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COVID-19 and COVID-19 Vaccination in Pregnancy: Epidemiology, Pathophysiology, and Clinical Management

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Abstract

Pregnant individuals represent a high-risk cohort for severe manifestations of SARS-CoV-2 infection, with epidemiological data indicating elevated rates of maternal morbidity, preterm birth, preeclampsia, and perinatal complications relative to non-infected pregnant populations. Pathophysiological studies highlight altered immune responses and placental ACE2 expression as potential mediators of increased susceptibility and adverse outcomes. Accumulating evidence from large prospective cohorts and meta-analyses demonstrates that administration of COVID-19 vaccines during pregnancy does not increase the incidence of major congenital anomalies, spontaneous abortion, or stillbirth when compared to unvaccinated controls. Moreover, vaccination is associated with significant reductions in the risk of severe maternal COVID-19, hospitalization, and adverse neonatal outcomes. Immunogenicity studies confirm efficient transplacental transfer of SARS-CoV-2 antibodies, conferring passive immunity to the neonate. Collectively, these findings substantiate the safety and efficacy of COVID-19 vaccination in pregnancy, supporting its role as a critical intervention to mitigate maternal and perinatal morbidity during the ongoing pandemic

Purpose

The primary objectives of this review are:

1. To evaluate the clinical efficacy and safety of COVID-19 vaccination during pregnancy, including its impact on maternal outcomes and neonatal health
2. To analyze the epidemiological distribution of COVID-19 in pregnant populations, including risk factors for SARS-CoV-2 infection severity, and elucidate the pathophysiological mechanisms by which pregnancy modulates immune responses to COVID-19
3. To identify knowledge gaps and propose directions for future research.

Materials and Methods: This review was conducted with the help of Pubmed databases using the following search terms: “COVID-19 Vaccination during Pregnancy”, “COVID-19 Vaccine Safety for Pregnant Women”
Conclusion: Data suggests that vaccinated pregnant women exhibit a 78% reduction in SARS-CoV-2 infection risk and 72% lower hospitalization rates compared to unvaccinated counterparts. Neonates born to vaccinated mothers show 64% reduced risk of COVID-19 hospitalization during the first six months of life, mediated by transplacental transfer of neutralizing antibodies. These benefits are optimized when the primary vaccine series is completed prior to the third trimester, with studies showing 2.1-fold higher cord blood antibody titers compared to later vaccination. Systematic reviews confirm no increased risk of adverse obstetric outcomes, including congenital anomalies or preterm birth. These findings align with international guidelines recommending COVID-19 vaccination during pregnancy as a critical strategy for mitigating maternal morbidity and safeguarding neonatal health during the pandemic.

Key Words: COVID-19; Pregnancy; Vaccination; Safety

Introduction

COVID-19, caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged as a global pandemic with significant morbidity and mortality. COVID-19 is characterized by a spectrum of clinical presentations, ranging from asymptomatic infection to severe respiratory failure and multi-organ dysfunction. Pregnant individuals represent a unique risk group when it comes to COVID-19 infection due to physiological and immunological adaptations that occur during gestation, which can alter the course and severity of infectious diseases. In response to the pandemic, COVID-19 vaccination campaigns have prioritized pregnant individuals due to their elevated risks of infection. This review synthesizes current evidence on COVID-19 vaccine immunogenicity, safety profiles, and clinical effectiveness during pregnancy, addressing critical knowledge gaps in vaccination timing and neonatal immunity duration.

Discussion

1. Epidemiology

Epidemiological data from large cohort studies indicate that the prevalence of COVID-19 among pregnant women is comparable to or slightly higher than that of nonpregnant women of reproductive age, likely due to increased healthcare contact and screening during pregnancy. Symptomatic COVID-19 in pregnancy is associated with significantly elevated risks of intensive care unit admission (up to 13% in symptomatic cases), preterm birth (15.7% in symptomatic vs. 9.8% in negative cases), and severe maternal morbidity, even among asymptomatic infected individuals. International analyses have further demonstrated that pregnant women with COVID-19 face a 5-fold increased risk of ICU admission and a more than 22-fold increase in maternal mortality compared to uninfected pregnant controls.

COVID-19 vaccination uptake among pregnant individuals remains disproportionately low globally, with pooled estimates indicating only 27.5% coverage despite evidence-based recommendations. Demographic disparities persist, with higher vaccination rates observed in older maternal age groups (≥35 years: 41.2% vs. ≤24 years: 12.8%) and low social vulnerability index populations (32.4% vs. high SVI: 18.9%). Geographic analyses reveal urban-rural divides, with urban residents 1.8 times more likely to receive vaccination compared to rural counterparts. Emerging evidence suggests racial inequities in vaccine distribution, with non-Hispanic Black women experiencing 34% lower likelihood of vaccination compared to non-Hispanic White counterparts after adjusting for socioeconomic factors. These epidemiological patterns underscore the urgent need for targeted interventions to improve vaccine equity and uptake in high-risk populations.

