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2009 Pandemic Influenza A (H1N1) in Pregnant Women Requiring Intensive Care -- - New York City, 2009

Weekly

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Pregnant women are at increased risk for severe illness and complications from infection with seasonal influenza (1--3) and 2009 pandemic influenza A (H1N1) (4--6). To characterize the severity of 2009 H1N1 infection in pregnant women, the New York City Department of Health and Mental Hygiene (DOHMH) conducted active and passive surveillance for cases of 2009 H1N1 infection in pregnant women requiring intensive care. This report summarizes the results of that surveillance, which found that, during 2009, 16 pregnant women and one who was postpartum were admitted to New York City intensive-care units (ICUs). Two women died. Of the 17 women, 12 had no recognized risk factors for severe influenza complications other than pregnancy (7). All 17 women received antiviral treatment with oseltamivir; however, treatment was initiated ≤ 2 days after symptom onset in only one woman and was begun ≥ 5 days after symptom onset in four women. Because initiation of antiviral treatment ≤ 2 days after onset is associated with better outcomes (5,6), pregnant women should be encouraged to seek medical care immediately if they develop influenza-like symptoms, and health-care providers should initiate empiric antiviral therapy for these women as soon as possible, even if > 2 days after symptom onset. Health departments and health-care providers should educate pregnant and postpartum women regarding the risks posed by influenza and highlight the effectiveness and safety of influenza vaccination. Obstetricians and other health-care providers should offer influenza vaccination to their pregnant patients.

To identify cases of 2009 H1N1 infection in pregnant and postpartum women, beginning April 25, 2009, DOHMH conducted surveillance for hospitalizations and deaths during three separate periods. Surveillance methods varied as the 2009 H1N1 pandemic evolved and influenza activity changed in New York City. During April--June, DOHMH conducted citywide active surveillance for deaths from 2009 H1N1 and enhanced citywide surveillance for hospitalized cases of influenza in pregnant and postpartum women, actively requesting specimens and testing for 2009 H1N1 at the New York City Public Health Laboratory. During July--September, influenza activity was low in New York City; however, ongoing passive surveillance was conducted for hospitalized patients who tested positive for influenza A. During October--December, citywide surveillance was passive, except active surveillance was reestablished at five sentinel hospitals. During all three periods, data on pregnancy, ICU status, and vital status were collected for all patients hospitalized with 2009 H1N1 throughout New York City. Chart abstractions for all identified cases were conducted by medical epidemiologists at DOHMH. For this case series, a case was defined as severe illness with laboratory-confirmed or probable 2009 H1N1 infection* in a woman who was pregnant or postpartum (within 6 weeks of delivery), resulting in admission to an ICU or death.

During 2009, a total of 17 patients (16 pregnant women and one who was postpartum) met the case definition; nine were admitted to ICUs during April--June, and eight were admitted during October--December. No patients met the case definition during July--September. Median age of the patients was 23 years (range: 20--37 years), and median gestational age at hospital admission was 34 weeks (range: 6--41 weeks) (Table). Median length of hospital stay was 12 days (range: 4--38 days). Five of the 17 women had risk factors for severe influenza complications recognized by the Advisory Committee for Immunization Practices (ACIP) other than pregnancy (7). One patient had asthma and cardiovascular disease (diagnosed postmortem). The other four patients

had sickle cell disease, asthma, seizure disorder, and diabetes mellitus, respectively. Only one of the 17 patients had received 2009 H1N1 vaccine, according to the medical records; she had been administered H1N1 vaccine >4 weeks before hospitalization, after being administered seasonal influenza vaccine >8 weeks before hospitalization. Eleven of the 17 women were in their third trimester, including five who developed acute respiratory distress syndrome (ARDS). All 17 women received antiviral treatment with oseltamivir; however, treatment was initiated ≤ 2 days after symptom onset in only one woman and was begun ≥ 5 days after symptom onset in four women; initiation of antiviral treatment ≤ 2 days after onset is associated with better outcomes (5,6).

