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Dolna 17, Warsaw,
Poland 00-773
+48 226 0 227 03
editorial_office@rsglobal.pl

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INFLUENZA IMMUNIZATION DURING PREGNANCY AS A STRATEGY FOR MATERNAL AND NEONATAL PROTECTION: BENEFITS, SAFETY AND CLINICAL RECOMMENDATIONS

Patrycja Jędrzejewska-Rzezak *(Corresponding Author, Email: patrycjaj@kul.lublin.pl)*
The John Paul II Catholic University of Lublin, Al. Racławickie 14, 20-950 Lublin, Poland
ORCID ID: 0000-0003-2144-5810

Monika Czekalska
Norbert Barlicki Memorial Teaching Hospital No. 1 of the Medical University of Lodz, Kopcińskiego 22, 90-153 Łódź, Poland
ORCID ID: 0009-0004-7091-5369

Natalia Kulicka
Lower Silesian Specialist Hospital, Kamieńskiego 73a, 51-124 Wrocław, Poland
ORCID ID: 0009-0002-9321-1693

Kinga Knutelska
The University Hospital in Cracow, ul. Jakubowskiego 2, 30-688 Kraków, Poland
ORCID ID: 0009-0003-0795-0228

Aleksandra Winsyk
University Clinical Hospital No. 4 in Lublin, 8 Jaczewskiego St., 20-964 Lublin, Poland
ORCID ID: 0009-0003-9780-3829

Paulina Gajniak
Poznań University of Medical Sciences, ul. Fredry 10, 61-701 Poznań, Poland
ORCID ID: 0000-0003-0402-6737

Maciej Karwat
Independent Public Health Care Center of the Ministry of the Interior and Administration in Krakow, Kronikarza Galla 25, 30-053 Kraków, Poland
ORCID ID: 0009-0007-5917-977X

Tytus Tyralik
Stefan Żeromski Specialist Hospital – Independent Public Healthcare Institution in Kraków, Osiedle Na Skarpie 66, 31-913 Kraków, Poland
ORCID ID: 0009-0001-7370-4610

Klaudia Bilińska
District Railway Hospital in Katowice, Panewnicka 65, 40-760 Katowice, Poland
ORCID ID: 0009-0003-4137-6135

Joanna Węgrzecka
Fedmed, ul. Widna 45, 06-400 Ciechanów, Poland
ORCID ID: 0009-0007-5714-3431

ABSTRACT

Influenza infection during gestation presents considerable hazards to both the mother and the fetus, including heightened hospitalization rates, severe respiratory problems, and negative newborn outcomes. Influenza vaccination is strongly advised as an efficacious prophylactic strategy to mitigate these hazards. This article evaluates the existing evidence regarding the safety, immunogenicity, and efficacy of influenza vaccines given during pregnancy. We examine the dual protective effect for both the mother and the newborn, highlighting the transplacental transfer of maternal antibodies and the resulting passive immunity during early infancy. Furthermore, we examine clinical guidelines from prominent health organizations, highlighting the significance of vaccination scheduling and methods to enhance vaccine acceptance among pregnant women. Our findings endorse influenza vaccination as an essential public health measure to safeguard the health of women and babies, and advocate for heightened awareness and implementation in prenatal care environments. Focus was directed on areas necessitating additional research and enhancements in clinical practice.

Aim of the study: The proportion of vaccinated pregnant women remains inadequate. Raising awareness of the possible health advantages of influenza vaccination for pregnant women and their developing fetuses is crucial. The significance of healthcare personnel is emphasized, and ways to improve pregnant women's awareness of the safety and benefits of vaccines during pregnancy are discussed.

Materials and methods: A review of the literature available in the PubMed and Google Scholar database was performed, using the key words: „influenza", „vaccine", „pregnancy", „pregnant woman", „maternal vaccination", „infant".

