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Acute and chronic respiratory diseases in pregnancy: Associations with placental abruption

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KEY WORDS

Respiratory disease
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Bronchitis

Objective: This study was undertaken to examine the associations between maternal respiratory diseases and placental abruption.

Study design: A population-based, retrospective cohort study was conducted to examine the associations between maternal respiratory diseases and abruption in the United States. Data on women who delivered singleton births ($n = 37,314,022$) were derived from the National Hospital Discharge Survey for the years 1993 to 2003. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes were used to identify pregnant women hospitalized for acute upper respiratory diseases, viral and bacterial pneumonia, acute bronchitis, and acute bronchiolitis, chronic bronchitis, asthma, and abruption. Relative risk (RR) and 95% CI were derived from multivariable logistic regression models to evaluate the associations after adjusting for maternal age, race, marital status, smoking, cocaine use, adequacy of prenatal care, maternal insurance status, geographic location, and year of birth (although data on smoking and cocaine use are likely underreported).

Results: The rate of abruption was 9.7 per 1,000 singleton births. The overall rate for acute respiratory conditions was 2.2 per 1000 pregnancies. Acute upper respiratory diseases (RR 3.2, 95% CI 3.0-3.4) and viral/bacterial pneumonia (RR 2.2, 95% CI 1.9-2.4) were associated with abruption. The rate of chronic respiratory conditions was 9.0 per 1,000 pregnancies. Chronic bronchitis was strongly associated with abruption (RR 31.8, 95% CI 29.6-34.3), but the association between asthma and abruption was modest (RR 1.1, 95% CI 1.0-1.2). Stratified analysis by maternal race showed that asthma was associated with abruption among black women but not white women.

Conclusion: Pregnancies complicated by acute and chronic respiratory diseases requiring hospitalization are associated with placental abruption.

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Placental abruption is one of most commonly encountered uteroplacental bleeding disorders with high rates of perinatal and maternal morbidity and mortality.^{1,2} The prevalence of abruption ranges between 5 and 20 per 1000 pregnancies,² and its cause still remains poorly understood, though a variety of socioeconomic and environmental factors have been implicated.³⁻⁵ The recurrence risk for abruption is about 10% to 15% in subsequent pregnancies.⁶

The prevalence of asthma during pregnancy is estimated to be between 37 and 84 per 1000 women in the United States.⁷ The condition is associated with an array of adverse pregnancy outcomes.⁸ Uncontrolled asthma can lead to reduced oxygenation at the maternal-fetal interface,⁹ which may be associated with increased risk of adverse pregnancy outcomes. The prevalence of community-acquired pneumonia among pregnant women is quite similar to that of the general population, although it has a much more virulent course during pregnancy.¹⁰ The incidence of community-acquired pneumonia is approximately 1.5 per 1000 pregnancies.^{11,12}

Despite the widespread use of antibiotics and recent advances in respiratory therapy, acute and chronic respiratory conditions during pregnancy remain important risk factors for maternal and fetal morbidity and mortality.^{8,12-15} Several studies have reported that respiratory diseases during pregnancy are associated with adverse pregnancy outcomes, including intrauterine growth restriction,¹⁶ preterm birth,^{13,17,18} small-for-gestational age births,^{12,19} and neonatal death.^{17,18} Although to our knowledge there has only been a single study from Canada that reported an association between asthma during pregnancy and placental abruption,⁸ the potential association between other forms of respiratory tract illnesses and placental abruption remains unknown. We examined these associations in a large population-based cohort of more than 37 million singleton pregnancies in the United States.

