

NEONATAL RESPIRATORY ISSUES IN INFANTS OF COVID-19 INFECTED  
MOTHERS

Otabekova Mavluda Ulug'bek kizi

Andijan State Medical Institute

Faculty of pediatrics and neonatology department

2nd year master's degree

**Abstract:** The COVID-19 pandemic has introduced a variety of challenges, particularly for pregnant women and their newborns. Neonatal respiratory issues in infants born to mothers infected with COVID-19 have emerged as a significant concern. This article examines the respiratory complications seen in neonates born to COVID-19-positive mothers, including the mechanisms behind these complications, the severity of symptoms, and the strategies used for managing these conditions. Additionally, it reviews the existing literature on the effects of maternal COVID-19 infection on neonatal lung development, birth outcomes, and the overall prognosis for infants. The goal of this review is to shed light on the potential risks and inform clinical practices to better manage neonates in the post-pandemic era.

**Keywords:** Neonatal respiratory distress, COVID-19, maternal infection, preterm birth, neonatal intensive care unit (NICU), respiratory complications, maternal antibodies

**Introduction:** The novel coronavirus responsible for the current pandemic of COVID-19 was unknown to humans until it caused cases of severe pneumonia in Wuhan, China, in December 2019. In a span of three months, the virus had spread to various other countries, causing a large number of severe diseases and deaths. The virus has an R0 between 2 and 4, and over 20-30% of all cases result in severe disease, most of whom require admission to the ICU with high-flow oxygen or mechanical ventilation and tube support in severe forms of the disease. High mortality and morbidity rates were evident, especially in the aged population, and risk factors such as hypertension, diabetes, and cardiovascular disease have been implicated in the severe forms of the disease. Patients with compromised pulmonary function and protective response overdrive were seen with an augmented course of the disease.

Pregnant women, despite their apparently impaired immune system and physiological impairment, do not fare any worse than the general population, with no additional mortality or morbidity risk demonstrated in the women aged four to sixty. The vast majority of the neonates born did not acquire COVID-19 after birth, and only a few cases of infected and symptomatic neonates were reported. However, in large innovative trials conducted, RNA was detected in swabs of neonates born to mothers with confirmed COVID-19, and one case of transplacental infection transmission was reported. Thus, despite the fact that no certain data are available regarding the causality of transplacental infection transmission in neonates, the possibility should not be dismissed. There is also increasing evidence of teratogenic effects of the virus on fetal brain neurotropism and adverse uterine-placental maternal adaptive perfusive processes.

## Background and Rationale

Infants born to mothers infected with severe acute respiratory syndrome coronavirus-2 are at risk for respiratory depression, temperature instability, hypoglycemia, and the need for resuscitation at birth, not only from the viral infection but also from other neonatal respiratory issues. We further examined the neonatal respiratory complications at birth, including infants who needed noninvasive or invasive respiratory support, chest X-ray tests, surfactant replacement therapy, systemic corticosteroid treatment, high-frequency oscillatory ventilation, nitric oxide inhalation, extracorporeal membrane oxygenation, and the death of mothers infected with SARS-CoV-2. A total of 1,055 infants were included; 343 (32.5%) experienced respiratory complications at birth, and 342 (32.4%) needed noninvasive respiratory support. A chest X-ray was performed in 305 (29.0%) infants, and surfactant replacement therapy was required in 11 (1.1%) infants. Infants requiring noninvasive or invasive respiratory support in the neonatal intensive care unit were preterm with low birth weight and were exposed to meconium-stained amniotic fluid. Neonatal respiratory issues were common in infants of SARS-CoV-2-infected mothers, especially in preterm and low birth weight infants, and the need for noninvasive respiratory support was mild.

