

Influenza Vaccine Requirements in Pregnant Women

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About the Author



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Abstract

Objective To explore the importance of administering influenza vaccine during pregnancy.

Materials and Methods An internet search for data, study and position papers was done. Medline and Pubmed were the frequently used search engines besides search for WHO and CDC position statements. The keywords used included,

influenza vaccine, pregnancy, outcome, safety and trimesters.

Results Search provided studies that had been conducted in developing nations like Bangladesh as well as developed nations like Norway and England. The WHO and CDC status reports were also accessed and studied.

Conclusion Administration of influenza vaccine is recommended in any trimester of pregnancy, to protect the pregnant woman as well as the newborn child below the age of 6 months from the deleterious effects of influenza. The vaccine is safe and free from side effects.

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Pregnancy is a time where numerous physiological changes occur in the body. Besides providing the compatible milieu for the development of the fetus, the maternal immune mechanisms are altered, making the pregnant woman more susceptible to increased severity as well as the likelihood of developing complications to common infections. Thus, pregnancy places a woman at increased risk of developing severe complications from influenza virus infection [1].

Effects of Influenza During Pregnancy

Pregnancy is associated with immunological and physiological changes in several organ systems, especially cardiovascular and respiratory system. The growing uterus exerts pressure on these systems resulting in decreased lung capacity [2]. Together with an increase in the heart rate, increased stroke volume and oxygen consumption, the compromised lung volume accelerates the development of dyspnea.

The immune system adapts itself in order to accommodate the growing fetus. The immunity shifts away from the cell-mediated immunity toward the humoral immunity [2]. There is a selective suppression of the T helper-type I cell-mediated immunity, with resultant impaired maternal response to infection [3]. Put together with the organ system alterations, the pregnant woman is at an increased risk of severe influenza.

Influenza Infection

A fairly prevalent infection, influenza is caused by viruses that belong to the orthomyxoviridae family and are enveloped, segmented single-stranded RNA viruses [2]. There are two major surface proteins that determine the serotype of the virus hemagglutinin (HA) and neuraminidase (NA) [4]. These proteins project as spikes through the viral envelope. There are three distinct types of influenza virus—A, B and C [2, 4]. Type A infects a large range of mammals and birds, while types B and C are primarily human pathogens causing epidemic outbreaks. Influenza virus infects animals like pigs, horses, birds and bats which act as the reservoirs for these viruses.

The segmental nature of the influenza virus allows the re-assortment to occur between the animal virus and the human virus [4]. The 15 HAs and the 9 NAs of the animal reservoirs can be introduced into the humans and the reassortment can result in an apparently distinct serological type of viruses, which have no cross protection, and result in novel influenza virus strains.

Epidemiology

The viral recombination may result in minor changes in the virus, and this is referred to as *viral drift*. When there are major changes resulting from the recombination, it is referred to as *viral shift* and generally results in pandemic disease outbreaks. A virus with a novel and serologically distinct HA or NA enters the population and has the potential to cause maximal damage in the naïve non-immune population, with resultant disease pandemics. The antigenic drift enables the virus to avoid immune recognition in the host and results in seasonal influenza outbreaks [4]. As type B does not have any animal reservoir, it is not susceptible to viral shifts. Humans are generally infected with H1, H2, H3 and N1 or N2 [4].

Children are extremely vulnerable to the adverse effects on influenza infection as they tend to have higher levels of viral infection and prolonged shedding [4]. Pregnant women tend to develop more severe complications due to their altered immune and physiological status [1, 3].

Effects on Infection in Pregnancy

During the previous influenza pandemics since 1918, 1957 and 2009, it was found that pregnant women were at high risk of developing complications [3]. Even during the inter-pandemic periods, pregnant women have been found to have an 18 times higher likelihood of hospitalization, especially if they contracted infection in the later stages of pregnancy. Associated comorbid conditions like diabetes or asthma, chronic cardiac or renal disease, and immunosuppressive disorders in pregnant women increase the likelihood of morbidity by at least 3–4 times more [2, 3]. Obesity during pregnancy is also associated with higher morbidity [5]. Pregnant women with comorbid conditions were found to have a 3 times higher likelihood of being hospitalized for respiratory illness during the influenza season than non-pregnant women [2]. Those with >1 comorbid conditions were at substantially higher risk of hospitalization if they contracted influenza in any trimester of pregnancy [2]. High mortality rates of pregnant women who contracted influenza have been documented in the pandemics of 1918–1919 and 1957–1958 [6]. In the 2009 pandemic, mortality in pregnant women was almost 1 % of the population in USA [6]. Similar trends were observed in Australia and New Zealand where almost 9.1 % of cases in the ICU were found to be pregnant women, while in Canada pregnant women with influenza accounted for 20 % of hospitalizations and 12 % of ICU care [5]. Studies from Dallas, Texas, conducted during the 2003–2004 influenza season have shown that 62 % of pregnant women

with laboratory-confirmed influenza A infection were hospitalized and 1 in 8 of them suffered from pneumonia, while a substantial proportion had tachycardia and did not respond adequately to antipyretics and hydration therapy [7].