Material and methods

Data source

A retrospective cohort study was conducted using data extracted from the National Hospital Discharge Survey (NHDS) for the years 1993 to 2003.²⁰ The National Center for Health Statistics (NCHS) conducts surveys on yearly basis that comprise discharges from noninstitutional hospitals, exclusive of federal, military, and Veteran Administration hospitals, located in the 50 states and the District of Columbia. It covers discharges from short stay, general hospitals with an average length of stay of less than 30 days, as well as pediatrics general hospitals. The initial sample was chosen in 1964 from the National Master Facility Inventory that included short-stay hospitals. This sample has been supplemented

periodically to include facilities opened since 1964. The sampling of hospitals for the survey was based on probabilities ranging from certainty for the largest hospitals to 1 in 40 for the smallest hospitals. A second stage systemic random sample of discharges was then selected from each sampled hospital.²⁰ The National Hospital Discharge Survey abstracts information on discharge diagnosis as well as demographics (age, gender, and race). Information on race was missing for up to 29% of the records in any given year (1993-2003).²⁰

We used the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes to identify mothers with the following hospital discharge conditions: acute respiratory conditions including acute upper respiratory diseases (ICD-9-CM 465.8 and 465.9), acute bronchitis (ICD-9-CM 466.0-466.19), and viral/bacterial pneumonia (ICD-9-CM 480.0-487.0), as well as chronic respiratory conditions including chronic bronchitis (ICD-9-CM 491.0-492.8 and 495.9-506.0) and asthma (ICD-9-CM 493.0-493.9). Data on singleton births (ICD-9-CM V270, V271, V301, V302, V3000, and V3001) and placental abruption (ICD-9-CM 641.21-641.23) were also extracted.

Placental abruption, defined as the premature separation of a normally implanted placenta, was the principal outcome. Factors that were considered to be associated with or influenced the risk of abruption included maternal age (categorized as 14-24, 25-34, and 35-49 years), maternal race (categorized as white, black, and others), marital status (married or unmarried), adequacy of prenatal care (adequate or inadequate), maternal smoking (yes or no), cocaine use (yes or no), insurance type (medicare, medicaid, indemnity, uninsured, and others), geographic location (Northeast, Midwest, South, and West) and birth year (1993-1994, 1995-1996, 1997-1998, 1999-2000, and 2001-2003).

The study was approved by the Institutional Review Board of UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ.

Statistical analysis

Distributions of maternal sociodemographic and behavioral characteristics as well as delivery year were examined according to their respiratory disease status (no condition, acute conditions and chronic conditions). Multivariable logistic regression analysis was performed to examine the associations between acute and chronic respiratory conditions and placental abruption before and after controlling for potential confounders including maternal age, maternal race, marital status, adequacy of prenatal care, maternal smoke, cocaine use, insurance type, geographic location, and birth year. Data on smoking and cocaine use are likely underreported in this dataset because the information was self-reported. We then repeated the analysis after stratifying the data

Table I Distribution of maternal characteristics among women with acute and chronic respiratory conditions: United States, 1993-2003

Characteristics	No condition (%) n = 36,902,006	Acute conditions (%) n = 80,533	Chronic conditions (%) n = 331,483
Maternal age (y)			
14-24	37.2	40.4	43.7
25-34	50.4	48.0	44.5
35-49	12.4	11.6	11.8
Maternal race			
White	74.1	75.4	68.7
Black	16.0	15.3	25.1
Others	10.0	9.3	6.3
Marital status			
Married	63.6	52.1	49.3
Unmarried	36.4	47.9	50.7
Inadequate prenatal care	1.6	0.5	1.9
Smoking	1.5	3.2	6.2
Cocaine use	0.3	0.4	0.6
Insurance groups			
Medicare	0.6	0.3	0.6
Medicaid	34.7	41.9	37.5
Indemnity*	55.2	51.6	52.9
Uninsured	4.5	3.0	3.5
Others	5.0	3.2	5.6
Geographic location			
Northeast	16.0	18.2	22.1
Midwest	19.3	20.9	27.7
South	39.9	37.6	26.8
West	24.8	23.2	23.4
Birth year			
1993-1994	15.0	16.7	10.7
1995-1996	16.3	20.7	13.8
1997-1998	19.5	16.0	17.8
1999-2000	19.1	21.3	20.6
2001-2003	30.0	25.3	37.2

All differences in proportion are statistically significant ($P < .001$).

* Indemnity = Worker's compensation, Blue Cross/Blue Shield.

by maternal race categories. Relative risk (RR) and 95% CI were used to describe the associations. All statistical analyses were performed with the use of the SAS version 9.1 (SAS Institute, Cary, NC).

