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CLINICAL MANIFESTATIONS OF COVID-19 IN THE NEWBORN: A NARRATIVE REVIEW

Indinara Arimateia Rodrigues da Silva*, Vanessa Cedraz dos Santos, Jaciele de Souza dos Santos, Juliane Batista Costa Teixeira, Chesney Mota Oliveira, Aisiane Cedraz Morais, Keyla Catharine Ribeiro Pereira, Juliana Silva Santos, Laisa Silva Santos and Rayciane Santos Suzart Ramos

Health Department, State University of Feira de Santana (UEFS)

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Corresponding author:
Indinara Arimateia Rodrigues da Silva

ABSTRACT

Objetivo: Investigar quais as manifestações clínicas apresentadas pelo recém-nascido infectadopor SARS-CoV-2. **Método**: Realizou-se umarevisão narrativa da literatura em 117 artigos, durante o mês de maio de 2020, tendo como período de referência os últimos quatro meses. Desses, foram selecionados 15 textos para análise, desenvolvida com base em artigos publicadosnas plataformas*The Jornal Pediatrics* e PUBCOVID19. **Resultados:** As características clínicas em neonatos são mais brandas que no adulto. Os indícios clínicos estão embasados na fisiopatologia da invasão celular por meio da Enzima Conversora de Angiotensina 2, presente no sistema respiratório e gastrointestinal. Dessa forma, as manifestações clínicas são altamente variáveis, sendo preferencialmente respiratórias como tosse, dispneia e coriza, além de hipertermia associados ou não a sintomas gastrointestinais como diarreia e vômitos. Indicadores atípicossuscitam uma resposta inflamatória similar à doença de *Kawasaki* e manifestações neurológicas. Sinais de alerta como a neutropenia grave indicam uma possível coinfecção.O diagnóstico atualmente é fundamentado em achados de opacidade em vidro fosco na TC de tórax, suspeita epidemiológica e rastreamento de contato. **Conclusão:** A população pediátrica é altamente vulnerável a doenças infecciosas. O curso da doença em pacientes pediátricos difere dos casos em adultos. A gravidade evolui leve.

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INTRODUCTION

At the end of 2019, the contemporary world began to live a new context presented by the emergence of the new Coronavirus called SARS-CoV-2, which appeared in China in the city of Wuhan (ZHU N *et al*., 2020). The first cases were reported as an outbreak of pneumonia of unknown origin, which soon after would be confirmed as the virus causing the disease 2019-nCoV or COVID-19 (LU R *et al*., 2020). The pathophysiological understanding of the virus is still restricted, but it is known that its clinical repercussion can range from a common cold to severe pneumonia, in its most severe reaches, groups with risk factors such as newborns (NB).NB who are in the neonatal period are understood as neonates, that is, up to 28 days after birth. The clinical manifestations of the infection are highly variable and are preferably respiratory, such as cough, dyspnea and runny nose, in addition to hyperthermia associated or not with gastrointestinal symptoms (BRAZIL, 2020a). The information obtained at the time of the study, approximately four months after the declaration of pandemic situation by the World Health Organization (WHO) is still ephemeral, but studies already state that newborns are less affected than adults by COVID-19.However, cases of deaths and greater severity have already been reported (DONG Y *et al*., 2020; DUARTE, 2020). A research conducted in mainland China shows that clinical manifestations are lighter, however, the NBs assume a higher risk position for infection (DONG *et al*., 2020) due to the immaturity of their immune system (BRAZIL, 2020b). The virus has high transmissibility and rapid dissemination from droplets and aerosols from person to person, with an average period of 5.2 days and can reach up to 12.5 days, being transmitted on average seven days after the onset of symptoms (BRAZIL, 2020a). The vertical transmission has so far not been validated.Reported cases of confirmed neonatal infection were presented causing a possible vertical contamination; however, these had close contact with people with confirmed positive results (PIERSIGILLI *et al*., 2020). Due to the volatile presentations of the disease and the nonspecific clinical picture, it is essential to identify which clinical indicators may be present in the NBs, so that the professional has sufficient knowledge to perform the appropriate behavior (VENTURINI *et al*., 2019). The signs presented by the baby should be easily understood and analyzed

