

GESTATIONAL AND NEONATAL OUTCOMES AFTER CORONAVIRUS INFECTION: A SYSTEMATIC REVIEW

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Abstract: Introduction: Covid-19 is a disease caused by the SARSCOV-2 virus. The first cases emerged in December 2019 in China and evolved into a global pandemic since 2020. In those infected, the clinical picture of the disease can range from mild or asymptomatic symptoms to severe forms with complications. It was found that during pregnancy there is a greater risk of maternal complications, especially when it occurs in the last trimester of pregnancy and puerperium, with an increase in cases of maternal death. **Goal:** To review the most prevalent possible gestational and neonatal complications in those infected with SARS-COV-2. **Methodology:** This is a systematic literature review with articles published in PubMed/MEDLINE, Scientific Electronic Library Online (SciElo), Latin American and Caribbean Health Sciences (Lilacs) databases published in the period between February 2020 and December 2021, with the descriptors: “pregnant women”, “neonates” and “SARS-CoV-2, with their translations into English, joined through the Boolean operator “AND” in the advanced search. Original publications were chosen. **Results/Discussion:** data were obtained from 2243 patients, all pregnant and with a confirmed diagnosis of SARSCoV-2. The most reported symptoms were: fever, cough, dyspnea and sore throat. A high prevalence of cesarean deliveries was found. Preterm birth was the most common obstetric complication, followed by PRMO. Significant percentages of neonates evolved with some type of respiratory disorder and died. **Conclusion:** the most prevalent clinical manifestations in pregnant women with COVID-19 were similar to those found in pregnant women without the infection; high percentages of obstetric and neonatal complications and cesarean deliveries have been described after COVID-19 infection.

Keywords: Pregnancy, newborns, SARSCOV-2.

INTRODUCTION

In December 2019, the first cases of pneumonia associated with infection with the SARS-CoV-2 virus were identified in China. Since then, COVID-19, the disease caused by this virus, has spread rapidly around the world and in March 2020 the World Health Organization (WHO) declared the new coronavirus a pandemic (UNA-SUS, 2020; REN et al, 2020). Since the beginning of the pandemic, there have been more than 490 million cases and 6 million deaths from COVID-19 worldwide. In Brazil, after more than 02 years of the first case, the number of infected reached more than 29 million with more than 660 thousand deaths (OPERAMUNDI, 2022; CORONAVIRUSBRASIL, 2022).

SARS-CoV-2 belongs to the family of coronaviruses that are known to cause illnesses ranging from the common cold to more serious illnesses such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS) (RABAAN et al, 2020). Its incubation period varies from 4 to 14 days. As it is an RNA virus, it is more prone to mutations and has a high power of dissemination. Its transmission can occur through contact with respiratory secretions and excretions of infected people and with contaminated objects when taken to the mouth, nose and eyes (ARAÚJO et al., 2020; MINISTRY OF HEALTH, 2020).

In those infected, the clinical picture of the disease can range from mild or asymptomatic pneumonia to severe forms with presentations that can lead to various complications such as respiratory failure and multiple organ failure (ARAÚJO et al., 2020).

There are population groups considered more susceptible to the development of the severe form of COVID-19, including those with chronic diseases such as diabetes mellitus, arterial hypertension, asthma, chronic

obstructive pulmonary disease; and smokers, obese individuals, over 60 years old, pregnant women, postpartum women and children under 5 years old (BRASIL. MINISTÉRIO DA SAÚDE, 2020).

It was found that during pregnancy there is a greater risk of maternal complications, especially in the last trimester of pregnancy and puerperium, with an increase in cases of maternal death, especially in developing countries. During pregnancy, immunological and cardiopulmonary changes occur that can cause greater sensitivity and increased clinical severity of pneumonia and some infectious diseases, including respiratory pathogens (BRASIL, 2020; RONDELLI et al., 2020)

In pregnancy, there is a progressive decrease in lung capacity and chest compliance, due to hormonal influences and increased uterine volume, which may predispose to the development of respiratory failure and hypoxemia due to COVID-19. Also, pregnancy presents with an increase in the state of hypercoagulability, motivated by the increase in the synthesis of clotting factors and the decrease in anticoagulant factors, which progressively occurs after the first trimester of pregnancy, predisposing the pregnant woman to a greater risk of cardiovascular complications due to this condition. disease (DASHRAATH et al, 2020; MARQUES-SANTOS et al., 2020).

