

Factor V Leiden and Risk for Pregnancy Loss

Meinardi JF et al., Ann Intern Med. 1999;130:736-739.

Factor V Leiden mutation, causing resistance to activated protein C, is the most common inherited predisposition to thrombosis known. It is associated with increased risks for venous thromboembolism and there is evidence associating it with obstetric morbidity including placental thrombosis.

In this retrospective study the authors looked to determine the risk for miscarriage (fetal loss \leq 20 weeks gestation), stillbirth (fetal loss $>$ 20 weeks gestation), or any fetal loss in carriers of the factor V Leiden mutation. They recruited patients referred to outpatient thrombosis clinics at university hospitals and identified 228 carriers (77 propositi and 151 of their relatives) and 121 noncarrier relatives as controls. All women were white. Patients were excluded if they had never been pregnant or if their only pregnancies had been ectopic or resulted in elective terminated. Among carriers, the risk for fetal loss was similar in propositi and relatives. The respective rates among carriers and non-carriers were 16.4% and 9.1% for fetal loss, OR 2.1 95% CI [1.35,3.33]; 13.5% and 7.4% for miscarriage, OR 2.08 95% CI [1.33,3.25]; and 2.9% and 1.7% for stillbirth, OR 1.60 95% CI [0.58,4.43]. The odds ratio in all categories was higher in homozygous carriers than heterozygous carriers and the difference in stillbirth was statistically significant when homozygous women were compared to controls. Interestingly 80% of the fetal losses occurred within the first 16 weeks of the study.

Comment: A similar retrospective study cited in the article (Preston FE - *Lancet* - 1996 Oct 5; 348(9032): 913-6) did not find a difference in the rate of fetal loss among 141 women with factor V Leiden and the control group, but the risk was higher with deficiencies of protein C, S, or antithrombin III. The study by Meinardi et al. adds to the evidence that a relationship exists between thrombophilia and pregnancy loss. However, the exact magnitude of the relationship is not known, nor is there any data to suggest that treatment with heparin or aspirin can alter the risk of an adverse outcome.

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