CLINICAL AND OBSTETRIC OUTCOMES IN PREGNANT WOMEN WITH COVID-19 IN THE BRAZILIAN AMAZON

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ABSTRACT

Objective: analyze the clinical-obstetric condition and the outcomes of pregnant women diagnosed with COVID-19 in a maternity hospital in the Brazilian Amazon. **Methods:** This is a case series in which we analyze clinical and obstetric records of pregnant women with COVID-19. The data were collectedin a maternity hospital in the northernmost Brazil. The outcomes evaluated were maternal death and hospital discharge before or after delivery. **Results:** We identified 17 pregnant women as confirmed COVID-19 cases. 15 patients were symptomatic, with the most common symptoms being dyspnea, cough, fever, and cephalea. One pregnant woman died on the way to the Intensive Care Unit, seven stable patients (41.2%) were discharged without delivery, and nine (52.9%) were discharged after delivery. Of the nine deliveries, six were cesarean sections, with one indication due to the COVID-19 condition, and the others according to obstetric indication. **Conclusions:** During the month in which Amapá presented the highest incidence of COVID-19 cases in Brazil, the findings of this small case group of COVID-19 in pregnant women suggest a severity level similar to those reported for non-pregnant patients.

INTRODUCTION

Since December 2019 there was a series of inexplicable cases of pneumonia reported in Wuhan, China. The government and Chinese researchers took measures to control the epidemic and carried out etiologic studies. On January 30th, 2020, the World Health Organization (WHO) announced the new 2019 coronavirus epidemic as a public health emergency of international concern. On February 11th, 2020, the WHO formally named the disease triggered by this virus as Coronavirus Disease 2019 (COVID-19). On the same day, the Coronavirus study group of the International Committee on Taxonomy of Viruses named it as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS□CoV□2) (Gorbalenya *et al.*, 2020). SARS-CoV-2 is an enveloped virus with a positive, non-segmented, single-stranded RNA genome, member of the Coronaviridae (CoV) family, causing a predominantly respiratory disease with a wide range of clinical severity, varying from asymptomatic or mildly

symptomatic conditions (fever, cough, dyspnea, myalgia, fatigue, and diarrhea) in a large proportion of patients to severe acute respiratory distress syndrome (ARDS) and fatal multiple organ failure (SU *et al.*, 2016; Huang *et al.*, 2020). Pregnant women represent a population particularly exposed to infectious lung diseases due to specific physiological changes during pregnancy (elevation of the diaphragm, increase in oxygen consumption, and edema in the respiratory tract). The pandemics of the Spanish flu in 1918, H1N1 flu in 2009, Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV), and the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) showed an excessive risk of severe forms for pregnant women (Chen *et al.*, 2020; Schwartz, 2020). Regarding the new 2019 Coronavirus, the direct impacts on the pregnancy-puerperal cycle are still uncertain, as research studies are very limited. The possibility of maternal-fetal transmission is still controversial. Additionally, the evidence does not determine if vaginal delivery presents more risk of maternal-fetal contamination than a cesarean delivery. The fetal impact of maternal infections for SARS-CoV-2 in the first and second trimester also needs to be clarified. Finally, the description of

newborn infection several days after birth recalls the need for strict prevention of infection in maternity hospitals (Chen *et al.*, 2020; Cui *et al.*, 2020). From this perspective, this research aims to analyze the clinical-obstetric conditions and outcomes of pregnant women diagnosed with COVID-19 in a maternity hospital in the Brazilian Amazon.

