Characteristics of Newborns from Mothers with SARS-CoV-2 Infection in a Portuguese Hospital

Características de Recém-Nascidos Filhos de Mães com Infecção por SARS-CoV-2 num Hospital Português

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ABSTRACT

Introduction: Guidance for pregnant women has been particularly problematic since the beginning of the COVID-19 pandemic. The aim of this study was to describe the characteristics and outcomes of pregnant women with SARS-CoV-2 infection and their newborns.

Material and Methods: Case review of clinical records of pregnant women with SARS-CoV-2 infection admitted for delivery and their newborns from April to December 2020 at a hospital in the Lisbon metropolitan area.

Results: From 1755 births, 81 (4.6%) were from SARS-CoV-2 positive mothers. Most (83.9%) were term newborns. Almost 16% were preterm, while there was an overall prematurity rate of 9.9%. Most women (88.6%) were asymptomatic. Rooming-in occurred in 80.8% cases and 19.2% newborns were admitted to the Neonatal Intensive Care Unit. From the total, 56.7% newborns were breastfed from birth and 43% had mixed feeding. None of the newborns had symptoms related to COVID-19 infection, and all had negative rt-PCR for SARS-CoV-2 at birth and at 48 hours of life. The majority (85.2%) was discharged home with their mothers.

Discussion: Pregnant women with COVID-19 have shown immune characteristics resembling healthy pregnancies, and it is not yet clear if SARS-CoV-2 can be vertically transmitted. Recent updates on neonatal guidance now recommend rooming-in and support the relative safety of breastfeeding.

Conclusion: This study supports other published articles regarding maternal and neonatal outcomes of SARS-CoV-2 infected pregnant women, including the absence of short-term adverse outcomes with rooming-in and breastfeeding.

Keywords: Breast Feeding; Infant, Newborn; Pregnancy; Rooming-in Care; SARS-CoV-2

RESUMO

Introdução: Desde o início da pandemia COVID-19, tem sido particularmente difícil obter orientações relativas a mulheres grávidas. Este estudo teve como objetivo descrever as características e resultados clínicos das grávidas com SARS-CoV-2 e dos seus recém-nascidos.

Material e Métodos: Revisão de processos clínicos de grávidas com infecção por SARS-CoV-2 admitidas para o parto, e dos seus recém-nascidos, no período de abril a dezembro de 2020 num hospital da área metropolitana de Lisboa.

Resultados: De um total de 1755 nascimentos, 81 (4,6%) foram de mães positivas para SARS-CoV-2. A maioria eram recém-nascidos de termo; 16% eram prematuros, sendo a taxa geral de prematuridade 9,9%. A maioria das grávidas (88,6%) foi assintomática. O alojamento conjunto ocorreu em 80,8% dos casos e 19,2% dos recém-nascidos foram admitidos na Unidade de Cuidados Intensivos Neonatais. A maioria dos recém-nascidos (56,7%) fez leite materno desde o nascimento e 43% fez aleitamento misto. Nenhum recém-nascido apresentou sintomas relacionados com a infeção por COVID-19 e todos foram negativos por rt-PCR para SARS-CoV-2 ao nascimento e às 48 horas. Do total, 85,2% dos recém-nascidos tiveram alta para o domicílio com a mãe.

Discussão: As grávidas com COVID-19 apresentam características imunológicas semelhantes a grávidas saudáveis e ainda não é clara a transmissão vertical do SARS-CoV-2. Atualizações recentes sobre as orientações neonatais recomendam o alojamento conjunto e apoiam a segurança da amamentação.

Conclusão: Este estudo corrobora resultados maternos e neonatais anteriores incluindo a ausência de resultados adversos a curto prazo com alojamento conjunto e amamentação.

Palavras-chave: Aleitamento Materno; Alojamento Conjunto; Gravidez; SARS-CoV-2; Recém-Nascidos

INTRODUCTION

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), responsible for the coronavirus disease 2019 (COVID-19), emerged in China in December 2019. Due to its rapid and massive spread, the World Health Organization (WHO) declared it a global pandemic in March 2020.

