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Respiratory Illness Hospitalizations Among Pregnant Women During Influenza Season, 1998–2008

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Abstract

To examine health care burden, pregnancy outcomes and impact of high risk medical conditions among pregnancy hospitalizations during influenza season. Length of stay, hospitalization charges, and delivery complications were compared between hospitalizations with and without respiratory illness and compared by presence of high risk medical conditions. Length of stay and hospital charges were significantly increased among respiratory illness hospitalizations versus non-respiratory hospitalizations. Among respiratory illness hospitalization, the odds of intrauterine fetal demise were increased (adjusted odds ratio (aOR) 2.50, 95 % confidence interval (CI) 1.97–3.18). Among live births, there were higher odds of preterm delivery (aOR 3.82, 95 % CI 3.53–4.14), cesarean delivery (aOR 3.47, 95 % CI 3.22–3.74), and fetal distress (aOR 2.33, 95 % CI 2.15–2.52). The presence of high risk medical conditions did not impact pregnancy outcomes. Among pregnant women hospitalized during influenza season, those with respiratory illness were more likely than those without respiratory illness to have poor perinatal outcomes, regardless of the presence of high risk conditions. Efforts to minimize influenza morbidity, including universal vaccination and early antiviral therapy should be promoted among all pregnant women.

Keywords

Health care burden; High risk condition; Influenza; Pregnancy; Respiratory illness

Introduction

The recent 2009 H1N1 influenza pandemic highlighted the risks pregnant women face from influenza. High rates of hospital and intensive care unit admissions among pregnant women with influenza were observed [1–4]. In addition to increased maternal morbidity, critically ill pregnant women with influenza during the 2009 pandemic had a higher percentage of poor

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delivery and neonatal outcomes, including increased operative deliveries, lower birth weight, preterm birth, admission to neonatal intensive care units, and neonatal death [2, 3, 5, 6]. The increased maternal and fetal morbidity experienced during the 2009 H1N1 pandemic was also observed in earlier influenza seasons and previous pandemics [7–10].

These elevated risks for complications have been observed among healthy pregnant women. However little is known about the impact of high risk medical conditions on influenza-related morbidity in pregnant women. In the general non-pregnant population, influenza-related complications are increased in the presence of certain high risk medical conditions. A study of patients with influenza hospitalized in the United States during the 2009 H1N1 pandemic found that over 70 % had at least one high risk medical condition [11]. Similar high proportions were reported in other studies [12]. In contrast, several studies found that approximately 30 % of pregnant women hospitalized with influenza during the 2009 H1N1 pandemic had a comorbid condition [2, 3].

In addition, little is known about the nationwide burden from influenza in pregnant women. This study aims to further explore the morbidity of influenza related hospitalizations among pregnant women using a nationwide sample of inpatient care, the Healthcare Cost and Utilization Project (HCUP) Nationwide Inpatient Database (NIS). This report expands on a previous report [13] by including data from more recent influenza seasons and examining charges associated with hospitalization. In addition we sought to explore the impact that high risk medical conditions have on pregnancy related influenza morbidity. We hypothesized that pregnant women hospitalized with respiratory illness increase the burden on the health care system by experiencing longer and more expensive hospitalizations, and that these women will be more likely to experience adverse pregnancy outcomes compared to those without respiratory illness. We expect high risk medical conditions to further increase the health care burden and adverse outcomes experienced by pregnant women.

Methods

Hospital discharge data were obtained from the HCUP NIS database from 1998 through 2008. The NIS is the largest collection of all-payer inpatient care data in the United States and provides patient and demographic diagnostic and procedural data on over 8 million hospital stays from over 1,000 hospitals annually. The NIS is a stratified probability sample of 20 % of all community hospitals in the United States based on a sampling frame using five strata: geographic region (Northeast, Midwest, West, and South), hospital size (based on number of beds), location (urban or rural), teaching status, and control (public, voluntary, or, proprietary). Community hospitals are defined by the American Hospital Association as all nonfederal general and specialty hospitals with an average length of stay less than 30 days whose facilities are open to the public. In 2008, the sampling frame for the NIS included approximately 95 % of all hospital discharges in the United States and participating states included 95 % of the United States population. To generate nationwide estimates of inpatient hospitalization the data are weighted. The weighting process accounts for changes in the number of states included over the years as well as different hospitals sampled each year. The data base provides diagnosis and procedure fields at each discharge coded by International Classification of Diseases, 9th revision, Clinical Modifications (ICD-9-CM).

