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Inflammatory markers as outcome predictors of COVID-19 in pregnant women

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Dear Editor,

We read with interest the article by Gündüz et al. on a cross-sectional study of 464 pregnant women with asymptomatic/mild (group 1) or severe (respiratory rate >24 and saturation <93%) SARS-CoV-2 infection (group 2) regarding the prognostic value of blood inflammatory markers for the outcome of COVID-19[1]. The neutrophil/lymphocyte ratio (NLR), the platelet/lymphocyte ratio (PLR), and the systemic inflammatory index (SII) were found to predict the outcome of COVID-19[1]. The study is excellent but has limitations that should be discussed.

The number of patients within each group differs markedly between the two groups. For this reason, a statistical comparison is problematic and not reliable.

The severity of SARS-CoV-2 infection was assessed only by the presence or absence of dyspnea. However, SARS-CoV-2 infections often manifest in extra-pulmonary organs[2]. Therefore, we should know the number of patients in whom the SARS-CoV-2 infection first manifested itself in organs other than the lungs.

Since D-dimer is increased per se due to the pro-thrombotic state in pregnancy, especially in the first and third trimester[3], it should not be used as an inflammatory parameter of COVID-19. The elevated D-dimer levels can lead to false positive results.

Patients with severe COVID-19 are susceptible to secondary infections due to immunosuppression by the SARS-CoV-2 virus[4]. Therefore, the number of pregnant women in whom the increase in inflammatory parameters was due to superinfection and not due to the COVID-19 infection should be clarified.

The prognosis of SARS-CoV-2 infection in pregnant women should not only be based on serum inflammatory markers, but also on monocyte distribution range, blood gas analysis, and imaging methods such as X-ray or CT of the lungs[5]. Antibody titres and CD3, CD4, and CD8 cell counts are even more specific than the inflammatory parameters evaluated for the study.

Another limitation is that the current medications taken regularly by the included women were not reported. Knowledge of current medications is critical, as multiple drugs can affect the blood parameters evaluated for the index study. For example, how many of the included patients had epilepsy and were taking anti-seizure drugs? The comorbidities are also absent. Knowledge of comorbidities is of crucial importance due to their impacts on the evaluated parameters.

There is no mention of the correlation between the inflammatory parameters and the outcome of the pregnancy. How many of the included patients had a stillbirth, an abortion, bleeding, premature rupture of membranes, placenta previa, or a cesarean section?

How many of the included patients had an elevated D-dimer level? Have these patients been screened for thrombosis? Another limitation of the study is that smoking status of pregnant women was not reported.

What was the cause of death of the two deceased patients? Did they die from COVID-19 or other causes? Have they been autopsied?

Overall, the interesting study has limitations that put the results and their interpretation into perspective. Clarifying these limitations would strengthen the conclusion and could improve the study. Inflammatory markers should not be the only predictors of COVID-19 in SARS-CoV-2-infected pregnant women.

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DATA ACCESS STATEMENT

All data are available from the corresponding author.

ETHICAL COMPLIANCE STATEMENT

The authors confirm that the approval of an institutional review board or patient consent was not required for this work. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this study is consistent with those guidelines. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

AUTHORS' CONTRIBUTIONS

JF: Conceptualization, Formal Analysis, Validation, Visualization, Writing – review & editing. **ACF:** Supervision, Validation. **FAS:** Supervision, Validation.

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