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POST- PARTUM HAEMORRHAGE : COAGULOPATHY MANAGEMENT AND THERAPEUTIC ASPECTS IN THE OBSTERIC INTENSIVE CARE UNIT

THESIS

DEFENDED AND PRESENTED PUBLICLY ON 14 /03/2022

By

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Born on November 06,1993 in Zambia

TO OBTAIN MEDICAL DOCTORATE DEGREE

KEYWORDS:

Coagulopathy -Post partum haemorrhage -Thromboelastometry -Blood transfusion -Fibrninogen

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ABBREVIATIONS

aPPT : Activated cephalin Time
BP : blood pressure
CCT : common coagulation tests.
DIC : disseminated intravascular coagulation
FFP : fresh frozen plasma
Hb : haemoglobin
HELLP : Haemolysis Elevated liver enzymes Low platelets
LBP : Labile blood products
MA : Marketing authorisation
MAP : Mean arterial pressure
PLT : platelet
POC : point of care
PP : platelet pellet
PPH : post-partum haemorrhage
PT : prothrombin time
PVC : peripheric veinous catheter
RBC : Red Blood Cell
rFVIIa : Factor VII activated recombinant
RPH : Retro placenta hematoma
RRT : renal Replacement therapy
TA : Tranexamic Acid
The : haematocrit
UTH : University Teaching Hospital.

PLAN

INTRODUCTION

By subscribing to the Millennium Development Goals (MDGs) [1], Morocco has committed to reducing maternal mortality by three quarters. According to World Health Organization (WHO) [2], around 830 women die every day worldwide from complications related to pregnancy or childbirth. In 2015 alone, 303,000 women died during or after pregnancy or childbirth [3].

In Morocco, the latest data reported by the ministry of health [4] showed a significant reduction in the maternal mortality ratio from 112 maternal deaths to 100,000 live births in 2010, to 72.6 in 2017. That is a reduction of around 35%. According to data reported by the Ministry of Health, PPHs represent 52% of maternal deaths.

PPH is a major cause of maternal morbidity and mortality worldwide. Risk factors include retained placenta, prolonged duration of the third stage of labour, previous caesarean section, and operative vaginal delivery. Occurrence and development of PPH are, however, unpredictable and can sometimes give rise to massive haemorrhage or even hysterectomy and maternal death. Severe haemorrhage can lead to coagulopathy causing further haemorrhage and requiring substitution with blood transfusions. [5]

PPH is defined by the world health organisation (WHO) [2] as blood loss of at least 500cc occurring within 24 hours of giving birth. We speak of severe bleeding when blood loss is more than 1000cc in the same time interval. Rapid cooperation between the obstetrician, the anaesthesiologist and the midwife are essential in providing an appropriate and optimal response to each case while avoiding the onset of serious complications (hypovolemic shock, intravascular coagulation disseminated, renal failure…). For this to happen, a good knowledge of the physio-pathological mechanisms, the risk factors, as well as regular monitoring by antenatal consultation (ANC) during the pregnancy is necessary to allow good primary prevention. Identifying high-risk pregnancies in time allows for good management of secondary complications.

MATERIALS AND METHODS

I. Study objectives

This work aims to analyse the epidemiological, clinical and Para clinical profile of postpartum haemorrhage in intensive care; As well as to determine the risk factors, clinical and laboratory profile of coagulopathy in postpartum haemorrhage. The different treatment modalities will also be discussed, in particular the transfusion of labile blood products, the infusion of fibrinogen and tranexamic acid.

II. Study Materials

II.1. Type and duration of the study

This is a retrospective, descriptive and analytical, non-interventional study during the period which extends from January 2014 to December 2020.

II.2. Study population

This study includes all cases of patients with postpartum haemorrhage and requiring hospitalization in the mother-child intensive care unit of the Hassan II University Hospital in Fez.

II.3. inclusion criteria

We retained as inclusion criteria for severe PPH:

- All patients presenting with PPH diagnosed clinically and requiring hospitalisation in the maternal intensive care unit.

II.4 exclusion criteria.

We excluded from this study patients whose charts were unusable due to insufficient information.

III. Study methods.

1. Data collection

All data will be collected from the computerized medical records of patients, including epidemiological parameters, diagnostic management, therapeutic management and progress. The results will be expressed in number, percentage, mean or mean ± standard deviation. The data will be processed using Microsoft Office Excel.

2. *Limitations of the study.*

- A great lack of information contained in the files, particularly the data of the initial care in the women that were referred.

  Below is the records keeping sheet that was used to collect data in our study:

RECORDS KEEPING SHEET

PATIENT'S IDENTITY

-Number in case study:

-Surname : - First name :

-Date of birth: -Age:

-patient index:

-Marital status: single □ married □ divorced □

HOSPITALISATION

-Method of admission: direct □ referral □

-Date of admission:

-Duration of hospitalisation:

-Date of delivery:

-Date of diagnosis of PPH:

PATIENT HISTORY

Medical history

-coagulopathy: □

-current medication: □ types.....

-nephropathy: □

-High blood pressure : □

-steatosis: □

-diabetes: □

-obesity: □

Surgical history

-C-section: □

-Gynaecological surgery: □

-other:……..

Gynaecological and obstetrical history:

-menarche:

-gesture:

-parity:

Pregnancy	progression	Method of delivery
1st		
2nd		
3rd		

-Retro placenta haemorrhage: yes □ No □

-pre-eclampsia: yes □ No □

- postpartum haemorrhages: yes □ No □ - cause…….

