EDITORIAL

Thrombophilia and Pregnancy

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Pregnancy is a state of hypercoagulation, most likely an adaptive mechanism, in order to reduce the risk of hemorrhage during and after the delivery. There are substantial changes in the haemostatic system during normal healthy pregnancy including rise in clotting factors I, VII, VIII, IX, and X, diminished protein S and fibrinolytic activity and resistance to activated protein C.[1] Reduced fibrinolytic activity is due to fivefold increase in PAI-1 (Plasminogen Activator Inhibitor type 1) levels.[2] In addition venous stasis increases during pregnancy as the lower-extremity veins dilate due to venous compression by the gravid uterus. Endothelial injury may also occur in antepartum or in postpartum period. The combination of these factors results in 4-5 times increased risk of venous thromboembolism (VTE) in the pregnant and postpartum patients.[3] The prevalence of VTE in pregnancy is 0.8-2.0 per 1,000 pregnancies and accounts for 1.1 deaths per 100,000 pregnancies.[4] The most important risk factor for women experiencing pregnancy-related VTE is prior personal history of VTE.[5] The second most common risk factor is thrombophilia [6 7] Studies have shown that at least 20%, and possibly over 50%, of pregnant patients diagnosed with VTE have thrombophilia.[8] There is a growing evidence that women with thrombophilia are also at risk of other vascular pregnancy complications, including recurrent fetal loss, pre-eclampsia, stillbirths, abruption and intrauterine growth restriction.

Thrombophilia can be Inherited or acquired. Inherited Thrombophilias are a group of genetic disorders, which can be classified as low or high risk based on the relative increased risk of VTE.

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Antiphospholipid antibody syndrome is considered as an acquired thrombophilia and its diagnosis is based upon clinical history and laboratory testing. Low-risk inherited thrombophilias include Heterozygous factor V Leiden, Heterozygous prothrombin G20210A mutation, Protein S deficiency and Protein C deficiency. High-risk inherited thrombophilias include Homozygous factor V Leiden, Homozygous prothrombin G20210A mutation, Compound heterozygous factor V Leiden with prothrombin mutation and Antithrombin deficiency. Ideally, evaluation for thrombophilia should be done when the patient is not pregnant, does not have an acute thrombotic event, and is not on anticoagulation therapy. ACOG (American College of Obstetricians and Gynecologists) recommends screening a patient for thrombophilia during pregnancy only if test results are likely to alter management. Screening should be performed when the presence of a thrombophilia may alter the intensity or duration of anticoagulation therapy. Screening is unnecessary when treatment is indicated for other reasons.[9] Thrombophilia screening may be considered in:

- Patients with a personal history of VTE that occurred in the setting of a transient nonrecurrent risk factor (eg, fractures, surgery, prolonged immobility) that was not estrogen- or pregnancy-related
- Patients with a first-degree relative with a prior VTE that occurred before age 50 years or with a prior diagnosis of high-risk thrombophilia.

Following are the recommended methods of evaluation of inherited thrombophilias in pregnancy:

- Factor V Leiden: Second-generation activated protein C resistance assay is reliable in pregnancy; if results are abnormal, evaluate for genotype for factor V Leiden mutation; if the patient is on anticoagulation therapy, consider evaluation of factor V Leiden mutation via genotype testing.
- Prothrombin G20210A mutation DNA analysis
- Protein C functional activity level
- Protein S free, total, and functional levels. (Protein S deficiency testing is less reliable in pregnancy, as levels decrease with increasing gestational age).
- Antithrombin-heparin cofactor assay

For Antiphospholipid antibody syndrome, in addition to specific clinical criteria for evaluation, laboratory criteria includes any one of the following (these laboratory findings must be abnormal twice, at least 12 weeks apart, to meet diagnostic criteria)[10]

- Anticardiolipin immunoglobulin G (IgG) or immunoglobulin M (IgM) antibodies greater than 99th percentile
- Antibeta2-glycoprotein I IgG or IgM antibodies greater than 99th percentile
- The presence of lupus anticoagulant

The factors that affect the decision, to provide Thromboprophylaxis, as well as the timing (antenatal or postpartum only) and intensity of therapy depends on the following:

- Any prior personal history of VTE
- The presence of high- versus low-risk thrombophilia
- The setting in which a prior VTE occurred (pregnancy/estrogen-related, idiopathic, or in the setting of non-recurrent risk factors such as fractures, surgery, or immobilization)

Early recognition of risk factors and judicious implementation of Thromboprophylaxis has significantly decreased maternal mortality due to thromboembolism

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