Profile of newborns of mothers with and without a COVID-19 diagnosis during pregnancy

Perfil de neonatos de mães com e sem diagnóstico de COVID-19 durante a gestação

Perfil de los recién nacidos de madres con y sin diagnóstico de COVID-19 durante el embarazo

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Abstract:
Objective: to analyze the birth conditions and general health status of newborns of mothers with and without a positive COVID-19 test during pregnancy. Methods: a descriptive, cross-sectional, retrospective, and analytical study using a non-probabilistic sample, conducted in a maternity ward of a hospital in the southern region of the city of São Paulo, SP, Brazil. Two data collection instruments were used from medical records: a semi-structured questionnaire to investigate data from the mothers; and another for evaluating the newborns. The χ2 test was used for comparison of qualitative variables, Student's t-test, Mann-Whitney test, and ANOVA for quantitative variables, and Pearson's correlation test. Results: 117 mothers and their respective newborns participated, distributed into two groups. Group I consisted of 63 mothers who tested negative for COVID-19 during pregnancy, and Group II consisted of 54 mothers who tested positive for the disease during pregnancy and their respective babies. Newborns of mothers who tested positive presented lower length and weight, larger head circumference, a higher chance of requiring oxygen, a higher proportion of prematurity, a greater number of days of hospitalization, as well as lower Apgar scores at one and five minutes. Conclusion: newborns of mothers who tested positive for COVID-19 during pregnancy presented a higher proportion of factors associated with complications in the indicators of birth conditions and general condition evaluated. The risk ratio for low birth weight, hospitalization, and lower Apgar scores was increased for mothers who tested positive compared to those who tested negative.
Keywords: COVID-19; Infant, Newborn; Apgar score; Pregnancy; Pregnancy complications.

Resumo:
Objetivo: analisar as condições de nascimento e o estado geral de saúde de recém-nascidos de mães com e sem teste positivo de COVID-19 durante a gestação. Método: estudo descritivo, transversal, retrospectivo de análise documental e analítico, com amostra não-probabilística, realizado em um hospital maternidade da zona sul da cidade de São Paulo. Foram utilizados dois instrumentos de coleta de dados dos prontuários: um questionário semiestruturado para investigação dos dados das mães; e outro, para avaliação dos neonatos. Foi utilizado teste do χ2 para comparação de variáveis qualitativas, teste t de Student, teste Mann-Whitney e ANOVA para variáveis quantitativas, e teste de correlação de Pearson. Resultados: participaram 117 mães e seus respectivos recém-nascidos, distribuídos em dois grupos. O grupo I foi formado por 63 mães que testaram negativo para COVID-19 durante a gravidez, e o grupo II, por 54 mães que testaram positivo para a doença durante a gravidez e seus respectivos neonatos. Os recém-nascidos de mães que testaram positivo apresentaram menor estatura e peso, maior perímetro cefálico, maior proporção entre os que necessitaram fazer uso de oxigênio, maior proporção de prematuridade, maior número de dias de hospitalização, bem como menor índice de Apgar no primeiro e no quinto minutos. Conclusão: os recém-nascidos de mães que testaram positivo para COVID-19 durante a gravidez apresentaram maior proporção de fatores associados a complicações nos indicadores de condições de nascimento e estado geral avaliados. A razão de risco para baixo peso, hospitalização e menor Apgar esteve aumentada para as mães que testaram positivo em relação às que testaram negativo.
Palavras-chave: COVID-19; Recém-nascido; Índice de Apgar; Gravidez; Complicações na gravidez.

