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COVID-19 and pregnancy

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TO THE EDITOR

Coronavirus disease 2019 (COVID-19) is an acute infectious respiratory disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. The novel coronavirus disease was first diagnosed and described in December 2019 in central China (city of Wuhan, Hubei province) (1). COVID-19 infection may range from mild infection of the upper respiratory tract, lower respiratory tract with life-threatening pneumonia with acute respiratory failure syndrome (1). This virus is broadly susceptible to all age, from the youngest newborns to the oldest. Pregnant women and their fetuses are at high risk to infect with a virus during outbreaks of infectious diseases (2). They are also more exposed to respiratory pathogens, so on that account they may be more susceptible to COVID-19 infection than the general population (1). Therefore, the epidemic has raised concerns about the possibility of vertical transmission of the virus from mother to fetus (3).

SARS-CoV-2 is the seventh member of the family of CoVs that infect humans. The genetic sequence of SARS-CoV-2 is $\geq 70\%$ similar to that SARS-CoV, and SARS-CoV-2 is capable of using the same cell entry receptor (ACE2) as SARS-CoV to infect humans. However, SARS-CoV-2 spike (surface spike glycoprotein) binds to human ACE2 with approximately 10-20-fold higher affinity than the SARS-CoV spike, making it easier to spread from human to human (4).

At the present time, there is only little data available about the risk of vertical transmission from mother to child due to the small number of published cases. Preliminary information suggests that pregnant women are not more severely affected than the general population (5), however the available research results show that there is a theoretical risk of vertical transmission, as the ACE2 receptor is widely expressed in the placenta. In the limited number of available cases in which newborns were born from mothers with COVID-19, there have been 2 neonates tested positive for SARS-CoV-2

from COVID-19-infected mothers. However, there have been no confirmed cases of vertical transmission among the 46 other neonates, born to COVID-19-infected mothers reported thus far (2).

The SARS-CoV epidemic occurred between November 2002 and July 2003. The largest published case series from 2004 about severe acute respiratory syndrome caused by SARS-CoV-1 comprised 12 pregnant women from Hong Kong with confirmed SARS-CoV (6). Clinical and laboratory findings of these cases were identical to those of non-pregnant patients, pneumonia was diagnosed in all 12 cases by CT scan. Ventilation treatment was indicated in four female patients; three of them died over the further clinical course from respiratory failure or sepsis. Seven women became ill during the first trimester. Four women suffered early abortion, two patients wanted termination of pregnancy for social indications, and one child was born at term and was healthy. Five patients contracted SARS after the 24th week of pregnancy. Vertical transmission of SARS-CoV was not detected in any of the cases with live-birth children (7).

At this point in time, there are two retrospective studies on pregnancies complicated by COVID-19 disease (8, 9). Over 19 cases were reported in all.

The first study ("Wuhan patient population") (9) comprises nine cases which were presented between 20th January 2020 and 31st January 2020, inclusively, at the Zhongnan Hospital of Wuhan University. The second study ("Hubei patient population") (8) reports of nine patients infected with SARS-CoV-2 and ten neonates who were treated between 20th January 2020 and 5th February 2020 in five hospitals in Hubei.

In both studies, the clinical symptoms of an infection with SARS-CoV-2 were identical to those of cases involving non-pregnant female patients (10). All cases had a high-risk exposure. Pneumonia developed in each case, typical infiltrates were detected by CT scan in both study populations. In the "Wuhan patient population" the laboratory results showed decreased white

blood cells and lymphocytes, mild thrombocytopenia and elevated liver function tests. None of the cases required mechanical ventilation. There were no fatalities either.

Moreover, The CDC does not have any evidence indicating the possibility of negative pregnancy outcomes for pregnant women with COVID-19, although two of the other coronaviruses SARS-CoV and MERS-CoV have been associated with more severe diseases and greater mortality in pregnant women (11, 12). Moreover, patients with SARS showed preferential activation of Th1 immunity, resulting in the marked elevation of proinflammatory cytokines (IFN- γ , IL-1 β , IL-6, and IL-12), leading to extensive lung damage. In contrast, patients with COVID-19 demonstrated activation of both Th1 and Th2 immunity, culminating in the presence of IFN- γ and IL-1 β in addition to IL-4 and IL-10. A range of immune responses that has been described and early adaptive response may be predictive of milder disease severity (13, 14). Interestingly, Dashraath et al. (2) pos-

tulated that changes in the hormonal milieu in pregnancy may result in the lesser severity of COVID-19 compared to that in nonpregnant individuals.

To conclude, COVID-19 is the latest in a series of diseases caused by emerging pathogens in the past two decades, from SARS to 2009 H1N1 influenza to Ebola and Zika virus disease. This situation is rapidly evolving and further research is needed to understand the clinical course and possible risks of transmission of SARS-CoV-2 through the placenta and pregnancy complications in infected mothers. Pregnant woman with confirmed infection and their fetuses should be closely monitored to be able to distinguish early any clinical symptoms and to prevent deterioration of mother and child. At the moment, it is not confirmed whether SARS-CoV-2 infection can impact the course of pregnancy or if pregnancy can aggravate the clinical course of COVID-19 disease. There is not enough indication of intrauterine virus transmission to the fetus either.

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