Results

In the NHDS data, between 1993 and 2003, there were 37,314,022 (unweighted $n = 306,051$) hospitalized women that delivered a singleton infant. The rates of acute and chronic conditions were 2.2 and 9.0 per 1,000 singleton pregnancies, respectively. Pregnant women hospitalized for acute and chronic respiratory conditions were examined for differences in maternal sociodemographic and

behavioral characteristics (Table I). Compared with women without respiratory conditions, those with acute and chronic respiratory conditions were more likely to be young, unmarried, smokers, cocaine users, enrolled in a Medicaid program, and be residents of Northeast and Midwest geographic locations. The frequency of acute respiratory conditions among white women was substantially higher than among black women. On the other hand, black women and those with inadequate prenatal care were more likely to have experienced chronic respiratory conditions that required hospitalization.

After controlling for maternal sociodemographic and behavioral factors, acute upper respiratory disease (RR 3.2, 95% CI 3.0-3.4) and viral and bacterial pneumonia (RR 2.2, 95% CI 1.9-2.4), but not acute bronchitis, were associated with abruption (Table II). Chronic bronchitis (RR 31.8, 95% CI 29.6-34.3) was associated with abruption, although the association with maternal asthma was of borderline significance (RR 1.1, 95% CI 1.0-1.2). Smoking and cocaine use were greatly underreported in this data set.

We further examined the association between respiratory diseases and abruption after stratifying the data by maternal race (Table III). The association with abruption was higher among white women with acute upper respiratory diseases, viral and bacterial pneumonia, as well as acute bronchitis and bronchiolitis. The association between viral and bacterial pneumonia and abruption was higher among black women. Of the chronic conditions, the association between chronic bronchitis and abruption was significantly higher among white women and between asthma and abruption was significantly higher among black women.

Comment

We examined the association between maternal respiratory diseases and placental abruption. Our population-based, retrospective cohort study of more than 37 million singleton deliveries in the U.S. between 1993 and 2003 shows that both acute and chronic respiratory conditions during pregnancy are associated with placental abruption. We speculate that acute and chronic respiratory conditions may trigger an inflammatory and hypoxic process at the maternal-fetal interface that consequently may lead to placental abruption.

Our finding of an association between asthma during pregnancy and abruption corroborates previous findings. A Canadian study reported an association between maternal asthma and placental abruption.⁸ However, a closer examination of our data shows that the association between asthma and abruption was confined to black women but not white women. This association may be attributable to disparity in access to health care that may have resulted in a higher asthma

Table II Association between respiratory diseases during pregnancy and placental abruption among hospitalized women with singleton pregnancies: United States, 1993-2003

Respiratory diseases	Total number of pregnancies	Placental abruption		
		Rate (%)	Unadjusted RR (95% CI)	Adjusted RR (95% CI)
No respiratory disease	36,902,006	0.96	1.0 (Reference)	1.0 (Reference)
Acute condition (any)*	80,533	2.29	2.4 (2.3-2.5)	2.4 (2.3-2.5)
Acute upper respiratory diseases	42,580	2.98	3.2 (3.0-3.4)	3.2 (3.0-3.4)
Viral and bacterial pneumonia	17,202	2.05	2.2 (1.9-2.4)	2.2 (1.9-2.4)
Acute bronchitis	21,507	1.05	1.1 (1.0-1.3)	1.0 (0.9-1.2)
Chronic conditions (any)*	336,175	1.40	1.4 (1.3-1.5)	1.3 (1.2-1.4)
Chronic bronchitis	3,818	25.09	34.5 (32.1-37.1)	31.8 (29.6-34.3)
Asthma	332,357	1.07	1.1 (1.0-1.2)	1.1 (1.0-1.2)
Any acute or chronic condition*	412,016	1.61	1.6 (1.5-1.7)	1.5 (1.4-1.6)

Adjustments were made for maternal age, race, marital status, prenatal care, insurance, geographic location, pregnancy year, tobacco smoke, and cocaine use.

* The number of women with acute conditions (n = 80,533) and chronic conditions (n = 336,175) may not add up to the total of "Any acute or chronic condition" (n = 412,016) because a woman may have received a diagnosis with more than 1 acute or chronic condition.

