

COVID-19, pregnancy outcomes, and the risk of preterm birth

COVID-19 e os desfechos na gestação e o risco de partos prematuros

COVID-19 y los desenlaces del embarazo y el riesgo de partos prematuros

 Paloma Aparecida Polaki¹,  Sara Borges Ferreira Gomes¹,  Luciana Paiva¹

 Breno Henrique Caneguim¹

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Abstract:

Objective: to characterize COVID-19 positive and negative pregnant women who gave birth and clinical outcomes, with an emphasis on the occurrence of premature births associated with SARS-CoV-2 infection. **Methods:** retrospective observational cohort study based on the analysis of medical records of pregnant women positive and negative for SARS-CoV-2 treated between January and December 2022, from which maternal and neonatal data were extracted (age, gestational age, type of delivery, etiology of prematurity, birth weight and APGAR score) and calculations of frequencies, proportions and measures of central tendency were performed to describe the outcomes related to the occurrence of premature births. **Results:** of 95 initially eligible records, 35 were from positive pregnant women and of these, 15 who gave birth at the institution, almost half presented premature birth, and all of these cases occurred in patients who tested positive for the infection. The majority of infections occurred in the first quarter of 2022, the period of circulation of the Ómicron variant. The main causes of prematurity were pre-eclampsia, high blood pressure and changes in amniotic fluid. Newborns born to infected mothers had, on average, adequate weight and good vitality levels in the first minutes of life. **Conclusion:** the occurrence of premature births was present among pregnant women diagnosed with SARS-CoV-2, highlighting the relevance of clinical monitoring of this population, but without direct evidence for SARS-CoV-2. The data reinforce the need for attention to maternal conditions during pregnancy and neonatal monitoring, especially in scenarios of viral infection.

Keywords: Pregnancy complications; Coronavirus; Infant, Newborn; Premature birth; SARS-CoV-2.

Resumo:

Objetivo: caracterizar as gestantes COVID-19 positivas e negativas que tiveram seus partos e os desfechos clínicos, com ênfase na ocorrência de partos prematuros associados à infecção pelo SARS-CoV-2. **Método:** estudo de coorte observacional retrospectivo baseado na análise de prontuários de gestantes positivas e negativas para SARS-CoV-2 atendidas entre janeiro e dezembro de 2022, dos quais foram extraídos dados maternos e neonatais (idade, idade gestacional, tipo de parto, etiologia da prematuridade, peso ao nascer e índice de APGAR) e realizados cálculos de frequências, proporções e medidas de tendência central para descrever os desfechos relacionados à ocorrência de partos prematuros. **Resultados:** de 95 prontuários inicialmente elegíveis, 35 eram de gestantes positivas e destas, 15 que realizaram o parto na instituição, quase metade apresentou parto prematuro, e todos esses casos ocorreram em pacientes com teste positivo para a infecção. A maioria das infecções ocorreu no primeiro trimestre de 2022, período de circulação da variante Ómicron. As principais causas de prematuridade foram pré-eclâmpsia, hipertensão arterial e alterações no líquido amniótico. Os recém-nascidos de mães infectadas apresentaram, em média, peso adequado e bons índices de vitalidade nos primeiros minutos de vida. **Conclusão:** a ocorrência de partos prematuros esteve presente entre gestantes com diagnóstico de SARS-CoV-2, evidenciando a relevância do monitoramento clínico dessa população, mas sem evidência direta para o SARS-CoV-2. Os dados reforçam a necessidade de atenção às condições maternas durante a gestação e ao acompanhamento neonatal, especialmente em cenários de infecção viral.

Palavras-chave: Complicações na gravidez; Coronavírus; Recém-nascido; Nascimento prematuro; SARS-CoV-2.

