studies are prone to bias as a result of differential accuracy of information from case and control parents,13 the register based studies may be biased by insufficient confounder control.14 Thus, there is still controversy about whether the apparent association between smoking and SIDS can be explained by differences in social factors or other lifestyle variables between smokers and non-smokers.

The putative effect of smoking on SIDS may be mediated through changes in the oxygen sensitivity of the peripheral arterial chemoreceptors, leading to increased vulnerability to hypoxic episodes.15,16 Furthermore, exposure to nicotine may influence the maturing of cardiorespiratory control, leading to cardiac arrhythmia.17 Finally, it has been suggested that nicotine may potentiate the lethal action of certain SIDS associated bacterial toxins.18

The aim of the present study was therefore to evaluate the association between smoking during pregnancy and SIDS, using prospectively collected data from a university ward, and making it possible to account for a number of potential confounders, including obstetric, sociodemographic, and lifestyle factors.

Population and methods

All pregnant women booking for delivery at the Department of Obstetrics and Gynaecology, Aarhus University Hospital, from September 1989 to August 1996 were invited to participate in the study. The women were asked to fill in three questionnaires: the first two before the routine antenatal visit at 16 weeks of gestation, and the third before the visit at 30 weeks of gestation.

Information from the first questionnaire was used to establish the women’s medical record. It provided information on medical and obstetric history, maternal age, and smoking habits before pregnancy and during the first trimester, and alcohol intake during pregnancy. The second questionnaire provided information on marital status, education, occupational status, and caffeine intake during pregnancy. The third questionnaire was used only to register smoking habits during pregnancy. Information about delivery was obtained from a birth registration form filled in by the attending midwife immediately after delivery. Before data entry, all birth registration
The women were defined as smokers if they smoked one or more cigarettes per day when 16 or 30 weeks pregnant. Only minimal changes in smoking habits appear after 16 weeks of gestation. Smoking was analysed in two categories (smokers versus non-smokers), and also in ordered categories: 0, 1–9, and 10 or more cigarettes per day.

### STATISTICAL ANALYSIS

The association between smoking during pregnancy and SIDS is presented as odds ratios (OR) with 95% confidence intervals (CI). Potential confounding variables were categorised as in Table 1. They were evaluated in logistic regression analyses, and if they changed the measure of association between smoking and SIDS by more than 10% they remained in the final model. All covariates were entered as ordinal, creating a number of dummy variables equal to the number of categories minus one.

To take into account the time of death after delivery, all measures of association were evaluated in a Cox regression analysis. However, as the results were similar to those from logistic regression analyses, they are not presented. Differences in mean birth weight were evaluated by analysis of variance. The attributable fraction (AF) was calculated from the following formula:

\[
AF = \frac{\text{proportion of exposed in the population} \times (OR - 1)}{\text{proportion of exposed in the population} \times (OR - 1) + 1}
\]

The study was approved by the regional ethics committee and by the Danish National Board of Health.

### Results

The study group consisted of 24,986 live born children. In 7450 (30%) pregnancies the mother was categorised as a smoker and in 17,536 (70%) pregnancies as a non-smoker. Among those categorised as non-smokers, 2642 (15%) had smoked before pregnancy but stopped during the first trimester. Among smokers, 3249 (44%) smoked 1–9 cigarettes per day, and 4201 (56%) 10 or more cigarettes per day. The mean number of cigarettes smoked per day was 9 (5).

The overall rate of SIDS was 0.80 per 1000 live births (n = 20). The median age at death among children who died from SIDS was 69 days (25% percentile 40 days; 75% percentile 109 days). The mean age at death was 27 days (95% CI 15 to 69 days) less among children born to women who had smoked during pregnancy compared with children of non-smokers.

The crude analysis showed that children of smokers had more than three times the risk of SIDS than children of non-smokers (table 2). Adjustment for parity, alcohol, and caffeine intake during pregnancy, maternal height and weight before pregnancy, years of school, occupational status, marital status, and number of antenatal care visits did not change the results. Adjustment for mother’s age reduced the risk of SIDS associated with SIDS by more than 10% they remained in the final model.
Table 2  Crude and adjusted OR of SIDS according to different categories of smoking habits during pregnancy

<table>
<thead>
<tr>
<th>Total no.</th>
<th>No. with SIDS</th>
<th>%</th>
<th>Adjusted* OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-smokers from 16 weeks gestation</td>
<td>17386</td>
<td>8</td>
<td>0.5</td>
</tr>
<tr>
<td>Smokers 1–9 cigarettes/day</td>
<td>7450</td>
<td>12</td>
<td>1.6</td>
</tr>
<tr>
<td>10+ cigarettes/day</td>
<td>3249</td>
<td>5</td>
<td>1.5</td>
</tr>
<tr>
<td>Non-smokers from 16 weeks gestation</td>
<td>17536</td>
<td>8</td>
<td>0.5</td>
</tr>
</tbody>
</table>

*Adjusted for maternal age.

with smoking (table 2). Mean birth weight was 323 g (95% CI 81 to 566 g) lower among children who died from SIDS than among surviving children. Adjustment for birth weight and gestational age at birth also reduced the risk of SIDS associated with smoking (OR = 2.9; 95% CI 1.2 to 7.2). Conclusions were not changed after adjustment for maternal age, birth weight, and gestational age at birth.

Discussion
In this prospective study of smoking during pregnancy and SIDS, children of women who smoked during pregnancy had an increased risk of SIDS compared with children born to women who had not smoked during pregnancy. Despite a small number of cases and controlling for possible confounders the association was statistically significant. The risk of SIDS increased with the number of cigarettes smoked per day during pregnancy.