in a judicious and individual way during this period, especially because the most severe respiratory distress syndromes appear concomitantly with other conditions characteristic of this phase. Concerning the behavior to be adopted, it should be based on the clinical picture of the mother and newborn, which requires following guidelines and recommendations of the protocols in force.The main guidelines for health professionals is the early identification of a condition with acute respiratory symptoms followed by isolation, team alternation, protection of professionals, pregnant women and newborns, stratification of symptomatic people and maximum protection of the team (BRAZIL, 2020c; PROCIANOY *et al*., 2020).In view of this, in order for nursing professionals to be able to recognize a neonate with suspected COVID-19, understand and act briefly, it is necessary to deepen and discuss the theme, allowing the construction of knowledge in the field of neonatal nursing. Thus, the aim of this article was to investigate the clinical manifestations of neonates infected with SARS-CoV-2, in order to provide subsidies that will help in the care practice and prevention of diseases.

METHODS

This is a narrative literature review. This is constituted by a broad analysis of the literature, which does not establish a rigorous methodology, but allows achieving and updating the knowledge on a specific theme from a theoretical perspective, being possible to synthesize the knowledge already existing in the literature by aggregating the authors'considerations and arguments in a way that directs the practice (ISER *et al*., 2020). Since this is a bibliographic analysis on the signs and symptoms of COVID-19 and the understanding of the repercussions on infants in the neonatal period, the selection included articles indexed in the databases The Journal of Pediatrics and PUBCOVID19, during May 2020, whose reference period was the past four months. The terms of indexation or descriptors Coronavirus infections, signs and symptoms, newborns were applied in isolation or in combination. The criterion used for inclusion of publications was to have the expressions used in the title or keywords, or that the abstract explicitly showed that the text was related to the association of clinical manifestations linked to newborns. The excluded articles did not present the established inclusion criterion and/or presented duplicity, i.e., publications retrieved in more than one of the databases. Dissertations and theses were also excluded. The initial search result in the databases returned 117 articles, 108 from The Journal of Pediatrics and 09 from PUBCOVID19. After the key information was collected, the titles and abstracts were firstly read, excluding 90 texts because they did not include the established age group. Subsequently, the 27 remaining texts were read completely, of which 15 were selected to write the article. The studies were initially classified according to the particularities of the sample, as well as those whose samples included neonates with clinical involvement by COVID-19.

