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Obstetric APS and thrombosis; modelling future risks

M Spaanderman, C Ghossein-Doha

Department of Obstetrics and Gynaecology, Maastricht University Medical Centre (MUMC), Maastricht, the Netherlands

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To diagnose obstetric history-based antiphospholipid syndrome (Ob-APS), it is recommended that women with recurrent pregnancy loss (RPL), a history of severe pre-eclampsia, eclampsia or features consistent with placental insufficiency (placental syndrome, PS) should be tested for antiphospholipid antibodies (aPL) (Miyakis et al. *J Thromb Haemost* 2006;4:295). The systemic biology of these pregnancy-related complications is still incompletely understood but includes an interplay between endothelial cell stimulation, (secondary) platelet activation, trophoblast impairment and Toll-like receptor-induced innate immunity activation. These factors may play a role in the clinical expression of APS and consequently underlie the variably reported beneficial effects of aspirin, low molecular weight heparins, and possibly corticosteroid and hydroxychloroquine treatment in the prevention of gestational complications.

The main types of aPL associated with adverse pregnancy outcome are lupus anticoagulant (LAC), anticardiolipin antibodies (aCL), and anti-beta-2 glycoprotein-1 antibodies (aB2GP1). Mean reported incidences in conjunction with RPL and PS vary between 15 and 18%, respectively (ASRM. *Fertil Steril* 2012;98:1103-11). Nonetheless, given the low incidence of RPL and severe PS, the absolute incidence of Ob-APS remains low. Therefore, detailed information from observational cohorts or randomised intervention studies regarding the impact of these antibodies on pregnancy in the absence or presence of treatment is scarce. Adjusted hazard ratios after Ob-APS for lifetime risk of deep vein thrombosis, pulmonary embolism, and cerebrovascular accident (transient ischaemic attack or stroke) are 1.9 (95% CI 1.5–2.3), 1.9 (95% CI 1.3–2.9) and 2.1 (95% CI 1.1–4.1), respectively, compared with women without thrombophilia (Gris et al. Blood 2012;119:2624). Although the relative risk is increased, the absolute risk is still low, and the relatively high number needed-to-treat may deter some clinicians from starting preventive antithrombotic treatment.

To deal with this concern, Ramires de Jesús G et al. (*BJOG* 2019; 126:656–61) a collaborative network, 'APS ACTION', studied the impact of the global antiphospholipid syndrome score (GAPSS) to stratify the risk of remote thrombosis in Ob-APS. The GAPSS combines the main types of aPL with vascular risk estimates (hyperlipidaemia and arterial hypertension). Different cardiovascular risk factors, hypertension, treated diabetes or hyperlipidaemia, obesity or smoking were included in a separate analysis. More than 60% of women with Ob-APS developed thrombosis after a mean period of 7.6 years. The risk of future thrombosis was not affected by age, concomitant auto-immune disease or specific obstetric history. The presence of any cardiovascular factor increased the risk of thrombosis, suggesting the importance of concurrent endothelial dysfunction to catalyse the process of thrombosis in the presence of aPL, especially when more than one subtype is present. The GAPSS also showed a potential role in assessing women's risk of future thrombosis, but there still appears to be a substantial overlap in scores between those with and without thrombotic complications. Moreover, the GAPSS includes anti-phosphatidylserine/prothrombin antibodies which are not mandatory in the work-up of Ob-APS. Nonetheless, this study shows that Ob-APS impacts not only reproductive performance but also remote health, and may be individually predicted by concurrent vascular risk factors. Although this study does not detail the additional effects of hormonal contraception on venous thrombosis, in women affected with Ob-APS at a reproductive age, it may be better to advise alternative non-hormonal contraceptive control.

Disclosure of interests

None declared. Completed disclosure of interest forms are available to view online as supporting information. ■