Received: 22 April 2020 | Revised: 24 April 2020 | Accepted: 27 April 2020

DOI: 10.1111/aogs.13887

LETTER TO THE EDITOR

Antenatal corticosteroid therapy and COVID-19: Pathophysiological considerations

Sir,

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has presented many challenges in health care, including obstetrics. Therefore, we read with great interest the special editorial published in *AOGS* regarding clinical recommendations for the management of coronavirus disease 2019 (COVID-19) in pregnant women.[1] As illustrated by the authors, the usefulness and safety of corticosteroids as an adjuvant therapy for COVID-19 pneumonia remains controversial. Corticosteroids may diminish the inflammatory response, a major factor for lung damage and acute respiratory distress syndrome in viral respiratory tract infection. However, previous studies on corticosteroid therapy in SARS coronavirus and Middle East respiratory syndrome coronavirus illustrated delayed viral clearance, with no survival benefit and perhaps even adverse outcomes.[2] Some patients with COVID-19 exhibit biphasic disease evolution with a mild presentation followed by a secondary respiratory deterioration due to a cytokine storm, despite decreasing viral load.[2] Therefore, timing of corticosteroid therapy might be particularly consequential, with early administration reducing inflammatory response and viral clearance during the initial phase.

While acknowledging the recommendations to administer corticosteroids for fetal lung maturation when preterm delivery is anticipated,[1] one must also consider the renin-angiotensin-aldosterone system, which is closely linked to the pathophysiology of COVID-19. SARS-CoV-2 gains access to its target cell by exploiting the membrane-bound angiotensin-converting enzyme 2 (ACE2).[3] ACE2 converts angiotensin II to angiotensin (1-7), which has vasodilator, anti-proliferative, and anti-fibrotic functional effects, in contrast to those of angiotensin II.[3] It is thought that viral infection downregulates ACE2, resulting in disproportionate angiotensin II activity, which may be a possible mechanism for organ injury in COVID-19. Animal studies have illustrated that glucocorticoids are potent inducers of ACE activity in the lung and so modulate local levels of angiotensin II, increase angiotensin II precursor processing, and upregulate angiotensin II receptors in vascular smooth muscle cells.[4,5] As angiotensin II seems to play a key role in the pathophysiology of COVID-19, its potentiation by corticosteroids might have a detrimental effect. Indeed, corroborating this theory, a small study illustrated correlation between increased plasma levels of angiotensin II, total viral load and lung injury severity.[4]

Despite the importance of antenatal lung maturation for neonates, uncertainties remain as to whether corticosteroids have any adverse effect on the clinical course of COVID-19 in the mother, and there is an urgent need to gather sufficient clinical data. Until then, especially during the early phase of the disease, we would proceed with caution regarding the administration of antenatal corticosteroids, considering the mother's clinical status and gestational age of the fetus, and ensuring an informed decision balancing benefits and risks.

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