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COMMENTARY

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# COVID-19 and pregnancy: An opportunity to correct an historic gender bias

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## Abstract

Current literature and clinical guidelines do not include pregnant women as an a priori risk group for COVID-19. However, a gender vision of health begs the question: Why are pregnant women not considered a risk group for COVID-19? The answer is clear: historically, most community scientific studies have not considered female gender, or pregnancy as a state, to be a focus of special interest or effort. Unfortunately, this bias seems to be maintained in the COVID-19 epidemic: most current guidelines for diagnosing SARS-CoV-2 infection during pregnancy apply the same standard criteria as for the general population.

This pandemic is an opportunity to begin redressing this historic gender bias against pregnant women, and to achieve this, we recommend two actions that are easy to implement, and would have a large impact. First, routinely test for SARS-CoV-2 infection in all pregnant women with clinical or epidemiological suspicion, regardless of gestational age or the clinical severity. Second, routinely test for SARS-CoV-2 infection in all pregnant women at admission for delivery. These actions are essential to understand the true impact of COVID-19 throughout pregnancy, and will improve how we manage many aspects of pre- and postnatal care.

It is the scientific community's responsibility to guide, even to anticipate, the recommendations of our respective governments' health policies. If we do not agree to consider pregnant women as a distinct priority subgroup of the population during this pandemic, once again we will miss an opportunity to overcome this historic bias.

**KEYWORDS**

COVID-19, female gender bias, pregnancy, SARS-CoV-2, vertical transmission

Current literature and clinical guidelines do not include pregnant women as a priori risk group for COVID-19. However, a gender vision of health begs the question: Why are pregnant women not considered a risk group for COVID-19? The answer is clear: historically, most community scientific studies have not considered the female gender, or pregnancy as a state, to be a focus of special interest or effort. Unfortunately, this bias seems to be maintained during the COVID-19 epidemic. Indeed, despite significant variation in protocols between hospitals, most current guidelines for diagnosing SARS-CoV-2 infection during pregnancy apply the same standard criteria as for the general population, namely performing one of the available molecular tests, such as quantitative reverse transcription polymerase chain reaction.[1-5] Even more striking, most protocols indicate testing in pregnant women only when their clinical severity justifies admission to hospital, that is, the same as for any other patient. As we respond to this challenging public health crisis, we should be careful not to perpetuate this historic bias.

  

COVID-19 infection in pregnant women creates additional challenges, for different reasons. The pathophysiological reasons include the involvement of both mother and fetus meaning that the complexity of the infection affects two populations simultaneously, each with their own implications in terms of fetal and maternal well-being; the unique, temporary, and complex immune status of the gestational period (eg, immunotolerance of the semiallogenic fetus), which may induce a state of increased susceptibility to certain intracellular pathogens; and the hypercoagulability of pregnancy itself, which is enhanced by SARS-CoV-2 infection.[6] Clinically, pregnant women with COVID-19 tend to present mild symptomatology, probably because of their younger age, the lower risk in women, their better health status, and the gestational immune state itself. Compared to the nonpregnant population, this good clinical tolerance likely leads to under-diagnosis, but does not necessarily imply a lesser impact on fetal development and well-being. From a logistical viewpoint, pregnant women are a generally healthy population that repeatedly interacts with the health system during a defined timeframe, generally culminating in hospital admission for delivery. All of these factors make pregnant women a differentiated, vulnerable subgroup of the population, and even more so in the context of the COVID-19 pandemic. Although the volume of data on the effects of COVID-19 in pregnancy is growing rapidly, current evidence is limited, and its impact remains largely unknown. Therefore, we cannot ignore the potential risk of infected pregnant women and the fetus.[7] Under the pandemic situation of COVID-19, special attention should be given to pregnant women.[8,9]

With COVID-19, we now have an opportunity to begin redressing this historic gender bias against pregnant women. We recommend two actions that are easy to implement, and would have a large impact:

