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DIAGNOSES AND COMPLICATIONS OF NEONATES OF COVID-19 POSITIVE MOTHERS

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Julia Kerr Catunda Machado[1] and Angelica Ferreira Gali[2]

ABSTRACT

Introduction: Pregnant women and newborns were characterized as a risk group during the SARS-CoV-2 virus pandemic. Vertical transmission from mother to newborn still seems unlikely, and there is a gap in the literature on the subject. Objectives: To identify the diagnoses of newborns born to mothers who were infected with SARS-COV-2 at the time of delivery, admitted to a Joint Accommodation or Neonatal Intensive Care Unit in a hospital in the interior of the state of São Paulo. Methodology: The research was carried out in a tertiary hospital in the interior of the state of São Paulo, through a cross-sectional study through the documentary analysis of medical records of newborns with 0 days of life until their discharge, admitted to the Joint Lodging and Neonatal ICU, whose mothers were positive with COVID-19 at delivery, from December 31, 2019 to September 30, 2022. Results: A total of 112 newborns of mothers diagnosed with COVID-19 were identified. Of these, 100 were housed together after birth, while 12 were transferred to the NICU. The average length of stay was 8 days in the NICU and a further 4 days in the rooming-in unit, totaling 12 days. All the newborns were breastfed and showed signs of respiratory distress, most of them mild. Only one required invasive mechanical ventilation, six non-invasive mechanical ventilation, and all received oxygen. Most had no radiological alterations and all tested negative in the RT-PCR test. As for laboratory tests, the scores varied, with half of the newborns born by normal delivery and only 3 of the 12 considered premature. Conclusion: The presence of COVID-19 in mothers did not cause substantial additional impacts on newborns, and none of the newborns tested were diagnosed positive for the disease, indicating no vertical transmission. Further studies are essential to gain a comprehensive understanding of the profile of this population group, including more in-depth investigations into the possible routes of contamination of newborns, preferably using a larger sample.

Keywords: Neonatology. Newborn. COVID-19.

[1] Master in Pediatrics, Santa Casa de Misericórdia de São Paulo
[2] Doctor from the University of Marília

INTRODUCTION

The *Severe Acute Respiratory Syndrome-related coronavirus 2* (SARS-CoV-2) virus emerged in China at the end of 2019, spreading rapidly around the world and making this situation a global pandemic decreed by the World Health Organization (WHO) in March 2020 (WORLD HEALTH ORGANIZATION, 2022). This scenario represented a serious public health problem with serious health, social, economic and political impacts, mainly saturating health systems, depleting supplies and human resources. Among the most affected countries, the following stand out: United States, India, Italy, China, Spain and Brazil (DE ROSE, PIERSIGILLI *et al.*, 2020, DOS SANTOS, *et al.*, 2020, MASCARENHAS, CAROCI-BECKER, *et al.*, 2020)element.

Transmission by the SARS-CoV-2 virus is much higher when compared to other viruses. Consequently, its mortality rate is higher due to its rapid transmissibility (COSTA, SANTOS, *et al.*, 2021)element. According to the WHO, as of September 2022, 606,459,140 cases have been confirmed worldwide, with a total of 6,495,110. In Brazil, these data represent around 34,526,148 confirmed cases and 684,853 deaths as a consequence of COVID-19 (WORLD HEALTH ORGANIZATION, 2022). To control contamination by the virus, the WHO and the Ministry of Health (MS) recommended social isolation, early detection of infection, notification, investigation and proper management of cases.

Most patients contaminated by the SARS-CoV-2 virus have fever, nasal congestion, runny nose, dry cough, dyspnea, myalgia, loss of taste and bilateral irregular pattern and/or ground-glass opacities, which can be seen on chest CT scans. In some cases, severe symptoms such as Severe Acute Respiratory Syndrome (SARG) may appear, being more common in the elderly and people with comorbidities (GÓES, DOS SANTOS, *et al.*, 2020, MASCARENHAS, CAROCI-BECKER, *et al.*, 2020, PESSOA, DO VALE, *et al.*, 2020)element.