KEYWORDS

Influenza, Vaccine, Pregnancy, Pregnant Woman, Maternal Vaccination, Infant

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1. Introduction

Influenza is a highly transmissible respiratory illness caused by prevalent RNA viruses from the Orthomyxoviridae family that propagate among humans. In individuals devoid of additional risk factors, it is typically a self-limiting illness and generally does not result in mortality. Nonetheless, certain identifiable patient groups are at heightened risk for severe infections with significant consequences. One of these groups consists of pregnant women. Influenza virus infection during pregnancy correlates with a heightened risk of hospitalization, respiratory problems, and negative obstetric outcomes, including preterm birth, low birth weight, or fetal demise. In the 2009 A/H1N1 influenza pandemic, numerous reports indicated a significantly more severe progression of the disease in pregnant women, an increased incidence of hospitalizations due to influenza, a greater necessity for oxygen therapy, extended stays in intensive care units, and detrimental effects of the infection on neonatal health.

Infections constitute the third primary cause of mortality in pregnant women. Statistics reveal that in 11 per 1,000 pregnant women, the disease leads to severe problems or mortality related to the virus (*Global Report on the Epidemiology and Burden of Sepsis : Current Evidence, Identifying Gaps and Future Directions*, 2020). International health organizations, including the World Health Organization (WHO), the Centers for Disease Control and Prevention (CDC), and the American College of Obstetricians and Gynecologists (ACOG), endorse influenza vaccination during pregnancy as a safe and effective preventive measure. Furthermore, the immunization of pregnant women benefits both the mother and the infant by facilitating the transplacental transfer of antibodies, thereby offering protection to the kid during the initial months of life, prior to the commencement of its own vaccinations.

Notwithstanding the accessibility of vaccinations and explicit guidelines, immunization rates among pregnant women remain inadequate in numerous countries, presenting a considerable challenge to public health.

This article delineates the present understanding of the efficacy and safety of influenza vaccinations during pregnancy, examines their advantages for both the mother and child, and evaluates the existing clinical guidelines. The objective of this work is to delineate avenues for future research and practices that may enhance the execution of this preventive approach in prenatal care.

2. The effects of influenza virus infection on a pregnant mother and her fetus

It is widely recognized that viruses induce various detrimental consequences during pregnancy and the perinatal period, affecting both the pregnant woman's health and the fetus. Two primary, non-exclusive modes of microbial impact can be identified: 1) direct vertical transmission to the fetus through the placental route or during delivery (e.g., cytomegalovirus or rubella virus), and 2) indirect damage to the maternal-fetal interface, resulting in significant disease and inflammation in the pregnant individual that impedes fetal and neonatal development (e.g., influenza virus, SARS-CoV-2 virus) (Creisher & Klein, 2024).

Pregnancy involves numerous physiological and immunological adjustments designed to facilitate fetal development and well-being (Bansal et al., 2021). Pregnant women exhibit heightened oxygen requirements, elevated heart rate, and diminished lung capacity. These alterations may result in a significantly more severe progression of viral infections in pregnant women and during the perinatal period. Consequently, modifications in the immune system heighten a woman's vulnerability to viral infections, while the deterioration of cellular immunity is crucial in combating such illnesses.

3. Influenza in pregnant women

Influenza is a contagious respiratory illness resulting from infection with influenza type A or B viruses. These viruses are classified within the Ortomyxoviridae family. Influenza A and B viruses circulate periodically among the population, but pandemic influenza arises from novel strains of the influenza A virus (Krammer et al., 2018).

Pregnant women face an elevated risk of severe illness and consequences, including mortality, due to seasonal infections and during pandemics (Mertz et al., 2017) (Vousden et al., 2021). Statistics from the USA during the 2009 flu pandemic reveal that 5% of influenza-related fatalities were pregnant women, while representing approximately 1% of the population (Siston et al., 2010). The seasonal influenza virus is documented to infect between 483 and 1,097 per 10,000 pregnant women annually (Katz et al., 2017)

The influenza virus is transmitted via respiratory droplets, with an incubation period of 2 to 5 days. The patient becomes infected throughout the incubation period of the disease and when clinical signs are evident in the influenza patient. The typical duration of contagion is 6 days, encompassing roughly 1-2 days prior to symptom manifestation and continuing for 5-7 days following their emergence.

