Prevention of thrombosis in pregnant women with suspected SARS-CoV-2 infection: clinical management algorithm

An emerging body of evidence suggests that the coronavirus disease 2019 (COVID-19) may predispose patients to venous thromboembolism (VTE). Increased levels of D-dimer are associated with a worsening condition of the patient. Risk assessment for VTE in all patients with COVID-19 admitted to hospital is recommended.

Most cases of COVID-19 during pregnancy are mild or asymptomatic, and clinical findings are similar to those in non-pregnant adults. However, pregnancy itself alters the body's immune system and the response to a viral infection can cause more severe symptoms. Recent reports warn of rapid maternal deterioration, coagulopathy¹ and maternal death in pregnant women diagnosed with COVID-19².

In pregnant women, the physiological hypercoagulability state and virus-related hypercoagulability may pose a uniquely increased risk for thrombotic-related morbidity. Thus, identifying women at risk is important for the successful provision of appropriate prophylaxis.

VTE risk assessment is complex as pre-existing conditions, together with new-onset or temporary risk factors, must be evaluated. Reduced mobility due to home confinement or hospital admission and pneumonia are associated with an increased risk of VTE in pregnant women. Multiple risk-assessment models have been developed to help estimate the risk of VTE in the pregnant population. The software tool, AnticoagObs, based on international guidelines^{3,4} is freely available (<http://www.anticoagulationinpregnancy.com/>).

International institutions⁵ recommend antenatal and postnatal prophylactic low-molecular-weight heparin in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-positive women. However, recommendations for scenarios such as SARS-CoV-2 exposure (close contact with a confirmed case) and/or suspected-COVID-19 (symptoms consistent with COVID-19, however, not yet confirmed) remain to be determined.

A national expert committee endorsed by the Spanish Society of Thrombosis and Haemostasis has built an algorithm for clinical management of pregnancy-associated VTE, adapted to the current SARS-CoV-2 pandemic (Appendix S1). It is important to update VTE risk factors that may worsen the severity of COVID-19 in pregnant women. Due to its role in promoting hypercoagulability, SARS-CoV-2 infection is included as an independent risk factor for VTE.

We propose: (1) in asymptomatic women with SARS-CoV-2 exposure, to reassess for VTE risk factors during pregnancy and puerperium, provide recommendations for isolation at home, and instruct the patient to contact a healthcare center or maternity unit if symptoms appear; and (2) in women suspected of COVID-19 with mild-to-moderate symptoms, to reassess for VTE risk factors and clinical severity, and monitor at home every 48–72 h via telephone contact. Pregnant women hospitalized for suspected COVID-19 with severe symptoms or any obstetric complications should be given a prophylactic weight-adjusted dose of heparin during admission and 1 month after discharge to prevent VTE. Due to the greater risk of VTE during the third trimester, extending prophylaxis until delivery and up to 6 weeks postpartum should be considered. Severe illness in a suspected COVID-19 patient should be managed as a confirmed SARS-CoV-2 infection.

For the first time, we present an algorithm including an approach for thromboprophylaxis for ambulatory

and hospitalized pregnant women with SARS-CoV-2 exposure and those with suspected COVID-19. Careful monitoring of pregnancies with COVID-19 to prevent major complications such as VTE is warranted. The antithrombotic and anti-inflammatory properties of heparin may improve disease outcome, providing that the use of heparin is safe for the mother and fetus.

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References

- Koumoutsea EV, Vivanti AJ, Shehata N, Benachi A, Le Gouez A, Desconclois C, Whittle W, Snelgrove J, Malinowski KA. COVID19 and acute coagulopathy in pregnancy. *J Thromb Haemost* 2020. DOI: 10.1111/jth.14856.
- Hantoushzadeh S, Shamshirsaz AA, Aleyasin A, Seferovic MD, Aski SK, Arian SE, Pooransari P, Ghotbizadeh F, Aalipour S, Soleimani Z, Naemi M, Molaei B, Ahangari R, Salehi M, Oskoei AD, et al. Maternal Death Due to COVID-19 Disease. *Am J Obstet Gynecol* 2020. DOI: 10.1016/j.ajog.2020.04.030.
- Royal College of Obstetricians and Gynaecologists. Reducing the Risk of Venous Thromboembolism during Pregnancy and the Puerperium. (Green-top Guideline No. 37a). 2015. <https://www.rcog.org.uk/en/guidelines-research-services/guidelines/37a/> [Accessed 10 June 2015].
- Bates SM, Greer IA, Middeldorp S, Veenstra DL, Prabulos AM, Vandvik PO. VTE, Thrombophilia, Antithrombotic Therapy, and Pregnancy: Antithrombotic Therapy and Prevention of Thrombosis, 9th Ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012; **141** (2 Suppl): e691S–e736S.
- Royal College of Obstetricians and Gynaecologists. Coronavirus (COVID-19) Infection in Pregnancy. Information for healthcare professionals. Version 7. 2020. <https://www.rcog.org.uk/globalassets/documents/guidelines/2020-04-09-coronavirus-covid-19-infection-in-pregnancy.pdf>

SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:

Appendix S1 Clinical management algorithm for prophylaxis of venous thromboembolism in pregnant women during COVID-19 pandemic