Information about smoking habits during pregnancy was obtained from a self-administered questionnaire completed by the pregnant women at 16 and 30 weeks of gestation. Because the data were collected prospectively, information about smoking could not be biased by the parents’ knowledge about the death of their child. With only 20 cases, it was not meaningful to assess any differential effect between smoking at weeks 16 and 30. Furthermore, among 8607 women (34%) information was missing about smoking habits at 30 weeks of gestation. In our population 30–40% of the smokers stopped smoking in early pregnancy, but after the first trimester very few stopped smoking. Thus, smoking habits at 16 weeks of gestation are a valid measure of smoking habits throughout pregnancy.

Women who stopped smoking before 16 weeks of gestation were categorised as non-smokers in the present study. However, if exposure in early pregnancy is associated with an increased risk of SIDS, compared with no exposure during the entire pregnancy, our result is an underestimation of the true association between smoking during pregnancy and SIDS.

Owing to careful prospective collection of information about maternal lifestyle, and sociodemographic and obstetric factors, we could adjust for a variety of potential confounders. Adjustment for maternal age marginally decreased the risk of SIDS associated with smoking. However, maternal age may represent a proxy for other factors associated with smoking and the occurrence of SIDS, for example, attitudes towards childcare. It is possible that controlling for those factors would further decrease the risk of SIDS associated with smoking. Furthermore, information about socioeconomic markers was missing in one third of all women which may constrain the possibility to fully adjust for these factors.

We did not have information on smoking by the mothers after delivery. However, this is likely to be closely associated with smoking habits during pregnancy. For outcomes assessed shortly after birth, any attempt to discriminate between effects of maternal smoking during pregnancy or after birth remains speculative. It is therefore possible that the association identified in this study may be caused by smoking exposure after delivery.

Unlike Schellsherrt and coworkers 1 we found that SIDS children had a lower mean birth weight than with surviving infants. Some children might be more vulnerable to tobacco exposure in utero, but it is also possible that women whose children died from SIDS smoked more than they actually reported, or smoked differently from mothers with surviving infants. Biochemical measures of tobacco exposure could throw light on this problem. The risk of SIDS was marginally reduced after adjustment for birth weight. Thus our result may indicate that smoking increases the risk of SIDS in addition to its effect on birth weight and preterm delivery.

Our study adds to earlier evidence for an association between smoking during pregnancy and SIDS. The study’s strengths are the possibility to adjust for a number of potential confounders and the fact that information about smoking habits during pregnancy was prospectively collected. Given the prospective nature of the study, the number of deaths is small: however, if the association between maternal smoking and SIDS found in this and previous studies reflects a causal relation, approximately 30–40% of all cases of SIDS could be avoided if all pregnant women stopped smoking in a population with 30% pregnant smokers.


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The editors will decide, as before, whether to also publish it in a future paper issue.

Protective role of cerebrospinal fluid in brain injuries

EDITOR,—We would like to offer a simple model of brain injury which explains many features of what is termed “closed skull” injuries—that is, those where damage results from the action of inertial forces only.

The model is easily constructed as follows. Fill a jam jar to the brim with water. Glue two threads to an egg, suspend the egg in the water, and screw the lid on tightly. If the jar is shaken horizontally as vigorously as possible, the egg will not usually touch the sides of the jar by a factor of 40–50, compared with those where damage results from the action of inertial forces only.

Standard fluid mechanics explains why the egg is not damaged by linear motion.1 The acceleration of the jar gives rise to three fluid acceleration reactions, and the viscous drag. Due to the horizontal pressure gradient, the acceleration of the egg relative to the jar by a factor of 40–50, compared with that would have been in the absence of the water. When the jar is rotated, inertia tends to keep the egg fixed in space and, as the water is incapable of exerting any significant moment on the egg, the thread breaks.

If we identify the egg with the brain, the water with the cerebrospinal fluid, the jar with the skull, and a broken thread with a bleeding bridging vein, we have a ready explanation for the generally accepted fact that brain injury is more easily caused by rotational than by linear acceleration.2

As the argument is based on known fluid mechanical principles, the important question is the extent to which the model represents a real head. The model ignores the presence of the brain stem. However, this approximation is justified, at least for small movements, because the neurovascular structures in the brain stem permit small linear and rotational movements of the brain before any significant forces come into play. Apart from the published animal studies, verification of this model would require experiments with an instrumented cadaver head or an advance in imaging technology to permit real time tracking of the brain’s movement.

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Oral steroids and inflammatory markers in asthma

EDITOR,—Although the recent paper by El-Radhi and colleagues presents interesting data about decreases in inflammatory markers during the resolution of acute asthma,1 some of their conclusions are not valid. Firstly, acute asthma has a tendency to resolve without corticosteroid treatment.2 As all of the children with acute asthma (quite rightly) received steroids, the observed effect may equally reflect processes associated with spontaneous resolution. Indeed, corticosteroids do not inhibit the release of eosinophil cationic protein (ECP) from eosinophils.3 Secondly, the normal controls are inadequate. Atopy per se is associated with increased serum levels of ECP,4 and it is therefore to be expected that the asymptomatic asthmatics will have higher ECP levels than the mostly non-atopic controls.

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CORRECTION

An error occurred in table 2 of Wisborg and colleagues’ recent paper (Arch Dis Child 2000;85:203–6). The correct figures are given in the table printed below:

Table 2 Crude and adjusted OR of SIDS according to different categories of smoking habits during pregnancy

<table>
<thead>
<tr>
<th>Total no. with SIDS</th>
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</tr>
<tr>
<td></td>
<td>10+ cigarettes/day</td>
<td>4201</td>
<td>7</td>
<td>1.7</td>
</tr>
</tbody>
</table>

*Adjusted for maternal age

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