REVIEW ARTICLE

CONTENTS

Vaccination in pregnancy: a systematic review of current evidence

Mária Gábor[1], Alena Schlosserová[1], Oxana O. Korchynska[2]
[1]PREŠOV UNIVERSITY IN PREŠOV, FACULTY OF HEALTH SCIENCES, PREŠOV, SLOVAK REPUBLIC
[2]UZHHOROD NATIONAL UNIVERSITY, UZHHOROD, UKRAINE

ABSTRACT

Aim: To summarize current recommendations and the state of knowledge on vaccination of pregnant women against influenza, pertussis, and Covid-19, and to highlight evidence on the efficacy and safety of vaccination during pregnancy.

Materials and Methods: A systematic literature review of studies published between 2014 and 2024 in the PubMed, Science Direct, Google Scholar, and NCBI databases was conducted. Of the total number of 31 studies found, 10 that met our required conditions were included. The inclusion criteria were peer-reviewed articles dealing with vaccination during pregnancy. Data selection and extraction were performed in accordance with PRISMA recommendations.

Conclusions: Vaccination of pregnant women appears to be a safe and effective way to protect mothers and their offspring. Emphasis should be placed on raising awareness and education in clinical practice.

KEY WORDS: pregnancy, vaccination, immunization, vaccine

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INTRODUCTION

Pregnancy is a specific period in a woman's life during which the body is more susceptible to infections that can pose a threat not only to the mother but also to the fetus. Vaccination of pregnant women is a preventive health measure that protects not only the mothers-to-be themselves, but also their unborn children from serious infectious diseases. Immunization during pregnancy reduces the risk of serious complications and also provides passive protection to newborns through transplacental transfer of maternal antibodies. Despite the scientifically proven benefits, there is still uncertainty among the general public about the safety of vaccination during pregnancy, which has a negative impact on vaccination rates.

According to international recommendations, vaccines are permitted during pregnancy in cases where their benefits outweigh the possible risks. Vaccinations during pregnancy are typically divided into routine vaccinations (recommended for all pregnant women), vaccinations indicated for health reasons, and vaccines that are contraindicated during pregnancy, which mainly include live attenuated vaccines [1].

Global health authorities such as the CDC, WHO, and ECDC (European Centre for Disease Prevention and Control) recommend influenza and dTap (diphtheria, tetanus, pertussis) vaccinations as safe, effective, and well tolerated during pregnancy [2,3].

AIM

To summarize current recommendations and the state of knowledge on vaccination of pregnant women against influenza, pertussis, and Covid-19, and to highlight evidence on the efficacy and safety of vaccination during pregnancy.

MATERIALS AND METHODS

A systematic literature review of studies published between 2014 and 2024 in the PubMed, Science Direct, Google Scholar, and NCBI databases was conducted. The paper also analyzes the available literature, recommendations from international health organizations (CDC, WHO, ECDC), as well as national legislative documents issued in Slovakia. Relevant results from epidemiological studies from the H1N1 influenza period (2009-2010) and the Covid-19 pandemic were also included. The keywords were compiled using the terms: "gravidita" and "tehotnosť" (pregnancy), "očkovanie" or

