A Literature Review on the Vaccination of COVID-19 in Pregnant and Breastfeeding Women: Effectiveness and Safety

by Fitriani Nur Damayanti

A Literature Review on the Vaccination of COVID-19 in Pregnant and Breastfeeding Women: Effectiveness and Safety

Fitriani Nur Damayanti[1]*, Alfina Aprilia Riafisari[1], Ayesha Hendriana Ngestiningrum[2]

[1]*Midwifery Study Program, Faculty of Nursing and Health, Universitas Muhammadiyah Semarang*, Semarang, Indonesia;
[2]*Department of Midwifery, Politeknik Kesehatan Kemenkes Surabaya, Surabaya, Indonesia*

Abstract

BACKGROUND: Pregnant women and breastfeeding women who are infected with the Coronavirus Disease 2019 (COVID-19) virus have a high risk, but pregnant women and women who breastfeed are not included in the initial vaccine trial for COVID-19. There are currently no clinical data on the use of the COVID-19 mRNA vaccine in pregnant and lactating women.

AIM: This study aims to get an overview of vaccinations for pregnant and lactating women.

METHODS: The method used in this paper is the Literature Review study. The data-based used in the source search were Google Scholar, PubMed, JAMA, and AJOG which aimed to collect themes regarding the discussion of COVID-19 Vaccination in Pregnant and Breastfeeding Women. The COVID-19 mRNA vaccine creates immunity in pregnant and lactating women.

RESULTS: IgG immunoglobulin after vaccination in pregnant, lactating, and nonpregnant women increased significantly and was stronger than pregnant women who were previously infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

CONCLUSION: Pregnant and lactating women have a stronger immune response after being vaccinated than pregnant women who were previously infected with SARS-CoV-2. Immune transfer to neonates occurs through the placenta and breast milk, antibodies are formed after vaccination in the third trimester of pregnancy. Immunogenicity and reactogenicity reactions after the vaccine are the same as for nonpregnant women. Therefore, education is needed by health workers to patients about the risks and benefits of vaccines for pregnant and lactating women.

Introduction

Coronavirus Disease 2019 (COVID-19) is a new infection caused by the novel coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first detected in Wuhan, China at the end of December 2019. Since then, the disease has spread rapidly worldwide and categorized as a pandemic by the World Health Organization on 11 March 2020. As of 7 April 2020, more than 1.3 million cases of SARS-CoV-2 have been confirmed worldwide, with nearly 80,000 cases related to death. Given the inability of governments around the world to contain infections and a lack of effective therapies or vaccines, federal entities, and pharmaceutical companies are rushing to develop life-saving interventions. Best practices are not available for obstetric care, and pregnant women may once again be excluded from effective and selective therapies from participating in clinical trials [1]. More than 73,600 infections and 80 maternal deaths have occurred in pregnant women in the America States alone as of March 1, 2021. SARS-CoV-2 infection was more severe in 126 pregnant women compared to nonpregnant women, with an increased risk of hospital admission, ICU admission, and death. Despite the higher risk, pregnant and breastfeeding women are not included in the initial vaccine trial for COVID-19, although the first vaccine trials began in pregnant women in February 2021 (Pfizer/BioNTech, ClinicalTrials.gov 130 Identifier: NCT04754594) [2].

Although the American College of Obstetricians and Gynaecologists and the Society for Maternal-Foetal Medicine are encouraging the Food and Drug Administration (FDA) to include pregnant women in authorizing the emergency use authorization (EUA) of the COVID-19 vaccine because of the increased risk of disease severity in the population of this, evidence on the immunogenicity of vaccines to guide patient decision-making and counseling providers is lacking [3], [4]. Approved new initial emergency COVID-19 vaccines, both use mRNA to deliver the SARS-CoV-2 Spike to boost the immune system [5], [6].

Currently, there are no clinical data on the use of the COVID-19 mRNA vaccine during breastfeeding, the FDA includes pregnant and nursing women in authorizing EUA of the COVID-19 vaccine because of the risk of increased disease severity. Many breastfeeding mothers are included in the priority category for vaccination, such as health care. The Academy of Breastfeeding Medicine

does not recommend stopping breastfeeding for mothers who are vaccinated against COVID-19. Nursing mothers should discuss the risks and benefits of vaccination with their health care providers about the risks of contracting COVID-19 and developing severe disease. Health care providers should use shared decision-making in discussing the benefits of vaccines to prevent COVID-19 and its complications, the risks of breastfeeding mothers and children, and the biological plausibility of the risks and benefits of vaccines for breastfed children [7].

