
















The use of antenatal corticosteroids for fetal maturation in COVID-19: clinical practice statement by the WAPM-World Association of Perinatal Medicine and the PMF-Perinatal Medicine Foundation

Themistoklis Dagklis¹ , Cihat Şen² , Ioannis Tsakiridis¹ , Cecilia Villalain³ ,
Karel Allegaert⁴ , Sven Wellmann⁵ , Satoshi Kusuda⁶ , Bernat Serra⁷ ,
Manuel Sanchez Luna⁸ , Erasmo Huertas⁹ , Nicola Volpe¹⁰ , Rodrigo Ayala¹¹ ,
Nelly Jekova¹² , Amos Grunebaum¹³ , Milan Stanojevic¹⁴ 

¹Third Department of Obstetrics & Gynaecology, Faculty of Health Sciences, School of Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece

²Perinatal Medicine Foundation and Department of Obstetrics & Gynecology, Memorial Babçelievler Hospital, Istanbul, Turkey

³Fetal Medicine Unit, Department of Obstetrics & Gynecology, University Hospital 12 de Octubre, Complutense University of Madrid, Madrid, Spain

⁴Department of Development and Regeneration, and Department of Pharmaceutical & Pharmacological Sciences, KU Leuven, Leuven, Belgium; and Hospital Pharmacy, Erasmus MC, Rotterdam, the Netherlands

⁵Department of Neonatology, University Children's Hospital Regensburg (KUNO), Hospital St. Hedwig of the Order of St. John, University of Regensburg, Regensburg, Germany

⁶Department of Pediatrics, Kyorin University, Tokyo, Japan

⁷Department of Obstetrics, Gynecology & Reproduction, Hospital Universitari Dexeus, Barcelona, Spain

⁸Neonatology Division and NICU, Hospital General Universitario "Gregorio Marañón" Complutense University of Madrid, Madrid, Spain

⁹Department of Obstetrics & Gynecology, San Marcos National University, Lima, Peru

¹⁰Fetal Medicine Unit, Department of Obstetrics & Gynecology, Azienda Ospedaliero-Universitaria di Parma, Parma, Italy

¹¹Department of Obstetrics & Gynecology, Centro Medico ABC Santa Fe, Mexico City, Mexico

¹²Department of Neonatology, University Hospital of Obstetrics & Gynecology "Maichin dom", Medical University Sofia, Bulgaria

¹³Department of Obstetrics & Gynecology, Barbara and Donald Zucker School of Medicine at Hofstra/Northwell and Lenox Hill Hospital, New York, USA

¹⁴Neonatal Unit, Department of Obstetrics & Gynecology, Clinical Hospital "Sveti Dub", Zagreb, Medical School, University of Zagreb, Croatia

Abstract

This statement follows the mission of the World Association of Perinatal Medicine (WAPM) in collaboration with the Perinatal Medicine Foundation (PMF), bringing together groups and individuals throughout the world with the goal of improving the use of antenatal corticosteroids (ACS) for fetal maturation in Coronavirus Disease 2019 (COVID-19). Pregnant women with COVID-19 are at increased risk of hospitalization, admission to intensive care unit and mechanical ventilation compared to non-pregnant patients. Thus, obstetricians may face the dilemma of initiating maternal corticosteroid therapy for maternal indication while weighing its potential adverse effects on the fetus. As there is no evidence on the effect of betamethasone in pregnant women with COVID-19, dexamethasone should be preferably used for fetal maturation, if available. As a recommendation, for pregnant women with COVID-19 who are oxygen dependent or under mechanical ventilation and meet the criteria for ACS, the usual doses of dexamethasone should be administered, followed by oral prednisolone 40 mg OD or intravenous hydrocortisone 80 mg BD for up to 10 days.

Keywords: Corticosteroids, fetal maturation, COVID-19.

Correspondence: Cihat Şen, MD. Department of Perinatal Medicine, Obstetrics and Gynecology, Perinatal Medicine Foundation and Istanbul University-Cerrahpasa, Istanbul, Turkey. **e-mail:** csen@perinatalmedicine.org / **Received:** February 5, 2022; **Accepted:** February 5, 2022

How to cite this article: Dagklis T, Şen C, Tsakiridis I, Villalain C, Allegaert K, Wellmann S, Kusuda S, Serra B, Luna MS, Huertas E, Volpe N, Ayala R, Jekova N, Grunebaum A, Stanojevic M. The use of antenatal corticosteroids for fetal maturation in COVID-19: clinical practice statement by the WAPM-World Association of Perinatal Medicine and the PMF-Perinatal Medicine Foundation. *Perinat J* 2022;30(1):12–13. doi:10.2399/prn.22.0301005

