

# Vaccination against flu and COVID-19 during pregnancy

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**SUMMARY:** *The incidence of emerging infectious diseases has increased during the past two decades and is expected to further increase. Special populations, such as pregnant women, might be at a higher risk and are more susceptible to or more severely affected by infectious diseases. The objective of this study was to recognize and emphasize the importance of the prevention of prenatal infections. The role of healthcare providers in reducing the incidence of infections is also crucial, as preventing infections in the pregnant woman, fetus, or infant is an important part of prenatal care.*

## INTRODUCTION

The incidence of emerging infectious diseases has increased during the past two decades and is expected to further increase. Viral pandemics threaten the general population; however, there are special populations, such as pregnant women, which might be at a higher risk and more susceptible to or more severely affected by infectious diseases<sup>2</sup>. Therefore, the World Health Organization (WHO) has classified pregnant and lactating women as high-risk populations<sup>3</sup>. Certain changes that occur in the immune system during pregnancy have been reported to increase the risk of respiratory failure and complicate the treatment of respiratory illness and might explain the increased risk of acquired infection and subsequent adverse effects<sup>4</sup>.

In December 2019, a new disease, now known as coronavirus disease 2019 (COVID-19) emerged as a major world threat. The pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has exposed vulnerable populations to an unprecedented global health crisis. Initially, the ability of SARS-CoV-2 to spread in the population was considered to be similar to that of influenza virus<sup>5</sup>. Of note, influenza A virus (novel H1N1 subtype) was first identified in April 2009<sup>6</sup> with WHO raising the influenza pandemic alert to its highest level in June 2009. Since then, seasonal influenza continues to be a major worldwide health hazard.

A comprehensive assessment of the outcomes of these 2 diseases during pregnancy could strengthen and focus our understanding of the specific preventive measures required in these populations, and help us define the future needs of healthcare facilities.

#### METHODS

The Medline, Google Scholar, Cochrane Library, and Scopus databases were searched for relevant articles published through the last 3 years, with no limitation on publication date.

#### INFLUENZA AND PREGNANCY

The clinical manifestation of influenza in pregnant women is similar to that in the general population. The most common symptoms include headaches, fever, myalgia, and malaise. These symptoms are usually accompanied by manifestations of respiratory tract illness, such as sore throat, cough, and a runny nose<sup>7</sup>. Other common features reported in affected individuals were vomiting and diarrhea. Importantly, it should be

mentioned that pneumonia is the major complication of influenza infection.

During the influenza pandemic of 2009, pregnant women had an estimated 4 times greater mortality rate compared with that during a regular season. Asthma, anemia, chronic obstructive pulmonary disease, chronic hypertension, obesity, and pregestational diabetes mellitus are examples of chronic comorbid illnesses that have been linked to an increased risk of severe maternal morbidity in pregnant women with influenza diagnoses<sup>8</sup>. In addition, pregnant women with influenza were more likely to be hospitalized for acute respiratory disease and to be admitted to an intensive care unit compared with the general population; however, the difference in mortality rate was not significant. Interestingly, the risk of hospitalization and death was higher in the third trimester of pregnancy<sup>9</sup>.

Apart from adverse maternal outcomes, influenza infection might also lead to neonatal complications. In a recent Korean study, children born to women with influenza were at an increased risk of preterm birth and low birth weight irrespective of gestational age<sup>10</sup>. Several studies have also reported that preterm birth is a risk factor for neonatal death among pregnancies<sup>11</sup>. Maternal hyperthermia, including fever, was shown to be a common clinical manifestation of influenza infection in pregnant women and a risk factor for problems with neural tube defects in offspring<sup>12</sup>. Pregnant women with hypoxemia and a high body mass index (BMI) on admission have also been associated with adverse outcomes following influenza infection. However, the vertical transmission of the influenza virus to the fetus appears to be extremely rare.

## COVID-19 AND PREGNANCY

Three-quarters of COVID-19 pregnant women were asymptomatic, which is a lower symptom prevalence than non-pregnant women. If they did experience symptoms, they were typically minor<sup>13, 14</sup>. The most common symptoms included cough, dyspnea, fever, and myalgia. The increased risk of severe disease during pregnancy usually appeared in the late second or third trimester. Risk factors for severe disease included being overweight or obese, >35 years old, having pre-existing comorbidity factors, and being Black, Asian, or minority ethnic<sup>15</sup>. Many studies suggested that pregnant women who were symptomatic with COVID-19 were at increased risk of preterm birth compared with uninfected women. However, in most cases, these preterm births were iatrogenic, and undertaken to improve maternal oxygenation. Women with severe SARS-CoV-2 infection should, therefore, be managed in units with access to appropriate neonatal units<sup>16</sup>. A systematic review of 108 pregnancies between December 8, 2019, and April 1, 2020, showed that 91 % of women delivered by cesarean section<sup>17</sup>. A national cohort study in England between May 29, 2020, and January 31, 2021, which included 342 080 women, of whom 3527 had laboratory-confirmed SARS-CoV-2 infection, showed that the rates of fetal death, preterm birth, preeclampsia, and emergency cesarean delivery were higher than those in uninfected women<sup>18</sup>. Another systematic review and meta-analysis of 39 studies, including 1316 pregnant women, which was published on September 2020 reported that SARS-CoV-2 was not non-transmitted from the mother to the fetus in utero during the study period<sup>19</sup>.