The symptoms of the condition generally do not differ markedly in pregnant women compared to the broader population. The patient exhibits a significant fever, pervasive fatigue, cephalalgia, musculoskeletal discomfort, malaise, pharyngitis, moderate rhinitis, a dry, exhausting cough, and shallow respiration. In individuals devoid of supplementary danger factors, the ailment typically resolves spontaneously between 3 to 7 days. Complications arise more frequently in pregnant women compared to the general population.

The recent proliferation of quick antigen testing, in conjunction with standard infection symptoms, is adequate for confirming influenza infection and promptly initiating treatment, especially for pregnant women. Should outpatient treatment prove ineffective, particularly in the presence of symptoms such as dyspnea, respiratory distress, thoracic pain, marked weakness, dehydration, or the manifestation of typical obstetric complications, the pregnant patient must be promptly referred for hospital care. Pregnant women experiencing a moderate progression of the disease, accompanied by chronic conditions that could precipitate a fast decline in health due to concurrent infection, should be hospitalized. These diseases encompass all circulatory system disorders, lung conditions, diabetes, renal diseases, and those with immunosuppression, irrespective of the underlying etiology.

Current research indicates that vertical transmission of the influenza virus through the placenta is exceedingly uncommon. However, illness in a pregnant woman may have detrimental effects on the growing fetus.

A 2017 meta-analysis by He et al. (He et al., 2017) revealed that influenza virus infection in pregnant women may correlate with low birth weight, stillbirth, and inferior APGAR scores relative to newborns of women without a history of influenza.

Ribeiro et al. (Ribeiro et al., 2018) discovered that pregnant women hospitalized for influenza virus infection, resulting in severe symptoms, faced an elevated risk of significant neonatal complications, including premature birth, low birth weight, fetal demise, and the necessity for cesarean section delivery.

In their 2020 study, Song et al. (Song et al., 2020) confirm that influenza virus infection in pregnant women dramatically elevates the incidence of preterm birth and low birth weight in babies. Furthermore, they underscore the observations concerning the long-term consequences for the kid resulting from a pregnancy complicated by maternal influenza infection. They signify a heightened risk of obesity in these children in the future. Older research also indicate the emergence of significant cognitive problems in these children into maturity.

4. Preventing influenza virus infections in pregnant women through vaccination

The most effective means of reducing flu problems in pregnant women and the fetus is to avoid illness altogether. A validated approach with demonstrated efficacy in preventing influenza infection is vaccination. The Centers for Disease Control and Prevention (CDC) and World Health Organization (WHO) jointly advocate for the vaccination of all pregnant women against influenza, irrespective of the pregnancy trimester. Numerous groups, both governmental and non-governmental across various countries, advocate for the vaccination of pregnant women against influenza (Cohen et al., 2023). Notwithstanding the consensus among the preeminent scientific organizations in gynecology and obstetrics - The American College of Obstetricians and Gynecologists (ACOG), Royal College of Obstetricians and Gynaecologists (RCOG), the proportion of vaccinated pregnant women remains inadequate (Etti et al., 2022) (Razzaghi et al., 2023).

Inactivated influenza vaccines comprising viral particles or surface proteins of the influenza virus, as well as a live intranasal vaccine, are available. Vaccines containing inactivated virus are authorized for pregnant women. They are delivered via intramuscular or deep subcutaneous injection. Live vaccinations are contraindicated for pregnant women. Recently, novel influenza vaccines, including cell culture vaccines and suggested vaccinations, have received approval. There are sporadic accounts of their application in pregnant women. As of now, no negative effects of providing these vaccines to pregnant women have been proven (Moro & Marquez, 2021) (Robinson et al., 2022).