Resumen:

Objetivo: caracterizar a las mujeres embarazadas positivas y negativas para COVID-19 que tuvieron sus partos y los desenlaces clínicos, con énfasis en la ocurrencia de partos prematuros asociados a la infección por SARS-CoV-2. **Método:** estudio de cohortes observacional retrospectivo basado en el análisis de historias clínicas de mujeres embarazadas positivas y negativas para SARS-CoV-2 atendidas entre enero y diciembre de 2022, de las cuales se extrajeron datos maternos y neonatales (edad, edad gestacional, tipo de parto, etiología de la prematuridad, peso al nacer e índice de APGAR), y se calcularon frecuencias, proporciones y medidas de tendencia central para describir los desenlaces relacionados con la ocurrencia de partos prematuros. **Resultados:** de las 95 historias clínicas inicialmente elegibles, 35 correspondían a mujeres embarazadas positivas para SARS-CoV-2 y, de estas, 15 tuvieron el parto en la institución; casi la mitad presentó parto prematuro, y todos estos casos ocurrieron en pacientes con prueba positiva para la infección. La mayoría de las infecciones ocurrió durante el primer trimestre de 2022, período de circulación de la variante Ómicron. Las principales causas de prematuridad fueron la preeclampsia, la hipertensión arterial y las alteraciones del líquido amniótico. Los recién nacidos de madres infectadas presentaron, en promedio, un peso adecuado y buenos índices de vitalidad durante los primeros minutos de vida. **Conclusión:** la ocurrencia de partos prematuros estuvo presente entre mujeres embarazadas con diagnóstico de infección por SARS-CoV-2, lo que evidencia la relevancia del seguimiento clínico de esta población, pero sin evidencia directa de una relación con el SARS-CoV-2. Los datos refuerzan la necesidad de prestar atención a las condiciones maternas durante el embarazo y al seguimiento neonatal, especialmente en contextos de infección viral.

Palabras clave: Complicaciones del embarazo; Coronavirus; Recién nacido; Nacimiento prematuro; SARS-CoV-2.

Corresponding Author: Breno Henrique Caneguim – breno.caneguim@uftm.edu.br

INTRODUCTION

In 2020, the World Health Organization (WHO) declared a global pandemic caused by the SARS-CoV-2 virus, the agent responsible for COVID-19, an infection that leads to inflammation of the respiratory system. The first confirmed cases were reported in China in December 2019, specifically in the city of Wuhan, while the first case in Brazil was detected and confirmed on February 26, 2020, in the city of São Paulo¹.

At the time, initial estimates indicated that approximately 80% of cases would be mild, 14% would present more severe symptoms, and only 6% would progress to critical status². In mild cases, the most common symptoms include fever, cough, dyspnea, runny nose, and myalgia; in severe and critical cases, respiratory difficulty is a prominent feature, frequently associated with the need for hospitalization and intubation. However, as the pandemic progressed and its global impact unfolded, these initial estimates were revised, given that approximately 6 million deaths caused by SARS-CoV-2 infection had been recorded worldwide by 2022³.

Faced with this scenario of rapid spread and high morbidity and mortality, accurate and early detection of the virus became essential for appropriate diagnosis and treatment in an effort to contain its spread⁴. In this context, the WHO approved two main types of diagnostic tests. The first is quantitative reverse transcription PCR (RT-PCR), considered the gold standard for diagnosing COVID-19, which can be performed using nasopharyngeal swabs, oropharyngeal samples, or saliva. The second type consists of rapid tests (RATs), which do not require specialized equipment to perform. Although RT-PCR offers higher sensitivity, its availability is generally restricted to hospitals and specialized clinics, a factor that contributed to the widespread use of rapid tests as the primary detection tool in local health services⁴.

In Brazil, data from the Ministry of Health highlight the magnitude of the pandemic's impact over the years. Regarding the rate per 100,000 inhabitants, 210,167 cases were recorded between March 27 and December 31, 2020, with 92.77 deaths per 100,000 inhabitants. In 2021, 52,895 cases and a mortality rate of 201.59 per 100,000 inhabitants were observed, whereas in 2022, 210,930 cases were recorded, with a mortality rate of 35.57 per 100,000 inhabitants. Regarding deaths, 4,154 were recorded in 2020, 632 in 2021, 1,159 in 2022, and 136 in 2023⁵.

