Acta Scientific PAEDIATRICS (ISSN: 2581-883X)

Volume 4 Issue 8 August 2021

Review Article

Challenges in the Diagnosis and Management of Newborns of COVID-19 Positive Mothers

Sufia Athar[1]*, Sarfraz Abedin[2] and Wasim Lodhi[3]

[1]Specialist Obstetrics and Gynecology, Al-Wakra Hospital, HMC, Qatar

[2]Specialist NICU, Pediatric, Al-Wakra Hospital, HMC, Qatar

[3]Consultant Obstetrics and Gynecology, North Middlesex University Hospital, London, UK

***Corresponding Author:** Sufia Athar, Specialist Obstetrics and Gynecology, Al-Wakra Hospital, HMC, Qatar.

Received: July 13, 2021

Published: July 26, 2021

Abstract

Coronavirus disease (COVID-19) pandemic has affected every nook and crook of the world. With the second and the impending third wave, the situation has further deteriorated. Neonates, being the vulnerable section of society, need more vigilance. With current recommendations, newborns of the infected mothers are being tested at birth. Considering the false-negative results of SARS-CoV-2, RT-PCR in children, neonates are liable to have higher false-negative results. Newer studies have revealed that neonates may develop the symptoms even after 5 - 21 days of birth. This may lead to delays in the diagnosis and the possibility of transmission of the disease to the caregivers. In this review, the current challenges in the diagnosis and management protocols of neonates are discussed, lightening the importance and protection for caregivers.

Keywords: Coronavirus Disease (COVID-19); SARS-CoV-2; RT-PCR

Introduction

The global COVID-19 pandemic has affected lives all around the globe. According to the recent WHO estimates nearly 162,800,00 cases and more than 3 million deaths were reported so far [1,2]. No age, no sex, no race could defy its spread. Earlier, neonates and children were at low risk. However, with the current scenario, even this group does not seem to be spared [3].

With the increase in the neonates being infected with the COVID-19 virus, the current CDC recommendation is to test all neonates of the infected mother for SARS-CoV-2 RNA by reverse transcription-polymerase chain reaction (RT-PCR) within the first 24 hours of birth [2,4]. For those neonates who test negative, a repeat RT-PCR is recommended at 48 hours of birth or earlier if planned for discharge [2,4]. However, the literature review suggests that neonates of infected mothers may develop symptoms in the two subsequent weeks, and even those that tested negative after birth develop symptoms and complications later [5].

This leads to insight into the need for repeat testing of the neonates between 7 - 10 days of birth. Current CDC guidelines do not recommend repeat testing unless symptoms are observed. Studies in children and adults have revealed a possible feco-oral transmission. Newborns that are tested negative within 24 hours of birth are advised routine newborn care. This may lead to transmission from these neonates to the caregivers. Considering the lower sensitivity of RT-PCR in neonates and delayed manifestations of COVID-19 symptoms in this group, a literature review was carried out to understand the challenges in the diagnosis and management of the neonates.

What do we know about neonates of COVID-19 infected mothers?

Recent reviews and meta-analysis on this cohort of the population have revealed that some neonates, tested negative at birth develop symptoms after 3 - 4 days and often need hospitalization. Some of the cases had severe complications and severe neonatal morbidity and mortality even though significant babies were tested in 24 hours of birth [4-6]. Trevisanuto., *et al*. 2021, in a systematic review, reported that the median age of testing positive in neonates of the infected mothers was 5 days and it ranged from 2 - 17 days. 77% of these were diagnosed during the hospital stay and 33% of neonates were admitted back after discharge from the hospital. 44% of these neonates had contact with infected mothers in hospital and home.

68% of these neonates were symptomatic with the onset of symptoms noted between 2 - 19 days of birth with a median of 10 days of birth. 11% required mechanical ventilation and 6% needed non-invasive respiratory support. Complications were noted in 6% of cases. The average hospital stay was 10 days [5].

Mullins., *et al*. 2021 reported that 0.9 - 2% of the infants of COVID-19 positive mothers were tested positive. In this study, only 9.5% of the neonates were tested in the PAN-COVID study, and 87.80% of neonates were tested in the AAP-SONPM study. Early neonatal death was noted in 0.2 - 0.3% [7].

In a study by Villar., *et al*. 2021,13% of the neonates tested were positive. But surprisingly, Severe Neonatal Morbidity index (SNMI), Severe perinatal morbidity and mortality index (SPMMI), and prolonged NICU stay were higher in neonates of infected mothers, who were tested negative for COVID-19 [8].

