Sudden Infant Death Syndrome and Maternal Depression

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Objective: To investigate whether there is an association between sudden infant death syndrome (SIDS) and perinatal depression.

Method: A case-control study design was used. Cases included women registered in a British primary care database with a live birth (1987–2000) and a subsequent SIDS death. Controls were women with a live birth born in the same year as the matched SIDS death, with infant survival for the first year of life.

Results: One hundred sixty-nine linked mother-infant cases of SIDS were matched with 662 mother-infant controls. The authors found that SIDS was independently associated with maternal depression in the year before birth (odds ratio [OR] = 4.93, 95% CI = 1.10 to 22.05), smoking (OR = 2.50, 95% CI = 1.29 to 4.88), and male sex (OR = 1.94, 95% CI = 1.04 to 3.64). There was weak evidence of an independent association of SIDS with depression in the 6 months after birth, before the index SIDS death (OR = 1.80, 95% CI = 0.71 to 4.56).

Conclusion: This study provides further evidence for an association between SIDS and perinatal depression, particularly antenatal depression. Health care professionals should ensure that women with perinatal depression are appropriately treated and are provided with clear advice on infant care practices that may prevent SIDS.

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Sudden infant death syndrome (SIDS) is the main cause of infant death in the first year of life and is defined as a sudden unexpected death of an infant (aged younger than 1 year) for which a careful history and postmortem examination fail to explain the cause of death.[1] The incidence of SIDS has fallen by 75% since initiation of the "Back to Sleep" campaign,[2,3] which encourages parents to place their babies supine, and the North American incidence of SIDS is now 0.5 per 1000 live births.[4] Maternal risk factors consistently identified, since the "Back to Sleep" campaign changed the epidemiology of SIDS, include smoking,[5,6] socioeconomic deprivation,[7,8] prematurity, intrauterine growth retardation and placental abnormalities,[6,9] and bedsharing when mothers are smokers.[10,11] Low birthweight infants[12,13] and male infants[14,15] are also at increased risk. Use of a pacifier is associated with a reduced risk of SIDS.[16,17]

Sudden infant death syndrome has been linked to psychiatric disorders in 3 studies. Postnatal depression was associated with SIDS in 2 prospective studies,[18,19] but both studies suffered from a high rate of missing data, used a self-report screening questionnaire as a measure of postnatal depression, and had small numbers of SIDS cases (33 and 22, respectively). A large study using data from the Danish Psychiatric Register and the Danish Medical Birth Register reported a relative risk of 5 for SIDS in the infants of women with schizophrenia after adjustment for birth weight and gestational age,[20] but mothers who had their first episode of schizophrenia after the SIDS death were included in this analysis, and this finding may therefore reflect reverse causality. Unlike the studies investigating SIDS and postnatal depression, there was no adjustment for socioeconomic status or smoking, which the authors acknowledge may have led to residual confounding.[20] It has also been reported that antipsychotics from breastmilk can produce increases in sleep apnea in neonates[21] and may be associated with SIDS,[21,22] but medication was not controlled for in the Danish study.[20]

The aim of this study was to investigate whether psychiatric disorders, particularly depressive disorders, are associated with SIDS and to examine the effect of potential confounders. Our null hypothesis was that there is no association between psychiatric disorders and SIDS.

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METHOD

Study Population and Study Design

This study uses data from the U.K. General Practice Research Database (GPRD) between 1987 and 2000. The GPRD was set up in 1987 and contains the computerized medical records of over 8 million primary care patients in the United Kingdom. Patients in the United Kingdom must be registered with a general practitioner in order to access secondary health care services, such as obstetric and mental health services; almost all pregnant women will therefore be included in the GPRD if they live in the catchment area of a GPRD general practice. Data recorded include prescription details, clinical events, preventive care provided, specialist referrals, hospital admissions, and the major patient outcomes. Clinical data are stored and retrieved by means of OXMIS (Oxford Medical Information System) codes[23] and, more recently, Read codes, which are cross-referenced to the *International Classification of Diseases* (ICD-9 and ICD-10), by the U.K. National Health Service Information Authority. The data collected are audited regularly, and the participating general practices have been subjected to a number of quality checks by the Office of National Statistics and the Medicines Control Agency, including internal validation by cross-checking within practices and by comparisons with national statistics.[24–26] Only practices that comply with this quality control (i.e., are "up to research standard" [UTS]) are retained in the database, and we only used data from subjects with at least 9 months of UTS data.

