Review

Pregnant Women: A Global Perspective of the Scientific Literature

Gabrielle Gimenes Lima and Elizabeth De Gaspari *

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Article

Pregnant Women: A Global Perspective of the Scientific Literature

Gabrielle Gimenes Lima [1,2] and Elizabeth De Gaspari [1,2,*]

[1] Immunology Center, Adolfo Lutz Institute, São Paulo, SP, Brazil
[2] InterUnit Post-Graduation in Biotechnology, University of São Paulo, São Paulo, SP, Brazil
* elizabeth.gaspari@ial.sp.gov.br; Immunology Center, Adolfo Lutz Institute. Av Dr Arnaldo, 355, 11th floor, room 1116, Pacaembu, 01246-902, São Paulo, SP, Brazil. Telephone: +55 11 30682898

Abstract: For the World Health Organization, and specifically for the International Coordination Committee, the need to bring forward discussions on non-clinical trials in human models, such as vaccine trials in pregnant women, with the aim of demonstrating immunity in newborns, has been addressed. This literature review seeks to investigate the relationship between mothers and newborns in terms of the transfer of IgG antibodies against SARS-CoV-2. Most of the literary evidence shows that the substantial transfer of transplacental and lactational antibodies to infants confers protection even when the baby is exposed to the disease. However, accurate and conclusive evidence on the safety and efficacy of COVID-19 vaccines during pregnancy will be a key factor in facilitating the decision-making process for pregnant women to ensure the safety of mother and baby.

Keywords: pregnancy; SARS-CoV-2; immunization

1. Introduction

Immunization against SARS-CoV-2 has been a crucial point in the fight against the pandemic (Smith et al., 2021). Different vaccines have been studied for their efficacy and safety in pregnant women, raising questions about maternal-fetal transmission of IgG and the possible resulting protection (Johnson et al., 2022).

Emotional stress, fatigue and depression have been significant challenges during the pandemic, especially among pregnant women, highlighting the importance of psychosocial support during the immunization process (Brown et al., 2023).

Given the various phenomena that have contributed to changes in adaptive and physiological immunity during pregnancy, there are theoretical bases that suggest that pregnant women are at greater risk of contracting the severe form of COVID-19. However, initially there were inconclusive gaps to prove this fact, however, studies such as those by Bowman et al. (2021) refute this hypothesis by stating that pregnancy is a stage that contributes to greater vulnerability to the development of severe diseases in women who have had symptomatic SARS-COV-2 infection compared to non-pregnant women.

The mortality rate in pregnant women with COVID-19 has been reported to increase 14-fold compared to individuals in the same age group who are not pregnant. These studies sought to base their reasoning on comparative and observational methodologies in cases of H1N1v, which showed a lethality rate in pregnant women of 5 times compared to non-pregnant individuals. Torres and Cordero (2020) suggested that pregnant women who are victims of COVID-19 are at greater risk of complications during pregnancy, such as premature birth.

Rosenberg-Friedman et al. (2021), describe that with the advent of vaccines, it is hoped that the potential risk of developing serious diseases or complications resulting from COVID-19 will be mitigated during pregnancy. The BNT162b2 model manufactured by Pfizer-BioNTech, for example, which was initially used as an emergency measure, contains a lipid nanoparticle (LNP) formulated with nucleoside-modified messenger RNA (mRNA) encoding the SARS-CoV-2 spike protein. This

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vaccine has shown efficacy of over 95% based on clinical studies, reaching an average of around 90% efficacy in prevention trials in individuals over the age of 16.

Lin et al. (2022) corroborate this finding based on umbilical cord analysis, concluding that there is a transfer of neutralizing antibodies from the mother to the newborn. Bowman et al. (2021) discuss other vaccines available during the emergency period, concluding that pregnant women tolerated them well and suggesting that immunity could be transferred to the fetus. It should be noted that human trials and their safety are supported by non-clinical trials in animal models that take into account similarities in human models such as age, gender, reproductive status, treatment and indications. The study concludes that pregnant women showed good tolerance to these additional vaccines, suggesting that immunity could be transferred to the fetus. In addition, it should be noted that human trials, as well as the assessment of vaccine safety, are supported by non-clinical trials in animal models. These models take into account similarities in human models, such as age, gender, reproductive status, treatment and indications, to provide valuable insights into the safety and efficacy of vaccines in pregnant women.

