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# Coagulation status, thrombelastography and complications occurring late in pregnancy

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**Abstract**

*Introduction*: There is much interest in the relationship between coagulation status and complications of pregnancy. The thrombelastograph (TEG) has been proposed as a useful, inexpensive tool to screen for patients with hypercoagulable states.
*Materials and methods*: We investigated 588 unselected pregnant women at booking, obtaining blood samples for TEG and thrombophilia investigation. Pregnancy outcome data was recorded.
*Results*: We found significant correlations between TEG parameters and the Prothrombin time (PT) and Activated Partial Thromboplastin time (APTT) ($p<0.01$) and with plasma Antithrombin level ($p<0.01$). There was no correlation between TEG and other thrombophilic defects (protein C, protein S, Factor V Leiden mutation, Prothrombin G20210A mutation, MTHFR C677T mutation and Lupus Anticoagulant). There was a significant association of TEG parameters with mid-trimester loss (MTL) but not with other adverse pregnancy outcomes.
*Conclusions*: The correlation between TEG and PT, APTT and antithrombin level supports its value in providing a global measure of haemostasis. Coagulation status at booking is associated with increased risk of MTL but not with complications occurring later in pregnancy.


## Introduction

Those who work in obstetric haematology are presented with the major challenge of interpret-

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ing the expanding body of literature relating to thrombophilia and adverse outcomes of pregnancy, and applying this to everyday clinical practice. In 1985, Branch et al. [1] described the association between the acquired Antiphospholipid syndrome (APS) and recurrent fetal loss. Subsequently, APS has also been associated with complications occurring later in pregnancy, including preeclampsia, intrauterine growth retardation and placental abruption [2]. The relationship of heritable thrombophilia with fetal loss was then investigated in the multicentre EPCOT study of 571 women. This showed positive correlation with antithrombin, protein C and protein S deficiencies but not with Factor V Leiden mutation [3]. In contrast, a recent meta-analysis of 31 studies of thrombophilic disorders and fetal loss found significant associations with Factor V Leiden and protein S deficiency; but not with the MTHFR mutation, protein C or antithrombin deficiency [4]. Kupferminc et al. [5] reported a three- to five-fold increased incidence of inherited thrombophilia defects in patients with late pregnancy complications in a case-control study, whereas a large UK population-based study concluded that five prothrombotic genotypes (including Factor V Leiden, Prothrombin G20210A and MTHFR C677T) are not associated with the development of preeclampsia or gestational hypertension [6].

However, most of the existing evidence in this area has been derived from retrospective data and there is a real need for large prospective studies. Clearly, the aetiology of adverse complications of pregnancy is multifactorial in which the presence of a thrombophilic defect is just one factor in the dynamic fetomaternal haemostatic process. Therefore a blood test, which could reliably predict for a hypercoagulable state would be another useful tool in the management of pregnant women.

Thrombelastography is considered a global test of whole blood coagulation. It measures the viscoelastic properties of whole blood as it is induced to clot in a low shear environment resembling venous blood flow. The resulting pictorial haemostasis profile is thus a measure of both the time taken for initiation and the kinetics of clot formation, the strength of the clot and its dissolution (Fig. 1). Hypercoagulable TEG parameters have been demonstrated in normal pregnancy [7], being maximal during labour [8], and returning to baseline by around 6 weeks postpartum [9].

The aims of this study were to investigate the relationship between TEG and thrombophilic defects and to determine whether TEG could be used as a screening test to identify women at risk of late pregnancy complications.

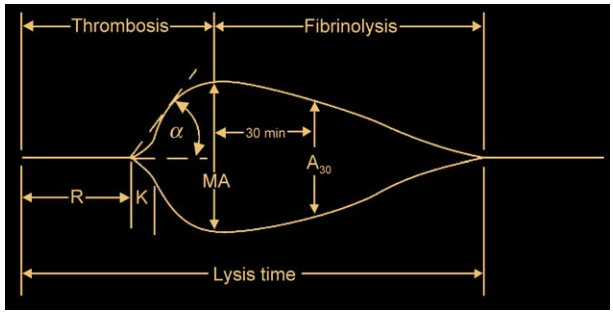


**Figure 1** The thromboelastograph trace [10]. Reaction (*R*) time is the period of time of latency from the time that the blood was placed in the TEG cup until the initial fibrin formation. *K* time is a measure of the speed to reach a certain level of clot strength (amplitude=20 mm) from the beginning of clot formation. Alpha ($\alpha$) angle measures the rapidity of fibrin build-up and cross-linking (clot strengthening). MA, or Maximum Amplitude, is a direct function of the maximum dynamic properties of fibrin and platelet bonding. MA represents the ultimate strength of the fibrin clot.

## Materials and methods

Ethical approval was granted from the local Research Ethics Committee. The unselected groups of pregnant women were recruited when attending antenatal booking clinic aiming for a total of 600 patients. Informed consent was required. A questionnaire covered personal and family history of thrombosis and obstetric complications, alcohol use, smoking, diabetes, hypertension and folic acid supplementation. Blood samples were taken for a thrombophilia screen and TEG analysis. Samples were analysed within 20 min of venepuncture in a research laboratory affiliated to a CPA-accredited laboratory participating in NEQAS. Results of all TEG analysis and thrombophilia tests were unknown to the clinician. Exclusion criteria for analysis were current multiple pregnancy, planned termination of pregnancy, fetal loss in the presence of congenital or karyotypic abnormalities or evidence of infection in the fetus or placenta. None of the recruited women were taking anticoagulants or antiplatelet agents.

### Thrombophilia tests

Sodium-citrated whole blood underwent double centrifugation at 2500 rpm (1200×*g*) for 15 min, followed by 4500 rpm (3500×*g*) for 10 min. The plasma obtained was separated and stored at −80