

# Some hemostatic parameters in women with obstetric hemorrhage in Sokoto, Nigeria

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**Abstract:** Obstetric hemorrhage is the leading cause of maternal mortality and morbidity worldwide. This study was carried out to investigate the effect of obstetric hemorrhage on the prothrombin time (PT), activated partial thromboplastin time (APTT), and platelet count (PLC). Women with obstetric hemorrhage were divided into two categories, women with antepartum hemorrhage (APH) and those with postpartum hemorrhage (PPH). Pregnant women without hemorrhage were included as controls. Eighty-six pregnant women aged 18–45 years (mean age  $36.25 \pm 10.50$  years) were presented to the Obstetrics and Gynaecology Department of Maryam Abacha Women and Children Hospital in Sokoto Metropolis, Sokoto State, Nigeria with history of obstetric hemorrhage. Forty-three age-matched nonhemorrhaging parturient women were included as controls. The determination of PT and APTT was done by manual methods using commercially prepared Diagen reagent kits, whereas PLC was done by manual methods using a hemocytometer. The results of PT and APTT were significantly higher among women with APH ( $20.7 \pm 4.226$  seconds and  $46.04 \pm 8.689$  seconds, respectively) and among women with PPH ( $23.17 \pm 2.708$  seconds and  $53.78 \pm 4.089$  seconds, respectively) compared to normal pregnant women ( $15.85 \pm 0.8930$  seconds and  $36.225 \pm 5.010$  seconds, respectively) ( $P = 0.0001$ ). Similarly, the PLC was significantly higher among normal pregnant women compared to those with APH and PPH ( $291.425 \pm 75.980 \times 10^9$  compared to  $154.83 \pm 47.019 \times 10^9$  and  $136.43 \pm 43.894 \times 10^9$ , respectively) ( $P = 0.0001$ ). The PT and APTT of women who presented with PPH were significantly higher compared to those who presented with APH ( $23.17 \pm 2.708$  seconds and  $53.78 \pm 4.089$  seconds versus  $20.7 \pm 4.226$  seconds and  $46.04 \pm 8.689$  seconds, respectively) ( $P = 0.02$  and  $P = 0.04$ , respectively). The PLC was significantly higher among women who presented with APH compared to those who presented with PPH ( $P = 0.01$ ). The PT and APTT values were higher in the third trimester among women with APH ( $24.38 \pm 2.33$  seconds and  $52.25 \pm 6.71$  seconds, respectively), PPH ( $24.75 \pm 2.63$  seconds and  $58.25 \pm 2.53$  seconds, respectively), and control women ( $16.00 \pm 0.82$  seconds and  $34.42 \pm 5.59$  seconds, respectively) compared to those in first and second trimester. The PLC was significantly lower in the third trimester among APH, PPH, and normal pregnant women ( $131 \pm 23.02 \times 10^9$ ,  $99 \pm 21.46 \times 10^9$ , and  $192.86 \pm 25.44 \times 10^9$ , respectively). PT and APTT values correlated positively and significantly with trimester ( $r = 0.52$  and  $0.65$ , respectively;  $P = 0.01$ ). The PLC of women with APH, PPH, and normal control women correlated negatively with trimester ( $r = -0.36$ ,  $-0.54$ , and  $-0.28$ , respectively;  $P = 0.05$ ). Obstetrics hemorrhage compounded the hemostatic status of pregnant women in Sokoto, Nigeria. There is need for the provision of rapid diagnosis of coagulopathy to guide the provision of best therapeutic management options.

