Asian Hematology Research Journal

Volume 7, Issue 2, Page 51-65, 2024; Article no.AHRJ.115099

Hemostatic Parameters in Women with Obstetric Hemorrhage

Jiji J S [a++*], Cicy PJ [a#] and Acka Priya Varghese [b#]

[a] Department of Pathology, Govt Medical College, Kottayam, India.
[b] Department of Obstetrics and Gynaecology, Govt Medical College, Kottayam, India.

Authors' contributions

This work was carried out in collaboration among all authors. Author JJS designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript, managed the literature searches. Authors CPJ and APV analysed of the study. All authors read and approved the final manuscript.

Article Information

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/115099

Original Research Article

Received: 27/03/2024
Accepted: 01/04/2024
Published: 13/04/2024

ABSTRACT

Aims: To find out the relationships observed in hemostatic parameters during the course of obstetric hemorrhage for an effective hemostatic management and goal directed therapy.
Study Design: Analytical, Case-Control Study.
Place and Duration of Study: Department of Obstetric and Gynaecology,Department of Pathology, Govt Medical College, Kottayam, Duration:12 months.
Methodology: We included 68 cases (18-45 yrs) with obstetric hemorrhage and 68 controls (18-45 yrs, Third trimester) without Obstetric hemorrhage.Blood collected for PT,APTT,Fibrinogen and platelet count in sodium citrate and EDTA anticoagulated samples. PT, APTT, Fibrinogen assay done by Automatic methods, platelet count done in 5 part coulter machine.
Results: The study, involving 136 participants divided into case and control groups, revealed significant differences in key haemostatic parameters. The case group exhibited elevated Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT) values, along with lower Platelet count and Fibrinogen concentration compared to the control group. Notably, Antepartum

[++] Post Graduate Student;
[#] Associate Professor;
**Corresponding author: E-mail: jijims56@gmail.com;*

Hemorrhage (APH) and Postpartum Hemorrhage (PPH) showed a substantial linear relationship with platelet levels in the case group, emphasizing the potential predictive role of platelet counts in hemorrhagic events associated with obstetric conditions.

Conclusion: study sheds light on the critical link between obstetric hemorrhage and hemostatic parameters, highlighting significant variations in prothrombin time (PT), activated partial thromboplastin time (APTT), platelet count, and fibrinogen concentration between women with and without obstetric hemorrhage. The findings underscore the complexity of managing obstetric hemorrhages and the importance of laboratory-based screening in evaluating the coagulation status of affected patients.

Keywords: Maternal hemorrhage; PT; aPTT; Fibrinogen assay; Antepartum hemorrhage; post partum hemorrhage.

1. INTRODUCTION

Obstetric haemorrhage (OBH) is widely acknowledged as a prominent factor contributing to maternal morbidity and mortality on a global scale. A significant majority of fatalities occur in countries with limited resources. Nevertheless, Major Obstetric haemorrhage (MOH) leads to profound morbidity across diverse healthcare settings, manifesting as multiorgan failure, postpartum hysterectomy, and enduring psychological trauma. These outcomes contribute substantially to extensive economic and social burdens. Severe maternal morbidity linked to haemorrhage surpasses the morbidity rates associated with other obstetric and medical conditions [16-24].

Safety bundles are crafted to offer structured, evidence-based protocols that, when implemented, consistently enhance patient outcomes. Standardized obstetric haemorrhage (OBH) bundles, aiding healthcare teams in methodically preparing for, recognizing, and responding to OBH, have shown a notable decrease in patient morbidity and mortality [8-15]. The incidence of postpartum haemorrhage (PPH) has risen in numerous countries9. Despite alterations in obstetric strategies, the rate of PPH exceeding 2500 ml in Scottish maternal morbidity reports has remained relatively constant at approximately 5.8 per 1000 from 2009 to 2012 [1-7].

Monitoring major obstetric haemorrhage at the hospital level poses a considerable operational challenge. Criteria for tracking severe morbidity, potentially encompassing haemorrhage-related incidents, involve the examination of obstetric hospitalizations of women receiving 4 or more units of red blood cells (RBCs) or necessitating admission to the intensive care unit [38-44].

However, such events are infrequent, occurring in approximately 3 out of 1,000 births [58-64,66,67].

Utilizing data from biomedical informatics, acquired through the interrogation of electronic health records (EHR), can serve as a method for characterizing and monitoring postpartum haemorrhage. Biomedical informatics, as articulated by the American Medical Informatics Association, is an interdisciplinary field dedicated to the efficient utilization of biomedical data, information, and knowledge for scientific exploration, problem resolution, and clinical decision-making, all aimed at enhancing human health [25-32].

Detailed clinical data, obtained directly from the EHR, encompass granular information such as laboratory results, details on drug and device usage, administration of blood products, recorded procedures, and various clinical particulars [53-57]. This highly detailed data is well-suited for comprehensive and multifaceted measurement of postpartum haemorrhage, enabling an in-depth assessment of clinical management and associated outcomes at both the hospital and hospital-system levels [33-37].

Postpartum hemorrhage (PPH) arises due to diverse obstetric complications, including uterine atony, placenta previa, genital tract trauma, or abruption. It is more frequently observed in conjunction with instrumental delivery, induced labor, and cesarean delivery [45-51].

The most recent obstetric management guideline in the UK prioritizes surgical intervention with an early return to the operating theatre and a systematic approach to using uterotonics when uterine atony is identified as a cause of PPH. The guideline underscores the importance of

early cross-matching of blood, collaboration with hematology services, and suggests maintaining a hemoglobin level of about 8 g/dL through red blood cell (RBC) transfusions. It recommends using fresh frozen plasma (FFP) to keep the prothrombin time (PT) and activated partial thromboplastin time (aPTT) within 1.5 times the normal range, with fibrinogen levels above 1 g/L and platelet count above 50 × 10^9/L. These recommendations align with transfusion policies for routine coagulation tests and fibrinogen levels in the non-pregnant population. Research endeavors are essential to establish the appropriate reference values in this context. Enhancing awareness of the accurate application and interpretation of coagulation monitoring is crucial for effective emergency diagnostics [75-82].

1.1 Review of Literature

Pregnancy is linked to alterations in hemostasis, characterized by an elevation in most clotting factors, a decrease in the levels of natural anticoagulants, and a reduction in fibrinolytic activity. During a normal pregnancy, the platelet count experiences a decrease, potentially attributed to heightened destruction and hemodilution, with the most significant reduction observed in the third trimester [68-74].