Coronavirus are single stranded RNA viruses, with a high rate of genetic mutations and recombinations, which enables them to escape the immune system causing new infections. They bond to angiotensin-converting enzyme-2 receptors, present in the epithelial cells of type II pneumocytes, kidney, intestine and blood vessels.[1] COVID-19 typically presents as an acute respiratory disease and pneumonia, although other systems may be affected.[2] Transmission occurs mainly via respiratory droplets and aerosols, but other transmission routes such as perinatal transmission have been described.[3] In the latter, it has been unclear whether it occurs via transplacental, transcervical or environmental exposure.

Pregnant women are not thought to be more susceptible to the infection than the general population.[4] However, according to evidence of similar viral illnesses and

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previous coronavirus infections, severe maternal and neonatal morbidity and mortality due to COVID-19 were likely to be expected in pregnancy. Nevertheless, recent reviews have shown that pregnant women with COVID-19 have immune characteristics resembling healthy pregnancies and show mild or no symptoms compared to non-pregnant women.[4,5]

The possibility of mother-to-fetus transmission of SARS-CoV-2 is currently highly debated, and the impact on the fetus may be different depending if the maternal infection occurs in the first, second or third trimesters. Miscarriage, preterm delivery, low birth weight, congenital infection and active infection of the newborn are potential adverse outcomes.[6]

The aim of this study was to describe the characteristics and outcomes of pregnant women with SARS-CoV-2 infection and their newborns and to analyze the differences between term and preterm newborns.

MATERIAL AND METHODS

Data was gathered through case review of clinical records of pregnant women admitted with SARS-CoV-2 infection at the time of delivery, and their newborns, in a hospital of the Lisbon metropolitan area, Hospital Professor Doutor Fernando Fonseca, EPE (HFF) from Abril to December 2020. Cases of fetal death were excluded. The study was approved by the Hospital Ethics Committee.

Since April 1st, all pregnant women admitted to the delivery room were tested for SARS-CoV-2 using real time Phanter Fusion® (Hologic) reverse transcriptase - polymerase chain reaction (rt- PCR) tests from both nasopharyngeal and oropharyngeal swabs. If women developed symptoms or revealed a positive epidemiologic context while admitted, a second test was performed.

The delivery room was divided into two circuits: one for admission and delivery of infected women and another for non-infected women ('clean' circuit). Both the maternity ward and the Neonatal Intensive Care Unit (NICU) were also divided into two circuits. In the NICU, a separate negative pressure room with capacity for four admissions was created, to admit newborns (term and preterm) from positive mothers who required special care.

The mother's medical history was reviewed. Data included: demographic and clinical characteristics, epidemiology, comorbidities, gestational age at diagnosis, duration of infection, presence and progression of symptoms, type of delivery, rooming-in and breastfeeding. A non-elective caesarian was considered if either maternal (pre-eclampsia/eclampsia, previous obstetric history, etc.) or fetal (fetal distress, pelvic presentation, macrosomia, etc.) conditions were described. At delivery, according to the hospital protocol, delayed cord clamping was initially not performed and skin- to-skin contact was allowed depending on maternal condition.

Women were considered asymptomatic or pre-symptomatic if they had a positive test for SARS-CoV-2 but no symptoms. According to the Centers for Disease Control and Prevention (CDC), maternal disease was classified as mild, moderate, severe and critical as follows: a) mild: fever, anosmia, cough, malaise, headache or gastrointestinal symptoms, without shortness of breath, dyspnea or abnormal chest imaging; b) moderate: evidence of lower respiratory disease by clinical assessment or imaging and an oxygen saturation ($SatO_2$) ≥ 94% on room air at sea level; c) severe: polypnea, $SatO_2$ < 94% on room air at sea level or lung infiltrates > 50%; d) critical: respiratory failure, septic shock and/or multiple organ dysfunction.