Methods

The method used in this paper is the Literature Review which aims to explore COVID-19 Vaccination in Pregnant and Breastfeeding Women. The review process begins by identifying journal articles that are relevant to the research topic. The databases used in the source search are Google Scholar, PubMed, JAMA, and AJOG. The search for articles was carried out by collecting themes around the discussion of the COVID-19 vaccine in pregnant and lactating women. The criteria for inclusion of a search for library sources is the year the article was published which was used from 2017 to 2021 in English and the full article. The keywords for the search were COVID-19 Vaccines and Pregnancy, COVID-19 Vaccination in Lactation, risks, benefits, and recommendations. The criteria for the articles included in the review are as follows cohort study, case study, review, and observational, Figure 1).
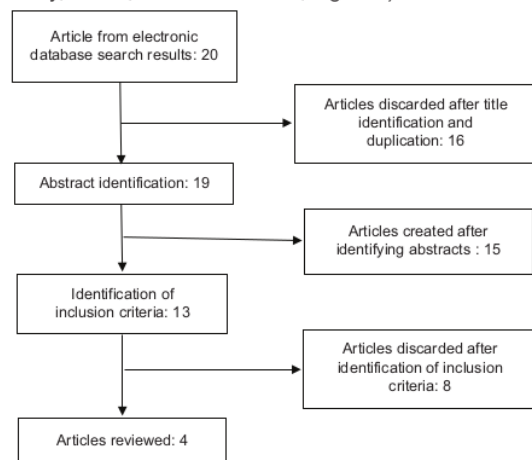

Figure 1: Flow chart of the included articles

Results

A literature search through an electronic database resulted in 10 articles with the potential to be reviewed. After identifying the abstract from article 10, article 7. The identification was then carried out in more detail to determine which articles were relevant and met the inclusion criteria in this review literature. From this identification, it is obtained article 5 which will be reviewed in this study. Identification criteria for articles included in the review are as follows cohort study, case study, review, and observational.

The four articles selected for review in this study were the results of research from the United States, namely, (Gray *et al.*, 2021), (Rasmussen *et al.*, 2020), (Gill and Jones, 2021). Articles from Texas, namely (Stafford *et al.*, 2021). The four articles constitute research: cohort study, case study, review, current commentary. A summary of the articles reviewed in this study can be seen in Table 1.

Table 1: Summary of articles reviewed

Author	Country	Research Title	Research methods	Result
Gray *et al.*, (2021)	USA	COVID-19 vaccine response in pregnant and lactating women: a cohort study	A cohort study	This study found that the COVID-19 mRNA vaccine produced strong immunity in pregnant women and breastfeeding women where the transfer of immunity to the neonate occurs via the placenta and breast milk, with immunogenicity and reactogenicity similar to that of nonpregnant women.
Rasmussen *et al.*, (2020)	USA	COVID-19 vaccines and pregnancy what obstetricians need to know	Current commentary	The mRNA vaccine exhibits reactogenicity in patients, with fever, fatigue, headache, chills, and muscle and joint pain. Fever (38°C or higher) occurred in 3.7% of participants after dose 1 and 15.8% after dose 2 of the mRNA vaccine. Neonates born to pregnant people with fever in the early trimester of pregnancy have been shown to have an increased risk for certain types of birth defects and the absolute risk is small. The risk associated with fever appears to be lowered by antipyretic drugs.
Gill and Jones, (2021)	USA	SARS-CoV-2 antibodies in neonatal cord blood after vaccination in pregnancy	A case report	The research result of this case is the transplacental part antibodies to SARS-CoV-2 are shown after vaccination in the third trimester of pregnancy.
Stafford *et al.*, (2021)	Texas, USA	The coronavirus disease 2019 vaccine in pregnancy: risks, benefits, and recommendations	Review	Overall, benefits a promising vaccine. However, the risks and benefits of the COVID-19 vaccine for pregnant women, foetuses, and new-borns should be discussed transparently with patients, the risk of neonatal transmission and overall infection-related morbidity and mortality in patients presenting asymptomatic is greatly reduced but has not been fully determined

COVID-19: Coronavirus disease 2019, SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2.

Ideally, after vaccination, antibodies have been formed which will provide protection for pregnant women and neonates. Studies evaluating neonatal immune responses to vaccines have demonstrated neonatal protection from transfer of antibodies through the placenta for a number of vaccines, including tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis; influenza virus; and respiratory viruses (Stafford *et al.*, 2021). This may also apply to the SARS-CoV-2 vaccine.

Although it is possible that neonatal antibodies originate from maternal infections that were not detected with SARS-CoV-2, this is unlikely given the frequency and high sensitivity of polymerase chain reaction testing [8].

