Influenza
Threat to Maternal Health

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KEYWORDS

• Influenza • Pregnancy • Respiratory illness • Maternal morbidity • Vaccination

KEY POINTS

- Increased morbidity and mortality have been associated with influenza infection in pregnancy, with infection in the third trimester the most common (approximately 50% of cases) and associated with a higher rate of complications.
- Prompt initiation of antiviral treatment decreases the likelihood of ICU admission and maternal mortality.
- Influenza vaccine is recommended in pregnancy regardless of trimester, with acceptance rates highest when the vaccine is offered at a physician's office.

INTRODUCTION

A maternal mortality rate of 1% was reported during the 2009–2010 influenza pandemic,[1] with influenza in pregnancy posing a serious risk to maternal health. A high level of suspicion coupled with prompt diagnosis and treatment is paramount to minimizing morbidity and mortality. Vaccination during pregnancy should be of high priority to improve both maternal and neonatal outcomes.

DISCUSSION

Influenza is an RNA virus of the Orthomyxoviridae family. There are 3 antigenic types of influenza: influenza A and influenza B both cause significant clinical disease and are associated with seasonal epidemics; influenza C causes only a mild respiratory illness without seasonality. Influenza A can be subtyped based on 2 surface glycoproteins—hemagglutinin (HA) and neuraminidase (NA). There are currently at least 16 antigenically distinct HAs and 9 distinct NAs and combinations of these 2 glycoproteins allow for the nomenclature of specific subtypes. Influenza B does not have these subtypes.

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Annual seasonal outbreaks occur with influenza cases first reported in approximately October with peak incidence in January–February and extension into May. Tropical climates may experience influenza activity throughout the year. Annual influenza vaccination is necessary to account for antigenic drift or subtle point mutations in surface antigens, which decrease host resistance to the pathogen. Occasionally with influenza A, an antigenic shift occurs. This is a significant change in the virus surface antigens (HA and NA), which leads to the emergence of a new subtype, often resulting in a global pandemic with increased morbidity and mortality. The last pandemic occurred with the emergence of the influenza A 2009 H1N1 strain.

INCREASED SEVERITY OF INFLUENZA IN PREGNANCY

Although pregnant women may not be more susceptible to influenza, higher morbidity and mortality have been associated with this infection in pregnancy. In a report of the influenza pandemic of 1918, pneumonia complicated approximately half of influenza infections in pregnancy and more than 20% of women died, with mortality highest in the third trimester.[2] Similar outcomes were reported during the pandemic of 1957.[3] Both immunologic and physiologic changes of pregnancy increase the potential severity of influenza in the gravid population. This was again highlighted during the 2009 H1N1 influenza A pandemic in which, despite aggressive hospitalization of pregnant women with influenza, 5% of deaths in the United States occurred among pregnant women whereas they composed only 1% of the population. Pregnant women are also more likely to experience severe disease requiring admission to an ICU. In comparison with years with only seasonal influenza, when only 40% of hospitalizations and 10% of deaths were among people age less than 65 years, in 2009 with the emergence of the H1N1 subtype, 90% of hospitalizations and 87% of deaths were among people less than 65 years,[4] highlighting the need for increased vigilance in the pregnant population, who more frequently experience adverse effects.

Gravid women experience a shift from helper T cell type1 (T_H1) to helper T cell type 2 (T_H2) immunity with suppression of cell-mediated and increased humoral immunity, likely secondary to the increased levels of estradiol and progesterone during pregnancy. For example, there is an increase in T_H2-type cytokines, such as interleukin (IL)-4, IL-5, IL-10, and IL-13, with suppression of inflammatory cytokines (**Table 1**), which theoretically may decrease susceptibility to acquisition of an illness, such as influenza, but also can affect efficient clearance of the pathogen.[5] The normal physiologic changes of pregnancy, especially at advanced gestational ages, also may predispose women to worse disease and need for more intensive care. In pregnancy, there is a 20% to 30% decrease in pulmonary functional residual capacity due to diaphragm elevation. In addition, there is an increased oxygen requirement and possible increased critical closing volume (the volume at which dependent parts of the lung begin to close during expiration), which can worsen respiratory illness.[6] More than 60% of pregnant women admitted for influenza infection are in the third trimester, with a small minority (<10%) in the first trimester.[1]

Regardless of the various possible causes, there is no doubt that influenza in pregnancy may have devastating consequences, requiring rapid diagnosis and treatment by an informed clinician to best prevent complications.

CLINICAL PRESENTATION

The inoculation period for influenza is 1 to 4 days, with a majority of women reporting a known exposure, most of whom are immediate family members. Individuals are usually infectious the day before as well as for 5 days after symptom onset. In a prospective