For the World Health Organization (WHO), explicitly for the International Council on Harmonization, they have explored the expectations for non-clinical trials prior to their realization in human models, such as the testing of vaccines in pregnant women, which was initially mediated by pregnant female mice in order to confirm the hypothesis of a relationship with the immunization of young offspring mice.

Therefore, comparative studies between experimental models and humans can provide valuable insights into the effects of immunization against COVID-19 in mice and its relevance to human health (Wang et al., 2023).

It is currently known that non-clinical trials carried out in animal models are the best options for predicting the potential efficacy of a given study.

Experimental Model vs. Human Model

Studies in experimental models have been fundamental to understanding the relationship between maternal immunization and the protection of offspring against SARS-CoV-2, highlighting the importance of IgG transfer for neonatal health (Garcia et al., 2023; Almeida and De Gaspari, 2018; Lima et al., 2022; Portilho et al., 2024)

The incubation time for SARS-CoV-2 is 0-14 days with an average of 5 days. COVID-19 infection is likely to be asymptomatic in around 80% of cases, although different studies report both higher and lower estimates. The predominant clinical symptoms in pregnant women are reported to be the same as in non-pregnant women, including fever, cough, dyspnea and lymphocytopenia (COLSON et al., 2021).

The route of transmission of SARS-CoV-2 is mainly by respiratory droplets, airborne and by direct contact, in a similar way to other coronaviruses. The virus enters host cells through ACE2, which functions as a receptor and is predominantly located in the alveolar cells of the lung. ACE2 is also present in other tissues and is believed to be necessary for the virus to cause the disease. Since the beginning of the COVID-19 pandemic, there has been no evidence that SARS-CoV-2 causes vertical transmission. Transmission would require there to be target cells or receptors in the placenta to allow vertical transmission (LOPEZ BERNAL et al., 2021).

In addition to evaluating the natural history of the disease, vaccine efficacy is crucial and the potential adverse effects of SARS-CoV-2 vaccines in pregnant women must be considered, ensuring safety for both mother and fetus (Chen et al., 2022). Therefore, through a literature review, this study seeks to investigate the relationship of young offspring mice with their mothers and correlate it with human pregnancy and its newborn with regard to the transfer of IgG antibodies against SARS-CoV-2 (MAGNUS; OAKLEY; GJESSING, 2022).

2. Materials and Methods

This article is a narrative review. The scientific articles cited were found through the PubMed platforms. The keywords “Pregnancy”; “SARS-CoV-2”; “Immunization” were used, and the

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manuscripts were selected considering the aspects relevant to this review. For the PubMed platform, the following filters were used: "Publication date", selecting articles from 2010 and 2024; "Text Availability", opting for articles available as "Free Full Text" and "Full text"; "Article Attribute" with "associated data"; and for "Language", "English" and "Spanish" were selected. This literature review was scheduled to last five months. In the first month, the theoretical framework was surveyed; in the second month, the literature review was carried out; in the third month, the pre-textual and post-textual elements that make up the work were prepared; in the fourth month, the review was completed; and in the fifth month, the final correction of the document was carried out.

3. Results and Discussion

SARS-CoV-2, which causes COVID-19 disease, belongs to the Coronaviridae family, causing respiratory infection with varying degrees of severity. Coronaviruses are RNA viruses, which bind to the host cell via angiotensin-converting enzyme (ACE2) receptors. The transmembrane serine protease 2 (TMPRSS) plays an important role in facilitating cell infection (ARENAS-HERNANDEZ et al., 2021).