- intra uterine foetal death: yes □ No □

current pregnancy

-gestational age:…….

-blood group:

-ante-natal monitoring: yes □ No □

-Macrosomia: yes □ No □

-Oligohydramnios: yes □ No □

-multiple foetuses: yes □ No □

- duration of labour: >12hrs <12hrs

-oxytocin: yes □ No □

-induced labour: yes □ No □

-Instrumental extraction: yes □ No □

-programmed c-section: yes □ No □

Indication…….

-Emergency c-section: yes □ No □

Indication……

Etiologies :

- uterine atony □
- placenta retention □
- uterine rupture □
- pelvic - cervical - vaginal lesions □
- Placenta previa □
- Placenta accreta □
- uterine inversion □
- Episiotomy □
- Coagulopathy □
- Other……..

Risk factors

- HELLP syndrome : yes □ No □
- RPH : yes □ No □
- Sub-capsular hepatic hematoma : yes □ No □
- Disseminated intra vascular coagulopathy : yes □ No □
- Eclampsia : yes □ No □
- Fatty liver : yes □ No □
- Pre-eclampsia : yes □ No □

Management of childbirth

- method of delivery: normal □ c-section □
- Analgesic : yes □ No □ type…….
- Oxytocin : yes □ No □ dose……..
- Anaesthesia : yes □ No □

  -loco-regional

  -general :

  Duration……..

- **State of new born** :
  - intra uterine growth retardation : yes □ No □
  - Induce prematurity : yes □ No □
  - Still born : yes □ No □
  - Apgar 1min 5min 10min
  - Other…….

Surgical management: yes □ No □

Procedure performed	*Yes/no*	*indication*
-Uterine revision		
-Resuture of tears		
-Hypogastric ligature		
-Triple ligature		
-Uterine suture:		
-Emergency hysterectomy		
- other ……		

Treatments received in operating room

Treatments/procedure	Yes/no	indication
intubation		
Transfusion:		
Quantity:		
drugs:		
-noradrenaline		
-diuretics		
-prostaglandin		
-oxytocin		
-phenylalanine		
-tranexamic acid		
Anaesthesia:		
-Propofol		
-Fentanyl		
-Curare		
-Midazolam		
Local regional anaesthesia:		
other …….		

ON ADMISSION

Clinical exam

-PPH diagnosis: yes □ No □

Quantity……

-state of consciousness: intubated: yes □ No □

-blood pressure:

-heart rate:

-SaO2

-temperature:

-presenting complaints:

lab work on admission

blood work	Admission Date : Time :	Day +….. Date: Time:	Day +…. Date: time:	Discharge Date: Time:
• Full blood count :				
○ Haemoglobin (g/dl) :				
○ White blood cells (/mm³) :				
○ Platelets (/mm³) :				
• Liver function test :				
○ GOT (UI/l) :				
○ GPT (UI/l) :				
○ GGT (UI/l) :				
○ Alkaline phosphatase (UI/l) :				
○ Total bilirubin (µmol /l) :				
○ Direct bilirubin (µmol /l) :				
• Haemostasis assessment :				
○ Prothrombin time PT (%) :				
○ Activated cephaeline Time (s) :				
○ Fibrinogen (g/l) :				
○ D-dimers (µg/ml) :				
• Albuminemia (g/l) :				
• Proteinemia (g/l) :				
• Natremia (mmol/l) :				
• Kalemia (mmol/l) :				
• Calcemia (mg/l) :				
• Chloremia (mmol/l) :				
• Alkaline reserves (mmol/l) :				
• CRP (mg/l) :				
• Glycemia (g/l) :				
• LDH (UI/l) :				
• Haptoglobin (g/l) :				

• Schistocytes (%) :				
• Uric Acid (mg/l) :				
• Magnesia (mg/l) :				
• Phosphoremia (mg/l) :				
• Lactates (mmol/l)				

• Cytobacteriological examination of urine :	Admission Date: Time:	Day+… Date: Time:	Day+…. Date: Time:	Discharge Date : Time:
o Leukocyturia(/mm³) :				
o Haematuria (/mm³) :				
o Culture :				

Radiological analysis :

-Abdominal echography : yes □ No □

-Kidney echography : yes □ No □

-Hepatic echography : yes □ No □

-Abdominal TDM : yes □ No □ other : ……

Treatment received in ICU :

- **standard care :**
  - Standard monitoring : yes □ No □
  - Peripheral IV : yes □ No □
  - Central veinous catheter : yes □ No □
  - Arterial catheter : yes □ No □
  - Gastric tube : yes □ No □
  - Urinary catheter : Yes □ No □

- Oxygen therapy : Yes □ No □
  - O2 mask : Yes □ No □
  - Non invasive ventilation : Yes □ No □
  - Intubation and ventilation : Yes □ No □

- **Vascular filling**: Yes □ No □

Nature of solute	quantity	duration
-SS 0,9%		
- Ringer Lactate		
- Synthetic Colloid		
- Albumin		
-other:		

Labile blood products :Yes □ No □

type	quantity	duration	indication
o red blood cell pellet			
o platelet pellet			
o fresh frozen plasma			

- Fibrinogen : Yes □ No □
    - Indication :……
- ventilation support : Yes □ No □

  -Indication : Neurologic □ Respiratory □ Hemodynamic □cardiac arrest

    - Induction/intubation:
        - Rapid sequence □ Standard□
        - Hypnotic : Propofol □ Thiopental □
        - Curare : Rocuronium bromide □ vecuronium bromide □ Succinylcholine□
        - Morphine : Fentanyl □ Sufentanyl □
    - Duration of intubation :
    - Maintenance of sedation: Fentanyl □ Midazolam □ Propofol □
- tracheotomy: Yes □ No □
- **<u>Medications received:</u>**

Medication type	Molecule	indication	dose	duration
antibiotic				
Analgesic				
Diuretic				
Gastric protection				
Anticoagulants				
Alkalinisation				
Vasoactive drugs				

Other…….

