

# Preeclampsia-Like Syndrome in a Pregnant Patient With Coronavirus Disease 2019 (COVID-19)



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## ABSTRACT

**Background:** Hypertension, proteinuria, and hepatic dysfunction have been described as manifestations of coronavirus disease 2019 (COVID-19) and are generally accepted as poor prognostic factors. However, these same findings can also occur in pregnant women with preeclampsia, thus creating a diagnostic challenge.

**Case:** We report a case of COVID-19 infection in an otherwise healthy pregnant patient with secondary hypertension, proteinuria, and significant hepatic dysfunction. Maternal placental growth factor (PIGF) testing was used to rule out preeclampsia. The patient received supportive care and improved significantly. She went on to have a spontaneous vaginal term delivery of a healthy male baby.

**Conclusion:** COVID-19 infection in pregnancy may present as preeclampsia-like syndrome. PIGF testing can be used to differentiate preeclampsia from COVID-19 and facilitate appropriate management.

## RÉSUMÉ

**Contexte :** L'hypertension, la protéinurie et la dysfonction hépatique ont été décrites comme des manifestations de la maladie à coronavirus 2019 (COVID-19) et sont généralement reconnues comme des facteurs pronostiques défavorables. Toutefois, ces mêmes manifestations sont parfois observables chez les femmes enceintes atteintes de pré-éclampsie, ce qui pose des difficultés diagnostiques.

**Cas :** Nous présentons un cas de COVID-19 chez une patiente enceinte autrement en bonne santé atteinte d'hypertension, de

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protéinurie et de dysfonction hépatique importantes secondaires à la maladie. Le dosage du facteur de croissance placentaire (PIGF) a été utilisé chez la mère pour exclure la pré-éclampsie. L'état de la patiente s'est grandement amélioré grâce au traitement symptomatique. Elle a finalement donné naissance à un garçon en bonne santé par accouchement vaginal spontané.

**Conclusion :** La COVID-19 pendant la grossesse peut se manifester comme un syndrome pré-éclamptique. Le dosage du PIGF peut permettre de distinguer la pré-éclampsie de la COVID-19 et faciliter la prise en charge adéquate.

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## INTRODUCTION

Growing evidence suggests that pregnant patients with coronavirus disease 2019 (COVID-19) infection are at increased risk of severe disease, including intensive care unit admission and need for mechanical ventilation, and overall mortality compared with non-pregnant individuals.<sup>1,2</sup>

Hypertension, proteinuria, and hepatic dysfunction have been described as manifestations of COVID-19 infection.<sup>3–5</sup> However, these same findings can also occur in pregnant women who develop preeclampsia, thus creating a diagnostic challenge.

We report a case of COVID-19 in an otherwise healthy pregnant patient with secondary hypertension and significant hepatic dysfunction and discuss the differential diagnosis, investigations, and management strategy.

**Keywords:** COVID-19; pregnancy outcome; preeclampsia; placenta growth factor

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## CASE

A healthy 39-year-old, G5 P1 woman, presented at 26<sup>4</sup> weeks gestation with progressively worsening dry cough and dyspnea that began approximately 5 days before admission. On presentation, she was afebrile with a blood pressure of 152/132, heart rate of 141 beats/min, respiratory rate of 20 per minute, and oxygen saturation of 96% on room air. An electrocardiogram showed sinus tachycardia. Computed tomography pulmonary angiogram was negative for pulmonary embolus but revealed patchy multifocal opacities, consistent with COVID-19 pneumonia, with limited evaluation of the upper abdomen that demonstrated no gross pathologies. Baseline laboratory investigations revealed hemoglobin of 106 g/L, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) of 72 and 64 U/L respectively, and normal leukocyte count, platelets, and creatinine. Obstetric ultrasound revealed an active baby, with normal Doppler flows. The patient was admitted to an internal medicine ward and was started on a prophylactic dose of low-molecular-weight heparin. COVID-19 infection was confirmed by a nasopharyngeal swab.

Initially, the patient had ongoing dyspnea, with O<sub>2</sub> desaturation on walk test. She received intramuscular betamethasone for fetal lung maturity, followed by intravenous dexamethasone daily. Her blood pressure subsequently normalized without medical therapy; however, repeat laboratory studies showed a progressive increase in hepatic enzymes, with an AST of 1154 U/L and ALT of 864 U/L. Hemoglobin levels decreased to 85 g/L, with lactate dehydrogenase (LDH) of 1018 U/L, and her albumin-creatinine ratio was 9.5. Platelets, creatinine, bile acids, complement (C3, C4), antinuclear antibody, and peripheral blood smear were normal.

Given the evolving clinical picture, a multidisciplinary discussion was conducted among the general internal medicine, maternal-fetal medicine, and infectious disease teams. Although the initial hypertension, anemia, severe hepatic dysfunction, and proteinuria could all be related to COVID-19, a possible diagnosis of preeclampsia with severe features could not be ruled out. Furthermore, diagnosis of preeclampsia with severe features would require different management, including treatment with magnesium sulfate and, ultimately, preterm delivery, with the potential for significant neonatal complications secondary to prematurity. To differentiate between these two entities, testing of maternal placental growth factor (PLGF) was conducted. The PLGF level was 158 pg/mL (normal >100 pg/mL), a value that rules out preeclampsia with very high negative predictive value.<sup>6</sup>

Over the next few days, the patient's condition improved. Her dyspnea resolved, with normalization of oxygen saturation on room air. AST and ALT levels gradually declined to 331 and 343 U/L, respectively, and the patient was discharged on day 13 for outpatient follow-up.

