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Maternal Smoking during Pregnancy and Sudden Infant Death Using the National Maternal and Infant Health Survey: A Case-Case Study

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ABSTRACT

We utilized data from the National Maternal and Infant Health Survey (*NMHIS*) *to analyze the risk of SIDS and other infant deaths among women who smoke during pregnancy adjusting for potentially modifiable risk factors such as secondhand smoke exposure and breastfeeding. The following variables were assessed with respect to risk for SIDS and other infant deaths*: *smoking exposure*, *level of education*, *infant and maternal age*, *infant and maternal birthweight*, *maternal BMI*, *gender*, *secondhand smoke exposure*, *breast feeding*, *prenatal vitamins*, *WIC*, *multiple gestation*, *sleep apnea monitor prescription*, *sleep apnea incidents and maternal alcohol use. Univariate analysis and multivariate logistic regression were performed to identify variables significantly associated with the odds of mortality from SIDS. Analysis utilized weighted estimates using SUDAAN* 9.0.0 *to adjust for design effects. A p-value* < 0.01 *was considered statistically significant. Women who smoked during pregnancy were 1.83 times more likely to give birth to an infant that died from SIDS versus some other cause of death*, *OR* (95%) = 1.83(1.33, 2.51). *Other Race infants and Black infants were more likely to suffer SIDS mortality than White infants*, *but the result was not significant in the final model. Other modifiable risk factors*, *such as secondhand smoke exposure and breast feeding*, *were not significant predictors of SIDS mortality. Independent of sociodemographic variables and other potential risk factors for SIDS death*, *maternal smoking was associated with an increased risk of SIDS death versus other death. This study highlights the importance of screening all pregnant women for tobacco use and emphasizes the importance of smoking cessation to decrease the risk of infant death from SIDS.*

***Keywords*:** *Sudden Infant Death*, *Smoking*, *Pregnancy*, *Passive Smoking*, *Breastfeeding*

1. Introduction

Sudden Infant Death Syndrome (SIDS) is the leading cause of postneonatal death among all racial and ethnic groups, representing nearly one-third of such deaths. The incidence of SIDS peaks in the second or third month of life, and subsequently decreases over the first year of life. Two components of cigarette smoke potentially responsible for a role in SIDS pathophysiology are carbon monoxide (CO) and nicotine. These toxins, which cross the placental barrier, have been demonstrated to alter the physiologic development of organs and tissues most susceptible to hypoxia damage, including the brain and heart in animal models [1-4]. Altered autonomic nervous system function has been described in infants born to mothers who smoked during pregnancy [5-7]. It has been hypothesized that CO exposure from maternal smoking may have an effect on postnatal electrophysiological remodeling which could predispose the infant heart to fatal arrythmias [3]. Exposure to CO in concentrations comparable to that of human smokers induced a statistically significant delay in action potential (AP) duration in a rat model [3]. The potential effect of CO exposure on AP duration is a plausible explanation for an arrhythmia resulting in sudden death.

In addition to CO exposure, nicotine exposure has also been implicated as a key cigarette component related to the cardiorespiratory events characteristic of SIDS [8]. Although not associated with restricting uterine blood flow, the cardiovascular effects of nicotine increase the fetal heart rate while decreasing fetal heart rate variability [9,10]. Studies demonstrating that pre-

natal exposure to cigarette smoke alters lung mechanics in infants and children have been bolstered by animal experiments linking nicotine to altered alveolar architecture, pulmonary hypoplasia, increases in collagen deposition and decreases in elastin content [11]. Nicotine is also known to adversely affect neural networks controlling respiration by acting as a fetal neuroteratogen [2].

While many toxic, infectious, metabolic, physiologic and socioeconomic factors have been proposed as causes of SIDS, less attention has focused on the role of modifiable behaviors such as smoke exposure (from maternal and secondhand exposures) and breast-feeding [12,13]. Smoking during pregnancy continues to be a significant public health problem, with 13.8% of women in 2005 admitting to this behavior while pregnant [14]. Smoking rates during pregnancy in the United Kingdom were 17% in the same year and the rates in Canada were 24% [15]. The role of secondhand smoke exposure in the pathophysiology of SIDS is less clear, as is the role of lower socioeconomic status which has been reported as an independent risk factor for SIDS [13]. The majority of studies performed to date are not based on a sample of infants' representative of the U.S. population.

