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Vaccination of pregnant women against COVID-19 under martial law: a narrative review

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Abstract

Background: Global vaccination programs against the coronavirus illness of 2019 (COVID-19) have been established as the primary measure to minimise and control the effects of the COVID-19 pandemic. During pregnancy, it is assumed that the expectant mother and her fetus are both in danger from the possibility of a viral infection.

Aim: to evaluate the safety and effectiveness of vaccination against COVID-19 for pregnant women and determine the impact of vaccination on pregnancy outcomes.

Methods: In this review, English studies from common databases such as Pubmed/MEDLINE, Web of Science, Scopus, and the Cochrane Library with the keywords "Vaccination," "pregnancy," and "pregnant women," combined with keywords, involving "COVID-19," were involved. The end date for this review is March 2022.

Scientific novelty: The main objective of this paper is to evaluate the effect of vaccination of pregnant women against COVID-19. Even though many studies assessed the efficacy of vaccination against COVID-19, most failed to determine the safety and effectiveness of COVID-19 vaccination for immunocompromised patients, especially pregnant women. Additionally, the impact of COVID-19 vaccination on neonatal outcomes was evaluated.

The practical significance of the obtained result: Concerns have also been raised about potential risks associated with vaccination during pregnancy or breastfeeding. Given these uncertainties, it is important for healthcare providers to carefully consider the risks and benefits of COVID-19 vaccination for pregnant women and their babies. Further research is needed to better understand the effects of vaccination on perinatal outcomes and to inform clinical decision-making around vaccine use in this population.

Conclusion: The COVID-19 vaccination is a safe and effective way to protect pregnant women from the virus. The benefits of getting vaccinated outweigh the risks, as pregnant women are at an increased risk of severe illness and complications from COVID-19. The Centers for Disease Control and Prevention (CDC) recommends that pregnant women get vaccinated, and many healthcare providers also recommend it. However, it is important for pregnant women to discuss their individual situation with their healthcare provider before making a decision about vaccination. Overall, getting vaccinated can help to protect both the mother and her unborn child from COVID-19.

Keywords: Vaccination, coronavirus, COVID-19, pregnant women, Neonatal outcomes.

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Introduction

Several COVID-19 vaccinations have been approved for emergency use to prevent severe COVID-19 disease caused by the SARS-CoV-2 virus. They have played an essential role in improving clinical outcomes and reducing the severity of the pandemic. Moreover, a unique immunisation strategy based on mRNA vaccines was developed during the pandemic [1,2]. The severity of the pandemic is globally recognised, and preventative measures such as good hygiene, masking, social distancing, and regular monitoring of health conditions are in place. As the pandemic spread worldwide, scientists worked on numerous vaccinations in order to help boost herd immunity and reduce the danger of viral infection [3,4].

Pregnancy is usually associated with a high incidence of various viral infections [5,6]. Immune changes during pregnancy may reduce the effectiveness of cell-mediated immune responses to infection [6]. Pregnant or recently pregnant women have an increased chance of suffering from a severe form of Covid-19, stillbirth, and preterm birth, according to the Centers for Disease Control and Prevention (CDC) [7,8]. Pregnancy is a risk factor for acquiring a severe SARS Cov-2 infection, according to the Society for Maternal and Fetal Medicine (SMFM) and the American College of Obstetricians and Gynecologists (ACOG) [9]. Pregnant women should be notified of the increased severity of covid-19, which includes invasive ventilation and intensive care unit admission when compared to non-pregnant women, and encouraged to take preventative measures to lower their risk of infection, such as getting the covid-19 vaccine to diminish their risk of developing a serious illness [10].

Research Problem

Most people have some fears about the vaccination against COVID-19 and have difficulties in finding good scientific evidence that help them to determine whether COVID-19 vaccination is safe and effective. These fears are doubled for immunocompromised individuals such as HIV patients and pregnant women. The lack of knowledge about the effects of immunisations during pregnancy and the safety of fetuses are two of the most common reasons pregnant women do not receive immunisation.

Research Focus

The safety and effectiveness of the approved COVID-19 vaccinations during pregnancy and their effects on the mother and fetus' immune systems were the main topics of this review.