All the above studies indicate that lots of neonates who are potentially infectious are tested negative at birth. This means that the sensitivity of RT-PCR is low in this age group. The other point to note is that symptoms were noted in neonates from 2-19 days of birth [5]. Neonates with the late manifestation of the disease suggest the need for continued vigilance and repeat tests to rule out potential positive cases even after the discharge.

Transmission of SARS-COV-19 virus from mother to the fetus

Dean., *et al*. 2020 suggested that transplacental infection is considered if a mother is infected with the COVID-19 virus with the last 2 weeks of childbirth or 2 days postpartum. Early exposure to the virus is considered if the neonate tests positive within 24 hours after birth from RT-PCR of the respiratory tract, and or if the virus is noted in the amniotic fluid, fetal blood, or umbilical cord blood. Persistence of infection is considered if the antibodies (SARS-CoV-2 IgM) are present > 24 hours-7 days of birth [9].

In neonates who develop symptoms later than 48 hours of birth, there are two probabilities, one is getting the late manifestation of symptoms and the other is acquiring the disease from the infected mother. If we investigate the transmission of the SARS-COV-19 virus, the current literature suggests that the COVID-19 virus can be transmitted through transplacental route, direct contact with infected mother/caregiver, and through droplet infection of the diseased.

In previous studies, placentas of women were noted to have intervillous or subchorionic fibrin, thrombotic vasculopathy, and ischemia. These findings explain the transplacental transmission and pathology of the fetal complications noted in-utero [10-13].

Neonates of infected mothers, who did not have trans-placental transmission may acquire the disease from droplets and direct contact with the mother, family members, or health caregivers. Transmission by this mode is low in neonates and children and usually mild disease in noted [14-16]. However, studies on neonates in this regard are sparse.

Sensitivity of the available diagnostic tests in neonates and children

In children, the sensitivity of rapid antigen tests and RT-PCR is noted to be lower than in adults [17,18]. In one study, nasal swab RT-PCR had 58.1% sensitivity and 97.7% specificity in children > 6 years. In kids, less than 6 years sensitivity and specificity were 66.7% and 97.8% respectively. In comparison to nasopharyngeal aspirate, lower sensitivity but higher specificity was noted for nasal swabs [18]. In an earlier study, the sensitivity of RT-PCR for respiratory syncytial virus (RSV) and Influenza A virus from a nose-throat swab in children was noted to be 93.1% and 91.9% respectively [19]. This indicates that SARS-CoV RT-PCR has a higher likelihood for false-negative results in children even more than other respiratory viruses. In neonates, studies in this regard were not found after an extensive search.

Pagani., *et al*. reported that SARS-CoV-2 IgG seroprevalence varies with age. This may suggest different sensitivity in different age populations [20]. Winichakoon., *et al*. have noted that a high cohort of the population tested negative by RT-PCR (nasopharyngeal/oropharyngeal swab) during the COVID-19 pandemic had false-negative results and similar findings were noted during the Middle East respiratory syndrome outbreak [21,22].

These studies indicate that in neonates of infective mothers, there is a need to repeat the RT-PCR.

The role of children in the transmission of SARS-CoV-2

Now let's review, the transmission of SARS-CoV-2 in children. The preponderance of this is higher in neonates. Studies have revealed prolonged viral shedding of this virus in infants and children as compared to adults [23-25]. In a study, viral-RNA was noted in stool samples in pediatric patients for more than 4 weeks though clearance from the respiratory passage was noted in two weeks after cessation of symptoms (mainly fever) [23]. Gou., *et al*. 2021 [26] in their research strongly suggested the evidence for gastrointestinal manifestations of SARS-CoV and the possibility of feco-oral transmission. Probably this would be more applicable in caregivers of neonates who are tested positive with mild disease and those who have false-negative results

Conclusion

All the above facts demand the need for additional testing of the neonates of diseased mothers around 5 - 10th day of birth. All these neonates need to be nursed with precautions for transmission to the caregivers for a minimum of 2 - 3 weeks of birth. On the other hand, it is equally important to follow CDC guidance for contact precautions from the infected mothers. Further studies in this regard are recommended.

The current situation of the pandemic is devastating and exhaustive for health care providers. Even a step to prevent the transmission of the disease would essentially decrease the global burden of the pandemic.