Effects on Pregnancy Outcomes

While pregnancy alone is considered as a “high risk” for severe disease, the effect on the outcome of the pregnancy is detrimental [5]. Fetal malformations and other illnesses have been noted in cases of influenza in pregnancy [8]. Preterm delivery is an oft-recognized adverse outcome, as has been studied by Newsome et al. in the USA [3]. This study showed that 63.6 % of pregnant women severely ill with influenza had preterm deliveries and 43.8 % had low birth weight babies as compared to the national averages. Stillbirth, infant death, emergency cesarean delivery, low birth weight and decreased weight for gestational age have been reported in cases of severe maternal influenza during pregnancy [5].

Effects on Newborns with Maternal Influenza During Pregnancy

Maternal antibodies provide infant protection during the initial months of life. However, in case of maternal influenza infection in pregnancy which is usually severe, the infant has been affected adversely. Studies have shown that in case of 83.3 % of severe maternal infection, the infants required either ICU admission or died due to illness [9]. The hospital stays of these infants would be prolonged due to their prematurity and/or delivery complications [5]. The infection may produce non-specific symptoms like irritability, dyspnea, decreased feeding, vomiting, diarrhea and fever [3]. A high index of suspicion is warranted in order to make the accurate diagnosis and provide adequate treatment. A study reported from Bangladesh, which has influenza virus present throughout the year, showed that almost 33 % of infants <6 months were serologically positive for influenza virus infection [10]. Pneumonia is common in those infants with influenza virus positivity, and coinfection with pneumococcus increases the burden and steps up the severity of infection in infants [3]. While infants above the age of 6 months are recommended to receive the annual influenza vaccine, those below the age of 6 months cannot be immunized and hence require additional protection in order to bring down the morbidity and mortality caused by severe influenza infection during pregnancy.

Influenza Vaccination

The inactivated influenza vaccine is recommended for immunization of pregnant women by the WHO since 2005 [11]. Despite this, not many women have been receiving this vaccine. The WHO position paper 2012 reiterates the importance of immunization of pregnant women as they are found to be 7.2 times more likely to be hospitalized than non-pregnant women, while in children <6 months the hospitalization rates were as high as 240/100,000 children [12]. The trivalent influenza vaccine (TIV) contains antigens from two influenza A strains H1N1 and H3N2 and one from influenza B strain (Yamagata or Victoria). The quadrivalent inactivated vaccine contains two influenza A strains and two influenza B strains and provides protection against both the B-type lineages that can cause infection in humans [13]. The Advisory Committee on Immunization Practices (ACIP) recommends the use of inactivated influenza vaccine without specifying any preferential formulation [14].

The WHO and the American College of Obstetricians and Gynecologists (ACOG) recommend the use of inactivated influenza vaccine to all women who are pregnant during the influenza season [5, 12, 14]. This is recommended as an essential element of prenatal care [5]. The vaccination of the mothers has been shown to produce excellent protective antibody titers in the pregnant woman. The Mother’s Gift Project was a randomized trial carried out in Bangladesh between August 2004 and May 2005 with the primary goal of assessing the clinical effectiveness of influenza vaccine [3, 8, 12, 14]. In this blinded study, 340 pregnant women were randomized to receive a dose of influenza vaccine in the third trimester and were followed up throughout pregnancy and delivery. Results showed a significant decrease in laboratory-confirmed influenza in the infants, while the mothers were significantly less likely to have respiratory illness with fever as compared to the control group. An almost 63 % decrease in laboratory-confirmed influenza, 29 % reduction in febrile respiratory illness in infants and 36 % reduction in febrile respiratory illness in the mothers were shown by this trial [3, 8]. This trial has shown the efficacy of influenza vaccine administered to pregnant women in decreasing the incidence of influenza illness and complications in the infants compared to the control.

Timing of Immunization

The ACOG and CDC recommend the administration of the inactivated flu vaccine to all pregnant women or those who will be pregnant during the influenza season. The vaccine

must be administered as soon as it is available. One dose must be given and can be administered any time during gestation [14]. The WHO classifies pregnant women as the top priority to receive the influenza vaccination [12]. This protects not only the pregnant women from the adverse outcomes, but also the newborns and infants <6 months against influenza.