Rooming-in and breastfeeding were allowed throughout the study period if the mother was asymptomatic or mildly symptomatic and able to comply with safety measures (frequent and careful hand and breast hygiene, use of facial mask, use of gloves while taking care of the newborn and keeping the newborn in the crib two meters away from the mother's bed). Mother and newborn were allocated in a COVID-19 postnatal ward in an individual room (without negative pressure) and instructions for contact, respiratory and breastfeeding precautions were explained. Medical and nursing staff did follow-up on compliance. A flyer regarding precautions related to COVID-19 and safety measures while taking care of the newborn was delivered upon admission.

The newborn data analyzed included: gestational age in weeks (wGA), birth weight, rt-PCR results collected from nasal swabs at birth and 48 hours of life and follow-up at 14 days of life. Birth weight definitions were: extremely low birth weight < 1000 g, very low birth weight < 1500 g, low birth weight < 2500 g and macrosomia > 4000 g. Light for gestational age was considered when weight was below the 10th percentile on Fenton`s growth charts. Prematurity was considered below 37 weeks of gestational age and late prematurity between 34 – 36 + 6 wGA. Newborns born from positive mothers were admitted to the NICU when in need of special care, if the mother was non-compliant with safety measures or in episodic situations when rooming-in was not available due to hospital management policies. In the NICU, newborns were admitted to a COVID-19 negative pressure ward, until two consecutive negative rt- PCR tests were obtained. Since it was not possible to ensure the safety control measures regarding transport of maternal milk to the NICU, these newborns were fed with formula while admitted. After two negative rt-PCR tests, admission followed the same procedures as other newborns.

All cases were evaluated by the hospital's social services and discharge conditions regarding compliance with social isolation measures were assessed. Clinical discharge followed standard policies. A telephone follow-up was performed after 14 days of delivery.

Statistical analysis was performed using SPSS 21.0 (SPSS, INC., Chicago, USA). For numerical variables with normal distribution, the mean and standard deviation were calculated. The median, minimum and maximum values were calculated for non-normal distribution variables.

RESULTS

During the study period there was a total of 1755 births and 81 (4.6%) were from SARS-CoV-2 positive mothers. A total of 68 (84%) were term newborns (group A) and 13 (16%) were preterm (group B), compared with an overall prematurity rate of 9.9%. The mean gestational age at delivery was 37.3 weeks. Most newborns were male (64.2%) and there were two twin pregnancies. Almost a quarter of cases (22.2%) occurred in June while November was the month with less cases (2.5%). Mean maternal age was 29.2 years old (minimum: 18; maximum: 44) and 64.6% were from African origin. The remaining were from Portugal (19%), Asian countries (8.9%) and Brazil (7.5%). A total of 45.6% women were employed; 43% were either unemployed or staying at home and in 11.4% there was no available data. The vast majority of women lived in municipalities served by the hospital while 7.4% lived in other areas, and were mostly in utero transfers.

Twenty women (25.3%) had comorbidities: sickle-cell trait (five); gestational diabetes (five); gestational diabetes, hypertension and obesity (four), chronic hepatitis B (two), human immunodeficiency virus (two), gestational hypertension (one) and previous cannabinoid consumption (one).

In sixty-seven women (84.8%), diagnosis of SARS-CoV-2 infection was made at hospital admission for delivery. Eight women (10.1%) had a positive result before delivery as the test was performed either because they had a positive epidemiological link, had symptoms or were admitted for pregnancy surveillance. Four women were admitted with a negative SARS-CoV-2 test and were diagnosed in the maternity ward after delivery. These women repeated the test either because they developed symptoms (three) or because a positive close epidemiological link was established (one). In only nine women (11.4%) a positive epidemiological context for COVID-19 was present (mainly family members) while the vast majority recalled no disease link.