MATERIALS AND METHODS

Study population, setting and data collection: The present research consists of a retrospective and descriptive case series, with a cross-sectional and quantitative design. We included pregnant women infected by COVID-19 confirmed by Reverse Transcriptase - Polymerase Chain Reaction Test (RT-PCR) or Quick-Test after a clinical condition of flu syndrome at a reference hospital in obstetric and neonatal care in the state of Amapá, North of Brazil, in May 2020. Suspected cases (without a confirmed diagnosis) were excluded. Seventeen pregnant women were identified at the research site. Data was collected at the Mother Luzia Women's Hospital (*Hospital MulherMãe Luzia*, HMML) in Macapá, capital of Amapá, the northernmost Brazilian state, which recorded the highest incidence of the country when the data of this research were collected. The health institution in question is the reference public maternity in the state for medium- and high-complexity Gynecology, Obstetrics, and Neonatology services and receives patients from other locations outside the capital. The study was approved by the hospital management and by the National Research Ethics Commission (*Comissão Nacional de ÉticaemPesquisa*, CONEP) under opinion No. 4,102,726. The researchers guaranteed the participants' anonymity, and the informed consent was waived as the data were retrospective. The data of the institution's medical records were obtained by means of a previously structured form. Demographics, clinical and obstetric information, as well as results of imaging tests during hospitalization were obtained.

Study Definitions: According to the Brazilian Ministry of Health,a confirmed case of COVID-19 is defined as a suspected case with positive results in laboratory tests: molecular biology, being RT-PCR or viral genome sequencing; immunological, such as the quick-test or serology, for detecting IgA, IgM, and IgG antibodies in samples collected after the seventh day of symptom onset (Brasil, 2020). Additionally, a chest x-ray can be carried out to detect early changes and a subsequent thorax Computed Tomography (CT) for presumptive diagnosis. Descriptive statistics were used to summarize the data; the results are presented as medians and interquartile ranges (IQR) or as means and standard deviations (SDs), as appropriate. The categorical variables were expressed as counts and percentages. For missing data, no attribution was made. The analysis was conducted with the IBM SPSS software, version 25.0.

RESULTS

During May 2020, 17 pregnant women with confirmed infection by COVID-19 in the hospital under study were identified. This number included pregnant women who had information reported in medical records from admission until outcome (death or hospital discharge). The mean age (± SD) of the pregnant women was 25 years old (± 1.93) (with a variation from 14 to 43). Nine (52.9%) declared to be brown-skinned; most of them (64.7%) were from the state's capital, and 47.1% did not have records about prenatal care. Regarding previous deliveries, most of them (70.6%) had two or more pregnancies, seven (41.2%) did not have any, three (17.6%) had one, and seven (41.2%) had more than one delivery. Regarding abortions, twelve (70.6%) never had one. Most of the pregnant women (52.9%) were in the third trimester. Table 2 shows the findings of the characteristics and vital signs of the pregnant women at the time of hospital admission. In the patients' evaluation, when they arrived at the hospital, there was presence of fetal movements in 88.2% of the cases.

Table 1. General characteristics of the patients at baseline

Characteristics		Frequency (n=17)
		n (%)
Age		
Mean (SD)		
25.4 years old (1.93)		
<18 years old		4 (23.5)
18-35 years old		11(64.7)
>35 years old		2(11.8)
Origin		
Capital		11(64.7)
Inland of the state		6(35.3)
Prenatal care		
Did not perform		4(23.5)
Did perform		5(29.4)
Not reported		8(47.1)
Declared skin color		
Brown		9(52.9)
White		1(5.9)
Black		1(5.9)
Asian		15.9
Not declared		5(29.4)
Number of pregnancies		
Median (IQR) 2 (1 - 4.5)	First Two or more	5(29.4)
		12(70.6)
Previous deliveries		
Median (IQR)		
1 (0 - 2)		
None (nulliparous)		7(41.2)
One		3(17.6)
More than one		7(41.2)
History of miscarriages		
None		12(70.6)
One		5(29.4)
Pregnancy trimester		
1st trimester		1(5.9)
2nd trimester		7(41.2)
3rd trimester		9(52.9)
Pre-existing diseases		
None		16(94.1)
Systemic Arterial Hypertension		1(5.9)