The Agency for Healthcare Research and Quality records data received from states into a consistent format and performs quality control procedures to confirm that data values are valid, internally consistent and consistent with established norms, when feasible. Edit procedures aim to make the data usable without extensive further editing. A more thorough overview of HCUP and NIS can be found elsewhere [14]. The NIS is available to the public and does not contain personal identifying information; therefore, the Centers for Disease Control and Prevention deemed this investigation to be exempt from review by an institutional review board.

Influenza season was defined using the information on the weekly percentage of positive viral isolates generated by World Health Organization (WHO) and National Respiratory and Enteric Virus Surveillance Systems Collaborating Laboratories, as has been reported previously [15]. Because HCUP provides only the month of hospitalization, the beginning month of the influenza season for each year was defined as the first fall or winter month containing at least 5 % of tests positive for influenza A non-subtyped, A (H1N1), A (H3N2), or influenza B. Similarly, the end of the influenza season was considered the last winter or spring month that included at least 5 % positive tests.

There is no patient identifier in the NIS, and therefore the unit of analysis is the hospital discharge record because one patient can be admitted multiple times. Our analysis included all pregnancy hospitalizations among women ages 15–44 years. Pregnancy hospitalizations were identified by the presence of any primary or secondary ICD-9-CM code of 640–679, V22, V23, and V27. Hospitalizations with codes indicating an ectopic gestation, molar pregnancy, or abortion (spontaneous and induced) were excluded. Delivery pregnancy hospitalizations were identified by the ICD-9-CM diagnosis codes 650, V27, procedure codes 72.0–72.9, 73.22, 73.59, 73.6, 74.0–74.2, 74.4, 74.99, and Diagnosis Related Group (DRG) codes 370–375. Pregnancy hospitalizations were also classified as delivery if any of the following outcomes were noted: preterm birth (ICD-9-CM diagnosis code 644.2), cesarean delivery (ICD-9-CM procedure codes 74.0-74.2, 74.4, 74.99 and DRG codes 370, 371), operative vaginal delivery (ICD-9-CM diagnosis code 669.5 and procedure codes 72.0–72.4, 72.6–72.7), intrauterine fetal demise or stillbirth (ICD-9-CM diagnosis codes 656.4, V27.1, V27.3, and V27.4), and fetal distress (656.3 and 659.7).

Respiratory illness was defined using codes for pneumonia and influenza (ICD-9-CM codes 480–488). High risk medical conditions were selected based on chronic medical conditions that confer a higher risk for influenza complications as specified by the Advisory Committee on Immunization Practices (ACIP) [16] and included the following: chronic pulmonary diseases including asthma (493), COPD (466), cystic fibrosis (277 and V77.6), and other chronic lung diseases (491–492, 494, 496, 500–506); chronic cardiac diseases including heart failure (428), arrhythmias (426–427), structural heart disease (393–398, 745–746), ischemic heart disease (412–414, 440), cardiomyopathies (425), and endocarditis (421); chronic renal disease (403–404, 585–587, V45.1, V45.11, V56); chronic hepatic disease (571); seizure disorders (345); hemoglo-binopathies (282); diabetes mellitus (250 and 648.0); HIV/AIDS (042, 795.71, V08); and chronic steroid use (V58.65).

Characteristics of pregnant women were compared between those hospitalized with respiratory illness and those hospitalized without respiratory illness. Characteristics examined included delivery status (delivered or undelivered), age group (15–24, 25–34, or 35–44 years), presence of at least one high risk medical condition, primary expected payer (public, private or other), hospital location (urban or rural), and geographic location (Northeast, Midwest, South or West). Comparisons were performed using Chi-square tests.

Lengths of stay and hospital charges (the amount hospitals billed for services) were compared between pregnancy hospitalizations with and without respiratory illness during influenza season. A log-linear model was used to analyze length of stay and a linear model was used to analyze hospital charges. Means were adjusted for age group, presence of at least one high risk medical condition, primary expected payer, hospital location, and geographic location. Hospital charges for each year were adjusted for inflation to 2008 dollars. Models were built separately for delivery and non-delivery hospitalizations. This methodology was then used to compare adjusted means of length of stay and hospital charges among pregnant women hospitalized during influenza season with respiratory illness, comparing those with and without high risk medical conditions.

