# Seasonal and 2009 pandemic influenza A (H1N1) virus infection during pregnancy: a population-based study of hospitalized cases

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We sought to describe characteristics of hospitalized reproductive-aged (15-44 years) women with seasonal (2005/2006 through 2008/2009) and 2009 pandemic influenza A (H1N1) virus infection. We used population-based data from the Emerging Infections Program in 10 US states, and compared characteristics of pregnant (n = 150) and nonpregnant (n = 489) seasonal, and pregnant (n = 489) and nonpregnant (n = 1088) pandemic influenza cases using $\chi^2$ and Fisher's exact tests. Pregnant women represented 23.5% and 31.0% of all reproductive-aged women hospitalized for seasonal and pandemic influenza, respectively. Significantly more nonpregnant than pregnant women with seasonal (71.2% vs 36.0%) and pandemic (69.7% vs 31.9%) influenza had an underlying medical condition other than pregnancy. Antiviral treatment was significantly more common with pandemic than seasonal influenza for both pregnant (86.5% vs 24.0%) and nonpregnant (82.0% vs 55.2%) women. Pregnant women comprised a significant proportion of influenza-hospitalized reproductive-aged women, underscoring the importance of influenza vaccination during pregnancy.

**Key words:** human, infectious, influenza, pregnancy, pregnancy complications, seasonal influenza, 2009 pandemic influenza

The emergence of 2009 pandemic influenza A (H1N1) virus (2009 H1N1) resulted in the first influenza pandemic in over 40 years. The Centers for Disease Control and Prevention (CDC) estimated that about 61 million people were infected, 274,000 were hospitalized, and about 12,740 died due to 2009 H1N1 in the United States.[1] About 90% of all hospitalizations and 87% of all deaths during the 2009 H1N1 pandemic were among people <65 years in contrast with experience from seasonal influenza when about 40% of all hospitalizations and 10% of deaths were found in this age group.[1] It is well recognized that pregnancy represents a risk factor for influenza complications and death during both pandemic and seasonal influenza.[2-6] Thus, with illness being widespread among the younger segments of the population

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Received Dec. 16, 2010; revised Feb. 4, 2011; accepted Feb. 14, 2011.

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Conflict of Interest: none.

Publication of this article was supported by the Centers for Disease Control and Prevention and the Association of Maternal and Child Health Programs.

0002-9378/$36.00 • © 2011 Published by Mosby, Inc. • doi: 10.1016/j.ajog.2011.02.037

during the 2009 H1N1 pandemic, it was expected that a higher proportion of pregnant women would be affected during the 2009 H1N1 pandemic than in previous influenza seasons. Early evidence during the 2009 H1N1 pandemic showed that pregnant women were disproportionally represented among hospitalized, intensive care unit (ICU)-admitted cases and deaths due to influenza.[7,8]

Using CDC's national pregnancy mortality surveillance data from 1998 through 2005, Callaghan et al[9] found that, on average, about 5 deaths can be attributable to seasonal influenza annually during the 8 influenza seasons studied. Through active surveillance for pregnancy-related mortality conducted during the 2009 H1N1 pandemic, 56 deaths due to influenza were identified among pregnant women with symptom onset from April 15, 2009, through Dec. 31, 2009.[10] Although data from 2009 H1N1 suggest much higher mortality in pregnant women than would be expected based on the previous years' pregnancy mortality surveillance in the United States, these estimates cannot be directly compared given disparate case ascertainment. Also, compared to seasonal influenza, attack rates were very high among persons in the childbearing age group with 2009 H1N1, and therefore, a commensurate increase in mortality consistent with the attack rates in this age group would have been expected. Thus, while the true magnitude of the difference in mortality between seasonal and 2009 H1N1 is not known, it is plausible that there was an excess mortality from influenza among pregnant women during 2009 H1N1. Most importantly, from the perspective of both public health and clinical obstetrics practice, there were considerably more pregnant women affected during 2009 H1N1 than during seasonal influenza.