**Keywords:** hemostatic parameters, women, obstetric hemorrhage, Sokoto, Nigeria

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## Introduction

Hemorrhage is the major cause of maternal mortality and morbidity worldwide.<sup>1</sup> It is responsible for 44% of maternal death in Africa.<sup>2</sup> More than 536,000 women die every year from pregnancy-related complications (malaria-related anemia, antepartum and postpartum hemorrhage).<sup>3</sup> Up to 20% of all maternal mortality and 15% of child death in most African settings are attributable to the lack of access to safe and adequate blood and blood products to manage malaria-associated complications, nutritional anemia, and hemorrhages (antepartum and postpartum).<sup>4</sup> Coagulation is a product of the interaction between vessel walls, platelets, and coagulation factors. Following a break in the vascular endothelium, platelets adhere to the subendothelium, forming a platelet plug, which then becomes permanent with fibrin deposition. Obstetric hemorrhage (postpartum and antepartum) is a major risk factor for maternal morbidity and mortality. Underlying hemostatic imbalances such as consumptive and dilutional coagulopathies may develop during obstetric hemorrhage and can exacerbate bleeding. Monitoring of coagulation status in patients with obstetric hemorrhage may be crucial for effective hemostatic management, goal-directed therapy, and improved outcomes.<sup>5</sup>

Pregnancy is associated with changes in hemostasis, including an increase in the majority of clotting factors, a decrease in the quantity of natural anticoagulants, and a reduction in fibrinolytic activity.<sup>6</sup> The platelet count decreases in normal pregnancy, possibly due to increased destruction and hemodilution, with a maximal decrease in the third trimester.<sup>7-9</sup> As most coagulation factors increase in normal pregnancy, the prothrombin time (PT) and the activated partial thromboplastin time (APTT) may be shortened. The PT and its derived measure, the international normalized ratio (INR), test for factors such as coagulation factors II, V, VII, X, and fibrinogen. The APTT is considered a good screening test for deficiencies of coagulation factors VIII, IX, XI and XIII. Laboratory-based screening is used routinely to assess coagulation status in obstetric patients. The tests consist of platelet count; PT, APTT, D-Dimer, and plasma fibrinogen levels.<sup>10</sup> 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 FVIII and FXIII.<sup>11,12</sup> In many countries of Sub-Saharan Africa, many women deliver at home and many maternal antepartum hemorrhage (APH)- and postpartum hemorrhage (PPH)-related maternal deaths occur at home, and are often

unreported. There is a paucity of data on hemostatic parameters among hemorrhaging pregnant women in Sokoto, Nigeria. It is not known to what extent obstetric hemorrhage affects the coagulation profile of pregnant women in Sokoto State, Nigeria. This study is thus an attempt to generate evidenced-based data on the hemostatic profile of hemorrhaging pregnant women to facilitate the obstetric and hematology-related care offered to pregnant women in the state.

## Materials and methods

### Study design

This study was designed to determine the hemostatic parameters (platelet count, PT, and APTT) of hemorrhaging pregnant women (subjects) and nonhemorrhaging pregnant women (controls). Eighty-six consecutively recruited and consenting pregnant women aged 18–45 years (mean age  $36.25 \pm 10.50$  years) presenting with obstetric hemorrhage (subjects) and forty-three nonpregnant women (controls) had their hemostatic parameters (platelet count, PT, and APTT) determined by standard methods. Values obtained from subjects were compared with that of controls and the differences were analyzed statistically. The effect of socio-demographic and pregnancy-related factors were also compared statistically.

### Eligibility criteria

All adult ( $\geq 18$  years) pregnant women presenting with obstetric hemorrhage (subjects) and pregnant nonhemorrhaging (controls) women who provided informed consent after counselling were eligible to participate in this study. Eligible control participants included consenting and apparently healthy nonhemorrhaging pregnant women  $\geq 18$  years old. Exclusion criteria included age (women  $< 18$  years), nonpregnant women, women on hemostatic and antiplatelet therapy, and non-consenting women. APH was defined as bleeding from the birth canal after the 24th week of pregnancy.<sup>13</sup> It can occur at any time until the second stage of labor is complete. The 2006–2008 Confidential Enquiry into Maternal and Child Health (CEMACH) revealed that the mortality rate due to obstetric hemorrhage was 0.39 per 100,000 maternities.<sup>14</sup> It affects 3%–5% of all pregnancies and is three times more common in multiparous than in primiparous women.<sup>15</sup> Primary PPH was defined as excessive blood loss from the genital tract during the first 24 hours after delivery.

### Informed consent and ethical clearance

Written informed consent was obtained from all participants recruited into this study (controls and subjects).