There were many uncertainties about the COVID-19 pandemic, especially in relation to the treatment and prevention of contamination of the disease. However, it is important to mention that even in the face of the pandemic scenario, the cycle of life continued, which generated doubts regarding the care to be taken in relation to pregnant women and newborns (NB) (GÓES, DOS SANTOS, *et al.*, 2020, MIMOUNI, LAKSHMINRUSIMHA, *et al.*, 2020, MINISTRY OF HEALTH, 2020)element.

Because of this, the Ministry of Health included women during the pregnancy-puerperal cycle and NB in the classification as risk groups (MASCARENHAS, CAROCI-BECKER, *et al.*, 2020)element. In pregnant women, symptoms can be present in a mild or moderate form and mostly asymptomatic. This scenario can lead to a high risk of neonatal

contamination during labor (PT) (COSTA, SANTOS, *et al.*, 2021, MASCARENHAS, CAROCI-BECKER, *et al.*, 2020)element.

Vertical transmission from mother to newborn still seems to be unlikely, but there is a gap in the present literature on the subject, most of which are carried out in China and with little scientific evidence. Pessoa et al, published a case study in 2020 where a 33-week-old pregnant woman with proven COVID-19 infection presenting with dry cough, dyspnea, and tomographic findings of ground-glass opacity and bilateral consolidations, underwent emergency cesarean section due to respiratory decompensation. The newborn was transferred to the Neonatal Intensive Care Unit (NICU) soon after birth and kept in respiratory and contact isolation. After 6 hours of life, his RT-PCR was collected, testing positive. Although there is such a gap regarding these findings, the positive result of this NB is worrying, and further investigations are needed (PESSOA, DO VALE, *et al.*, 2020)element.

According to a systematic review published in 2021 where the objective was to evaluate the relationship between COVID-19, pregnancy and neonates, it was possible to identify that all included studies diagnosed the SARS-CoV-2 virus in parturients through RT-PCR testing. However, most studies have highlighted the possibility of a false negative result in patients who could be infected with the virus. The false negative result can occur due to insufficient viral load, sampling in the initial or late stage of the disease, and unstructured collection sites (FORATORI-JUNIOR, MOSQUIM, *et al.*, 2021)element. In the same study, of the 279 neonates evaluated, only ten tested positive for SARS-CoV-2 after at least 30 hours of delivery.

Some authors believe that vaginal delivery may carry a risk of vertical transmission of COVID-19, however, the hypothesis that best explains the non-viral transmission from mother to child is due to the fact that the receptor of angiotensin-converting enzyme 2 (ACE2) of COVID-19 has low expression in all precursor cells of the maternal-fetal interface. In some studies, the placenta, umbilical cord, amniotic fluid, and breast milk were tested and there were no positive results for the presence of the virus. However, it should be noted that there may have been a false negative result as previously mentioned (FORATORI-JUNIOR, MOSQUIM, *et al.*, 2021, SALVADOR-PINOS, MARTINEZ, *et al.*, 2022)element.

Knowing that the transmission of the virus occurs through contamination by droplets, aerosols and contact, during labor of women who are suspected or contaminated with SARS-CoV-2, the team must be aware of the diagnosis and prepared to follow all safety recommendations (SILVA, ROCHA, *et al.*, 2021)element.

According to the study published in 2021, two stages are extremely important during the birth process, namely: hand hygiene with water and liquid soap or alcohol gel preparation (70%) and use of personal protective equipment (disposable apron, surgical mask or upper, procedure gloves, goggles, face shield, caps and shoe covers). Some studies have recommended early clamping of the umbilical cord and separation of mother and child after birth for 14 days, however, there is not enough evidence to confirm the benefit of this action. In addition, separating mother and baby can negatively impact the adaptation of the NEWBORN (SILVA, ROCHA, *et al.*, 2021)element.

