

# Coronavirus Sars-Cov-2 A Puzzle Still to Be Solved in Pregnancy

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## Abstract:

**Introduction:** The new corona virus detected in China, SARS-CoV-2, spreads rapidly among the cities of the world, and produces a clinical picture that receives the name of COVID-19, capable of inducing disease with increased risk in pregnant women of complications for her and for the product of conception.

**Objective:** to show in relation to COVID-19 and pregnancy the main findings that try to explain the infection and the disease.

**Materials and methods:** this reflective type of writing was based on the documentary review of information available in digital repositories on aspects of COVID-19 infection in pregnant women. Results: the documentary information of what was found is categorized into four subchapters: pregnancy physiology and susceptibility to SARS-CoV-2, maternal-fetal transmission of SARS-CoV-2, recommendations for obstetric management in COVID-19 and future research in COVID-19 and pregnancy.

**Discussion and conclusions:** SARS-CoV-2 infection and COVID-19 disease in pregnant women are explained in an effort to offer researchers and health professionals condensed information on the matter for consensual obstetric management that culminates with the issuance of recommendations and the approach of aspects that are considered necessary to investigate.

**Keywords:** pregnancy, SAR-CoV-19; pandemic; emergency; prevention and control (Source: DeCS, Bireme)

## Introduction

The new coronavirus detected in China, SARS-CoV-2, spreads rapidly among cities around the world, and produces a clinical condition called COVID-19, capable of inducing illness in pregnant women (it is estimated that the prevalence of SARS-CoV-2 infection in women presenting in labor ranges between 3 and 20%, but rates cannot currently be compared between populations because universal screening is not a common health practice), especially viral pneumonia, which at Just as pneumonia due to other causes negatively affects the product of conception, since it can trigger premature rupture of membranes, spontaneous abortion, premature birth, intrauterine fetal death, intrauterine growth retardation and neonatal death after birth [1, 2].

The magnitude of the health problem in pregnant women can be really important, due to the fact that asymptomatic infection is 15 times higher in obstetric patients in relation to surgical patients [3] and because the number of laboratory confirmed cases of SARS-CoV-2 infection is higher than

expected in pregnant women, the latter according to reports from the Center for Disease Prevention and Control (CDC), however, most specialists in the area believe that the data are insufficient to conclude reliably whether or not pregnancy increases susceptibility to SARS-CoV-2 [4], what is conclusive is that the infection, as in non-pregnant people, is more common among economically disadvantaged pregnant women [5, 6].

In relation to the severity of the disease in pregnant women, comparative studies between them and non-pregnant women, adjusted for age and comorbidity, have shown that COVID-19 is more serious among those who are pregnant because they have a higher risk of hospital admission, as well as need of oxygen therapy and endotracheal intubation, they are also 3 times more likely to be admitted to intensive care units (3.9 versus 10.5 per 1,000) and have a mortality rate, as well as 1.7 times more likely to die [4, 7, 8].

Hence the importance of determining the characteristics that define COVID-19 in pregnant women. In this sense, it is convenient to highlight that there

are several aspects to investigate in relation to COVID-19 and pregnancy. The objective of this paper is to show in relation to COVID-19 and pregnancy the main findings that try to explain the infection and the disease in an effort to offer researchers and health professionals condensed information for consensual obstetric management, since, It includes recommendations, as well as offers theoretical support about the variables that need to be investigated to maximize results in the fight against this important public health problem.

### Methodology

This reflective writing was based on the documentary review available in digital repositories on aspects of COVID-19 infection in pregnant women, based on the use of descriptors or keywords closely related to the topic. Repeated documents and those without clear or original conclusions were excluded. All original documents published until November 2022 were included. The analysis of the relevant ideas allowed them to be grouped into 4 subchapters in the results section, in order to facilitate their reading.

### Data analysis techniques

Document analysis was used because it allows obtaining data from secondary sources of information. Mainly articles published in peer-reviewed, indexed and prestigious scientific journals that contained information on COVID-19 and pregnancy were reviewed.

### Results

As a result of the analysis of documentary information, the findings were categorized into four subchapters: physiology of pregnancy and susceptibility to SARS-CoV-2, maternal-fetal transmission of SARS-CoV-2, recommendations for obstetric management in COVID-19 and future research in COVID-19 and pregnancy.