- Technical use of extra renal purification : Yes □ No □
  - Indication :
  - Technique :
  - State date :
  - Number of sessions :

EVOLUTION

- PPH :
  - Diuresis : Recovery □ / Persistence of oligo-anuria □
  - Normalisation of renal function : yes □ No □
  - Blood pressure :
  - pulse :
- Complications linked to stay in ICU :
  - Nosocomial infections : yes □ No □
    - Type :
    - Germ :
    - Treatment :
  - Thromboembolic complications : yes □ No □
  - Bronchial congestion and atelectasis : yes □ No □
  - Skin and osteo articular complications : yes □ No □
  - Psychiatric complications :yes □ No □
  - Neurological : yes □ No □
- Evolution at the end of stay in ICU :

  Recovered □ Death □ Sequelae □
- Total duration of stay:

RESULTS

I. Study populations.

Total number PPH cases recorded in the maternal ICU from 2014 -2020 that meet the inclusion and exclusion criteria which were 100.

II. Patient characteristics

II.1. Age

The average age of the patients in our study was 31.55 +/- 6.0 with the youngest being 19 and the oldest being 49. The distribution by age group is shown in figure 1.

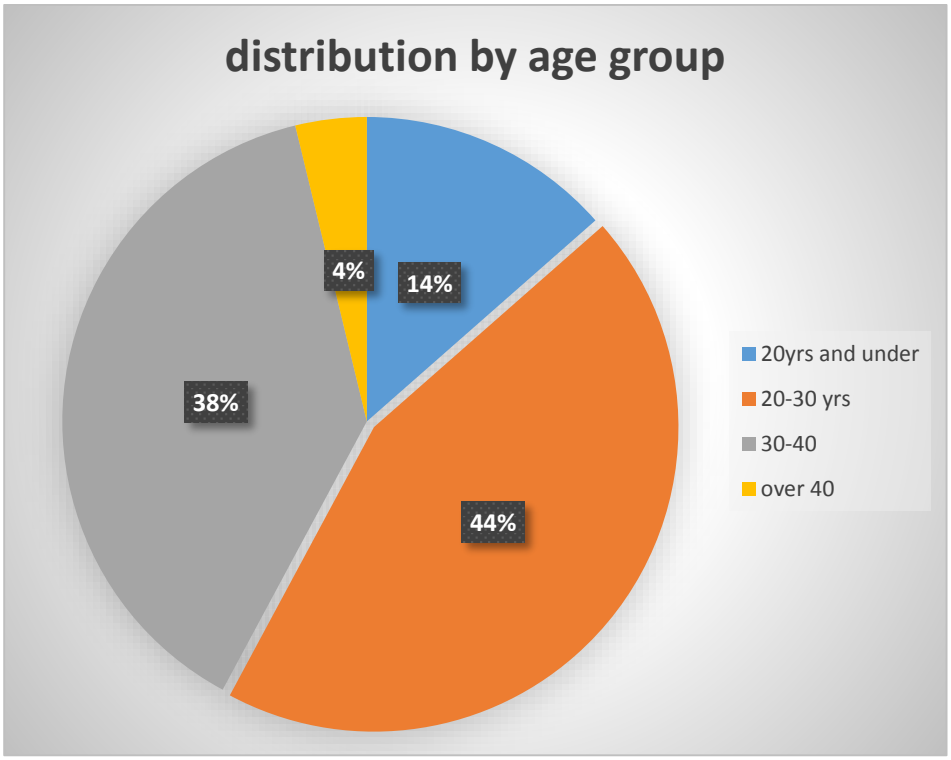

Figure 1: representation by age group of patients who presented with severe PPH.

II.2. Method of hospitalisation.

The breakdown by method of hospitalisation either on referral or self-initiated Is shown in figure 2