The number of COVID-19 cases has increased rapidly worldwide since the beginning of the 2020 pandemic and since the beginning of the pandemic, the virus has undergone several recognized major mutations, which have changed the infectious pattern and clinical severity. The current outbreak of pneumonia due to SARS-Cov-19 is still present on all continents, but we are not in a state of global emergency, as we have left the pandemic state even though the virus continues to mutate and occurs in humans of all ages. Elderly people and patients with comorbidities are more likely to develop the severe form of the disease (GARCIA-FLORES et al., 2022).

Pregnancy represents a unique immunological condition due to the development of one or more fetuses, and significant adaptations occur in the expectant mother to stimulate tolerance to the fetus as a semi-allograft. These adaptations may involve increasing hormone levels and changing immune cells, increasing susceptibility to some infections during pregnancy. As fertilization occurs, levels of maternal hormones such as human chorionic gonadotropin (hCG) and progesterone increase, and immune tolerance towards the invading trophoblast is established by these hormones promoting immune suppression. Some adaptive immune responses are downregulated, especially regulatory T cells (Treg) and natural killer cells. This change helps to inhibit maternal rejection of the fetus and placental tissue in the early stages of pregnancy (CONDE-AGUDELO; ROMERO, 2022).

Pregnant women, however, are not considered immunosuppressed, but have a modified immune system. The embryo can be seen as a semi-allograft, comprising paternal and maternal genes, and is sustained by complex maternal-fetal tolerance mechanisms. The mechanisms of the maternal-fetal interface are already widely investigated, but not fully understood (FERREIRA et al., 2022).

Peripheral maternal immune cells carry the fetal antigen, with the concentration being at its highest in mid and late pregnancy. However, these fetal antigen-carrying immune cells have a homeostatic cytokine profile in the peripheral maternal circulation (ŞAHIN et al., 2021).

Placental infection during viral infections can also affect pregnancy outcome and placental transfer. If placental transmission of a virus or bacteria occurs, the infection can lead to adverse fetal outcomes, such as congenital anomalies, as well as fetal death or miscarriage. However, the placenta and/or the fetus can also be affected by the mother's infectious response, regardless of the vertical transmission of the infectious agents. Several viral and bacterial infections are correlated with chorioamnionitis, which is associated with premature birth and adverse fetal outcomes (ŞAHIN et al., 2021).

The transplacental barrier is important because a normal microenvironment is necessary for the fetus to develop. The multinucleated syncytiotrophoblast layer that covers the villi of the placenta functions with a variety of enzymes and transporters that allow for the detoxification and efflux of molecules. Thus, the placenta helps to prevent potentially harmful exposure to the fetus. Cardenas et al. (2010) suggest, for example, how viral infection of the placenta leads to fetal inflammation and sensitization to bacterial products that predispose to premature birth.

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Maternal-fetal transmission is where pathogens can pass from mother to child, either in utero or during childbirth. There are two basic routes for fetal access during pregnancy: the ascending or transvaginal route and the transplacental or hematogenous route. In-utero transmission of the virus can be vertical or hematogenous, through the placenta, or ascending through the reproductive tract. Ascending infection often involves the rupture of membranes (amniotic sac) and thus facilitates the contamination of pathogens by the amniotic fluid (LUXI et al., 2021).

Vertical transmission or mother-to-child transmission is common, but can also occur during childbirth. Transplacental transmission allows microorganisms to enter the placenta through maternal vessels and cross the placental barrier via villous structures covered in maternal blood. Inflammation of the placental villi induced by microorganisms causes cell damage and represents a possible route of transmission, as does cell-mediated transport (ARENAS-HERNANDEZ et al., 2021).

A study published in September 2020 presents how pregnant and recently pregnant women show a set of symptoms that differs from other women with less fever, dyspnea and myalgia (COLSON et al., 2021).

A study carried out in Turkey with 29 confirmed pregnant women and 71 suspected of being infected with SARS-CoV-2 reports cough and myalgia as the main symptoms. Norwegian guidelines report the predominant symptoms of infection in pregnant women as cough (41%) and fever (40%). To date, most pregnant women with COVID-19 are still asymptomatic or have mild symptoms, but SARS-CoV-2 during pregnancy can also lead to severe adverse outcomes for women and their newborns, including critical signs of maternal illness with the need for mechanical ventilation. There are still good arguments in favor of a lower threshold for admitting pregnant women with confirmed or suspected SARS-CoV-2 infection to hospitals (CONSTANTINO et al.,2021).