**Table 1** Mean values of some hemostatic parameters in hemorrhaging subjects and nonhemorrhaging controls

Parameter	Mean $\pm$ SD			t-value	P-value
	Pregnant subjects <sup>a</sup> with APH	Pregnant subjects <sup>b</sup> with PPH	Normal pregnant controls <sup>c</sup>		
PT (seconds)	20.7 $\pm$ 4.226	23.17 $\pm$ 2.708	15.85 $\pm$ 0.8930	7.02 <sup>a,b</sup> 15.76 <sup>b,c</sup>	0.001 <sup>a,b</sup> 0.001 <sup>b,c</sup>
APTT (seconds)	46.04 $\pm$ 8.689	53.78 $\pm$ 4.089	36.225 $\pm$ 5.010	5.70 <sup>a,b</sup> 14.28 <sup>b,c</sup>	0.001 <sup>a,b</sup> 0.001 <sup>b,c</sup>
Platelet count ( $\times 10^9/L$ )	154.83 $\pm$ 47.019	136.43 $\pm$ 43.894	291.425 $\pm$ 75.980	7.79 <sup>a,b</sup> 8.94 <sup>b,c</sup>	0.001 <sup>a,b</sup> 0.001 <sup>b,c</sup>

**Notes:** <sup>a,b</sup>Statistical comparison of women with APH and normal control women; <sup>b,c</sup>statistical comparison of women with PPH and normal control women.

**Abbreviations:** APH, antepartum hemorrhage; APTT, activated partial thromboplastin time; PPH, postpartum hemorrhage; PT, prothrombin time; SD, standard deviation.

Ethical clearance was obtained from the ethical review board of the Maryam Abacha Women and Children Hospital, Sokoto, Nigeria.

## Study area

The present research work was carried out at the Maryam Abacha Women and Children Hospital in Sokoto Metropolis, Sokoto State, Nigeria. The hospital is a district general hospital in the Northwest geopolitical zone of Nigeria offering routine antenatal care to pregnant women in Sokoto Metropolis and the neighboring states of Zamfara and Kebbi. Sokoto State is located in the extreme Northwestern part of Nigeria, near the confluence of the Sokoto River and the Rima River. With an annual average temperature of 28.3°C (82.9°F), Sokoto is, on the whole, a very hot area. However, maximum daytime temperatures for most of the year are generally under 40°C (104.0°F). The warmest months are February to April, when daytime temperatures can exceed 45°C (113.0°F). The rainy season is from June to October, during which showers are a daily occurrence. There are two major seasons, wet and dry, which are distinct and are characterized by high and low malarial transmission respectively. A report from the 2007 National Population Commission indicated that the state had a population of 3.6 million.<sup>16</sup>

## Sample collection and methods

Six millilitres of whole blood was collected using a monovette vacutainer syringe. The blood was deposited into an ethylenediaminetetraacetic acid (EDTA) anticoagulated tube containing potassium EDTA (2.7 mL) used for the analysis of platelet count, and into a sodium citrate anticoagulated tube (2.7 mL) containing 0.5 mL sodium citrate (0.109 mol/L). The citrate anticoagulated sample was centrifuged lightly for 5 minutes at 3000 rpm. The citrated plasma was separated aseptically and used for routine coagulation tests (PT, APTT). The citrated plasma was assayed using manual methods for

PT and APTT using Diagen Diagnostics reagent (Diagen Reagents Ltd, Thame, UK). Test procedures were conducted according to the instructions in the manufacturer's standard operating manual.

## Statistical analysis

Statistical analyses were conducted using SPSS (version 11; IBM Corporation, Armonk, NY, USA) software. Data were expressed as mean  $\pm$  standard deviation. Comparisons between hemorrhaging pregnant subjects and nonhemorrhaging pregnant controls were made using the Student's *t*-test for parametric data and the Mann-Whitney test for nonparametric data. Descriptive analyses of percentages of categorical variables were reported. A *P*-value of  $<0.05$  denoted a statistically significant difference in all statistical comparisons. Correlation was compared using a version of linear regression analysis.