According to a publication by the Ministry of Health, it is recommended that in cases of asymptomatic or symptomatic pregnant women who do not have clinical changes, the routine of clamping the umbilical cord should be maintained. Regarding skin-to-skin contact and breastfeeding, it is recommended that these should be performed on asymptomatic mothers who have not had home contact with people contaminated by the virus. Otherwise, it is recommended that skin-to-skin contact and breastfeeding be carried out after all the parturient's hygiene care, such as bathing, changing masks, caps, nightgowns, and sheets (SILVA, ROCHA, *et al.*, 2021)element.

Thus, after all the information cited, it is necessary to highlight the importance of investigating the profile of these NB, children of mothers who were diagnosed with COVID-19. It is necessary to characterize how these NB presented themselves after birth so that there is a better understanding of the association between COVID-19, pregnancy and NB.

OBJECTIVES

GENERAL OBJECTIVE

To analyze the diagnoses of newborns born to mothers infected with SARS-CoV-2, who were within the period of viral transmissibility at the time of delivery, encompassing rooming-in and NICU neonates admitted to a public and tertiary hospital in the interior of the State of São Paulo, from December 31, 2019 to September 30, 2022.

SPECIFIC OBJECTIVES

- To determine, through documentary analysis, through medical records, the outcome of neonates born to mothers infected with COVID-19 and compare them with current scientific evidence.
- To evaluate whether the variables to be studied of the newborns (birth weight, Apgar, gestational age – New Ballard, weight gain/loss, RT-PCR, laboratory and imaging tests, length of stay in rooming-in and NICU, breastfeeding, respiratory

distress, prematurity, sepsis, and other possible pathologies) may be related to maternal infection.

- To analyze the data regarding demographic aspects, need and type of ventilatory support used, complications, length of hospital stay, main diagnosis and clinical outcome.
- To correlate the results found with those of other studies of the same profile.
- To contribute, based on the discussion of the data collected, in the process of forming the cultural repertoire of health professionals, about COVID-19 and its relationship in neonatology, to improve care in the service.

MATERIALS AND METHODS

RESEARCH DESIGN

This will be a cross-sectional analytical observational epidemiological study, which will be developed through the documentary analysis of medical records of pregnant women and newborns from a public hospital in São Paulo.

PROCEDURES

The study will be developed from the documentary analysis of the medical records of pregnant women with positive SARS-CoV-2 and within the period of transmission at the time of delivery admitted to the Obstetric Center, and of their neonates in the Rooming-in and NICU, in the period between December 2019 and September 2022. According to information from the hospital's Department of Technology and Informatics (IT), in the aforementioned period, 112 occurrences of mothers with a positive COVID test at the time of delivery were recorded. This corresponds to the size of the population whose electronic medical records will be analyzed to compose the results of this research.

Data will be collected regarding maternal infection, birth weight, Apgar score, sex, gestational age – New Ballard, weight gain/loss, RT-PCR, laboratory and imaging tests, length of stay in rooming-in and NICU, breastfeeding, respiratory distress, prematurity, sepsis, and other possible complications (Appendix 1)

INSTRUMENTS

The data will be collected from the Rooming-in and NICU admissions record book of the hospital where the study will be carried out and the analysis of the collected data will be done by computing them in Excel tables and the results will be evaluated through statistical analysis.

STATISTICAL ANALYSIS

Statistical analysis will be performed using specialized software, with normality tests applied to the data to determine the choice between parametric or non-parametric methods. Continuous variables will be described by means and standard deviations. Comparisons between groups will be made by chi-square or Fisher's exact for categorical variables. A significance level of 5% ($p < 0.05$) will be considered. Multivariate analyses will be conducted to adjust for potential confounders.

