

Pregnancy & Thrombophilia

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There are two main adverse experiences that are associated with thrombophilia and pregnancy. First second is maternal venous thromboembolism (VTE) and second are pregnancy complications including placental infarction, miscarriage, intrauterine growth retardation, preeclampsia, abruption, and intrauterine death. Asymptomatic women with congenital deficiencies of antithrombin, protein C, or protein S have approximately an eight-fold increased risk of VTE during the pregnancy compared to normal control subjects. Approximately 60% of women who develop VTE during pregnancy have factor V Leiden. Other thrombophilic disorders such as prothrombin gene mutation, hyperhomocystinemia, and persistent antiphospholipid antibodies are probably associated with an increased risk of VTE during pregnancy and the puerperium. Clinical experience suggests that women with antithrombin deficiency have a higher risk of VTE than women with other thrombophilias and should be treated more aggressively. The antepartum management of pregnant women with known thrombophilia and no prior history of VTE are controversial. In a review of pregnant women with antithrombin, protein C, or protein S deficiency, less than 2% of the women experienced VTE during the pregnancy. Unfortunately, there are no prospective studies addressing this issue. Women who have a history of VTE with or without thrombophilia are believed to have a higher risk of recurrence in subsequent pregnancies. The estimated rate of recurrence of VTE during the pregnancy in women with a history of VTE has varied between 0% and 13% depending on the inclusion criteria and population that is studied.

MATERNAL RISKS FOR VENOUS THROMBOEMBOLISM

Fatal pulmonary embolism (PE) remains a common cause of maternal mortality. Mortality can be reduced by aggressively investigating symptomatic women when they present with a clinical suspicion of deep vein thrombosis (DVT) or PE and by treatment and/or prophylaxis in women who have an increased risk of DVT and/or PE. The true incidence of venous thromboembolism (VTE) associated with pregnancy is not known but there is a strong clinical impression that the risk is increased compared to the incidence in non-pregnant women. The risk appears to be higher following cesarean section (particularly emergency cesarean section) compared with vaginal delivery. VTE appears to occur in all trimesters with equal prevalence. There is a striking predisposition for DVT to occur in the left leg, approximately 90% of the time. In addition, a greater proportion of thrombi during the pregnancy are in the iliofemoral veins and are therefore more likely to embolize to the lungs. Similar to the situation in non-pregnant individuals, the clinical diagnosis of DVT and PE during the pregnancy is difficult. This is compounded by chronic leg swelling and pain as well as chest pain and dyspnea, which are common complaints during pregnancy and are usually not associated with VTE. In a recent study of consecutive pregnant patients presenting with a clinical suspicion of DVT, the prevalence of DVT was less than 10% compared to approximately 25% in non-pregnant women with similar complaints.

PLACENTAL AND FETAL RISKS.

Thrombophilia is present in two-thirds of women with a history of recurrent abortions, intrauterine fetal death, intrauterine growth restriction (IUGR), and severe early-onset preeclampsia. In a study that examined 65 women with pregnancy-related complications, 37 (61%) had evidence of acquired or congenital thrombophilia (Bar J, et.al., Thromb Res. 2001). Among these included 22 (36%) women with protein S deficiency; 1 (2%) with protein C deficiency; 2 (3%) with activated protein C resistance (APC-R), 2 (3%) with IgG antiphospholipid antibodies; 1 (2%) with a circulating anticoagulant; and 9 (15%) with a combined defect.

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Brenner B, Kupferminc MJ. (Best Pract Res Clin Obstet Gynaecol. 2003) reviewed the growing body of evidence suggesting that thrombophilia plays a significant role in the development of obstetric complications. Although the majority of women with thrombophilia will have an uneventful pregnancy, case-control studies have demonstrated that thrombophilia is more prevalent in women with pregnancy loss and early-onset pre-eclampsia. Placental abruption and severe intrauterine growth restriction (IUGR) may also be associated with thrombophilia. Placental pathological findings in women with thrombophilia include thrombosis and fibrin deposition potentially to a greater degree than in normal pregnancy. Several groups have suggested that heparin prophylaxis at low doses combined with aspirin could be efficacious in preventing pregnancy-related complications in women with inherited thrombophilia and a history of prior obstetric complications (Grandone E et.al., Fertil Steril. 2002). Kupferminc MJ et.al., (Hypertens Pregnancy. 2001) administered prophylactic low molecular weight heparin and aspirin to women patients with obstetric complications and an inherited thrombophilia. Patients who were found to be homozygous for the methylenetetrahydrofolate reductase mutation also received folic acid supplementation throughout their pregnancy. Their results suggested that women may benefit from treatment with combined low molecular weight heparin and aspirin in subsequent pregnancies. Tzafettas J, et.al., (Clin Exp Obstet Gynecol. 2002) suggested that thromboprophylaxis during pregnancy may be effective in preventing pregnancy-related complications in women with a history of prior complications but without an underlying thrombophilia

Mello G, and colleagues (Hypertension. 2004) reported on their investigations of the effect of LMWH on the pregnancy outcome, on maternal blood pressure values, and on uteroplacental flow in nonthrombophilic women with history of preeclampsia. Women were randomized in 2 groups: 41 treated with Fragmin[®] and 39 untreated (control group). Fragmin[®] reduced the risk of preeclampsia by 74%, of fetal growth restriction by 78% and the severity of early onset preeclampsia by 88%. In women treated with Fragmin[®] the relative risk for preeclampsia was 0.26, and the relative risk for fetal growth restriction was 0.14. Blood pressures, as well the resistance indexes of both uterine arteries were lower in the treated group. These investigators concluded that Fragmin[®] reduces the recurrence of preeclampsia, of negative outcomes, and the resistance of uteroplacental flow, and also prevents maternal blood pressure increase in women with a previous history of preeclampsia.

Riyazi N, et.al., (Eur J Obstet Gynecol Reprod Biol. 1998) studied 276 women with a history of preeclampsia and/or fetal growth restriction. Ninety (33%) of these women with preeclampsia and 15 (5%) with intrauterine growth restriction had abnormalities of the coagulation system. Of the 90 women with coagulation abnormalities including protein S deficiency, activated protein C (APC) resistance and/or elevated Anti-phospholipid antibodies had a subsequent pregnancy and were treated with the combination of aspirin and low molecular weight heparin. In subsequent pregnancies, the birth weight of babies born to patients with a coagulation abnormality were higher than in the group with no disorder. These authors concluded that low molecular weight heparin appears to have a favorable effect on the pregnancy outcome of women with a history of preeclampsia and/or fetal growth restriction and documented thrombophilia.

This information is provided to supplement your consultation visit. If you have questions, please contact Dr Valentino or a member of his nursing staff.