A modifiable intervention, sleep position, has been studied more closely. As a result of the *Back to Sleep Campaign* that was implemented in 1994, SIDS mortality rates in the U.S. have declined for all ethnic groups [16]. However, even after the implementation of the *Back to Sleep Campaign*, non-Hispanic Black infants were 2.14 times more likely to die from SIDS than Non-Hispanic White infants [17]. This finding is particularly problematic considering White women are much more likely to smoke during pregnancy than Black women [14,18]. This suggests that there may be an interaction between race and smoking status although this has not been reported to date.

This study utilized the 1988 National Maternal and Infant Health Survey (NMIHS) to examine the effect of maternal smoking status during pregnancy and secondhand smoke exposure on the prevalence of death due to sudden infant death syndrome (SIDS) using a nationally representative sample of infant deaths from the U.S. population. Previous studies utilizing the NMIHS to examine the relationship between maternal smoking and SIDS were incomplete, failing to account for breast feeding or secondhand smoke exposure [19,20]. The analysis presented in this manuscript accounts for both maternal smoking, as well as secondhand smoke exposure during pregnancy. Additionally, the analysis presented in this paper considers whether or not the infant was breast fed, a variable previously identified as an important protective factor against postneonatal death [21].

2. Methods

The 1988 National Maternal and Infant Health Survey (NMIHS) were conducted by the National Center for Health Statistics (NCHS) to assist researchers in studying factors related to poor pregnancy outcomes. The survey is a nationally representative sample of 9953 (74.2% response rate) women who had live births, 3309 (69.3%) that had late fetal deaths and 5332 (65.3%) who had infant deaths in 1988. The mother's questionnaire included information on prenatal care and health habits, including tobacco smoke exposure, previous and subsequent pregnancies, characteristics of the parents and the baby's health through 6 months of age. Only the infant death group from the total study population was analyzed for this report. This study was approved by the University of Miami Institutional Review Board.

Data were abstracted from the birth certificate for the following information: birthweight, gender, gestational age, maternal age, infant race and parity. Data were abstracted from the maternal questionnaire for maternal education level, history of cigarette smoking during pregnancy, and history of alcohol use during pregnancy.

The NMIHS and Longitudinal Follow-Up drew stratified systematic samples from live births and infant deaths that were registered in 48 states, the District of Columbia, and New York City in 1988; and from fetal deaths that were registered in 46 states, the District of Columbia, and New York City in 1988. To increase the reliability of the data, Black infants were oversampled in the live-birth, fetal-death, and infant-death components of the NMIHS because Black infants have rates of low birthweight and infant mortality about twice that of White infants [22]. Very low-birthweight (<1.500 g) and moderately low-birthweight (1500 - 2499 g) infants were oversampled in the live-birth component to obtain a sufficient number of high-risk births for special studies.

The live-birth and fetal-death components were restricted to women 15 years of age or over, and the infant-death component included women under 15 years of age. Mothers included in this study were women who had infant deaths and responded to the questionnaire from the NMIHS (N = 5332). The two study groups in the analysis consisted of (1) SIDS deaths, as defined by an ICD-9-CM code recorded as 798.0; and (2) other deaths consisting of all other infant deaths [23]. This data was obtained from linkage of the birth certificates and death certificates.

The following study independent variables were ex-

pressed both continuously and categorically: smoking exposure, level of education, infant and maternal age, infant and maternal birthweight, maternal BMI, gender, secondhand smoke exposure, breast feeding, prenatal vitamins, WIC, multiple gestation, sleep apnea monitor prescription, sleep apnea incidents, and maternal alcohol use.