Resumen:
Objetivo: analizar las condiciones de nacimiento y el estado general de salud de los recién nacidos de madres con y sin prueba positiva de COVID-19 durante el embarazo. Método: estudio descriptivo, transversal, retrospectivo, de análisis documental y analítico, con muestra no probabilística, realizado en un hospital materno de la zona sur de la ciudad de São Paulo, SP. Brasil. Se utilizaron dos instrumentos de recopilación de datos de los historiales clínicos: un cuestionario semiestructurado para investigar los datos de las madres y otro para evaluar a los recién nacidos. Se utilizó la prueba χ2 para comparar variables cualitativas, la prueba t de Student, la prueba de Mann-Whitney y ANOVA para variables cuantitativas, y la prueba de correlación de Pearson. Resultados: participaron 117 madres y sus respectivos recién nacidos, distribuidos en dos grupos. El grupo I estaba formado por 63 madres que dieron negativo en la prueba de COVID-19 durante el embarazo, y el grupo II, por 54 madres que dieron positivo en la prueba de la enfermedad durante el embarazo y sus respectivos recién nacidos. Los recién nacidos de madres que dieron positivo presentaron menor estatura y peso, mayor perímetro cefálico, mayor proporción entre los que necesitaron oxígeno, mayor proporción de prematuridad, mayor número de días de hospitalización, así como menor índice de Apgar en el primer y quinto minuto. Conclusión: los recién nacidos de madres que dieron positivo en COVID-19 durante el embarazo presentaron una mayor proporción de factores asociados a complicaciones en los indicadores de las condiciones de nacimiento y el estado general evaluados. La razón de riesgo de bajo peso, hospitalización y menor Apgar fue mayor para las madres que dieron positivo en comparación con las que dieron negativo.
Palabras-clave: COVID-19; Recién-nacido; Puntaje de Apgar; Embarazo; Complicaciones del embarazo.

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INTRODUCTION

COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was declared a pandemic by the World Health Organization (WHO) on March 11, 2020[1-2]. Two years later, in March 2022, it had already accumulated approximately half a billion confirmed cases and six million deaths[3]. Analyses of its possible origins point to unintentional emergence, although this theory should not be discarded, as evidence supports the hypothesis that SARS-CoV-2 originated from coronaviruses present in animals, which implies the need for virus sequencing and identification of the potential intermediate host[4].

The syndrome, whose first identified case occurred in December 2019 in China, has had a strong impact on global public health[5-7], prompting the world to undertake numerous efforts in the search for control and reduction of its consequences[7]. Data released by the COVID-19 Observatory[8] show record numbers of deaths in Brazil, as well as critical levels of occupancy of Intensive Care Unit (ICU) beds.

COVID-19 and the corresponding restrictions have resulted in severe limitations to the provision of neonatal care[9], although maternal and neonatal health is related to health care throughout the life course, considered a priority within the Sustainable Development Goals and the 2030 Development Agenda[10-11].

In this scenario, it is also emphasized that, to date, limited data are available on the effect of COVID-19 on pregnancy and on maternal and perinatal outcomes[12]. It is noted that the first two trimesters of pregnancy present increased inflammatory responses, but the third represents a phase of lower immunological activity, making mothers and babies vulnerable targets; therefore, encountering any infectious pathogen can bring complications to both the expectant mother and the unborn baby[13]. Thus, the present article aimed to analyze the birth conditions and general health status of newborns of mothers who did test positive or negative for COVID-19 in a hospital maternity ward.

METHODS

This is a descriptive, cross-sectional, retrospective documentary analysis study. It considers information from the medical records of newborns and mothers who gave birth at the maternity ward of a municipal public hospital located in the M'boi Mirim district, in the southern part of the city of São Paulo, between June and December 2020.

This study was conducted and managed by two nationally relevant social health organizations. The hospital was inaugurated in 2008 and is considered a reference for the care of more than half a million people in the region where it is located. As part of its structure, its

maternity ward has 22 beds in the Neonatal Conventional Intermediate Care Unit (NICUCo), 10 beds in the Neonatal Intensive Care Unit (NICU), as well as 5 pre-delivery rooms and 10 operating rooms[14-15].

In 2018, the maternity hospital performed more than 79,000 consultations, in addition to 1,691 deliveries. It is considered the 41st best hospital in Latin America, and is the only public service among those evaluated in the 2018 ranking[16]. In addition, it was the first, at the municipal level, to receive, in 2014, the highest level accreditation seal granted by the National Accreditation Organization in recognition of the quality and safety of the care provided by the unit, a title currently maintained[15].

As in other cross-sectional studies[17], in the first phase, the PICO proposal[18] was used to develop the guiding question, an acronym for the four components of the proposal: P – patient or population; I – intervention or exposure; C – comparison or control; O – outcome.