Logistic regression was used to calculate adjusted odds of delivery outcomes among those with versus those without respiratory illness, controlling for characteristics indicated above. Intrauterine fetal demise was examined among all pregnancy hospitalizations and preterm birth, cesarean delivery, and fetal distress were examined among hospitalizations with live births. Among pregnant women hospitalized during influenza season with respiratory illness, the odds of these outcomes were then compared among those with and without high risk medical conditions.

SAS-callable SUDAAN version 9.2 (RTI, Research Triangle Park, North Carolina) was used for all analyses to account for the complex sampling design and to provide weighted estimates. Data analyses were performed independently by two programmers for accuracy.

Results

There were an estimated 17,548,022 pregnancy hospitalizations over the 10 influenza seasons examined, and of those, 56,337 (0.3 %) had a diagnosis of respiratory illness. Selected characteristics of pregnancy hospitalizations during influenza seasons 1998 through 2008 are shown in Table 1. A greater proportion of women hospitalized with respiratory illness were aged 15–24 or 35–44 than those without respiratory illness ($P < 0.0001$). Those with respiratory illness were more likely than those without respiratory illness to remain undelivered during their hospitalization (69 vs. 10 %, $P < 0.0001$) and have at least one high risk medical condition (29 vs. 5 %, $P < 0.0001$). Those hospitalized with respiratory illness were also more likely to have Medicaid/Medicare as the intended payer (51 vs. 40 %, $P < 0.0001$) and to be located in rural areas (16 vs. 13 %, $P < 0.0001$).

Among both delivery and non-delivery hospitalizations, the average length of stay was significantly increased for respiratory illness hospitalizations when compared with non-respiratory hospitalizations (Table 2). Among delivery hospitalizations, the average length of

stay was 7.0 days for hospitalizations with respiratory illness compared with 2.6 days for hospitalizations without respiratory illness ($P < 0.0001$). Among non-delivery hospitalizations, the average length of stay was 4.1 days for hospitalizations with respiratory illness compared with 3.0 days for hospitalizations without respiratory illness ($P < 0.0001$).

Hospital charges were significantly increased when respiratory illness was present among both delivery and non-delivery hospitalizations (Table 2). The difference in charges with or without respiratory illness was greatest among delivery hospitalizations. The average hospital charge among delivery hospitalizations with respiratory illness was $35,204 compared with an average of $9,444 without respiratory illness ($P < 0.0001$).

Among hospitalizations with respiratory illness, the presence of at least one high risk medical condition further increased the average length of stay and hospital charges (Table 2). The difference was more prominent among delivery hospitalizations, with an average length of stay of 9.1 days if at least one high risk medical condition was present versus 6.9 days among those without high risk medical conditions ($P < 0.0001$). Among delivery hospitalizations, the average charges were also greater among those with at least one high risk medical condition ($50,873 vs. $31,326 among those without high risk medical conditions, $P < 0.0001$).

Selected pregnancy outcomes and mode of delivery for hospitalizations with and without respiratory illness are shown in Table 3. Among live births, the odds of preterm birth were higher among women with respiratory illness than among women without respiratory illness (adjusted odds ratio (aOR) 3.82, 95 % confidence interval (CI) 3.53–4.14). Fetal distress was also more likely among live births when respiratory illness was present (aOR 2.33, 95 % CI 2.15–2.52). Among all delivery hospitalizations, women with respiratory illness were more likely to experience fetal demise (aOR 2.50, 95 % CI 1.97–3.18) than women without respiratory illness. Women with respiratory illness were more likely to deliver by cesarean section than women without respiratory illness (aOR 3.47, 95 % CI 3.22–3.74). Among delivery hospitalizations of women with respiratory illness, having at least one high risk medical condition was associated with a higher risk for cesarean delivery (aOR 1.44, 95 % CI 1.22–1.70), but not for preterm birth, fetal distress, or fetal demise (Table 4).

Comment

Our findings demonstrate increased hospital burden, adverse pregnancy outcomes, and cesarean deliveries among hospitalized pregnant women with respiratory illness, compared to hospitalized pregnant women without respiratory illness, during the influenza season. Among hospitalizations with respiratory illness, the presence of high risk medical conditions did not impact pregnancy outcomes.