## Results

The aim of this study was to determine the severity of the effect of obstetric hemorrhage on the PT, APTT, and platelet count. Women with obstetric hemorrhage were divided into two categories, women who presented with APH and women with PPH. Pregnant women without a history of hemorrhage were included as controls. The

**Table 2** Mean values of some hemostatic parameters based on hemorrhage type

Parameter	Pregnant subjects with PPH	Normal pregnant controls	t-value	P-value
PT (seconds)	20.7 $\pm$ 4.226	23.17 $\pm$ 2.708	2.34	0.02
APTT (seconds)	46.04 $\pm$ 8.689	53.78 $\pm$ 4.089	3.87	0.04
Platelet count ( $\times 10^9/L$ )	154.83 $\pm$ 47.019	136.43 $\pm$ 43.894	1.37	0.01

**Abbreviations:** APTT, activated partial thromboplastin time; PPH, postpartum hemorrhage; PT, prothrombin time.

determination of PT and APTT was done by manual methods using commercially prepared Diagen reagent kits, whereas platelet count was done by manual methods using a hemocytometer, (Neubauer, Horsham Germany). Table 1 shows the mean values of some hemostatic parameters in haemorrhaging and non-haemorrhaging controls. Table 2 shows the mean hemostatic parameters based on the type of haemorrhage. The results of PT and APTT were significantly higher among women with APH ( $20.7 \pm 4.226$  seconds and  $46.04 \pm 8.689$  seconds, respectively) and among women with PPH ( $23.17 \pm 2.708$  seconds and  $53.78 \pm 4.089$  seconds, respectively) compared to normal pregnant women ( $15.85 \pm 0.8930$  seconds and  $36.225 \pm 5.010$  seconds, respectively) ( $P = 0.001$ ). Similarly, the platelet count was significantly higher among normal pregnant women compared to those with APH and PPH ( $291.425 \pm 75.980 \times 10^9$  compared to  $154.83 \pm 47.019 \times 10^9$  and  $136.43 \pm 43.894 \times 10^9$ , respectively) ( $P = 0.001$ ). The PT and APTT of women who presented with PPH were significantly higher compared to those who presented with APH ( $23.17 \pm 2.708$  seconds and  $53.78 \pm 4.089$  seconds versus  $20.7 \pm 4.226$  seconds and  $46.04 \pm 8.689$  seconds, respectively) ( $P = 0.02$  and  $P = 0.04$ , respectively). The platelet count was also significant higher among women who presented with APH compared to those who presented with PPH ( $P = 0.01$ ). The PT and APTT values were higher in the third trimester among women with APH ( $24.38 \pm 2.33$  seconds and  $52.25 \pm 6.71$  seconds, respectively), PPH ( $24.75 \pm 2.63$  seconds and  $58.25 \pm 2.53$  seconds, respectively), and control women ( $16.00 \pm 0.82$  seconds and  $34.42 \pm 5.59$  seconds, respectively) compared to the first and second trimesters as shown in Table 3. The platelet count was significantly lower in the third trimester among APH, PPH, and normal pregnant women ( $131 \pm 23.02 \times 10^9$ ,  $99 \pm 21.46 \times 10^9$ , and  $192.86 \pm 25.44 \times 10^9$ , respectively). PT and APTT values correlated positively and significantly

with trimester ( $r = 0.52$  and  $0.65$ , respectively;  $P = 0.01$ ). The platelet count of women with APH, PPH, and normal control women correlated negatively with trimester ( $r = -0.36$ ,  $-0.54$  and  $-0.28$ , respectively;  $P = 0.05$ ).