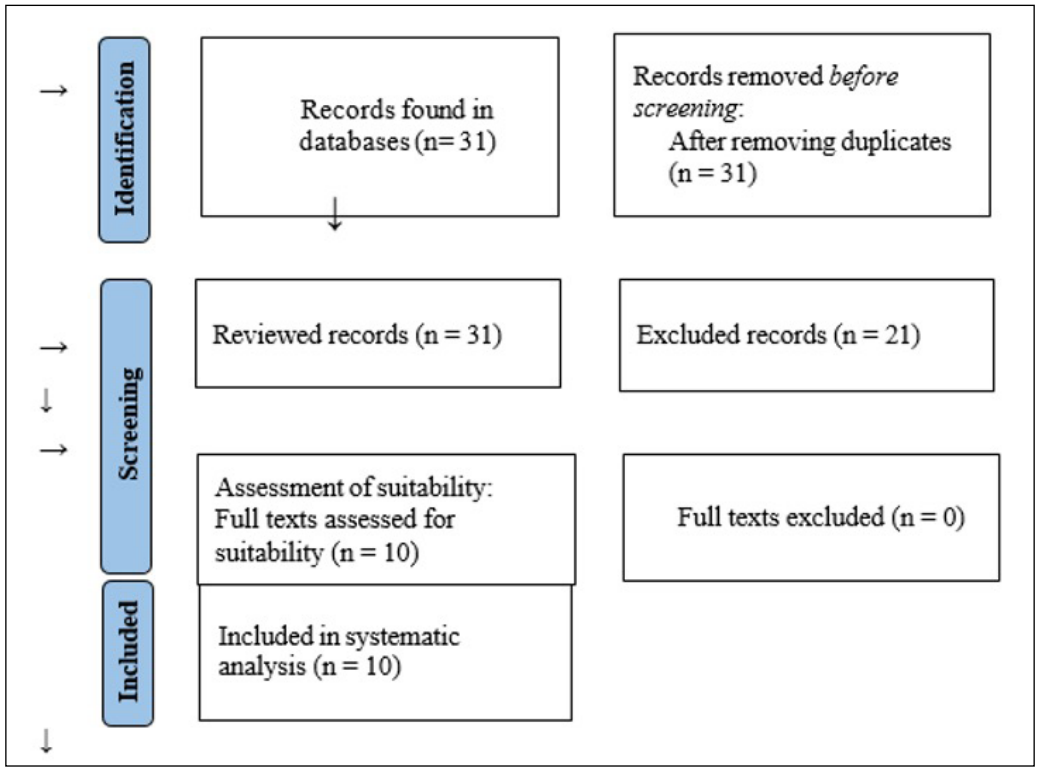

Fig. 1. PRISMA flow diagram
Picture taken by the authors

"vaccination" or "imunizácia" (immunization), and "vakcína" (vaccine). We filtered the studies regardless of their form or language of publication, with the condition that they were published between 2014 and 2024. In total, we found 31 studies, of which 10 met our criteria (Fig. 1 PRISMA flow diagram). Two independent reviewers evaluated the studies, and a third reviewer resolved any disagreements.

REVIEW AND DISCUSSION

An analysis of the studies found points to the safety of vaccination during pregnancy against three infectious diseases: whooping cough (Tdap), influenza, and COVID-19. No evidence of serious adverse effects or adverse pregnancy and perinatal outcomes was found in the vaccine comparison (Table 1).

Vaccination against whooping cough (Tdap) during pregnancy has been evaluated as safe in several studies, including cohort studies and meta-analyses of randomized clinical trials [4,5]. The results showed that administration of the Tdap vaccine in the second and third trimesters is not associated with an increased risk of preeclampsia, premature birth, or low birth weight. In addition, significantly higher levels of pertussis antibodies, which protect infants in the first months of life, were found in newborns of vaccinated mothers. The study by Gomme et al. (2022) confirmed that the highest levels of IgG in umbilical cord blood were achieved when vaccination was given before 31 weeks of gestation, with an optimal interval of at least 7.5 weeks before delivery.

Influenza vaccines have also demonstrated an excellent safety profile in several studies. A randomized controlled study [7] found no serious adverse events (SAEs) after vaccination (such as fetal death, severe preeclampsia, fetal damage), and most local or systemic reactions were mild. The findings of a meta-analysis by Nunes and Madhi (2018) are significant, showing that influenza vaccination of pregnant women reduces the risk of laboratory-confirmed disease in infants by 48% and hospitalizations by up to 72%. A cohort study by Regan et al. (2023) confirms that influenza vaccination does not increase the risk of miscarriage when administered before or during pregnancy.

