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Venous thromboembolism associated with pregnancy and hormonal therapy

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Venous thromboembolism (VTE) is a major cause of maternal morbidity and mortality during or early after pregnancy and in women taking hormonal therapy for contraception or for replacement therapy. Post-thrombotic syndrome, including leg oedema and leg pain, is an unrecognized burden after pregnancy-related VTE, which will affect more than two of five women. Women with a prior VTE, a family history of VTE, certain clinical risk factors and thrombophilia are at considerably increased risk both for pregnancy-related VTE and for VTE on hormonal therapy. This review critically assesses the epidemiology and risk factors for pregnancy-related VTE and current guidelines for prophylaxis and treatment. We also provide information on the risk of VTE related to hormonal contraception and replacement therapy.

Pregnancy-related venous thromboembolism

Epidemiology and clinical burden

Venous thromboembolism (VTE) is a major complication to pregnancy, both in the antenatal- and in the postnatal-periods, and occurs in 0.5–2.2 women per 1000 pregnancies [1–7]. Some studies have found a higher incidence of VTE either during pregnancy [1,2] or in the postnatal period [4], whereas

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other studies have found no difference between the ante- and postnatal periods [3,6,7]. The risk of VTE is increased in all three trimesters (Fig. 1), but the risk is probably highest in the last trimester and at delivery [5,7]. The risk of postnatal venous thrombosis is very high during the first three weeks postpartum (Fig. 1), then rapidly declines, but a small increased risk for VTE probably sustains beyond 6 weeks until 12 weeks postpartum [5,7].

Deep vein thrombosis (DVT) is the dominant phenotype during pregnancy, whereas pulmonary embolism (PE) occurs more often in the postpartum period [7]. During pregnancy 80–90% of the DVTs affect the left limb [7,8], which may be explained by the compressing effect of the growing uterus on the left iliac vein and the pulsatile compression of the left iliac vein by the right iliac artery [9]. Moreover, DVTs during pregnancy are most often high proximal DVTs that affect the ileofemoral veins rather than the calf veins and poplitaeal–femoral vein transition [6,7,10]. This proximal distribution of DVTs during pregnancy represents a diagnostic challenge, since symptoms, such as lower abdominal pain, pelvic girdle pain, back pain and leg oedema, are less specific for thrombosis and are common in pregnancy.

The clinical burden of pregnancy-related VTE is not well known, but is probably associated with important short-term and long-term morbidity. In developed countries, fatal PE maintains to be one of the leading causes of maternal deaths in pregnancy [11], but the number of fatal PEs has been relatively stable despite a steady decrease of maternal deaths [6]. Prevention and treatment of pregnancy-related PE is a major challenge, and two-thirds of these fatal PEs could possibly be ameliorated with proper prophylactic measures [12].

Little is known of the long-term consequences of pregnancy-related VTE. The post-thrombotic syndrome (PTS) takes months or years to develop after DVT, and is characterised by swelling and oedema, a feeling of heaviness and pain, itching and discolouration of the skin, and even skin ulcers in severe cases. In proximal DVT outside pregnancy (defined as any DVT from the poplitaeal vein and proximal) approximately 20–50% will develop some degree of PTS, 5–10% being severe [13,14]. This risk may be substantially higher for more proximal DVT affecting the upper thigh and/or the iliac veins [15]. Use of elastic compression stockings may significantly reduce the risk of PTS [16]. In a long-term follow-up of women with pregnancy-related DVT, 42% developed any degree and 7% severe PTS after 3–16 years [17], and the women with a history of pregnancy-related DVT had reduced quality of life [18]. These data suggest that pregnancy-related VTE is associated with a considerable unrecognized clinical burden, and that improved preventive measures, treatment and follow-up is necessary for optimal care of these women.

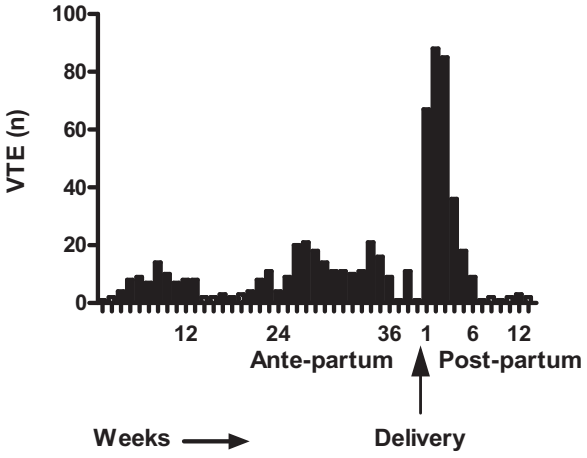

Fig. 1. The frequency of venous thromboembolism (VTE) during and early after pregnancy – from Ref. [7], with permission.