Alongside the progression of cases, the constant mutation of the SARS-CoV-2 virus and the emergence of new variants reinforced the importance of vaccination as a central strategy for controlling the pandemic, combined with non-pharmacological measures⁶. In Brazil, according to the Ministry of Health, 341,048,280 vaccine doses were administered in 2021, 160,829,899 in 2022, and 15,139,818 in 2023, totaling 517,017,997 vaccines administered to Brazilians across those three years up to the time of this research⁵.

In this broader context, it is relevant to consider specific population groups that are more vulnerable to infection and its complications. Initially, the elderly and individuals with comorbidities were classified as high-risk groups. However, as the pandemic progressed, there was an increase in the number of pregnant women infected with SARS-CoV-2, many of whom experienced complications associated with the infection⁷. Although the impact of vaccination on this group is still under investigation, preliminary data have indicated safety and the potential transfer of antibodies to newborns, as well as an association with a reduction in preterm births when comparing vaccinated and unvaccinated pregnant women⁸.

The heightened vulnerability of pregnant women can be understood in light of physiological changes inherent to pregnancy, such as reduced respiratory functional residual capacity, diaphragm elevation, and respiratory tract mucosal edema, as well as immunological alterations that increase susceptibility to viral infections⁹. Furthermore, factors such as age over 35, obesity, diabetes, hypertension, the presence of comorbidities, and third-trimester pregnancy can contribute to more severe cases of COVID-19 and outcomes such as preterm birth¹⁰. Preterm births are defined as those occurring between 22 and 37 weeks of gestation¹¹. However, the outcomes linking SARS-CoV-2 infection to maternal-fetal health are still not entirely clear².

In this regard, studies have investigated potential underlying mechanisms, including the presence of the virus in placental tissues. There are reports of SARS-CoV-2 expression in the placentas of infected women¹². In one specific case, a pregnant woman who tested positive for COVID-19 had her pregnancy terminated at 22 weeks due to placental abruption and severe preeclampsia; virus-like particles were detected in placental cells, although viral expression was not identified in fetal tissues. In this same case, PCR testing was positive for the virus in placental swabs and amniotic fluid, and the newborn required respiratory support in the ICU¹².

Supporting these findings, studies conducted in the United States indicate a higher infection rate among pregnant women compared to non-pregnant women in the 20–29 age group¹³. Furthermore, a meta-analysis involving 111 studies demonstrated increased odds of preterm birth, pre-eclampsia, stillbirth, neonatal mortality, and maternal mortality in pregnant women testing positive for SARS-CoV-2 compared to uninfected women. It is noteworthy that the increased risks of stillbirth and preeclampsia are associated with inflammatory changes affecting the placenta¹⁴.

Despite advances, the impact of SARS-CoV-2 on pregnancy still requires further investigation, particularly regarding effects ranging from fetal implantation through development and delivery to neonatal health. The presence of asymptomatic cases poses an

additional challenge for the detection and monitoring of these pregnant women¹². Similarly, although many newborns of SARS-CoV-2-positive mothers are asymptomatic, there are reports of symptoms such as dyspnea, fever, gastrointestinal manifestations, vomiting, and abdominal distension, even though most cases show good recovery following appropriate treatment⁹.

Within this context, the present study focuses on a teaching hospital located in a city in the Triângulo Sul region of the state of Minas Gerais, Brazil; during the pandemic, this facility served as a referral center for the care of pregnant women and newborns infected with SARS-CoV-2. Within its macro-region, the hospital serves 27 municipalities in Minas Gerais, providing comprehensive coverage through the Unified Health System (*Sistema Único de Saúde* - SUS) and operating with a capacity of 306 active beds¹⁵.

Thus, this study aims to characterize pregnant women, that tested positive and negative for COVID-19, who gave birth at the facility, as well as their clinical outcomes, with a particular focus on the occurrence of preterm births associated with SARS-CoV-2 infection.

