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Review

COVID-19 Vaccination and Pregnancy

Natalia Ignaszak-Kaus[1,*,†], Karolina Chmaj-Wierzchowska[1,†], Katarzyna Wszołek[1], Maciej Wilczak[1]

[1]Department of Maternal and Child Health, Poznan University of Medical Sciences, 60-535 Poznań, Poland
*Correspondence: natalia.ignaszak@gmail.com (Natalia Ignaszak-Kaus)
[†]These authors contributed equally.

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Abstract

Objectives: A review to assess the safety, efficacy, COVID-19 vaccination acceptance and awareness in pregnant women. **Machanism**: Pregnant women diagnosed with COVID-19 are characterized by more frequent hospitalization in intensive care units and are at three times higher risk of preterm; their newborns more often need invasive ventilation. Vaccination is the most effective preventive measures against SARS-CoV-2, but there are still questions about safety and immune response. Pregnant women were not included in study groups during phase III clinical trials. **Findings in Brief**: Vaccination during pregnancy is not associated with an increased risk of obstetric or neonatal complications; scientific communities recommend vaccination for pregnant women, those planning for pregnancy and those who are breastfeeding. Unfortunately, knowledge regarding COVID-19 vaccination and willingness to take vaccine during pregnancy is low. **Conclusions**: General practitioners and obstetricians have a large role in increasing public awareness of COVID-19 vaccination. No evidence of teratogenicity of the vaccine has been found.

Keywords: COVID-19 vaccination; COVID-19 vaccination and pregnancy; infection of COVID-19 during pregnancy; safety of COVID-19 vaccination

1. Introduction

It has been 2 years since COVID-19, caused by SARS-CoV-2, was declared a pandemic in March 2020 [1]. Despite the fact that the infection is asymptomatic in two-thirds of pregnant women, the symptomatic course of the disease is more severe compared to that in nonpregnant women. Pregnant women diagnosed with COVID-19 are characterized by more frequent hospitalization in intensive care units, need for mechanical ventilation and extracorporeal membrane oxygenation, and death rate, and the risk of severe course of the disease is the highest in the third trimester [2–5]. Fortunately, they usually require symptomatic treatment. Women who are infected with SARS-CoV-2 and present disease symptoms have less favorable obstetric outcomes than healthy women or infected women without infection symptoms. Symptomatic patients are at three times higher risk of preterm delivery (mainly iatrogenic), and intrauterine fetal demise. Moreover, the newborns of affected mothers more often need invasive ventilation and admission to the neonatal intensive care unit which is related to a higher percentage of preterm births (mainly iatrogenic- urgent cesarean section performed to save the mother) [2,5,6].

The most effective approach to prevent the severe course of COVID-19 seems to be preventive measures against SARS-CoV-2, which includes hand hygiene, avoidance of close contact with an infected person, and vaccination [7]. Analyses of the effectiveness of preventive vaccinations should take into account the type of vaccine, the number of doses administered, the variant/subvariant of the virus, the existence of comorbidities and medications taken, especially immunosuppressive ones, and the time elapsed since the administration of individual doses [8].

Currently, vaccination with mRNA vaccines is recommended for pregnant women, both by researchers evaluating the safety of these vaccines and by internationally recognized scientific societies that monitor the health status of particular social groups [9–14].

The position statement published by the Polish Society of Gynecologists and Obstetricians in April 2021 also indicated the advisability of vaccination for pregnant women. However, due to the lack of data on evidence-based medicine during the time, it was suggested that unless there is an emergency to administer the vaccine, vaccination should be postponed until the completion of organogenesis in the fetus [15]. In Poland, preparations based on mRNA technology were highly preferred, as a larger number of published observational studies have demonstrated safety of using this sort of vaccination among pregnant women [15].

2. COVID-19 Vaccines Recommendations

The combined positions of societies and expert groups on COVID-19 vaccination in pregnant women are presented in Table 1 (Ref. [2,11–16]).

Table 1. Recommendations and positions of societies and expert groups on COVID-19 vaccination in pregnant women, including the preferred formulation.