ORCID ID: T. Dagklis 0000-0002-2863-5839; C. Şen 0000-0002-2822-6840; I. Tsakiridis 0000-0003-4337-7871; C. Villalain 0000-0002-9456-4100; K. Allegaert 0000-0001-9921-5105; S. Wellmann 0000-0001-9230-6266; S. Kusuda 0000-0001-5318-8877; B. Serra 0000-0002-1749-3628; M. S. Luna 0000-0001-9543-7392; E. Huertas 0000-0002-9851-8419; N. Volpe 0000-0003-4209-5602; R. Ayala 0000-0003-2548-3208; N. Jekova 0000-0002-2701-5996; A. Grunebaum 0000-0002-0308-0232; M. Stanojevic 0000-0002-3124-5575

Pregnant women with Coronavirus Disease 2019 (COVID-19) are at increased risk of hospitalization, admission to intensive care unit and mechanical ventilation compared to non-pregnant patients. Thus, obstetricians may face the dilemma of initiating maternal corticosteroid therapy for maternal indication while weighing its potential adverse effects on the fetus.^[1] On the other hand, the neonatal benefits of antenatal corticosteroids (ACS) in women at high risk of preterm birth within the next 7 days have been well established.^[2]

The use of glucocorticoids as a means of immunomodulatory therapy in oxygen dependent COVID-19 patients is supported by the results of the Randomized Evaluation of COVID-19 Therapy (RECOVERY) trial;^[3] the use of dexamethasone for up to 10 days significantly reduced 28-day mortality in COVID-19 patients receiving invasive mechanical ventilation or oxygen without invasive mechanical ventilation (29.3% vs. 41.4%; RR: 0.64; 95% CI: 0.51–0.81) and in those receiving oxygen without invasive mechanical ventilation (23.3% vs. 26.2%; RR: 0.82; 95% CI: 0.72–0.94). Conversely, there was a trend towards increased mortality in those patients receiving no respiratory support at randomization (17.8% vs 14.0%; RR: 1.19; 95% CI: 0.91–1.55).^[3] It is worthy of note that only six pregnant women were included in the RECOVERY trial and, as per protocol for pregnant women, they received either oral prednisolone or intravenous hydrocortisone instead of dexamethasone, as these, contrary to dexamethasone, do not cross the placenta in significant quantity.^[4] Based on this safety signal of possibly increased mortality among patients with mild COVID-19 receiving dexamethasone, the indications for ACS should be limited to obstetrical indications with expected preterm delivery within the next 7 days.^[5] As there is no evidence on the effect of betamethasone in pregnant

women with COVID-19, dexamethasone should be preferably used for fetal maturation, if available.

Recommendation

- For pregnant women with COVID-19 who are oxygen dependent or under mechanical ventilation and meet the criteria for ACS, the usual doses of dexamethasone (4 doses of 6 mg IM at 12 h intervals) should be administered, followed by oral prednisolone 40 mg OD or intravenous hydrocortisone 80 mg BD for up to 10 days.

Research funding: None declared.

Author contributions: All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

Conflicts of interest: Authors state no conflict of interest.

Informed consent: Not applicable.

Ethical approval: Not applicable.

References

1. Allotey J, Stallings E, Bonet M, Yap M, Chatterjee S, Kew T, et al.; PregCOV-19 Living Systematic Review Consortium. 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. [PubMed] [CrossRef]
2. Dagklis T, Tsakiridis I, Papazisis G, Athanasiadis A. Efficacy and safety of corticosteroids' administration for pulmonary immaturity in anticipated preterm delivery. *Curr Pharm Des* 2021;27:3754–61. [PubMed] [CrossRef]
3. Group RC, Horby P, Lim WS, Emberson JR, Mafham M, Bell JL, et al.; RECOVERY Collaborative Group. Dexamethasone in hospitalized patients with Covid-19. *N Engl J Med* 2021; 384:693–704. [PubMed] [CrossRef]
4. Kemp MW, Newnham JP, Challis JG, Jobe AH, Stock SJ. The clinical use of corticosteroids in pregnancy. *Hum Reprod Update* 2016;22:240–59. [PubMed] [CrossRef]
5. Vidaeff AC, Aagaard KM, Belfort MA. Antenatal corticosteroids in COVID-19 perspective. *World J Exp Med* 2021;11: 37–43. [PubMed] [CrossRef]

This work is licensed under the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 Unported (CC BY-NC-ND4.0) License. To view a copy of this license, visit <http://creativecommons.org/licenses/by-nc-nd/4.0/> or send a letter to Creative Commons, PO Box 1866, Mountain View, CA 94042, USA.

Publisher's Note: The content of this publication does not necessarily reflect the views or policies of the publisher, nor does any mention of trade names, commercial products, or organizations imply endorsement by the publisher. Scientific and legal responsibilities of published manuscript belong to their author(s). The publisher remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.