Most women (88.6%) were asymptomatic and only nine (11.3%) presented SARS-CoV-2 related symptoms: seven (77.7%) had mild disease (fever, cough, malaise) and two (22.3%) presented with severe illness: one 32 wGA with respiratory distress, pneumonia and supplementary oxygen need (delivered by cesarean at 34 wGA due to deterioration of the mother's respiratory status) and the other, 34 wGA twin pregnancy, with simultaneous pre-eclampsia diagnosis, that developed respiratory distress with pneumonia and need of noninvasive mechanical ventilation (delivered immediately). Both women with severe disease were previously healthy with no identifiable comorbidities.

Most births (69.3%) were dystocic: cesarean (58.2%) and forceps / vacuum (11.3%). Cesarean was exclusively due to COVID-19 maternal infection in 18.5% of the cases, and due to lack of progress in labor in 7% cases. The remainder were due to maternal or fetal illness (10% and 22.7% respectively). Maternal illness included pre-eclampsia (three); human immunodeficiency with high viral load (two); COVID-pneumonia (two) and previous cesarean (one). The fetal reasons for cesarean were fetal distress (ten); fetal growth restriction (three); macrosomia (three); breech presentation (two). Table 1 describes maternal characteristics.

At delivery, a bath was given to 61.7% newborns while skin to skin contact was promoted in only 12% cases, all delivered by eutocic birth. Rooming-in occurred in most cases (80.8%) and in 16 cases (19.2%) there was direct admission to the NICU due to prematurity (ten); temporary absence of rooming-in capacity (four), respiratory distress (one); intended for adoption (one). Most newborns (56.7%) were breastfed from birth, and 43% had mixed feeding, mostly due to NICU admission.

None of the newborns had symptoms related to COVID-19 infection, and all had negative rt-PCR for SARS-CoV-2 at birth and 48 hours. There was one death – an extreme premature of 26 wGA, with *Pseudomona aeruginosa* associated septic shock, on the 41st day of life.

As for an analysis of newborns by group, in group A (term newborns; n = 68) the mean gestational age was 39 weeks (minimum 37; maximum 41), and mean birth weight was 3301 g (minimum: 2360; maximum 4700). Rooming-in occurred in 76.5% of the cases. Six newborns (8.8%) were admitted to the NICU until discharge due to: transient tachypnea of the newborn (one); adoption (one) and temporary absence of rooming-in capacity (four). Eight term newborns (11.8%) stood partially with their mothers during hospital admission: three were admitted first to the NICU as mothers (two) or the newborn (one) needed special immediate care, being relocated afterwards; and five were first roomed-in and were later transferred to the NICU due to: mothers becoming symptomatic (two); mother not complying with

Table 1 – Characteristics of SARS-CoV-2 positive pregnant women

Variable (n = 79)	**Yes**	**No**
Age	29.2 years (min.:18; max.: 44)	
African origin	51 (64.6%)	28 (35.4%)
Presence of comorbidities	20 (25.3%)	59 (74.7%)
Positive epidemiological link	9 (11.4%)	70 (88.6%)
Positive RT- PCR at admission	67 (84.8%)	12 (15.2%)
Symptomatic	9 (11.3%)	70 (88.6%)
Delivery by cesarian	47 (58.2%)	32 (40.5%)

min.: minimum; max.: maximum

safety procedures (one) and the unavailability of rooming-in (two). The mean length of hospital stay was 4.4 days (minimum: 2; maximum: 26). The longest stay was due to social factors (adoption).

There was a total of 13 preterm newborns (group B), mostly late preterm (84.6%). The mean gestational age was 33 weeks (minimum: 26; maximum: 36) and mean birth weight 1080 g (minimum: 0.760; maximum: 3000). There were two low birth weight preterm newborns (16.9%). There were only three cases of spontaneous prematurity (23%), one being a twin pregnancy. Two (15.3%) were due to fetal growth restriction and the other cases (53.8%) were mostly due to maternal illness: pre-eclampsia (four), COVID-19 pneumonia (two), chorioamnionitis (one); diabetic ketoacidosis (one).