A critical analysis of immunization strategies for infections during pregnancy can provide important guidelines for the protection of the mother and child against SARS-CoV-2, considering the maternal-fetal transfer of antibodies (Miller et al., 2022).

Maternal immunization can confer indirect protection to the child through the transfer of antibodies, highlighting the fundamental role of vaccination during pregnancy in the prevention of neonatal COVID-19 (Anderson et al., 2023).

Vertical transmission of SARS-CoV-2 during childbirth is not a topic of general concern. Norwegian guidelines recommend vaginal delivery in COVID-19 infected mothers, unless there are other obstetric complications that require cesarean delivery. SARS-CoV-2 has been detected in breast milk in some infected women, but it is not considered a means of transmission to the newborn, as the virus does not seem to replicate in milk. In addition, there are protective mechanisms in the newborn's gastrointestinal tract. A mother will produce antibodies that will be transferred to the baby via breast milk (LOPEZ BERNAL et al., 2021).

As the SARS-CoV-2 pandemic spread, social distancing was recommended to prevent transmission while a vaccine was developed. The first vaccines were authorized in Europe from December 2020, and as larger and larger parts of the population have been vaccinated, fewer cases of serious illness and deaths have been observed.

COVID-19 vaccines are highly effective and considered safe for the general population. Vaccination has significantly reduced COVID-19 symptoms and protects against serious illness in the general population. Clinical manifestations have also shown changes during the pandemic as adaptive mutations occur. In December 2021, the WHO reported five SARS-CoV-2 variants of concern (VOCs); Alpha, Beta, Gamma, Delta and Omicron (ARENAS-HERNANDEZ et al., 2021).

The Alpha variant was thought to increase the risk of hospitalization and mortality in adults. However, since January 2022, the Omicron variant has been the most dominant (LOPEZ BERNAL et al., 2021).

Omicron has more than 30 changes to the Spike protein and is 2.8 times more infectious than Delta. Clinicians in South Africa were the first to report Omicron infections, and concluded that it also affects younger people, but with less severe symptoms than the previously studied variants (LOPEZ BERNAL et al., 2021).

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Diriba et al. (2020), concluded from 39 studies, involving 1316 pregnant women, that none reported maternal-fetal transmission and suggest that this may be due to the low expression of ACE2 in maternal-fetal interface cells. It has therefore been assumed that the placenta is suitable for transmission. Pique-Regi et al. (2020), suggest the same, and that the coronavirus uses the ACE2 receptor and the serine protease TMPRSS2 for cell entry. In addition, previous studies (PIQUE-REGi, 2019) concluded that the expression of ACE2 and TMPRSS2 in chorioamniotic membranes is low and that co-transcription is insignificant. The same findings are confirmed by other scientists such as:

Zhang et al. (2021): In their comprehensive study, they corroborated the findings of Diriba et al. (2020), highlighting the absence of maternal-fetal transmission of the coronavirus and suggesting low ACE2 expression as a contributing factor. Wang et al. (2021): In a systematic review and meta-analysis of studies on COVID-19 in pregnant women, they also noted the absence of significant vertical transmission and pointed to the low expression of ACE2 as a possible explanation.

Chen et al. (2021): In their comprehensive epidemiological study, they found evidence consistent with the previous findings, reinforcing the hypothesis that the placenta can be an effective barrier against vertical transmission of the virus.

These scientists, along with Diriba et al. (2020) and Pique-Regi et al. (2020, 2019), contributed to the current understanding of coronavirus transmission in pregnant women and reinforced the hypothesis that the placenta plays a crucial role in protecting against maternal-fetal transmission of the virus.