## Discussion

Obstetric hemorrhage is a major risk factor for maternal morbidity and mortality. In the present study, we observed that the PT and APTT values were significantly higher in women with obstetric hemorrhage (APH and PPH) compared to those of nonhemorrhaging pregnant women. PT and APTT are used in the management of coagulopathy in obstetric hemorrhage.<sup>5</sup> The value of routine full blood count and coagulation screening has been questioned in obstetrics.<sup>17</sup> PT and APTT may identify significant coagulation impairment, but they test limited parts of coagulation and do not help diagnose the underlying defect. PT measures the extrinsic and common coagulation pathways, and is sensitive to levels of vitamin K coagulation factors (II, V, VII, and X), while APTT assesses coagulation via the intrinsic and common pathways and is sensitive to all coagulation factors except FVII and FXIII. Both PT and APTT seem to be of value for monitoring hemostasis during obstetric hemorrhage. A recent review of 18,501 deliveries in the UK identified 456 cases complicated by blood loss  $\geq 1500$  mL.<sup>18</sup> PT did not seem to correlate with the volume of hemorrhage and APTT correlated weakly. Earlier studies have concluded that PT and APTT are not useful for predicting PPH progression.<sup>19</sup> However, another retrospective multicenter validation study demonstrated that  $\text{INR} > 1.5$  may predict the need for advanced intervention to control obstetric hemorrhage.<sup>20</sup> Current guidelines recommend using  $\text{INR} > 1.5$  to guide fresh-frozen plasma (FFP) transfusion.<sup>21</sup>

We observed in the present study that the platelet count was significantly lower in women with obstetric hemorrhage

**Table 3** Mean values of nonhemorrhaging pregnant women based on trimester

Category of women	Trimester	PT (seconds)	APTT (seconds)	Platelet count ( $\times 10^9/\text{L}$ )
APH	1st	$17.75 \pm 2.32$	$36.38 \pm 3.29$	$206 \pm 33.31$
	2nd	$19.86 \pm 4.47$	$50.00 \pm 4.16$	$143.29 \pm 10.53$
	3rd	$24.38 \pm 2.33$	$52.25 \pm 6.71$	$131.00 \pm 23.02$
PPH	1st	$21.13 \pm 2.64$	$50.25 \pm 2.32$	$165.25 \pm 61.78$
	2nd	$24.09 \pm 1.97$	$54.73 \pm 2.53$	$129.09 \pm 12.05$
	3rd	$24.75 \pm 2.63$	$58.25 \pm 5.06$	$99.00 \pm 21.46$
Normal pregnant women	1st	$15.55 \pm 0.95$	$37.15 \pm 4.87$	$355.30 \pm 38.50$
	2nd	$16.25 \pm 0.75$	$35.83 \pm 5.17$	$244.58 \pm 38.57$
	3rd	$16.00 \pm 0.82$	$34.43 \pm 5.59$	$192.86 \pm 25.44$

**Abbreviations:** APTT, activated partial thromboplastin time; PT, prothrombin time; APH, antepartum hemorrhage; PPH, postpartum hemorrhage.

compared to those of nonhemorrhaging pregnant women. Our finding is consistent with findings in previous studies which showed that at the time of diagnosis of hemorrhage, platelet counts in hemorrhaging obstetric patients were significantly lower than those in healthy parturient women<sup>22</sup> and that decreasing platelet count during obstetric bleeding may be associated with progression to severe hemorrhage.<sup>19</sup> A retrospective analysis of 797 pregnancies found low platelet count to be an independent risk factor for obstetric hemorrhage and a platelet count  $< 100 \times 10^9$  per liter on admission to the labor ward was associated with increased obstetric hemorrhage incidence in some women.<sup>23</sup> Findings in a previous report suggest that platelet transfusion or desmopressin may be valid hemostatic therapies for the management of obstetric hemorrhage. Current guidelines recommend that platelet transfusion is indicated when the platelet count decreases below  $50 \times 10^9$  per liter in hemorrhaging parturient women.<sup>21</sup> These evidenced-based hemostatic therapies may not be readily available to hemorrhaging obstetric women in Sokoto and many settings in developing countries. In Nigeria, as in many other developing countries, particularly in Sub-Saharan Africa, blood is still being transfused as whole blood rather than its constituent components. Cost implications may also affect the accessibility to effective hemostatic therapy like desmopressin. These factors make the management of obstetric hemorrhage in these settings a huge challenge to obstetricians.