#### Physiology of pregnancy and susceptibility to SARS-CoV-2

Until now, there are clear reports that pregnant women have a higher risk of serious illness in relation to the rest of the population due to the physiological changes of this stage, among which the reduction of residual volume, elevation of the diaphragm, inability to eliminate pulmonary secretions, the decrease in lung size as the fetus grows, increased risk of thromboembolic disease and alterations in cellular immunity [4]. Risk factors for serious disease include older age (>34 years), black race, overweight or obesity, and comorbidities (chronic lung disease, high blood pressure, and diabetes) [9, 10]. In relation to the clinical evolution in 25 % of pregnant women persist symptoms for more than 8 weeks after their onset [11]. Pregnant women are also at greater risk of developing pre-eclampsia/eclampsia when infected with SARS-CoV-2 [12].

However, in pregnant women, the clinical course described may involve asymptomatic infection (rarely reported), rhinitis/pharyngitis or mild pneumonia that in most cases resolves satisfactorily (however, when pneumonia is severe, mortality can reach 25%, exceeding well as that registered in the general population), but the clinical diagnosis can be complicated, since, in a fifth of healthy pregnant women, gestational rhinitis is common, as well as physiological dyspnea (due to the greater demand for oxygen due to the increase in metabolism), maternal anemia and fetal oxygen consumption). Furthermore, it is unknown whether the immune regulation (due to its dominant Th2 environment) of pregnancy influences the pathogenesis and virulence of SARS-CoV-2 as the exaggerated inflammatory response described in the disease is suppressed and is associated with a worse prognosis [13-15].

It is known that infected mothers can transmit the virus through respiratory droplets during breastfeeding, but transmission of SARS-CoV-2 through breast milk has not yet been definitively proven. Likewise, in the case of vertical transmission, there are several reports in which SARS-CoV-2 nucleic acid is not detected by RT-PCR in placenta, amniotic fluid, umbilical cord blood, vaginal swabs, breast milk or swab samples of the neonate's

throat. However, a few studies report positivity but lack clinical information and information on the viral isolation procedure, so perinatal infection cannot be ruled out. There are reports of IgM anti SARS-CoV-2 in newborns and its indication as proof of vertical transmission in the understanding that the immunoglobulin due to its structural configuration does not cross the placenta, however, this is not conclusive proof, because it is also known that Morphological alterations of the placenta allow the passage of IgM, consequently, they may be false positives [16].

#### Maternal-fetal transmission of SARS-CoV-2

There are several viruses capable of crossing the placental barrier and reaching the fetus, among these are Zika, cytomegalovirus and rubella. In this sense, transmission can occur during pregnancy, the beginning of labor, during childbirth (intrapartum) or later. birth (through breastfeeding or contact with the mother or other infected people [postpartum]), in the case of SARS-CoV-2 transmission seems rare [17, 18], because the infection is not associated with high levels of viremia and the placenta may not express high levels of factors that facilitate virus entry into the cell (angiotensin converting enzyme II and cellular transmembrane serine protease 2) [19-23]. There is information that the majority of SARS-CoV-2 infections in those born to infected mothers are associated with infected caregivers and that breastfeeding is safe because SARS-CoV-2 has not been detected in breast milk [24, 25]. Furthermore Systematic reviews do not report an increase in infection in the late postnatal period (infection that occurs after 72 hours of birth) in children of infected women who breastfeed [26].

Similarly, in the susceptibility of the placenta to SARS-CoV-19, the reports on the interaction of angiotensin 2 as a receptor for this coronavirus at the placental level are contradictory; some authors have found transient overexpression and increased activity of angiotensin 2, and others obtain very low expressions at the maternal-fetal interface. Now, in severe cases of COVID-19 (SARS-CoV-2 infection alone is not an indication for termination of pregnancy) where mothers suffer from severe acute respiratory failure, early termination of pregnancy, after week 32 is really beneficial for maternal treatment and rehabilitation (vaginal delivery is not contraindicated in patients with COVID-19, as there is no convincing evidence of vertical transmission, cesarean section should only be resorted to if there are severe complications resulting from the infection), but The postnatal deterioration of the former pregnant mother may continue, so follow-up is required. It is certain that social distancing measures are effective in reducing the transmission of the disease in pregnant women, as well as for the rest of the population, and that the use of systemic corticosteroids as routine use in the treatment of COVID-19 is not It is the option in pregnancy due to its immunosuppressive role and predisposition to maternal hyperglycemia [14, 27].

#### Recommendations for obstetric management in COVID-19

Based on what has been stated so far, international health organizations and specialists in the area establish the following recommendations for obstetric management in COVID-19 [2, 28-31]:

1. Careful monitoring of asymptomatic pregnant or recently pregnant women with epidemiological contact history.
2. The encouragement of prenatal, postpartum and postabortion control as appropriate (in case of infection, postpone routine visits until the isolation period is over, in these cases telephone or web consultations can be used) as well as the treatment of complications in if there are. It is recommended that pregnant women recovering from SARS-CoV-2 infections evaluate fetal growth 14 days after cure or 21 days after the previous fetal biometry.
3. In relation to the management of the infection in pregnancy, it is recommended to maintain maternal oxygen saturation at least 95%. Antiviral therapy should not be denied or suspended, nor should systemic steroids, especially in those who require supplemental oxygen or mechanical ventilation., and anticoagulation is recommended. Pregnant and breastfeeding women should be vaccinated against SARS-CoV-2.