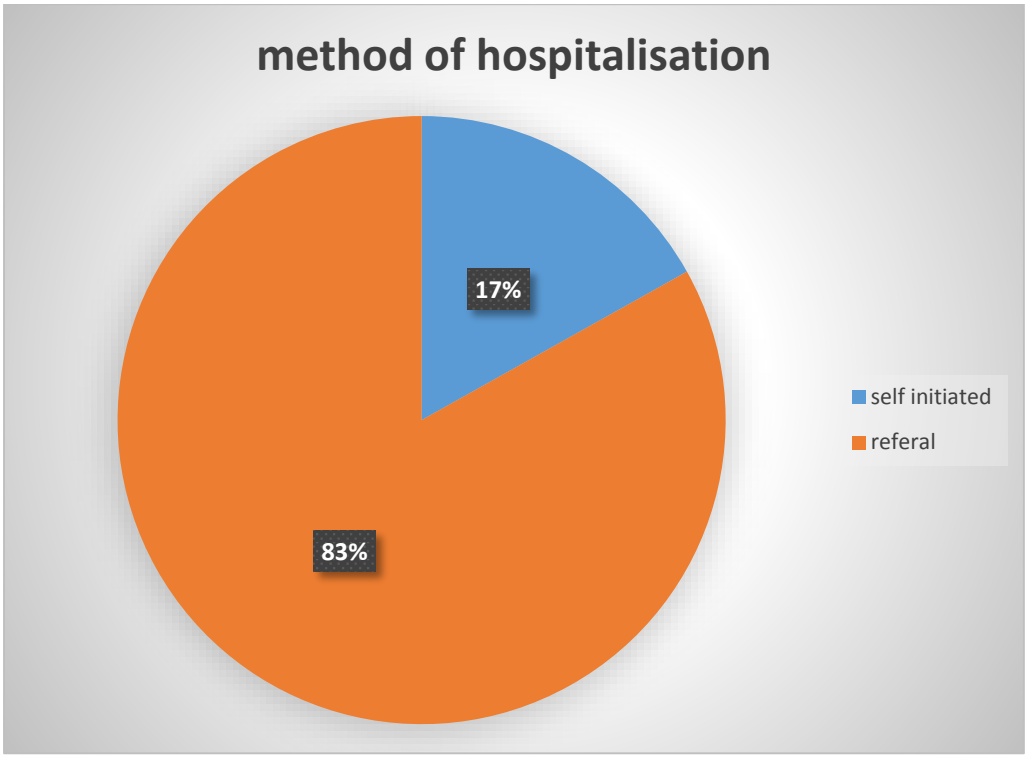

Figure 2: breakdown by method of admission either on referral or self-initiated with patients presenting PPH.

II.3. Duration of hospitalisation

Patients in our study had an average duration of hospitalisation of 3.59 days with a minimum of 1day and a maximum of 33days.

The distribution of duration of hospitalisation is shown in figure 3.

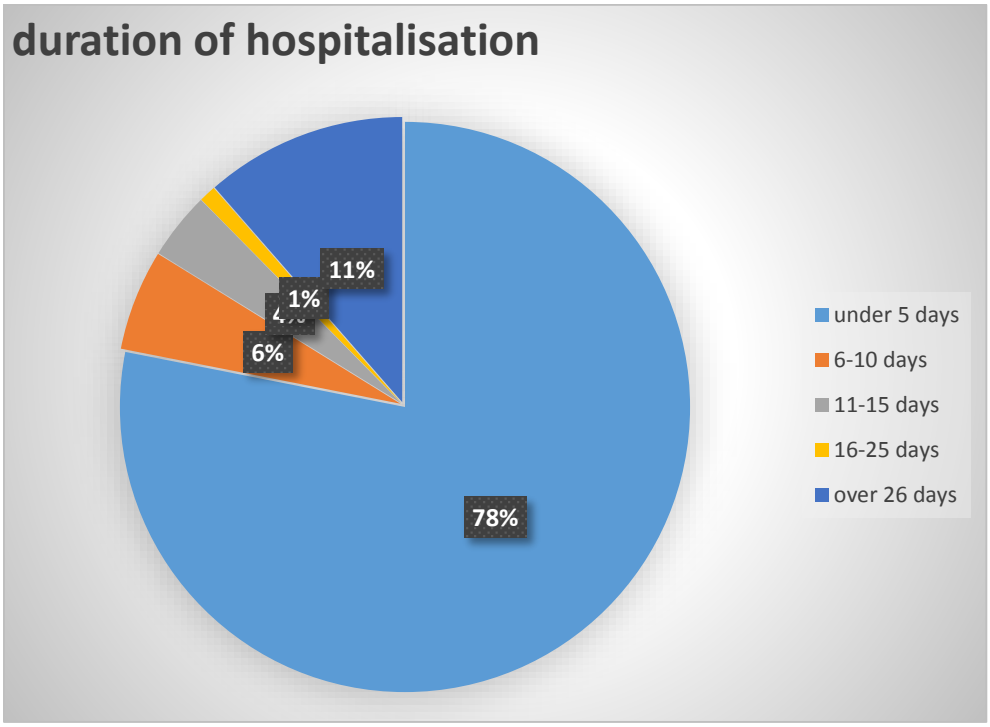

Figure 3: breakdown in duration of hospitalisation of patients who presented with PPH.

II.4. Gravidity

The average gravidity in our group of study was 3.14 with a minimum of 1 and a maximum of 9.