The proposal resulted in the following question: *What are the birth conditions and general health status of newborns of mothers who tested positive for COVID-19 during pregnancy compared to newborns of mothers who tested negative for the disease during pregnancy?*

Medical records of mothers aged 18 to 40 years old, with or without COVID-19 infection, and of their newborns were included, provided they were available in the hospital's record system. Records with incomplete information were excluded.

The records considered were those of mothers with scheduled deliveries between June and December 2020 and their respective newborns. A semi-structured questionnaire was used to collect information from mothers and newborns, which was subsequently tabulated in Microsoft Excel® and used for statistical analysis.

The questionnaire, previously prepared by the researchers, consisted of sociodemographic questions (name initials, age, race/color, place of birth, marital status, occupation, and family income), obstetric history (number of pregnancies, number of live births, number of miscarriages, number and type of previous deliveries, gestational age, type of delivery, prenatal care, complications during the pre-partum, delivery, and postpartum periods), and health and lifestyle habits (pre-existing comorbidities, diagnosis or history of COVID-19, weight, height, BMI, alcohol consumption, tobacco use, medication use, and/or illicit drug use).

Regarding the newborn, only information pertaining to the post-birth period was considered (early neonatal period: the interval between birth and the moment the baby reaches 6 days, 23 hours, and 59 minutes). The following data was collected: mother's initials, time of birth, sex, questions related to health status (head circumference, weight, length, information

about COVID-19, need for oxygen or ventilation, complications, need for hospitalization, and mortality), APGAR score, and bilirubin test.

The Brazilian Ministry of Health[19] recommends the use of the APGAR score at the first and fifth minutes of the baby's life as an important resource for recording the baby's birth conditions and for a good understanding of their health status, to be considered for subsequent care.

This method takes into account factors such as heart rate, respiratory effort, muscle tone, skin color, and reflex irritability, the total sum of which can range from 0 to 10. The higher the score obtained, the better the physiological condition of the newborn; 0 to 3 indicates a sign of severe anoxia; between 4 and 6, moderate anoxia; and 7 an adequate standard[20].

Jaundice is considered a frequent problem in the neonatal period. Bilirubin is defined as an elevated blood concentration of indirect bilirubin, when greater than 1.3 to 1.5 mg/dL, or direct bilirubin greater than 1.5 mg/dL, provided that this is considered to be greater than 10% of the total bilirubin value[21].

The assessment of bilirubin levels in newborns is a practice encouraged by the Brazilian Society of Pediatrics (*Sociedade Brasileira de Pediatria* - SBP)[22], which highlights it as a marker for neonatal jaundice, which, consequently, can be aggravated by bilirubin encephalopathy. Actions to control and reduce the progression of these comorbidities are important public health measures[22].

The normality of the data was tested using the Korolmorgov-Smirnov test. Statistical analysis was performed using the χ^2 test for comparison of qualitative variables, Student's t-test, Mann-Whitney test and ANOVA for quantitative variables, and Pearson's correlation test. A significance level of 5% was adopted for all statistical procedures.

To predict the impact of the various risk factors considered on the occurrence of climacteric symptoms, a logistic regression methodology was employed, using the intensity of these symptoms as the dependent variable, according to the following standardization: code 0 = mild symptoms; code 1 = severe symptoms. As independent variables, all those that showed a significant association with the occurrence of significant symptomatology were considered. The GraphPad Prism for Windows version 6.0 software was used for the statistical procedures. All risk analyses were adjusted for the patient's weight, given that there was a difference between the groups.

The research began after approval by the Research Ethics Committee (CEP) of the São Paulo Municipal Health Department, substantiated opinion no. 4,868,369. Ethical and legal

aspects were respected, as established by Resolution no. 466/2012 of the National Health Council (CNS).

RESULTS

This study included medical records related to 117 mothers and their respective babies, who were divided into two groups. Group I consisted of mothers who tested negative for COVID-19 during pregnancy (n=63), and Group II consisted of those who tested positive for COVID-19 during that period (n=54).

The analysis of clinical and anthropometric characteristics revealed that most mothers who tested positive had higher body weight, were married, had fewer than five prenatal visits, a lower proportion of pre- and delivery complications, and a lower proportion with associated comorbidities (Table 1).

Table 1. Anthropometric and clinical characteristics of mothers with a positive and negative history for COVID-19, São Paulo/SP, Brazil, 2020.

