Introduction

The placenta is a unique organ with dual blood circulation, functioning throughout foetal development. Placental trophoblasts express and produce coagulation components, participating not only in haemostasis but also in placental vascular development and differentiation ***(Lanir et al., 2003)***.

For pregnancy to proceed normally, the placenta must be allowed to develop and grow appropriately so that an adequate blood supply is available to promote growth of the developing foetus. Failure of the normal uterine physiological changes to occur and development of the intra-placental pathology will ensure placental insufficiency and the features that accompany are failing placenta i.e. repeated spontanous miscarriage (RSM), intra-uterine growth retardation (IUGR), pre-term delivery, placental abruption and pregnancy-induced hypertension ***(Robertson et al., 2006)***.

Thrombotic lesions of the placenta are a common feature in women with recurrent foetal loss and adverse pregnancy outcomes. However, the aetiology of foetal loss and associated adverse conditions of pregnancy is unknown. It is believed that these are associated with abnormal placental vasculature and haemostatic disturbances leading to inadequate maternal foetal circulation ***(Vora et al., 2009)***.

Thrombophilia involves genetic and acquired conditions that increase the risk of venous thromboembolism, but are usually undiagnosed because most carriers are asymptomatic ***(Kovalevsky et al., 2004)***.

There is growing evidence that women with thrombophilia are at an increased risk of venous thrombo-embolism and severe obstetric complications ***(Dudding and Attia, 2004)***.

Repeated spontanous miscarriage (RSM) is usually defined as the loss of three or more consecutive pregnancies prior to 28 weeks of pregnancy ***(Crosignani and Rubin, 1991)*** or even 20 ***(Bricker and Farquharson, 2002)*** and within this definition is a large and heterogeneous group of patients with many different causes of miscarriage are being defined ***(Kovalevsky et al., 2004)***.

Repeated spontaneous miscarriage (RSM) affects 2–5% of the couples attempting to reproduce ***(Coulam et al., 1997)***, despite knowledge of various inherited risk factors associated with venous thromboembolism (VTE), no definite cause can be found in about 50% of patients ***(Ulander, 2007)***.

Thrombosis in decidual vessels is believed to be one such cause, leading to intrauterine growth retardation, fetal death, and possibly repeated spontaneous miscarriage ***(Carp et al., 2002)***.

Thrombophilia has been recently implicated in early pregnancy loss by impairing the initial vascularization process occurring at implantation, which is necessary for successful pregnancy ***(Azem et al., 2004 and Kujovich, 2004)***. It is well established that inherited or acquired thrombophilic factors and their combinations can lead to increased risk of thrombosis ***(Younis et al., 2000)***.

Acquired thrombophilia is associated with thrombophilic factors with no inherited characteristics, such as antiphospholipid antibodies (APA) which include anticardiolipin antibody (ACA) and lupus anticoagulant (LA), the detection of which seems to be higher in the first trimester in women who have antiphospholipid syndrome (APS) ***(Couto et al., 2005)***.

Inherited factors for thrombophilia include mutations in factor V gene, prothrombin gene and methylenetetrahydrofolate reductase (MTHFR) genes

which are risk factors for thrombosis, in addition to a higher frequency of RSM and other pregnancy complications ***(Couto et al., 2005)***.

The mutation in the factor V gene has been identified as the molecular basis for activated protein C (APC) resistance and has been named factor V Leiden. This leads to a hypercoagulable state, with clear association between recurrent spontaneous miscarriage and factor V Leiden ***(Foka et al., 2000)***.

The mutation in the prothrombin gene is associated with elevated prothrombin levels and is a risk factor for thrombosis ***(Couto et al., 2005)***.

The mutation in the MTHFR gene leads to a reduction in the activity of MTHFR enzyme ***(Lane et al., 1996)***. The reduced enzyme activity results in decreased synthesis of 5-methyltetrahydrofolate which is the primary methyl donor in the conversion of homocysteine to methionine. Plasma homocysteine concentrations is elevated and acts as a risk factor for venous and arterial thrombosis ***(Margaglione et al., 1998)*** and increased risk of stroke, myocardial infarction and peripheral arterial disease ***(De-Stefano et al., 1996)***.

Some cases of recurrent first trimester miscarriage (the loss of three or more consecutive pregnancies at less than 12 weeks' gestation) may have a thrombotic aetiology. The evidence for this comes from histological studies reporting microthrombi to be a common finding in the placental vasculature of pregnancies among women with RSM ***(Rai et al., 1996)***.