METHODS

This is a quantitative, retrospective observational cohort study based on the medical records of women treated between January and December 2022. Data extraction took place from May to November 2023, involving the analysis of records from pregnant patients that tested positive or negative for COVID-19, who underwent antigen testing (rapid test) at the Hospital das Clínicas (HC) of a federal university located in the Triângulo Sul region of Minas Gerais. Non-pregnant patients (whether SARS-CoV-2 positive or negative) from the same period and cases of twin pregnancies were excluded from the study.

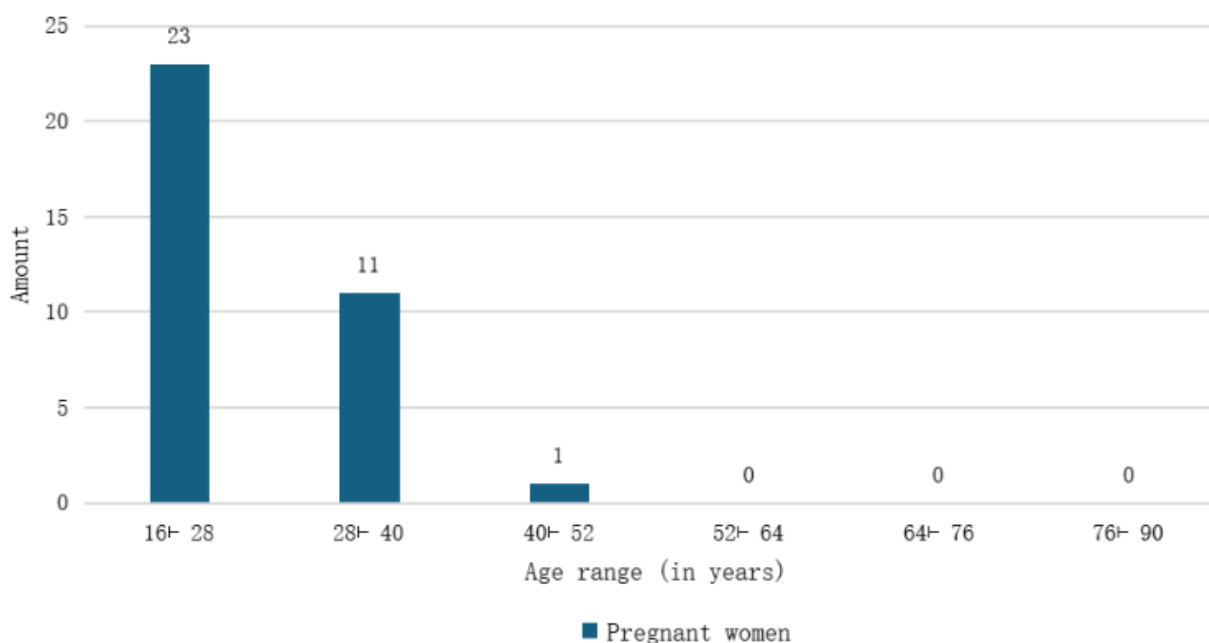
Medical records were analyzed on HC computers using the University Hospital Management Application (*Aplicativo de Gestão para Hospitais Universitário* - AGHU). The following data were obtained: gestational age at the time of testing, primiparity status, indication for Cesarean section, etiology of preterm birth, newborn weight, APGAR score, and the need for neonatal resuscitation. These data were subsequently tabulated in Microsoft Excel® to calculate frequencies, proportions, and measures of central tendency, which were used to describe outcomes related to preterm births.

The study was reviewed and approved by the Ethics Committee of the Hospital das Clínicas of the Universidade Federal do Triângulo Mineiro (HC/UFTM) (opinion no. 5.626.720).

RESULTS

The analysis of medical records yielded a total of 93 records of pregnant and non-pregnant patients who underwent SARS-CoV-2 antigen testing at the HC between January and December 2022. Of this total, two patients had twin pregnancies, and 56 records belonged to non-pregnant women. Thus, out of the 91 records, 35 women were pregnant, ranging in age from 16 to 52 years, and were included in the study ([Figure 1](#)).

Figure 1. Number of pregnant patients testing positive or negative for COVID-19 by age group, Uberaba/MG, Brazil, 2023.