During her outpatient follow-up, AST and ALT continued to decline and eventually normalized. Blood pressure measurements and serial ultrasound scans for fetal growth were normal. She went on to have a spontaneous vaginal delivery of a healthy 3880 g male baby at 39<sup>2</sup> weeks gestation.

## DISCUSSION

Data regarding the effects of COVID-19 on pregnancy course and outcomes continue to accumulate as the pandemic spreads. Recent studies have reported that pregnant women with COVID-19 are at increased risk for severe disease, mechanical ventilation, and intensive care unit admission.<sup>1,2</sup> COVID-19 in pregnancy also significantly increases the risk for preterm delivery and maternal death.<sup>7</sup>

Hepatic dysfunction is a common finding in COVID-19 and is considered an indicator of poor prognosis.<sup>3</sup> Proteinuria is also a common manifestation of COVID-19 and is considered a risk factor for severe disease.<sup>5</sup> New-onset hypertension has also been described in COVID-19.<sup>4</sup> Endothelial dysfunction has been suggested as the mechanism for both manifestations: The severe acute respiratory syndrome coronavirus 2 accesses host cells by binding to angiotensin-converting enzyme 2, expressed in endothelial cells, and can cause endothelial dysfunction resulting in hypertension, kidney injury, and proteinuria, as well as diabetes and thrombosis.<sup>8</sup>

New-onset hypertension, proteinuria, and severe hepatic dysfunction are also clinical manifestations of preeclampsia<sup>9</sup>; therefore, differentiating between preeclampsia and COVID-19 in pregnancy can be challenging. Moreover, management strategies are different: Whereas the treatment of severe COVID-19 infection consists of steroids, antiviral drugs, and supportive care, treatment of preeclampsia with severe features is usually delivery.<sup>9</sup> An increased incidence of preeclampsia has been reported among pregnant women with COVID-19.<sup>7</sup> However, it is possible that some of those cases were misdiagnosed as preeclampsia, thus potentially contributing to the high incidence of provider-initiated preterm delivery in pregnant patients with COVID-19.<sup>1,2</sup>

PLGF is a placental-related angiogenic marker that is considered highly specific for preeclampsia. Women with

preeclampsia are characterized with low-levels of PIGF and a high sFlt-1/PIGF ratio. Thus, PIGF can be used to distinguish between these two entities, with levels >100 pg/mL ruling out preeclampsia with a high degree of certainty.<sup>6</sup> Additional support for the use of PLGF in this situation can be found in a recent publication by Mendoza et al.,<sup>10</sup> who described a preeclampsia-like syndrome in five of 42 (12%) pregnant women with severe COVID-19 and used the sFlt-1/PIGF ratio to rule out preeclampsia in four of those cases.

## CONCLUSION

COVID-19 infection in pregnancy can present with manifestations imitating preeclampsia. Greater awareness of this situation, along with possible use of PIGF as an ancillary test, can assist in ruling out preeclampsia and thus avoid unnecessary provider-initiated preterm delivery, with improved neonatal outcomes. Additional studies are needed to further investigate the association between COVID-19, preeclampsia, and the preeclampsia-like syndrome described in this report.

**Consent:** The woman whose story is told in this case report has provided signed permission for its publication.

## REFERENCES

1. Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ* 2020;370:m3320.
2. Subbaraman N. Pregnancy and COVID: what the data say. *Nature* 2021;591:193–5.
3. Parohan M, Yaghoubi S, Seraji A. Liver injury is associated with severe coronavirus disease 2019 (COVID-19) infection: a systematic review and meta-analysis of retrospective studies. *Hepatol Res Off J Jpn Soc Hepatol* 2020;50:924–35.
4. Mandal AKJ, Kho J, Metaxa S, et al. COVID-19 and late-onset hypertension with hyporeninaemic hypoaldosteronism. *Int J Clin Pract* 2021;75:e13773.
5. Yang Q, Yang X. Incidence and risk factors of kidney impairment on patients with COVID-19: a meta-analysis of 10180 patients. *PLoS ONE* 2020;15:e0241953.
6. Zeisler H, Llubra E, Chantraine F, et al. Predictive value of the sFlt-1:PIGF ratio in women with suspected preeclampsia. *N Engl J Med* 2016;374:13–22.
7. Di Mascio D, Khalil A, Saccone G, et al. Outcome of coronavirus spectrum infections (SARS, MERS, COVID-19) during pregnancy: a systematic review and meta-analysis. *Am J Obstet Gynecol MFM* 2020;2(2, Supplement):100107.
8. Hypertension, thrombosis, kidney failure, and diabetes: is COVID-19 an endothelial disease? A comprehensive evaluation of clinical and basic evidence - PubMed. Available at: <https://pubmed.ncbi.nlm.nih.gov/32403217/>. Accessed on May 4, 2021.
9. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' task force on hypertension in pregnancy. *Obstet Gynecol* 2013;122:1122–31.
10. Mendoza M, Garcia-Ruiz I, Maiz N, et al. Pre-eclampsia-like syndrome induced by severe COVID-19: a prospective observational study. *BJOG Int J Obstet Gynaecol* 2020;127:1374–80.