Table 2. Characteristics and vital signs of the patients at hospital admission

Variables at Admission	Frequency (n=17)
	n(%)
Perception of Fetal Movements	
Absent	2(11.8)
Present	15(88.2)
Loss of Amniotic Fluid	
Without loss	9(52.9)
With loss	5(29.4)
Not recorded	3(17.6)
Blood Pressure	
Normotensive	13(76.5)
High blood pressure	4(23.5)
Temperature	
Afebrile	16(94.1)
Febrile	1(5.9)
Heart Rate	
Normal	6(35.3)
Tachycardia	11(64.7)
Respiratory Rate	
Eupnea	2(11.8)
Tachypnea	1(5.9)
Not recorded	14(82.4)
Oxygen Saturation	
Median (IQR)	
98 (97 – 99)	
<95%	1(5.9)
95-100%	16(94.1)
Fetal Heart Rate	
Adequate	16(94.1)
Inadequate	0(0)
Not recorded	1(5.9)
Reason for Seeking Assistance	
Obstetric reason	7(41.2)
Flu syndrome	6(35.3)
Both	4(23.5)

Table 3. Clinical and obstetric evolution of the pregnant women with COVID-19

CHRACTERISTIC	Frequency (n=17)
	n (%)
Onset of the COVID-19 symptoms	
≤7 days before hospital admission	8(47.1)
>7 days before hospital admission	5(29.4)
After hospital admission	4(23.5)
SpO$_2$ <95% episode	
Yes	7(41.2)
No	10(58.8)
Use of supplementary O$_2$	
Received supplementary O$_2$	6(35.3)
Did not receive supplementary O$_2$	11(64.7)
Disorder episode in FHR	
Yes	1(5.9)
No	16(94.1)
Obstetric disorders	
Post-term pregnancy	3(17.6)
Hyperemesis gravidarum	2(11.8)
Oligohydramnios	2(11.8)
Eclampsia	1(5.9)
Prolonged labor	1(5.9)
Fetal macrosomia	1(5.9)
Syphilis	1(5.9)
Urinary tract infection	1(5.9)
Clinical Manifestations	
Asymptomatic	2(11.8)
Symptomatic	15(88.2)
Dyspnea	12/15 (80)
Cough	11/15 (73.3)
Fever	10/15 (66.7)
Cephalea	10/15 (66.7)
Chest pain	8/15 (53.3)
Anosmia	7/15 (46.7)
Asthenia	7/15 (46.7)
Emesis	5/15 (33.3)
Diarrhea	3/15 (20)
Sore throat	3/15 (20)
Shivering	2/15 (13.3)
Epistaxis	2/15 (13.3)
Diagnosis method	
Quick Text	9(52.9)
RT-PCR	7(41.2)
Thorax CT	1(5.9)
Thorax CT	
Did not perform	11(64.7)
Did perform	6(35.3)
Bilateral ground-glass opacity	5/6 (85.7)
Findings with incomplete report	1/6 (14.3)
Hospitalization time (days)	
Up to 3 days	7(41.2)
3-7 days	2(11.8)
More than 7 days	8(47.1)
Outcome	
Maternal death	1(5.9)
Discharge without delivery	7(41.2)
Discharge after delivery	9(52.9)
Delivery (n=9)	
Normal	3(33.3)
Cesarean	6(66.7)
Obstetric indication	5/6 (83.3)
Indicated due to COVID-19	1/6 (16.7)