In our study, the presence of respiratory illness increased the odds of preterm birth, cesarean delivery, and fetal distress. These findings may partially explain the higher charges and increased length of stay among delivery hospitalizations and are consistent with what has been observed during previous influenza seasons. In one study, women hospitalized in 2009 with severe H1N1 influenza had an average gestational age of 34.8 weeks at delivery [2]. In

another study of pregnant women with H1N1 influenza in 2009 admitted to intensive care units, among 60 births after 20 weeks' gestation, 39 % were preterm and 57 % were admitted to a neonatal intensive care unit [5]. Increased odds of preterm birth, cesarean delivery and fetal distress were previously reported among pregnant women with respiratory illness during influenza seasons 1998 though 2002 [13]. Our study also demonstrated that pregnancies complicated by respiratory illness had increase odds of intrauterine fetal demise. Although high rates of stillbirth were reported during the influenza pandemics of 1918 and 1957, appropriate comparison groups were not available [7, 8]. There have been several reports documenting transplacental transfer of influenza virus from the mother to amniotic fluid and fetal tissue [17]. However, further investigation is needed to explore the effects of influenza in pregnancy and the potential pathophysiological relationships between maternal exposure, infection, and fetal loss.

It has been suggested that the presence of high risk medical conditions in pregnancy increases the rate of hospitalization during the influenza season when compared to pregnant women without high risk conditions [9, 10]. However, our findings suggest that among delivery hospitalizations during the influenza season, having a high risk medical condition in addition to a respiratory illness does not have as much impact on perinatal outcome as respiratory illness alone. Physiologic alterations to the respiratory, cardiovascular and immune systems during pregnancy may confer a higher risk for severe consequences of infections, even among otherwise healthy pregnant women [18].

A major strength of this study is the use of a large sample of nationwide hospitalizations over a period of ten influenza seasons. In addition, there are few studies looking at the specific impact of high risk medical conditions on influenza related pregnancy complications. However, there are several limitations inherent with the use of diagnosis codes which should be considered. Laboratory confirmation of influenza was not available; nonetheless diagnostic testing is not always performed particularly if clinical suspicion of influenza infection is high [19]. The codes for influenza and pneumonia were chosen as a proxy for influenza based on the assumption that respiratory hospitalizations during influenza seasons can be largely attributed to these diagnoses. However it is possible that use of these codes for our analyses overestimated the impact of influenza and we also cannot determine what proportion of these effects might be attributable to influenza versus other respiratory illnesses. We were unable to examine certain factors which might impact outcomes, such as race/ethnicity, gestational age, and influenza vaccination status. Some of the diagnosis codes for comorbidities examined, such as asthma, may have poor sensitivity [20]. Finally, due to the cross-sectional nature of the analysis, our study cannot determine causality between influenza and increased health care burden, adverse pregnancy outcomes, or cesarean delivery.

In conclusion, our study demonstrates that pregnancy complications and higher health care charges are associated with respiratory illness during the influenza season among pregnant women. The risk of poor pregnancy outcomes among pregnant women with such illness do not appear to be substantially affected by the presence of high risk medical conditions. Obstetric providers should have heightened awareness that all pregnant women hospitalized with respiratory illness during influenza season may be at risk for severe morbidity. CDC's

Advisory Committee on Immunization Practices (ACIP) and the American College of Obstetricians and Gynecologists (ACOG) recommend universal vaccination of pregnant women with inactivated influenza vaccines [21, 22]. Vaccination of pregnant women can lead to improved outcomes both for mother and infant, including reduced risks of maternal influenza, prematurity, small for gestational age, and laboratory-confirmed infant infection [23, 24]. CDC also recommends early antiviral treatment of pregnant women with suspected influenza in order to minimize severe illness [25]. Efforts to minimize morbidity from influenza, such as universal vaccination, prompt evaluation, and early antiviral therapy, should be strongly promoted among all pregnant women.

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Table 1

Selected characteristics of pregnancy hospitalizations during influenza season (1998–2008)

Characteristic	Hospitalization with respiratory illness (%) (N = 56,337)	Hospitalization without respiratory illness (%) (N = 17,491,685)
Status at discharge*		
Delivered	31.0	90.5
Undelivered	69.0	9.5
Age*		
15–24	40.7	36.0
25–34	44.2	50.1
35–44	15.2	14.0
Presence of high risk medical condition*,a		
≥ 1	29.1	4.6
None	70.9	95.4
Primary payer*		
Public	51.2	39.6
Private	41.1	54.2
Other	7.7	6.2
Hospital location*		
Urban	84.3	86.8
Rural	15.7	13.3
Geographic location*		
Northeast	16.3	18.2
Midwest	25.4	23.6
South	37.4	32.3
West	20.8	25.9