Research Questions

1. What are the types of COVID-19 vaccines?
2. Is the vaccination against COVID-19 safe and effective for pregnant women?
3. What is the impact of vaccination against COVID-19 on pregnancy outcomes?
4. What is the risk of pregnant women being infected with COVID-19?

Research Aim

Therefore, this review was performed in order to evaluate the safety and effectiveness of vaccination against COVID-19 for pregnant women and to determine the impact of vaccination on pregnancy outcomes.

Research Methodology

General Background

The studies that were found using each set of keyword combinations were then pooled to create an impartial collection of publications. Studies and/or articles that weren't subjected to peer review, as well as proposals, procedures, reviews, letters, and opinions, were eliminated. The references include publications that were chosen in terms of their relativity to the topic. The research is concentrated on providing an overview of the effect of vaccination of pregnant women against COVID-19.

Data Analysis

In this review, English studies from common databases such as Pubmed/MEDLINE, Web of Science, Scopus, and the Cochrane Library with the keywords "Vaccination," "pregnancy," and "pregnant women," combined keywords involving "COVID-19," were involved. The end date for this review is March 2022.

Research Results

The result of the search using the chosen search strategy was 2367 articles. These articles to choose as well as the articles related to the topic were screened. A full-text screening of 344 articles after excluding the remaining article by title and abstract screening was accomplished. Finally, 51 articles to gather information about the topic and write this review were used (Figure 1).

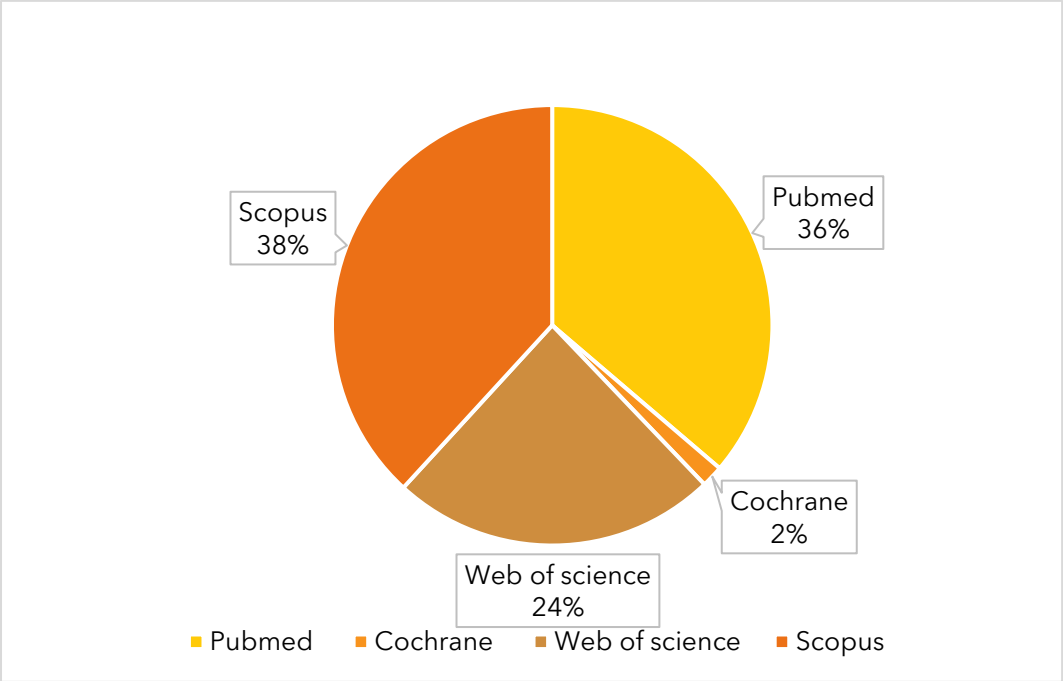

Figure 1. Research results

Literature review

The COVID-19

In late 2019, the COVID-19 outbreak first appeared in Wuhan, Hubei, China, and it has since quickly spread worldwide [11]. The virus responsible was discovered to be the 2019 new coronavirus [12]. The World Health Organization (WHO) later renamed this virus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). WHO declared COVID-19 a pandemic and recommended aggressive action from all nations due to the infection's rapid spread and worldwide effects [13]. The discovery that SARS-CoV-2 may transmit from person to person through respiratory vay and close contact presented a significant challenge to public health as the infection's transmission rate accelerated [14].