Ten preterms (76.9%) were admitted to the NICU and the three late preterm newborns (35 and 36 wGA) were roomed-in with their mothers since birth. The mean hospital stay in this group was 12.3 days (minimum: 5; maximum: 41). Most newborns (61.5%) received exclusive maternal breastfeeding during the hospital stay, which was kept on follow-up at 14 days in 15.4%. Table 2 reflects the characteristics of the newborns.

As for preterm and term newborns, there were significantly more SARS-CoV-2 symptomatic women delivering preterms (30.7% *vs* 7.3%, p = 0,01) while there were no differences amongst women with previously diagnosed co-morbidities (23.1% *vs* 25%, p = 0.56). Breastfeeding was also different between groups. The rate of exclusive breastfeeding during the hospital stay (91.2%) and on 14-day follow-up (83.9%) was higher in term newborns, and when comparing newborns (term and preterm) admitted to the NICU with those with rooming-in during all hospital stay, the former presented a significantly lower exclusive breastfeeding rate at discharge (62.5% *vs* 96.4%, p = 0.001).

All SARS-CoV-2 positive mothers were evaluated by the hospital's social services regarding income, number of co-inhabitants and availability of isolation conditions at home for both mother and newborn. The mean number of co-inhabitants was three (minimum: 0; maximum: 9), and in two situations it was considered that there were no conditions of social isolation at home. Most newborns were discharged home with their mothers (85.2%) and 9.9% with a designated family member that previously tested negative for SARS-CoV-2 (while the mother remained admitted at the hospital or had been previously discharged home); three newborns were transferred to the pediatric ward while awaiting resolution of the social situation. On the 14th day of life, a follow-up phone call was performed with an 87.6% response rate. All newborns contacted remained healthy with no related SARS-CoV-2 symptoms.

DISCUSSION

Lisbon and Tagus Valley was the second most affected region with SARS-CoV-2 infection in Portugal with 133 739 cases by the end of December 2020. Amadora, which is part of the Lisbon and Tagus Valley region, is Portugal's most densely populated municipality with 7363 inhabitants/km^2 and is served by a single hospital - Hospital Professor Doutor Fernando Fonseca, EPE. The municipality of Sintra, even though it is highly populated, it has a lower population density, with 1184 inh/km^2, and is served by two hospitals, one of which being HFF.

HFF has a level III Neonatal Intensive Care Unit (NICU) and a level III Obstetrics Department. It has been certified with the baby friendly hospital initiative since 2010. It serves a population of more than 600 000 inhabitants in the municipalities of Amadora and Sintra and has around 2800 births per year.

Of the resident population in Amadora, 10% are of foreign origin, 3.8% live in low-income neighborhoods, and the unemployment rate is 15%, all higher than in the rest of the country.[7] This is reflected in this study, where the majority of infected women (81.1%) were of foreign origin, and almost half (43%) unemployed or staying at home. The mean maternal age was 29.2 years and 64.6% were of African origin. All infected pregnant women were evaluated by the hospital's social services after delivery, but only a residual number was considered not to have conditions of social isolation at home. Ethnic disparities in incidence and outcomes of COVID-19 infection have been reported in pregnant and non-pregnant women worldwide, and possible reasons suggested for these disparities include social and health behaviors, co-morbidities and potential genetic influences.[4]

Many of the initial cases of SARS-CoV-2 infection reported outside of China were imported or linked to travelers, which was also the case in Portugal. Worldwide, health

Table 2 – Characteristics of newborns from SARS-CoV-2 positive mothers

Variable (n = 81)	**Preterms** (n = 13)	**Term newborns** (n = 68)
Mean gestational age at diagnosis	33 wGA (min.:26; max.: 36)	39 wGA (min.: 37; max.: 41)
Mean birth weight	1080 g (min.: 0,76; max.: 3000)	3301g (min.: 2360; max.: 4700)
Admission at NICU	10 (77%)	6 (8.8%)
Rooming-in	3 (23%)	54 (79.4%)
Feeding on maternal milk until discharge	61.5%	91.2%
Feeding on maternal milk at 14th day of life	38.5%	83.9%
Mean length of hospital stay	12.3 days (min.: 5; max.: 41	4.4 days (min.: 2; max.: 26)

min.: minimum; max.: maximum; NICU: Neonatal Intensive Care Unit

officials adopted the 'Test-Track-Trace' strategy, through intensive epidemiological investigations coupled with isolation of cases and quarantine of close contacts. However, community transmission became widespread, and the ascertainment of the infection source became difficult to establish.[8,9] In our report, an epidemiological link could only be established in 11.4% of the cases, although follow up and contact tracing was not performed by hospital staff but rather by public health professionals.