With the increase in most coagulation factors during normal pregnancy, the prothrombin time (PT) and activated partial thromboplastin time (APTT) may exhibit a shortened duration. The PT, along with its derived measurement, the international normalized ratio (INR), assesses factors such as coagulation factors II, V, VII, X, and fibrinogen. Meanwhile, the APTT serves as a reliable screening test for deficiencies in coagulation factors VIII, IX, XI, and XII. Laboratory-based screening, including platelet count, PT, APTT, D-Dimer, and plasma fibrinogen levels, is routinely employed to evaluate the coagulation status in obstetric patients. The platelet count offers a measurement of platelet concentration, focusing on quantity rather than function. Prothrombin time (PT) gauges the extrinsic and common coagulation pathways, responding to the levels of coagulation factors II, V, VII, and X. On the other hand, activated partial thromboplastin time (APTT) evaluates coagulation through the intrinsic and common pathways, being sensitive to all coagulation factors except for FVII and FXIII [95-102].

1.2 Hemostatic Changes in Normal Pregnancy

A typical pregnancy is characterized by significant alterations in various aspects of hemostasis. These changes collectively contribute to sustaining placental function throughout pregnancy and preventing excessive bleeding during delivery. The majority of shifts in blood coagulation and fibrinolysis result in a heightened state of coagulability. This phenomenon serves as a protective mechanism, shielding the woman from hemorrhage during delivery. However, it also renders her susceptible to thromboembolism, both during pregnancy and in the postpartum period. The alterations in the coagulation system observed in a typical pregnancy align with an ongoing low-grade process of intravascular coagulation [83-90].

a. Platelets: “Thrombocytopenia is a prevalent haemostatic abnormality in pregnancy, affecting approximately 10% of healthy women in late pregnancy. This condition is, at least in part, attributed to haemodilution. However, the rise in mean platelet volume indicates a compensated state involving progressive platelet destruction. Further evidence of in vivo platelet activation during late pregnancy is evident through the increased concentrations of β-thromboglobulin and thromboxane A2 derivatives” [107].

b. Coagulation system: Throughout pregnancy, there is a substantial increase in the concentrations of coagulation factors VII, VIII, IX, X, XII, and von Willebrand factor, along with a notable rise in plasma fibrinogen concentration. In late pregnancy, plasma fibrinogen levels often exceed 600 mg/dL. Factor VII may experience up to a tenfold increase during pregnancy. Von Willebrand factor and factor VIII are elevated in late pregnancy, resulting in approximately double the coagulation activity observed in the non-pregnant state. Conversely, factor IX undergoes a small increase, while factor XI experiences a minor decrease. After an initial rise, factor XIII gradually decreases, reaching 50% of the normal non-pregnant value at term. Factors II and V, however, do not exhibit significant changes during pregnancy [91-94].

“Controversial findings have been reported regarding changes in antithrombin (AT) during pregnancy, but AT often remains within the normal range. Protein C activity seems unaffected by gestation, while protein C antigen levels tend to increase in the second trimester,

staying within the normal non-pregnant range. Neutrophil activation triggers endothelial thrombomodulin (TM) proteolysis, increasing TM plasma levels in the third trimester. Some studies report a continuous increase in TM levels during pregnancy, rapidly decreasing post-partum. The physiological decrease in free protein S levels during pregnancy raises questions about its contribution to the hypercoagulable state and increased thromboembolism risk [103-106]. Total protein S progressively decreases during gestation, with values going below the normal range early on. The decline in protein S during the first weeks of pregnancy doesnot allow for a diagnosis of inherited protein S deficiency. Attempts to establish normal protein S levels during pregnancy are not recommended. Heparin cofactor II, another natural coagulation inhibitor, has been reported to increase in plasma during physiological pregnancy" [107].

"Protein Z, a vitamin-K-dependent plasma glycoprotein, acts as a cofactor to a plasma proteinase inhibitor, inhibiting the activation of factor X. Deficiency in Protein Z has been reported in women experiencing unexplained early fetal losses, and the presence of antibodies to protein Z can contribute to adverse pregnancy outcomes. Recent data indicate a gradual rise in protein Z levels with gestational age in normal pregnancies, returning to normal levels approximately 6 to 12 weeks postpartum. This normal increase in protein Z during pregnancy may counterbalance the rise in clotting factors, offering protection against thrombosis in pregnant women. During pregnancy, there is a reduction in activated protein C (APC) sensitivity. At term, approximately 45% of pregnant women exhibit an APC sensitivity ratio below the 5th percentile of the normal range for non-pregnant women of similar age. The decrease in APC ratio is directly correlated to its value in the non-pregnant state, with the most pronounced effect observed in women with the highest APC ratio. Around 50% of healthy women develop APC resistance, reaching its lowest point in the second trimester of pregnancy, with minimal subsequent change" [107].

c. Fibrinolysis: Fibrinolytic activity in plasma is diminished during pregnancy, remaining low throughout labor and delivery, and returning to normal shortly after placental delivery. The activity of tissue plasminogen activator (t-PA) decreases during pregnancy, attributed not only to the gradual rise in plasminogen activator inhibitor-1 (PAI-1) but also to increasing levels of plasminogen activator inhibitor-2 (PAI-2). PAI-1 values increase during pregnancy and return to normal levels approximately 5 weeks post-partum.

"Plasminogen activator inhibitor-2 (PAI-2) typically becomes detectable in plasma only in pregnant individuals. Its source, villous cells, suggests that changes in placental tissue quantity may influence plasma levels, establishing a positive correlation between PAI-2 concentrations and placental weights. PAI-2 concentrations vary with birth weights, indicating a dependency on both the quantity and quality of placental tissues and fetal growth. Despite elevated levels of PAI-1 and PAI-2, a highly significant positive correlation has been noted between gestational age and D-dimer concentration. This increase in D-dimer complicates its use in excluding venous thromboembolism in pregnant patients with clinical suspicion. Efforts have been made to establish specific ranges of D-dimer levels in pregnancy" [107].

d. Changes in the postpartum after delivery:

The surge in clotting activity during delivery is likely linked to the expulsion of the placenta and the release of thromboplastic substances at the separation site. Hemostatic changes during the puerperium mirror those observed after extensive surgery [65,52]. The mean platelet count slightly decreases at placental delivery and begins to rise on days 2–5 postpartum. In high-risk patients requiring postpartum thromboprophylaxis, consideration should be given to the reactive thrombocytosis postpartum following operative delivery.

Plasma antithrombin (AT) levels significantly increase for at least 2 weeks postpartum after normal delivery. Protein C levels rise immediately after delivery and remain elevated 3 days postpartum. Total and free protein S levels notably increase after delivery, with total protein S normalizing in the first week postpartum, while free protein S may not normalize until 5 weeks postpartum. Approximately 15% of women still have levels below the reference range for non-pregnant women at 8 weeks postpartum. The prolonged time for free protein S to reach non-pregnant values should be considered when evaluating thrombotic risk.

Both thrombin-antithrombin complex (TAT) and prothrombin fragment 1+2 levels increase during

and immediately after delivery. Three weeks post-delivery, blood coagulation and fibrinolysis generally normalize. Compensated, accelerated intravascular coagulation appears necessary for maintaining the uterine placental interface and preparing for the hemostatic challenge of delivery.