Mild COVID-19 cases included such symptomatics as myalgia, fever, a sore throat, and malaise but no dyspnea, shortness of breath, or abnormal chest imaging that would suggest lower respiratory tract disease. Mild COVID-19 infection accounts for 81% of symptomatic infections [15]. During chest ex-ray or physical examination, patients with moderate illness show signs of lower respiratory disease, but they nevertheless maintain an oxygen saturation of 94% or more in room air at sea level. The critical condition is characterised by multiorgan deficiency, septic shock, and respiratory deficiency [16].

COVID-19 in pregnancy

It is generally acknowledged that particular respiratory infections, such as varicella pneumonia and H1N1, increase the risk of mortality and severe morbidity in pregnant women [17]. This includes an increased risk of developing a serious disease when infected with COVID-19-related viruses as well as other viral respiratory illnesses like influenza [18,19]. Regarding COVID-19, the limited information does not suggest that pregnant people women are more likely to acquire an infection or have severe morbidity (such as the need for ICU hospitalisation or fatality) than non-pregnant women [20,21].

Some research has raised questions about the possibility that pregnant women may be more vulnerable to COVID-19 because they may generally be more susceptible to respiratory infections [22]. According to the evidence, pregnant women are no more susceptible to this specific virus than the general public [23]. The non-pregnant and pregnant populations have vulnerable subgroups; doctors must be aware of these high-risk groups and treat them appropriately. Individuals with pre-existing diabetes are particularly susceptible to the negative consequences of COVID-19 infection [24].

The pregnant woman experiences several physiological changes throughout most of the gestational period that mimic numerous disorders and raise her exposure to infectious diseases. Many organ systems change during

pregnancy, but the cardiovascular and respiratory systems are most affected. Red blood cell mass and blood plasma volume rapidly elevate during pregnancy and reach a peak in the third trimester [25,26]. Physiological dilutional anemia appears when the volume of blood plasma increases beyond the mass of blood cells. Increased exhaustion is one of the symptoms of anemia in pregnancy, which is a major cause of morbidity. Lower extremities edema and tachycardia are two additional symptoms of physiologic morbidity brought on by the concomitant rise in heart rate and decreased systemic vascular resistance. Patients also enhance total minute ventilation in the respiratory system by increasing total tidal volume. Pregnancy-related physiological dyspnea is caused by respiratory alkalosis caused by increased ventilation throughout the pregnancy.

According to statistics, between 60 and 70 percent of women feel dyspnea and shortness of breath with exertion, with occurrence rates rising in the second trimester [27]. Diagnosing lung disease during pregnancy is challenging due to these physiologic changes. COVID-19 infection has a broad range of presenting symptoms, which makes this challenge more difficult. Regarding the presence of shortness of breath (30%) and cough (52%), symptoms of COVID-19 in pregnancy are comparable to infections in the general population. However, compared to the general population, pregnant women were less likely to suffer symptoms of diarrhea (14%), headache (41%), chills (38%), and fever (34%) [28] **(Figure 2)**.

