

Adverse Outcomes in Pregnant Women Hospitalized With Respiratory Syncytial Virus Infection: A Case Series

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We identified 10 women hospitalized with respiratory syncytial virus infection during pregnancy. Diagnoses included pneumonia/atelectasis (5), respiratory failure (2), and sepsis (2). Six had obstetrical complications during hospitalization, including 1 induced preterm birth. One required intensive care unit admission and mechanical ventilation. Four infants had complications at birth.

Keywords. respiratory syncytial virus; pregnancy; respiratory infections; maternal infections; maternal vaccines.

Respiratory syncytial virus (RSV) infection during pregnancy has not been well described; however, it is an increasingly recognized cause of acute respiratory illness (ARI), which may be clinically severe and result in hospitalization [1, 2]. A technical consultation group convened by the Centers for Disease Control and Prevention has emphasized the need to characterize RSV infection during pregnancy, with a priority of describing burden, risk factors for severe disease, and pregnancy and neonatal outcomes [3]. In this retrospective study, we identified pregnant women who were hospitalized with RSV infection.

METHODS

Using a validated algorithm, we identified pregnant women at Kaiser Permanente Southern California aged 14–49 years whose pregnancies ended in a live birth between 1 August 2010 and 30 April 2017 [4]. The study was restricted to live births because the algorithm does not accurately identify the timing of nonlive birth outcomes in relation to the RSV infection. Cases were defined as women who were hospitalized during pregnancy (outside of delivery) and tested positive for RSV by viral

culture or polymerase chain reaction in the 2 weeks prior to or during hospitalization. Medical records for RSV hospitalization and delivery were reviewed.

RESULTS

We identified 275 349 pregnant women who met our inclusion criteria. Of those, 1057 were tested for RSV during pregnancy and 25 (2%) were positive. Ten of the 25 women with a positive RSV test were identified as hospitalized cases (Table 1). In comparison, 1159 women were tested for influenza during this time. Testing for both RSV and influenza increased with each season of the study.

Medical History: Current Pregnancy

Median age at RSV hospitalization was 30.5 years (range, 20–42). Seven women were multigravida and 3 were primigravida. Nine had at least 1 comorbid condition: asthma (1), diabetes mellitus (2), hypothyroidism (1), obesity (5), and tobacco smoking during pregnancy (2).

Medical records were reviewed for conditions preceding hospitalization for RSV. Two women had been previously hospitalized: 1 for mastitis and 1 for ARI. Five had pregnancy complications or risk factors, including short cervix, trisomy 21 (on noninvasive prenatal testing), preeclampsia, short pregnancy interval, and fetal macrosomia with polyhydramnios. Eight had received influenza vaccine and 2 had received tetanus, diphtheria, and acellular pertussis vaccine.

RSV Hospitalizations

On admission for the RSV-associated hospitalization, 9 women were in their third trimester; median gestational age was 31 weeks (range, 27–37). The 10 women were hospitalized for a median of 3 days (range, 2–8). Diagnoses included acute upper respiratory tract infection (2), pneumonia (4), asthma exacerbations (2), respiratory failure (2), atelectasis (1), and sepsis (2). RSV infection was included among the discharge diagnoses of 4 and influenza infection of 2. Although all were tested for influenza, only 1 woman had a positive test; this was not identified on her discharge diagnosis. All 10 received albuterol during hospitalization; 8 received antibiotics, 6 oseltamivir, and 3 prednisone.

In 6 of the 10 women, a pregnancy complication was noted during the RSV hospitalization. One had exacerbation of her preexisting short cervix without preterm labor, which was thought to be a result of her respiratory symptoms. Three developed preterm contractions, 2 of whom had coinfections (influenza and urinary tract infection). One was induced for preeclampsia and delivered during the RSV hospitalization.