Anonymized data are stored in 4 tables linked by a unique patient identifier. Patients' maternal records are linked to their baby's records in the GPRD through a household number. This household number was used with the date of delivery from the maternal record and matched with the baby's birthday (which is given as the first day of the month of birth in the GPRD to maintain confidentiality) to identify the babies born to the subjects during the study period. Data on babies were extracted from maternal and/or infant records where available.

Cases

Cases included women registered with a general practice in the GPRD who had a live birth between 1987 and 2000 with a subsequent diagnosis of SIDS (in the maternal or infant record). A diagnosis of SIDS is recorded by the general practitioner when provided with the diagnosis by secondary services, i.e., after clinical, pathologic, and forensic investigation.

Controls

Controls included women registered with a general practice in the GPRD with a live birth born in the same index year as the index SIDS baby, with infant survival for the first year of life, and mother and baby matched for general practice and maternal age (± 2 years). Four controls were searched for in the database to optimize the statistical power of the study.

Measures

Potential predictors of SIDS were taken from records up to 3 years before the index SIDS date where available and included demographic details, medical and psychiatric history (i.e., details of history of any medical or psychiatric diagnosis, hospital referrals, letters or admissions), illicit drug use, and smoking and alcohol consumption. As it is difficult to date accurately the beginning of a new depressive episode, an episode of antenatal depression is here defined as a clinical diagnosis of depression (ICD-10 codes F32–F38) recorded by the general practitioner in the year before delivery. Postnatal depression was defined as a new prescription of antidepressants or a new depressive episode recorded in the first 6 months postpartum, but "any" depressive episodes postpartum (new or a continued depressive episode) were also examined.

Analysis

Data were initially transferred into a relational database (Access, Microsoft Corp., Redmond, Wash.) to create appropriate data files (Access tables). Stata v8.1 (Stata Corp., College Station, Tex.) was used for data analysis. A descriptive analysis investigating the distribution of the variables and comparing cases and controls was carried out. Conditional logistic regression models were then used to investigate the association between these variables and SIDS. With 130 cases and 520 controls, an odds ratio (OR) of 2.5 would be detectable, with 85% power, using a 5% significance level.

Ethical approval was obtained from the Scientific Ethical Advisory Group, which decides whether studies using data from the GPRD should receive ethical approval.

RESULTS

There were 1768 records of SIDS, but this number included duplicate codes and cases where the same SIDS baby was coded in the infant and maternal record. When the infants were linked to the mothers using household number, 178 cases were identified. No controls could be identified for 8 of these cases, and 1 mother appeared twice in the database with 2 different household numbers making it impossible to know which children were hers. Thus, a dataset with 169 cases of SIDS and 662 controls was left, although infant data were only available for 132 of the cases. One case had 2 SIDS infants, and in this instance, data were collected for the first SIDS infant.