The majority of the women were between 36 and 40 weeks of gestation at the time of testing; the minimum recorded gestational age was 13 weeks, and the maximum was 41 weeks. Most of these pregnant women (specifically 21 of them) tested positive for COVID-19 between January and March 2022 ([Chart 1](#)). Table 1 also shows that, among the 35 pregnant women, 43% (15 patients) gave birth at the HC, while 57% (20 patients) did not give birth at that hospital.

Chart 1. Gestational age of patients at Hospital das Clínicas da UFTM (HC-UFTM) at the time of testing, Uberaba/MG, Brazil, 2023.

Pregnant woman	Gestational age	Date of testing	Positive for COVID-19	Birth at HC-UFTM
Patient 1	25 weeks and 4 days	03/01/2022	Yes	No
Patient 2	32 weeks and 1 day	07/01/2022	No	No
Patient 3	37 weeks and 5 days	12/01/2022	Yes	Yes
Patient 4	39 weeks and 3 days	11/01/2022	No	Yes
Patient 5	40 weeks	14/01/2022	Yes	No
Patient 6	40 Semanas e 1 day	16/01/2022	Yes	Yes
Patient 7	13 weeks	18/01/2022	No	No
Patient 8	38 weeks	21/01/2022	Yes	No
Patient 9	30 weeks	21/01/2022	No	No
Patient 10	34 weeks and 1 day	24/01/2022	Yes	Yes
Patient 11	40 weeks	26/01/2022	No	No
Patient 12	37 weeks and 3 days	30/01/2022	Yes	Yes
Patient 13	37 weeks and 5 days	02/02/2022	Yes	No
Patient 14	39 weeks	04/02/2022	No	No
Patient 15	36 weeks	28/01/2022	Yes	Yes
Patient 16	41 weeks	08/02/2022	Yes	Yes
Patient 17	38 weeks and 3 days	25/02/2022	Yes	Yes
Patient 18	35 weeks and 2 days	21/05/2022	Yes	Yes
Patient 19	39 weeks and 4 days	19/02/2022	No	No
Patient 20	24 weeks and 4 days	19/02/2022	Yes	No
Patient 21	31 weeks and 1 day	17/03/2022	No	No
Patient 22	38 weeks and 4 days	21/04/2022	Yes	No
Patient 23	30 weeks and 1 day	10/05/2022	No	No
Patient 24	27 weeks and 5 days	10/05/2022	No	No
Patient 25	36 weeks and 1 day	28/04/2022	Yes	Yes
Patient 26	36 weeks and 3 days	18/05/2022	Yes	Yes
Patient 27	39 weeks and 5 days	28/05/2022	No	No
Patient 28	37 weeks and 3 days	03/06/2022	Yes	Yes
Patient 29	40 weeks	28/07/2022	No	No
Patient 30	36 weeks and 5 days	02/08/2022	Yes	No
Patient 31	34 weeks and 5 days	01/08/2022	No	No
Patient 32	38 weeks	24/08/2022	Yes	Yes
Patient 33	39 weeks and 4 days	08/10/2022	Yes	Yes
Patient 34	28 weeks and 4 days	27/12/2022	No	No
Patient 35	36 weeks and 4 days	29/12/2022	Yes	Yes

Data obtained from the medical records of the 15 pregnant women who gave birth at the HC showed that 14 tested positive and 1 tested negative for COVID-19 at the time of delivery ([Chart 2](#)). Regarding these 15 women, 7 had preterm deliveries, and all tested positive for COVID-19; there were 8 non-preterm deliveries, with 7 testing positive and 1 testing negative for COVID-19.

Chart 2. Data obtained from the medical records of patients who gave birth at the University Hospital, Uberaba/MG, Brazil, 2023.