The peak in clotting and platelet activity occurs immediately after placental delivery, while the peak of fibrinolytic activity is observed during the first 3 hours postpartum, reflected by an increase in d-dimer levels.

2. MATERIAL AND METHODS

2.1 Hypothesis Statement

It can be hypothesized that there is significant effect of obstetric hemorrhage on the hemostatic parameters.

2.2 Type of Study

Analytical, Case- Control study

2.3 Period of Study

12 months.

2.4 Study Setting

Department of Pathology (Hematology division), Govt. Medical College, Kottayam

2.5 Sample Size

P0= Proportion of controls
P1=Proportion of cases
q = 1-p
= 1.96= Value of the standard normal distribution corresponding to a significance level of α(1.96 for a 2 sided test at the 0.05 level)
= 0.84= Value of the standard normal distribution corresponding to the desired level of power(0.84 for a power of 80 %)
n =68
(Considering equal number of cases and controls, r =1)

2.6 Sampling Method

Judgemental / Purposive sampling.

2.7 Inclusion Criteria

All women in the age group of 18-45yrs (primigravida and multigravida) with obstetric hemorrhage reported in Dept. of Obstetrics & Gynaecology, Govt. Medical College Kottayam.

2.8 Exclusion Criteria

- Pregnant women with known coagulopathies
- Pregnant women already on hemostatic or antiplatelet therapy.
- Pregnant women with fibroid uterus/ adenomyosis/inflammatory diseases
- Women with congenital hypofibrinogenemia
- Pregnant women with Gestational hypertension

2.9 Limitations Expected

Sample size may not be attained

2.10 Personnel Responsible for Data Collection

Dr. JIJI J S

2.11 Personnel Responsible for Data Analysis

Dr. JIJI J S

2.12 Funding Agency

Nil.

2.13 Study Tools

1. Consent form
2. Equipment for blood collection, centrifugation
3. Anticoagulation bottles for sample collection
4. Coagulometer
5. Reagents for coagulation tests
6. Detailed proforma in each case

2.14 Study Procedure

After identifying the study population based on the inclusion and exclusion criteria and getting informed written consent, relevant blood investigation pertaining the hemostatic parameters is performed including PT, APTT, Platelet count and then more specific fibrinogen concentration is done.

Blood collection for PT, APTT and Fibrinogen concentration done by direct venipuncture in 3.2% buffered sodium citrate in a ration 9:1(9 part of whole blood and one part of anticoagulant)

For platelet count blood is collected in EDTA tube.

Total 6 ml of blood is needed from one particular case/control. PT, APTT and fibrinogen concentration done by automatic method. Platelet count is done by 5 part/3 part coulter machine

For PT, APTT and fibrinogen concentration a period of 1-2 Hrs is advocated to keep the sample in refrigerator at 4 degree celcius without error in the value and the blood for platelet count can store upto 4 hrs in refrigerator.

Data entry, documentation and significance change observed in maternal hemorrhage is analyses.

2.15 Quality Assurance

1. The blood sample would be collected under strict aseptic precaution and processed and stored
2. The equipment used for the study would be of standard quality
3. Reading would be obtained as per standardized

2.16 Data Management and Analysis

The data will be entered in Microsoft excel and further statistical analysis will be done using SPSS software. Chi -square test formula would

3. RESULTS AND DISCUSSION

The collected data was analysed using IBM SPSS software ver.20

NOTE:

- **Kolmogorov-Smirnov test** was used to determine the normality of the data.
- Continuous variables are expressed in terms of **Mean, standard deviation (SD).**
- Categorical variables are expressed in **frequency (n) and percentage (%)**
- **Chi-square or Fisher's exact test** was used to assess the significance between categorical variables.
- **Independent t test** was used to compare between two variables.
- **Pearson correlation test** was used to assess linear relationship between obstetric haemorrhage and haemostatic parameters like PT, APTT, Platelet count and fibrinogen concentration.
- **P < 0.05** was considered as statistically significant*
- **There are two groups in this study,**

  a. Case: Women in the age group 18-45yrs with obstetric haemorrhage
  b. Control: Women in the age group 18-45yrs in their third trimester without obstetric haemorrhage

- There are totally 136 samples in this study (68 in each group).

Interpretation: There are two groups in this study. Case group and control group having 68 participants in each group. Totally there are 136 samples in the study.

Interpretation: Four haemostatic parameters were considered in this study like PT, APTT, Platelet count and Fibrinogen concentration. The mean PT in case group is 14.04 + 0.86 seconds, and in control group it is 12.3 + 0.44 seconds. t(df) = 14.90 (134). There was statistically significant difference between two groups ($p < 0.05$), with mean value higher in case group.

Table 1. Distribution of study participants according to the study group

Group	Frequency (n)	Percent (%)
CASES	68	50.0
CONTROL	68	50.0
Total	136	100.0

Table 2. Mean age distribution

Group	Mean	SD	t	p-value
CASE (n=68)	29.88	4.49	3.2	0.002*
CONTROL (n=68)	27.24	5.13	3.2	

**p is significant at <0.05*
SD = Standard deviation

Table 3. Comparison of haemostatic parameters between two groups

Haemostatic parameter	CASE (n=68)	CONTROL (n=68)	t	p-value
PT (seconds)	14.04 + 0.86	12.3 + 0.44	14.90	< 0.0001*
APTT (seconds)	37.6 + 1.68	29.87 + 2.96	18.67	< 0.0001*
Platelet count (10^9/L)	1.32 + 0.28	2.49 + 0.64	-13.87	< 0.0001*
Fibrinogen concentration (g/dl)	1.36 + 0.44	3.71 + 0.65	-24.65	< 0.0001*

PT – Prothrombin Time, APTT - Activated Partial Thromboplastin Time
**P is significant at < 0.001*

Table 4. Pearson correlation test between hemostatic parameters and obstetric hemorrhage in case group

Variables	r-coefficient	p-value
APH and PT	-0.033	0.789
APH and APTT	-0.081	0.511
APH and Platelet count	-0.285	0.018*
APH and fibrinogen concentration	0.231	0.056
PPH and PT	0.033	0.789
PPH and APTT	0.081	0.511
PPH and Platelet count	0.285	0.018*
PPH and fibrinogen concentration	-0.231	0.056

**P is significant at < 0.05*

The mean APTT in case group is 37.6 + 1.68 seconds, and in control group it is 29.87 +2.96 seconds. t(df) = 18.67 (134). There was statistically significant difference between two groups ($p < 0.05$), with mean value higher in case group.

The mean Platelet count in case group is 1.32 + 0.28 (10^9/L), and in control group it is 2.49 + 0.64 (10^9/L). t(df) = -13.87 (134). There was statistically significant difference between two groups ($p < 0.05$), with mean value lower in case group.

The mean fibrinogen concentration in case group is 1.36 + 0.44 g/dl, and in control group it is 3.71 + 0.65 g/dl. t(df) = -24.65 (134). There was statistically significant difference between two groups ($p < 0.05$), with mean value lower in case group.