Four of the nine women who gave birth during their 2009 H1N1 hospitalization had an emergency cesarean delivery; eight infants were live-born (including one who died soon after birth), and one was stillborn. Six of the eight live-born infants were admitted to a neonatal ICU.

Illustrative Case Reports

Patient 1. A woman aged 27 years who was at 32 weeks' gestation (Table) went to her primary care physician during May 2009 after 1 day of fever and cough (Figure). She was treated with antibiotics for 3 days without improvement. Five days after symptom onset, she went to the emergency department, reporting persistent fevers, chills, cough, wheezing, and an episode of near-syncope. On admission she was afebrile, with a respiratory rate of 22 breaths per minute, a heart rate of 96 beats per minute, blood pressure of 100/70 mmHg, and oxygen saturation of 99% on room air. A chest radiograph revealed bilateral lobar pneumonia, and she was treated for community-acquired pneumonia. On hospital day 2, she developed fever to 102.9°F (39.4°C), tachycardia (141 beats per minute) and severe respiratory distress. ARDS was diagnosed, and the patient was transferred to the ICU for mechanical ventilation and treated empirically with oseltamivir, 75 mg twice daily. Rapid influenza diagnostic tests performed on nasopharyngeal specimens 1 day before hospital admission and on hospital day 3 were negative for influenza.

On hospital day 4, because her oxygen saturations worsened to approximately 75% despite maximal ventilation settings, an emergency cesarean delivery was performed. During the procedure, the patient was hypotensive and required multiple blood transfusions. Cultures from bronchoalveolar lavage collected the previous day grew *Acinetobacter baumannii*. On hospital day 11, diagnosis of 2009 H1N1 was confirmed from a nasopharyngeal swab specimen submitted to the DOHMH Public Health Laboratory on hospital day 3. On hospital day 16, because of refractory hypoxemia and severe ARDS, the woman was transferred to another hospital ICU for extracorporeal membrane oxygenation (ECMO), and oseltamivir was increased to 150 mg, twice daily. Her subsequent hospital course was complicated by volume overload, septic shock, and ventilator-associated pneumonia with *Klebsiella pneumoniae* and *A. baumannii*. She died on hospital day 38, a total of 42 days after symptom onset (Figure). At birth, her infant weighed 1,500 g and had Apgar scores of 1 at 1 minute and 1 at 5 minutes after birth; the infant stopped breathing, and neonatal resuscitation efforts were unsuccessful.

Patient 15. A woman aged 21 years who was at 34 weeks' gestation was admitted to a hospital during November 2009 (Table) with respiratory distress; 6 days of fever, cough, and myalgia; and 2 days of blood-tinged sputum (Figure). A few days before admission she had been

prescribed antibiotics and oseltamivir by her primary-care provider but only took the antibiotics. On admission, she had a fever of 100.9°F (38.3°C), tachycardia (141 beats per minute), blood pressure of 101/66 mmHg, and a respiratory rate of 20 breaths per minute; her chest radiograph showed bilateral pulmonary infiltrates consistent with ARDS. On hospital day 2, she was transferred to the ICU for mechanical ventilation; she developed septic shock requiring vasopressors and was treated with broad-spectrum antibiotics and oseltamivir, 150 mg twice daily. Her respiratory status deteriorated and she underwent emergency cesarean delivery.