Pregnant woman	Gestational age	Positive for COVID	Primiparity	Indication for Cesarean section	Etymology	Weight of newborn	APGAR	Need for resuscitation
Patient 1	37 weeks and 5 days	Yes	No	No	None	3070g	9/10	NR
Patient 2	39 weeks and 3 days	No	No	No	None	2855g	9/9	NR
Patient 3	40 weeks and 4 days	Yes	Yes	No	None	3508g	6/8	NR
Patient 4	34 weeks and 1 day	Yes	Yes	No	Anhydramnios	2225g	9/9	NR
Patient 5	37 weeks and 4 days	Yes	No	No	None	3455g	NI	NR
Patient 6	36 weeks and 1 day	Yes	No	Yes	High blood pressure	2635g	9/9	NR
Patient 7	33 weeks and 1 day	Yes	Yes	Yes	Low-lying placenta	NR	NR	NR
Patient 8	38 weeks and 4 days	Yes	No	No	None	3685g	9/9	NR
Patient 9	35 weeks	Yes	No	No	None	2265g	8/9	NR
Patient 10	36 weeks and 3 days	Yes	No	Yes	Preeclampsia	NR	NR	NR
Patient 11	35 weeks and 3 days	Yes	Yes	No	None	3020g	9/9	NR
Patient 12	37 weeks and 3 days	Yes	Yes	No	None	NR	NR	NR
Patient 13	38 weeks and 1 day	Yes	No	No	None	3650g	9/9	NR
Patient 14	39 weeks and 4 days	Yes	No	No	None	3420g	9/9	NR
Patient 15	36 weeks and 4 days	Yes	No	No	PPROM + Fetal Tachycardia	2790g	8/9	NR

Key: NR = Not Reported; **PPROM** = Preterm Premature Rupture of Membranes; **g** = grams

DISCUSSION

Of the 35 pregnant women included in the study, 21 tested positive for SARS-CoV-2 between January and March 2022. A new variant of the virus, known as Omicron, had emerged in South Africa in late 2021, with the first case recorded in Brazil in early 2022. Due to its rapid spread, this variant caused a surge in cases in Brazil, with approximately 186,000 cases recorded daily and a total of 6,246 deaths linked to the new variant by February 2022¹⁶.

Given the high mutation rate of the Omicron variant, the immune response was less effective compared to other variants¹⁷; however, as vaccination coverage expanded, the number of cases began to decline from April 2022 onwards¹⁶. Furthermore, the rise in cases during this period coincided with the easing of mask-wearing mandates in Brazil and globally¹⁸.

Previous studies indicate that the average age of pregnant patients infected with COVID-19 generally ranges from 22 to 46 years¹⁹; this aligns with the data from the current study, where the patients' average age was 23 years. Of the 35 pregnant women in this study, 15 gave birth at the HC; 14 of these women tested positive for COVID-19, and one tested negative. Seven births were classified as preterm, all involving patients who tested positive for COVID-19, with five attributed to specific causes: high blood pressure, anhydramnios, low-lying placenta, preeclampsia, and preterm premature rupture of membranes (PPROM) combined with fetal tachycardia.

However, only two cases of preterm birth had no identifiable underlying cause. It is important to highlight that SARS-CoV-2 infections can alter and damage both the maternal and fetal immune systems, potentially leading to pregnancy complications such as fetal death, preterm birth, intrauterine growth restriction, and preeclampsia²⁰. Furthermore, due to the increased cardiopulmonary strain experienced by pregnant women during the second and third trimesters, viral infection can result in heightened respiratory distress, potentially leading to fetal distress, miscarriage, or preterm birth²⁰.

Understanding the potential causes of preterm birth is crucial for prevention and proper clinical management. A case study demonstrated a higher frequency of preterm births among primigravid patients²¹. Among the 15 pregnant women who delivered at the HC, five reported this as their first pregnancy; three of these cases were preterm births, with gestational ages ranging from a minimum of 33 weeks and 1 day to a maximum of 35 weeks, and all patients tested positive for COVID-19.

Pregnant women with a gestational age of over 28 weeks (third trimester) should be alert to any clinical signs associated with COVID-19, as they are at higher risk of preterm birth²². Data released by the Brazilian Obstetric Observatory on COVID-19 for 2020 and 2021 show that

the highest number of deaths among pregnant women with Severe Acute Respiratory Syndrome (SARS) occurred during the third trimester (703 deaths), followed by the second trimester (390 deaths) and the first trimester (89 deaths)²³.