Table 4. Main medications used in the pregnant women diagnosed with COVID-19

Medication	Frequency (n=17)
	n (%)
Antibiotics	
Used	16(94.1)
Not used	1(5.9)
Corticosteroids	
Used	10(58.8)
Not used	7(41.2)
Hydroxychloroquine	
Used	3(17.6)
Not used	14(82.4)
Anticoagulant (Clexane)	
Used	1(5.9)
Not used	16(94.1)
Ivermectin	
Used	5(29.4)
Not used	12(70.6)
Antipyretic + Analgesic	
Used	15(88.2)
Not used	2(11.8)
Non-steroid anti-inflammatory	
Used	5(29.4)
Not used	12(70.6)
Antiemetic	
Used	8(47.1)
Not used	9(52.9)
Antiviral (Oseltamivir)	
Used	3(17.6)
Not used	14(82.4)

presented COVID-19 symptoms up to one week before admission, five (29.4%) more than one week before, and four (23.5%) after admission. Episodes of SpO2 changes (<95%) in six pregnant women were recorded at some time of the hospitalization and, thus, these women received supplemental oxygen through a nasal cannula. Almost all the pregnant women (94.1%) asserted not having pre-existing diseases. Concerning the main obstetric disorders, there were three cases of post-term pregnancy, two cases of hyperemesis gravidarum (HG), and two cases of oligohydramnios. Fifteen patients were symptomatic, with the most common symptoms being dyspnea, cough, fever, and cephalea. Regarding the diagnosis, in addition to the suspicion due to the flu condition, nine (52.9%) were confirmed through the immunological quick-test, seven (41.2%) through the RT-PCR test, and only one by a highly suggestive thorax CT. Six women had a thorax CT record; however, for one, the full report was not included; in the others, bilateral ground-glass opacity was found. Eight pregnant women were hospitalized for more than 7 days, another seven women were discharged in less than three days, and two between 3 and 7 days. One pregnant woman died on the way to the ICU, seven stable patients (41.2%) were discharged without delivery, and nine (52.9%) were discharged after delivery. Of the nine deliveries, six were cesarean sections, with one indication due to the COVID-19 condition, and all the others according to obstetric indication. The drug therapy (Table 4) consisted of the administration of antibiotics for almost all pregnant women (94.1%); the majority (58.8%) used some corticosteroid. The polemical hydroxychloroquine and ivermectin drugs were administered to three and five pregnant women, respectively.

DISCUSSION

We reported one of the first case series of pregnant women diagnosed with COVID-19 in Brazil, specifically in the Amazon region. We included 17 patients admitted to a hospital in the North region between May 05 and May 28th, 2020. The clinical characteristics of these pregnant women infected by the new coronavirus were similar to those of adults in the general population infected by COVID-19, as evidenced in other studies (Chen *et al*., 2020b; Yu *et al*., 2020). By observing the characteristics of the pregnant women at admission, our findings show that only one woman presented fever, thus suggesting that fever may not be a useful criterion to determine the presence and

In addition, the majority (52.9%) did not present loss of amniotic fluid via the vagina at admission. Regarding the vital signs, 76.5% were admitted normotensive (systolic blood pressure between 120 and 139 mmHg and diastolic blood pressure between 80 and 89 mmHg), almost all (94.1%) were afebrile, and 64.7% presented tachycardia (>100 bpm). The respiratory rate was not recorded in 82.4% of the cases, and oxygen saturation (SpO2) presented adequate values (95%-100%) in sixteen (94.1%) pregnant women. Fetal heart rate (FHR) was adequate (120 bpm-160 bpm) in all cases recorded. Regarding the reason for seeking assistance, seven pregnant women (41.2%) were specifically admitted for obstetric reasons, six (35.3%) for flu syndrome, and four (23.5%) for both reasons. Table 3 refers to the patients' clinical and obstetric evolution, in which eight (47.1%)