Society	Recommendations	Recommended vaccine/comment	Last updated	Status of recommendations
Royal College of Obstetricians And Gynecologists (RCOG) [2]	*Vaccination against COVID-19 is strongly recommended and should be offered to all pregnant women. Pregnant women are recognized as a priority group for vaccination.*	*Pregnant women should be offered the Pfizer-BioNTech or Moderna vaccines unless they have already had one dose of the Oxford-AstraZeneca vaccine, in which case they can complete the course with the same vaccine or with an mRNA vaccine (provided there are no contraindications to either).*	March 7, 2022	Current
The American College of Obstetricians and Gynecologists (ACOG) [11]	*The ACOG recommends to vaccinate all eligible persons aged 12 years and older, including pregnant and lactating individuals.*	*The mRNA COVID-19 vaccines are preferred over the J&J/Janssen COVID-19 vaccine for all vaccine-eligible individuals, including pregnant and lactating individuals, for primary series, primary additional doses (for immunocompromised persons), and booster vaccination.*	April 28, 2022	Current
Centers for Disease Control and Prevention (CDC) [12]	*COVID-19 vaccination is recommended for people who are pregnant, breastfeeding, trying to get pregnant now, or might become pregnant in the future.*	*No safety concerns were found in animal studies. Studies in animals receiving a Moderna, Pfizer-BioNTech, or Johnson & Johnson's Janssen (J&J/Janssen) COVID-19 vaccine before or during pregnancy found no safety concerns in pregnant animals or their babies.*	April 19, 2022	Current
Society for Maternal-Fetal Medicine (SMFM) [13,14]	*Pregnant, postpartum, and lactating people and those considering pregnancy should receive the COVID-19 vaccination [14].*	*A clinical preference for all individuals to receive an mRNA COVID-19 vaccine over the Janssen Biotech (J&J) COVID-19 vaccine [13].*	January 1, 2022 [13] March 3, 2022 [14]	Current
Polish Society of Gynecologists and Obstetricians (PTGiP) [15]	*COVID19 vaccines should be offered to pregnant and lactating women. [...] each vaccination should be consulted with the obstetrician in charge of the pregnancy. However, we suggest that, if there is no indication for urgent vaccination of the pregnant woman, the above procedure be performed after the period of organogenesis.*	*Due to the existence of far more observations and safety evaluations of vaccination of pregnant women with mRNA vaccines, they are the preferred ones to be used first in the fight against COVID-19 pandemic in pregnant women.*	April 26, 2021	Current
Strategic Advisory Group of Experts on Immunization (SAGE) of WHO [16]	*WHO has identified pregnant women as a priority-use group for COVID-19 vaccination, given the increased risk of severe outcomes. WHO recommends the use of all available type of vaccines in pregnant women when the benefits of vaccination to the pregnant woman outweigh the potential risks.*	*Developmental and reproductive toxicity (DART) studies have not shown harmful effects of the COVID-19 vaccines in pregnant animals and their foetuses. […] On the basis of previous experience with use of other inactivated vaccines used during pregnancy, the effectiveness of all type of vaccines in pregnant women is expected to be comparable to that observed in nonpregnant women of similar age. WHO does not recommend delaying pregnancy or terminating pregnancy because of vaccination. […]* *WHO recommends the same use of vaccine in breastfeeding and non-breastfeeding women.*	December 20, 2021– June 6, 2022	Current

3. Safety of Vaccines

Pregnant women were not included in study groups during phase III clinical trials. Similarly, immunocompromised individuals were also not included. Nevertheless, COVID-19 vaccines are still recommended for immunocompromised individuals because they are not live vaccines [17] and provide substantial protection against severe infection.

Bleicher *et al*. [18] performed a comparative study analyzing the effect of vaccination during pregnancy on complications such as genital tract bleeding, gestational diabetes, gestational hypertension, fetal growth disorders, miscarriage, and preterm delivery [18]. Their study included 326 patients, both vaccinated and unvaccinated. Both groups had a similar percentage of obstetric complications. However, vaccinated individuals were found to have a significantly lower risk of COVID-19 infection (1.5% vs 6.5%, $p = 0.024$, odds ratio 4.5, 95% confidence interval 1.19–17.6).