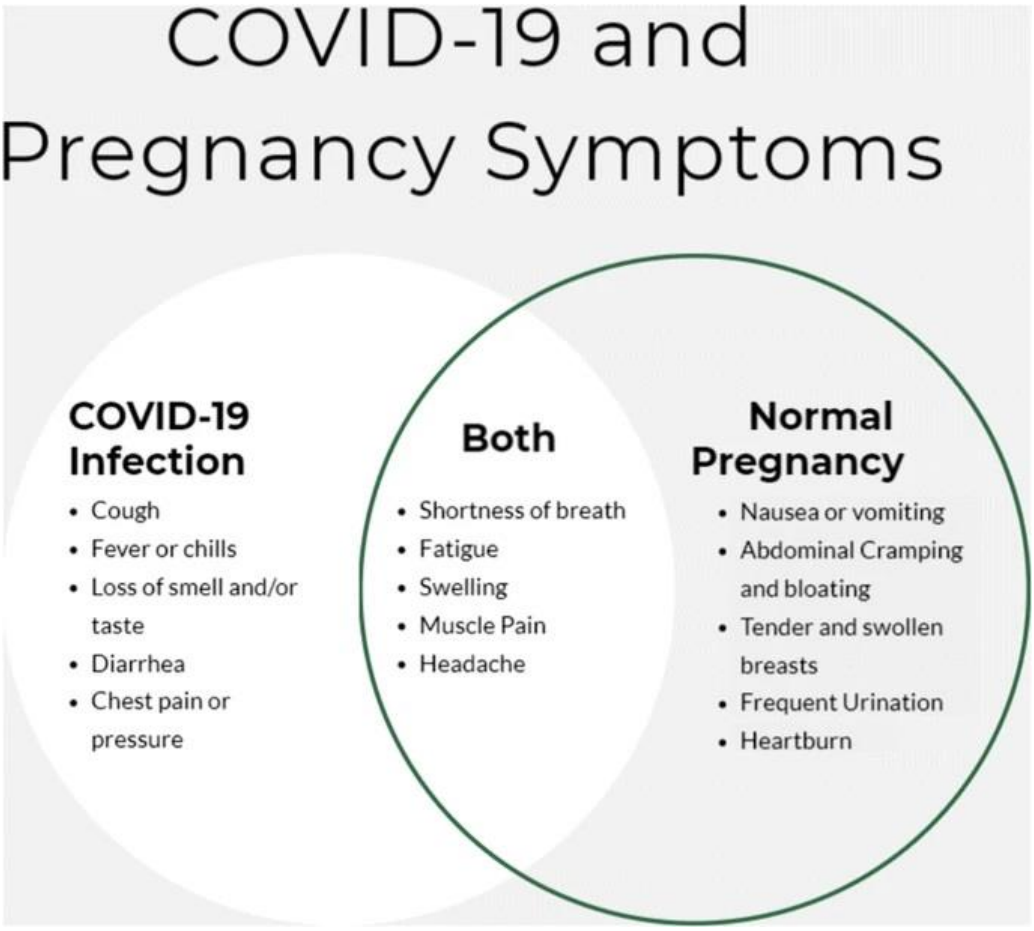

Figure 2. COVID-19 and pregnancy symptoms [29].

Pregnancy outcomes

Wei et al. performed a systematic review and meta-analysis in order to determine the relationship between the infection with COVID-19 during pregnancy and the outcomes of pregnancy. They involved forty-two articles, including 438548 pregnant women. They found that COVID-19 in pregnancy is accompanied by preterm birth, stillbirth, preeclampsia, and maternal ICU admission compared with cases without COVID-19. Contrary to asymptomatic COVID-19, symptomatic COVID-19 was linked to a higher risk of premature birth and cesarean delivery [30]. The exact processes behind the relationship between preeclampsia and COVID-19 are still unknown. Researchers have found evidence that SARS-CoV-2 may cause renin-angiotensin system malfunction and vasoconstriction via binding to angiotensin-converting enzyme 2 receptors [31]. Most women had cesarean sections because of fetal distress and premature membrane rapture (PROM) to prevent vertical transmission and decrease unfavorable neonatal and perinatal outcomes [32,33]. Elective cesarean sections were also performed to reduce women's respiratory discomfort [32,34]. Pregnant women's most important laboratory results were

Lymphocytopenia, increased liver enzymes, and leukocytosis. On chest CT scans, consolidation lesions, and sporadic ground glass shadows were the most often found abnormalities. Concerns have been raised about infection-related pre- or postpartum maternal deaths [35].