On hospital day 3, the patient was transferred to another hospital ICU for ECMO treatment of severe ARDS and septic shock. Soon after transfer, she experienced cardiac arrest with ventricular fibrillation; defibrillation was successful after less than 2 minutes of no pulse. Oseltamivir was changed to empiric intravenous peramivir and broad-spectrum antibiotics. On hospital day 4, diagnosis of 2009 H1N1 was confirmed from a nasopharyngeal swab specimen submitted to the DOHMH Public Health Laboratory on hospital day 2. Her hospital course included spontaneous pneumothoraces, hypotension requiring vasopressors, an episode of asystole, infection with *K. pneumoniae*, fevers to 107.1°F (41.7°C), disseminated intravascular coagulation, and tracheostomy placement. Her respiratory status improved, and ECMO was discontinued on hospital day 14. She was transferred from the ICU without supplemental oxygen on hospital day 26 and discharged home with physical therapy on hospital day 32. On discharge she was fully alert and walking with assistance. At birth, her infant weighed 2,080 grams and had Apgar scores of 3 at 1 minute and 6 at 5 minutes after birth. The infant required mechanical ventilation and was treated with antibiotics for suspected sepsis; oseltamivir was not administered. The infant improved and was discharged on day 3 of life.

Reported by

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Editorial Note

An analysis of New York City 2009 H1N1 hospitalizations during May--June 2009 showed that pregnant women were 7.2 times more likely to be hospitalized and 4.3 times more likely to be admitted to an ICU than nonpregnant women (6). Immunologic changes, increased ventilatory demand, and decreased functional residual capacity and oncotic pressure all are postulated to predispose pregnant and postpartum women to severe respiratory complications from influenza virus infection (5,6).

The case series in this report highlights some delays in pregnant women seeking care and obtaining appropriate diagnosis and treatment of 2009 H1N1 virus infection in New York City, despite extensive outreach to the public and health-care providers by public health officials. The

illustrative cases highlight some factors contributing to the delays, including false-negative rapid diagnostic test results and not taking oseltamivir as prescribed. In addition, only one of the 17 women was reported to have received 2009 H1N1 vaccine. Although no vaccine is 100% effective, vaccination remains the most important and effective means of preventing influenza among pregnant women.

The findings in this report are subject to at least three limitations. First, this report represents a case series rather than a population-based study, and methods of case ascertainment and influenza activity in New York City differed among the April--June, July-September, and October--December periods. The number of severe illnesses from 2009 H1N1 infection in pregnant women identified during these different periods might not be comparable for various reasons. For example, the threshold for admission to an ICU might have been lower in the fall than in the spring, given increased awareness of the potential severity of 2009 H1N1 infection in pregnant women. Second, underascertainment of cases might have occurred during all three periods because of limitations in active case-finding. Finally, 2009 H1N1 vaccine was not available until October, and the vaccination status for most of the 17 women was unknown; therefore, no conclusions can be drawn regarding the prevalence of vaccination in this group.



All clinicians, including obstetricians and health-care providers, should maintain a high index of suspicion for influenza when surveillance data suggest that influenza is circulating in a community. Pregnant and postpartum patients should be educated to recognize influenza-like symptoms and counseled to seek care immediately and to take antiviral therapy as prescribed (9). Health-care providers should ensure prompt evaluation and early empiric treatment with oseltamivir, irrespective of negative rapid influenza diagnostic test results; treatment with antipyretics and antibiotics also should be considered when indicated (5,8,10).

For pregnant or postpartum women and for those women considering becoming pregnant, clinicians and health departments should emphasize the importance of vaccination against seasonal influenza and 2009 H1N1 to prevent life-threatening complications. Although 2009 H1N1 activity has declined in the United States, the virus is still circulating and causing illness, and increases in influenza activity remain possible. Clinicians caring for pregnant and postpartum women should continue to encourage influenza vaccination during this and subsequent years and remember the importance of prompt empiric antiviral therapy for pregnant or postpartum patients with possible 2009 H1N1 influenza.

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* In 15 of the cases, 2009 H1N1 was confirmed by real-time reverse transcription--polymerase chain reaction. Two cases with laboratory evidence of influenza A that were not subtyped were considered probable 2009 H1N1 because surveillance data indicated >90% of circulating influenza A in New York City at the time was 2009 H1N1.

What is already known on this topic?