A study published in *The New England Journal of Medicine* analyzed obstetric outcomes and side effects in more than 35,000 pregnant women [10]. The analysis included women who were vaccinated at least 30 days before their last menstrual period and women in different stages of pregnancy. The data used for the study were obtained from the v-safe application for reporting adverse reactions to COVID-19 vaccines and the VAERS (Vaccine Adverse Event Reporting System). VAERS is a vaccine safety surveillance system established by the Centers for Disease Control and Prevention (CDC) and the US Food and Drug Administration (FDA) in 1990 [19]. Of the early adverse events that possibly occur after vaccination, pregnant women slightly more likely experienced injection-site pain than nonpregnant women, but less likely reported symptoms such as myalgia, chills, headache, or fever. To assess obstetric outcomes, randomly selected patients who were indicated on the app as currently pregnant were contacted. About 4000 women agreed to further analysis and were included in the study. Of these, 2.3% were vaccinated during the periconceptional period without knowing that they were pregnant, 28.6% were vaccinated in the first trimester of pregnancy, 43.3% in the second trimester, and 25.7% in the third trimester. The frequency of preterm deliveries and fetus growth disturbances in this studied population of pregnant women was similar to that of the general population (9.4% and 3.2%, respectively). Spontaneous miscarriage was the most common complication, but its frequency was not higher than that in the general population (12.6%). Congenital malformations were found in 2.2% of term pregnancies; however, the cases did include any woman who received the vaccine before pregnancy or in the first trimester.

The published studies on side effects reported by pregnant women have not shown complications other than those observed in the general population [20]. Injection-site pain and fatigue after vaccination were the most common complications reported by pregnant women [21]. Among almost 8000 women included in the study, these complaints were reported by 91.4% and 31.3%, respectively. One study described a case of immune thrombocytopenia that occurred after 13 days of vaccination (Moderna mRNA-1273 vaccine) in the first trimester of pregnancy [22]. However, after treatment with corticosteroids, the patient was discharged from the hospital in good condition, with no further complications. Another similar case was described in Qatar [23]. Pregnant women in the 8th week of pregnancy had a relapse of immune thrombocytopenia purpura (ITP) after the introduction of the first dose of Pfizer SARS-CoV2 vaccine, which worsened further after the second dose. Fortunately, without serious complications. The authors suggest, that women with history of ITP should have delayed the second dose of vaccine in pregnancy. Mendes-de-Almeida *et al*. [23] present more fatal case. A pregnant woman in the 23th week of pregnancy developed intracerebral hemorrhage localizated in the left temporal lobe associated with vaccine-induced thrombotic thrombocytopenia (VITT) 12 days after the ChAdOx1 nCOVID-19 vaccination [24]. She underwent urgent neurosurgery for hematoma drainage and decompressive craniectomy. Unfortunately, after these procedures, obstetric ultrasound detected fetal death. The patient died 17 days after vaccination with refractory intracranial hypertension. To the best of our knowledge, abovementioned study was only one which has shown an association between vaccination during pregnancy and increased risk of maternal or neonatal complications. Fu *et al*. [25] presented a systematic review of 23 studies where they shown safety, high efficacy and no significant vaccine-related adverse events. A large multicenter study analyzed the potential impact of the vaccine on the risk of preterm delivery and fetal growth abnormalities [26]. The study included over 36,000 unvaccinated and only 10,000 vaccinated pregnant women. The subjects received different types of vaccines. There was no evidence showing that the vaccinated group had a higher rate of preterm births or babies with too low a weight for gestational age (i.e., SGA). In another study, Kharbandy *et al*. [27] assessed whether COVID-19 vaccination was associated with an increased risk of miscarriage. This study included over 100,000 pregnant women who received both mRNA and vector vaccines. In the studied population, only 13,000 had a miscarriage. However, no correlation between pregnancy loss and earlier vaccination (in the 28 days preceding miscarriage) was found. An important piece of evidence supporting that vaccines do not affect the fetus is a paper demonstrating that IgM antibodies are not detected in cord blood [28]. This confirms that vaccination has no effect on the fetal immune system. Both this study and another one which showed that Spike protein was not found in the placenta and cord blood indicate that the vaccine does not penetrate the placental barrier [29]. The summary of

Table 2. The safety of COVID-19 vaccination in pregnant women.