Bibliography

1. World Health Organization. WHO Coronavirus Disease (COVID-19) Dashboard (2021).
2. Centers for Disease Control and Prevention. "Evaluation and Management Considerations for Neonates at risk for COVID-19" (2021).
3. Ludvigsson JF. "Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults". *Acta Paediatrics* 109 (2020): 1088-1095.
4. "Evaluation and Management Considerations for Neonates At Risk for COVID-19". CDC (2020).
5. Trevisanuto D., *et al*. "Coronavirus infection in neonates: a systematic review". *Archives of Disease in Childhood - Fetal and Neonatal Edition* 106 (2021): 330-335.
6. Juan J., *et al*. "Effect of coronavirus disease 2019 (COVID-19) on maternal, perinatal and neonatal outcome: systematic review". *Ultrasound in Obstetrics and Gynecology* 56 (2020): 15-27.
7. Mullins E., *et al*. "Pregnancy and neonatal outcomes of COVID-19: co-reporting of common outcomes from PAN-COVID and AAP-SONPM registries". *Ultrasound in Obstetrics and Gynecology* 57 (2021): 573-581.
8. Villar J., *et al*. "Maternal and Neonatal Morbidity and Mortality Among Pregnant Women With and Without COVID-19 Infection: The INTERCOVID Multinational Cohort Study". *JAMA Pediatrics* (2021).
9. Algarroba GN., *et al*. "Visualization of SARS-CoV-2 virus invading the human placenta using electron microscopy". *American Journal of Obstetrics and Gynecology* 223.2 (2020): 275-278.
10. Ng WF., *et al*. "The placentas of patients with severe acute respiratory syndrome: a pathophysiological evaluation". *Pathology* 38 (2006): 210-218.
11. Li M., *et al*. "The SARS-CoV-2 receptor ACE2 expression of maternal-fetal interface and fetal organs by single-cell transcriptome study". *PLoS ONE* 15 (2020): e0230295.
12. Blumberg DA., *et al*. "Vertical Transmission of SARS-CoV-2: What is the Optimal Definition?" *The American Journal of Perinatology* 37 (2020): 769-772.
13. Vivanti AJ., *et al*. "Trans-placental transmission of SARS-CoV-2 infection". *Nature Communications* 11 (2020): 3572.
14. Solís-García G., *et al*. "Epidemiología, manejoyriesgodetransmisiónde SARS-CoV-2 enunacohortedehijosdemadresafectasde COVID-19". *Anales de Pediatría* 94 (2021): 173-177.

15. Laws RL., *et al*. "Symptoms and Transmission of SARS-CoV-2 Among Children — Utah and Wisconsin". *Pediatrics* 147.1 (2021): e2020027268.

16. Posfay-Barbe KM., *et al*. "COVID-19 in children and the dynamics of infection in families". *Pediatrics* 146.2 (2020): e20201576.

17. González-Donapetry P., *et al*. "SARS-CoV-2 Working Group. Think of the Children: Evaluation of SARS-CoV-2 Rapid Antigen Test in Pediatric Population". *The Pediatric Infectious Disease Journal* 40.5 (2021): 385-388.

18. Di Pietro GM., *et al*. "Diagnosis of SARS-CoV-2 in children: accuracy of nasopharyngeal swab compared to nasopharyngeal aspirate". *European Journal of Clinical Microbiology and Infectious Diseases* 40 (2021): 1155-1160.

19. Pagani G., *et al*. "Seroprevalence of SARS-CoV-2 IgG significantly varies with age: results from a mass population screening (SARS-2-SCREEN-CdA)". *Med Rxiv* (2020).

20. Winichakoon P., *et al*. "Negative nasopharyngeal and oropharyngeal swabs do not rule out COVID-19". *Journal of Clinical Microbiology* 58 (2020): e00297-e00220.

21. Memish ZA., *et al*. "Respiratory tract samples, viral load, and genome fraction yield in patients with Middle East respiratory syndrome". *The Journal of Infectious Diseases* 210 (2014): 1590-1594.

22. Xing YH., *et al*. "Prolonged viral shedding in feces of pediatric patients with coronavirus disease". *Journal of Microbiology, Immunology and Infection* 53 (2019): 473-480.

23. Li X., *et al*. "The role of children in transmission of SARS-CoV-2: A rapid review". *Journal of Global Health* 10 (2020): 011101.

24. Widders A., *et al*. "SARS-CoV-2: the viral shedding vs infectivity dilemma". *Infection, Disease and Health* 25.3 (2020): 210-215.

25. Liu P., *et al*. "Dynamic surveillance of SARS-CoV-2 shedding and neutralizing antibody in children with COVID-19". *Emerging Microbes and Infections* 9 (2020): 1254-1258.

26. Guo M., *et al*. "Potential intestinal infection and faecal-oral transmission of SARS-CoV-2". *Nature Reviews Gastroenterology and Hepatology* 18 (2021): 269-283.

Volume 4 Issue 8 August 2021