## VACCINES

WHO has emphasized that pregnant women were recommended as the highest priority group for inclusion in influenza immunization programs. The Advisory Committee on Immunization Practices of the CDC recommends that all pregnant women, those who may become pregnant, and those who have recently given birth receive any licensed, age-appropriate inactivated influenza vaccine or the recombinant quadrivalent influenza vaccine during any trimester of pregnancy. The administration of the flu vaccine is recommended to be performed at the end of October, before the increased flu activity, thus allowing the more efficient protection of the pregnant woman. U. S. Food and Drug Administration (FDA)-licensed influenza vaccines are produced annually to protect against the 3 or 4 flu viruses that scientists anticipate to circulate each year<sup>20</sup>. Typically, these influenza vaccines include the live attenuated dominant strains of influenza A and B. However, pregnant women should not receive a live attenuated influenza vaccine due to concerns about the safety of a live vaccine<sup>21</sup>. As a result, vaccination rates among pregnant women are low. Persistent concerns about vaccine safety and the fear of genetic abnormalities remain the dominant barrier to vaccination<sup>22</sup>. Interestingly, 3 retrospective studies evaluating maternal safety, found no correlation between influenza vaccines and maternal adverse events<sup>23</sup>. Moreover, the effectiveness of influenza vaccines against influenza-like illness in pregnant women was demonstrated in a Cochrane review of observational studies published in 2018<sup>24</sup>. More recently, 3 systematic studies published by WHO did not detect an increased risk of miscarriage, fetal death, mortality preterm birth, or congenital

anomalies among pregnant women who received the flu vaccine<sup>25,26,27</sup>. To summarize, maternal influenza immunization has actually been associated with a reduced risk of mortality<sup>28</sup>.

In just a few months, huge efforts have been thrown into the race to develop a vaccine against SARS-CoV-2 infection. On December 11, 2020, FDA issued the first Emergency Use Authorization (EUA) for a 2019 coronavirus disease prevention vaccine (COVID-19) to people aged 16 and over. The first COVID-19 vaccines available in the United States were messenger RNA (mRNA) vaccines, BNT162b2 (Pfizer–BioNTech) and mRNA-1273 (Moderna). These were followed by the licensing of other vaccines. The Joint Committee on Vaccination and Immunisation (JCVI) has recognized that the potential benefits of vaccination are particularly important for some groups of pregnant women. These groups include women who are at very high risk of getting infected or women with clinical conditions that put them at high risk for suffering serious complications from COVID-19. Moreover, there has been increasing evidence about the safety and effectiveness of COVID-19 vaccination during pregnancy. Several studies have suggested that the benefits of receiving a COVID-19 vaccine outweigh any known or potential risks of vaccination during pregnancy. As none of the COVID-19 vaccines contain a live virus, they cannot make anyone sick with COVID-19, including pregnant women and their babies. Whereas, pregnant women with COVID-19 are at increased risk of complications that can affect pregnancy and the developing baby. Shimabukuro et al. evaluated the pregnancies of women who were vaccinated from December 14, 2020, to February 28, 2021. Their

preliminary findings did not show any obvious safety signals among pregnant women who received mRNA COVID-19 vaccines<sup>29</sup>. There was no correlation between receiving an mRNA COVID-19 vaccine and a higher incidence of spontaneous abortion, according to studies conducted by many groups on a total of 2456 pregnant women<sup>30,31</sup>. In a study of more than 40 000 pregnant women, COVID-19 vaccination during pregnancy was not associated with delivering an infant small for their gestational age or preterm birth<sup>32</sup>.

Finally, a systematic review and meta-analysis from articles published up to 1 November 2022 showed a decrease in the odds of preterm births among vaccinated pregnant women. Neonates of vaccinated women had also lower risk of ICU admission. It is worth mentioning that during the Omicron period, maternal vaccination did not reduce the risk of neonatal SARS-CoV-2 infection (33)

#### CONCLUSION AND RECOMMENDATIONS

Due to the serious consequences for mothers and infants, the prevention of prenatal infections is a critical component of the broader management of maternal and child health. Pregnant women can take steps to minimize the chance of developing a potentially harmful illness during pregnancy. This is achieved by practicing good hygiene, receiving prenatal care and immunizations, receiving good nutrition, and taking precautions to avoid exposure to dangerous infections. The role of healthcare providers in reducing the incidence of infections is also crucial, as preventing infections in the pregnant woman, fetus, or infant is an important part of prenatal care. However, despite the recommendations for vaccination against

influenza and COVID-19 during pregnancy, vaccination rates remain low.

### **Competing Interests**

The author has no relevant financial or non-financial interests to disclose.

**Conflicts of Interest:** The authors declare no conflicts of interest.

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