Neonatal outcomes

Clinical symptoms include fever, feeding intolerance, disseminated intravascular coagulation, birthing problems, bleeding, cyanosis, edema, rash, pneumonia, and dyspnea have been reported in neonates born from COVID-19-infected pregnant women [36]. Babies born to women with COVID-19 had a greater risk of admission to the neonatal intensive care unit (NICU) and stillbirth than babies born to women without COVID-19 [37,38]. The vertical transmission seems infrequent, and most babies born to mothers who caught COVID-19 during pregnancy are healthy. Most newborns with COVID-19 experience a modest illness course with unchanged outcomes. Yet, there are numerous reports of COVID-19 having a significant negative influence on the neonatal brain of infected newborns. Some follow-up studies imply that children born during the pandemic have a higher frequency of behavioral and neurodevelopmental issues [39].

COVID-19 vaccination

There are currently several types of COVID-19 vaccines that have been authorized for emergency use around the world. These vaccines work in different ways to help protect against the virus.

1. mRNA vaccines: These vaccines, such as Pfizer-BioNTech and Moderna, use a small ammount of genetic material called messenger RNA (mRNA) to instruct cells to produce a protein found on the surface of the virus. The mRNA method is ideally suited for the creation of vaccines against recently emerging viruses like SARSCoV-2 because of its flexibility, speedy development, safety, and powerful immunogenicity. MRNA vaccines against COVID-19 were effectively created at a rate never before achieved, building on significant technological advancement and advancement in the mRNA vaccine platform over the previous ten years. However, given that COVID-19 vaccines are the first mRNA vaccines to be approved for sale, some problems with potential large-scale manufacturing and the vaccine's long-term storage stability may arise [40,41].

2. Viral vector vaccines: These vaccines, such as AstraZeneca and Johnson & Johnson, use a harmless virus (such as adenovirus) to deliver genetic material from the COVID-19 virus into cells. This also triggers an immune response. The replication-deficient chimpanzee adenoviral vector chAdOx1 is used in chimpanzee adenovirus immunization. It is integrated with the surface spike protein's genomic code and has been genetically modified to match the SARS-CoV-2 spike protein [40].

3. Inactivated or killed virus vaccines: These vaccines, such as Sinovac and Sinopharm, use a dead or inactivated version of the COVID-19 virus to stimulate an immune response. So it cannot cause disease but still stimulates an immune response in the body. The killed vaccine for COVID-19 is made by growing large quantities of the virus and then treating it with chemicals or heat to render it inactive. This type of vaccine has been used successfully for other diseases such as polio, hepatitis A, and influenza. The killed vaccine remains an important tool in the fight against COVID-19 and will continue to be studied and improved upon as we learn more about this novel virus.

4. Protein subunit vaccines: These vaccines contain harmless pieces of proteins found on the surface of the COVID-19 virus to trigger an immune response. In the case of COVID-19, protein subunit vaccines use a piece of the spike protein found on the surface of the SARS-CoV-2 virus. This spike protein allows the virus to enter human cells and cause infection. To create a protein subunit vaccine, scientists first identify which part of the virus they want to target. In this case, they focus on the spike protein. They then use genetic engineering techniques to produce large quantities of just that part of the virus in a laboratory setting. Once enough of the spike protein has been produced, it is purified and used as the main component of the vaccine. When injected into a person's body, this purified spike protein triggers an immune response that helps protect against future infections [42].

One advantage of protein subunit vaccines is that they are generally considered safe and well-tolerated. Because they only contain a small ammount of the virus or bacteria, there is little risk of causing an actual infection. Additionally, because they do not contain live viruses or bacteria, they can be safely given to people with weakened immune systems [43].

Several COVID-19 vaccines currently in development use protein subunits as their main component. These include Novavax's NVX-CoV2373 vaccine and Sanofi/GSK's adjuvanted recombinant protein-based vaccine candidate [44].

All of these vaccine types are effective at preventing severe illness and hospitalization from COVID-19. It is important for individuals to receive whichever vaccine is available to them in their area in order to help protect themselves and others from the spread of the virus.