The distribution of patients according to gravidity is represented in fig.4

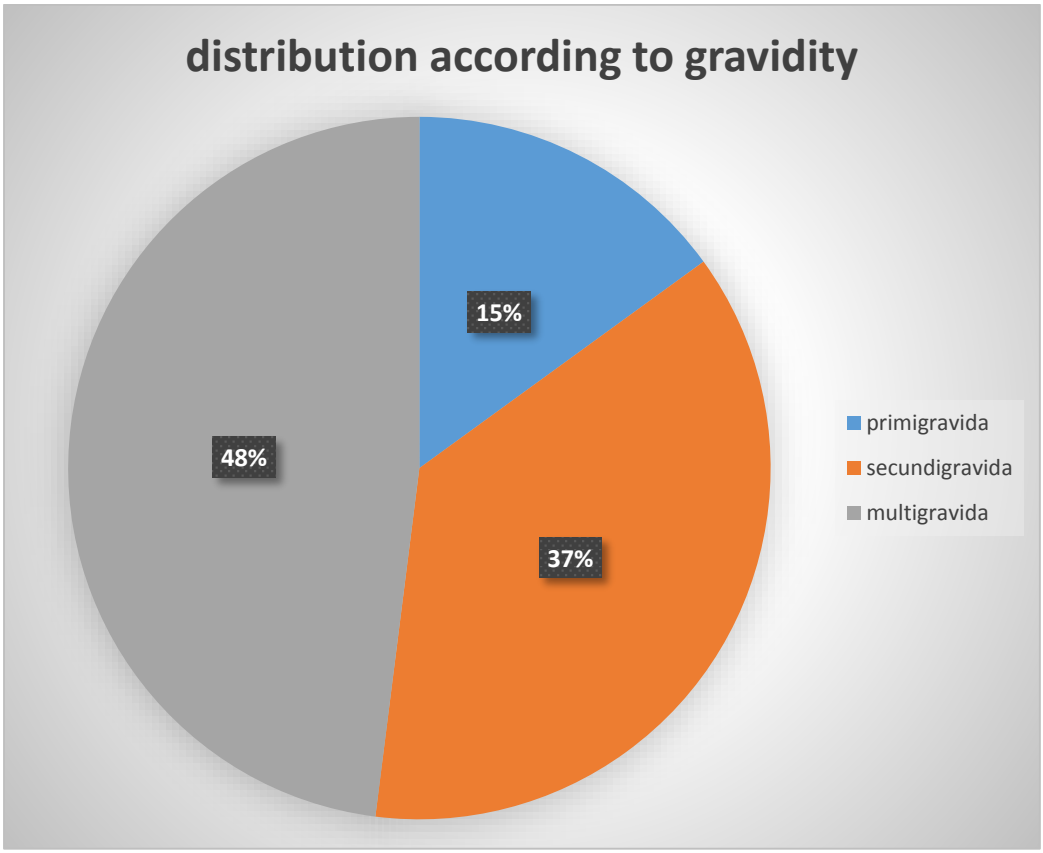

Figure 4: representation of patients who presented with PPH according to their gravidity.

II.5 Gestational age

The average gestational age in our group of study was 37.49weeks with the maximum of 42 and the minimum of 20 weeks.

The distribution of patients according to gestational age is represented by the figure 5.

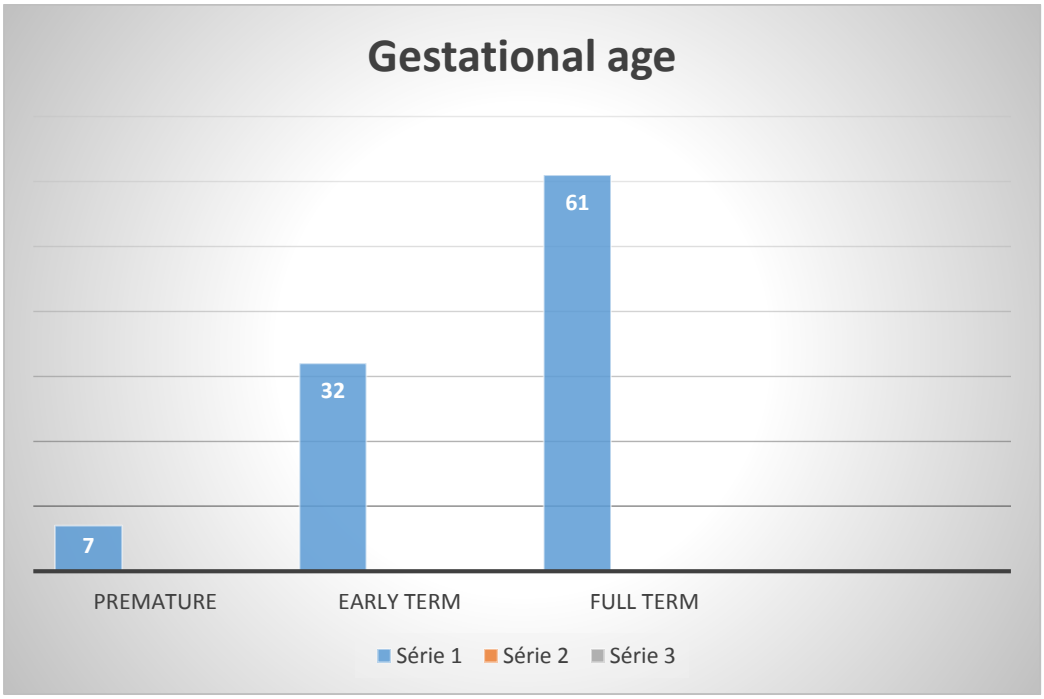

Figure 5: represents the distribution of patients who presented PPH according to gestational age.

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II.6. Antenatal surveillance

Antenatal monitoring was observed in 68% of the patients. The distribution of patients who observed anti natal monitoring is shown in figure 6.

