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Interpreting COVID-19 outcomes in pregnancy needs knowledge of prevalent conditions in that time frame



We thank Sarkar et al¹ for their interest in our manuscript. We had shown that relatively worse outcomes during parturition in COVID-19-positive mothers were associated with other confounding risk factors for pregnancy.² The multivariate analysis did not reveal COVID-19 to be an independent risk factor, and we hypothesized that patients with other such risk factors are more likely to be referred to a specialized center.

We would like to clarify that the data were collected during the first wave and not the second wave in India. Our university was one of the first in the country to have a dedicated COVID-19 hospital. Again, this hospital was the first in the state to have full facilities for cesarean delivery. Of all the consecutive pregnancies, only those who were delivering in this hospital between June 2020 and November 2020 were included.

Because it was a government-designated COVID-19 hospital, most patients were admitted by referral from other healthcare facilities (facilities for cesarean delivery were not available in other COVID-19 hospitals). Simultaneously, a non-COVID-19 hospital was running, where the deliveries of COVID-19-negative patients took place. We do not have the exact data on how many were referral admissions in each section, but they would be much more than in the COVID-19 section than in the non-COVID-19 section.

Most hospitals around the world were stretched for resources, including manpower, at the peak of the COVID-19 waves. Fortunately, we did not face any dire shortages, and all the resources were shared proportionately between the COVID-19 and non-COVID-19 sections. Postpartum hemorrhage was more in the univariate analysis and not on multivariate analysis, whereas cesarean deliveries were higher in the COVID-19 group even on multivariate regression. There could be 3 reasons for this. First, in the initial stages, cesarean deliveries were preferred to minimize the risk of neonatal transmission. Second, the other

(non-COVID-19) preexisting risks factors were greater in the COVID-19 group. Third, hypoxemia in the mother might lead to more fetal distress (poor tocograms) in babies, leading to more cesarean deliveries in a few cases.

The higher proportion of referrals might account for the lower APGAR scores in the newborns. In case any other healthcare facility detected fetal distress and the mother was found to be positive for COVID-19, it would refer the patient to our center. The time taken for transfer to our center might lead to lower APGAR scores, but the quick operative delivery and a strong neonatal intensive care unit backup ensured that this did not translate into neonatal mortality.

We thank Sarkar et al¹ for bringing out this important message that it is imperative to interpret the COVID-19 outcomes in the light of the background, at the time of the study. COVID-19 and its management have evolved rapidly since its emergence, to its current status, where postvaccination breakthrough infections are major issues. ■

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Statins to prevent or treat preeclampsia: sometimes it is too late



TO THE EDITORS: The use of pravastatin in obstetrics has become an important subject addressed in several publications in the *American Journal of Obstetrics & Gynecology*.^{1,2} Two randomized placebo-controlled clinical trials on the efficacy of pravastatin to treat women with early-onset preeclampsia or prevent term preeclampsia did not show evidence of benefit.^{1,3} This is in contrast with the results of preclinical studies, including case reports where pravastatin—either as a treatment or as a prophylaxis—seemed to be effective.¹ What positive pravastatin reports have in common is that the medication was administered in the first trimester of pregnancy or at the beginning of the second trimester of pregnancy.¹ The rationale for statin administration is to reverse the angiogenic or antiangiogenic imbalance that is detected before the clinical recognition of preeclampsia⁴ and other great obstetrical syndromes, such as fetal death⁵ and massive perivillous fibrin deposition.⁶ Pravastatin can improve the angiogenic or antiangiogenic profile when administered early. Thus, we believe that the appropriate approach to test the efficacy of pravastatin is to administer it as soon as an abnormal angiogenic or antiangiogenic profile is detected. Longitudinal studies show that abnormalities in placental growth factor, soluble fms-like tyrosine kinase-1, and endoglin are detectable at different times in pregnancy according to the specific obstetrical syndrome.⁴ For example, the abnormalities are detected earlier in patients with massive perivillous fibrin deposition than in patients destined to develop preeclampsia.⁶ We believe that the lack of efficacy of pravastatin to prevent late-onset preeclampsia when started at 36 weeks of gestation³ may reflect that the medication has been administered too late in pregnancy and that some patients with late-onset preeclampsia do not have an abnormal angiogenic or antiangiogenic profile.⁶ We believe that future trials on the efficacy of pravastatin to prevent preeclampsia or other adverse pregnancy outcomes should select patients based on the abnormality in the angiogenic or antiangiogenic profile and the medication be started early in the mid-trimester of pregnancy to increase the likelihood of a therapeutic effect, which is unlikely to be realized when the drug is

started at 36 weeks of gestation. The initiation of pravastatin in the second trimester of pregnancy would decrease the potential teratogenic risk of pravastatin when administered in the first trimester of pregnancy. ■

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