British Journal of Anaesthesia **109** (6): 851–63 (2012)
Advance Access publication 16 October 2012 · doi:10.1093/bja/aes361

BJA

Haemostatic monitoring during postpartum haemorrhage and implications for management

C. Solomon[1]*, R. E. Collis[2] and P. W. Collins[3]

[1] Department of Anaesthesiology and Intensive Care, Salzburger Landeskliniken SALK, 48 Müllner Hauptstrasse, 5020 Salzburg, Austria
[2] Department of Anaesthesia, University Hospital of Wales, Cardiff, UK
[3] Department of Haematology, School of Medicine, Cardiff University, Cardiff, UK

* Corresponding author. E-mail: solomon.cristina@googlemail.com

Editor's key points

- Postpartum haemorrhage (PPH) is a major cause of maternal mortality worldwide.
- Monitoring of coagulation in PPH must take account of pregnancy-induced changes in coagulation status.
- Point-of-care testing may have advantages in guiding replacement therapy.
- There is a need for specific studies of haemostatic therapies in PPH.

Summary. Postpartum haemorrhage (PPH) is a major risk factor for maternal morbidity and mortality. PPH has numerous causative factors, which makes its occurrence and severity difficult to predict. Underlying haemostatic imbalances such as consumptive and dilutional coagulopathies may develop during PPH, and can exacerbate bleeding and lead to progression to severe PPH. Monitoring coagulation status in patients with PPH may be crucial for effective haemostatic management, goal-directed therapy, and improved outcomes. However, current PPH management guidelines do not account for the altered baseline coagulation status observed in pregnant patients, and the appropriate transfusion triggers to use in PPH are unknown, due to a lack of high-quality studies specific to this area. In this review, we consider the evidence for the use of standard laboratory-based coagulation tests and point-of-care viscoelastic coagulation monitoring in PPH. Many laboratory-based tests are unsuitable for emergency use due to their long turnaround times, so have limited value for the management of PPH. Emerging evidence suggests that viscoelastic monitoring, using thrombelastography- or thromboelastometry-based tests, may be useful for rapid assessment and for guiding haemostatic therapy during PPH. However, further studies are needed to define the ranges of reference values that should be considered 'normal' in this setting. Improving awareness of the correct application and interpretation of viscoelastic coagulation monitoring techniques may be critical in realizing their emergency diagnostic potential.

Keywords: blood coagulation tests; point-of-care systems; postpartum haemorrhage; thrombelastography

Postpartum haemorrhage (PPH) is excessive blood loss after childbirth, and has been defined as blood loss >500 ml within 24 h of normal vaginal delivery, or >1000 ml after Caesarean section,[1 2] although alternative definitions have been used to describe PPH and its severity.[3–6] Although PPH typically occurs within 24 h of childbirth (primary PPH), haemorrhage may occur any time up to 12 weeks postpartum (secondary PPH). PPH is the leading cause of maternal mortality worldwide, estimated to be responsible for around 143 000 deaths each year.[7] PPH also contributes significantly to maternal morbidity and is a major reason for intensive care admission and hysterectomy in the postpartum period.[8–10]

The causes of PPH are varied, and have been classified according to their underlying pathophysiology[11] (Fig. 1). Excessive bleeding is often exacerbated by acquired coagulation abnormalities, and coagulopathies vary markedly depending on underlying aetiology. Primary coagulation defects are occasionally direct causes of PPH. Although historically categorized under 'thrombin', recent studies suggest that acquired fibrinogen deficiency, rather than thrombin generation, may be the major coagulation abnormality associated with obstetric bleeding.[12–15] Similar observations have been made during blood loss in trauma[16] and major surgery.[17]

The diversity of potential triggers makes the occurrence and severity of PPH difficult to predict. Many cases have no identifiable risk factor.[3] However, episodes of PPH with differing causes may have common pathological progression, with measurement of haemostatic impairment potentially providing important information for diagnosis and therapeutic intervention. Bleeding leads to loss and consumption of coagulation factors, which may be exacerbated by dilutional coagulopathy after volume resuscitation. Coagulation defects may be compounded by hyperfibrinolysis. Rapid correction of coagulopathies that develop during PPH may be crucial for controlling bleeding and improving outcomes. However, appropriate haemostatic intervention may depend on the availability of tests which allow rapid diagnosis of the cause of bleeding. In this review, we discuss the normal changes in clotting factors during pregnancy, the importance of coagulation failure during major PPH, tests that