Continuous measures are reported as means with 95% confidence intervals and comparisons between the two study groups (SIDS deaths vs. other deaths) used the t-test for independent samples. Categorical measures are reported as percents with 95% confidence intervals and were compared using a Chi-square test. Multivariate logistic regression was performed to identify variables significantly associated with the odds of mortality from SIDS. Interactions between maternal smoking status and all other covariates were tested. All analyses utilized weighted estimates and were performed using SUDAAN 9.0.0 (Research Triangle Institute, Cary, NC) to adjust for design effects. A p-value < 0.01 was considered statistically significant, given the very large sample size.

3. Results

Mothers of White infants were significantly more likely to smoke during pregnancy (39.1%) than mothers of Black infants (34.0%) or mothers of Other Race infants (23.2%) ($p < 0.001$). Mothers who smoked during pregnancy were significantly less likely to take prenatal vitamins, breast-feed the infant, and have more than a high school education. Mothers who smoked during pregnancy were also significantly more likely to give birth to multiples, use the government sponsored nutrition program, *Women*, *Infants and Children* (*WIC*) program, and drink alcohol during pregnancy. **(Table 1)**

Table 1. Weighted baseline characteristics of mothers who smoked and did not smoke during pregnancy (N = 38,917).

Characteristic	Non-smokers (%)	Smokers (%)	p-value
Used Vitamins	76.9	73.4	<0.001
Ever Breast fed	43.5	30.0	<0.001
Born Preterm(<37 weeks)	57.5	55.0	<0.001
Multiple Gestation Pregnancy	10.4	11.4	0.002
Used WIC	27.7	36.3	<0.001
LBW (<2.500 g)	58.9	58.7	0.756
Used Alcohol	34.3	58.1	<0.001
Maternal Education			
<High school	21.8	36.1	<0.001
High school Graduate	35.8	42.4	
Some college	42.3	21.4	
Race			
White	60.9	39.1	<0.001
Black	66.0	34.0	
Other race	76.8	23.2	

3.1. Univariate Analysis

A comparison of study categorical and continuous variables, stratified by maternal race, between the SIDS deaths and other deaths are presented in **Tables 2** and **3**. All covariates included in the weighted univariate analyses, with the exception of breast feeding and use of prenatal vitamins, were significantly different between the two infant death groups ($p < 0.001$). A significantly greater proportion of mothers smoked during the 12 months preceding delivery in the SIDS mortality group (53.3%) compared to the other mortality group (34.2%). This finding held for both Black and White races, although a higher proportion of White smokers were represented in the SIDS mortality group. In addition to the significant variables reported in the unweighted analysis, maternal prepregnancy BMI was significantly lower in the SIDS mortality group (22.93) compared to the other mortality group (23.27). The lower maternal prepregnancy BMI among the SIDS mortality group was not observed for Black infants. Maternal birth weight was significantly greater for the SIDS mortality group (3184 g) compared to the other mortality group (3122 g). This relationship was observed among White infants, but there was no significant difference in maternal birthweight between SIDS mortality groups for Black or Other Race infants.

3.2. Multivariate Logistic Regression Analysis, Weighted and Adjusted for Design Effects

After adjustment of standard errors using SUDAAN, the overall model was significant ($p < 0.001$). Smoking during pregnancy, use of a sleep apnea monitor, an infant that stopped breathing, infant age at death, maternal age, and infant birthweight were significant predictors of SIDS mortality. **(Table 4)** Women who smoked during pregnancy were 1.83 times more likely to give birth to an infant that died from SIDS versus some other cause of death, OR (95% CI) = 1.83 (1.33, 2.51). Secondhand smoke exposure through the presence of household smokers was not significantly associated with infant death from SIDS in the final model. Use of a sleep apnea monitor and an infant that was previously noted to have stopped breathing were significantly protective factors against SIDS death in the model. Infants older at the time of death and infants born to older mothers were slightly less likely to die from SIDS. The odds ratio and 95% CI for a 1 gram increase in infant birthweight were nearly indistinguishable from 1.00, but the birthweight

Table 2. Baseline categorical characteristics (weighted) of 1988 NMIHS cohort for infant mortality groups (*N* = 38,917).

