

Commentary

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Maternal mortality due to pandemic influenza A H1N1 2009 virus in Colombia

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The report by Rojas-Suarez et al. [11] describes clinical information on 23 maternal deaths from pandemic A(H1N1)2009 influenza (2009 H1N1) infection in Colombia. Their clinical experiences mirror what we experienced in the United States during this same time period. Using Centers for Disease Control and Prevention (CDC) surveillance data through the end of 2009, we described 56 deaths from 2009 H1N1 among pregnant women in the United States and showed that pregnant women had a disproportionately higher risk of mortality than the general population [12].

The experience with pregnant women during the 2009 H1N1 influenza pandemic is a reminder of the risks of influenza to pregnant women. Compared to the general population, pregnant women with influenza are more likely to develop severe disease and to die [10]. In addition to the considerable risks for the pregnant woman, there can also be adverse effects on her fetus including increased risk of spontaneous abortion, preterm delivery, low birth weight, and fetal death [10]. Therefore, vaccination and prompt empiric therapy are particularly critical for pregnant women in preventing and treating infection and for preventing adverse fetal effects. Of note, in the Colombian case series [11], none of the women who died had received influenza vaccination and many did not receive prompt antiviral therapy.

In the United States, influenza vaccination is recommended for all women who will be pregnant during influenza season, regardless of trimester [1]. In the wake of the 2009 H1N1 pandemic, influenza vaccination coverage for pregnant women increased. However, coverage

has been relatively stable since then with approximately 50% of pregnant women being vaccinated [7], leaving significant room for improvement. We have learned that health care providers play a critical important role in promoting influenza vaccine. In a recent study, pregnant women whose health care providers recommended and offered influenza vaccination were more likely to receive the influenza vaccine (73.6%) compared with women who received only a recommendation but no offer (47.9%) and women who received neither a recommendation nor an offer (11.1%) [2].

In addition to vaccine, we also know that pregnant women infected with influenza benefit from prompt antiviral therapy. In our series of 56 deaths among pregnant women with influenza [12], only one death occurred in a pregnant patient who received treatment within 2 days of symptom onset; women who received antiviral therapy more than 4 days after symptom onset were six times more likely to be admitted to an intensive care unit and over 50 times more likely to die than women treated within 2 days after symptom onset. Multiple studies from the 2009 H1N1 pandemic demonstrated that early initiation of antiviral therapy decreased severe morbidity and mortality among pregnant women [8].

As we reflect on the recent influenza pandemic in 2009–2010, our collective global clinical experiences may hold important lessons for the challenges ahead. Although this paper [11] focuses on the effects of a pandemic strain of influenza, it is important to remember that seasonal influenza also presents a significant risk to pregnant women [9]. The 2012–2013 influenza season was moderately severe in the United States, with higher rates of hospitalization and death compared with recent years. Specific data about how pregnant women fared during the 2012–2013 season are not available. However, during that season, 149 children died of influenza; with the exception of the 2009–2010 H1N1 pandemic season, this is the highest number of pediatric deaths reported since 2004 when influenza-associated pediatric mortality became nationally notifiable, emphasizing that seasonal influenza continues to represent a significant threat to human health [4]. Thus, it

is critical that we continue to encourage pregnant women to be vaccinated for seasonal influenza.

Our experience in recent years has also highlighted the unpredictable nature of influenza, with the emergence and maintenance of several novel influenza viruses with pandemic potential. A highly pathogenic strain of avian influenza A (H5N1) was first reported in humans in 1997 in Hong Kong. Culling of poultry in Hong Kong and implementation of other measures resulted in control of the outbreak, but the virus reemerged in 2003. Cases of H5N1 continue to be observed, with 633 human cases and 377 deaths reported to the World Health Organization (WHO) in 15 countries in Asia, Africa, the Pacific, Europe and the Near East since November 2003. As of July 5, 2013, 23 human cases and 17 deaths were already reported in 2013 [14]. Most cases have had exposures to birds, and sustained, efficient human-to-human transmission, a factor necessary for development of a pandemic, has not been observed. Several pregnant women with H5N1 have been reported, including one case with severe multi-organ involvement resulting in her death and transmission of H5N1 to her fetus [13].

In 2011, 12 cases of another novel influenza virus, influenza A H3N2 variant (H3N2v) (the term “variant” refers to influenza viruses that normally circulate in pigs when they are found in people) were identified in the United States, and 309 additional cases were reported from 12 states in 2012. Thus far in 2013, 16 cases from three states have been reported (as of August 15, 2013). Most cases of H3N2v illness in humans have been mild, although several hospitalizations and one death have occurred. Most cases had prolonged exposure to pigs at agricultural fairs, and no sustained, efficient human-to-human transmission has been observed, although limited human-to-human transmission occurred [5].

