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Is COVID-19 a risk factor for severe preeclampsia? Hospital experience in a developing country

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To the Editor:

We have read with great interest the article published by Todros [1]; it states that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and preeclampsia have common pathophysiological characteristics, as shown by inflammatory changes. In the present work, we want to report our experience in a reference hospital of Peru regarding the clinical course of hypertensive disorders of pregnancy in pregnant women with SARS-CoV-2 infection.

Coronavirus disease 2019 (COVID-19) has been shown to cause systemic complications such as high blood pressure, kidney disease, thrombocytopenia, and liver injury [2]. The angiotensin-converting enzyme 2 (ACE2) receptor mediates the SARS-CoV-2 action that causes vasoconstriction resulting from renin-angiotensin system dysfunction [3]. During pregnancy, ACE2 plays an important role in the regulation of arterial pressure and expresses itself in excessive amounts in placental tissue, including syncytiotrophoblast, cytotrophoblast, endothelium, and vascular smooth muscle of the villi [4]. Intrauterine infection caused by COVID-19 can alter ACE2 expression, promoting a preeclamptic state. Mendoza, in his case series, postulates a preeclampsia-like syndrome in patients with severe SARS-CoV-2 infection, who meet the criteria for preeclampsia but who recover without delivery, only after the improvement of the respiratory condition [2].

Regarding the histopathological findings, Shaness et al. have shown that the placentas of patients with SARS-CoV-2 infection show a higher prevalence of decidual arteriopathy and other characteristics of poor maternal vascular perfusion such as decidual arteriopathy that includes atherosclerosis; fibrinoid necrosis and mural hypertrophy of membrane arterioles; changes that would reflect a systemic inflammatory state of hypercoagulability; findings similar to placental changes in hypertensive disorders of pregnancy; and changes related to oligohydramnios, fetal growth restriction, premature delivery, and fetal death [5]. While it is true that the reported cases are of patients with severe SARS-CoV-2 infection, the pathophysiology proposed so far would make us think that SARS-CoV-2 infection is a pro-inflammatory state, even in asymptomatic patients, that could be a risk factor for developing preeclampsia.

At the Obstetrics Department of a Peruvian Social Security hospital, from March to April 2020, Huerta et al [6] reported the first series of cases of pregnant women with COVID-19 in Peru. This study included 41 female patients, of which 68% were asymptomatic, 19.5% had mild infection and 4.8% had severe pneumonia that required enter the intensive care unit and non-invasive ventilation. The most frequent type of delivery was caesarean section (76.5%) and the most frequent indication was a history of caesarean section (48.3%) followed by presenting dystocia (20.7%) and hypertensive disorders of pregnancy in 10.3%. Also, leukocytosis was evidenced in 26.8%, thrombocytopenia in 14.6% and transaminasemia in 31.7% of patients. No maternal deaths or fetal deaths were reported.

Furthermore, at the same Department of the above-mentioned Hospital, from May 2020 to date, we have treated 20 pregnant women with a serological diagnosis of SARS-CoV-2 infection who developed preeclampsia (**Table 1**). Eleven patients were pregnant at term, and there was only one twin pregnancy. Regarding the respiratory symptoms, 16/20 (80%) patients were asymptomatic, with the remaining patients exhibiting mild symptoms. The most frequent findings in their laboratory tests were as follows: hypertransaminasemia, 40%–65%; leukocytosis, 30%; lymphopenia, 15%; and elevated C-reactive protein levels, 10%. Of all the patients, 15% (3/20) met the criteria for gestational hypertension and 15% (3/20) met the criteria for preeclampsia without signs of severity, whereas 70% (14/20) met the criteria for severe hypertensive disorders of pregnancy, comprising nine patients with severe preeclampsia; two with eclampsia; and five with hemolysis, elevated liver enzymes and low platelet count syndrome. The main route of delivery was cesarean section, which was performed in 85% (17/20) patients; one hysterectomy was performed for placenta accreta. The fetal death rate was 9.5% (2/20). Furthermore, 71% of the newborns had appropriate weight for their gestational age and 9.5% were small for gestational age. Only one newborn tested positive in the nasopharyngeal swab test for SARS-CoV-2 within the first 24 hours of life.

In conclusion, based on these preliminary findings, we suggest that SARS-CoV-2 infection, by inducing a pro-inflammatory state, predisposes pregnant women to a greater severity of the course of preeclampsia, even when severe respiratory symptoms are absent. We suggest the need for more scientific evidence to confirm this possible association.

Declaration of interests

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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Case	Age	Gestational Age	Parity	Symptoms	White blood cell x 10^3 (Lymphocytes %)	AST (U/L)	Delivery	Hypertensive Pregnancy Disorder
1	39	39	Multiparity	Asymptomatic	7.5 (16.7)	64	Caesarean Section	Severe Preeclampsia
2	33	34	Multiparity	Asymptomatic	9.1 (31.9)	53	Caesarean Section	Severe Preeclampsia
3	43	40	Multiparity	Asymptomatic	12.3 (28.4)	36	Caesarean Section	Severe Preeclampsia
4	21	36	Nulliparity	Asymptomatic	7.4(25.6)	42	Caesarean Section	Mild Preeclampsia
5	31	33	Nulliparity	Asymptomatic	9.3 (27)	53	Caesarean Section	Severe Preeclampsia
6	33	38	Multiparity	Asymptomatic	7.7 (22.2)	14	Caesarean Section	Gestational Hypertension
7	45	38	Multiparity	Asymptomatic	14.5 (32.8)	25	Caesarean Section	Severe Preeclampsia
8	42	40	Multiparity	Headache	8.8 (19.2)	51	Vaginal Delivery	Gestational Hypertension
9	32	40	Multiparity	Asymptomatic	19.2 (4.73) *	39	Vaginal Delivery	Mild Preeclampsia
10	37	40	Multiparity	Asymptomatic	8.4 (35.3)	16	Caesarean Section	Severe Preeclampsia
11	45	34	Nulliparity	Asymptomatic	6.0 (15.8) *	27	Caesarean Section	Severe Preeclampsia and Eclampsia
12	33	39	Multiparity	Asymptomatic	10.2 (33.9)	27	Caesarean Section	Gestational Hypertension
13	29	34	Multiparity	Asymptomatic	18 (3.7) *	904	Caesarean Section	Severe Preeclampsia and Eclampsia
14	39	39	Multiparity	Asymptomatic	11 (27)	64	Cesarean Hysterectomy	Hellp Syndrome
15	29	36	Nulliparity	Asymptomatic	6.8 (21.6)	449	Caesarean Section	Hellp Syndrome
16	32	37	Multiparity	Asymptomatic	10.1 (27.5)	16	Caesarean Section	Mild Preeclampsia
17	17	23	Nulliparity	Cough	7.9 (17.7)	59	Caesarean Section	Hellp Syndrome+
18	27	23	Nulliparity	Cough	7.8 (17.8)	54	Caesarean Section	Hellp Syndrome
19	24	39	Nulliparity	Asymptomatic	12.7 (22.9)	33	Caesarean Section	Severe Preeclampsia
20	31	33	Multiparity	Fever	9.3 (29.9)	288	Vaginal Delivery	Hellp Syndrome +

Table 1. Clinical and biochemical characteristics of patients with serological diagnosis of COVID-19 and Hypertensive Pregnancy Disorders. Source: Data obtained from the Obstetrics inpatient Department. Hospital Nacional Edgardo Rebagliati Martins. March-August 2020. AST: Aspartate aminotransferase. * Patients with lymphopenia (lymphocytes <1000 cells/mm^3). + Patients who had stillbirth.