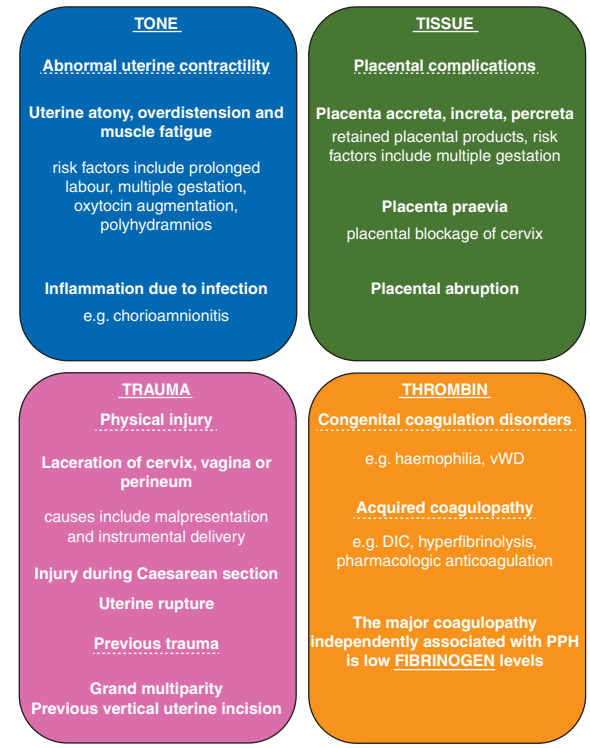

Fig 1 Major risk factors associated with PPH. Conditions are classified according to pathophysiology. DIC, disseminated intravascular coagulation; vWD, von Willebrand's disease; PPH, postpartum haemorrhage.

are available for monitoring haemostasis, and the implications of coagulation monitoring for PPH management strategies.

Methodology

We conducted a literature search for articles describing haemostasis testing/coagulation monitoring in the obstetric setting, using PubMed with the following search terms with no filters applied: [blood coagulation tests (MeSH)] and obstetric; [thrombelastography (MeSH)] and obstetric; [blood coagulation tests (MeSH)] and [peripartum period (MeSH)]; [thrombelastography (MeSH)] and [peripartum period (MeSH)]; [blood coagulation tests (MeSH)] and [postpartum hemorrhage (MeSH)]; [thrombelastography (MeSH)] and [postpartum hemorrhage (MeSH)]; [postpartum hemorrhage (MeSH)] and [Blood coagulation (MeSH)]; [postpartum hemorrhage (MeSH)] and [Blood coagulation factors (MeSH)]. In total, 674 articles were retrieved. Articles published after 1991 were screened (abstract if available, whole article if not) and retained if the use of laboratory coagulation tests, point-of-care (POC) coagulation coagulation monitoring, or measurement of individual coagulation factors/inhibitors was reported during healthy pregnancy, obstetric complication, or PPH. After screening, 121 articles remained; these formed the evidence-base for the review and included review articles, *in vitro* and *ex vivo* experimental studies, case-reports, and prospective and retrospective clinical investigations. The evidence was supplemented with reports of interest known to the authors, and with references cited within articles used in the review.

Coagulation status during pregnancy and the peripartum period

Marked changes in haemostasis are observed during pregnancy.[18] In comparison with the non-pregnant state, procoagulant levels are generally elevated (Fig. 2), but antagonists of coagulation decrease or remain unchanged. This hypercoagulable state may reduce the risk of haemorrhage during delivery and the postpartum period. In contrast, platelet counts typically decrease during pregnancy,[19] although the clinical significance of this is uncertain.[15] Haemostasis can be further influenced by anaemia and pre-eclampsia. Anaemia (haemoglobin <11 or 10.5 g dl^{-1} in second trimester)[20] affects $\sim$20% of pregnant women worldwide[21] and is associated with increased blood loss and likelihood of transfusion during delivery.[22] Similarly, pre-eclampsia, which occurs in 0.4–2.8% of births,[23] is associated with haemostatic abnormalities including thrombocytopenia and disseminated intravascular coagulopathy.[24]

Standard coagulation tests; assessment of bleeding risk in obstetric patients

The routine coagulation screen

Laboratory-based screening is used routinely to assess coagulation status in obstetric patients. The tests consist of platelet count, prothrombin time (PT), activated partial thromboplastin time (aPTT), with plasma fibrinogen levels also routinely determined in many centres.[12 15 25 26] Platelet count provides a measure of platelet concentration but not function. PT measures the extrinsic and common coagulation pathways, and is sensitive to levels of coagulation factors (F) II, V, VII, and X, whereas aPTT assesses coagulation via the intrinsic and common pathways and is sensitive to all coagulation factors except FVII and FXIII.[25 27] The aPTT is shorter in pregnancy because of the raised FVIII and so is relatively insensitive to haemostatic impairment. Both the PT and aPTT are relatively insensitive to plasma fibrinogen levels, which are typically measured indirectly using the Clauss assay.[28] In this method, fibrinogen concentration is inversely proportional to the time taken for the clot to form, and so gives a measure of functional fibrinogen (FF).

The value of routine full blood count and coagulation screening has been questioned in obstetrics[29 30] and other settings.[31 32] PT and aPTT may identify significant coagulation impairment, but they test limited parts of coagulation and do not help diagnose the underlying defect. These tests may also generate a high number of false-positive and false-negative results.[31] Pre-procedural coagulation screening is therefore not generally recommended unless a complication associated with haemostatic impairment