Finally, as of April 1, 2013, WHO reported identification of human infections of a novel low pathogenic avian

influenza A (H7N9) virus in China [3]. To date, there have been 135 confirmed human cases associated with this virus. Most cases have been severely ill, and over 30% of cases have died [15]. Although most cases were among elderly males, at least two pregnant women with H7N9 have been reported [6]. Case investigations suggest that most people with H7N9 were infected following contact with infected poultry or contaminated environments. A few small clusters of H7N9 infection have occurred and, thus, human-to-human transmission cannot be ruled out; however, no sustained human-to-human transmission has been observed. The terms “low pathogenic” and “highly pathogenic” with regard to avian influenza viruses refer to the severity of influenza in chickens; infection in chickens with low pathogenic viruses is subclinical. Thus, the fact that H7N9 is a low pathogenic avian influenza virus means that infected chickens cannot be easily detected based on clinical illness, which complicates control measures.

The 2012–2013 influenza season and recent outbreaks of novel influenza viruses with pandemic potential stress the importance of remaining vigilant. Obstetric health care providers should continue to focus on ways to integrate influenza vaccination into prenatal care. In addition, pregnant women who are suspected to have influenza should receive prompt antiviral treatment. Based on our experience with the 2009 H1N1 pandemic, these strategies save lives.

Disclaimer: 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.

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References

- [1] Advisory Committee on Immunization Practices. Prevention and control of influenza with vaccines: interim recommendations of the Advisory Committee on Immunization Practices (ACIP), 2013. *MMWR Morb Mortal Wkly Rep.* 2013;62:356.
- [2] CDC. Influenza vaccination coverage among pregnant women: 2011–12 influenza season, United States. *MMWR Morb Mortal Wkly Rep.* 2012;61:758–63.
- [3] CDC. Emergence of avian influenza A(H7N9) virus causing severe human illness – China, February–April 2013. *MMWR Morb Mortal Wkly Rep.* 2013;62:366–71.
- [4] CDC. Influenza activity – United States, 2012–13 season and composition of the 2013–14 influenza vaccine. *MMWR Morb Mortal Wkly Rep.* 2013;62:473–9.
- [5] CDC. Situation summary on influenza A (H3N2) variant viruses (“H3N2v”), <http://www.cdc.gov/flu/swineflu/h3n2v-situation.htm>. Accessed August 15, 2013. 2013.
- [6] Gao HN, Lu HZ, Cao B, Du B, Shang H, Gan JH, et al. Clinical findings in 111 cases of influenza A (H7N9) virus infection. *N Engl J Med.* 2013;368:2277–85.
- [7] Kennedy ED, Ahluwalia IB, Ding H, Lu PJ, Singleton JA, Bridges CB. [Monitoring seasonal influenza vaccination coverage among pregnant women in the United States.](#) *Am J Obstet Gynecol.* 2012;207:59–16.
- [8] Mosby LG, Rasmussen SA, Jamieson DJ. 2009 Pandemic influenza A (H1N1) in pregnancy: a systematic review of the literature. *Am J Obstet Gynecol.* 2011;205:10–8.

- [9] Rasmussen SA, Jamieson DJ, Bresee JS. Pandemic influenza and pregnant women. *Emerg Infect Dis*. 2008;14:95–100.
- [10] Rasmussen SA, Jamieson DJ, Uyeki TM. Effects of influenza on pregnant women and infants. *Am J Obstet Gynecol*. 2012;207:S3–8.
- [11] Rojas-Suarez J, Paternina-Caicedo A, Cuevas L, Angulo S, Cifuentes R, Parra E, et al. Maternal mortality due to pandemic influenza A H1N1 2009 virus in Colombia. *J Perinatal Med*. 2014;42:19–26.
- [12] Siston AM, Rasmussen SA, Honein MA, Fry AM, Seib K, Callaghan WM, et al. Pandemic 2009 influenza A(H1N1) virus illness among pregnant women in the United States. *J Am Med Assoc*. 2010;303:1517–25.
- [13] Theiler RN, Rasmussen SA, Treadwell TA, Jamieson DJ. Emerging and zoonotic infections in women. *Infect Dis Clin North Am*. 2008;22:755–72, vii–viii.
- [14] World Health Organization. Cumulative number of confirmed human cases for avian influenza A(H5N1) reported to WHO, 2003-2012. http://www.who.int/influenza/human_animal_interface/H5N1_cumulative_table_archives/en/. Accessed August 12, 2013.
- [15] World Health Organization. Human infection with avian influenza A(H7N9) virus – update. http://www.who.int/csr/don/2013_08_11/en/. Accessed on August 15, 2013.

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