There was no significant difference in the duration of data available ($p = .94$). Thirty-seven (22%) cases and 178 (27%) controls had no detailed information on the infants ($\chi^2 = 1.751$, $p = .186$). Consequent to the matching

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Table 1. Characteristics of Cases of Sudden Infant Death Syndrome (SIDS) and Controls

Variable, N (%)	Cases of SIDS	Controls	Odds Ratio (95% CI)	p Value
Male infant	83 (63)	242 (50)	1.64 (1.11 to 2.42)	.01
Smoker	93 (70)	224 (40)	3.39 (2.19 to 5.26)	< .001
Alcohol > 14 U/wk vs alcohol 0–14 U/wk	3 (3)	10 (2)	2.17 (0.48 to 9.80)	.32
Depression 6 mo postpartum	13 (16)	24 (8)	1.93 (0.84 to 4.45)	.12
Postnatal depression (new episode)	9 (11)	23 (8)	1.39 (0.53 to 3.59)	.50
Depression in year before birth	7 (9)	6 (2)	4.21 (1.18 to 14.98)	.03

procedure, maternal age, year of delivery, and general practice did not differ between exposed and unexposed groups.

The mean age of the mothers was 26 (SD = 5.5) years. The sex of the baby was known in 78% of cases and 73% of controls ($\chi^2 = 1.75$, df = 1, p = .19) and was more likely to be male in SIDS cases (Table 1). Other demographic and clinical characteristics are given in Table 1.

No cases or controls had a diagnosis of schizophrenia or bipolar disorder prior to the SIDS death or during the first year postpartum, although 2 controls subsequently developed schizophrenia later according to their case records. There was no history of substance misuse recorded in cases or controls, and there was no significant difference in alcohol consumption per week recorded in cases or controls (p = .71). No cases or controls had a psychiatric admission in the 3 years prior to the pregnancy. One control but no cases had a psychiatric admission during pregnancy. One control and 1 case had a psychiatric admission in the first year after the baby was born, and 1 other control had 2 psychiatric admissions in the year after birth (p = .52, Fisher exact test). Seventeen cases (13%) and 39 controls (8%) had a nonpsychiatric admission during pregnancy (OR = 1.62, 95% CI = 0.85 to 3.10, p = .15). There was no difference in the number of (nonpsychiatric) hospital admissions prior to the pregnancy (p = .4, N = 616) in the cases or controls. During pregnancy, no cases or controls were prescribed antidepressants or anticonvulsants; only 1 case and 1 control were prescribed hypnotics/anxiolytics, and 1 case and 1 control were prescribed neuroleptics. In the 6 months after birth, 1 control but no cases were prescribed antidepressants. Smoking data were more likely to be unrecorded in cases (N = 36 [21%]) compared with controls (N = 95 [14%]) (OR = 1.79, 95% CI = 1.10 to 2.93, p = .02). Nevertheless, where smoking information was recorded, cases were more likely to be recorded as smokers than controls (OR = 3.39, 95% CI = 2.19 to 5.26). Variables included in the final regression model are given in Table 2.

Depression in the year before birth was independently associated with SIDS, although depression after the birth was not significantly associated with SIDS (this was true whether only new cases of depression recorded [postpartum depression] were examined or any case of depression in the 6 months after birth, including chronic depression, was investigated). However, there was evidence of a trend in the relationship between depression in the 6 months after birth and SIDS in the multivariate analysis (adjusted for smoking and infant sex) (OR = 1.80, 95% CI = 0.71 to 4.56, p = .21).

Table 2. Final Regression Model for Factors Associated With Sudden Infant Death Syndrome (SIDS)

Cases of SIDS	Odds Ratio	z	p Value	95% CI
Depression in year before birth	4.93	2.09	.037	1.10 to 22.05
Infant sex (male vs female)	1.94	2.07	.038	1.04 to 3.64
Smoker	2.50	2.70	.007	1.29 to 4.88

DISCUSSION

This study found that SIDS was associated with a history of depression in the year before birth. Depression in the 6 months after birth, whether a new episode of depression (postnatal depression) or chronic depression, was not independently significantly associated with SIDS, though this may reflect a lack of statistical power—there was evidence of a trend for depression after birth to be associated with SIDS in the analysis and multivariate analyses. We also confirmed the consistently reported association between maternal smoking and SIDS and male sex of the baby and SIDS.