In addition, symptoms that are common during pregnancy can delay the diagnosis and management of Covid-19 in those with mild respiratory tract symptoms. Estrogen-mediated gestational rhinitis manifests with severe nasal congestion and rhinorrhea, which can mask the coryza symptoms of covid-19. Likewise, physiological dyspnea due to accelerated metabolism, anemia and oxygen consumption by the fetus can make diagnosis difficult and favor community transmission (DASHRAATH et al, 2020)

The main gestational and perinatal outcomes identified in the studies are: higher number of cesarean sections, preeclampsia, gestational hypertension, premature rupture of membranes, placenta previa, premature births, abortion and fetal distress (DIRIBA; AWULACHEW; GETU, 2020; EGLOFF et al, 2020).

As it is a disease of recent knowledge, there is not enough evidence available to define the definitive effect of covid-19 during pregnancy (AKHTAR et al., 2020).

Furthermore, the possibility of vertical transmission by SARS-COV-2 cannot be ruled out. Work on the correlations of transplacental transmission is still limited. Despite this, emerging studies suggest that vertical transmission is possible and likely occurs in a minority of cases, especially during the third trimester of pregnancy (MUSA et al., 2021).

This study aimed to review the most prevalent possible gestational and neonatal complications in those infected with SARS-COV-2.

METHODOLOGY

This is a Systematic Review (SR) that followed the recommendations of the Top Items for Reporting Systematic Reviews and Meta-analysis (PRISMA).

Searches for articles were carried out in the electronic databases PubMed/MEDLINE, Scientific Electronic Library Online (SciElo), Latin American and Caribbean Health Sciences Literature (Lilacs), using the terms “pregnant women”, “neonates” and “SARS-CoV-2, with their English translations, joined through the Boolean operator “AND” in the advanced search.

The search took place in November 2021 and was restricted to articles published from February 2020 onwards in English. The screening of articles took place between

December 2021 and February 2022.

All included studies had their reference lists screened to find pertinent studies that the search could not have found in the database. As inclusion criteria, articles on COVID during pregnancy were used that reported: symptoms presented by pregnant women, obstetric complications, mode of delivery and neonatal complications.

In the combined search in the databases, 595 articles were found. All these articles were screened by the researchers using the Rayyan application, which, after removing duplicates and articles that did not meet the inclusion criteria, left a total of 46 articles for full-text analysis. Articles from literature reviews and meta-analysis were also excluded, as shown in flowchart 1.