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Table 1. Characteristics and Outcomes of Pregnant Women Hospitalized for Respiratory Syncytial Virus Infection

Characteristic	No. N = 10
Medical history (current pregnancy) ^a	
Median age, years (range)	30.5 (20–42)
Comorbid conditions ^b	9
Median number of previous pregnancies (range)	1.5 (0–7)
Median number of previous births (range)	1 (0–4)
Influenza vaccine	8
Tetanus, diphtheria, and acellular pertussis vaccine ^c	2
Hospitalizations	2
Preexisting pregnancy complications or risk factors ^d	5
Respiratory syncytial virus hospitalization	
Median gestational age, weeks (range)	31 (27–37)
Days hospitalized (range)	3 (2–8)
Discharge diagnosis ^d	
Acute upper respiratory infection	2
Asthma exacerbation	2
Atelectasis	1
Pneumonia	4
Respiratory failure	2
Sepsis	2
Complications ^e	
Coinfection	2
Intubation	1
Preeclampsia	1
Preterm contractions	3
Preterm induction of labor	1
Neonatal hypoglycemia	1
Short cervix	1
Medications ^e	
Albuterol	10
Antibiotics	8
Oseltamivir	6
Prednisone	3
Delivery hospitalization	
Median gestational age, weeks (range)	39 (36–40)
Cesarean delivery	5
Complications ^e	
Chorioamnionitis	1
Intrauterine growth restriction	1
Preeclampsia	1

^aAt time of respiratory syncytial virus hospitalization admission.

^bComorbidities included asthma, diabetes mellitus, hypothyroidism, obesity, and tobacco smoking during pregnancy.

^cAn additional 5 pregnant women, previously unvaccinated, received this vaccine after discharge.

^dPreexisting pregnancy complications included short cervix, trisomy 21 (on noninvasive prenatal testing), preeclampsia, short pregnancy interval, and fetal macrosomia with polyhydramnios.

^eA pregnant woman may have had more than 1 diagnosis, medication, or complication.

Delivery Hospitalizations

The median gestational age at delivery was 39 weeks (range, 36–40). The median interval from RSV hospitalization admission to delivery was 8 weeks (range, 0–11). Three women had complications during their delivery hospitalization. In addition to the woman induced during her RSV hospitalization, another was induced at 38 weeks for worsening preeclampsia

that, at 36 weeks, was present during RSV hospitalization and worsened after discharge. There were 5 cesarean deliveries, including 1 related to chorioamnionitis and cephalopelvic disproportion.

Case Summaries of Severe RSV Infection

Patient 1 was a 25-year-old woman, G1P0, with a history of poorly controlled type 1 diabetes mellitus. Complications of her current pregnancy included excessive gestational weight gain, mild preeclampsia, fetal macrosomia, and polyhydramnios. At 36 weeks, she was evaluated for influenza-like illness and admitted for preeclampsia. A chest X ray revealed left lower lobe consolidation, and she was diagnosed with pneumonia and sepsis. On hospital day 2, labor was induced for preeclampsia and was complicated by oxygen desaturation and elevated blood pressure. Her infant was delivered by cesarean delivery and transferred to neonatal intensive care for hypoglycemia. During postpartum recovery, the patient developed dyspnea, tachycardia, and hypoxia. Her clinical condition stabilized by postpartum day 3, and she was discharged postpartum day 5 with her infant.

Patient 2 was a 20-year-old woman, G1P0, with a history of allergic rhinitis. She was admitted at 30 weeks for dyspnea and worsening cough. Her exam was significant for bilateral wheezing and trace edema in the extremities. She was started on albuterol and prednisone. Her symptoms worsened, she developed acute respiratory failure, and was admitted to intensive care and intubated. Her symptoms improved on supportive therapy, she was extubated, and 2 days later discharged with a prednisone taper. At 39 weeks, labor was induced for intrauterine growth restriction.

