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CORRESPONDENCE

The Potential Confounders Hiding in a United States Cohort About Severe Acute Respiratory Syndrome Coronavirus 2 Infection During Pregnancy

To the Editor—With great interest, we read the article by Regan et al [1]. In their cohort study, the authors investigated the association between prenatal severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and increased risk of adverse pregnancy outcomes. These findings support previous studies that suggest maternal SARS-CoV-2 infection harms fetal health. However, there are some issues that should be discussed.

First, SARS-CoV-2 infection may not be the only risk factor of adverse pregnancy outcomes after adjustment in this cohort. This study was based on de-identified administrative claims and electronic health records data from OptumLabs Data Warehouse [2]. However, some confounders recorded in electronic health records data were not considered in this study, such as parity. A comparative study showed that primary cesarean delivery contributes to the increasing rate of patients' refusal to undergo vaginal delivery, thus inducing the secondary or repeat cesarean delivery [3]. Moreover, SARS-CoV-2–infected pregnancy complicated with high-risk gestational factors should be considered when evaluating the risk of adverse pregnancy outcomes. For example, previous studies indicated that maternal obesity is linked to a greater risk of preterm birth [4]. As a result, we suggest that importing the known residual confounders into the adjusted model would improve the precision of this study.

Second, personal factors were effect modifiers for the association between coronavirus disease 2019 (COVID-19) and clinician-initiated events, including induced abortion, cesarean delivery, and clinician-initiated preterm birth. The administrative codes cannot reflect the exact condition. The preference of patients may influence the decisions of the doctors [3]. On the other hand, doctors may execute clinician-initiated events for COVID-19 patients for other reasons than SARS-CoV-2 infection. The personal factors were residual confounders to the outcomes. Owing to the large infected-to-uninfected ratio in this study, we propose that matching the infected and uninfected cases by time-dependent propensity score matching can minimize the impact of the residual confounders [5]. After sequential matching with time-dependent propensity score, the effect of exposure can be identified by the Cox regression model used in this cohort.

Note

Potential conflicts of interest. All authors: No potential conflicts of interest.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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