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Immunization of Newborns Born to Mothers with SARS-CoV-2 Infection: A Narrative Review

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Annotation: Background: The COVID-19 pandemic raised concerns about neonatal susceptibility, placental antibody transfer, and the timing and safety of routine immunizations. Objective: To synthesize evidence from 2020–2025 on vertical transmission of SARS-CoV-2, maternal–fetal antibody transfer (after infection or vaccination), neonatal immune features, and implications for routine vaccination of infants born to mothers with COVID-19. Methods: Narrative review of peer-reviewed studies and authoritative guidelines (WHO, ACOG, AAP). Results: Vertical transplacental transmission is rare (<1–3%). Efficient transfer of maternal IgG to SARS-CoV-2 occurs, with magnitude depending on timing of infection or vaccination. Maternal mRNA vaccination in pregnancy reduces COVID-19 hospitalizations in infants <6 months and increases infant antibody titers. No evidence supports delaying routine newborn vaccines (HepB at birth; BCG per national policy) solely due to maternal COVID-19. Conclusions: Routine immunization schedules should be followed for neonates of mothers with COVID-19; individualized assessment is warranted for premature or clinically unstable infants.

Keywords: COVID-19; SARS-CoV-2; newborn; maternal antibodies; transplacental transfer; vaccination; Hepatitis B; BCG; WHO; AAP.

Introduction

SARS-CoV-2 infection during pregnancy prompted re-evaluation of neonatal risks and early life vaccination strategies. Beyond the direct question of congenital infection, key issues include the efficiency and durability of maternal–fetal antibody transfer following infection or vaccination and whether maternal disease alters the safety or immunogenicity of routine newborn vaccines. This narrative review summarizes contemporary evidence and practice guidance relevant to immunization of newborns born to mothers with COVID-19 [4,16].

Methods

We searched peer-reviewed literature (2020–2025) in MEDLINE/PubMed and major journals (NEJM, JAMA Pediatrics, Nature Portfolio, BMJ, iScience), alongside guidance from WHO, ACOG, and AAP. Priority was given to cohort studies, systematic reviews, and authoritative guidance with clear methodology and relevance to neonatal immunization. Given the breadth of the topic and evolving evidence base, this review is narrative rather than systematic.

Results

Most studies demonstrate very low rates of confirmed in utero SARS-CoV-2 transmission. Recent cohorts and systematic reviews estimate congenital infection rates typically below 1% and rarely exceeding 2–3%, with higher risk associated with severe maternal disease and short intervals between infection and delivery. These data support routine neonatal care with appropriate infection control but do not warrant alterations to standard immunization schedules solely due to maternal COVID-19 [10,18].

Maternal–Fetal Antibody Transfer After Infection or Vaccination

Multiple cohorts show robust transplacental transfer of anti-SARS-CoV-2 IgG following maternal infection, with cord blood titers correlating with maternal titers and the interval from infection to birth.

Some studies reported comparatively reduced transfer versus influenza/pertussis antibodies when maternal infection occurred late in the third trimester, likely reflecting limited time for placental transport. mRNA vaccination during pregnancy induces high maternal titers with efficient transfer; infant IgG can persist for months (often into the second half-year of life). Transfer ratios and infant titers are influenced by trimester of vaccination and time since maternal immunization [1,5,19].

Impact of Maternal COVID-19 Vaccination on Infant Outcomes

Maternal mRNA vaccination during pregnancy is associated with reduced risk of COVID-19 hospitalization in infants younger than six months. Boosters in pregnancy further augment the magnitude and quality of antibody responses measured in early infancy. These findings underpin public-health recommendations to vaccinate pregnant individuals, both for maternal protection and indirect infant protection [3].

Neonatal Immune Features in the Context of Maternal COVID-19

Reports describe transient alterations in neonatal inflammatory markers and lymphocyte subsets among infants born to mothers with COVID-19; however, these changes have not been linked to diminished vaccine responsiveness in early life. Available data do not indicate increased frequency of serious adverse events after routine newborn vaccines in this population. Causes of Immune Suppression in Newborns Born to Mothers with COVID-19 [2,8].