Characteristic	SIDS Death (%)	Other Death (%)	*p*-value
N	5215	33,702	
Gender			
Female	40.8	44.1	<0.001
Male	59.2	55.9	
Mother Smoked 12 Months Preceding Delivery			
Black	47.1	32.0	<0.001
White	59.3	35.9	<0.001
Other Race	32.4	20.8	<0.001
Smokers in Home During Pregnancy			
Black	47.1	45.3	0.230
White	56.7	38.3	<0.001
Other Race	39.3	33.7	0.090
Mother Drank Alcohol 12 Months Preceding Delivery			
Black	35.8	31.1	0.001
White	54.5	48.7	<0.001
Other	32.4	26.0	0.038
Mother Ever Breastfed			
Black	15.5	16.8	0.367
White	43.0	43.8	0.481
Other Race	61.9	46.4	<0.001
Mother's Education Level			
Total			
High School Graduate	38.3	38.3	<0.001
Some College	26.7	35.9	
Black			
High School Graduate	39.2	40.1	<0.001
Some College	19.6	29.5	
White			
High School Graduate	39.9	38.4	<0.001
Some College	27.3	38.8	
Other			
High School Graduate	26.0	27.3	<0.001
Some College	29.8	46.2	
Prenatal Vitamin Use			
Black	63.6	65.6	0.140
White	78.0	80.9	<0.001
Other Race	82.5	75.4	0.017
WIC Use During Pregnancy			
Black	60.8	43.6	<0.001
White	39.4	21.7	<0.001
Other	52.8	25.8	<0.001
Multiple Gestation Birth			
Black	6.4	11.4	<0.001
White	5.5	12.5	<0.001
Other Race	2.3	11.7	<0.001
Premature Birth < 37 weeks			
Total	21.6	62.6	<0.001
Black	32.6	73.4	<0.001
White	17.4	58.6	<0.001
Other	17.2	52.3	<0.001
Apnea Monitor Prescribed			
Total	2.4	2.5	<0.001
Black	3.3	1.6	<0.001
White	1.9	2.8	<0.001
Other	0.0	1.2	<0.001*
Infant Ever Stopped Breathing			
Total	17.2	5.2	<0.001
Black	16.3	4.4	<0.001
White	17.8	5.4	<0.001
Other	4.2	5.2	<0.001*

*indicates insufficient sample size (at least 1 cell had a count of 0).

Table 3. Baseline continuous measures (weighted) of 1988 nmihs cohort for infant mortality groups (*N* = 38,917).

Characteristic	SIDS Death (Mean; 95% CI)	Other Death (Mean; 95% CI)	*p*-value
N	5215	33,702	
Number of Cigarettes/Day After Knowledge of Pregnancy			
Black	7.9 (7.3, 8.6)	8.1 (7.8, 8.4)	0.680
White	12.3 (11.9, 12.7)	9.1 (8.9, 9.3)	<0.001
Other	13.9 (10.8, 17.0)	6.8 (5.9, 7.7)	<0.001
Maternal Level of Education (Years)			
Black	11.6 (11.5, 11.7)	12.1 (12.0, 12.2)	<0.001
White	11.9 (11.8, 12.0)	12.5 (12.4, 12.5)	<0.001
Other Race	10.9 (10.4, 11.4)	12.1 (11.8, 12.3)	<0.001
Maternal Age (Years)			
Black	22.8 (22.5, 23.1)	24.1 (24.0, 24.2)	<0.001
White	24.5 (24.3, 24.7)	26.2 (26.1, 26.3)	<0.001
Other	23.8 (23.1, 24.5)	29.1 (28.8, 29.5)	<0.001
Maternal BMI			
Black	23.8 (23.5, 24.1)	24.0 (23.9, 24.2)	0.207
White	22.6 (22.4, 22.7)	23.0 (22.9, 23.1)	<0.001
Other	23.2 (22.8, 23.7)	21.7 (21.5, 22.0)	<0.001
Maternal Birth weight (Kg)			
Black	3.00 (2.95, 3.05)	3.00 (2.98, 3.02)	0.993
White	3.25 (3.23, 3.27)	3.17 (3.16, 3.18)	<0.001
Other	3.16 (3.06, 3.25)	3.16 (3.12, 3.21)	0.876
Child's Birth weight (Kg)			
Black	2.86 (2.82, 2.90)	1.47 (1.44, 1.49)	<0.001
White	3.19 (3.16, 3.21)	1.90 (1.88, 1.92)	<0.001
Other	3.17 (3.10, 3.24)	2.03 (1.95, 2.10)	<0.001
Gestational Age (Weeks)	38.4 (38.3, 38.5)	31.6 (31.5, 31.7)	<0.001
Infant Age at Death (Days)	96.6 (94.5, 98.6)	54.9 (53.7, 56.1)	<0.001