Variables	Group I - Positive Mother	Group II - Negative Mother	p
Age (years)	27.1±5.9	28.1±6.6	0.22
Weight (kg)	82.1±12.9	76.1±13.3	**0.008**
BMI (kg/m²)	27.9±2.4		
Married (%)	84.5	55.5	**0.002**
Single (%)	14.5	45.5	**0.001**
Number of pregnancies	2.5±1.5	2.8±1.7	0.19
Live births	1.1±1.2	1.3±1.4	0.21
Number of miscarriages	0.41±0.79	0.6±1.2	0.17
Cesarean Section (%)	39.6	33.3	0.12
Vaginal Birth (%)	60.4	66.3	0.14
Pre-natal (%)	83.0	98.4	**0.04**
Prepartum complications (%)	18.8	34.9	**0.0032**
Complications during birth (%)	3.7	23.8	**0.001**
Postpartum complications (%)	1.8	4.7	0.23
Commorbidies (%)	26.4	38.0	**0.02**
Alcohol (%)	5.6	3.1	0.58
Tobacco (%)	3.7	14.2	0.08
Illicit drugs (%)	1.8	11.1	0.09
Medications (%)	28.3	31.7	0.21

BMI = body mass index.

Regarding the characteristics of the newborns, group II, consisting of mothers who tested negative for COVID-19, had a larger head circumference, shorter length, a lower proportion of oxygen use, greater use of non-invasive ventilation, higher oxygen saturation, a higher proportion of hospitalizations, and a greater number of days of hospitalization, in addition to a lower APGAR score at one and five minutes (Table 2).

Table 2. Anthropometric and clinical characteristics for newborns of mothers with a positive and negative history for COVID-19, São Paulo/SP, Brazil, 2020.

	NB of mother tested negative COVID-19 (standard deviation) (n = 63)	NB of mother tested positive COVID-19 (standard deviation)(n = 54)	p
Weight (kg)	3.11±0.45	2.85±0.75	0.016
Low weight (%)	11.3	25.3	0.052
Head circumference (cm)	33.6±1.3	45.8±3.8	**0.003**
Length	47.2±1.7	32.7±2.1	**0.007**
Ambient air (%)	88.9	80.3	0.17
Supplemental O_2 (%)	11.1	1.5	**0.005**
NIV	0	9.5	**0.009**
OTI (%)	0	3.1	0.36
Hemoglobin saturation (%)	97±3	98±3	**0.009**
Hospitalization (%)	14.8	26.9	0.05
Reason for hospitalization			
Hipoglycemia (%)	9.2	1.5	**0.01**
Prematurity (%)	1.8	15.8	**0.0003**
Congenital abnormalities (%)	1.8	3.1	0.45
Other	0	3.1	0.36
Stillbirth	0	3.1	0.36
Days of hospitalization	3.8±3.6	17.6±17.9	**0.03**
Apgar first minute	8.4±0.8	7.6±2.3	**0.007**
Apgar fifth minute	9.6±0.5	9.1±1.9	**0.02**

Key: NB = newborn; NIV = non-invasive ventilation; OTI = orotracheal intubation.

The risk of low birth weight was assessed among newborns of mothers who tested positive and negative for COVID-19, and it was found to be 2.7 times higher in positive conditions (Figure 1). The risk of oxygen therapy use in the first 10 hours after birth was also assessed among newborns of mothers who tested positive and negative for COVID-19. It was observed that this risk was 1.6 times higher in mothers who tested positive (Figure 2).

The risk of hospitalization among newborns of mothers who tested positive and negative for COVID-19 was also assessed. It was found to be 1.9 times higher in positive conditions (Figure 3).