Due to its recent emergence, vaccination against Covid-19 is still the subject of observational studies and systematic reviews. An analysis [10] involving more than 17 million pregnant women found no association between vaccination and adverse outcomes, regardless of vaccine type or trimester of administration. A cohort study [11] from 2022 showed that the rate of preterm birth was lower in vaccinated (5.5%) compared to unvaccinated (6.2%) pregnant women. Umbilical cord blood samples from mothers who had been vaccinated with mRNA vaccines against SARS-CoV-2 showed effective transplacental transfer of neutralizing antibodies [12], which were still detectable after 12 months.

Table 1. Vaccine safety during pregnancy

Type of vaccine	Side effects in the mother	Impact on pregnancy	Effects on the fetus/newborn	Conclusion on safety
Tdap (whooping cough)	- mild pain at the injection site - low subfebrile temperatures - no serious reactions	- does not increase the risk of preeclampsia, premature birth, miscarriage, or IUGR	- significantly higher IgG levels - no increased risk of SAE	Safe in the 2nd and 3rd trimesters
Influenza	- local reactions (pain, fatigue) - no fever - no systemic complications	- does not increase the risk of miscarriage or complications during pregnancy	- 48% lower incidence of influenza - 72% fewer hospitalizations	Safe throughout pregnancy
Covid-19 (mRNA and others)	Typical post- vaccination symptoms: fatigue, headache, fever (short-term) - Lower risk of severe Covid-19 in mothers	- does not increase the risk of premature birth, miscarriage, preeclampsia, or low birth weight	- effective transplacental transfer of antibodies - long-term protection (neutralizing antibodies ≥ 6–12 months)	Safe, ideally to be administered in the third trimester

Source: compiled by the authors of this study

The studies analyzed showed that vaccination of pregnant women does not pose a risk to either the mother or the child. On the contrary, vaccination has a prophylactic effect, with the mother's immune response providing passive immunity to the newborn and reducing the risk of infection during the first months of life.

In Slovakia, it is recommended to vaccinate with the dTap combination vaccine. This vaccination is recommended during the third trimester of pregnancy, preferably between weeks 28 and 38. It protects the mother from the disease itself and also transfers maternal antibodies to the fetus, which protects the newborn from the disease until it is vaccinated (Decree of the Ministry of Health of the Slovak Republic No. 585/2008 Coll.) [13]. Every pregnant woman should receive the Tdap vaccine regardless of her previous medical history during each pregnancy. Women who have not previously been vaccinated with Tdap should be vaccinated immediately after giving birth [14]. These recommendations are based on evidence of the high efficacy and safety of the vaccine and are consistent with the practice in more than 40 countries worldwide, where vaccination in the third trimester is standard [15].

In connection with influenza, it is important to recall the experience of the influenza A (H1N1) pandemic in 2009/2010, when it became apparent that pregnant women were one of the most at-risk groups. The WHO therefore included them among the priority groups for vaccination, along with children, seniors over 65, and the chronically ill. Statistics showed an increased risk of hospitalization, acute respiratory distress syndrome (ARDS), and mortality in unvaccinated pregnant women compared to those who were not pregnant. Based on these data, the CDC recommends flu vaccination in the fall months regardless of gestational age, including in the first trimester [2,13]. Furthermore, the results of studies [7,8] show that influenza vaccines are safe for both the mother and the fetus and reduce the risk of serious perinatal complications.

At the European level, there is some heterogeneity in the approach to vaccinating pregnant women (Table 2). Some countries allow vaccination in all trimesters, while others recommend vaccination only in the second or third trimester. These differences highlight the need to harmonize recommendations across EU member states. As stated by Aldoosari et al. (2023) [15], the implementation of clear national strategies and a unified communication line on the part of the state contribute to higher immunization rates.

Perceptions of vaccine safety are a key factor in pregnant women's decisions. Studies from 2021 and 2022 have shown that vaccination with the Tdap vaccine during pregnancy is not associated with an increased incidence of adverse effects (e.g., preeclampsia, partus praematurus, or intrauterine growth retardation). On the contrary, children of vaccinated mothers had significantly higher levels of specific antibodies, which supports the effectiveness of transplacental transfer [4, 5].