Table 4. Results of multiple logistic modeling* to assess the association between maternal smoking and infant mortality from sids (weighted), (*N* = 8,264).

Characteristic	OR (95% CI)	*p*-value
Smoked During Pregnancy		
No	1.00	
Yes	1.83 (1.33, 2.51)	<0.001
Alcohol During Pregnancy		
No	1.00	
Yes	1.10 (0.81, 1.49)	0.527
Household Smokers		
Yes	1.00	
No	0.90 (0.67, 1.20)	0.476
Maternal Age	0.95 (0.92, 0.98)	<0.001
Maternal Level of Education		
Some college	1.00	
High school Graduate	1.07 (0.75, 1.54)	0.703
< High school	0.93 (0.62, 1.38)	0.707
Multiple Gestation Pregnancy		
No	1.00	
Yes	1.69 (0.83, 3.48)	0.151
Child Gender		
Female	1.00	
Male	1.13 (0.85, 1.51)	0.400
Child Race		
Black	1.00	
White	0.93 (0.69, 1.25)	0.623
Other	1.96 (0.89, 4.30)	0.095
Gestational Age	0.96 (0.92, 1.01)	0.120
Infant Birthweight	1.04 (1.01, 1.06)†	<0.001
Infant Breastfed		
No	1.00	
Yes	1.02 (0.74, 1.42)	0.885
Used Sleep Apnea Monitor		
No	1.00	
Yes	0.21 (0.10, 0.44)	<0.001
Infant Stopped Breathing		
No	1.00	
Yes	0.68 (0.47, 0.97)	0.034
Infant Age at Death	0.99 (0.99, 1.00)	<0.001

effect was significant in the model ($p < 0.001$). For a 100 gram increase in infant birthweight, there was a 4% increased risk of death from SIDS as opposed to another cause. Other Race infants and Black infants were more likely to suffer SIDS mortality than White infants, but the result was not significant in the final model. An infant born as a twin or higher order gestation pregnancy was 1.69 times more likely to suffer SIDS mortality, but again, this result was not significant ($p < 0.151$). The analysis checked for interaction between smoking status and all other variables included in the final model and found no interaction present.

4. Discussion

The NMIHS provides a unique opportunity to gather information on a representative sample of live births and infant deaths occurring in the United States. The NMIHS continues to be the only nationally representative survey that provides information on such a wide range of health behaviors and pregnancy outcomes in conjunction with birth and demographic information. For these reasons, it remains an extremely valuable research tool despite the fact that the data reflect population characteristics that are now over 15 years old.

In this case-case study, the major finding is that smoking during pregnancy increased the risk of infant death from SIDS versus some other cause by 83%. Both in this study cohort and many other populations, women who smoke in pregnancy tend to have different sociodemographic characteristics than non-smokers [18, 24]. Because these factors may also be associated with risk for SIDS, concern exists that associations may reflect sociodemographic confounding rather than a causal relationship. However, in this study, adjustment for factors such as maternal education and race only minimally influenced effect sizes. We found no evidence of an interaction between race and maternal smoking status.

Several researchers have corroborated the maternal smoking and SIDS relationship. Taylor and Sanderson used the NMIHS to conduct a study of risk factors for SIDS and found maternal smoking during pregnancy was significantly more common among infants that died from SIDS than in infants dying from other causes, OR (95% CI) = 1.97 (1.59, 2.45) [20]. They did not control for breast feeding or other smokers in the home during pregnancy. Schoendorf and Kiely, who also analyzed the NMIHS data, but stratified the analysis by race, and only included normal birthweight babies, demonstrated that maternal smoking is a more significant risk factor for SIDS than for other postneonatal deaths [19].