Figure 1. Relative risk of low weight for mothers who tested positive and negative for COVID-19, São Paulo/SP, Brazil, 2020.
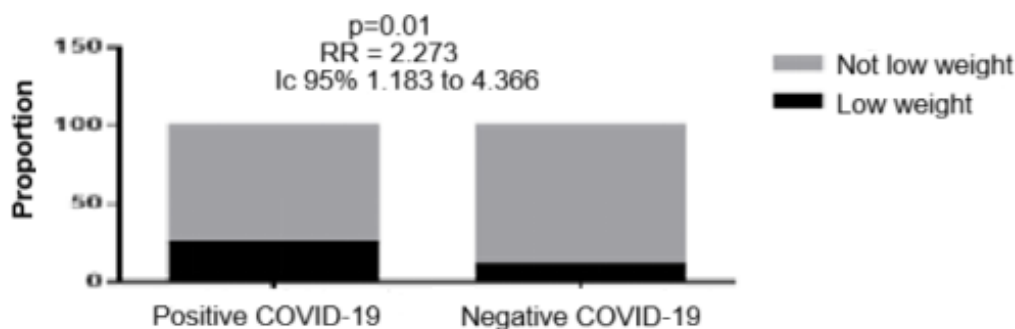

Figure 2. Relative risk for use of oxygen in the first 10 hours after birth for mothers who tested positive and negative for COVID-19, São Paulo/SP, Brazil, 2020.
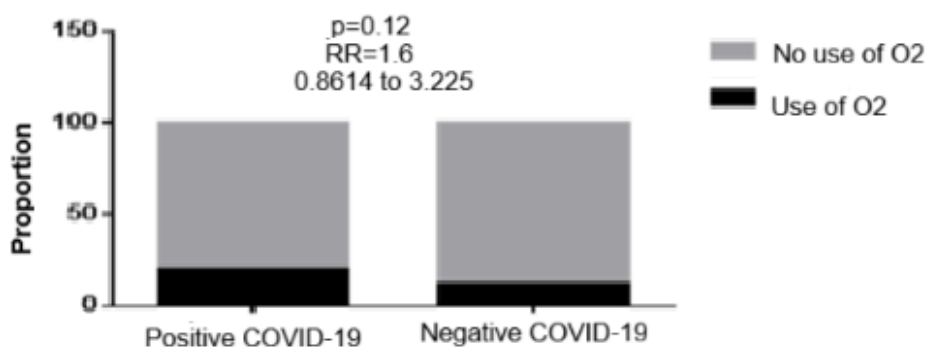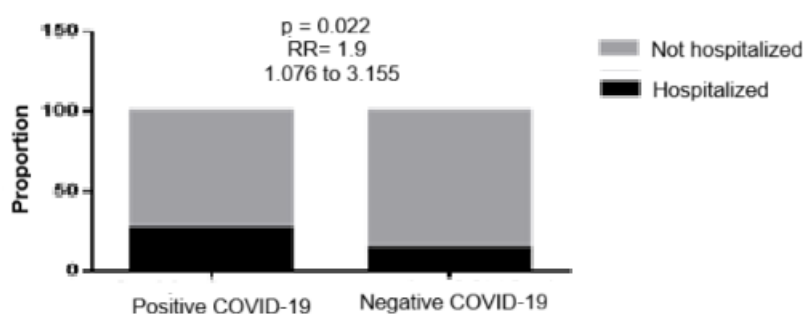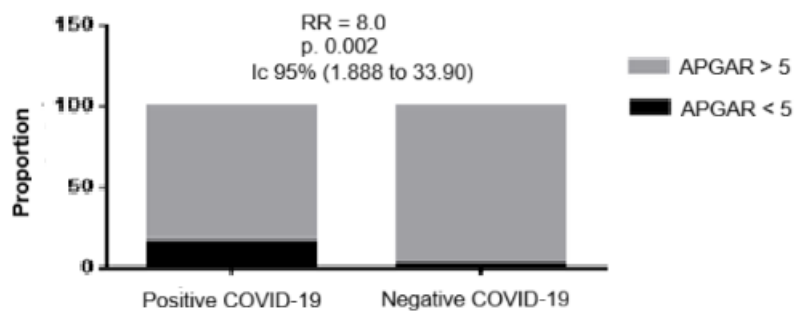

Figure 3. Relative risk of hospitalization for newborns of mothers who tested positive and negative for COVID-19, São Paulo/SP, Brazil, 2020.


The APGAR score at one and five minutes was less than 5 points among newborns of mothers who tested positive and negative for COVID-19. It was found that this score was 8 times higher in positive contexts (Figure 4).

Figure 4. Relative risk for APGAR under 5 points in the first and fifth minute for mothers who tested positive and negative for COVID-19, São Paulo/SP, Brazil, 2020.