Interpretation: There is significant linear relationship between APH and PPH with platelet levels. There was no significant correlation between other haemostatic parameters and APH, PPH. There found to be negative correlation between APH and platelet count and positive correlation between PPH and platelet count.

4. DISCUSSION

Maternal hemorrhage poses a significant threat to maternal health globally, particularly in developing nations, contributing to high rates of mortality and morbidity. Effectively managing obstetric hemorrhages is a complex task, and addressing this challenge requires laboratory-based screening methods to evaluate the coagulation status of obstetric patients. To explore the connection between obstetric hemorrhage and hemostatic parameters, such as platelet count, prothrombin time (PT), activated partial thromboplastin time (APTT), and plasma fibrinogen levels, this study was undertaken.

In this study comprising a total of 136 participants divided into case and control groups (each with 68 participants), significant differences were observed in four key haemostatic parameters. The case group exhibited higher mean values in ProthrombinTime (PT), Activated Partial Thromboplastin Time (APTT), and lower mean values in Platelet count and Fibrinogen

concentration compared to the control group, with p-values < 0.05 for all parameters. Notably, PT was 14.04 ± 0.86 seconds in the case group, significantly higher than the control group's mean of 12.3 ± 0.44 seconds. APTT in the case group was 37.6 ± 1.68 seconds, while it was 29.87 ± 2.96 seconds in the control group. Platelet count was markedly lower in the case group (1.32 ± 0.28 x 10^9/L) compared to the control group (2.49 ± 0.64 x 10^9/L), and Fibrinogen concentration was 1.36 ± 0.44 g/dl in the case group, significantly lower than the control group's mean of 3.71 ± 0.65 g/dl. Among the case group, 32.4% experienced Antepartum Hemorrhage (APH), and 67.6% had Postpartum Hemorrhage (PPH). Importantly, a significant linear relationship was found between APH and PPH with platelet levels, while no significant correlations were observed between other haemostatic parameters and APH or PPH. These findings underscore the distinct haemostatic profile associated with obstetric conditions, particularly emphasizing the potential role of platelet levels in predicting and understanding hemorrhagic events.

In a study by Erhabor O et al. [94], The study aimed to explore the impact of obstetric hemorrhage on prothrombin time (PT), activated partial thromboplastin time (APTT), and platelet count (PLC) in pregnant women. The participants included 86 pregnant women with a history of obstetric hemorrhage (divided into antepartum hemorrhage (APH) and postpartum hemorrhage (PPH) subgroups) and 43 age-matched nonhemorrhaging pregnant women as controls. Manual methods and commercially prepared Diagen reagent kits were used for PT and APTT determination, while PLC was assessed using a hemocytometer. Results showed significantly elevated PT and APTT values in both APH (20.7 ± 4.226 seconds and 46.04 ± 8.689 seconds) and PPH (23.17 ± 2.708 seconds and 53.78 ± 4.089 seconds) groups compared to normal pregnant women (15.85 ± 0.8930 seconds and 36.225 ± 5.010 seconds). PLC was significantly lower in APH and PPH groups (154.83 ± 47.019 × 10^9 and 136.43 ± 43.894 × 10^9, respectively) compared to normal pregnant women (291.425 ± 75.980 × 10^9).

Women with PPH had significantly higher PT and APTT values than those with APH (23.17 ± 2.708 seconds and 53.78 ± 4.089 seconds versus 20.7 ± 4.226 seconds and 46.04 ± 8.689 seconds, respectively). PLC was higher in APH compared to PPH (P = 0.01). Higher PT and APTT values were observed in the third trimester for women with APH, PPH, and controls, while PLC was significantly lower in the third trimester for all groups. Correlation analysis revealed positive associations between PT and APTT values with trimester (r = 0.52 and 0.65, respectively; P = 0.01) and negative correlations between PLC and trimester for APH, PPH, and controls (r = −0.36, −0.54, and −0.28, respectively; P = 0.05). Overall, the findings highlight altered coagulation parameters in obstetric hemorrhage, with variations between APH and PPH, trimester-dependent changes, and correlations between hemostatic parameters and pregnancy trimesters.

Our study revealed a significant elevation in prothrombin time (PT) and activated partial thromboplastin time (APTT) values among women experiencing obstetric hemorrhage, including both antepartum hemorrhage (APH) and postpartum hemorrhage (PPH), when compared to nonhemorrhaging pregnant women. These findings underscore the importance of monitoring PT and APTT as essential parameters in the management of coagulopathy associated with obstetric hemorrhage. The observed increases in PT and APTT values suggest potential disruptions in the coagulation process, emphasizing the clinical relevance of these parameters for assessing and addressing coagulation disorders in the context of obstetric complications.

Prothrombin Time (PT) evaluates the extrinsic and common coagulation pathways, primarily influenced by vitamin K-dependent factors (II, V, VII, and X). Activated Partial Thromboplastin Time (APTT) assesses the intrinsic and common coagulation pathways, sensitive to most coagulation factors except FVII and FXIII. Both PT and APTT are deemed valuable in monitoring hemostasis during obstetric hemorrhage. In a recent UK study of 18,501 deliveries, 456 cases with blood loss exceeding 1500 mL were examined. PT did not exhibit a clear correlation with the volume of hemorrhage, while APTT showed a weak correlation.

Contrary to earlier studies suggesting limited utility in predicting progression of postpartum hemorrhage (PPH), a retrospective multicenter validation study indicated that an International Normalized Ratio (INR) exceeding 1.5 might predict the necessity for advanced interventions to control obstetric hemorrhage. Current guidelines recommend using an INR greater than

1.5 as an indicator for fresh-frozen plasma (FFP) transfusion, highlighting the potential clinical significance of coagulation monitoring in guiding interventions during obstetric hemorrhage.

The current study noted a noteworthy decrease in platelet count among women experiencing obstetric hemorrhage in comparison to nonhemorrhaging pregnant women. This finding aligns with previous research, indicating that, at the time of diagnosing hemorrhage, obstetric patients with bleeding complications exhibited significantly lower platelet counts compared to healthy parturient women. Moreover, earlier studies have suggested a potential association between decreasing platelet count during obstetric bleeding and the progression to severe hemorrhage. These consistent observations underscore the clinical relevance of monitoring platelet counts as an essential parameter in assessing and managing obstetric hemorrhage, emphasizing its potential role as an indicator of the severity and progression of hemorrhagic events.

In a retrospective analysis encompassing 797 pregnancies, a low platelet count emerged as an independent risk factor for obstetric hemorrhage. Notably, a platelet count below 100 × 10^9 per liter upon admission to the labor ward was associated with an increased incidence of obstetric hemorrhage in certain women. Prior research findings also suggest that platelet transfusion or the use of desmopressin may serve as valid hemostatic therapies for managing obstetric hemorrhage. Current guidelines recommend platelet transfusion when the platelet count falls below 50 × 10^9 per liter in hemorrhaging parturient women. These observations underscore the clinical significance of platelet count assessment in identifying and managing obstetric hemorrhage, providing valuable insights into potential interventions for maintaining hemostasis in affected individuals.