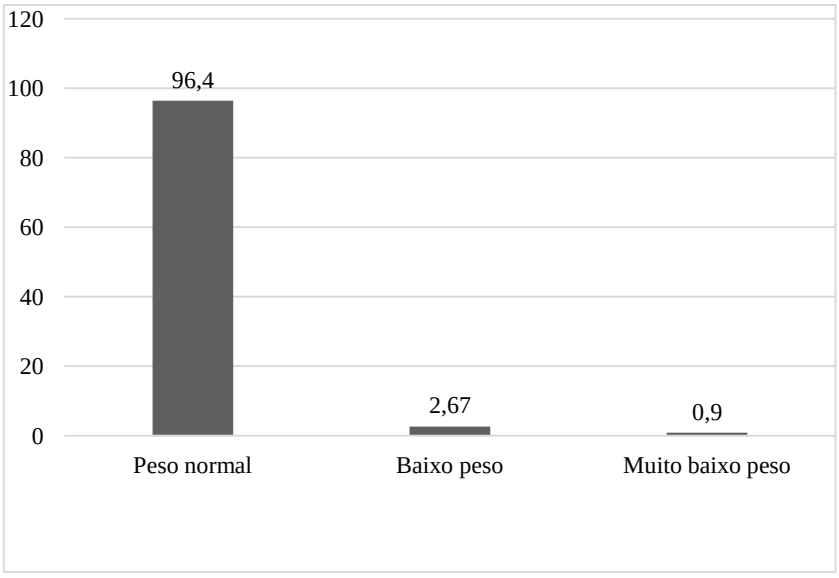
ETHICAL ISSUES

The research will be submitted to the approval of the Research Management System of the University of Western Paulista (UNOESTE) and the Plataforma Brasil to later begin the study of the medical records strictly following the current ethical standards, ensuring confidentiality of the name of the institution from which the documents, mentioned above, were analyzed. Due care will be taken so that the data does not identify the participants in the research and in future publications.

RESULTS

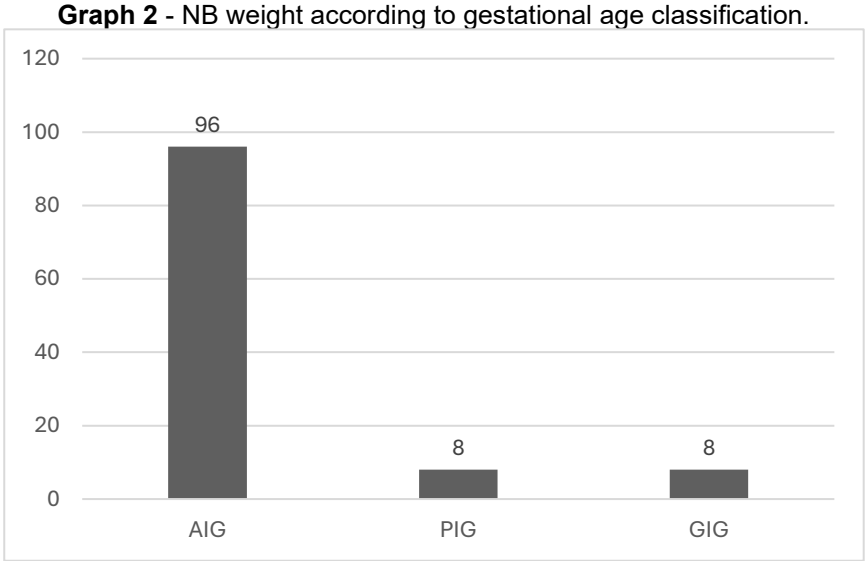
We identified 112 newborns (NBs) born to mothers diagnosed with COVID-19. Of the NBs identified, 100 went to the rooming-in unit after birth and 12 needed to be transferred to the NICU. The weight of the NBs can be seen in Graph 1, while the weight classified according to gestational age can be seen in Graph 2.

Graph 1 - Weight of NBs classified as normal weight, low weight and very low weight.



Legend: low weight: <2500gr; very low weight: less than 1500gr; extreme low weight: less than 1000gr.

Graph 2 - NB weight according to gestational age classification.