Author	N (numer of patients)	Country	Study design	Outcome	Vaccination type	Population type
Bleicher *et al*. [18]	326 patients	Israel, Canada	Prospective cohort observational study: compare the difference between groups (vaginal bleeding, pregnancy loss, hypertension, gestational diabetes, and preterm birth)	The rate of composite pregnancy complications was similar between vaccinated and non-vaccinated group (15.8% vs 20.1%, $p = 0.37$), respectively. The risk for COVID-19 infection was significantly lower in the vaccinated group (1.5% vs 6.5%, $p = 0.024$, Odds Ratio: 4.5, 95% confidence interval 1.19–17.6)	Pfizer-BioNTech, BNT162b2	Vaccinated and non-vaccinated pregnant women
Shimabukuro *et al*. [10]	35,000 (4000 pregnant)	USA	Analyzed obstetric outcomes and side effects; the data used for the study were obtained from the v-safe application for reporting adverse reactions to COVID-19 vaccines and the VAERS	Pregnant women slightly more likely experienced injection-site pain, but less likely reported symptoms such as myalgia, chills, headache, or fever. The frequency of preterm deliveries and fetus growth disturbances Spontaneous misscariage was the most common complication, but its frequency was not higher than that in the general population	mRNA COVID-19 vaccines	Vaccinated women, including those who are pregnant and vaccinated at last 30 days before the last period and during pregnancy
Kachikis *et al*. [21]	8000	USA	A cohort study investigates short-term reactions associated with COVID-19 vaccines among pregnant and lactating individuals vs individuals neither pregnant nor lactating but planning pregnancy	Injection-site pain and fatigue after vaccination were the most common complications reported by pregnant women these complaints were reported by 91.4% and 31.3%, respectively	Pfizer-BioNTech BNT162b2 vaccine or Moderna mRNA-1273 vaccine	Pregnant and non-pregnant vaccinated women
Fu *et al*. [25]	23 studies	Canada	A systematic search of MEDLINE, Embase, PubMed, medRxiv, and bioRxiv To summarize the safety, immunogenicity, and effectiveness of COVID-19 vaccines in pregnancy and lactation	COVID-19 vaccination in pregnant and lactating individuals is immunogenic, does not cause significant vaccine-related adverse events or obstetrical and neonatal outcomes	Pfizer-BioNTech BNT162b2, Moderna mRNA-1273, Johnson & Johnson and AstraZeneca vaccine	Vaccinated pregnant and lactating individuals
Lipkind *et al*. [26]	46,079	USA	Multicenter retrospective cohort study to evaluate risk for preterm and SGA at birth among vaccinated and unvaccinated pregnant women, accounting for time-dependent vaccine exposures	Vaccination during pregnancy was not associated with preterm birth (adjusted hazard ratio [aHR] = 0.91; 95% CI, 0.82–1.01) and not associated with SGA at birth (aHR = 0.95; 95% CI, 0.87–1.03)	mRNA COVID-19 vaccine	Pregnant vaccinated and non-vaccinated women

Table 2. Continued.

Author	N (numer of patients)	Country	Study design	Outcome	Vaccination type	Population type
Kharbanda *et al*. [27]	105,446	USA	Data from 8 health systems over seven 4-week surveillance periods from December 15, 2020, through June 28, 2021, were included	Spontaneous abortions did not have an increased odds of exposure to a COVID-19 vaccination in the prior 28 days compared with ongoing pregnancies (adjusted odds ratio, 1.02; 95% CI, 0.96–1.08)	BNT162b2 (Pfizer-BioNTech), mRNA-1273 (Moderna) vaccines and Ad26.COV.2.S (Janssen)	Pregnant vaccinated and non-vaccinated women
Beharier *et al*. [28]	213	Israel	Maternal and fetal blood samples were collected from parturients prior to delivery and from the umbilical cord following delivery, respectively. COVID sera IgG and IgM titers were measured	Vaccine elicits strong maternal humoral IgG response (anti-S and RBD) that crosses the placenta barrier and approaches maternal titers in the fetus within 15 days following the first dose. IgG transfer ratio at birth was significantly lower for third-trimester as compared with second trimester infection. Fetal IgM response was detected in 5 neonates, only in the infected group	BNT162b2 mRNA vaccine	Pregnant: vaccinated (n = 86); PCR-confirmed SARS-CoV-2 infected during pregnancy (n = 65), and unvaccinated noninfected controls (n = 62)
Prahl *et al*. [29]	20	USA	The transplacental transfer of mRNA vaccine products and functional anti-SARS-CoV-2 antibodies during pregnancy and early infancy	Products of mRNA vaccines are not transferred to the fetus during pregnancy, however timing of vaccination during pregnancy is critical to ensure transplacental transfer of protective antibodies during early infancy	mRNA-1273 (Moderna) and BNT162b2 (Pfizer)	Vaccinated pregnant

VAERS, Vaccine Adverse Event Reporting System.

Table 3. Immune response and efficacy of COVID-19 vaccines in pregnant women.