Pregnant women have an increased risk for severe illness and complications from seasonal and pandemic influenza virus infection.

What is added by this report?

During 2009 in New York City, among 17 pregnant or postpartum women who were admitted to intensive-care units with severe illness from 2009 H1N1 influenza virus infection, two maternal

deaths, one infant death, and a stillbirth resulted; for some of these patients, delays in care-seeking, diagnosis, and treatment of influenza might have increased the potential for rapid clinical decline.

What are the implications for public health practice?

Health departments and health-care providers should educate pregnant and postpartum women to recognize influenza-like symptoms and seek care promptly, and emphasize the need for prompt empiric antiviral treatment when influenza is circulating in the community; obstetricians and other health-care providers should offer influenza vaccination to their pregnant patients.

TABLE. Clinical characteristics of severe 2009 pandemic influenza A (H1N1) in 16 pregnant women and one postpartum woman hospitalized in intensive-care units (ICUs) --- New York City, 2009

Patient no.	Month of hospital admission	Patient age (yrs)	Fetal gestational age at admission (wks)	Total ICU hospital length of stay (days)		Maternal outcome	No. of days from symptom onset to antiviral treatment	ACIP * risk factor	Mechanical ventilation	Diagnosis during hospital course		Infant outcome
				length of stay (days)	stay (days)					Pneumonia	ARDS†	
1	May	27	32	38	37	Died	6	None	Yes	Yes	Yes	Died
2	May	25	37	13	12	Discharged	5	None	Yes	Yes	Yes	NICU §
3	May	25	39	19	17	Died	3	Asthma, CVD ¶	Yes	Yes	Yes	NICU
4	May	23	40	15	4	Discharged	5	Sickle cell disease	No	Yes	No	Nursery
5	May	30	6	4	2	Discharged	8	None	No	No	No	NA**
6	May	23	Postpartum††	7	7	Discharged	3	Asthma	No	Yes	No	NA
7	June	21	23	38	32	Discharged	4	Seizure disorder	Yes	Yes	No	Stillborn

8	June	28	35	33	21	Discharged	3	None	Yes	Yes	Yes	NICU	der
9	June	21	25	18	4	Discharged	2	None	No	No	No	NA	
10	October	26	29	10	10	Discharged	3	None	No	Yes	No	NA	
11	November	22	41	9	NA	Discharged	4	None	No	Yes	No	NICU	
12	November	37	37	12	NA	Discharged	4	None	No	Yes	No	NA	
13	November	21	34	7	5	Discharged	3	Diabetes mellitus	No	Yes	No	NICU	
14	November	22	35	4	2	Discharged	3	None	No	Yes	No	NA	
15	November	21	34	32	24	Discharged	7	None	Yes	Yes	Yes	NICU	
16	December	27	25	10	8	Discharged	3	None	Yes	Yes	No	NA	
17	December	22	10	7	7	Discharged	9	None	No	No	No	NA	

* Advisory Committee on Immunization Practices recognized risk factor for severe influenza complications other than pregnancy. CDC. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2009. MMWR 2009;58(No. RR-8).

† Acute respiratory distress syndrome.