Similar conclusions can be drawn for vaccination against COVID-19, even though it is a relatively new disease, but available data from large observational and population studies suggest its safety. A meta-analysis [10] involving a large sample of pregnant women showed no increase in the incidence of miscarriage, premature birth, or intrauterine growth retardation. Similar results are confirmed by Dick et al. (2022) [11] in a large cohort study, confirming that vaccination does not lead to adverse obstetric complications. In addition, serological test results show effective transfer of neutralizing antibodies across the placenta, with levels detectable in newborns [12].

The question of why, despite positive evidence regarding the safety and efficacy of vaccines, their

uptake among pregnant women remains suboptimal in many countries is the subject of ongoing research. Woodcock et al. (2023) [16] discuss the statistics of rising and falling influenza vaccination rates in relation to age and ethnicity. Based on a retrospective cohort study, they found that uptake of the seasonal influenza vaccine among pregnant women increased during the decade preceding the Covid-19 pandemic, but remained suboptimal. Adeyanju et al. (2021) [17], in their study, identify the determinants of influenza vaccine hesitancy among pregnant women in Europe. The most commonly reported factors were psychological determinants, such as risk perception, concerns about vaccine safety, insufficient information, anti-vaccination attitudes, and low trust in the healthcare system.

Healthcare professionals play a crucial role in women's decision-making regarding vaccination. The study by Barrett et al. (2018) [18] emphasizes that midwives, gynecologists, and obstetricians are the most important sources of trustworthy information for pregnant women. Their active recommendation of vaccination significantly increases vaccine uptake. Kynčl et al. (2023) [19], in their study from the Czech Republic, note that the availability of the vaccine directly at the facility where a woman receives prenatal care, along with informed consent and reimbursement of the vaccine, are key factors in improving vaccination strategies. In conclusion, currently available evidence supports vaccination of pregnant women against Tdap, influenza, and COVID-19 as a safe and effective preventive measure that reduces morbidity and mortality not only in mothers but also in their newborns. However, to improve vaccination practices in clinical settings, systematic education of healthcare professionals, increased availability of vaccines in prenatal care, and trustworthy communication with pregnant women are essential.

CONCLUSIONS

Based on the available scientific evidence, it can be concluded that vaccination of pregnant women against pertussis (Tdap), influenza, and COVID-19 is safe, effective, and contributes to the protection of both mother and newborn. Studies confirm that administering these vaccines during pregnancy is not associated with an increased risk of adverse pregnancy or neonatal outcomes. On the contrary, it reduces the risk of infections during the early neonatal period.

The findings of this systematic review support the validity of recommendations made by both national and international health authorities. An important factor influencing vaccination uptake remains the awareness of pregnant women and the proactive approach of healthcare personnel. In line with this, we recommend strengthening the education and support of gynecologists in providing reliable and up-to-date information about vaccination during pregnancy.

The systematic review was conducted in accordance with the PRISMA 2020 methodological recommendations, which ensured the transparency, reproducibility, and informative value of the conclusions reached.\

STUDY LIMITATIONS

The systematic analysis faces several limitations. Only a small proportion of the total number of studies searched were included in the review, which may have affected the breadth and representativeness of the results. The included studies differed in design, sample size, and geographical and cultural context, which complicates their comparison. In the case of COVID- 19 vaccination, most of the available data are short-term, and therefore it is not possible to fully assess the long-term effects. We also did not include unpublished data, which may pose a potential risk of publication bias. Despite these limitations, the work provides a valuable overview of current knowledge on the safety of vaccination during pregnancy.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

CORRESPONDING AUTHOR

Oxana O. Korchynska
Uzhhorod national university,
3 Narodna Squ., 88000 Uzhhorod, Ukraine
e-mail: xena.0474@gmail.com

ORCID AND CONTRIBUTIONSHIP

Mária Gábor: 0009-0006-4160-2675 A B D
Alena Schlosserová: 0000-0002-1747-1429 E F
Oksana O. Korchynska: 0000-0001-7265-4829 E

A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article

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