Patient 3 was a 40-year-old woman, G8P4. She was admitted at 29 weeks for asthma exacerbation and acute hypoxemia. She also complained of dysuria and had a history of urinary tract infections. Her medical records were incomplete; however, her discharge note indicated diagnoses including respiratory failure and sepsis with acute organ dysfunction. During hospitalization she received prednisone and albuterol nebulizer treatments, intravenous ceftriaxone and azithromycin, and oral nitrofurantoin. She was discharged on hospital day 5 and had an uncomplicated spontaneous vaginal delivery at 40 weeks.

DISCUSSION

Of the 25 pregnant women in our study who had a positive RSV test, 10 (40%) were hospitalized for ARI. A cross-sectional study of ARI during pregnancy found that RSV contributed to 10%–14% of ARI in pregnant women [5], and serologic findings suggest that 20%–30% of women of child-bearing age are infected with RSV annually [6, 7]. However, severe RSV infection that requires hospitalization during pregnancy is likely underdetected due to infrequent testing [2]. Of the 10 pregnant women in our study who were hospitalized with RSV, 4 were diagnosed with pneumonia, 2 with respiratory failure (1 requiring mechanical ventilation), and 2 with sepsis. One woman

in our study, diagnosed with pneumonia and preeclampsia, was induced during her RSV hospitalization.

Published reports of RSV infection in hospitalized pregnant women are rare. The first case series of RSV infection during pregnancy identified 3 cases; 2 were hospitalized, required mechanical ventilation, and resulted in preterm delivery [2]. In a recently reported retrospective study of ARI-related hospitalizations during pregnancy, Regan et al found 8 of 21 (38%) RSV cases were diagnosed with pneumonia [1]. Several large prospective studies have evaluated the incidence of RSV among pregnant women with influenza-like illness. None were hospitalized; however, subsequent preterm birth was reported in 11% and 29% of women [8–10]. Our study findings emphasize that RSV infection during pregnancy can be clinically severe and may be accompanied by pregnancy complications.

Nine of the 10 women in our study had at least 1 comorbid condition; the most common was obesity (50%). In addition, 1 woman had a history of asthma and 2 had coinfections (1 tested positive for influenza, another had a urinary tract infection). This is similar to Wheeler et al's case series, where all 3 cases had either preexisting asthma or a coinfection. Five women in our study had a pregnancy complication or risk factor prior to their hospitalization for RSV. Prior pregnancy complications (40%) and asthma (20%) were reported with a similar frequency by Regan et al. An additional cross-sectional study of ARI in pregnancy identified 8 women with RSV, 1 of whom was hospitalized; she had a history of asthma and was pregnant with dichorionic diamniotic twins [11].

Nine women in our study were in their third trimester at the time of RSV hospitalization. These findings appear to be consistent with previous studies of RSV and influenza hospitalizations during pregnancy. Of the 21 RSV hospitalizations in pregnant women reported by Regan et al, 67% were in their third trimester [2]. In addition, all 3 cases identified in Wheeler et al's case series were in their third trimester [1]. Studies of influenza infection during pregnancy have found that women in the third trimester are at greater risk of hospitalization [12, 13]. The severity of RSV and influenza infection during pregnancy is likely due to physiologic changes that affect the respiratory system and immunologic changes to accommodate the fetus, as well as preexisting comorbidities such as obesity or asthma [14, 15].

This study is limited to a single integrated healthcare system. In addition, only hospitalized cases were included and thus represent a more severe presentation of RSV in pregnancy. Previous studies have also reported that RSV screening among pregnant women with ARI is infrequent [2]. As a result of these limitations, it is likely that some potential cases were not identified. By limiting this study to pregnancies ending in live births, it is possible that additional cases involving fetal death or loss during early pregnancy were not identified. An additional limitation includes inconsistent testing for other respiratory pathogens.

The information presented here may inform the benefits of maternal vaccination for an RSV vaccine intended to protect

infants. Additional studies may help to identify the true burden of severe disease among pregnant women, as well as specific risk factors that lead to hospitalization.

Notes

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