No studies to date have compared characteristics of pregnant women with seasonal and pandemic influenza. Use of a population-based influenza surveillance system presents an opportunity to not only examine if severity of influenza illness was higher during the 2009 H1N1 pandemic than during previous influenza seasons, but also to assess changes in clinical practices with regard to pregnant women during the 2009 H1N1 pandemic. The main objective of this study is to describe and compare sociodemographic factors, medical history, and clinical characteristics of hospitalized pregnant and nonpregnant reproductive-aged women (15-44 years) with seasonal and 2009 pandemic influenza A (H1N1) virus infection. Additionally, this study examines characteristics of pregnant and nonpregnant women with confirmed seasonal influenza and 2009 H1N1 who were admitted to an ICU, assesses the benefit of antiviral treatment among pregnant women with 2009 H1N1, and reviews pregnancy outcomes among women hospitalized with 2009 H1N1 after Sept. 1, 2009.

## Materials and methods

We used population-based surveillance data collected by CDC's Emerging Infections Program (EIP) Network for influenza-associated hospitalizations among women of reproductive age (15-44 years at the time of hospital admission) from Oct. 1, 2005, through April 30, 2010. The EIP influenza surveillance catchment area expanded slightly during this time period. In 2009, EIP influenza surveillance was conducted in 62 counties covering 13 metropolitan areas in the following 10 states: California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New Mexico, New York, Oregon, and Tennessee. Detailed information about the composition of the EIP surveillance catchment area by county for each influenza season is provided elsewhere.[11,12]

For this analysis, a case was defined as a reproductive-aged (15-44 years) woman residing in the surveillance area, who was admitted to a surveillance-area hospital and had laboratory confirmation of influenza A infection within 14 days of admission during any one of the 2005/2006 through 2008/2009 influenza seasons or during the 2009 H1N1 pandemic. For influenza seasons 2005/2006, 2006/2007, and 2007/2008, EIP influenza-surveillance was conducted from Oct. 1 through April 30 of the following year each season. For the 2008/2009 season, data were collected from Oct. 1, 2008 through April 15, 2009 when the 2009 H1N1 virus was first identified by CDC. For the purpose of this analysis, we used all data collected from reproductive-aged women with confirmed 2009 H1N1 infection from April 15, 2009, through April 30, 2010.

Testing for influenza was based on decisions made by individual clinicians during each influenza season and the 2009 H1N1 pandemic, and reflects clinical practice recommendations available during the index influenza season. Laboratory confirmation of influenza infection involved a positive result from a viral culture, a direct or indirect fluorescent antibody staining, a rapid antigen test or real-time reverse-transcriptase polymerase chain reaction (rRT-PCR), or documentation of a positive test result in the patients' medical records.[11] Cases were identified prospectively through state-mandated illness reporting systems or retrospectively through review of hospital admissions, discharge or infection control logs, and/or laboratory lists.

Medical records data on sociodemographic, medical history, influenza vaccination status, and clinical course and management were abstracted on all identified cases using a standardized data collection form. EIP employed consistent data collection and reporting protocols throughout influenza seasons from 2005/2006 through 2009/2010. Data were collected on the following preexisting medical conditions that confer a higher risk for influenza complications as specified by the Advisory Committee on Immunization Practices: asthma, cystic fibrosis, other chronic lung disease, cardiovascular disease, chronic metabolic disease, hemoglobinopathy, neuromuscular disorder, cancer, renal disease, immunosuppressive condition, cognitive or seizure disorder, and pregnancy.[13] To determine a patient's influenza vaccination status, several approaches were utilized. In cases where the influenza vaccination status was not recorded or recorded as unknown on medical records, the state vaccination registry was checked; if the information was not recorded in the registry or no state registry existed for adults, 3 separate attempts were made to contact the patient's primary care provider and obtain this information. If these efforts