

LETTER TO THE EDITOR

Reply: Neurological disease in pregnant females with COVID-19 may not only be attributable to SARS-CoV-2

To the Editor,

We appreciate the interest and observations of Professor Finsterer¹ regarding our recently published review article.² The other three pregnant women with COVID-19 and neurological complications,³⁻⁵ which he identified, were not included in our original article, even though we had been careful during the search process using broad terms in several combinations as described in the Methods section.² He summarized¹ a new stroke case⁵ and two new cases of Guillain-Barré syndrome (GBS)^{3,4} in pregnant women with COVID-19. Therefore, we have herein revised 10 patients with central nervous system (CNS) involvement (48%) and 11 patients with peripheral nervous system (PNS) involvement (52%) in order to compare with our previous results.²

Updated results have demonstrated that the median maternal age remained 32 (27.5–34.5) years, and the median gestational age was reduced to 32 (28–36) weeks. Interestingly, the woman who had suffered a stroke was in the 7th week of gestation.⁵ Notwithstanding, there was no statistical difference when comparing these results before² and after including the new cases. Only one new case⁵ presented migraine with aura as a previous medical condition (total = 8/21, 38%). Two new cases^{4,5} presented normal blood tests (abnormal blood tests = 15/17, 88%), and one new case⁴ presented changes in the chest image (total = 11/11, 100%). Two women^{3,4} also received immunotherapy (total = 15/19, 79%). We found no differences when the CNS and PNS involvement subgroups were compared for all the above variables.

Two women diagnosed with GBS^{3,4} were admitted to ICU (total = 11/21, 52%), but only one⁴ developed acute respiratory distress syndrome (ARDS; total = 9/21, 43%) and required mechanical ventilation (total = 9/21, 43%). When updating the results, we observed similar rates of ARDS, ICU admission, and mechanical ventilation when comparing the subgroups of CNS and PNS involvement. It is important to observe that we had previously emphasized the risk of ICU admission among pregnant women with COVID-19 and CNS involvement,² but this association did not remain significant when we increased the sample. It is necessary to obtain a larger sample to properly assess the association between neurological complications in pregnancy and the severity of COVID-19, as well the maternal and fetal outcomes in these women.

The woman with GBS and ARDS⁴ underwent a surgical delivery due to obstetric recommendations (total = 12/18, 67%), and the newborn evolved well despite a diagnosis of COVID-19, with no respiratory symptoms (total poor fetal outcome = 3/16, 19%). The other two women^{3,5} were still pregnant during the follow-up period and presented good outcomes. Only the women with GBS and severe COVID-19⁴ remained with disabilities after being discharged (poor neurologic outcome = 2/21, 9.5%).

We agree that neurological conditions in pregnant women with COVID-19 may not only be attributable to the SARS-CoV-2 infection.¹ The COVID-19 pandemic limited further investigations and possibly led to the misidentification of neurologic complications in infected patients. Therefore, it was challenging to study the causal relationship, especially in pregnant women. However, growing evidence in the general population has demonstrated an actual relationship between neurological complications and SARS-CoV-2, even in the presence of other predisposing factors, such as pregnancy.² Physiological immune modulation^{2,3} and modifications in the coagulation system^{2,5} linked to pregnancy and the puerperal period possibly exacerbate the direct and indirect effects of SARS-CoV-2 infection² on the nervous system. It is also possible that neurological conditions which occur or worsen during the perinatal period (e.g., eclampsia² and migraine⁵) may influence the occurrence of neurological complications related to COVID-19.

Despite the methodological limitations in the published case reports, including the new three cases,³⁻⁵ we have only included pregnant women with a confirmed diagnosis of COVID-19 and an appropriately investigated neurological disease in our review.² Although it is not possible to verify all the data in each case, especially analyzing the coincidence of the COVID-19 and the neurological complication, we believe that a relationship between the two conditions is probable during pregnancy due to the expected scarcity of other predisposing factors for severe diseases. Generalization of the results is limited, mainly because these 21 case reports published until November 2021 did not represent the actual prevalence of COVID-19 with complications from neurologic conditions in pregnant women. Discussion on this theme should warn of neurological manifestations in pregnant women with COVID-19 as signs of neurological disorders, regardless of respiratory symptoms.

KEYWORDS

COVID-19, guillain-Barré syndrome, neurological disease, pregnancy, stroke

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None.

AUTHOR CONTRIBUTIONS

JEM and PASRF equally involved in design, literature review, discussion, drafting of the manuscript, critical comments, and final approval.

CONFLICT OF INTEREST

The authors report no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this letter are available from the corresponding author upon reasonable request.

PEER REVIEW

The peer review history for this article is available at <https://publons.com/publon/10.1111/ane.13663>.

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