Soon after the beginning of the pandemic, a national emergency plan was declared with a strict lockdown applied from 18th of March to the 4th May, and mobility restrictions during December. Although there was an increase of daily cases from March onwards, the monthly number of cases in pregnant women did not differ significantly in our study.

Following national guidelines, initial COVID-19 testing (in the general population) was only performed in symptomatic individuals. In July, and according to recommendations from the WHO and the European Centre for Disease Prevention and Control, testing was extended to suspected cases and close contacts as contact tracing was considered essential to halt the transmission of COVID-19.[9]

In hospital settings worldwide, universal screening test using rRT-PCR tests in nasopharyngeal swabs was adopted for specific situations, such as for obstetric patients and healthcare workers, with the CDC recommending universal screening for all pre-admission patients, depending on testing capacity and disease prevalence. This testing strategy may result in false-negative test in patients who are tested during the incubation period, and which later become infectious.[10] On the other hand, screening asymptomatic patients will detect individuals with low viral loads (either at early or late onset of disease) and therefore with a level of contagiousness that could be potentially negligible, although clear data on the relationship between virus load and contagiousness is still missing.[11] These issues were documented in this study, where four women were admitted with negative SARS-CoV-2 and were afterwards diagnosed in the maternity ward: three developed symptoms and one was re-tested after establishment of an epidemiological link. Nevertheless, there are many potential benefits of universal SARS-CoV-2 screening. In hospitalized patients, detection of asymptomatic infection can guide hospital isolation policies, bed assignments, and use of personal protective equipment. For healthcare workers, it might improve workforce depletion by unnecessary quarantine, reduce transmission in asymptomatic cases, contain the virus in healthcare settings, and protect hospital staff from infection.[12]

Worldwide, the incidence of infection in pregnant women at any gestational age is still unclear, as universal screening tests are not generally used, except in the presence of symptoms or at admission for delivery. In our study, of all pregnant women admitted for delivery, 4.6% were positive, but most (88.6%) were asymptomatic for SARS-CoV-2 infection. These results concur with other studies where universal screening is performed prior to delivery.[13]

In the symptomatic group (11.3%), seven women had mild disease and two met criteria for severe disease, requiring non-invasive ventilation. The predominant features of symptomatic patients were cough, fever and dyspnea, and did not differ based on gestational age. Similar clinical manifestations have also been described in other cohort studies.[14,15] In our study there was a significant higher number of preterm births in symptomatic women (p = 0.01) suggesting that symptomatic disease could be associated with prematurity.

Comorbidities considered as risk factors for disease severity, such as obesity, hypertension, diabetes and immunodeficiency, occurred in 25.3% of the cases but none amongst symptomatic women. Previous studies have also reported that pregnant women do not appear to be at an increased risk of severe illness compared with non-pregnant women in the general population.[5,16] The estimated mortality rate for pregnant patients is 0.6% - 2%, which is comparable to the general population, with those with critical disease at the time of presentation accounting for the majority of deaths.[14] In our study there was no significant association between women with previous comorbidities and prematurity and no maternal deaths were reported.