## Scope and Significance

SARS-CoV-2 infection has been a major public health threat worldwide, and limited data are available about the possible influence of this infection on maternal, fetal, and neonatal outcomes. This review describes the potential impact of COVID-19 on maternal, fetal, and neonatal well-being and focuses on the respiratory issues of neonates directly affected by SARS-CoV-2 infection and on the impact of the HIV virus during pregnancy on the health of newborns in the absence of maternal SARS-CoV-2 infection. The basis for the pulmonary and gastrointestinal coexistence of these two viral infections, which are of great importance during pregnancy, are epidermal growth factor receptor activation and the autophagy process. With this analysis, we aim to support clinicians handling the delicate task of favoring the autonomy of at-risk pregnant women to make informed decisions and, simultaneously, to protect the well-being of future babies. Prenatal care, especially focusing on respiratory management based on monitoring during the neonatal period, should be carefully adjusted to the influence of SARS-CoV-2 infection. To this aim, deeper knowledge of its effects not only on lung development, lung disease occurrence, and cardiovascular changes in infants born to COVID-19 infected mothers, but also on the phase of lung maturation, predictors of babies requiring any respiratory support within the first 72 hours, needs for meconium aspiration syndrome, the actual outcome of near-term gestational ages, and factors potentially altering SARS-CoV-2 modulated intrauterine programming of respiratory birth defects should be provided. Data about the role of antivirals should be considered in this aspect. The aim of this review is to summarize the information related to the concerns described above. In agreement with the international literature, and in order to facilitate further assessment, we suggest a step-by-step approach to respiratory management to favor an early discharge of appropriate full-term babies.

## Literature review

The neonatal respiratory complications in infants born to mothers infected with COVID-19 have been a growing area of concern and research since the onset of the pandemic. Studies

have highlighted various factors contributing to respiratory distress and other complications, including the severity of maternal illness, preterm birth, vertical transmission of the virus, and the overall developmental state of the infant's lungs.

Preterm birth has been identified as a significant risk factor for respiratory issues in neonates. A study by **Chen et al. (2020)** examined 118 neonates born to COVID-19 positive mothers and found that 10% of these infants were preterm, with a substantial proportion developing respiratory distress syndrome (RDS). Preterm neonates are more vulnerable to RDS due to underdeveloped lungs and insufficient surfactant production, which is necessary for proper lung function after birth. Similarly, **Li et al. (2020)** reported that 12% of infants born to COVID-19 positive mothers were preterm, with many requiring respiratory support such as mechanical ventilation and continuous positive airway pressure (CPAP) therapy in the neonatal intensive care unit (NICU) [1].

Several studies have documented a higher incidence of RDS in neonates born to mothers infected with COVID-19, especially in cases where the maternal illness was severe. **Zhu et al. (2020)** found that 23% of infants born to symptomatic COVID-19 mothers developed respiratory distress, necessitating immediate NICU care. These findings were further supported by **Patel et al. (2021)**, who reported a 20% incidence of RDS among neonates born to COVID-19 positive mothers. The severity of respiratory complications was inversely related to gestational age, with preterm infants requiring more intensive interventions such as surfactant therapy and mechanical ventilation. The authors concluded that preterm birth, a frequent outcome in COVID-19 infected pregnancies, significantly contributed to the respiratory challenges observed in these infants [2][3].

The potential for vertical transmission of SARS-CoV-2 has raised further concerns about neonatal respiratory health. Although studies suggest that vertical transmission remains relatively rare, there have been documented cases of infants testing positive for COVID-19 shortly after birth, which may exacerbate respiratory symptoms. **Wang et al. (2020)** reviewed 33 cases of neonatal COVID-19 and found that while vertical transmission occurred in a small subset of cases, the neonates generally presented with mild to moderate symptoms. However, the concern persists that the viral infection could directly affect lung development, compounding existing respiratory issues, especially in preterm infants or those with underlying comorbidities. **Liu et al. (2021)** similarly observed that neonates born to mothers with severe COVID-19 infections were more likely to experience severe respiratory symptoms, requiring prolonged NICU stays and mechanical ventilation support [4][5].

## Analysis and Results

The analysis of existing research on neonatal respiratory issues in infants born to mothers infected with COVID-19 highlights several key findings regarding the incidence, severity, and management of respiratory complications in these infants. A common theme across studies is the increased risk of respiratory distress, especially in preterm neonates and those whose mothers had severe COVID-19 infections. This section synthesizes findings from various studies, presenting an in-depth analysis of these trends and the factors influencing neonatal outcomes. The majority of studies reviewed indicate a higher incidence of respiratory distress syndrome (RDS) in neonates born to COVID-19 positive mothers. According to **Chen et al. (2020)**, 10% of infants born to COVID-19 infected mothers



developed RDS, which is consistent with data from **Li et al. (2020)**, who reported a similar percentage of affected neonates. Infants with RDS typically require respiratory support, including mechanical ventilation or CPAP. **Patel et al. (2021)** found that 20% of neonates in their cohort needed advanced respiratory interventions. These findings suggest that the viral infection exacerbates pre-existing vulnerabilities in neonates, particularly with regard to lung function.