Author	N (numer of patients)	Country	Study design	Outcome	Vaccination type	Population type
Collier *et al*. [30]	131	USA	A prospective cohort study to evaluate the immunogenicity of COVID-19 messenger RNA (mRNA) vaccines in pregnant and lactating women	Binding, neutralizing, and functional nonneutralizing antibody responses as well as CD4 and CD8 T-cell responses were present in pregnant, lactating, and nonpregnant women following vaccination. Binding and neutralizing antibodies were also observed in infant cord blood and breast milk. Binding and neutralizing antibody titers against the SARS-CoV-2 B.1.1.7 and B.1.351 variants of concern were reduced, but T-cell responses were preserved against viral variants	mRNA-1273 (Moderna) or BNT162b2 (Pfizer-BioNTech)	Pregnant, lactating, and neither pregnant nor lactating women who were vaccinated or had confirmed SARS-CoV-2 infection
Gray *et al*. [31]	168	USA	To evaluate the immunogenicity and reactogenicity of coronavirus disease messenger RNA vaccination in pregnant and lactating women compared with: nonpregnant controls and natural coronavirus disease infection in pregnancy	Vaccine-induced antibody titers were equivalent in pregnant and lactating compared with nonpregnant women. All titers were significantly higher than those induced by severe acute respiratory syndrome coronavirus 2 infection during pregnancy ($p < 0.0001$). Vaccine-generated antibodies were present in all umbilical cord blood and breast-milk samples	BNT162b2 Pfizer/BioNTech or mRNA-1273 Moderna	Vaccinated pregnant and lactating women compared with nonpregnant controls pregnant women who had confirmed SARS-CoV-2 infection during pregnancy
Prabhu *et al*. [32]	122	USA	Women vaccinated during pregnancy; The relationship between maternal and cord blood IgG levels and between IgG placental transfer (neonatal/maternal) ratio and time was studied	The earliest detection of antibodies in women occurred 5 days post–vaccine dose 1, and the earliest detection of antibodies in cord blood occurred 16 days post–vaccine dose 1. Maternal IgG levels were significantly higher, week by week, starting 2 weeks after the first vaccine dose (p = 0.005 and 0.019, respectively), as well as between the first and second weeks after the second vaccine dose (p = 2e-07). Maternal IgG levels were linearly associated with cord blood IgG levels (R = 0.89, $p < 2.2e-16$). The placental transfer ratio correlated with the number of weeks elapsed since maternal vaccine dose 2 (R = 0.8, p = 2.6e-15)	BNT162b2 Pfizer/BioNTech or mRNA-1273 Moderna	Vaccinated pregnant women, All tested negative for SARS-CoV-2 infection
Halasa *et al*. [33]	379	USA	Case-control study at 20 pediatric hospitals in 17 states, to assess effectiveness of maternal completion of a 2-dose primary mRNA COVID-19 vaccination series during pregnancy against COVID-19 hospitalization in infants	Among 379 hospitalized infants aged <6 months (176 with COVID-19 [case-infants] and 203 without COVID-19 [control-infants]), the median age was 2 months, 21% had at least one underlying medical condition, and 22% of case- and control-infants were born premature (<37 weeks gestation). Effectiveness of maternal vaccination during pregnancy against COVID-19 hospitalization in infants aged <6 months was 61% (95% CI, 31%–78%)	mRNA COVID-19 vaccine	Infants of vaccinated during pregnancy and non-vaccinated women

Table 4. COVID-19 vaccination acceptance and awareness in pregnant women.

