

Severe maternal morbidity and mortality associated with COVID-19: The risk should not be downplayed

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Nordic countries have a long tradition of collecting health-related population data meticulously and reporting them transparently. Such data provide firm grounds for making good decisions and as a result the public health institutions in Scandinavia enjoy the trust of society. The COVID-19 pandemic has, however, resulted in a completely new situation, as we are now exploring in uncharted waters. Based on reports from China,¹⁻³ Italy,⁴ USA⁵ and perhaps with the good intention of reducing anxiety among this vulnerable population group, it has been widely publicized that pregnant women are not at increased risk of susceptibility, infectivity and severity of COVID-19 compared with the general population or non-pregnant women, although a systematic review of 108 cases of laboratory-confirmed pregnancies with COVID-19 has reported the possibility of increased risk of severe disease among pregnant women.⁶

Recently, the Public Health Agency of Sweden released a report on pregnant and early postpartum women diagnosed with COVID-19 who required intensive care during the period between 19 March and 20 April 2020 (reference number: 01907-2020). This report is based on rigorously collected surveillance data that were extracted from the Swedish National quality registry on Intensive Care (SIR), and a summary has been published in AOGS.⁷ A total of 53 women with COVID-19 between the ages of 20 and 45 years received intensive care. Of those women, 13 were or had recently been pregnant. Six of these 13 women required invasive mechanical ventilation. An analysis based on an estimate of the total number of pregnant and non-pregnant women in the population of Sweden revealed that the relative risk (RR) for pregnant and early postpartum women (<1 week) with COVID-19 to receive intensive care was 5.4 (95% confidence interval [CI] 2.89-10.08) and the RR to require invasive mechanical ventilation was 4.0 (95% CI 1.75-9.14) compared with non-pregnant women of similar age. This risk remained higher (RR 3.5, 95% CI 1.86-6.52) even after accounting for 50% more

pregnancies in the denominator to include possible miscarriages and early intrauterine deaths. Although the results are based on a relatively small number of COVID-19 cases and details regarding comorbidities are lacking, the risk is significant enough not to be ignored.

Published case series from China have not reported any maternal deaths related to COVID-19.¹⁻³ However, maternal mortalities associated with COVID-19 have been reported recently from several other countries in the mainstream news and social media (<https://ripe-tomato.org/2020/04/05/covid-19-in-pregnancy-news-reports/>) as well as in the scientific literature.^{8,9} The Public Health Agency of Sweden has also reported one maternal death, which was not included in the data analysis of pregnant women admitted to intensive care. Maternal deaths due to COVID-19 are happening not only in low-income countries with restricted resources and poorer healthcare systems^{8,9} but also in highly developed countries with excellent resources and healthcare facilities and traditionally very low maternal mortality ratios. Furthermore, it is very likely that maternal deaths are under-reported.

If and why pregnant women may be at risk of developing more severe disease has not been elucidated yet. Physiologically, one would expect pregnant women to be more vulnerable than non-pregnant women of reproductive age. Increased susceptibility to hypoxemia due to pregnancy-associated anatomical and physiological changes in the cardio-respiratory system leading to high oxygen demands, a hypercoagulable state increasing the risk of pulmonary microvascular thrombosis, and altered immune function causing unfavorable inflammatory response could all have an important role in the pathophysiology and impact the clinical course/outcome of COVID-19 in pregnant women.¹⁰⁻¹² However, it may also be possible that the highly adaptive immune system in pregnancy may be potentially advantageous in defending against the infection. Further studies are needed to explore these possibilities.

One major problem when studying COVID-19-associated complications in pregnancy is not knowing the denominator. An alternative is to study the entire pregnant population, but universal testing using real-time PCR, the current gold standard method, is resource-intensive. More information is likely to be available when reliable serological testing becomes widely available. As women usually provide blood samples during pregnancy for routine antenatal tests and these are often stored in biobanks, testing is possible to assess seroconversion in stratified unselected samples. National quality registries can also be of great value in this regard, as illustrated by the recent report of the Public Health Agency of Sweden.

Robust estimates of disease severity are still lacking, and the proportionate risk of severe maternal morbidity and mortality related to COVID-19 cannot be determined without analyzing large-scale population-based data from several countries adjusting for several confounding factors and outcome modifiers. Real clinical data are more nuanced, but they are more likely to reflect the reality when compared with simulation models based on assumptions. We must remain cautious while interpreting and generalizing the findings from small, uncontrolled studies. Therefore, the need for rigorous data collection and transparent reporting cannot be overemphasized.¹¹ However, on the basis of available data, and in line with the precautionary principle, the risk of COVID-19 in pregnancy should not be downplayed to avoid falsely reassuring healthcare professionals and the public. Women should be advised to take necessary precautions to avoid infection during pregnancy.

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