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Can COVID-19 in pregnancy cause pre-eclampsia?

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In this issue of *BJOG*, Mendoza and colleagues report in an observational study the occurrence of a pre-eclampsia-like syndrome in six out of eight pregnant women with novel coronavirus disease (COVID-19) who were admitted to the intensive care unit with severe pneumonia (Mendoza et al. *BJOG* 2020;127:1374–80). There were no symptoms of pre-eclampsia among the 34 pregnant women who had mild forms of COVID-19. Importantly, the authors recorded not only routine laboratory test results, but also measured biophysical and biochemical markers that are typically altered in women with pre-eclampsia (uterine artery pulsatility index on Doppler ultrasound, serum soluble fms-like tyrosine kinase-1 [sFLT-1] and placental growth factor [PlGF]). Such markers were normal in five of the six women, in whom the symptoms of pre-eclampsia resolved after improvement of the maternal clinical situation.

The intriguingly high cumulative incidence of pre-eclampsia symptoms in women with severe COVID-19 needs to be interpreted with caution because of the observational nature of the study, the small number of pregnant women with severe infection and the possible role of confounding factors. The normal biomarker results in most cases, nevertheless, suggest that severe COVID-19 can lead to symptoms that mimic those of pre-eclampsia in the absence of defective placentation, which is further corroborated by the resolution of the symptoms without the delivery of the placenta when overall clinical improvement occurs. It is plausible that such manifestations are the result of widespread inflammation and endothelial damage, in a process that has been termed 'cytokine storm', responsible for many of the symptoms of the coronavirus-related organ injury (Mehta et al. *Lancet* 2020;395:1033–4) This mechanism includes activation of inflammation pathways that convert arachidonic acid to prostaglandins, thromboxane and eicosanoids, ultimately provoking significant cytokine release. The cascade of events, however, does not appear to influence the levels of specific pre-eclamptic angiogenic and anti-angiogenic markers such as sFLT-1 and PlGF.

A normal sFLT-1 : PlGF ratio in women with clinically suspected pre-eclampsia can be reliably used to predict the short-term absence of disease (Zeisler et al. *N Engl J Med* 2016;374:13–22). Although the definition of pre-eclampsia has changed over the last 20 years to incorporate less specific clinical features of end-organ damage, biomarkers will probably become part of the disease definition in the years to come or, at least, a valuable tool to select subgroups of women at higher risk of pre-eclampsia-related morbidity and mortality who require closer monitoring or immediate delivery.

While larger cohorts derived from national data sets or international registries of COVID-19 in pregnancy will be essential to confirm or refute this association, the preliminary data published in this study indicate that delivery during severe COVID-19 should not be based on pre-eclampsia symptoms alone, particularly at early gestational ages, and that the use of ultrasound and serum biomarkers such as the sFLT-1 : PlGF ratio might help to guide clinical management by distinguishing hypertension and endothelial dysfunction caused by COVID-19-related inflammation from true pre-eclampsia.

Disclosure of interests

None declared. A completed disclosure of interests form is available to view online as supporting information. ■