Author	N (numer of patients)	Country	Study design	% of acceptance	Risk factors of nonacceptance vaccination	Common concerns
Levy *et al*. [34]	662	USA	Survey study given to pregnant women; There were 31 questions regarding sociodemographics, vaccination history, previous COVID-19 symptoms and diagnoses, attitudes toward vaccines in pregnancy, and beliefs about the COVID19 vaccination specifically	381 of 653 women (58.3%; 95% CI, 54.5−62.2) would accept the COVID-19 vaccine while pregnant. Trust in the information received about vaccinations was the strongest predictor of COVID-19 vaccination acceptance	Younger age, Black or African American race, Hispanic ethnicity, having less than a bachelor's degree, and declining the seasonal influenza vaccine	Primary concern was risk to the fetus or neonate (45.8%), followed by vaccine side effects (17.7%)
Battarbee *et al*. [35]	915	USA	Cross-sectional survey among pregnant women enrolled in a prospective COVID-19 cohort study	Only 41% reported they would get a vaccine; Receipt of influenza vaccine during the previous season was associated with higher odds of vaccine acceptability (aOR 2.1, 95% CI, 1.5–3.0)	Non-Hispanic Black and Hispanic women had lower odds of accepting a vaccine compared with non-Hispanic White women	The most frequently cited concern was vaccine safety for their pregnancy (82%)
Huddleston *et al*. [36]	2506	USA	Survey study given to pregnant women	57.4% getting vaccinated during pregnancy; among the unvaccinated, only 35.7% reported vaccine acceptance The predictors of higher odds of vaccination were increasing education and income, living in a metropolitan area, and worry over COVID-19, being counseled about vaccination by a provider was a strong predictor of getting vaccinated compared with receiving no counseling	The predictors of lower odds of vaccination were being of the Black race compared with White race and being counseled by a provider not to vaccinate compared with no counseling	No information
Townsel *et al*. [37]	4379: pregnant, breastfeeding, trying to conceive and other women of a reproductive age	USA	Cross-sectional, opt-in online survey of the entire employee workforce at an academic medical center in the U.S. Primary outcome was receipt of or intent to receive the COVID-19 vaccine, classified as: received, delayed or declined	Compared to other women of reproductive age, pregnant participants were six times more likely to delay COVID-19 vaccination and twice as likely to decline, those who were trying to conceive had nearly three times the odds of delaying and declining the vaccine compared to the referent. Very few physicians delayed or declined the vaccine	Allied health professionals were slightly more likely to reject the vaccine compared to nurses. Non-Hispanic Black participants had a fourfold increased chance of both declining and delaying, whereas Non-Hispanic Asian participants were significantly less likely to decline and delay the vaccine compared to non-Hispanic White participants	33.2% ($n = 1456$) of all participants and 44.5% ($n = 113$) of pregnant participants expressed at least one concern. The highest rates of concern were observed for safety and effectiveness of the vaccine, which were highest among pregnant and trying to conceive participants

Table 4. Continued.

Author	N (numer of patients)	Country	Study design	% of acceptance	Risk factors of nonacceptance vaccination	Common concerns
Razzaghi *et al*. [38]	135,968	USA	Data from Vaccine Safety Datalink (VSD), were analyzed to assess receipt of COVID-19 vaccine during pregnancy	22,197 (16.3%) of whom had received ≥1 dose of a vaccine during pregnancy. Among these 135,968 women, 7154 (5.3%) had initiated and 15,043 (11.1%) had completed vaccination during pregnancy	Receipt of ≥1 dose of COVID-19 vaccine during pregnancy was lowest among women aged 18–24 years (5.5%), Hispanic (11.9%) and non-Hispanic Black (Black) women (6.0%)	No information
Kuciel *et al*. [39]	118	Poland	An anonymous online survey was distributed to assess the level of acceptance of COVID-19 vaccination among pregnant and lactating women for themselves and their children in Poland	The trust of pregnant and breastfeeding women and women who have offspring in government, in healthcare professionals, in scientific authorities, and sound scientific data is strongly associated with vaccine acceptance and may influence an individual's decision to perceive recommended actions as beneficial to the society as a whole. Pregnant women are 4 times more likely to trust government health information than non-pregnant women (OR = 4.150; $p = 0.009$)	Breastfeeding women declared that they vaccinate their children as opposed to non-breastfeeding women ($p = 0.001$) Therefore, they were determined to get vaccinated themselves ($p = 0.006$) Women aged 35–40 believed less that vaccinations were safe and effective in opposite to 30–35 Women with lower education think less that vaccinating children is safe and effective in preventing infectious diseases compared to women with higher education ($p = 0.055$)	No information

abovementioned reviews and studies are presented in the Table 2 (Ref. [10,18,21,25–29]).