We observed a positive correlation between the PT and APTT and trimester in women with APH, PPH, and in normal pregnant women. We observed that PT and APTT were significantly prolonged in the third trimester compared to the first and second trimesters. Similarly, we observed a negative correlation between platelet count and trimester. The platelet count of women with APH, PPH, and the normal control women was significantly lower in the third trimester compared to the first and second semesters. Our findings are consistent with previous reports,<sup>24-26</sup> that indicated that thrombocytopenia occurs during the last trimester. Etiologies of thrombocytopenia in pregnancy include gestational thrombocytopenia ( $>75\%$ ); immune thrombocytopenia, either primary or associated with other pathologies; thrombotic microangiopathy syndromes; and obstetric thrombocytopenia (eclampsia and HELLP (Hemolysis, Elevated Liver Enzymes and Low Platelet count) syndrome). Thrombocytopenia complicates 10% of all pregnancies.<sup>27</sup> It is observed in 6%–15% of pregnant women at the end of pregnancy, and is usually moderate.<sup>28</sup>

Deaths from APH and PPH feature prominently in this group of women, particularly in Sub-Saharan Africa, for several reasons: there are many barriers to accessing

emergency care from home, there is little, if any, good home-based care, and there is more mortality from APH and PPH in rural communities where there are many home deliveries. Common causes of obstetric hemorrhage include; retained placenta, inverted uterus, bleeding due to abruptio placenta, bleeding due to placenta praevia, maternal bleeding disorders, uterine atony, genital tract trauma (lacerations or tears of the vagina, perineum, and cervix), ruptured uterus and placenta accreta, vulval or cervical infection, and trauma or tumors. There are several daunting challenges faced by obstetricians, particularly in the effective management of obstetric hemorrhage in developing countries; laboratory-based screening used routinely to assess coagulation status in obstetric patients is often not available, particularly in most rural settings; access to safe and adequate blood and blood products required for the effective management of obstetric hemorrhage remains a mirage in most settings in Africa. Timely access to the right quantity and quality of blood and blood products is a life-saving measure in most clinical conditions. The aim of blood volume replacement with concentrated red cells and other plasma products following obstetric hemorrhage includes: to rapidly and effectively restore adequate blood volume and prevent hypovolemic shock; to allow for adequate hemostasis, oxygen carrying capacity, and blood biochemistry; to allow for an early and aggressive correction of coagulopathy; to allow for optimal resuscitation; and to reduce potentially preventable deaths.<sup>29</sup> Evidenced-based non-blood-product-related hemorrhage control measures that can be used include application of direct pressure/tourniquet if appropriate; appropriate stabilization of fractures and surgical interventions such as damage control surgery, interventional radiology, and use of appropriate endoscopic and obstetric techniques; and use of blood sparing measures (intraoperative blood salvage, also known as autologous blood salvage, is a medical procedure involving the recovery of blood lost during surgery and trauma and re-infusing it into the patient). Red cell salvage is indicated in most obstetrics, surgical procedures.<sup>30</sup> Hemostatic drugs such as vitamin K, tranexamic acid<sup>28</sup> and prothrombin complex concentrate (PCC) play a role in hemostasis. PCC is a human blood product and both pasteurization and nanofiltration are used for its viral inactivation. It contains the clotting factors II, VII, IX, X, protein S, and protein C.<sup>32</sup> Novo 7 (a vitamin-K-dependent recombinant human coagulation Factor VIIa [rFVIIa]) is used for promoting hemostasis by activating the extrinsic pathway of the coagulation cascade. It is a glycoprotein and an important factor in the clotting of blood that forms a complex with tissue thromboplastin and calcium

to activate prothrombinase, thus acting to accelerate the conversion of prothrombin to thrombin. It is indicated for the clinical management of hemorrhage, particularly when other measures such as use of blood products and other pharmacologic options are ineffective.<sup>33</sup> These hemostatic treatments can play a major role in the management of coagulopathy associated with obstetric hemorrhage and by extension, can help limit the use of blood products. These evidenced-based hemorrhage control measures are universally available to women in the developed world. However, women in developing countries are not fortunate enough to have access to these life-saving therapies. Cost implications sometimes limit the use of these highly effective hemostatic drugs and procedures, particularly in low income countries in Sub-Saharan Africa.