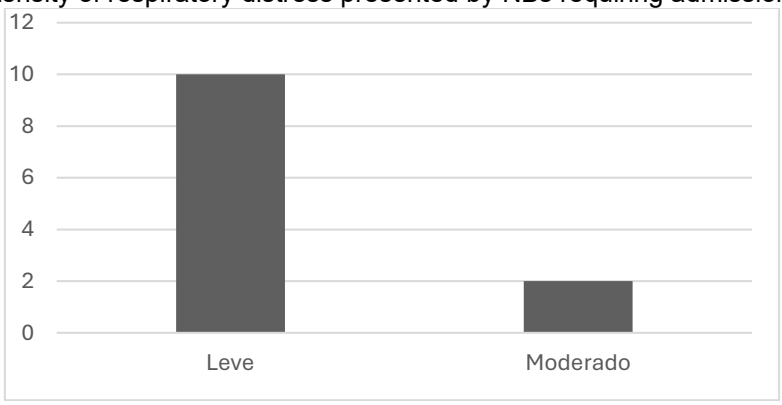


Key: AIG - appropriate for gestational age; SGA - small for gestational age; LGA - large for gestational age.

The data described below is for NBs who were transferred to the NICU (Table 1 - Profile of NBs of mothers with COVID-19 transferred to the NICU). The average length of stay in the NICU was 8 days and in the rooming-in unit 4 days, totaling an average of 12 days in hospital. All the NBs were breastfed.

All the NBs had signs of respiratory discomfort, most of them mild (10) and only two with moderate discomfort (Graph 3). With regard to ventilatory support, only one NB required invasive mechanical ventilation, six needed non-invasive mechanical ventilation and all had O2 supply at some point during their hospitalization, totaling an average of 2 days of oxygen supply. Only one had a chest X-ray with atelectasis, the other 11 had no radiological alterations.

Graph 3 - Intensity of respiratory distress presented by NBs requiring admission to the NICU



100% of the NBs had a negative RT-PCR. With regard to laboratory tests, one NB had a blood count score of 3, three had a score of 2, six had a score of 1 and two had a score of 0. With regard to the route of delivery, 50% of the NBs were born by normal delivery. Of the 12 NBs, only 3 were considered premature.

Of the 12 patients who required admission to the NICU, 9 had an APGAR score of 8/9 in the first and 5th minutes of life, respectively, which corresponds to 75% of the patient sample. The remaining 25% had an APGAR of 7/8 points in the same assessment, and the only premature patient of the 12 included in the study was included in this second group, with an APGAR of 7/8 in the 1st and 5th minutes of life, respectively (Table 1).

Table 1 - Profile of NBs of mothers with COVID-19 transferred to the NICU.

RN	Weight	Gender	APGAR	NB	IG	Premature?
1	1605g	M	7/8	35S6D	35S6D	Yes
2	3900g	M	8/9	39S	38S4D	No
3	2952g	F	8/9	36S	36S5D	Yes
4	2480g	F	8/9	36S3D	36S3D	Yes
5	3175g	M	8/9	38S	38S	No
6	3160g	F	7/8	39S1D	39S	No
7	3210g	M	8/9	37S3D	38S	No
8	3400g	F	7/8	38S2D	38S	No
9	2900g	M	8/9	37S1D	37S4D	No
10	3100g	M	8/9	38S3D	38S	No
11	3530g	F	8/9	39S	39S3D	No
12	2850g	M	8/9	37S2D	37S	No
***Caption**: NB – New Ballard; IG – Gestational age.*						

DISCUSSION

According to this research, of the 112 NBs identified as having a COVID-19 positive mother, only 12 were transferred to the NICU. As in the study by SCHWARTZ et al, no confirmed cases of COVID-19 were found in the NBs (SCHWARTZ E GRAHAM AL, et al, 2020). When tested, all showed negative results for RT-PCR. Although there are still many disagreements between authors regarding the vertical transmission of COVID-19, a large number of them corroborate our findings and state that this is a rare event. Most of the evidence published to date indicates that the virus is not able to cross the placenta and infect the amniotic fluid, implying that this contamination occurs shortly after birth.