*Chi square $P<0.0001$

[a]High risk medical conditions include conditions for which influenza vaccination is recommended by the Advisory Committee on Immunization Practices (chronic cardiac disease, chronic pulmonary disease, diabetes mellitus, chronic renal disease, malignancies, and immunosuppressive disorders)

Table 2

Length of stay and hospital charges of pregnancy hospitalizations by delivery status and presence of high risk medical conditions during influenza season (1998–2008)

	Delivery hospitalizations (N = 15,843,026)				Non-delivery hospitalizations (N = 1,704,996)			
	Adjusted mean length of stay[a]		Adjusted mean hospital charges[a]		Adjusted mean length of stay[a]		Adjusted mean hospital charges[a]	
	Days (SE)	*P* value	$ (SE)	*P* value	Days (SE)	*P* value	$ (SE)	*P* value
Respiratory illness[b]								
Yes	7.01 (0.14)	<0.0001	35,204 (1,144)	<0.0001	4.10 (0.06)	<0.0001	17,743 (4,469)	<0.0001
No	2.57 (0.01)		9,444 (92)		2.97 (0.02)		9,606 (187)	
High risk medical condition (among respiratory illness)[c]								
Yes	9.11 (0.33)	<0.0001	50,873 (2,967)	<0.0001	4.64 (0.12)	<0.0001	21,027 (975.56)	<0.0001
No	6.89 (0.17)		31,326 (1,101)		4.06 (0.07)		16,622 (495)	

SE standard error

[a]Means are adjusted for the following characteristics, using log-linear modeling for length of stay and linear modeling for hospital charges: age, primary expected payer, hospital location, and geographic location

[b]Also adjusted for presence of high risk medical conditions

[c]High risk medical conditions include conditions for which influenza vaccination is recommended by the Advisory Committee on Immunization Practices (chronic cardiac disease, chronic pulmonary disease, diabetes mellitus, chronic renal disease, malignancies, and immunosuppressive disorders)

Table 3

Odds of selected pregnancy outcomes among delivery hospitalizations, by presence of respiratory illness during influenza season (1998–2008)

Outcome	Respiratory illness present (N = 17,136) N (%)	Respiratory illness absent (N 15,722,564) N (%)	aOR (95 % CI)[a]
Preterm birth[b]	4,420 (25.8)	1,140,648 (7.3)	3.82 (3.53–4.14)
Cesarean delivery[b]	10,185 (59.4)	4,415,731 (28.1)	3.47 (3.22–3.74)
Fetal distress[b]	4,700 (27.4)	2,093,426 (13.3)	2.33 (2.15–2.52)
Intrauterine fetal demise[c]	333 (1.9)	102,993 (0.7)	2.50 (1.97–3.18)

a*OR* adjusted odds ratio, *CI* confidence interval

[a]Adjusted for the following characteristics: age, primary expected payer, hospital location, geographic location, and presence of high risk medical conditions (including conditions for which influenza vaccination is recommended by the Advisory Committee on Immunization Practices: chronic cardiac disease, chronic pulmonary disease, diabetes mellitus, chronic renal disease, malignancies, and immunosuppressive disorders)

[b]Among live births only

[c]For intrauterine fetal demise, total N for respiratory illness present = 17,468; total N for respiratory illness absent = 15,825,557

Table 4

Odds of selected delivery outcomes among delivery hospitalizations with respiratory illness, by presence of high risk medical condition status during influenza season (1998–2008)

Outcome	≥1 High risk medical condition (N = 3,917) N (%)	No high risk medical condition (N = 13,218) N (%)	aOR (95 % CI)[a]
Preterm birth[b]	1,102 (28.1)	3,317 (25.1)	1.13 (0.94–1.35)
Cesarean delivery[b]	2,611 (66.7)	7,574 (57.3)	1.44 (1.22–1.70)
Fetal distress[b]	1,106 (28.2)	3,595 (27.2)	1.07 (0.90–1.27)
Intrauterine fetal demise[c]	107 (2.7)	225 (1.7)	1.53 (0.89–2.62)

aOR adjusted odds ratio, *CI* confidence interval

High risk medical conditions include conditions for which influenza vaccination is recommended by the Advisory Committee on Immunization Practices (chronic cardiac disease, chronic pulmonary disease, diabetes mellitus, chronic renal disease, malignancies, and immunosuppressive disorders)

[a] Adjusted for the following characteristics: age, primary expected payer, hospital location, geographic location

[b] Among live births only

[c] For intrauterine fetal demise, total N for high risk medical condition present = 4,025; total N for respiratory illness high risk medical condition absent = 13,444