4. Immune Response and Efficacy

Many studies have analyzed the immune response after vaccination in pregnant women. A majority of these showed that the response in these women was the same as that in nonpregnant women. One study confirmed that the immune response, as measured by the increase in both IgG antibodies (humoral immunity) and T lymphocytes (cellular response), is identical in nonpregnant, pregnant, and breastfeeding women [30]. Similar findings were reported by Gray *et al*. [31], who indicated that the immunogenicity of the vaccine was comparable in pregnant, nonpregnant, and breastfeeding groups. The authors also detected IgG antibodies in cord blood and breast milk. An analysis performed at a large academic center in New York revealed that antibody production starts 5 days of vaccination in pregnant women, and the antibodies are found in the cord blood after 16 days of vaccination [32]. This suggests that vaccination up to 2 weeks before delivery provides passive protection to the newborn. Halas *et al*. [33] evaluated the need for hospitalization of children under 6 months of age who were diagnosed with COVID-19. The authors found that children of mothers who were vaccinated before 20 weeks of gestation had a 32% lower risk of hospital treatment than children born to women who were not vaccinated. In contrast, vaccination after the 20th week minimized the risk of hospitalization by as much as 80%. These differences are probably due to the decrease in antibody concentrations with increasing time since vaccination and seem to suggest that women who were vaccinated in early pregnancy should receive a booster dose. However, it is important to remember that vaccination is primarily intended to protect the woman from the severity of the disease and it is not advisable to postpone it in order to maximize the possible benefits to the newborn. Table 3 (Ref. [30–33]) summarized abovementioned studies.

5. Vaccination Acceptance and Awareness among Pregnant Women

Studies analyzing the willingness of pregnant women to be vaccinated have not shown promising results. A majority of them indicate a low acceptance of vaccination, ranging between 30% and 58% [34–36]. In a review by Battarbee *et al*. [35], 41% of pregnant women expressed a willingness to get vaccinated. The main reason for refusal stated by participants was concern about the safety of the vaccine (82% of respondents). Women who had previously received the influenza vaccine were significantly more willing to be vaccinated for COVID-19. However, it seems comforting that women who received information on the vaccine from their doctors were more likely to agree to vaccination. The US study attributed the low acceptance of vaccination among pregnant women to a lack of confidence in the efficacy of the vaccine and fear of side effects, especially on the fetus [34,37]. Among different populations, vaccination rates were lower among African-American and Latino pregnant women. The rates were also shown to be the lowest in the youngest age group [38]. It was found that only 5.5% of women aged 18–24 years had received the vaccine. According to a Polish study, the faith of pregnant and breastfeeding women in the vaccine is strongly related to the opinions of the government, medical authorities, and health care workers [39]. Thus, the dissemination of accurate information on vaccination by medical personnel and social campaigns is very important. This can significantly increase the level of trust and awareness regarding the effectiveness and safety of the vaccine and consequently increase the percentage of vaccinated pregnant women. The abovementioned studies and reviews are summarized in the Table 4 (Ref. [34–39]).

6. Summary

This study indicates that pregnant women must be vaccinated to protect against COVID-19. This population is at a higher risk of more severe disease and is more susceptible to infection compared to the general population. Vaccination during pregnancy is not associated with an increased risk of obstetric or neonatal complications, and no evidence of teratogenicity of the vaccine has been found. Scientific communities around the world, including the American College of Obstetricians and Gynecologists (ACOG), the Royal College of Obstetricians and Gynecologists (RCOG), the Society for Maternal-Fetal Medicine (SMFM), as well as the World Health Organization (WHO) and CDC, recommend vaccination for pregnant women as well as those planning for pregnancy and those who are breastfeeding. Knowledge regarding COVID-19 vaccination and willingness to take vaccine during pregnancy is low; information campaigns and, above all, general practitioners and obstetricians have a large role in increasing public awareness of COVID-19 vaccination. Every pregnant woman should be informed of the possibility, and indeed the necessity, of vaccination, and refusal should be recorded in the medical file. Vaccine for COVID-19 can also be given with other vaccinations; however, an interval of 14 days between other vaccines is recommended, with the exception of the seasonal influenza virus vaccine which can be given concurrently.

Abbreviations

ACOG, The American College of Obstetricians and Gynecologists; CDC, Centers for Disease Control and Prevention; FDA, Food and Drug Administration; ITP, immune thrombocytopenia purpura; RCOG, Royal College of Obstetricians And Gynecologists; SGA, small-for-gestational-age; SMFM, Society for Maternal-Fetal Medicine; VAERS, Vaccine Adverse Event Reporting System; WHO, World Health Organization; VITT, vaccine-induced thrombotic thrombocytopenia.

Author Contributions

NIK and KCW designed the research study. KW analyzed the data, searched publications in PubMed. MW provided help and supervisored the study. NIK, KCW wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest. MW, KW, KCW is serving as one of the Guest editors of this journal. We declare that MW, KW, KCW had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to SM.

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