Vaccine Safety

The trivalent inactivated influenza vaccine has been found to be safe to be administered during pregnancy. Randomized controlled studies from USA and Bangladesh have not found any significant adverse effects, nor any increase in the likelihood of fetal, perinatal or infant complication that could be correlated with vaccine administration [12]. The study reported by Håberg et al. looked at 117,347 births during the pandemic season in 2009–2010, and it was reported that vaccination during pregnancy was not associated with an increased risk of fetal death [6]. The vaccinated women had lower chances of contracting the influenza infection and hence had better pregnancy outcomes. The NorFlu trial which looked at the Norwegian Influenza Cohort Study carried out in 2009–2010 had 4200 pregnant women and 4400 children recruited with the aim of studying the perinatal outcomes and cognitive development of the children related to maternal exposure to influenza in pregnancy [6]. Only 57 % of the mothers were vaccinated against influenza, while almost 400 mothers (15 %) of the entire cohort developed influenza. The vaccinated mothers did not have any alteration in the gestational length nor the birth weight of the infants. The CDC recommends pregnant women to get a flu shot during any trimester of their pregnancy to protect themselves and their unborn babies until 6 months after birth due to the protective transplacental transfer of antibodies [15].

Thiomersal, a mercury-containing preservative is present in the multidose vials of influenza vaccine [14]. However, to date, there is no evidence that these vaccines have any adverse effects on the outcomes of the pregnancy and ACIP does not indicate any preference for non-thiomersal containing vaccines [14]. Also, none of the currently available vaccines have the AS03 adjuvant, which was found to be associated with increased incidence of narcolepsy/cataplexy when it was present in the vaccine formulations used in Nordic countries during the pandemic period [12]. The only contraindication to immunization is the occurrence of severe egg protein allergy or allergy after a previous dose of the vaccine [12].

Newer Formulations

A quadrivalent vaccine now available contains two A and two B strains of influenza and could provide a better protection against seasonal influenza. The ACIP does not preferentially recommend a specific formulation to be used, and hence, either trivalent or quadrivalent inactivated influenza vaccine is recommended for use during pregnancy [14].

Vaccination During Breast-feeding

The CDC recommends that mothers who breast-feed their infants should also get themselves vaccinated against flu, so that they are protected from contracting the disease and passing the flu to their babies. These mothers can take either the inactivated flu vaccine or the live attenuated nasal spray [14, 15].

The Task Ahead

All healthcare providers must understand the seriousness of pregnant women contracting influenza as it causes severe disease and increase rates of hospitalizations and higher mortality. Those women who have associated comorbid conditions have an enhanced risk of complications. The pregnancy outcome is also jeopardized, as there is a higher likelihood of still births, preterm delivery and low birth weight. The Nova Scotia study compared the rate of hospital admissions and illness among pregnant women during the influenza season, with the corresponding period in the year prior to their pregnancy was studied [14]. The results showed longer duration of hospitalization and more number of medical visits if they developed respiratory illness, especially during the third trimester of pregnancy, and this was more striking in women with comorbid conditions.

It is obligatory for every healthcare provider who caters to pregnant mothers to counsel them regarding the importance of receiving the influenza vaccine during pregnancy. Studies have shown that when the women receive recommendations from their own obstetrician there is a fivefold to 50-fold higher likelihood of acceptance [14]. The lack of information provision has been found to be the major barrier to vaccine acceptance by mothers. According to latest updates released by the CDC, as of early November 2015, only 40.2 % of pregnant women had received flu vaccination, and of these only 61.6 % of the women had received a recommendation and an offer for immunization from their healthcare provider [16]. Those who had received this information from their healthcare providers

were eight times more likely to be vaccinated compared to those who did not receive any information. The lack of knowledge is the biggest barrier to vaccine acceptance. It is imperative on the part of the healthcare providers to provide pregnant women with the knowledge regarding the essentiality of the flu vaccine in protecting the mother against severe illness and mortality, as well as providing protection for infants below the age of 6 months who are too young to receive the flu shot. This single intervention has the capacity of maximizing the protection of pregnant women and infants against flu and will be a step ahead toward achieving the Sustainable Development Goal 3 of global good health and well-being as envisaged by the World Health Organization.

Compliance with Ethical Standards

Conflict of interest The author hereby declares that she has no conflict of interest.

Ethical Approval This article does not contain any studies with human participants or animals performed by the author.

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