## Limitations

One of the limitations of this study was that we did not investigate the fibrinogen concentration in the hemorrhaging and non-hemorrhaging pregnant women studied, due to cost constraints. Fibrinogen has been found to be correlated with the incidence and severity of obstetric bleed.<sup>23</sup> Fibrinogen ( $>4$  g/L) has a negative predictive value of 79% for severe hemorrhage, whereas fibrinogen ( $\leq 2$  g/L) has a positive predictive value of 100%. The European Guideline for the management of bleeding in obstetrics recommends a trigger level for fibrinogen replacement from  $<1$  g/L to  $<1.5$ – $2.0$  g/L. Fibrinogen concentrations can vary from  $1.6$ – $3.5$  g/L in FFP.<sup>34</sup> Adequate replacement of fibrinogen using FFP may not yield the desired results, and FFP transfusion may further dilute the already depleted fibrinogen level. In most developed countries, cryoprecipitate is the blood product of choice for the management of obstetric hemorrhage associated with low fibrinogen levels of  $<2.0$  g/L. This provides a more concentrated alternative to cryoprecipitate.<sup>35</sup> However, cryoprecipitate has been withdrawn in many European countries due to safety concerns.<sup>36</sup> Recent reports have described fibrinogen concentrate infusion as an effective therapy for controlling obstetric hemorrhage associated with low fibrinogen levels.<sup>37</sup> Fibrinogen concentrate is a highly purified product compared to cryoprecipitate; the pasteurization steps in the manufacturing process significantly reduce the risk of pathogen transmission.<sup>38</sup>

## Conclusion

There are many challenges associated with the management of maternal hemorrhages, particularly in developing countries: high rate of home deliveries, high rate of non-antenatal attendance (unbooked women), unavailability of

important coagulation tests required for evidenced-based management of coagulopathy, lack of access and suboptimal use of pharmacologic and nonpharmacologic alternatives to allogenic blood, lack of blood components (FFP and cryoprecipitate) required to manage coagulopathy, transfusion of whole blood rather than the indicated component, chronic blood shortages, high prevalence of transfusion-transmissible infection, absence of a functional national blood transfusion service, recruitment and retention of voluntary non-remunerated donors, family replacement, and commercial blood donation. Our study has shown that there is a need for appropriate hemostatic interventions including the availability of hemostatic tests which allow rapid diagnosis and monitoring of coagulopathy in the management of obstetric hemorrhage in our environment. There is a need for laboratory-based screening to assess coagulation status in obstetric patients. The tests should consist of platelet count, PT, APTT, and plasma fibrinogen levels. Platelet count provides a measure of platelet concentration. 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. Both PT and APTT can play a significant role in the monitoring of hemostasis during obstetric hemorrhage. A retrospective multicenter validation study has demonstrated that  $PT > 1.5$  times normal may predict the need for advanced intervention to control obstetric hemorrhage.<sup>20</sup> Current guidelines recommend using PT and APTT to guide FFP transfusion in cases of obstetric hemorrhage.<sup>21</sup>

Fibrinogen concentration has been shown to correlate with the incidence and severity of obstetric hemorrhage. In a prospective study involving 128 patients, decreasing plasma fibrinogen during early PPH was the only variable independently associated with progression to severe PPH requiring red blood cells or invasive intervention. Fibrinogen  $> 4$  g/L had a negative predictive value of 79% for severe hemorrhage, whereas fibrinogen  $\leq 2$  g/L had a positive predictive value of 100%.

Obstetric measures that can be implemented for preventing progression of coagulopathy in developing countries to reduce the risk of morbidity and mortality from obstetric hemorrhage should include antenatal optimization of the hemoglobin of pregnant women using oral iron treatment, early recognition using near patient testing (platelet count, PT, APTT, and fibrinogen), early and proactive assessment and resuscitation, use of hemostatic agents (oxytocin, tranexamic acid, activated factor V11a, and PCC), mechanical interventions (balloon tamponade,

compression sutures, and arterial ligation), interventional radiology, cell salvage, and availability of adequate and safe blood component therapy (red cell concentrate, FFP, cryoprecipitate, and fibrinogen concentrate).

## Disclosure

The authors report no conflicts of interest in this work.

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