

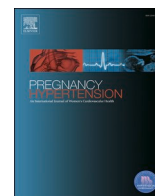


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# Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health

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## Is COVID-19 disease a risk factor for preeclampsia? Should aspirin be considered for prophylaxis of preeclampsia in these patients?

Dear editor,

We have read the study by Jayaram et al. [1] and wanted to congratulate the authors for this article on a major challenge in the current pandemic COVID-19 infection and make some minor contributions.

Since December 2019, a novel coronavirus has spread worldwide, and we still have limited information about this virus, especially in pregnancy. There is no consensus on some aspects of the disease in pregnancy. One of the most important current issues in the COVID-19 pandemic is the relationship between COVID-19 infection and preeclampsia (PE) in pregnancy. Most studies have shown that the risk of PE is increased in pregnant women with COVID-19 disease. In this infection, a PE-like syndrome develops and leads to similar symptoms, signs, and lab tests changes. Therefore, a big challenge is how to differentiate between the two. COVID-19, primarily a respiratory infection, can have marked multiorgan effects leading to renal, hepatic, gastrointestinal (GI), cardiovascular, central nervous system (CNS), and hematological injuries. In both COVID-19 and PE, vascular endothelial damage occurs that leads to multiorgan damage. In COVID-19 infection, headache, nausea and vomiting, blurred vision, epigastric pain, decreased platelet count, increased in liver enzymes, lactate dehydrogenase (LDH), uric acid, soluble fms-like tyrosine kinase 1 (sFLT-1), sFLT-1/PIGF (placental growth factor) Ratio and proteinuria can mimic PE. The important point is that these changes are progressive in PE, but the changes secondary to COVID-19 go away as the disease improves.

Increased sFLT-1 and sFLT/PIGF Ratio can predict PE. It has been recently hypothesized that CoV-2-dependent coagulopathy may be promoted by an imbalance between pro-angiogenic and anti-angiogenic factors. In particular, in COVID-19 patients, high levels of sFLT-1, PIGF, and a high ratio of sFLT-1/PIGF have been detected [2]. These factors are relevant predictive factors for in-hospital mortality in COVID-19 patients [3,4].

Placental changes caused by this infection include maternal vascular malperfusion with infarcts and increased fibrin deposition. In COVID-19 disease, the amount of PIGF and sFLT-1 increases due to vascular endothelial damage. Attention to these changes should be considered for the subsequent effects of the COVID-19 infection on adverse pregnancy outcomes. We suggest these patients should be followed for the level of these markers after the disease improves and determine whether these changes are reversible or not? There are several ways to determine whether placental injury persisted after COVID-19 infection improvement: placental changes on ultrasound, placental and endothelial serum markers, and placenta biopsy. It seems that the study of biomarkers is easier and safer than histopathological examination, and also it occurs earlier than ultrasound changes. This follow-up is important in terms of the prevention of adverse outcomes of pregnancy such as PE, especially when COVID-19 infection occurs in first and second trimesters. Low-dose aspirin prophylaxis is recommended in women at high risk of PE and should be initiated between 12 and 28 weeks of gestation (optimally before 16 weeks). Low-dose aspirin (60–100 mg/day) inhibits the expression of sFLT-1 in hypoxia-induced human cytotrophoblasts [5]. Is moderate to severe COVID-19 infection a major risk factor to the development of PE or not? Is the presence of this disease alone is an indication for aspirin to prevent adverse outcomes of pregnancy? How to determine which patients with COVID-19 infection will progress to PE? Is baseline level of placental serum markers and their trend helpful? Some issues need to be studied further in the future.

### Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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DOI of original article: <https://doi.org/10.1016/j.preghy.2021.07.248>.

<https://doi.org/10.1016/j.preghy.2021.11.001>

Received 19 September 2021; Accepted 3 November 2021

Available online 11 November 2021

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Sedigheh Hantoushzadeh<sup>a</sup>, Maasoumeh Saleh<sup>b,\*</sup>, Behnaz Nouri<sup>c</sup>, Zahra Panahi<sup>d</sup>

<sup>a</sup> Department of Fetal-Maternal Medicine, Tehran University of Medical Sciences, Imam Khomeini Hospital, Tehran, Iran

<sup>b</sup> Department of Fetal-Maternal Medicine, Tehran University of Medical Sciences, Shariati Hospital, Tehran, Iran

<sup>c</sup> Student Research Committee, Alborz University of Medical Sciences, Karaj, Iran

<sup>d</sup> Department of Obstetrics and Gynecology, Maternal-Fetal Neonatal Research Center, Tehran University of Medical Sciences, Valiasr Hospital, Tehran, Iran

\* Corresponding author.

E-mail addresses: [hantoushzadeh@tums.ac.ir](mailto:hantoushzadeh@tums.ac.ir) (S. Hantoushzadeh), [salehmaasoumeh@yahoo.com](mailto:salehmaasoumeh@yahoo.com) (M. Saleh).