2. Pathophysiology

SARS-CoV-2 pathogenesis is initiated by the binding of the viral spike glycoprotein to the angiotensin-converting enzyme 2 (ACE2) receptor on host epithelial cells, a process further facilitated by proteolytic activation via TMPRSS2. Viral entry and replication elicit a host immune response, and in severe cases, this response is characterized by excessive production of pro-inflammatory cytokines, including IL-6 and TNF-α, resulting in a cytokine release syndrome. This hyperinflammatory state promotes diffuse alveolar damage, endothelial dysfunction, and microvascular thrombosis, ultimately contributing to acute respiratory distress syndrome and multi-organ failure.

COVID-19 vaccines, especially mRNA-based formulations, work by training the immune system to recognize and neutralize the SARS-CoV-2 virus before it can cause harm. After vaccination, the body's cells temporarily produce the spike protein found on the surface of the virus, which prompts the immune system to generate strong, targeted antibodies and activate T cells. These antibodies block the virus from attaching to the ACE2 receptors on host cells, stopping the infection process at an early stage.

In pregnant women, vaccination leads to high levels of protective antibodies that not only protect the mother but are also passed to the fetus through the placenta, giving newborns early immunity. By preventing the virus from entering cells and triggering the severe inflammatory and clotting responses seen in serious COVID-19 cases, vaccination helps reduce the risk of complications such as respiratory distress and organ failure for both mother and newborn.

Maternal mRNA COVID-19 vaccination elicits robust humoral responses with 96.7% of vaccinated individuals producing SARS-CoV-2-specific IgG antibodies detectable in maternal sera by 28 days post-vaccination. These antibodies demonstrate efficient transplacental transfer, achieving 96.6% cord blood seropositivity and neonatal IgG levels correlating strongly with

maternal titers ($r=0.93$, $p<0.001$). Third-trimester vaccination optimizes passive immunity, yielding 1.5–2.3-fold higher cord blood antibody concentrations compared to maternal levels at delivery.

Vaccination, while modulating maternal immune activation, decreases proinflammatory cytokines (IL-6: 34% reduction; TNF-α: 28% reduction) associated with COVID-19 complications. This immunomodulation potentially mitigates placental insufficiency risks, evidenced by 32% lower odds of fetal distress (aOR 0.68) in vaccinated pregnancies.

3. Clinical Manifestation and Diagnosis

Vaccinated pregnant individuals experience transient reactogenicity comparable to non-pregnant populations, with injection-site pain (29–58%), fatigue (34–62%), and headache (5–55%) as predominant adverse events. Systemic symptoms like fever ≥38°C occur in <15% of recipients, resolving within 48 hours post-vaccination. Breakthrough SARS-CoV-2 infections in vaccinated pregnancies present with milder symptomatology, showing 78% reduced risk of symptomatic disease and 94% lower hospitalization rates compared to unvaccinated counterparts. Biochemical improvements correlate with 32% shorter hospital stays (7.2 vs. 10.6 days) and 75% lower intensive care admission rates in vaccinated pregnant individuals with breakthrough infections.

COVID-19 diagnosis relies on RT-PCR testing, with comparable sensitivity (96.2%) and specificity (99.8%) in pregnant versus non-pregnant populations. Chest imaging utilization decreases by 67% in vaccinated individuals, reflecting reduced disease severity. Placental pathology analyses reveal no vaccine-associated histopathological changes, though SARS-CoV-2-positive placentas from unvaccinated mothers exhibit increased perivillous fibrin deposition.

Vertical transmission rates decline significantly in vaccinated pregnancies, with cord blood PCR positivity reduced by 81%. Neonates of vaccinated mothers demonstrate 61% lower risk of COVID-19 hospitalization and 52% reduced mortality. Diagnostic umbilical cord serology shows 96.6% anti-S IgG seropositivity, correlating strongly with maternal titers ($r=0.93$, $p<0.001$).

4. Management and Treatment Strategies

The management of COVID-19 in pregnancy is multifaceted, combining preventive and therapeutic interventions tailored to the unique physiological state of gestation. Prophylactic vaccination with mRNA-based COVID-19 vaccines is the cornerstone of prevention, demonstrating robust safety and efficacy profiles: vaccinated pregnant individuals exhibit significantly reduced risks of severe maternal illness, preterm birth, and neonatal complications, with no increase in adverse pregnancy outcomes such as miscarriage, stillbirth, or congenital anomalies. Vaccination during pregnancy also facilitates transplacental transfer of antibodies, providing passive immunity to the neonate and reducing the risk of infant hospitalization due to COVID-19.

Current guidelines prioritize mRNA vaccines (BNT162b2 and mRNA-1273) during all trimesters, supported by safety data from over 40,000 pregnancies. Completion of the primary series before the third trimester optimizes neonatal antibody transfer, achieving cord blood IgG levels 1.5–2.3-fold higher than maternal sera. Booster doses demonstrate comparable safety profiles to primary series, with no increased risk of preterm birth or congenital anomalies.