RESULTS ANDDISCUSSION

The study conferred the reflection of the main clinical manifestations presented by newborns affected by COVID-19 as well as the warning signs of evolution to a poor prognosis.This narrative review highlights some vulnerability factors to which newborns are exposed, such as immaturity of the immune system, emphasizing the higher risk of premature babies because they are more prone to infections, as well as those with congenital malformations or severe comorbidities. The main findings show that the disease process of neonates is directly linked to the exposure of the infection in the foci in the body, where each affected system defines the clinical manifestation. Authors point out the limitations of the newborn's immune system due to deficiency in the response to invasive pathogens as a result of the deficit in the innate and adaptive mechanism of birth, which makes the NB susceptible to infections. Therefore, extreme preterm infants have 5-10 times higher chance of infection (DINIZ *et al*., 2014; RIZZON, 2011). Throughout the research, the scarcity of scientific studies of confirmed neonatal positive cases was limited.Zumla (2016) claims thatinfections with the human coronavirus (HCoV) strains HCoV-229E, HCoV-OC43, HCoV-NL63 and HCoV-HKU1 generally result in mild, self-limited infections of the upper respiratory tract, such as the common cold. In contrast, in Brazil, about 13 babies have died victims of COVID-19 and cases of greater severity have already been reported (DUARTE, 2020). Recent studies Zhu N *et al*. (2020) and Chen H *et al*. (2020) show that pregnant women usually evolve well to the presence of the virus; however, these results make explicit the increase of comorbidities in this population, revealing the higher risk of complications during pregnancy due to COVID-19, such as the possibility of premature deliveries. Thus, attention is drawn to the possible complications resulting from a premature delivery, as well as the preparation of care units for cases such as these. Entering the hospital tonic, Brazil (2020b) describes the role of nursing in the environment of the delivery unit and care for the newborn, highlighting the performance of a good anamnesis for an adequate management in the admission of pregnant women, establishing flows for care, separating COVID-19 suspected or confirmed patients; precautions necessary to prevent the transmission of COVID-19 by contact,droplets and aerosols between patients, family members and health professionals; ensuring bonding and encouraging the presence of asymptomatic fathers and mothers; management of the newborn and their safe and timely hospital discharge. With the health crisis and the intense social changes, there is still concern about the inference of the pandemic in the healthy growth of those babies. In general, the SARS-CoV-2 virus, of the Coronaviridae family, has pathophysiology based on the ability of cell invasion through the Angiotensin-Converting Enzyme 2 (ACE-2), present in the respiratory and gastrointestinal system, whose incoming receptor (CESPEDES *et al*., 2020) is similar to the SARS-C that caused the Coronavirus epidemic in China in 2003 (BOSH, 2003). The results indicate the variation in clinical presentation from asymptomatic infections, mild upper airway infection (Influenza Syndrome) to Severe Acute Respiratory Syndrome (SARS), evolving to severe respiratory failure and Cardiorespiratory Arrest (CRA); acute cardiac injury and secondary infection or co-infection (ZHU N *et al*., 2020; VENTURINI *et al*., 2020; BRAZIL, 2020c; YALING *et al*.; W-H Z, 2020). The same studies generally indicate that SARS-COV-2 infection identified by upper respiratory symptoms such as dry cough, rhinorrhea, respiratory distress, tachypnea, and fever; however, neonates may present atypical signs such as vomiting and diarrhea and other gastrointestinal signs such as intolerance to feeding or impaired feeding. Upper respiratory signs precede gastrointestinal signs. One of the main explanations suggested for the occurrence of milder symptoms and the lowest involvement in this age group by the virus is supported by studies that show the lower production of ACE-2 and immaturity of ACE-2 receptors in the lower respiratory tract, humoral immune responses and underdeveloped cells (FERNANDES, 2020).

To She *et al*. (2020), the virus is highly contagious when compared to SARS-CoV in 2003 with over 1000 cases worldwide; the MERS-CoV outbreak in June 2012 with 1180 and the SARS-CoV-2, which, in less than 25 days, reached the mark of 1,297 cases in China. The mean incubation period of COVID - 19 in children is longer than in adults, being approximately 6.5 days, and 5.4 days in adults. Characterized as a generalized infection manifesting clinically through exposure to infection in the foci in the body, being transmitted especially through respiratory droplets, aerosols and close contact. As already mentioned, SARS-CoV-2 binds to the ACE-2 receptor, thus the virus has as binding site the cells that express the receptor, stimulating a chain response. The first cells that express ACE-2 receptors are the cells of the human mucosa, such as the lips, eyelids and nasal cavities, which are exposed to air. Evidence indicates that soon after, there is contamination of the conjunctival epithelium by infectious droplets and body fluids. Ocular complications in infected patients caused by respiratory virus may lead to acute respiratory tract infection.Similarly, receptors are present in the lung, also reflecting on lung function. Researchers also found the presence of ACE-2 receptors in the gastrointestinal system especially in stratified stomach epithelial cells, and in intestinal epithelial cells in the ileum and colon, clarifying the occurrence of