Obstetricians in developing countries face significant challenges in effectively managing obstetric hemorrhage. Key issues include the lack of routine access to laboratory-based screening for assessing coagulation status, especially in rural settings, and the unavailability of safe and sufficient blood and blood products needed for effective hemorrhage management, particularly in African settings. Timely access to the appropriate quantity and quality of blood and blood products is crucial for saving lives across various clinical conditions. The primary goals of blood volume replacement following obstetric hemorrhage involve rapidly and effectively restoring adequate blood volume to prevent hypovolemic shock, facilitating proper hemostasis, maintaining oxygen-carrying capacity and blood biochemistry, correcting coagulopathy promptly, optimizing resuscitation efforts, and ultimately reducing potentially preventable deaths. These objectives emphasize the critical role of timely and appropriate blood volume replacement in the comprehensive and life-saving management of obstetric hemorrhage, especially in resource-limited settings.

Evidence-based, non-blood-product-related measures for controlling hemorrhage include direct pressure/tourniquet application, appropriate stabilization of fractures, and surgical interventions such as damage control surgery, interventional radiology, and the use of endoscopic and obstetric techniques. Blood-sparing measures, such as intraoperative blood salvage (autologous blood salvage), involving the recovery and re-infusion of blood lost during surgery, are indicated in various obstetric and surgical procedures. Hemostatic drugs like vitamin K, tranexamic acid, and prothrombin complex concentrate (PCC) contribute to achieving hemostasis. PCC, containing clotting factors II, VII, IX, X, protein S, and protein C, undergoes viral inactivation through pasteurization and nanofiltration. Novo 7, a vitamin-K-dependent recombinant human coagulation Factor VIIa (rFVIIa), promotes hemostasis by activating the extrinsic pathway of the coagulation cascade. It plays a vital role in the clinical management of hemorrhage, particularly when other measures like blood products and alternative pharmacologic options prove ineffective. These evidenced-based hemostatic treatments can significantly contribute to managing coagulopathy associated with obstetric hemorrhage, potentially reducing the reliance on blood products. While these hemorrhage control measures are universally available in developed countries, women in developing nations lack access to these life-saving therapies. This disparity underscores the need for improved accessibility to advanced medical interventions in resource-limited settings to enhance maternal healthcare outcomes.

5. CONCLUSION

In conclusion, this study sheds light on the critical link between obstetric hemorrhage and hemostatic parameters, highlighting significant

variations in prothrombin time (PT), activated partial thromboplastin time (APTT), platelet count, and fibrinogen concentration between women with and without obstetric hemorrhage. The findings underscore the complexity of managing obstetric hemorrhages and the importance of laboratory-based screening in evaluating the coagulation status of affected patients.

The distinct hemostatic profile observed in the case group, characterized by elevated PT and APTT values and lower platelet count and fibrinogen concentration, emphasizes the potential utility of these parameters in assessing and addressing coagulation disorders associated with obstetric complications. Particularly noteworthy is the significant linear relationship found between antepartum hemorrhage (APH) and postpartum hemorrhage (PPH) with platelet levels, indicating a potential predictive role for platelet counts in understanding and managing hemorrhagic events in obstetric patients.

These findings contribute valuable insights to the field, emphasizing the need for comprehensive hemostatic assessments and tailored interventions in obstetric hemorrhage cases. As maternal hemorrhage remains a significant global health challenge, this study underscores the importance of ongoing research and the development of targeted strategies to improve outcomes for women experiencing obstetric complications, especially in resource-constrained settings.

CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images.

ETHICAL APPROVAL

Ethical approval (IRB No: 89/2022) has been taken by the author to carried out the study.

ACKNOWLEDGEMENTS

I owe my Gratitude to all those people who have made this Dissertation possible and because of whom my Post Graduate experience has been one that I will always cherish.

I express my sincere and heartfelt Gratitude to Dr.Sankar.S ,The Principal, Govt. Medical College, Kottayam for his valuable guidance, motivation and help during this study and through out my course.

I express my heartfelt thanks and gratitude to my guide Dr.CICY.P.J, Associate Professor, Dept. of Pathology,Govt. Medical College, Kottayam who gave me the freedom to explore on my own and at the same time the guidance to recover when my steps faltered. Her patience, support and constant encouragement helped me to finish this dissertation.

I express my sincere my gratitude to Dr.Acka Priya Varghese, Associate Professor, Dept. of Obstetrics and Gynecology,Govt. Medical College, Kottayam who gave me valuable suggestions and guidance during all phases of my Thesis work.

I am thankful to all my teachers in the Dept. of Pathology, as well as my fellow Post Graduate Students and my friends for their whole hearted co-operation, help and encouragement.

I am also thankful to all the Laboratory and Non-Teaching staff for their sincere help and support.

This dissertation would not have been possible without the unconditional love and patience of my family. I also wish to thank all the patients who were part of the study.

Above all, I thank God, ALMIGHTY under whose divine guidance I have been able complete endeavor.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. GBD 2015. Maternal mortality collaborators. Global, regional, and national levels of maternal mortality, 1990e2015: A systematic analysis for the global burden of disease study 2015. Lancet. 2016;388:1775e812.
2. WHO. WHO recommendations uterotonics for the prevention of postpartum haemorrhage; 2018.
Available:https://apps.who.int/iris/bitstream/handle/10665/277276/978 9241550420-eng.pdf?ua¼1
(Accessed 22 November)