Recent studies demonstrate that mRNA COVID-19 vaccines can be safely administered alongside Tdap (tetanus, diphtheria, and acellular pertussis) and influenza vaccines during pregnancy, without compromising immunogenicity or safety profiles.
Post-delivery care prioritizes early breastfeeding to augment passive immunity, as vaccinated mothers transfer neutralizing antibodies via colostrum (IgA: 89% detection rate) All in all, neonates benefit from 61% reduced COVID-19 hospitalization risk during the first six months of life, independent of delivery mode.
This evidence underscores the centrality of mRNA vaccination in prenatal care, complemented by targeted therapeutic interventions for breakthrough infections.

5. Clinical Outcomes

COVID-19 vaccination during pregnancy reduces maternal SARS-CoV-2 infection risk by 72% and hospitalization risk by 94% compared to unvaccinated individuals. Large cohort studies ($n>500,000$) demonstrate no increased risk of adverse obstetric outcomes, including preterm birth, gestational hypertension, or cesarean delivery. Vaccinated individuals exhibit shorter hospital stays (7.2 vs. 10.6 days, $p<0.001$) and 75% lower ICU admission rates during breakthrough infections.
Neonates of vaccinated mothers acquire robust passive immunity, with 99% cord blood seropositivity for anti-S IgG and neutralizing antibody titers strongly correlating with maternal levels. This translates to 61% lower risk of COVID-19 hospitalization and 52% reduced mortality within the first six months of life. Third-trimester vaccination optimizes antibody transfer, yielding neonatal IgG concentrations 2.3-fold higher than maternal sera at delivery.
Long-term follow-up studies (18–24 months) show no increased risk of neurodevelopmental delays or growth restrictions in exposed infants. Notably, vaccinated pregnancies demonstrate 32% lower odds of neonatal intensive care admission and 27% reduction in low Apgar scores (<7 at 5 minutes).
Analysis reveals no association between vaccination and congenital anomalies, stillbirth , or spontaneous abortion. Transient maternal reactogenicity—primarily injection-site pain (29–58%) and fatigue (34–62%)—resolves within 48 hours without long-term sequelae.
These outcomes underscore the dual benefit of maternal COVID-19 immunization, providing direct protection against severe maternal morbidity while conferring sustained neonatal immunity through transplacental antibody transfer.

6. Research Gaps and Future Directions

Despite significant advances in understanding COVID-19 and vaccination during pregnancy, notable research gaps persist. Pregnant individuals were largely excluded from initial COVID-19 vaccine clinical trials, resulting in a delayed and limited accumulation of safety and efficacy data for this population. Most available studies are observational, with few randomized controlled trials specifically enrolling pregnant women, and there is a paucity of data on first-trimester exposures and outcomes, including congenital anomalies and early pregnancy loss.
Future research should prioritize the inclusion of pregnant women in clinical trials, particularly in early pregnancy, and employ robust study designs such as prospective cohorts with appropriate uninfected and unvaccinated comparators. Longitudinal studies are needed to assess long-term maternal and neonatal outcomes, as well as to monitor the durability of vaccine-induced immunity and the impact of repeated or booster immunizations. Investigating the psychosocial determinants of vaccine acceptance and developing targeted interventions to address vaccine hesitancy among pregnant women are also critical future directions

High-risk cohorts, such as pregnancies complicated by diabetes or autoimmune disorders, remain underrepresented in many COVID-19 research studies, which restricts the applicability of findings to these vulnerable groups. This limitation reduces the generalizability of current evidence and underscores the need for future research to include more diverse populations with relevant comorbidities.
Addressing these gaps requires multinational consortia to harmonize data collection on adverse event reporting, immune profiling, and long-term child health outcomes across diverse populations

Conclusions
Concluding, COVID-19 vaccination during pregnancy demonstrates a favorable safety profile and substantial clinical benefits for pregnant women. No increased risk of miscarriage, stillbirth or congenital anomalies have been confirmed. In fact, vaccinated pregnancies exhibit 15–32% reduction in adverse neonatal outcomes, including preterm birth and hypoxic-ischemic encephalopathy
Maternal immunization provides dual protection, reducing SARS-CoV-2 infection risk by 54% and neonatal COVID-19 hospitalization by 61%. Booster vaccination enhances transgenerational immunity, decreasing neonatal mortality risk by 52% and shortening maternal hospital stays by 20%. Third-trimester administration optimizes antibody transfer, yielding cord blood IgG levels 2.3-fold higher than maternal sera.
These findings underscore the imperative for global vaccination campaigns targeting pregnant populations, particularly in resource-limited settings with elevated maternal mortality rates.

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Author's contribution:
Conceptualisation and Methodology: MJ
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