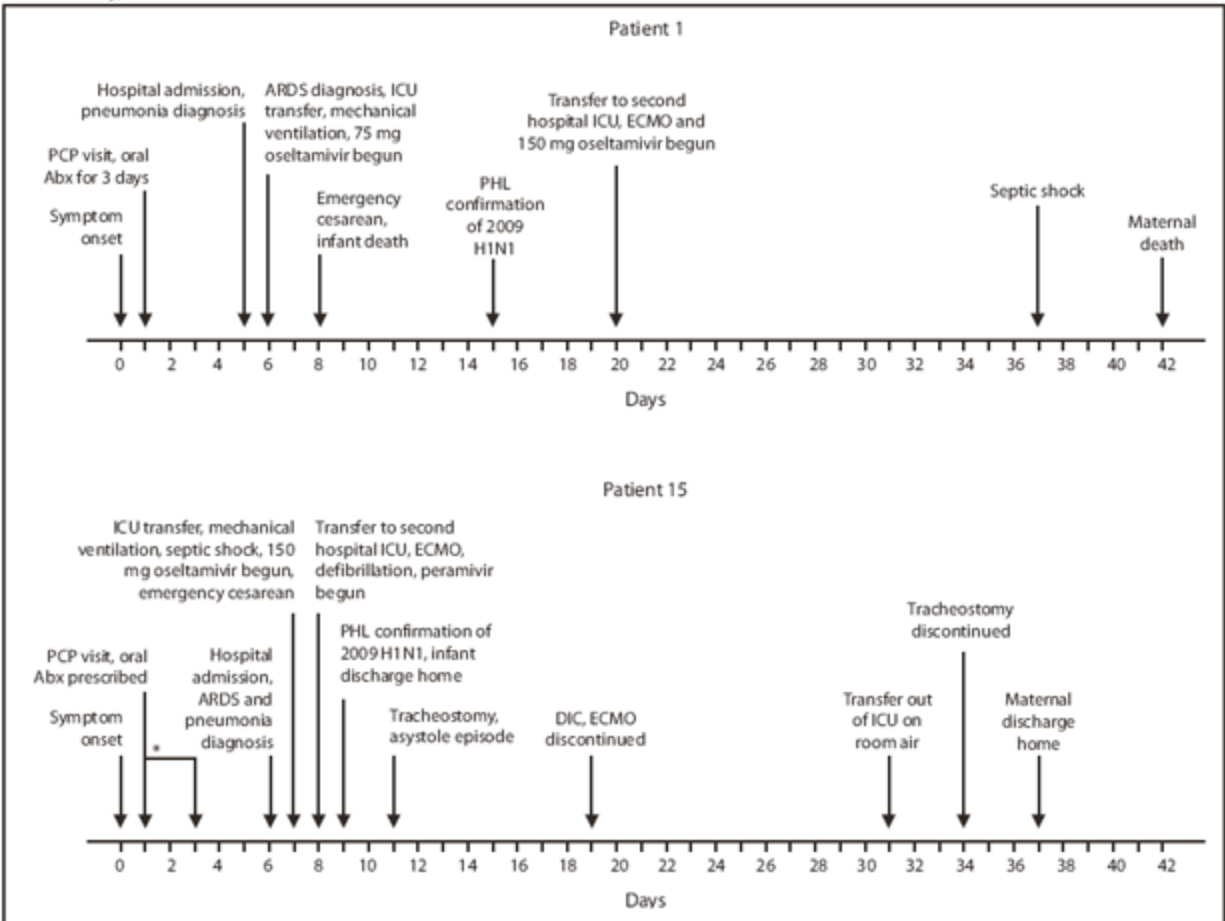
§ Neonatal ICU.

¶ Cardiovascular disease diagnosed postmortem.

** Not available. Patient was discharged before giving birth.

†† <2 weeks after delivery.

FIGURE. Timeline of key events in two cases of severe 2009 pandemic influenza A (H1N1) in pregnant women hospitalized in intensive-care units --- New York City, 2009



Abbreviations: PCP = primary-care provider, Abx = antibiotics, ICU = intensive-care unit, ARDS = acute respiratory distress syndrome, PHL = New York City Department of Health and Mental Hygiene Public Health Laboratory, ECMO = extracorporeal membrane oxygenation, DIC = disseminated intravascular coagulation.

* Date of PCP visit was not confirmed but was 1--3 days after symptom onset.

Alternate Text: The figure above shows two timelines of key events in the treatment cases of two pregnant women (patient 1 and patient 15) who were hospitalized in New York City intensive care units with 2009 pandemic influenza A (H1N1) during 2009.

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