The primary contraindication for influenza vaccination is anaphylactic responses following prior delivery of the vaccine. Vaccinations for women with a documented allergy to hen's egg protein should be conducted under specialized supervision in medical facilities equipped to provide immediate specialist assistance in the case of an anaphylactic reaction. Moreover, contraindications encompass, as with other vaccines, acute diseases accompanied by fever (Nypaver et al., 2021).

The CDC's latest report specifies the most advantageous timing for administering the flu vaccine to pregnant women. Vaccination is typically advised against in July and August because of the risk for diminished immunity to infection during the peak flu season. Vaccine during these months may be advisable for women in the third trimester of pregnancy, as it diminishes the risk of influenza in infants during their initial months of life, when they are ineligible for vaccine, due to the mother's immunization. Women in the first and second trimester should preferably receive vaccination in September or October, unless we foresee that vaccination would be unfeasible during that period (Cohen et al.,2023).

5. The safety and efficacy of influenza vaccines in pregnant women

Numerous research and meta-analyses conducted over several decades conclusively affirm the substantial safety of influenza vaccinations in pregnant women, benefiting both the mother and the developing fetus. The overwhelming majority of scientific research does not identify any detrimental consequences during pregnancy subsequent to the administration of the influenza vaccine. An observational study, Vaccine Safety Datalink (VSD), found an association between influenza vaccination in pregnant women and an elevated risk of miscarriage within four weeks of vaccination in women who had received a vaccine containing the same virus in the preceding season. This study was conducted during the 2010/2011 and 2011/2012 seasons (Donahue et al., 2017). This connection was not validated in trials performed in later seasons (Donahue et al., 2019). No negative health impacts have been documented in infants or school-age children whose moms received influenza vaccinations during pregnancy.

Influenza vaccines, as to any other medication, may induce negative effects. Flu vaccines typically have a limited incidence of documented adverse effects post-vaccination. When they occur, they typically manifest as localized reactions, including erythema, discomfort, or edema at the injection site; systemic symptoms reported post-vaccination, such as a mild elevation in temperature or myalgia and arthralgia, are infrequently observed. These reactions typically resolve spontaneously within several days (Rand & Olson-Chen, 2023) .

Given these data, it is essential to underscore that the advantages of influenza vaccination in pregnant women much surpass the potential hazards linked to this intervention.

Multiple studies have established that influenza vaccination during pregnancy does not elevate the risk of miscarriage, preterm birth, fetal demise, stillbirth, low birth weight, cesarean delivery, congenital anomalies, or neurological and psychomotor developmental abnormalities (Nichol et al., 2023)(Lopatynsky-Reyes et al., 2023)(Getahun et al., 2024).

A systematic evaluation by Wolfe et al. (Wolfe et al., 2023) published in 2023 concluded that influenza vaccination during pregnancy does not correlate with an elevated risk of unfavorable pregnancy outcomes or severe maternal non-obstetric complications. The analysis encompassed 63 research, comprising 29 studies that assessed seasonal influenza vaccine (trivalent and quadrivalent) vs no vaccination. The meta-analyses yielded no statistically significant correlations with preterm birth, spontaneous pregnancy loss, or low birth weight. Descriptive studies for stillbirth, congenital abnormalities, and severe maternal non-obstetric events similarly revealed no significant relationships with risk. Nevertheless, the authors underscore that these findings derive from studies of inferior methodological quality that frequently failed to adequately account for confounding variables and temporal inaccuracies. It is advised to undertake subsequent studies with enhanced control over these variables to elevate the quality of evidence and provide more accurate evaluations of the safety of influenza vaccination during pregnancy.

The overall anticipated efficacy of the influenza vaccine is 38% (Cohen et al., 2023). The alterations in the immune system experienced by women during pregnancy seemingly do not influence the immunogenicity of influenza vaccinations, so the efficacy of influenza immunization in pregnant women parallels that observed in the general population (Nunes et al., 2016). A published study demonstrated a 40% decrease in the risk of hospitalization from influenza among pregnant women (Thompson et al., 2019).

