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

Magnus Westgren1 | Karin Pettersson1,2 | Henrik Hagberg3 | Ganesh Acharya1,2,4

1Division of Obstetrics and Gynecology, Department of Clinical Science, Intervention and Technology (CLINTEC), Karolinska Institutet, Stockholm, Sweden
2Department of Women’s Health, Karolinska University Hospital, Stockholm, Sweden
3Department of Obstetrics and Gynecology, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden
4Women’s Health and Perinatology Research Group, Department of Clinical Medicine, UiT, The Arctic University of Norway, Tromsø, Norway

Correspondence: Ganesh Acharya
Email: ganesh.acharya@ki.se

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 systems8,9 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.

© 2020 Nordic Federation of Societies of Obstetrics and Gynecology

Acta Obstet Gynecol Scand. 2020;99:815–816.

wileyonlinelibrary.com/journal/aogs | 815
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. 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.

ORCID

Ganesh Acharya https://orcid.org/0000-0002-1997-3107

REFERENCES

1. Chen L, Li Q, Zheng D, et al. Clinical characteristics of pregnant women with Covid-19 in Wuhan, China. N Engl J Med. 2020. https://doi.org/10.1056/NEJMc2009226

2. Yan J, Guo J, Fan C, et al. Coronavirus disease 2019 (COVID-19) in pregnant women: a report based on 116 cases. Am J Obstet Gynecol. 2020. pii: S0002-9378(20)30462-2. https://doi.org/10.1016/j.ajog.2020.04.014

3. Qiancheng X, JIan S, Lingling P, et al. Coronavirus disease 2019 in pregnancy. Int J Infect Dis. 2020. https://doi.org/10.1016/j.ijid.2020.04.065

4. Ferrazzi EM, Frigerio L, Cetin I, et al. COVID-19 Obstetrics Task Force, Lombardy, Italy: executive management summary and short report of outcome. Int J Gynaecol Obstet. 2020. https://doi.org/10.1002/ijgo13162

5. Breslin N, Baptiste C, Gyamfi-Bannerman C, et al. COVID-19 infection among asymptomatic and symptomatic pregnant women: two weeks of confirmed presentations to an affiliated pair of New York City hospitals. Am J Obstet Gynecol MFM. 2020;100:118. https://doi.org/10.1016/j.ajogmf.2020100118

6. Zaigham M, Andersson O. Maternal and perinatal outcomes with COVID-19: a systematic review of 108 pregnancies. Acta Obstet Gynecol Scand. 2020. https://doi.org/10.1111/aogs13867

7. Collin J, Byström E, Carnahan AS, Ahnne M. Pregnant and postpartum women with SARS-CoV-2 infection in intensive care in Sweden. Acta Obstet Gynecol Scand. 2020

8. Amorim MMR, Takemoto MLS, Fonseca EB. Maternal deaths with Covid19: a different outcome from mid to low resource countries? Am J Obstet Gynecol. 2020. https://doi.org/10.1016/j.ajog.2020.04.023

9. Hantoushzadeh S, Shamshirsaz AA, Aleyasin A, et al. Maternal death due to COVID-19 disease. Am J Obstet Gynecol. 2020. https://doi.org/10.1016/j.ajog.2020.04.030

10. Koumoutsea EV, Vivanti AJ, Shehata N, et al. COVID19 and acute coagulopathy in pregnancy. J Thromb Haemost. 2020. https://doi.org/10.1111/jth14856

11. Liu H, Wang LL, Zhao SJ, Kwak-Kim J, Mor G, Liao AH. Why are pregnant women susceptible to COVID-19? An immunological viewpoint. J Reprod Immunol. 2020;139:103122. https://doi.org/10.1016/j.jri.2020.103122

12. Liang H, Acharya G. Novel corona virus disease (COVID-19) in pregnancy: what clinical recommendations to follow? Acta Obstet Gynecol Scand. 2020;99(4):439-442. https://doi.org/10.1111/aogs.13836