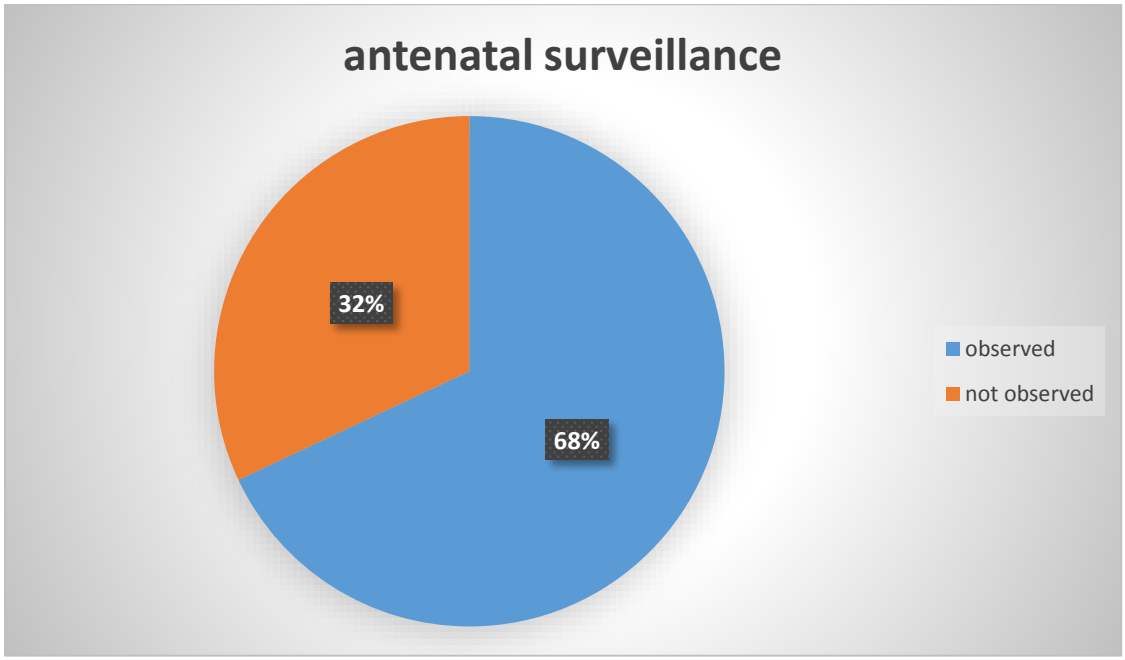


figure 6: represents the distribution of patients who presented with PPH that observed antenatal surveillance.

II.7. Obstetric history

No particular obstetric history was observed in 57% of the patients while in the rest of the 43% presented with abortion, preeclampsia, placenta abruption and still births. table 1 depicts a distribution in percentile of obstetric history in our study cohort.

Table 1: shows the distribution of obstetric history in patients who presented with PPH

Obstetrical history	Number of cases/percentages
No history	57%
c-section	16%
Abortion	8%
RPH	9%
PPH	4%
Still births	3%
Pre-eclampsia	3%

II.8. Distribution of Risk factors

The risk factors found and their percentages are shown in figure.7

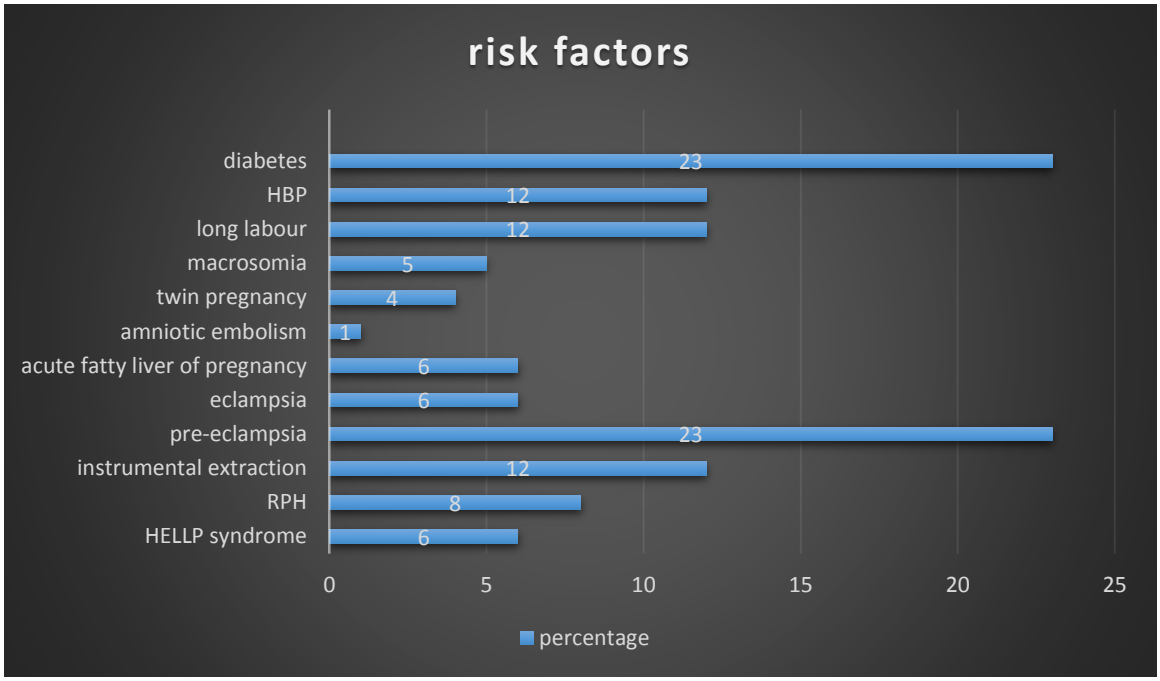


Figure 7: distribution of risk factors in patients presenting PPH.

The graph shows that the implicated risk factors are HBP and diabetes at 12% and 23% respectively, with long labour and instrumental extraction at 12% and pre-eclampsia at 23%.

II.9. Labour and delivery

9.1 Place of delivery

The breakdown of place of delivery is represented in figure 8.