The impact of COVID-19 infection during pregnancy depends on the trimester in which occurs, with evidence suggesting that miscarriage is more common in the first trimester.[4] The lack of differentiated syncytiotrophoblasts during the first and second trimesters predisposes to increased transplacental infectivity of certain pathogens in early pregnancy. Moreover, the histopathological changes (vascular malperfusion, inflammation and thrombosis) documented in the placenta of infected women, may contribute to the disruption of the maternal-placental interface and play a role in adverse fetal outcomes. Currently, the PRIORITY study (Pregnancy CoRonavirus Outcomes RegIsTry) is recruiting pregnant women with known or suspected COVID-19 disease to understand its clinical course and risks of complications such as miscarriage, stillbirth, preterm labor, and neonatal health.[14,17]

In our study, the mean gestational age at delivery was 37.3 weeks. There was a 16% prematurity rate amongst COVID-19 pregnant woman, mostly late prematurity (84.6%) and 16.4% of newborns with low birth weight. This is higher than the national prematurity rate which is around 8%. This might be justified by the high number of iatrogenic prematurity due to maternal disease (38.4%), mostly hypertension and/or pre-eclampsia. Similar results have been reported in a systematic review that compared obstetric outcomes in combined coronavirus infections and found that SARS-CoV2 resulted in higher rates of preterm birth and pre-eclampsia.[18] The hormonal profile of normal gestation is characterized by an early increase of all components of the renin-angiotensin-aldosterone system, including angiotensin-converting enzyme 2 (ACE2), which is responsible for converting angiotensin Ang I to Ang-(1-9) and Ang II to Ang-(1-7) (vasodilatory, antithrombotic, and

anti-inflammatory activities). During pregnancy, low blood pressure is maintained through a balance between being refractory to the pressor effect of Ang II and increased levels of Ang-(1-7) which exhibit systemic vasodilatory responses. In pre-eclampsia, this balance is lost, with an over-exaggerated Ang II blood pressure response and decreases Ang-(1-7) levels. SARS-CoV-2 binds to ACE2 receptors and causes its down-regulation (increasing Ang II and decreasing Ang-(1-7), which might exacerbate pre-existing pre-eclampsia.[18]

In pregnant women with SARS-CoV-2 infection, there is no formal indication for routine cesarean delivery except for obstetrical reasons, although in many case reports, it was the preferred mode of delivery, with the aim of minimizing the chance of cross infection and ensuring staff safety. The delivery room management should be performed according to standard procedures, without changes in the practice of delayed cord clamping and skin-to-skin contact. Initial care of the newborn should not be delayed due to COVID-19, and if needed, neonatal resuscitation should be performed according to national guidelines.[1] In this study cesarean delivery occurred in 58.2% of cases (the overall national cesarean rate is 36%). Most cesarean deliveries were due to obstetric or fetal reasons (32.7%), but in 18.5% of cases it was due to COVID infection, where the aim was to minimize the risk of cross infection between mothers and healthcare workers. More than half of newborns had a bath with chlorhexidine and skin-to-sin contact was performed in only a minority of cases (11%). There was no data available regarding delayed cord clamping. Although not part of standard procedures, a bath after delivery may help remove virus particles that are potentially present on the newborn's skin as it is a standard established procedure in other potentially vertically transmitted viral infections.

A recent review has reported that SARS-CoV-2 RNA was isolated in amniotic fluid, placenta, umbilical cord, and breast milk.[18] Nevertheless, it is not yet clear if SARS-CoV-2 can always be transmitted from mother to infant. Although viremia is seen in 1% of the cases, suggesting that placental and fetal seeding might be rare, transplacental transmission has been recently confirmed by comprehensive virological and pathological investigations.[3,19] In this study, all newborns tested negative for COVID-19 at birth and 48 hours after, although routine PCR, histological or immunohistochemistry tests were not performed for placenta, amniotic fluid, umbilical cord or breast milk.

The benefits of breast milk for neonatal health are universally recognized, and the WHO recommends that every neonate should be breastfed for at least six months. These recommendations apply to SARS-CoV-2 positive mothers as long as basic hygiene measures are followed.[14] Despite this, breastfeeding in these newborns has been a controversial topic and although various guidelines endorse the relative safety of breastfeeding whilst infected with COVID-19, more data is needed. SARS-CoV-2 RNA has been isolated from breast milk samples, but it is still unclear whether it has a potential infectious capacity. Additionally, SARS-CoV-2 IgG has been identified in breast milk samples from positive mothers, raising the question of a potential protective role of breast milk in these situations.[19] Combining all this, some mothers may express concern about breastfeeding.