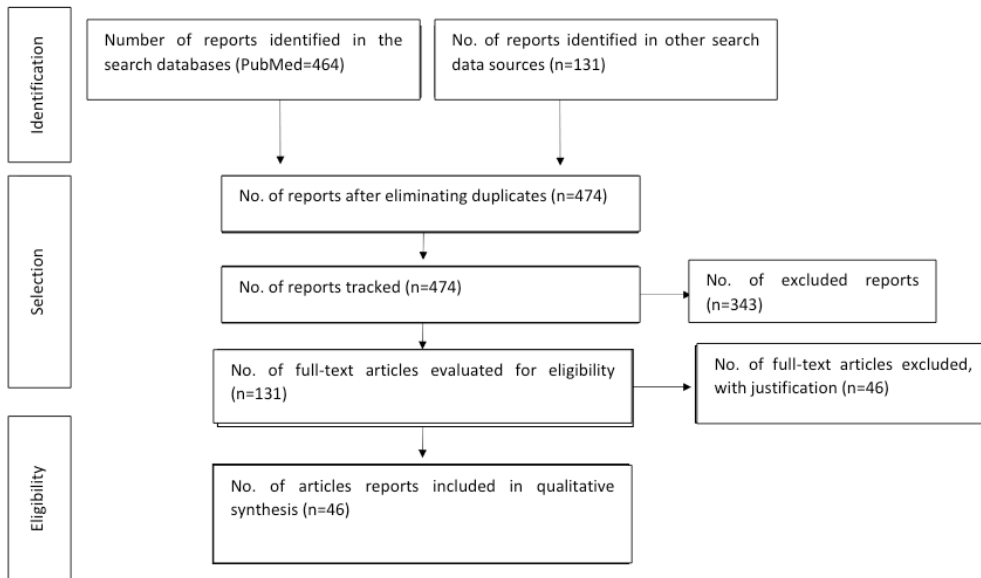
This work was developed with its own resources and had the institutional support of the State University of Feira de Santana. Regarding ethical feasibility, this research meets the requirements of Resolution 466/12 and its complementary ones, therefore, the research team is aware of the need and importance of secrecy and anonymity of the research subjects (BRASIL, 2012).

RESULTS

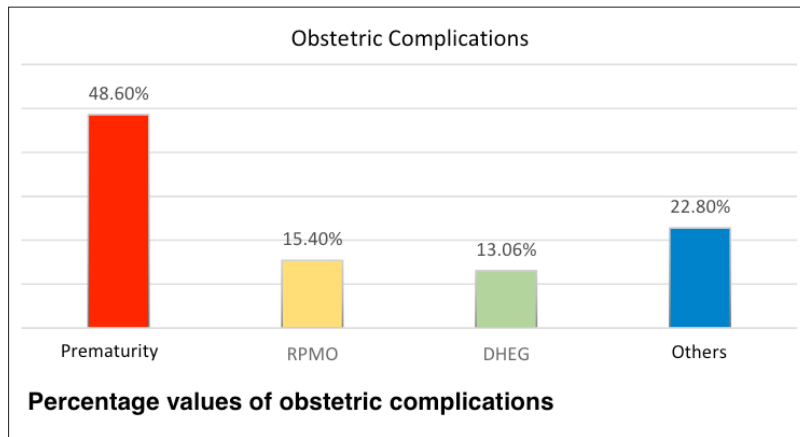
Of the 46 articles reviewed, data were obtained from 2243 patients, all pregnant and with a confirmed diagnosis of SARSCoV-2. Of these, 1850 pregnant women had given birth by the end of the studies.

The most reported symptoms were: 693 had fever (27.7%), followed by cough with 668 cases (26.7%), dyspnea 301 cases (12.0%) and sore throat 172 cases (6.9%). Less common general symptoms include nausea, vomiting, abdominal pain, nasal congestion, dysgeusia, and fatigue. Only 2.8% of all pregnant women required hospitalization in Intensive Care Units (ICU) and less than 2% died.

Of the 1,850 deliveries reported, 921 were

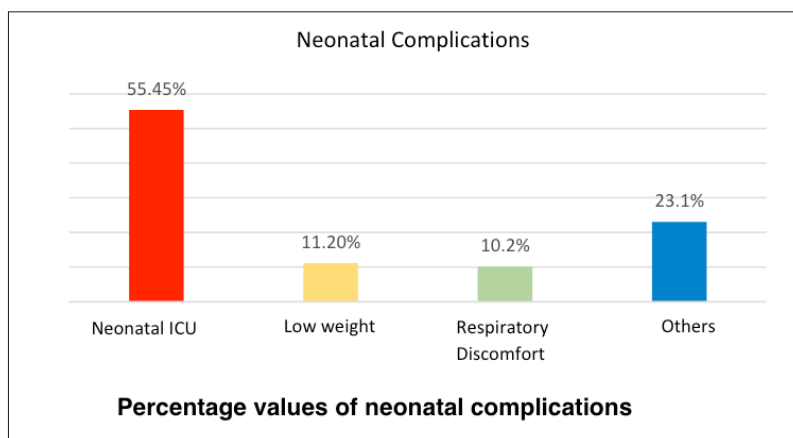


Flowchart 1: Systematic Review



Graph 1: Frequency of obstetric complications

Source: Author, 2022.