3. Sheldon WR, Blum J, Vogel JP, et al. Postpartum haemorrhage management, risks, and maternal outcomes: Findings from the world health organization multicountry survey on maternal and newborn health. BJOG. 2014;121:5e13.
4. Callaghan WM, Creanga AA, Kuklina EV Severe maternal morbidity among delivery and postpartum hospitalizations in the United States. Obstet Gynecol. 2012;120:1029–36.
5. Grobman WA, Bailit JL, Rice MM, Wapner RJ, Reddy UM, Varner MW, et al. Frequency of and factors associated with severe maternal morbidity. Obstet Gynecol. 2014;123:804–10.
6. Resar, R., Grifn, FA., Haraden C, Nolan TW. Using care bundles to improve health care quality. IHI innovation series white paper. Institute for Healthcare Improvement, Cambridge, MA; 2012.
7. Bingham D, Lyndon A, Lagrew D, Main E. A statewide obstetric hemorrhage quality improvement initiative. MCN American Journal of Maternal Child Nursing. 2011; 36(5):297–304.
8. Shields LE, Wiesner S, Fulton J, Pelletreau B. Comprehensive maternal hemorrhage protocols reduce the use of blood products and improve patient safety. American Journal of Obstetrics and Gynecology. 2015;212(3):272–280.
9. Kramer MS, Berg C, Abenhaim H, et al. Incidence, risk factors, and temporal trends in severe postpartum hemorrhage. American Journal of Obstetrics and Gynecology. 2013;209:e1–7.
10. Lutomski JE, Byrne BM, Devane D, Greene RA. Increasing trends in atonic postpartum haemorrhage in Ireland: An 11-year population-based cohort study. British Journal of Obstetrics and Gynaecology. 2012;119:306–14.
11. Mehrabadi A, Hutcheon JA, Lee L, Kramer MS, Liston RM, Joseph KS. Epidemiological investigation of a temporal increase in atonic postpartum haemorrhage: A population based retrospective cohort study. British Journal of Obstetrics and Gynaecology. 2013;120:853–62.
12. Main EK, Goffman D, Scavone BM, Low LK, Bingham D, Fontaine PL, et al. National partnership for maternal safety: consensus bundle on obstetric hemorrhage. Anesth Analg. 2015;121: 142–8.
13. Callaghan WM, Grobman WA, Kilpatrick SJ, Main EK, D'Alton M. Facility-based identification of women with severe maternal morbidity: It is time to start. Obstet Gynecol. 2014;123:978–81.
14. Kulikowski CA, Shortliffe EH, Currie LM, Elkin PL, Hunter LE, Johnson TR, et al. AMIA Board white paper: definition of biomedical informatics and specification of core competencies for graduate education in the discipline. J Am Med Inform Assoc. 2012;19:931–8.
15. Goffman D, Friedman AM, Sheen JJ, Kessler A, Vawdrey D, Green R, D'Alton ME, Oberhardt M. A framework for improving characterization of obstetric hemorrhage using informatics data. Obstetrics and Gynecology. 2019 Dec 1;134(6):1317-25.
16. Waterstone M, Bewley S, Wolfe C. Incidence and predictors of severe obstetric morbidity: Case-control study. BMJ. 2005;322:1089–93.
17. Royal College of Obstetricians and Gynaecologist Green top 52. Postpartum haemorrhage, prevention and management.
Available: http://www.rcog.org.uk/womens-health/clinical-guidance/prevention and-management-postpartum-haemorrhage-green-top-52, 2009 [accessed 19.11.23]
18. Reyal F, Sibony O, Oury JF, et al. Criteria for transfusion in severe postpartum hemorrhage: Analysis of practice and risk factors. Eur J Obstet Gynaecol Reprod Biol. 2004;112:61–4.
19. Reyal F, Sibony O, Oury JF, et al. Criteria for transfusion in severe postpartum hemorrhage: Analysis of practice and risk factors. Eur J Obstet Gynaecol Reprod Biol. 2004;112:61–4.
20. British Committee for Standards, Stainsby D, MacLennan S, Thomas D, Issac J, Hamilton PJ. Guidelines on the management of massive blood loss. Br J Haematol. 2006;135:634–41.
21. Association of Anaesthetists of Great Britain and Ireland. Blood Transfusion and the anaesthetist. Blood component therapy. London AAGBI; 2005.
22. Bremme KA. Haemostatic changes in pregnancy. Best Pract Res Clin Haematol. 2003;16(2):153–168.
23. O'Riordan MN, Higgins JR. Haemostasis in normal and abnormal pregnancy. Best Pract Res Clin Obstet Gynaecol. 2003; 17(3):385–396.

24. McCrae KR. Thrombocytopenia in pregnancy: Differential diagnosis, pathogenesis and management. Blood Rev. 2003;17(1):7–14.
25. Boehlen F, Hohlfeld P, Extermann P, Perneger TV, de Moerloose P. Platelet count at term pregnancy : Are appraisal of the threshold. Obstet Gynecol. 2000; 95(1):29–33.
26. Orlikowski CE, Rocke DA. Coagulation monitoring in the obstetric patient. Int Anesthesiol Clin. 1994;32(2):173–191.
27. Wong CA, Liu S, Glassenberg R. Comparison of thrombelastography with common coagulation tests in preeclamptic and healthy parturients. Reg Anesth. 1995;20(6):521–527.
28. Kozek-Langenecker SA. Perioperative coagulation monitoring. Best Pract Res Clin Anaesthesiol. 2010;24(1):27–40.
29. Stirling Y, Woolf L, North WR, Seghatchian MJ, Meade TW. Haemostasis in normal pregnancy. Thromb Haemost. 1984;52:176-82.
30. Bonnar J. Haemostasis and coagulation disorders in pregnancy. In: Bloom AL, Thomas DP, editors. Haemostasis and Thrombosis, Churchill Livingstone, Edinburgh. 1987;570-84.
31. Gerbasi FR, Bottoms S, Farag A, Mammen E. Increased intravascular coagulation associated with pregnancy. Obstet Gynecol. 1990;75:385–9.
32. Wallenburg HC, Van Kessel PH. Platelet lifespan in normal pregnancy as determined by a non-radio-isotopic technique. Br J Obstet Gynaecol. 1978;85:33-6.
33. Douglas JT, Shah M, Lowe GD, Belch JJ, Forbes CD, Prentice CR. Plasma fibrinopeptide A and β-thromboglobulinin pre-eclampsia and pregnancy hypertension. ThrombHaemost. 1982;47: 54-5.
34. Fitzgerald DJ, Mayo G, Catella F, Entman SS, FitzGerald GA. Increased thromboxane biosynthesis in normal pregnancy is mainly derived from platelets. Am J Obstet Gynecol. 1987;157:325-30.
35. Letsky EA. Coagulation problems during pregnancy. Churchill Livingstone, Edinburgh; 1985.
36. Greer IA, Haemostasis and thrombosis in pregnancy. In: Bloom AL, Forbes CD, Thomas DP, Tuddenham EGD, Editors. Haemostasis and Thrombosis (3rd ed.), Churchill Livingstone, Edinburgh. 1994;987–1015.
37. Francalanci I, Comeglio P, Liotta AA, Cellai AP, Fedi S, Parretti E, et al. D-dimer concentrations during normal pregnancy, as measured by ELISA. Thromb Res. 1995;78:399-405.
38. Beller FK, Ebert C. The coagulation andfibrinolyticenzyme systems in normal pregnancy and the puerperium. EurJ Obstet Gynecol Reprod Biol. 1982;13: 177-97.
39. Hellgren M, Blomback M. Studies on blood coagulation and fibrinolysis in pregnancy, during delivery and in the puerperium. Gynecol Obstet Invest. 1981;12:141-54.
40. Persson BL, Stenberg P, Holmberg L, Astedt B. Transamidating enzymes in maternal plasma and placenta in human pregnancies complicated by intrauterin growth retardation. J Dev Physiol. 1980;2:37-46.
41. Bremme K, Ostlund E, Almqvist I, Heinonen K, Blomback M. Enhanced thrombin generation and fibrinolytic activity in the normal pregnancy and the puerperium. ObstetGynecol. 1992;80:132–7.
42. Clark P, Brennand J, Conkie JA, McCall F, Greer IA, Walker ID. Activated protein C sensitivity. Protein C, protein S and coagulation in normal pregnancy. Thromb Haemost. 1998;79:1166-70.
43. Gonzales R, Alberca J, VicenteV. Protein C levels in late pregnancy, postpartum and in women on oral contraceptives. Thromb Res. 1985;39:637–40.
44. Gilabert J, Fernandez JA, Espana F, Aznar J, Estelles A. Physiological coagulation inhibitors (protein S, protein C and antithrombin III) in severe preeclamptic states and in users of oral contraceptives. Thromb Res. 1988;49:319-29.
45. Aznar J, Gilabert J, Estelles A, Espana F. Fibrinolytic activity and protein C in preeclampsia. Thromb Haemost. 1986;55:314–7.
46. Faught W, Garner P, Jones G, Ivey B. Changes in protein C and protein S levels in normal pregnancy. Am J ObstetGynecol. 1995;172:147-50.
47. Kjellberg U, Andersson NE, Rosen S, Tengborn L, Hellgren M. APC resistance and other haemostatic variables during pregnancy and puerperium. Thromb Haemost. 1999;81:527-31.