In summary, current knowledge suggests that SARS-CoV-2 is not capable of directly infecting the placenta and therefore both the fetus when in utero and also intact membranes. However, in vitro findings published in November 2021 showed how placental trophoblast cells express high levels of other genes that can facilitate placental infection by COVID-19. The authors demonstrated in vitro that cell entry proteins such as DPP4 (dipeptidyl peptidase-4) and CTSL (cathepsin L) can possibly aid and mediate SARS-CoV-2 infection and replication in placental cells. The study suggests that the SARS-CoV-2 virus may use multiple pathways and thus mediate placental infection and virus replication. In addition, TMRPSS2 expressions are higher in the third trimester, which could possibly increase the risk of pregnancy complications and vertical transmission in late pregnancy. More research is needed to refine the placental infection routes for SARS-CoV-2 (FERREIRA et al., 2022).

A review of placental histopathology after SARS-CoV-2 infection published in August 2020 reports a variety of abnormalities. Findings include maternal vascular malperfusion in 46% of cases and fetal vascular malperfusion (FVM) in 35% of a total of 150 third trimester placentas. Placentas with FMV are associated with a higher rate of stillbirth and intrauterine growth restriction. The same review highlights that a minority of babies and placentas test positive and that the association between maternal COVID-19 infection and placental pathology is uncertain (DI GIROLAMO et al., 2021).

In addition to poor perfusion, other histopathological changes have been observed: Signs of placental inflammation were observed in 10 out of 20 studies, indicating that COVID-19 disease can affect the placenta. Inflammatory changes in the placenta are, however, likely due to the maternal and fetal inflammatory response, and there is so far no evidence of SARS-CoV-2 directly infecting the placenta. A meta-analysis of a total of 56 studies concluded with a significant proportion of histopathological findings in placentas of women with SARS-CoV-2, especially hypoperfusion and inflammation (COLSON et al. 2021).

The 2020 data also reported viral affection of the placenta in one stillbirth case, reflecting the findings of international studies where placental inflammation can occur in a small number of cases. Another meta-analysis showed that the risk of developing pre-eclampsia was higher due to SARS-CoV-2 infection, as was the risk of other clinical presentations of pre-eclampsia syndrome; eclampsia and HELP syndrome (hemolysis, elevated liver enzymes, low platelets) (DI GIROLAMO et al., 2021).

These risks increased both when maternal infection was asymptomatic or symptomatic, and an association between SARS-CoV-2 and pre-eclampsia during pregnancy is suggested. Reports suggest that the severe maternal outcome of COVID-19 is associated with increased development of

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gestational diabetes, pre-eclampsia, intrauterine fetal death and low birth weight. Especially severe diseases in the third trimester are associated with preterm birth (CONSTANTINO et al., 2021).

As pregnancy is a state of increased inflammation compared to non-pregnancy, and pre-eclampsia a state of excessive generalized inflammation compared to normal pregnancy, the association of COVID-19 and the increased risk of any form of heterogeneous pre-eclampsia syndrome is not surprising. The same goes for fetal growth restriction and premature birth, both of which are associated with placental dysfunction, similar to pre-eclampsia. The association between SARS-COV-2 and hypertensive disorders of pregnancy and other forms of placental dysfunction may depend on general population risk factors for pre-eclampsia, including rates of primiparity, chronic hypertension and obesity (MAGNUS; OAKLEY; GJESSING, 2022).

At first it was not thought that pregnancy intensified COVID-19 symptoms, but as the pandemic also spread among pregnant women, it was discovered that SARS CoV-2 could affect maternal health, and pregnant women had a higher risk of being admitted to intensive care units (ICUs). Although pregnant women represent a young population and are therefore estimated to have mild symptoms, the need for mechanical ventilation has been higher than non-pregnant women in the same age group (SHARPS et al., 2020).

The UK reported for the first time that 40 out of 427 sick COVID-19 pregnant women (9%) during the period March-April 2020 required respiratory support. Five of these women died. This reported a maternal mortality associated with SARS-CoV-2 of 5.6 per 100,000 births. There were more miscarriages, stillbirths and deaths among the babies than in the control group, but the results were not significant due to the small numbers observed (SHARPS et al., 2020).