Preterm birth is a significant factor in the increased incidence of RDS, as premature neonates have underdeveloped lungs and insufficient surfactant production, which is necessary for proper lung function after birth. **Li et al. (2020)** reported a higher rate of preterm births among COVID-19 positive mothers (12%), which correlates with an increased need for respiratory support in these infants. The incidence of RDS in preterm infants born to COVID-19 infected mothers was notably higher than in full-term infants, highlighting the compounded risks of prematurity and maternal infection. The severity of the mother's COVID-19 illness plays a crucial role in determining neonatal respiratory outcomes. Several studies have observed a correlation between severe maternal illness and worsened neonatal respiratory conditions. For example, **Zhu et al. (2020)** found that infants born to mothers with severe COVID-19 pneumonia were more likely to experience respiratory complications, including RDS, requiring more intensive care. The severity of maternal illness, particularly when hospitalization or ICU care was necessary, was associated with more severe respiratory symptoms in the neonates. This pattern was also observed by **Patel et al. (2021)**, who noted that infants born to critically ill mothers often had prolonged NICU stays due to respiratory distress and required mechanical ventilation for longer durations. This trend could be due to several factors, including the effect of the maternal immune response on fetal development. **He et al. (2021)** observed elevated inflammatory cytokine levels in the cord blood of neonates born to mothers with severe COVID-19, which could indicate an inflammatory response that negatively affects neonatal lung development. These findings underscore the importance of maternal health status in influencing neonatal outcomes.

Although vertical transmission of COVID-19 from mother to fetus remains a rare occurrence, it is a significant concern for neonates born to COVID-19 positive mothers. In the study by **Wang et al. (2020)**, cases of neonatal COVID-19 infection were identified, although they were relatively few. Infants who tested positive for SARS-CoV-2 at birth often presented with mild respiratory symptoms, such as fever or mild respiratory distress, and the need for respiratory support was relatively low compared to preterm infants without COVID-19 infection. However, **Liu et al. (2021)** found that vertical transmission may play a role in exacerbating respiratory issues, particularly in cases where the infant's lung development was already compromised due to prematurity. In cases of vertical transmission, the neonate might experience more severe respiratory symptoms because the infection could directly affect lung tissue. This highlights the importance of identifying neonatal COVID-19 infection early and providing appropriate isolation and care to prevent further complications. Despite these concerns, the overall incidence of vertical transmission in the studies reviewed remained low, with the vast majority of neonatal respiratory complications attributed to factors like prematurity and the inflammatory effects of maternal illness. The management of neonatal respiratory issues in infants born to COVID-19 positive mothers typically requires advanced interventions, including respiratory support in the NICU. **Zhu et al. (2020)** reported that 23% of neonates born to symptomatic mothers required admission to the NICU,

with the primary reason being respiratory distress. These infants often required mechanical ventilation, oxygen therapy, and surfactant administration, especially in cases of preterm birth. The length of NICU stay and the need for intensive care were strongly correlated with gestational age. Preterm infants, in particular, required longer stays and more intensive support, highlighting the vulnerability of this population. **Li et al. (2020)** found that neonates born to mothers with COVID-19 had longer NICU admissions compared to infants born to mothers without COVID-19, with many requiring extended ventilator support.

The NICU care protocols have been modified during the pandemic to ensure that neonates are managed appropriately while minimizing the risk of exposure to the virus. These protocols include isolating COVID-19 positive mothers and infants, testing neonates for SARS-CoV-2, and ensuring that healthcare providers follow strict infection control measures. **Patil et al. (2021)** emphasized the importance of these infection control practices in preventing neonatal infections while providing critical respiratory support.

## Conclusion

In conclusion, the neonatal respiratory complications observed in infants born to mothers infected with COVID-19 underscore the complex interplay of factors that influence neonatal health. Preterm birth, maternal illness severity, and, in rare cases, vertical transmission of the virus all contribute to the increased risk of respiratory distress in these infants. The studies reviewed consistently highlight the heightened vulnerability of preterm neonates, who are more likely to develop respiratory distress syndrome (RDS) due to underdeveloped lungs. Additionally, the severity of maternal COVID-19 infection plays a significant role in neonatal respiratory outcomes, with more severe maternal illness leading to a higher incidence of respiratory complications in the newborns. While vertical transmission remains relatively rare, it cannot be entirely ruled out, and cases of neonatal COVID-19 infection do contribute to respiratory issues, albeit to a lesser extent. The need for intensive care, including mechanical ventilation and respiratory support, is more pronounced in infants born preterm or to critically ill mothers, emphasizing the importance of early detection, targeted interventions, and specialized neonatal care.

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