Among the pregnant women participating in this study, gestational ages ranged from a minimum of 31 weeks to a maximum of 40 weeks, and the majority of those who gave birth at the HC were in their third trimester. In another case study involving 23 women, 19 tested positive for COVID-19 during the third trimester, with 7 of these cases resulting in preterm births²⁴. Of these, 4 patients went into labor following PPRM, and 3 required preterm delivery due to respiratory distress²⁴. These findings corroborate the data from the present study, as all 15 pregnant women who gave birth at the HC were in their third trimester; 14 tested positive for COVID-19, and 1 tested negative. Regarding the 7 cases of preterm birth at the HC, the timing of the positive infection test coincided with the gestational age at the time of delivery.

Among the 15 deliveries that took place at the HC, three COVID-19-positive pregnant women required a cesarean section due to conditions such as high blood pressure, low-lying placenta, or pre-eclampsia. Research has shown that, among COVID-19 positive pregnant women, approximately 23.4% underwent labor induction; of these, 86.7% were asymptomatic, while only 13.3% exhibited mild symptoms²⁵. Among the latter group, 66.7% successfully delivered vaginally following induction, while others did not; consequently, Cesarean sections were performed without complications²⁵. However, some studies indicate that the mode of delivery is not altered by SARS-CoV-2 in positive or suspected cases, given that the virus has been detected in vaginal secretions or amniotic fluid only in very rare instances²⁶. There is no evidence that a Cesarean section reduces the risk of neonatal infection. Nevertheless, Cesarean sections are the most common mode of delivery for patients with severe illness in intensive care units or those who are intubated²⁶.

Newborn weight and APGAR scores are key determinants of neonatal mortality²⁷. The APGAR score is a method used to assess a newborn's vitality in the first few minutes after birth. It involves evaluating five signs, each scored from 0 to 2, resulting in a total score ranging from 0 to 10. Regarding birth weight, the WHO classifies newborns weighing less than 2,500g as having low birth weight²⁷. Upon comparing the data obtained in this study, it was observed that among the seven deliveries classified as preterm involving pregnant women who tested positive for COVID-19 during the third trimester, the mean birth weight of the newborns was 2,587g (with one newborn weighing 2,225g), while the birth weight was not reported for two of the preterm deliveries. However, while COVID-19 in pregnant women may not be associated with

low birth weight²⁸, SARS-CoV-2 infection in pregnant women can have a direct impact on the occurrence of preterm births and low neonatal birth weight²⁹.

Therefore, it is important to conduct studies on this topic to obtain concrete data regarding whether the virus affects neonatal birth weight. Regarding the APGAR scores of the newborns, the premature infants in the study showed good scores, ranging from a low of 8/9 to a high of 9/9. The relationship between APGAR scores and COVID-19 requires further investigation; however, studies indicate that the majority of newborns born to mothers who tested positive for the infection have APGAR scores of 7 or above³⁰.

CONCLUSION

Based on the data obtained in this study, cases of preterm birth were observed among women diagnosed with COVID-19, particularly those with comorbidities and those in the third trimester of pregnancy. These findings should be interpreted with caution given the study's descriptive nature, as it is not possible to establish associations or draw statistical inferences regarding the variables analyzed.

Despite limitations inherent to the retrospective design, such as the lack of complete data prior to 2022 and the small sample size of pregnant women who gave birth at the institution, the findings cannot be generalized.

Nevertheless, the results highlight the importance of clinical monitoring for pregnant women in the context of COVID-19, especially when risk factors for preterm birth are present. Furthermore, the findings underscore the need for multicenter studies with larger samples and prospective designs to deepen the understanding of maternal and neonatal outcomes. Regarding newborns of mothers who tested positive for SARS-CoV-2, the importance of longitudinal follow-up is emphasized to better elucidate potential long-term effects on child health and development.

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