4. The contemplation of childbirth as a way to terminate the pregnancy even in confirmed SARS-CoV-2 infection (individualized for each case) and the completion of the pregnancy by cesarean section only if medically indicated.
5. That newborns of mothers with suspected, probable or confirmed SARS-CoV-2 infection must have standard infant feeding (breastfeeding as the main) and general care in an event where respiratory hygiene with the use of a mask is deprived, washing hands and disinfecting surfaces.
6. Finally, pregnant women must receive psychosocial support, be treated with respect and dignity, and be accompanied by trained and multidisciplinary health personnel in this complex COVID-19 pandemic situation.

#### Future research in COVID-19 and pregnancy

Research on COVID-19 and pregnancy, given the scientific evidence reported, should focus on aspects such as susceptibility to SARS-CoV-2 infection, evaluation of complications in pregnant women and children in the perinatal stage, and of course on definitively elucidating the existence or not vertical transmission. Likewise, there is not enough data on the impact of COVID-19 on pregnant populations, nor on the incidence of vaccination in this group of women (that is, on safety), nor on protection of the infant through antibodies contained in breast milk against SARS-CoV-2 natural or post-vaccine or on the scoring systems for evaluating clinical deterioration and the need for admission to maternal intensive care.

#### Discussion

Pregnancy is considered an independent risk factor for severe disease in those women who acquire SARS-CoV-2 infection, particularly if they suffer from chronic diseases such as diabetes mellitus or preeclampsia, perhaps attributable to the peculiar physiological changes that occur in the cardiorespiratory system of the pregnant woman, a situation that is complicated by the low acceptance rates of vaccination against SARS-CoV-2 in this group [32-36].

SARS-CoV-2 is also attributed with the ability to severely affect the product of conception, because the placenta can be damaged by the virus, with hypoperfusion and inflammation that leads to fetal decomposition and a greater risk of perinatal morbidity and mortality, without However, placental histopathological abnormalities in pregnancies complicated with SARS-CoV-2 infection require more and in-depth investigations, given that the studies published in this regard were carried out with small samples, with heterogeneous evaluation of results and without the incorporation of criteria of inclusion, which makes it difficult to objectively extrapolate the evidence [37-41].

The increase in the number of reports of the significant prevalence of signs of arteriopathy in pregnant women with SARS-CoV-2 infection undoubtedly suggests the potential connection between infection by this virus and alteration of placental function, despite , from the opinions found between those who have found overexpression and increased activity of angiotensin 2 and those who report low expression of this receptor in the maternal-fetal interface (receptor through which SARS-CoV-2 enters the host cells).

What there is agreement on is the mechanism responsible for the risk of fetal death in pregnancy, explained by the effect of the SARS-CoV-2 virus on the decrease in placental perfusion induced by alterations in the hemodynamic state of the mother. It is an indirect pathogenic mechanism; in addition, alternatively, the increase in proinflammatory mediators in the host in response to the viral infection is mentioned as a viral mechanism of placental damage, which leads to the appearance of histopathological anomalies related to inflammation [42- 45].

Finally, it should be noted that crucial evidence on the real role of SARS-CoV-2 infection on pregnancy is missing or unclear, especially due to the existence of research reports in pregnant women with mild symptoms or

atypical infections without significant differences in regarding fetal growth compared to those pregnancies complicated by SARS-CoV-2 infection [46].

#### Conclusions

The clear definition of the pathogenic mechanism, clinical evolution, transmission, diagnosis and treatment of COVID-19 is crucial for the care of pregnant women as a population vulnerable to infectious disease outbreaks because it is known that, without SARS-CoV-2, they are already especially and disproportionately affected by respiratory diseases with high morbidity and mortality, due to the compromise of their immunological and mechanical functions. There is no doubt that the field of premises to be revealed regarding the impact of COVID-19 on pregnancy is vast, and therefore, crucial to safeguard the life of the fetus and its mother based on obstetric management supported by consensus and recommendations. of best practices resulting from research with strict methodological protocols (with the aim of avoiding bias), the only valid process to obtain a solid theoretical basis for SARS-CoV-2 infection during pregnancy.

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#### Conflict of interest declaration

As authors of the article we declare that there is no conflict of interest.

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