In the early stages of the pandemic, several medical organizations recommended the temporary maternal-infant physical separation, in order to protect newborns from acquiring SARS-CoV-2 infection from mothers with COVID-19 at the time of delivery. This recommendation ran counter to mother-infant rooming-in practices and to its multiple advantages, including supporting effective breastfeeding. Later, multicenter studies from Italy and USA supported the most recent updates on neonatal guidance, which now recommend rooming-in unless mothers are too ill to care for their newborn.[20]

In our hospital, rooming-in and breastfeeding from SARS-CoV-2 positive mothers have been allowed since the beginning of the pandemic, as long as the mother was asymptomatic or mildly symptomatic and considered capable of following infection control recommendations. As a result, most newborns (80.8%) were roomed-in with their mothers, and 56.7% received exclusive breast milk (not extracted) within the first hour of birth. Most mothers understood the need for compliance with basic hygiene measures, including wearing surgical facemask during breastfeeding and all of them showed confidence in the staff's recommendations regarding rooming-in and breastfeeding. The success of breastfeeding, during hospital stay and on follow up, as expected, was higher amongst newborns roomed-in from birth and amongst term newborns.

From the beginning of the pandemic, clinicians from all specialties have been challenged to offer optimal care to infected patients and provide adequate advice to individuals that have been potentially affected by the virus. Professional societies have also had difficulty in providing clinical guidance, which was particularly problematic in the initial stages of the pandemic, given the limited information about this new disease. Developing guidance for pregnant mothers and their newborns was no exception, and although national and international guidelines initially recommended temporary maternal-infant physical separation and absence of breastfeeding, in this study, baby friendly practices with rooming-in and direct breastfeeding were allowed since the beginning of the pandemic. To our knowledge, at the time, this was an innovative approach in the Portuguese neonatal setting, which later became the standard of care in neonatal guidance.

Upon discharge, there was 87.6% adherence to telephone visits. None of the newborns reported to have any symptoms consistent with COVID-19 and none had emergency department visits or hospital admissions related with COVID-19. The results regarding the absence of short-term adverse neonatal outcomes with rooming-in and breastfeeding concur with other published articles.[21] The success of breastfeeding during hospital stay was significantly higher amongst newborns roomed-in compared to newborns admitted to the NICU (p = 0.001).

Follow-up at 14 days of life was based exclusively on

clinical criteria and rt-PCR test was not performed, so although none of newborns developed symptoms we could not formally exclude SARS-CoV-2 infection at this time. This study has several limitations. Mothers were considered infected with SARS-CoV-2 and contagious if they tested positive at admission since tests regarding viral load were not performed at this time, and no other biological product was analyzed. As previously mentioned, asymptomatic women identified as having rt-PCR positive test results only by obstetric screening practices rather than by illness have an uncertain onset of infection and therefore unclear infectiousness. Furthermore, newborns born to mothers who were infected with SARS-CoV-2 during pregnancy and tested negative at admission were not included in this study.

CONCLUSION

Most pregnant women with COVID-19 in our study were asymptomatic with few or no adverse outcomes, while the symptomatic group reported a higher prematurity rate, and higher newborn NICU admission. Despite this, short-term infant outcomes were good. Although there is a better understanding nowadays of viral dynamics, evidence of how it affects pregnant women and their newborns is still poorly understood. Fetal infection, although rare, has been described, while newborn infection might be associated mostly with the level of infectiousness (viral shedding) of the mother, thus emphasizing the importance of following recommended infection control and prevention practices.

AUTHORS CONTRIBUTION

All the authors had an equal contribution to the literature research, draft and distribution of the questionnaire, analysis of the results and draft of the paper.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

COMPETING INTERESTS

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