**Recommendation 1.** Routinely test for SARS-CoV-2 infection in all pregnant women with clinical or epidemiological suspicion, regardless of gestational age or clinical severity. Our experience with COVID-19 to date suggests that there is no vertical transmission to the fetus in women who acquire the infection during the third trimester, although there are still only a few series of published cases.[10] In contrast, we have very little information on the impact of the disease when infection occurs during the first half of pregnancy. As in other viral infections, the prevalence and severity of maternal and/or fetal involvement probably varies according to gestational age at the time of the infection, so we do not know how it might impact viability (possible increase in abortion rate at a very early gestational age), risk of teratogenicity or fetal congenital anomalies (due to the infection itself, or to its symptoms, such as fever), immune responses and potential risks from the cytokine-storm infection, or vascular and/or placental status (such as altered expression of angiotensin-converting enzyme 2, angiogenic disbalance, hypercoagulability, and prothrombotic status). We also do not know whether its impact might differ according to pre-existing comorbidities, especially obesity and hypertensive diseases of pregnancy. Therefore, although there is no reliable evidence to support the possibility of vertical transmission of COVID-19, the maternal infection and inflammation that occurred in response to the viral infection could affect the developing fetus and even postnatal life. Facing this lack of evidence, we cannot acquire this knowledge about an emerging unknown disease if we cannot confirm the diagnosis. Infected but otherwise low-risk pregnant women with mild disease might not need clinical assessment, but irrespective of gestational age and clinical severity, they should be tested to confirm the diagnosis. Only then will we know the true impact of SARS-CoV-2 infection throughout pregnancy, in terms of maternal morbidity, mortality, and perinatal outcomes.

**Recommendation 2.** Routinely test for SARS-CoV-2 infection in all pregnant women at admission for delivery. We know that most pregnant women with COVID-19 at delivery are asymptomatic and undiagnosed. Recent experience has shown that 13.7% of asymptomatic pregnant women at delivery were SARS-CoV-2-positive (1 in 8 women attended in labor); moreover, 88% of antepartum women who were infected at admission were asymptomatic.[11] In our setting (tertiary hospital, catchment population 800 000), we have confirmed SARS-CoV-2 infection at admission in 4 of 155 asymptomatic pregnant women (2.6%, unpublished data). Although these results cannot be extrapolated elsewhere (they depend on the prevalence of infection in each geographic area), they highlight the risk of infection and underdiagnosis in asymptomatic pregnant women. Considering this, and given the risk of asymptomatic viral shedding, some centers have begun systematic screening of patients in labor and delivery.[11,12] Universal screening for SARS-CoV-2 has important benefits for optimal management, such as the respiratory isolation area during labor and maternal hospitalization, the protection measures taken by health professionals and family members, neonatal care (such as breastfeeding advice, which itself is important for public health in the long-term) and the postpartum discharge schedule (early return home).

Based on these arguments, we have gone beyond the general recommendations of our regional and national governments, and have recently adopted these two recommendations in our hospital, in consensus with other hospitals in the surrounding territory (Metropolitan North Territory, Barcelona, Catalonia). However, this is not a widespread policy in Spain, or elsewhere for that matter. The absence of this priority from current guidelines for managing pregnancy during the COVID-19 pandemic, as well as the currently sparse technical resources in many hospitals, are the two key factors that explain the difference in strategy between centers.

Even further, the historical exclusion of pregnant individuals from research trials directly and unjustifiably contravenes their right to patient autonomy and self-determination. Omitting pregnant women from research magnifies their vulnerability and excludes them from gold standard evidence-based medicine. Only by including pregnant women in research, with the appropriate standards, will we be able to begin remedying gender-biased policies and producing real evidence that is gender applicable and inclusive.

It is the scientific community's responsibility to guide, even to anticipate, the recommendations of our respective governments' health policies. If we do not agree to consider pregnant women as a distinct priority subgroup of the population during this pandemic, once again we will miss an opportunity to overcome this historic bias.

## CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

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