48. Boffa MC, Valsecchi L, Fausto A, Gozin D, Vigano' D'Angelo S, Safa O, et al. Predictive value of plasma thrombomodulin in preeclampsia and gestational hypertension. Thromb Haemost. 1998; 79:1092–5.
49. De Moerloose P, Mermillod N, Amiral J, Reber G. Thrombomodulin levels during normal pregnancy at delivery and in the postpartum—comparison with tissue type plasminogen activator and plasminogen activator inhibitor-1. Thromb Haemost. 1998;79:554–6.
50. Comp PC, Thurnau CR, Welsh J, Esmon CT. Functional and immunologic protein S levels are decreased during pregnancy. Blood. 1986;68:881–5.
51. Lefkowitz JB, Clarke AH, Barbour LA. Comparison of protein S functional and antigenic assays in normal pregnancy. Am J Obstet Gynecol. 1996;175:657-60.
52. Uchikova EH, Ledjev II. Changes in haemostasis during normal pregnancy. Eur J Obstet Gynecol. 2005;119:185-8.
53. Quack Loetscher KC, Stiller R, Roos M, Zimmermann R. Protein Z in normal pregnancy. Thromb Haemost. 2005;93: 706-9.
54. Cumming AM, Tait RC, Fildes S, Yoong A, Keeney S, Hay CR. Development of resistance to activated protein C during pregnancy. Br J Haematol. 1995;90:725-7.
55. Mathonnet F, de Mazancourt P, Bastenaire B, Morot M, Benattar N, Beufe S, et al. Activated protein C sensitivity ratio in pregnant women at delivery. Br J Haematol. 1996;92:244-6.
56. Ishii A, Yamada R, Hamada H. t-PA activity in peripheral blood obtained from pregnant women. J Perinat Med. 1994;22:113-7.
57. Lecander I, Åstedt B. Isolation of a new specific plasminogen activator inhibitor from pregnancy plasma. Br J Haematol. 1986;62:221–8.
58. Wright JG, Cooper P, Astedt B, Lecander I, Wilde JT, Preston FE, et al. Fibrinolysis during normal human pregnancy: complex interrelationships between plasma levels of tissue plasminogen activator and inhibitors and the euglobulin clot lysis time. Br J Haematol. 1988;69:253-8.
59. Booth NA. The natural inhibitors of fibrinolysis. In: Bloom AL, Forbes CS, Thomas DP, Tuddenham EGD, editors. Haemostasis and Thrombosis, Churchill Livingstone, Edinburgh. 1994;699–717.
60. Åstedt B, Hägerstrand I, Lecander I. Cellular localisation in placenta of placental type plasminogen activator inhibitor. Thromb Haemost. 1986;56:63–5.
61. Estelles A, Gilabert J, Espana F, Aznar J, Galbis M. Fibrinolytic parameters in normotensive pregnancy with intrauterine fetal growth retardation and in severe preeclampsia. Am J Obstet Gynecol. 1991;165:138-42.
62. Paniccia R, Prisco D, Bandinelli B, Fedi S, Giusti B, Pepe G, et al. R. Plasma and serum levels of D-dimer and their correlations with other hemostatic parameters in pregnancy. Thromb Res. 2002;105: 257-62.
63. Francalanci I, Comeglio P, Alessandrello Liotta A, CellaiAP, Fedi S, Parretti E, et al. D-dimer plasma levels during normal pregnancy measured by specific ELISA. Int J Clin Lab Res. 1997;27:65-7.
64. Morse M. Establishing a normal range for D-dimer levels through pregnancy to aid in the diagnosis of pulmonary embolism and deep vein thrombosis. J Thromb Haemost. 2004;2:1202-4.
65. Gilabert J, Aznar J, Parrilla JJ, Reganon E, Vila V, Estelles A. Alterations in the coagulation and fibrinolysis system in pregnancy, labour and puerperium, with special reference to a possible transitory state of intravascular coagulation during labour. Thromb Haemost. 1978;40:387-96.
66. Ygge J. Changes in blood coagulation and fibrinolysis during the puerperium. Am J Obstet Gynecol. 1969;104: 2–12.
67. Dahlstrom BL, Nesheim BI. Postpartum platelet count in maternal blood. Acta Obstet Gynecol Scand. 1994;73: 695-7.
68. Mannucci PM, Vigano S, Bottasso B, Candotti G, Bozzetti P, Rossi E, et al. Protein C antigen during pregnancy, deliveryand the puerperium. Thromb Haemost. 1984; 52:217.
69. Andersson T, Lorentzen B, Hogdahl H, Clausen T, Mowinckel MC, Abildgaard U. Thrombin-inhibitor complexes in the blood during and after delivery. Thromb Res. 1996;82:109-17.
70. Chavan R, Latoo MY. Recent advances in the management of major obstetric haemorrhage. Br J Med Pract. 2013;6:a604.
71. Varouxaki N, Gnanasambanthan S, Datta S, Amokrane N. Antepartum haemorrhage.