Serum levels of indirect and direct bilirubin were analyzed in newborns of mothers who tested positive and negative for COVID-19 during pregnancy. No statistically significant difference was observed in serum levels (Figure 5).

Figure 5. Analysis of indirect and direct bilirubin for newborns of mothers who tested positive and negative for COVID-19, São Paulo/SP, Brazil, 2020.
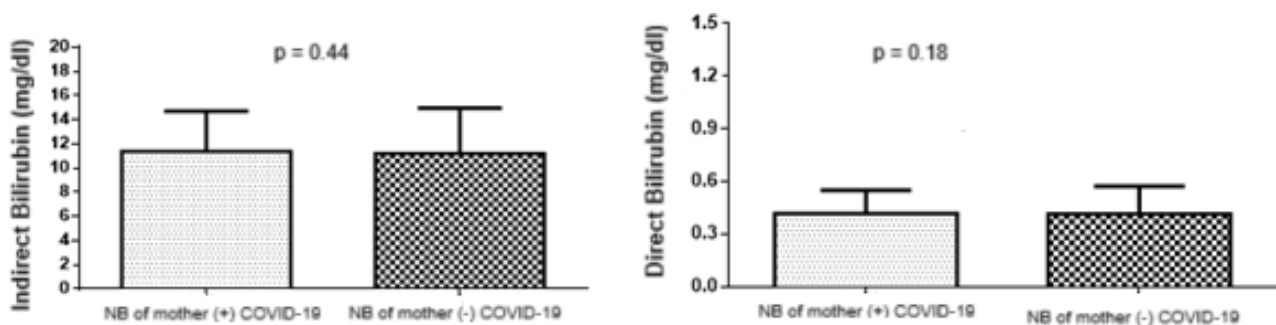
DISCUSSION

Newborns of mothers who tested positive during pregnancy have shorter length and weight, larger head circumference, a greater chance of needing oxygen, a higher proportion of prematurity, a greater number of days and proportion of hospitalization, lower APGAR scores at one and five minutes, and a higher risk of low birth weight.

One of the first studies on COVID-19 suggested the possibility of vertical transmission due to the virus's behavior, such that a neonate born by cesarean section to a mother with COVID-19 presented elevated levels of IgM, IgG, and inflammatory cytokines hours after birth[23].

Another study that evaluated placental and amniotic membrane samples from pregnant women diagnosed with severe COVID-19 in the peripartum period[24], in which placental and amniotic membrane swabs were performed on 11 patients, observed SARS-CoV-2 RNA in samples from three of them, with newborns who had negative RT-PCR tests and were asymptomatic from the first to the fifth day of life. Even without clinical signs evidencing vertical transmission, such as contamination of the newborn, the findings of viral RNA in placental and membrane samples suggest exposure[25].

In the present study, newborns of mothers who had COVID-19 during pregnancy had lower birth weight. Conversely, research contests this assertion and explains that there is no association between the syndrome and prematurity, nor is there evidence that low birth weight is justified by maternal disease[26]. However, a systematic review revealed that the most common findings among newborns of pregnant women with coronavirus were prematurity (n = 65; 34.5%) and low birth weight (n = 32; 17.0%)[5].

Another study analyzing the risk of developing severe neonatal infection revealed that neonatal infection was uncommon and mild, and there was no increase in prematurity. Low birth weight among newborns of mothers who tested positive for COVID-19 is still a controversial topic; however, it seems to be related to the severity of the disease that developed in the mother of the neonate.

Another finding of the present study was that newborns of mothers who tested positive for COVID-19 required oxygen therapy. An investigation to examine the clinical and ventilatory characteristics of neonates born to mothers infected with COVID-19 showed that a cohort with the characteristics of a mean gestational age of 34.4 weeks; 57.14% were male, and the average birth weight was 2,358g. All newborns were tested for COVID-19, and six tested positive.

Regarding ventilatory support, 63.64% used some type of resource, while 33.33% did not resort to any type[27]. Studies on the need for oxygen or mechanical ventilation in children of post-COVID-19 mothers are scarce. One study, involving four babies of post-COVID-19 mothers, indicated that two presented with skin rashes of unknown etiology at birth, and one with facial ulcerations. One infant manifested tachypnea and was sustained by non-invasive mechanical ventilation for three days[28].