Additional studies corroborate the efficacy of immunizations for pregnant women and the diminished risk of newborns acquiring influenza during their initial months of life, when they are ineligible for vaccination, highlighting the significant advantage of maternal immunization. The underdevelopment of the immune system during the initial six months of a child's life may contribute to a heightened incidence of influenza, perhaps resulting in severe cases that necessitate hospitalization (Nunes et al., 2016). Vaccination of pregnant women against influenza is expected to decrease the risk of influenza in infants by 70% and also diminishes the incidence of febrile respiratory diseases by about 30% in this patient cohort (Nunes & Madhi, 2018a).

Passive immunity in neonates, attained via transplacental transfer of IgG antibodies from an immunized mother, is a crucial method for safeguarding the newborn from influenza. Evidence indicates the transfer of IgA antibodies via breastfeeding from an immunized mother; however, the impact seems to be considerably less pronounced (Nunes & Madhi, 2018b).

Vaccination against the group offers significant advantages in safeguarding both the pregnant lady and the newborn. Implementing a vaccination program for pregnant women fulfills the objectives of vaccination, as articulated by Atzinger and Henna, on two levels: safeguarding the vaccinated individual (first level) and ensuring the protection of future generations (final level) (Atzinger & Henn, 2020).

6. Enhancing vaccination rates during pregnancy - strategies for improvement

The proportion of pregnant women vaccinated against influenza remains inadequate. The largest proportion of immunized pregnant women is observed in nations where obstetricians actively advocate for the influenza vaccination program and encourage patient participation. The CDC estimated that in March 2025, 38% of pregnant women in the USA were vaccinated against influenza *(Influenza Vaccination Coverage, Pregnant Women, United States*, 2025*)*. The data regarding the percentage of pregnant women vaccinated against influenza in Poland is inadequate. The queried databases include a singular research done by Jurga et al. (Jurga et al., 2024). Among the surveyed pregnant women, 12.2% received this immunization.

Consequently, it is imperative to enlighten both physicians and patients by providing them with credible, scientifically validated information regarding influenza vaccination during pregnancy. All scientifically baseless claims regarding the detrimental effects of vaccines on the body of a pregnant woman and the fetus should be vigorously opposed.

The following are pre-established methods that, if effectively executed, can enhance pregnant women's awareness of the safety and advantages of immunizations during pregnancy(Sebghati & Khalil, 2021).

1. The family doctor's responsibility includes educating and reminding patients about immunizations inside primary health care facilities, as well as disseminating informational brochures targeted at pregnant individuals.

2. Professional conduct of healthcare practitioners - educating about the advantages of immunization for both the expectant mother and her fetus.

3. Facilitate access to vaccinations by suggesting their administration during routine obstetric check-ups, so eliminating the need for pregnant women to reschedule appointments solely for immunization purposes.

4. Acknowledging women's apprehensions about the safety of immunization for the fetus and addressing these concerns with current medical knowledge, while educating healthcare professionals in this domain.

5. Involving midwives in the promotion of vaccinations by annually enhancing their knowledge regarding vaccinations for pregnant women, so bolstering their confidence in recommending and providing these vaccinations.

The aforementioned strategies are entirely suitable for all vaccinations advised for pregnant women, not solely for influenza vaccination, and should be executed to safeguard against infectious complications in a cohort of pregnant women who represent a specific risk group for severe illness.

7. Future Directions for Research and Clinical Practice

Although substantial data endorses the advantages of influenza vaccination during gestation, some domains necessitate additional investigation and enhancements in clinical practice (Chittajallu et al., 2025). Future developmental trajectories can be categorized into various fundamental dimensions.

Innovative vaccination formulations and technology

Advancements in biotechnology create chances to manufacture vaccines with enhanced immunological characteristics and safety profiles. Vaccines utilizing novel platforms, such as mRNA, are especially promising and have demonstrated excellent efficacy in several indications. Future research should concentrate on evaluating their safety and immunogenicity in pregnant women, along with their capacity to confer long-term protection to both mother and child. The creation of universal vaccinations that encompass a wider range of influenza virus strains may diminish the necessity for annual vaccine reassessment.