severity of COVID-19, which is supported by a study on the clinical characteristics of COVID-19 in China, where patients often did not present fever (Guan *et al*., 2020). Therefore, the need for paying attention to diagnostic protocols that require fever for testing for COVID-19 is emphasized, as they may delay diagnosis. Also at admission, we verified that most of the patients (64.7%) were admitted with tachycardia. In 14 (82.4%) cases, the respiratory rate was not recorded, and almost all presented oxygen saturation and fetal heart rate with adequate values. In the research study by Savasi *et al*. (2020) it was identified that heart and respiratory rates were significantly higher at the admission of women with a severe progression of the disease. In COVID-19, acute respiratory insufficiency due to acute hypoxemia is the primary manifestation in the severe form of the disease. In this study, seven pregnant women presented SpO2 below 95% at some time during their hospitalization, and four received supplemental oxygen through a nasal cannula to improve the condition. For He *et al*., (2020) the objective of the treatment through a nasal cannula must be maintained until SpO2 is above 95% for patients without chronic pulmonary disease; in addition, the patients must wear a surgical mask to reduce the risk of droplet or aerosol transmission of the virus. Therefore, providing supplemental oxygen for patients with COVID-19 can be beneficial when the public health resources enable its implementation (Shenoy; Luchtel; Gulani, 2020). Changes in the fetal heart rate can be an early indicator of maternal respiratory deterioration, that is, the combination of effects, such as maternal hypoxia and decrease in oxygen transfer through the placenta, can cause changes in the fetal heart rate (Rasmussen *et al*., 2020; Gracia-Perez-Bonfils *et al*., 2020).However, the outcomes show that only one pregnant woman presented elevated fetal heart rate (>160 beats per minute) at some time during hospitalization; the other women did not present any abnormality. During hospitalization, two women were completely asymptomatic and, among the symptomatic ones, the most common symptoms reported were dyspnea, cough, fever, cephalea, and chest pain. The clinical manifestations due to COVID-19 for these women were similar to those of other research studies with pregnant and non-pregnant populations (Huang *et al*., 2020; Chen *et al*., 2020; Li *et al*., 2020).

In this study sample, six of the nine deliveries were cesarean; however, five were strictly indicated for obstetric reasons, such as cases of oligohydramnios, post-term pregnancy, and eclampsia. In addition, there were three premature deliveries, but their causes were not related to COVID-19 pneumonia, as well as in another study (Chen *et al*., 2020). The number of cesarean deliveries, despite not having obstetric indication, draws the attention. The literature shows that this type of delivery is associated with increased morbidity during immediate postpartum due to an increase in the risk of thromboembolic disease, blood loss, and infections (Sandall *et al*., 2018).Accordingly, it is important that vaginal delivery occurs for women with respiratory diseases whenever possible, so as to minimize postpartum complications. As in another study, 12 this case series did not have a uniform therapeutic management, mainly because it is an unprecedented disease where there is no validated treatment to control the infection and more robust evidence is still in progress. We observed that for daily care and, according to the symptoms, analgesics and antipyretics were administered in 88.2% of the women; additionally, as a hospital protocol, almost all received antibiotics (ceftriaxone and azithromycin). We highlighted that ten women received some type of glucocorticoid (commonly betamethasone and prednisone), five used ivermectin, and three used hydroxychloroquine. It is worth noting that recent data show that the use of glucocorticoids, especially dexamethasone, can result in lower mortality in patients with the severe form of the disease (RECOVERY Collaborative Group *et al*., 2021). On the other hand, the use of hydroxychloroquine has shown negative evidence, with more side effects when compared to placebos (Boulware *et al*., 2020). The use of ivermectin has uncertain evidence, despite positive results in laboratories. In human beings, possibly effective concentrations, based on in vitro studies, would be physiologically unattainable (Chaccour *et al*., 2020).

Conclusion

In summary, of the seventeen patients in this study, only one died, and the others did not develop severe pneumonia. From this perspective, based on the findings and the research studies found, there is currently no evidence strongly suggesting that COVID-19 infection during pregnancy can lead to severe adverse outcomes. The research limitations were the small sample; the low record of laboratory information due to difficulties in carrying out the exams, aggravated by the high demand due to the pandemic; and the lack of information on the neonates, as their medical records were located separately from the maternal ones, which made it impossible to assess APGAR scores, newborn infections or neonatal deaths.

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