Another study[23] sought to describe the clinical presentations, radiological and laboratory findings, and outcomes of COVID-19 disease in individuals 90 days or older, analyzing 36 babies and finding that none of them received antiviral medication. It has been found that infants aged 90 days or older may manifest a severe form of COVID-19.

Multisystem inflammatory syndrome in children, although rarely reported in infants, is a possible complication of COVID-19 and may be associated with significant morbidity and mortality. The need for ventilatory support for these newborns may be linked to the fact that the virus promotes airway inflammation, predisposing to alterations in the ventilation-perfusion ratio. It can be inferred that the more symptoms the mother presents, the greater the risk of the newborn manifesting respiratory difficulties[23].

Also, an increased risk of hospitalization was observed in children of mothers who tested positive for COVID-19. In a systematic review that included 50 studies reporting information

from 441 pregnant women and 391 newborns, the primary outcomes were maternal health characteristics and adverse pregnancy outcomes, neonatal outcomes, and SARS-CoV-2 infection in newborns. It was found that, of the 441 women affected by COVID-19 during pregnancy, 387 gave birth. There are nine reported maternal deaths. In pregnant women with COVID-19, the most common symptoms were fever (56%), cough (43%), myalgia (19%), dyspnea (18%), and diarrhea (6%)[29].

Pneumonia was diagnosed by computed tomography in 96% of pregnant women with the disease. Pregnancy complications included cesarean delivery (80%), preterm labor (26%), fetal distress (8%), and premature rupture of membranes (9%). Six stillbirths (2%) are reported. The most common comorbidities associated with pregnant women with COVID-19 were hypertensive disorders (10%), diabetes (9%), placental disorders (2%), co-infections (3%), uterine scarring (3%), and hypothyroidism (3%). Among newborns of mothers with COVID-19, preterm birth (25%), respiratory distress syndrome (8%), and pneumonia (8%) were reported, and the number of days of hospitalization was higher than average. There were four neonatal deaths reported[29].

In another study, 30 newborns of post-COVID-19 mothers were evaluated, of whom 28 had negative PCR test results for SARS-CoV-2. Among their mothers, 15 reported fever, nine presented with cough, and twenty had cesarean deliveries. The median term birth was 37 weeks, and 20 newborns were male. Most were asymptomatic, except for the three who presented with shortness of breath. Two of them were intubated and both died, the first from severe sepsis, and the second from severe hyaline membrane disease. The length of hospital stay for these babies was longer than the hospital average[30].

CONCLUSION

This study showed that newborns of mothers who tested positive for the disease during pregnancy have shorter length and lower weight, larger head circumference, a greater chance of needing oxygen, a higher proportion of prematurity, a greater number of days of hospitalization and a higher proportion of hospitalization, as well as lower APGAR scores at one and five minutes.

The limitations of the present study are related to the fact that the newborns were not tested to verify whether any changes were due to a positive COVID-19 test. Another factor that could not be controlled concerns which periods of gestation the mother tested positive for coronavirus. Probably, the effects on newborns are different in terms of symptoms depending

on gestational age. Furthermore, the retrospective cross-sectional design does not allow establishing causal relationships.

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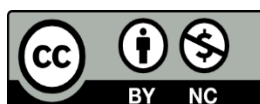**How to cite this article (Vancouver)**
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How to cite this article (ABNT)
FERRARI, A. P.; SOUZA, A. C.; VASQUES, T. P.; PORTO, E. F. Profile of newborns of mothers with and without a COVID-19 diagnosis during pregnancy. **Revista Família, Ciclos de Vida e Saúde no Contexto Social**, Uberaba, MG, v. 13, e025025, 2025. DOI: https://doi.org/10.18554/refacs.v13i00.8237. Access in: *insert day, month and year of access*.

How to cite this article (APA)
Ferrari, A. P., Souza, A. C., Vasquez, T. P., & Porto, E. F. (2025). Profile of newborns of mothers with and without a COVID-19 diagnosis during pregnancy. Rev. Fam., Ciclos Vida Saúde Contexto Soc., 13, e025025. Retrieved in *insert day, month and year of access* from https://doi.org/10.18554/refacs.v13i00.8237