The transplacental portion of the SARS-CoV-2 antibody after infection in pregnancy has been reported. A recent study evaluating the vertical transmission of SARS-CoV-2 as well as the transplacental antibody pathway after infection in pregnancy showed a low rate of vertical transmission of the virus as well as a low rate of transplacental antibody transfer. That this low rate of antibody transfer may expose the neonate to infection. After vaccination, pregnant women have a stronger immune system than pregnant women infected with SARS-CoV-2. From a study by Gill and Jones 2021, showing that trials comparing neonatal immune response in vaccinated pregnant women and pregnant women with SARS-CoV-2 infection, antibodies to SARS-CoV-2 are formed after vaccination in the third trimester of pregnancy [8].

IgG immunoglobulin after vaccination in pregnant, lactating, and non-pregnant women increased significantly and was stronger than pregnant women who were previously infected with SARS-CoV-2. This increase results in an increase in IgG levels in the blood, which means the transfer of IgG to the neonate via the placenta and breast milk. Following the EUA for the COVID-19 mRNA vaccine, safety information has been tracked by the CDC using the V-safe smartphone app. The V-safe data showed no significant difference in post-vaccination reactions in pregnant versus nonpregnant women aged 16–54 years. While the side effect profile of pregnant women who receive the COVID-19 vaccine does not differ significantly from that of nonpregnant women, the relatively high incidence of fever (up to 32% after the second dose) raises theoretical concerns for pregnant vaccine recipients, although the level of risk is controversial [2].

Discussion

The mRNA vaccine in pregnant women and nursing mothers has good benefits. However, the risks and benefits of the COVID-19 vaccine for pregnant women, fetuses, and newborns should be discussed transparently with patients, the risk of neonatal transmission, and overall infection-related morbidity and mortality in patients presenting asymptomatic is greatly reduced but not fully proven. Breastfeeding mothers can be given the COVID-19 vaccination if the body temperature is below 37.5°C; no contact with sufferers or suspected COVID-19 within the last 14 days; and no symptoms of fever, cough, runny nose, and shortness of breath for the last 7 days [3].

The COVID-19 mRNA vaccine shows side effects in patients such as fever, fatigue, headaches, chills, muscle, and joint pain. Patients with fever (38°C or higher) occurred in 3.7% of patients after dose 1 and 15.8% after dose 2 of the mRNA vaccine. Babies born to pregnant women who have a fever in the early trimester of pregnancy are at risk for birth defects. The risks associated with fever can be reduced with antipyretic drugs [9].

In Indonesia, the Corona vaccine produced by Sinovac Biotech is the first inactivated COVID-19 vaccine that has received EUA after undergoing phase 3 clinical trials. Inactivated vaccines are made from microorganisms that have been killed, so they are expected to be safer than live attenuated vaccines. In the general population, the side effects of inactivated COVID-19 vaccine based on studies are fever, myalgia, headache, nausea, fatigue, and redness or pain at the injection site. Therefore, in general, the inactivated COVID-19 vaccine actually has a good safety profile. However, data for pregnant women is not yet available. Based on the Circular Letter of the Ministry of Health of the Republic of Indonesia number HK.02.02/I/368/2021, breastfeeding mothers can be given the COVID-19 vaccine but pregnant women have not been advised to receive this vaccine. However, the administration of other inactivated viral vaccines such as influenza has been advocated and used safely in pregnant women for decades [9], [10], [11].

The mRNA-type COVID-19 vaccine, that is, thought to be safer for pregnant and lactating women. This is because mRNA vaccines do not contain viruses but only contain genetic components designed to resemble the genetic material of viruses. After the mRNA vaccine has successfully formed antibodies, the genetic component of the mRNA will be destroyed. The mRNA vaccine is not expected to cross the placenta although the antibodies formed can cross the placenta and provide the fetus with immunity. In addition, during lactation, vaccine mRNA lipids are thought not to reach breast tissue although vaccine-stimulated antibodies and T-cells can reach breast milk [8], [10].

Conclusion

This type of COVID-19 mRNA vaccine is considered quite safe for pregnant and lactating women. Pregnant and lactating women have a stronger immune response after being vaccinated than pregnant women who were previously infected with SARS-CoV-2. The transfer of immunity to the neonate occurs through the placenta and breast milk, antibodies are formed after vaccination in the third trimester of pregnancy. Immunogenicity and reactogenicity reactions after vaccine are the same as in nonpregnant women. Meanwhile, the mRNA vaccine is a newer technology, so studies on its long-term safety profile in pregnant

women are not yet available. Therefore, further research is needed on the safety of this vaccine and education by health workers to patients about the risks and benefits of the vaccine for pregnant and lactating women.

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