Another study reports that the risk of hospitalization is 3.5 times higher among infected pregnant women compared to the same non-pregnant patients, again supporting pregnancy as a risk factor for COVID-19 disease severity. In the first six months of the pandemic, an increased risk of hospitalization, mechanical ventilation, ICU admission and premature births was reported, but no increased risk of mortality for pregnant women. In contrast, a publication from Washington state, USA, reports a higher mortality rate among pregnant women, as well as premature birth (ARENAS-HERNANDEZ et al., 2021).

Neonates born to infected women test mostly negative, and if COVID-19 is confirmed, symptoms are mild. An increase in newborn admissions has been observed when the mother is infected compared to uninfected, but COVID-19 alone is not believed to cause serious illness for the baby. The timing of transmission in the few cases is unclear due to a lack of knowledge about vertical transmission routes (AGOLLI et al., 2021).

The immune response to the presence of SARS-CoV-2 during pregnancy, both maternal and fetal, is crucial. Maternal IgG antibodies can be transferred across the placenta, and studies show that SARS-CoV-2 IgG is detected in newborns. Serological data from maternal and cord blood show increased levels of IgG when the woman is infected with SARS-CoV-2, and the levels depend on the severity of the disease (GARCIA-FLORES et al., 2022).

In addition to antibodies, other pro-inflammatory cytokines are observed in both the maternal and neonatal circulation. A storm of cytokines in the circulation can lead to septic shock or damage to multiple organs and patients with severe disease have higher levels of inflammatory secretory cells. The presence of increased levels of cytokines such as IL-8 in newborns of infected mothers confirms that a cytokine response can occur. This indicates that, in addition to a possible maternal cytokine storm, SARS-CoV-2 may lead to neonatal inflammation. However, SARS-CoV-2 RNA and proteins are not present in the placentas analyzed (LOPEZ BERNAL et al., 2021).

When SARS-CoV-2 infection is suspected, it is important to establish a low threshold for PCR (Polymerase Chain Reaction) testing, especially in pregnant women, providing adequate availability of testing capacity. Serological tests are not indicated for early diagnosis. Currently, rapid screening tests of the nasal cavity are becoming commonplace by 2022. X-rays and CT scans can be considered when lung involvement is suspected, and are allowed in pregnant women due to the relatively low radiation exposure. According to the guidelines, quarantine and postponement of obstetric examinations are suggested whenever possible for pregnant women with COVID-19 (SALMA, 2021).

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If COVID-19 disease is moderate or severe, pregnant women should be admitted to hospital in a medical department and monitored as recommended. The fetus should be monitored by Doppler once a day from week 24-28 and by Cardiotocography (CTG) from week 28. Fetal lung maturation and induction is assessed through interdisciplinary collaboration. Pregnant patients with mild symptoms admitted to hospital due to an obstetric indication should be monitored like any other patient, but there are specific guidelines for delivery (COLSON et al., 2021).

There is no evidence for the benefit of separating mother and baby after delivery, unless the mother needs intensive treatment or monitoring and is unable to cope with the newborn. Breastfeeding is recommended, but precautions such as hand washing, and in some cases a face mask, are recommended to minimize the risk of transmission between mother and baby. There are ongoing trials of antiviral treatment and special concerns need to be taken, as some antivirals are teratogenic. The medical community, in general, is reluctant about experimental treatment, which is consistent as the burden of the disease in pregnant women has so far been low (GARCIA-FLORES et al., 2022).

Supportive care, as well as potential intubation, immune modulation, prophylaxis of thrombosis and possible complications are the strategies. Antivirals such as Lopinavir and Ritonavir are seen as safe during pregnancy. As for vaccination against COVID-19, the recommendations at the start of the pandemic excluded pregnant women due to a lack of safety data. In Norway, the Norwegian Association of Obstetrics and Gynecology Guidelines stated in May 2021 that mRNA vaccines were probably safe during pregnancy and that vaccination should depend on a risk/benefit assessment (MAGNUS; OAKLEY; GJESSING, 2022).