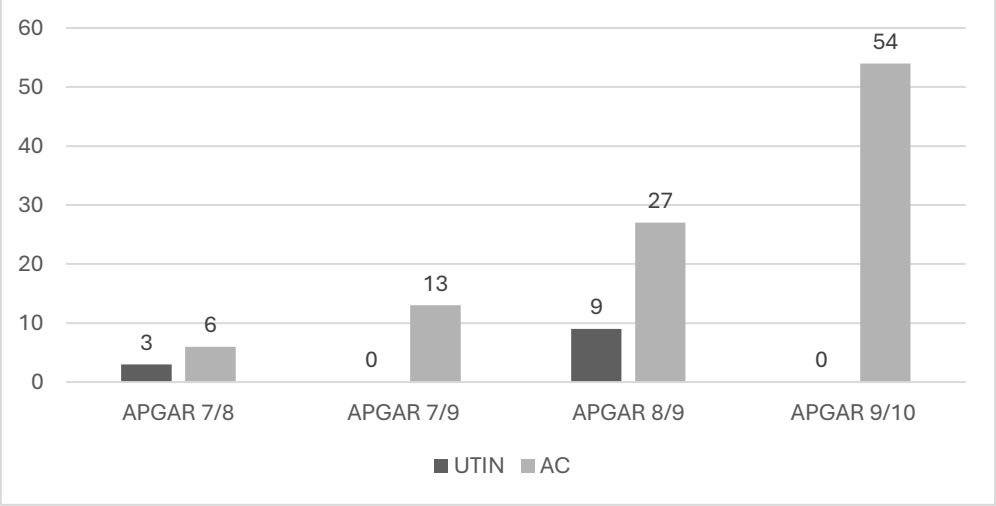
Regarding the main repercussions of SARS-CoV-2 in newborns of pregnant women who had COVID-19, some authors cite prematurity, low birth weight and the need for cesarean delivery (CASTRO, et al, 2020, TRIPPELLA, et al, 2020). This evidence does not corroborate our findings, where 96% of NBs were of normal weight, and of the 12 NBs transferred to the ICU, only 3 were considered premature and 50% of deliveries were

cesarean sections. This difference between the results may be related to the small sample of positive newborns in this study.

Of the 112 NBs born to mothers with COVID-19, only 12 were transferred to the NICU, which represents around 10% of the total. Although our number of NICU admissions was low, most studies report that NICU admission is recurrent in this population (SMITH, et al, 2020).

All the NBs in this study had 5th minute APGAR scores above 5 (Graph 4), which means that many of them did not need assistance to establish breathing 5 minutes after birth. APGAR values in studies of newborns whose mothers had COVID-19 during pregnancy were above 7 in most cases. However, in some cases of premature birth and in cases where the newborns had COVID-19, this index was lower. These findings are in line with our results, where premature NBs had lower APGAR values (DUBEY P et al, 2020; ONCEL et al, 2021).

Graph 4 - APGAR of patients admitted to the NICU vs. patients admitted directly to rooming-in.



Caption: NICU: neonatal intensive care unit; AC: rooming-in.

The results indicate that all the newborns showed signs of respiratory distress, although most were classified as mild. This suggests a possible influence of the mother's condition on the babies' respiratory health. It is important to note that most of the newborns did not show any significant radiological changes.

The results of OLIVEIRA et al, 2023 corroborate our findings where 100% of NBs needed ventilation support, whether invasive or non-invasive, in the first hours of life. This was probably not due to COVID-19 infection, as none of the NBs had positive APGAR RT-PCR (DUBEY P et al, 2020; ONCEL et al, 2021).

It is noteworthy that the average length of stay in the NICU was 8 days, and later, in the rooming-in unit, it was another 4 days, totaling an average of 12 days in hospital for these

newborns. All of them were breastfed, a crucial practice for their healthy development, despite the mother's condition (DUBEY P et al, 2020).

Based on the above, the data obtained is essential for defining the target profile, highlighting the main clinical and epidemiological characteristics of both neonates and their mothers. This information is essential to guide the development of health policies aimed at promoting neonatal health and reducing the associated risks. In addition, it is necessary to clarify the neonatal outcomes of newborns whose mothers were infected with SARS-COV-2, in order to implement effective measures for prevention, management of complications and appropriate treatment for the entire population.

CONCLUSION

COVID-19 in mothers did not result in additional significant impacts on newborns, and the newborns tested were not diagnosed with the disease, providing no evidence of vertical transmission. It is crucial to conduct further research to fully understand the profile of this population group and especially the routes of contamination of newborns, ideally with a larger sample.

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