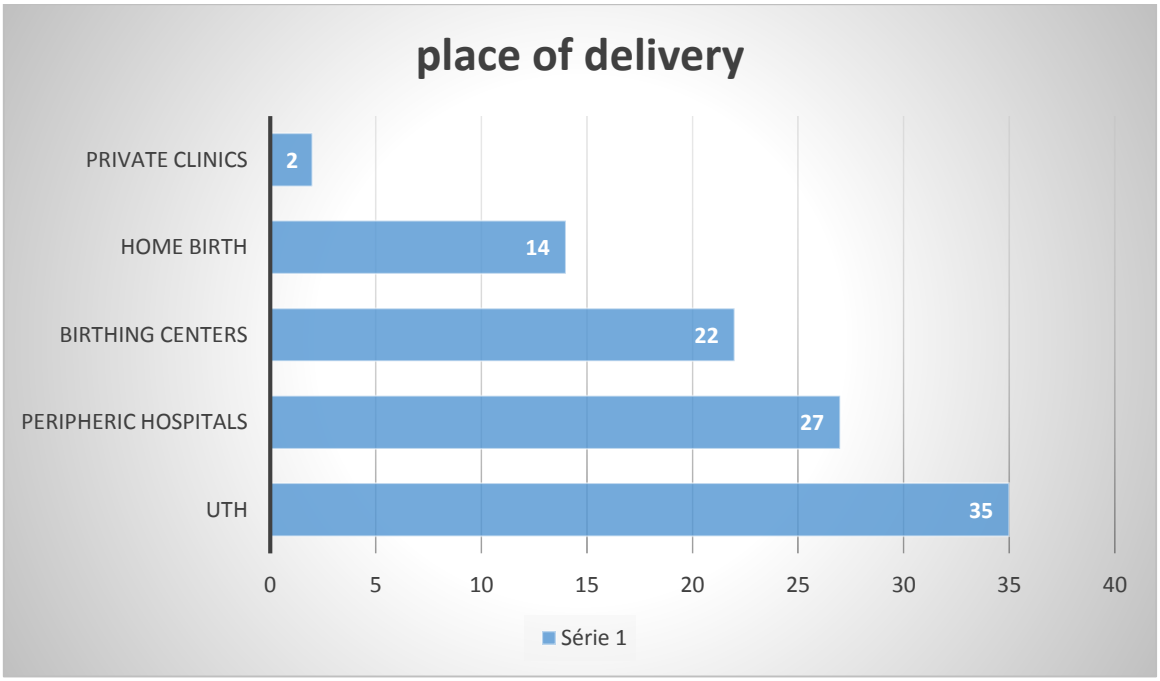


Figure 8: represents the distribution of places of delivery in patients with PPH

86% of our patients gave birth in medical facilities. We also note that 65% of cases had deliveries outside the University Teaching hospital but were later referred to the UTH for further treatment.

II.9.2 Method of delivery

The breakdown in method of delivery is illustrated in figure 9.

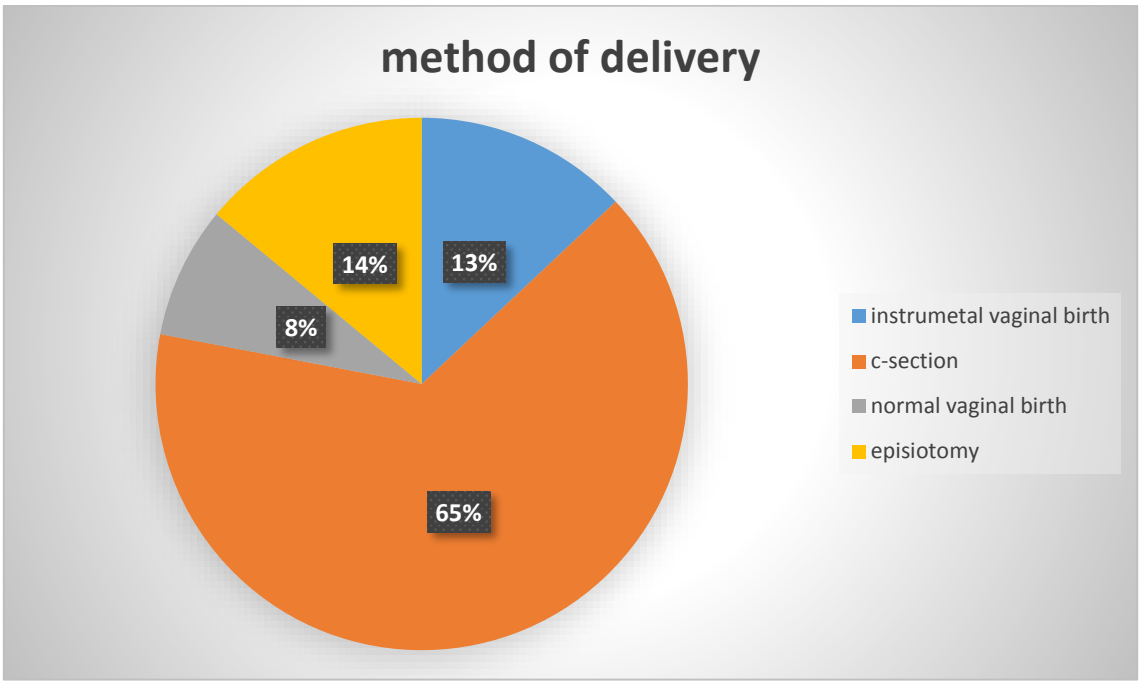


Figure 9: represents the distribution of method of delivery in patients with PPH

II.10. summary of patient's profiles

A summary of all patient profiles is illustrated in table 2:

Table 2: a summary of patients that presented severe PPH.

Average age	31.55 +/-6
Average gravidity	3.14+/- 5
Full term pregnancies	61%
Medically assisted deliveries	92 %

II.11. state of new born babies

The state of new born babies was recorded in only 96% of our patients and is illustrated in the table 3.