digestive symptoms in some babies. This information guides emergency and management plans in units containing children during the pandemic (SHE *et al*., 2020). Some atypical cases with skin rashes triggering an inflammatory response similar to Kawasaki disease (CASTRO, 2020), fever and neurological manifestations have been reported; however, there is no scientific basis to prove the relationship between these findings and the virus (CHACÓN-AGUILAR *et al*., 2020).However, one draws attention to the risk of rapid evolution to severe conditions. A systematic review pointed out the case of a 23-day-old neonate with COVID-19, presenting symptoms with low fever and mild respiratory symptoms, which evolved to severe neutropenia over a period of five days, which implies a possibility of a different pathway of immune response and secondary infections (VENTURINI, 2020). In that sense, She *et al*. (2020) describe that the presence of covid-19 involvement may lead pediatric cases to five clinical types, with asymptomatic, mild, common, severe and critically severe infection, with symptom fever as the most common, lasting from 1 to 8 days, routine blood tests showed normal results or with change in c-reactive protein temporarily.A severe case involving a child reported in the study started with gastrointestinal symptoms, with no evident respiratory manifestations, but progressed rapidly to acute respiratory distress syndrome. It should be noted thatthe presence of significant comorbidities, such as congenital anomalies, sickle cell anemia and or developmental delay associated with long-term dependence on technological support, increases the likelihood of severe complications.One of the main adversities encountered in care refers to the correct screening for the definition of the suspected case in the light of clinical manifestations, since no specific clinical picture for neonatal COVID-19 infection is defined (SHEKERDEMIAN *et al*., 2020; SHE *et al*., 2020).

Thus, it is essential to adopt clinical management correctly since the initial contact with health services. It is necessary to consider and differentiate each case, namely: the definition of suspected case of NB is established in NB of mothers with a history of suspected or confirmed infection by COVID-19 between 14 days before delivery and 28 days after delivery; or NB directly exposed to people infected with COVID-19,whether close persons or professionals directly involved in their assistance. Confirmation should be based on the positive result for COVID-19 through reverse polymerase-transcriptase chain reaction (RT-PCR), in samples of the respiratory tract with swab collection, one sample from the oropharynx and another from the nasal cavity (BRASIL, 2020b). The diagnostic criteria for symptomatic NBsfor COVID-19 infection include at least one clinical symptom including unstable body temperature, low activity or inadequate feeding or shortness of breath; chest x-ray findings showing abnormalities containing unilateral or bilateral ground-glass opacities, multiple lobular or subsegmental areas of consolidation;or an indication of high risk for COVID-19 infection with COVID-19 diagnosed in the patient's family or caregivers; and or intimate contact with people with suspected or confirmed COVID-19; or patients with pneumonia of unexplained cause (BRAZIL, 2020c). The main route of transmission is the horizontal, form an infected mother or health care provider, through droplets or by contact with biological material subsequently infected. Precaution measures such as using masks, the distance between mother-baby, except during breastfeeding and the hygiene of hands and surfaces are considered fundamental actions to prevent the transmission of the virus to newborns (BRAZIL, 2020b). Thus, neonatal care aims to protect the health team and close contacts, avoiding the evolution of cases to death. The process begins from the moment the team is notified of the hospital admission of a mother with suspected or confirmed COVID-19, in which a complete anamnesis should be performed to identify perinatal risk factors and plan actions (BRAZIL, 2020d).

CONCLUSION

The pediatric population is identified as highly vulnerable to infectious diseases. Consequently, this public requires careful observation during an infectious outbreak. Although statistics show the low probability of NB and children evolving with severe conditions caused by SARS-CoV-2 infection.The information suggests the lack of a compulsory pattern in this cohort, leaving several gaps in knowledge, adding to the fact that the data found in the literature are instantaneous, taking into account that the course of the pandemic is active in several places of the world.The course of the disease in pediatric patients differs from cases in adults. Gravity evolves mildly. The scenario of challenges and uncertainties for the general population requires self-care actions and respect for prevention measures in order to achieve the protection of the collective and the individual. Acting responsibly consequently reduces the rates of spread of the virus preventing the involvement of risk groups and or with risk factors such as newborns, since it has been proven that the transmission in this group occurs horizontally. It is believed that the reflections presented during the work add to the formation of a new look towards newborns, as a vulnerable group, thus improving the response of specific care actions. Therefore, it triggers the possibility of criticality, relating the convergences between the newborn and COVID-19, basing the efficient clinical management, as well as the implementation of relevant strategies.

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