Table III Association between respiratory diseases and placental abruption among hospitalized women with singleton pregnancies by maternal race: United States, 1993-03

Respiratory diseases	Placental abruption: Adjusted RR (95% CI)	
	White women	Black women
No respiratory disease	1.0 (Reference)	1.0 (Reference)
Acute conditions		
Acute upper respiratory diseases	4.4 (4.1-4.6)	—
Viral and bacterial pneumonia	2.5 (2.2-2.9)	3.3 (2.8-3.8)
Acute bronchitis and acute bronchiolitis	1.5 (1.3-1.8)	—
Any acute condition	3.2 (3.0-3.3)	1.1 (1.0-1.3)
Chronic conditions		
Chronic bronchitis	42.0 (38.9- 45.4)	—
Asthma	0.9 (0.8-1.0)	1.5 (1.4-1.6)
Any chronic condition	1.4 (1.3-1.5)	1.5 (1.4-1.6)
Any acute or chronic condition	1.8 (1.7-1.9)	1.5 (1.4-1.5)

Adjustments were made for maternal age, marital status, prenatal care, insurance, geographic location, pregnancy year, tobacco smoke, and cocaine use.

hospitalization rates among black women²¹⁻²³ compared with white women.

We noted a strong association between chronic bronchitis and placental abruption (Tables II and III). Although this association persisted after adjustment for several potential confounders, it is likely that active exposure to smoking is underreported. Furthermore, the possibility of our reported associations being affected by residual confounding (because unmeasured factors such as passive exposure to smoking) cannot be overlooked.

Because therapeutic regimens are not well documented in these data, we were unable to separate patients by their medication type. The possibility that medications used for treatment of asthma such as corticosteroids may cause abruption in some asthmatic pregnant women cannot be ruled out, and the risk of placental abruption caused by these drugs at prophylactic doses remains unknown. According to various studies on asthma

and preventive medications during pregnancy, adverse pregnancy outcomes as a result of asthma medications used during pregnancy appears to be minimal than risks associated with largely uncontrolled asthma.^{9,24-26}

Our finding regarding the association of acute conditions (viral and bacterial pneumonia) and chronic conditions (asthma) with placental abruption is important. Although we were able to demonstrate an association between upper-respiratory disorders and abruption, the direction of causation remains unknown, suggesting that future studies should examine the nature of associations and the direction of causation by which maternal respiratory diseases and the potential for other environmental irritants such as passive smoking or corn dust²⁷ may be associated with abruption.

Our study has limitations. Although we adjusted the analysis for several maternal sociodemographic and behavioral characteristics, data on smoking and cocaine

use during pregnancy are underreported in the data. The observation that women diagnosed with acute and chronic respiratory conditions tend to report smoking and cocaine use more often than women without these conditions (Table I), may lead to a differential misclassification with regard to smoking during pregnancy. Such misclassification, if present, will likely result in relative risks being driven away from null.²⁸ Whether a true association between respiratory disease and abruption persists, or if the association is largely mediated through smoking/cocaine use in our study remains unknown. Our findings therefore warrant cautious interpretation. Data on maternal race were missing for up to 20% of records in a given year between 1995 and 2001 and for up to 30% of records thereafter. However, a previous sensitivity analysis that examined hospitalization and mortality from asthma in this data did not change the rate of outcomes.²¹ Finally, our findings are based on data on women that required hospitalization involving serious conditions. Thus, the reported prevalences of respiratory tract conditions are likely underestimated, thereby limiting generalizability to pregnant women seen as outpatients. On the other hand, the strengths of the study include its large sample size, the fact that it is a population-based cohort study with a better quality dataset adequately capturing discharge diagnosis of abruption and respiratory disorders, and controlling for potential confounding factors.

Conclusions

The study suggests that maternal acute and chronic respiratory diseases during pregnancy that require hospitalization are associated with placental abruption. Future studies should examine the nature of associations and the direction of causation, especially to shed light on whether the associations are driven by exposures to maternal smoking and cocaine use before and during pregnancy.

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