During acute SARS-CoV-2 infection, elevated maternal levels of pro-inflammatory cytokines such as IL-6, IL-1β, TNF-α, and IFN-γ can cross the placental barrier or alter placental cytokine signaling [9,20].

Chronic intrauterine exposure to these mediators leads to “fetal inflammatory response syndrome” (FIRS), which can suppress normal thymic maturation and result in transient T-cell lymphopenia in the neonate [12].

SARS-CoV-2 infection can cause placental vasculitis, microthrombosis, and villous hypoperfusion, impairing nutrient and oxygen transport [7].

Hypoxia and oxidative stress in utero disturb hematopoietic stem-cell niches in the fetal liver and bone marrow, reducing the development of B- and T-lymphocyte precursors and altering innate immune activation after birth [11,15].

Maternal infection generates antibodies that are efficiently transferred to the fetus, but prolonged maternal immune activation may suppress fetal immune training [3]. The newborn receives high levels of maternal IgG, which may transiently inhibit endogenous antibody production (a phenomenon known as immune masking) [17].

Additionally, a limited transplacental transfer of IgA and IgM results in lower mucosal protection in the respiratory and gastrointestinal tracts. Maternal COVID-19, particularly if associated with antibiotic use, corticosteroids, or Cesarean delivery, can lead to altered colonization of the infant gut [14].

Reduced exposure to maternal vaginal and intestinal flora delays the establishment of beneficial bacteria such as Bifidobacterium and Lactobacillus, which are critical for immune tolerance and regulatory T-cell induction. This dysbiosis predisposes the newborn to inflammation and impaired vaccine responsiveness [18].

Inflammatory and metabolic stress in the maternal–fetal environment triggers epigenetic modifications (DNA methylation, histone acetylation) in fetal immune genes regulating cytokine production and antigen presentation. Alterations in cortisol and leptin signaling further modulate neonatal immune development, contributing to transient immunosuppression during early postnatal life [7].

Preterm delivery, neonatal hypoxia, and prolonged hospitalization (e.g., NICU care with oxygen therapy or antibiotics) are more frequent among infants of COVID-positive mothers. Such stressors cause oxidative damage to lymphocytes and reduce the pool of naïve T-cells, compromising both

innate and adaptive responses. The immune weakening observed in some neonates born to mothers with COVID-19 is multifactorial—driven by maternal inflammation, placental injury, altered antibody dynamics, microbiome dysbiosis, and epigenetic programming [4].

Most alterations are transient, resolving within weeks to months, yet they highlight the need for close immunological monitoring and timely vaccination of these infants [1].

Implications for Routine Newborn Vaccines

Hepatitis B: The universal birth dose (within 24 hours) remains indicated. For HBsAg-positive mothers, standard prophylaxis (HepB vaccine plus HBIG) applies without modification for maternal COVID-19 status. BCG: Administer per national policy when the infant is clinically stable; defer in the presence of acute illness or significant respiratory compromise. Other inactivated vaccines (e.g., DTP-containing, IPV, Hib, pneumococcal) should begin at the usual chronological age. There is no evidence to support delaying routine vaccines solely because the mother had COVID-19 [10].

Special Situations

Preterm or clinically unstable infants may require individualized timing of BCG and other vaccines, consistent with standard neonatal practice. Where severe maternal disease occurred close to delivery, clinicians may consider baseline immune evaluation of the infant; however, routine serologic testing is not required before immunization [13].

Practical Recommendations

- Adhere to national/WHO routine immunization schedules for newborns of mothers with COVID-19.
- Administer the Hepatitis B birth dose on time; follow standard HBIG protocols when indicated.
- Provide BCG when the infant is clinically stable; defer only for standard clinical reasons.
- Encourage maternal COVID-19 vaccination during pregnancy to enhance infant protection in early life.
- Avoid unnecessary deferral of vaccines based solely on maternal COVID-19 history [12, 20].

Conclusions

Evidence accumulated through 2025 supports routine immunization of newborns born to mothers with SARS-CoV-2 infection without additional delays or modifications. Maternal infection or vaccination results in transplacental transfer of functional IgG that may provide temporary infant protection, while timely active immunization remains essential to establish durable immunity.

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