Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter #1 Response to letter to Editor by Dr. Sarkar et al. for' who said differentiating preeclampsia from COVID-19 infection was easy? Refers to PII: S2210-7789(21)00539-0 Letter #2 Response to letter to Editor by Dr. Hantoushzadeh et al. for' is COVID-19 disease a risk factor for preeclampsia? Should aspirin be considered for prophylaxis of preeclampsia in these patients?' Refers to PII: S2210-7789(21)00538-9

Dear Editors,

Thank you for the opportunity to respond to the letter submitted by Dr. Sarkar and his team. We are thankful for their interest in our study [1].

Dr. Sarkar et al. requested additional information about several patients from Table 2 that were COVID-19 positive and did not have a preeclampsia work-up. These patients were judged by the adjudicators as having either gestational hypertension (n = 2) or chronic hypertension (n = 1). At the time of their evaluation both gestational hypertension patients were laboring with just two isolated mild range blood pressure values. Neither patient exhibited proteinuria nor other clinical symptoms of preeclampsia. The patient with pre-existing chronic hypertension was admitted for induction of labor and was normotensive throughout the episode of care (no anti-hypertensive medication). The last patient presented with the elevated serum creatinine alone in the setting of kidney injury linked to chemotherapy for cervical cancer complicating the current pregnancy. This patient was also normotensive throughout the episode of care.

Despite strives for consistency, diagnostic evaluation of hypertensive disorders of pregnancy are recommended clinically with a high degree of clinical subjectivity. For example, it is more likely for patients who are approaching delivery or are in active labor not to undergo preeclampsia work-up because labor pain and anxiety could be associated with hypertension. A diagnostic work up of pre-eclampsia is frequently ordered only if the suspicion for pre-eclampsia is high based on clinical ground.

The question about the frequency of COVID-19 testing is important. During our study we consistently followed the CDC guidelines which frequently changed. There was no difference in the frequency of testing between the two groups.

We would like to thank Dr. Hantoushzadeh and her team for the interest in our study and insightful recommendations for future research directions.

As mentioned in our study we focused primarily on the episode of care. Our analysis included patients only if >20 weeks of gestation [1]. We agree inflammation could be the pathophysiologic link between COVID-19 infection and preeclampsia. In addition to the research cited in the letter, it has been established that there is a pro-inflammatory shift with the coronavirus disease and this heightened state of inflammation is associated with increased severity of the disease [2,3]. Future research should determine for how long the sFlt-1/PlGF ratio remains elevated after disease resolution in COVID-19 patients who are not pregnant any longer. Similarly, if the above markers correlate with the viral load, remains unknown at the time of this writing. We are yet to determine if this vascular endothelial dysfunction leads to long-term sequelae reported in the COVID-19 affected population and if low dose aspirin prevent those effects.

The association between TNF-α and hypertension is well known, and its correlation with sFlt-1/PlGF ratio was also established in animal models [4]. Anti-TNF treatment has also been demonstrated to improve this imbalance and improve hypertension [4–6]. In recent studies patients with chronic illnesses on anti-TNF agents were noted to have fewer hospitalizations and mortality as compared to those who did not receive anti-TNF agents [7,8]. Moreover, in preeclampsia, our group previously demonstrated steroids leads to a transitory improvement of laboratory values and clinical syndrome [9]. These changes occurred independent of sFlt-1/PlGF ratio implying inflammation alone is linked to clinical manifestations of preeclampsia. It is entirely plausible COVID-19 infection may mimic an inflammatory response characteristic to preeclampsia. The point of our paper, however, is that preeclampsia symptoms are non-specific and despite being transitory increase the complexity of the clinical presentation by triggering a preeclampsia work-up which by itself raises costs and hospitalization time.

To conclude, further studies need to be done to understand the link between preeclampsia symptoms and COVID-19 infection in the pregnant population and if targeted treatments are warranted. A few of the ongoing NIH clinical trials such as ACTIV-1 and ACTIV-4 will provide us with a better understanding of utility of therapeutics that are considered non teratogenic in the COVID-19 population [10].

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