It was expected that Black infants would be at an increased risk for SIDS considering the fact that previous studies have identified Black race as a pertinent risk factor. The final model of the present study suggested Black infants are at a slightly increased risk for death from SIDS compared to White infants; however, this result was not significant. Infants of "Other Race" were actually 1.96 times more likely to suffer SIDS mortality than Black infants, although this result also failed to reach statistical significance. Only 34 valid "Other Race" infants were included in the SIDS analysis, most of which were Asian or American Indian. Hispanic eth-

nicity was distributed among White, Black, and Other Race infants and was not readily isolated in this analysis. Although race was not a significant predictor of SIDS mortality, future studies should pay special attention to American Indians, a group in which SIDS accounted for 81.8% of infant deaths in addition to representing a group where smoke exposure during pregnancy is highly prevalent. These results further highlight the importance of counseling women against smoking during pregnancy and providing access to cessation programs.

Bed-sharing and sleep position have been implicated as risk factors for SIDS and pacifier use during sleep has been implicated as a protective factor for SIDS; however, these variables were not available for analysis in the NMIHS [25,26]. The NMIHS and Longitudinal Follow-Up were conducted prior to the initiation of the *Back to Sleep* campaign. Sleep behaviors are pertinent variables to consider as risk factors for SIDS mortality because of their possible impact on the infant's control of arousal mechanisms, but due to limitations of the dataset, only smoke exposure could be assessed [27].

In addition to smoking during pregnancy, use of a sleep apnea monitor and the infant having ever stopped breathing were significantly associated with risk of SIDS mortality. Use of a sleep apnea monitor decreased the risk of SIDS mortality by 79%, and noticing the infant had stopped breathing reduced the risk of SIDS mortality by 32%. The univariate analysis indicates Black infants that died from SIDS were more likely to have been prescribed a sleep apnea monitor and that infants that stopped breathing were more likely to have died from SIDS; however, the final regression model found the association reversed. There were high percentages of missing cases for both of these variables, possibly reducing the validity of conclusions drawn about these relationships. An analysis of the NMIHS using SIDS deaths and live controls also described a protective effect of home apnea monitoring [28].

It is important to note when interpreting the analysis that a distinction should be made between statistical significance and clinical significance. The large sample size produced by weighting often times results in very small *p*-values that reflect small effect estimates of questionable clinical relevance. In **Table 1**, for example, one might expect a significantly higher percentage of preterm infants to be born to smokers rather than to non-smokers, rather than vice-versa. Prematurity is a common characteristic among infants suffering all causes of mortality; and it is likely that the statistically significant difference seen between smokers and non-smokers regarding prematurity is the product of the large sample size, and not a clinically important observation.

SIDS continues to be a major cause of postneonatal death. Although lower than in 1988, the prevalence of smoking during pregnancy continues to be substantial, both in the U.S. and other Western countries. With overall smoking prevalence among women increasing in many countries, maternal smoking is clearly an important international health issue. In many developing countries, the lack of adequate health facilities, and tobacco education or control programs can increase the health risks of maternal smoking on the fetus and infant. Importantly, this analysis found neither race, nor socioeconomic status, were significantly associated with SIDS risk, suggesting universal tobacco screening and education during pregnancy should be undertaken. Finally, while many health benefits of breast feeding have been identified, this study failed to find a significant protective effect of breast feeding in reducing the risk of SIDS mortality. Further study of this topic is needed before breast feeding can be recommended or discounted as a modifiable risk factor in the prevention of SIDS. The relationship between maternal smoking status and SIDS was clear. The importance of abstaining from tobacco smoke exposure during and after their pregnancy should be stressed when educating all pregnant women how to maintain a healthy pregnancy and smoking cessation guidance should be made available to all pregnant women with a positive screen.

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