Strengths of the present study include a larger sample size than in previous studies of SIDS and psychiatric disorders, a population-based case-control design, and control for many potential confounding variables. However, residual confounding by factors not available on the GPRD is possible, e.g., use of a pacifier and bedsharing. This study was not able to examine whether the association between depression and SIDS was due to low birthweight or prematurity, as there were limited primary care infant data. However, there is increasing evidence that antenatal depression is associated with prematurity, low birthweight, and obstetric complications,[27–30] so these factors could explain the association found here. Antenatal depression (which often continues into the postnatal period), may also lead to changes in neuroendocrine exposures in utero,[31] which could have an impact on fetal development.

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The association may also be explained by smoking and substance misuse, which were not adequately recorded. It was noted in this and other studies that women with psychiatric disorders are less likely to have their smoking and alcohol status recorded during pregnancy,[32] despite the increased frequency of smoking and substance misuse in this population.[33]

This study depends on general practitioner codings of SIDS, which could contain random or systematic bias. We were not able to validate the SIDS diagnosis, as pathology reports were not available, and it is possible that general practitioners overestimated SIDS; however, as SIDS is a diagnosis of exclusion, overestimation is unlikely to occur, as general practitioners wait for the results of the pathologic investigation before concluding a death is a SIDS death.

We controlled for general practice as a proxy for neighborhood (and socioeconomic status), though there is some debate as to how accurately neighborhoods can act as a proxy for socioeconomic status.[34] Socioeconomic status represents many factors reflecting social position, income, occupation, education, and ownership of resources. There is a dose-response relationship between SIDS and socioeconomic deprivation, with the risk of infant death increasing with greater exposure to adverse social circumstances.[8] It has been suggested that smoking explains the association between socioeconomic difficulties and SIDS, but the prevalence of maternal smoking (during pregnancy) in mothers of SIDS infants is twice that expected in control mothers with similar levels of socioeconomic deprivation.[35] Socioeconomic status may act as a distal factor in the causal pathway of SIDS, with depression the proximal risk factor, though the association found in this study does not necessarily indicate causality. However, if this association is causal, how could depression lead to SIDS?

There is some evidence that infants who subsequently succumb to SIDS may be vulnerable in some way—developmental problems and admission to the hospital after the first week of life are significantly associated with SIDS[36]; risk factors for SIDS also include prematurity or the presence of immature cardiorespiratory control mechanisms.[28,37] Women with antenatal depression are at higher risk of adverse obstetric outcomes, and antenatal depression may therefore increase the risk of having a vulnerable infant. Other possible etiologic factors include prescribed drugs such as phenothiazines[21,38,39] or antidepressants during pregnancy; antidepressants are known to be related to arousal dysfunction in neonates exposed to selective serotonin reuptake inhibitors in the third trimester of pregnancy.[40] Prescribed medication seems unlikely to be a contributory factor here though, as very few women in this study population were prescribed medication during pregnancy or postpartum, and phenothiazines are now clearly not recommended for infants under the age of one. One study of new mothers with high levels of social deprivation found that psychological vulnerability (operationally defined as the presence of personality disorder and/or a score of more than 11 on the Edinburgh Postnatal Depression Scale, indicating possible postnatal depression) and negative feelings about the baby either prenatally or postnatally were significantly associated with behaviors associated with SIDS risk (e.g., the baby was not always placed supine to sleep; the baby was exposed to smokers at home).[41] Mothers with perinatal depression may find it difficult to optimize behaviors associated with SIDS risk.[32]

In conclusion, this case-control study using prospectively recorded primary care data found an association between perinatal depressions and SIDS, particularly depression in the year prior to birth. Depression is a treatable condition, and our findings again highlight the importance of detection and treatment of depression in pregnancy. Midwives and primary care professionals also need to emphasize the importance of minimizing SIDS by advising new mothers with depression to reduce their infant's exposure to smoke and to place the baby supine to sleep.

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