COVID-19 vaccination in pregnancy

The recent recommendation about using the COVID-19 vaccine in pregnancy is that the vaccine should be used as early as possible for the maternal benefit due to the substantial rise in SARS-CoV-2-related mortality among pregnant women. It is essential to understand how COVID-19 vaccination affects pregnancy and, consequently, placental antibody transfer to provide vaccine recommendations for this population group [45]. A cohort analysis showed that humoral immunity developed during pregnancy, with reactivity and reactogenicity comparable to those seen in non-pregnant women; vaccine-induced antibody titers were the same in both groups of women. On the other hand, few studies have discovered decreased immunity during pregnancy in comparison to that seen in women who received vaccinations but were not expectant [45,46]. Prabhu et al. [47] studied 122 pregnant woman with SARS-CoV-2 and found that IgG level was 43.6% following the first dosage of mRNA-based vaccination; 98.5% following two doses. Besides, two weeks after the initial dosage of the vaccine, maternal IgG levels were noticeably increased each week by week.

Regarding the antibody transfer to the fetus, by four weeks after the first immunisation dosage, IgG antibodies were present in all but one cord blood sample.

Atyeo et al. [45] studied the concentration of the Fc portion of the antibodies after mRNA-based COVID vaccination. After the first dosage, they found that Fc receptor antibody concentrations were considerably lower in pregnant women than in non-pregnant women. After the second dosage, Fc receptor antibody concentrations rose substantially but remained lower than in non-pregnant women.

Discussion

Several published studies reported that COVID vaccination was very effective in reducing the risk of infection and the severity of the disease. A wide-scale analysis of Scotland population was performed by Goldshtein et al. [48]. They included 126149 unvaccinated and 18399 vaccinated pregnant women. About 77% of COVID infections, 90% of hospital admissions, and 98% of critical care admissions were in the unvaccinated group. A previously published study also examined the efficacy of maternal vaccination against covid-19-related hospital admittance in newborns during the first six months of life. The incidence of hospital admission with COVID was significantly higher in infants whose mothers were not vaccinated. They discovered that maternal vaccination during pregnancy reduced the risk of covid-19-related hospital admittance in children under 6 months by 61%.

Regarding the effect of COVID vaccination on perinatal outcomes. Several studies reported that the perinatal adverse effects did not increase after maternal vaccination. Perinatal outcomes refer to the health outcomes of both mother and baby during pregnancy, childbirth, and postpartum. Various factors can affect these outcomes, including maternal health status, environmental factors, and medical interventions such as vaccination.

Theiler et al. [49] reported that the incidence of preterm birth was 9.3% in the vaccinated woman and 8.5% in the unvaccinated woman. The rates of cesarean deliveries were 31.4% in the vaccinated woman, unvaccinated 29.8%. NICU admission: vaccinated 0.07%; unvaccinated 0.6%. The difference in these perinatal outcomes was not significant between both groups.

Kharbanda et al. [50] reported that the incidence of spontaneous abortion was 8.6% SAB that occurred within 28 days of vaccination.

Concerning the adverse events of COVID-19 side effects in pregnancy. Typically minor to severe symptoms follow the covid-19 vaccination, and they start to appear three days after receiving the vaccination. The majority start the day after the immunisation and pass in one to two days. The second dose is linked to more serious and regular side effects. Pregnancy-related vaccine adverse effects appear to be comparable to those in non-pregnant individuals, with pain at the injection site, fatigue, headaches, and myalgia being the most common signs.

Conclusions and Implications

1. COVID vaccination in pregnancy is a safe and effective way to protect both the mother and the developing fetus from the virus.
2. The Centers for Disease Control and Prevention (CDC) recommends that pregnant individuals receive the COVID vaccine, as they are at an increased risk of severe illness and complications from COVID-19.
3. Studies have shown that COVID vaccines do not increase the risk of miscarriage or other adverse pregnancy outcomes.
4. Pregnant individuals who contract COVID-19 are at a higher risk of preterm birth, stillbirth, and other complications, making vaccination even more important.
5. Vaccination during pregnancy can also provide passive immunity to newborns, who are unable to receive the vaccine themselves until they are at least 12 years old.

6. It is important for healthcare providers to educate pregnant patients about the benefits of vaccination and address any concerns or questions they may have.

7. By getting vaccinated during pregnancy, individuals can help protect themselves, their unborn child, and their community from the spread of COVID-19.

Declarations

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Data sharing statement

Data supporting the findings and conclusions are available upon request from the corresponding author.

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