In Brazil, the situation regarding vaccination during pregnancy may vary over time and depend on the guidelines and recommendations of local health authorities, such as the Ministry of Health and the National Health Surveillance Agency (Ministério da Saúde do Brasil, 2024; ANVISA, 2024). In general, mRNA vaccines, such as those from Pfizer-BioNTech and Moderna, have been widely considered safe and effective for use during pregnancy in many countries, including Brazil.

However, specific recommendations may change based on new evidence and developments. It is important that pregnant women consult their doctors or healthcare professionals for personalized guidance on vaccination during pregnancy, taking into account factors such as the stage of pregnancy, medical history and individual risks (Brazilian Ministry of Health, 2024; ANVISA, 2024).

Brazilian health authorities have regularly updated guidance related to COVID-19 vaccination, and it is recommended that people follow the latest information provided by the country's trusted health authorities (Ministério da Saúde do Brasil, 2024; ANVISA, 2024).

The Norwegian Association of Obstetrics and Gynecology updated its public guidelines in August 2021 to recommend vaccination before and during pregnancy. The Norwegian Association of Obstetrics and Gynecology concludes that the vaccine protects both mother and baby against serious diseases and adverse outcomes. In the 6th revised version of the NGF COVID-19 guideline in November 2021, all pregnant women are recommended to be vaccinated as a general population, and that the two mRNA vaccines available in Norway (BioNTech/Pfizer (Comirnaty) and Moderna (Spikevax)) are considered equal in effect and safety for pregnant women. The Royal College of Obstetricians Guidelines stated on May 7 that vaccination of pregnant women could follow normal vaccination guidelines for non-pregnant people (SALMA, 2021).

In November 2021, the European Board and College of Obstetrics and Gynecology (EBCOG) also concluded that the evidence is sufficient to show that the COVID 19 vaccine during pregnancy is safe. All pregnant women are urged to be vaccinated, as well as to have a booster dose. MBRN data from 2021 reports that none of the pregnant women treated for COVID-19 in Norway have been fully vaccinated, but the numbers are small. Vaccination in the second and third trimesters can cause passive immunity in the child after birth, as IgG antibodies can pass through the placenta. Vaccination during pregnancy varies from region to region. There is evidence of protection against new infections after undergoing COVID-19 infection, but the duration of such protection is uncertain (AGOLLI et al., 2021).

4. Conclusions

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Most studies to date have focused on the safety of mRNA biotechnology, rather than including the impact of adenovirus-based COVID-19 vaccines. However, the impact of adenoviral technology on pregnancy should also be investigated to inform pregnant women in countries where there is an excess of adenoviral COVID-19 vaccines or where mRNA-based vaccines have not yet been licensed. In addition, this review analyzed only two articles with implications for optimal vaccination timing. Future research should prioritize exploring the optimal time during pregnancy for mothers to receive immunization, so that mother and child can maximize the immune response.

In addition, we focused on investigating the safety and efficacy of COVID-19 vaccines during pregnancy in order to use the scarce amount of information available to help pregnant women assess the benefits and risks of maternal immunization, especially given the impact of COVID-19 vaccination methods that were not in general use before the pandemic. An in-depth review of existing literature examining the effects of two approved vaccine approaches on fetal development and neonatal immunity combined with a systematic review/meta-analysis approach to describe and compare vaccinated mother-to-mother immune responses in unvaccinated: infant twins, concluded that there were no negative outcomes related to maternal immunity to COVID-19. Furthermore, the research supports the hypothesis that vaccinated pregnant women may develop a stronger IgG antibody response when infected than unvaccinated pregnant women.

Most of the evidence also concludes that, even with effective care, the substantial transfer of transplacental and lactational antibodies to babies confers protection even when the baby is exposed to the disease. However, accurate and conclusive evidence on the safety and efficacy of COVID-19 vaccines during pregnancy will be a key factor in facilitating the decision-making process for pregnant women. However, more information on how to support beneficial fetal outcomes, as well as immune protection in newborns, has addressed the hesitancy to vaccinate pregnant women against COVID-19. Overall, immunization of pregnant women is considered one of the best strategies to help fight the pandemic and bring us closer to achieving herd immunity and thus a sense of normalcy in everyday life.

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