Graph 2: Frequency of neonatal complications

Source: Author, 2022.

cesarean sections (49.8%). Of these, 443 (48%) were for elective surgeries, many out of concern for unfavorable outcomes from COVID-19. The most common obstetric indications were dystocia, fetal distress and preeclampsia, respectively. Another 106 cesarean deliveries did not have their indications disclosed in the studies.

Preterm delivery was the most common obstetric complication in 354 cases (48.7%), followed by Premature Rupture of the Ovular Membranes (PRMO) with 112 cases 15.4% and Specific Hypertensive Disease of Pregnancy (DHEG) 95 cases 13%. Abnormal placental insertion, venous thromboembolism, miscarriage and threatened miscarriage were less frequently reported in the reviewed articles, corresponding together 13 cases (1.8%) as shown in graph 1.

A total of 1842 neonates were evaluated. Of these, 37 tested positive for COVID (2%), 336 (18%) required care in a neonatal ICU, 104 (5.6%) evolved with some type of respiratory disorder and 12 (0.6%) were death, as shown in graph 2.

DISCUSSION

Patients with COVID-19 may present with different clinical conditions, ranging from asymptomatic or mild infections to severe conditions with ARDS and multiple organ failure. Acute infections tend to manifest with the signs and symptoms of a common cold. After these initial symptoms, the most common are fever, cough and dyspnea. About 80% of those infected recover without the need for hospital care (GOULARTE et al., 2020).

The results of this systematic review indicated that the most prevalent clinical manifestations in pregnant women with COVID-19 were similar to those described in the general population with COVID-19, including fever, cough, myalgia, shortness of

breath, and diarrhea.

These results are in agreement with a retrospective study with 116 pregnant women infected with SARS-CoV2 developed in China, which demonstrated that the clinical changes, even in patients with pneumonia, from COVID-19 during pregnancy were similar to women in general (YAN et al., 2020).

Although some studies point out that the outcomes of COVID-19 in pregnant women are similar to those in non-pregnant women, others indicate that this disease favors the development of gestational complications. Martinez-Portilla et al., 2021, reported in a cohort of 289,331 women of childbearing age, including 7,705 pregnant women, that despite the mortality rate due to COVID-19 being similar between pregnant and non-pregnant women, the chances of death, pneumonia and ICU admission were higher in pregnant women.

COVID-19 infection has several clinical repercussions that are still unknown (CHI; GONG; GAO, 2021; WEI et al., 2021). In pregnancy it is no different, however some studies have correlated complications such as prematurity DHEG, PRMO with COVID-19. A meta-analysis and systematic review study showed that pregnant women with COVID-19 are 1.82 times more likely to have preterm birth (OR 1.82, 95% CI 1.38 to 2.39), one of the main obstetric complications described (WEI et al., 2021). This study was corroborated by another that also indicated prematurity as the main adverse outcome, which occurred in 24.74% of pregnant women, followed by PMR in 8.49% of pregnancies (CHI; GONG; GAO, 2021).

Some studies report that COVID-19 may be associated with an increased risk of developing HDPE (CHI; GONG; GAO, 2021; VILLAR et al., 2021). These findings are based on the hypothesis that in preeclampsia,

autoantibodies play an important role in its pathophysiology and, as a pro-inflammatory disease, COVID may be associated with a higher risk of its development (QUINONEZ et al., 2021) (QUINONEZ et al., 2021) (CHI; GONG; GAO, 2021).