Surveillance of the enduring consequences of vaccination

The majority of studies conducted thus far have concentrated on the short-term evaluation of vaccine safety and efficacy. It is essential to perform longitudinal studies to evaluate the effects of vaccination on children's health over an extended duration, encompassing immune system development and potential immunological consequences. The enduring safeguarding of the mother, particularly concerning repeated gestations and vaccines, continues to necessitate elucidation.

Integration of influenza vaccination with additional prenatal interventions

Enhancing prenatal care may necessitate improved integration of influenza vaccine with other standard health interventions, like pertussis immunization and vitamin deficiency prevention initiatives. A comprehensive approach that addresses all facets of maternal and fetal health may enhance vaccine acceptability and elevate overall health outcomes. Investigation is required into efficient organizational and educational frameworks that facilitate such integration.

Education and Mitigating Obstacles to Vaccination

Notwithstanding explicit instructions, immunization rates among pregnant women continue to be poor in numerous countries. Future initiatives should prioritize the formulation of teaching programs for both patients and healthcare personnel to successfully address misconceptions and apprehensions regarding vaccine safety. The utilization of digital resources, social marketing, and the engagement of opinion leaders can enhance acceptability and faith in immunization.

8. Summary

Influenza is a highly transmissible respiratory illness caused by prevalent RNA viruses from the Orthomyxoviridae family. Pregnant women face an increased susceptibility to serious illnesses. Infections represent the third highest cause of mortality among pregnant women, with 11 per 1, 000 cases resulting in serious complications or death associated with the virus.

Viruses induce various detrimental consequences during pregnancy and the perinatal period, affecting both the pregnant woman's health and the fetus. Pregnant women exhibit heightened oxygen requirements, elevated heart rate, and diminished lung capacity, which may result in a significantly more severe progression of viral infections in pregnant women and during the perinatal period. The immune system modifications heighten a woman's vulnerability to viral infections, while the deterioration of cellular immunity is crucial in combating such illnesses.

Preventing influenza virus infections through vaccination is the most effective means of reducing flu problems in pregnant women and the fetus. The Centers for Disease Control and Prevention (CDC) and World

Health Organization (WHO) jointly advocate for the vaccination of all pregnant women against influenza, regardless of the pregnancy trimester. Vaccination against influenza during pregnancy is an established and endorsed preventive measure that effectively safeguards both the mother and the newborn against severe problems associated with influenza infection. A multitude of studies validate the vaccine's safety in pregnant women and its efficacy in decreasing hospitalizations, premature deliveries, and influenza cases in babies throughout the initial months of life. Notwithstanding explicit recommendations from international health organizations, vaccination rates within this demographic remain inadequate, attributable to factors such as ignorance, misinformation, and confusion among both patients and certain healthcare professionals. Consequently, enhancing understanding, fostering confidence in immunizations, and including immunization into standard prenatal care is crucial.

From the standpoint of advancing medicine, it is essential to investigate novel vaccine technologies, assess the long-term consequences of immunization, and develop systemic solutions to enhance the accessibility and acceptance of immunizations among pregnant women. Influenza vaccination during pregnancy safeguards persons and constitutes a component of a comprehensive public health plan designed to enhance health metrics for mother and child populations.

Disclosure

Author's contribution:
Conceptualization: Patrycja Jędrzejewska-Rzezak
Metoholody: Joanna Węgrzecka, Kinga Knutelska,
Formal analysis: Paulina Gajniak, Tytus Tyralik,
Investigation: Klaudia Bilińska, Maciej Karwat, Patrycja Jędrzejewska-Rzezak
Writing - Rough Preparation: Aleksandra Winsyk, Natalia Kulicka
Writing-Review and Editing: Monika Czekalska, , Tytus Tyralik
Data curation: Joanna Węgrzecka, Kinga Knutelska, Paulina Gajniak, Aleksandra Winsyk
Visualisation: Maciej Karwat, Monika Czekalska
Project administration: Natalia Kulicka, Klaudia Bilińska

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