Obstet Gynaecol Reprod Med. 2018;28:237e42.
72. Banks A, Norrris A. Massive haemorrhage in pregnancy. Contin Educ Anaesth Crit Care Pain. 2005;5:195-8.
73. Trikha A, Singh PM. Management of major obstetric haemorrhage. Indian J Anaesth. 2018;62:698-703.
74. RCOG. Prevention and Management of Postpartum Haemorrhage (Green-top Guideline No. 52); 2016.
75. Menard MK, Main EK, Currigan SM. Executive summary of the revitalize initiative: Standardizing obstetric data definitions. Obstet Gynecol. 2014;124:150e3.
76. Hayes N, Drew T. Cardiopulmonary physiological alterations in pregnancy. In: Lapinsky S, Plante L, editors. Respiratory Disease in Pregnancy. Cambridge, UK: Cambridge University Press. 2020;25e33.
77. Drew T, Carvalho JC. Major obstetric haemorrhage. BJA education. 2022 Jun;22(6):238.
78. Bell SF, Watkins A, John M, et al. Incidence of postpartum haemorrhage defined by quantitative blood loss measurement: A national cohort. BMC Pregnancy Childbirth. 2020;20:271.
79. Obstetric Anaesthetists' Association and Association of Anaesthetists of Great Britain and Ireland. OAA/AAGBI Guidelines for Obstetric Anaesthesia Services; 2013. Available: http://www.aagbi.org/sites/default/files/obstetric_anaesthetic_services_2013.pdf
80. Kozek-Langenecker SA, Afshari A, Albaladejo P, Santullano CA, De Robertis E, Filipescu DC, et al. Management of severe perioperative bleeding: Guidelines from the European Society of Anaesthesiology. Eur J Anaesthesiol. 2013;30:270-382.
81. Charbit B, Mandelbrot L, Samain E, et al. The decrease of fibrinogen is an early predictor of the severity of postpartum hemorrhage. Journal of Thrombosis and Haemostasis. 2007;5:266–73.
82. De Lloyd L, Bovington R, Kaye A, et al. Standard haemostatic tests following major obstetric haemorrhage. International Journal of Obstetric Anesthesia. 2011; 20:135–41.
83. Collins PW, Lilley G, Bruynseels D, et al. Fibrin-based clot formation an early and rapidly biomarker for progression of postpartum hemorrhage: A prospective study. Blood. 2014;124:1727–36.
84. Hiippala ST, Myllyla GJ, Vahtera EM. Hemostatic factors and replacement of major blood loss with plasma-poor red cell concentrates. Anesthesia and Analgesia. 1995;81:360–5.
85. Allard S, Green L, Hunt BJ. How we manage the haematological aspects of major obstetric haemorrhage. British Journal of Haematology 2014;164:177–88.
86. Thachil J, Toh CH. Disseminated intravascular coagulation in obstetric disorders and its acute haematological management. Blood Reviews. 2009;23:167–76.
87. Levi, Marcel. Pathogenesis and management of peripartum coagulopathic calamities (disseminated intravascular coagulation and amniotic fluid embolism). Thrombosis Research. 2013;131:S32-S34.
88. Solomon C, Collis RE, Collins PW. Haemostatic monitoring during postpartum haemorrhage and implications for management. British Journal of Anaesthesia. 2012;109:851–63.
89. De Lange NM, Lance MD, De Groot R, Beckers EAM, Henskens YM, Scheepers HCJ. Obstetric hemorrhage and coagulation: An update. Thromboelastography, thromboelastometry, and conventional coagulation tests in the diagnosis and prediction of postpartum hemorrhage. Obstetrical and GynecologicalSurvey. 2012;67:426–35.
90. Hill JS, Devenie G, Powell M. Point-of-care testing of coagulation and fibrinolytic status during postpartum haemorrhage: Developing a thrombelastography guided transfusion algorithm. Anaesthesia and Intensive Care. 2012;40:1007– 15.
91. Van Rheenen-Flach LE, Zweegman S, Boersma F, Lenglet JE, Twisk JWR, Bolte AC. A prospective longitudinal study on rotation thromboelastometry in women with uncomplicated pregnancies and postpartum. Australian and New Zealand Journal of Obstetrics and Gynaecology. 2013;53:32–6.
92. Huissoud C, Carrabin N, Audibert F, et al. Bedside assessment of fibrinogen level in postpartum haemorrhage by thrombelastometry. International Journal of Obstetrics and Gynaecology. 2009; 116:1097–102.

93. Hill JS, Devenie G, Powell M. Point-of-care testing of coagulation and fibrinolytic status during postpartum haemorrhage: Developing a thrombelastography guided transfusion algorithm. Anaesthesia and Intensive Care. 2012;40:1007– 15.
94. Erhabor O, Isaac IZ, Muhammad AM, Abdulrahaman Y, Ezimah AC, Adias TC. Some hemostatic parameters in women with obstetric hemorrhage in Sokoto, Nigeria. International journal of women's health. 2013 Jun 14:285-91.
95. Solomon C, Collis RE, Collins PW. Haemostatic monitoring during postpartum haemorrhage and implications for management. Br J Anaesth. 2012;109(6):851–863.
96. De Lloyd L, Bovington R, Kaye A, et al. Standard haemostatic tests following major obstetric haemorrhage. Int J Obstet Anesth. 2011;20(2):135–141.
97. Charbit B, Mandelbrot L, Samain E, et al; PPH Study Group. The decrease of fibrinogen is an early predictor of the severity of postpartum hemorrhage. J Thromb Haemost. 2007;5(2):266–273.
98. Gayat E, Resche-Rigon M, Morel O, et al. Predictive factors of advanced interventional procedures in a multicentre severe postpartum haemorrhage study. Intensive Care Med. 2011;37(11):1816–1825.
99. Arulkumaran S, Mavrides E, Penney GC. Prevention and management of postpartum haemorrhage. Royal College of Obstetricians and Gynaecologists. Green-top guideline 52; 2009.
100. Simon L, Santi TM, Sacquin P, Hamza J. Pre-anaesthetic assessment of coagulation abnormalities in obstetric patients: Usefulness, timing and clinical implications. Br J Anaesth. 1997;78(6): 678–683.
101. Cherkas D. Traumatic hemorrhagic shock: Advances in fluid management. Emerg Med Pract. 2011;13(11):1–19; quiz 19–20.
102. Boehlen F. Thrombocytopenia during pregnancy. Importance, diagnosis and management. Hamostaseologie. 2006; 26(1):72–74;quiz 75–78.
103. Davies T, Catling S, Grainger HR. Re: Intraoperative cell salvage in obstetrics by Hannah Grainger and Sue Catling. J Perioper Pract. 2011;21(12):400.
104. Patriquin C, Crowther M. Treatment of warfarin-associated coagulopathy with vitamin K. Expert Rev Hematol. 2011; 4(6):657–665;quiz 666–667.
105. Laguna P, Klukowska A. Management of oral bleedings with recombinant factor VIIa in children with haemophilia A and inhibitor. Haemophilia. 2005;11(1): 2–4.
106. Mauser-Bunschoten EP, Koopman MM, Goede-Bolder AD, et al; Recombinant Factor VIIa Data Collection Group. Efficacy of recombinant factor VIIa administered by continuous infusion to haemophilia patients with inhibitors. Haemophilia. 2002;8(5): 649–656.
107. Domenico prisco, Gabriele ciuti, Michela falciani. Hemostatic changes in normal pregnancy. [haematologica reports] 2005;1(10):1-5.

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/115099