The high rate of cesarean deliveries compared to vaginal deliveries, whether in patients with mild or severe COVID-19, was higher than the worldwide rate of cesarean sections in women without the infection, according to work by Betran et al. 2021 involving 154 countries, pointed out that on average 21.1% of women underwent cesarean section, ranging from 5% in Sub-Saharan Africa to 42.8% in Latin America and the Caribbean.

Keita et al (2021) reported in a cohort carried out in France that the number of cesarean deliveries in pregnant women with Covid-19 corresponded to 52% of deliveries. Previous studies in the United States and China have also reported a high rate of cesarean sections (PRABHU et al., 2020; WU MCGOOGAN, 2020).

Cesarean delivery, although a common procedure worldwide and essential to save lives, when well indicated, is still a surgery with significantly higher morbidity than vaginal delivery, both in the short term, such as infections and bleeding, and in the long term. term, such as risk of developing placenta accreta, spectrum disorder in future pregnancy, so it needs to be well indicated to reduce maternal and neonatal morbidity (NAÇÕES UNIDAS BRASIL, 2021).

Among the findings in this review, we found Only 2.8% of all pregnant women required hospitalization in Intensive Care Units (ICU) and less than 2% died.

The high rate of cesarean sections in pregnant women with COVID-19 may be related to concerns about the possibility of vertical transmission. Emerging evidence,

although limited, suggests that vertical transmission is possible (ROTTENSTREICH et al., 2021).

Regarding vertical transmission of SARS-CoV-2, it was not described in this review, however, there are controversies about its prevalence in the literature.

Egloff et al. (2020) demonstrate that maternal-fetal transmission is very rare, possibly less than 1% after maternal SARS-CoV-1 infection. According to these authors, they believe that vertical transmission during pregnancy via the placenta is probably greater when there is an increase in gestational age, since the angiotensin-converting enzyme 2 is necessary for cellular integration of the virus into the placenta, and is present at very low levels in the placenta. human placenta during the first trimester of pregnancy and there are no data on the expression of this receptor in 2nd and 3rd trimester placentas (EGLOFF et al., 2020). This study also found that more than 18% (336/1842) of neonates required admission to a neonatal ICU.

Patane et al 2020 were the first to describe the presence of SARS-CoV-2 RNA on the fetal side of the placenta in 2 cases of mothers who received a diagnosis of COVID-19, as well as newborns who tested positive for SARS -CoV-2 soon after birth. These findings support the possibility of vertical transmission of SARS-CoV-2 from mother to fetus in utero (PATANÈ et al., 2020).

For Silva et al. 2020, respiratory disorders are among the main causes of admission to a neonatal ICU, and there are several possible causes, ranging from prematurity and surfactant deficiency to the clinical repercussions of a systemic disease.

Other studies have correlated COVID-19 with higher rates of NICU admission and the presence of respiratory disorders in neonates, IUGR and low birth weight (42.86%) in neonates born to COVID-19 positive mothers

(MASCIO et al., 2020; SMITH et al., 2020). In our review, we found about 74 (12%) had IUGR or LBW

Muse et. al. (2021), in a systematic review of systematic reviews with 54,413 pregnant women infected with SARS-CoV-2 and more than 30,840 newborns of infected mothers, found that more than 800 neonates tested positive through throat swab RT-PCR for SARS-CoV-2. Most of the studies reviewed in this paper suggested that neonates who tested positive for COVID-19 became infected postnatally due to environmental exposure (MUSA et al., 2021).

CONCLUSION

The findings of this study indicate that the most prevalent clinical manifestations in pregnant women with COVID-19 were similar to those found in pregnant women without the disease.

A significant number of obstetric and neonatal complications were found in infected pregnant women and their neonates, suggesting that this infection may be related to unfavorable outcomes during pregnancy, both for the mother and the fetus.

Vertical transmission of SARS-COV-2, however, remains controversial, requiring further studies to better understand its prevalence.

The high number of cesarean deliveries, motivated by concern about unfavorable outcomes from COVID-19, supports the need to search for more evidence and studies on the safety of vaginal delivery.

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