Table 3: state of new born babies in patients that presented severe PPH.

State of new Born	Number of cases	Percentage
Live births	48	46.08 %
Still born	29	27.84 %
Needed resuscitation upon delivery	9	8.64 %
Neo-natal death	7	6.72 %
Hospitalised in NICU	3	2.88 %

III. POSITIVE DIAGNOSIS

III.1. clinical exam

III.1.a Quantity of blood loss after delivery

The evaluation of the quantity of blood loss was done subjectively, to this effect the use of the collection bag is not normally done in delivery rooms, the quantity of blood loss was reported according to 3 categories: minimal, moderate and severe as illustrated in the figure 10.

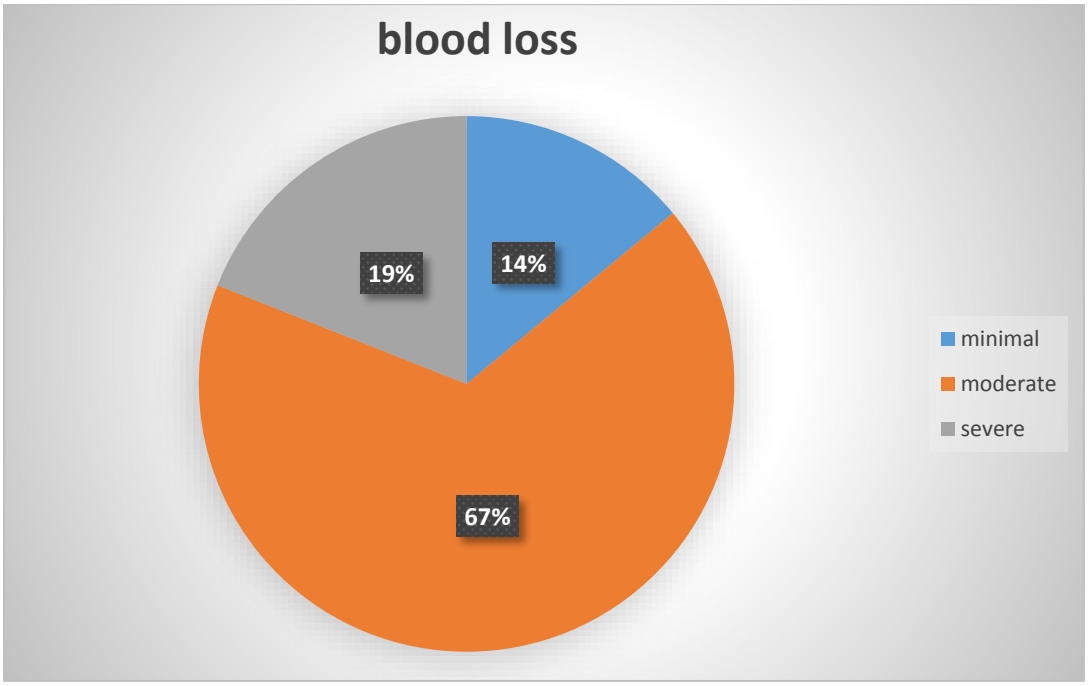


figure 10: illustrates the breakdown of the severity of blood loss in patients presenting PPH .

III.1.b. The hemodynamic status.

The evaluation of the hemodynamic effects was made at the time of diagnosis of postpartum haemorrhage, and was based on pulse, urine output, BP, heat of the extremities, pallor, as well as evaluation of consciousness. Table 4 illustrates the hemodynamic status of the patients at the time of diagnosis.

Table 4: illustrates the breakdown of the clinical characteristics of the patients that presented with PPH on admission and diagnosis.

variables	Number of cases/ average/ +/- standard deviation	%	Extremes
Breathing rate (c/min)	24.3 +/- 10.18	-	10-65
Heart rate (b/min)	103.6 +/- 19.44	-	56-140
Systolic BP (mmHg)	105.9	-	30-200
Diastolic BP (mmHg)	62.4	-	10-100
Temperature	37.8 +/- 0.99	-	35-40
Glasgow score	12+/- 1.2	-	5-15
Diuresis (ml/24hrs)	669 +/- 48.66	-	0-2200

III.2 .Laboratory results

It was noted that most patients experienced severe blood loss and had HB as low as 3g/dl with a PT as low as 16%. The kidney function was terribly altered in 8 patients who ended up needing dialysis. The fibrinogen levels were also terribly altered with levels as high as 6.45g/l and as low as 0.31 causing sever blood loss and or intra vascular disseminated coagulopathies. Table 5 gives us a breakdown of the lab work.

Table 5: illustrates the average laboratory results of patients presenting severe PPH on admission or diagnosis.

Laboratory results	Average +/- standard deviation	extremes
Haemoglobin (g/dl)	8.44 +/- 8.914	3-14.2
Fibrinogen (g/l)	2.19 +/- 1.45	0.31-6.45
Prothrombin time PT (%)	78.29 +/- 20.06	16-100
Activated cephalin time (s)	33.55 +/- 5.49	30-48.8
Uraemia (mmol/l)	0.47+/-0.458	0.07-3.46
Creatinine (mmol/l)	15.16 +/- 17.6	4-121
Kalemia (mmol/l)	4.87+/-4.3	2.9-5.8
Calcemia (mg/l)	80.06 +/- 9.1	61-109
Natremia (mmol/l)	136.61 +/- 6.3	122-152
Haematocrit (%)	30.7 +/- 7.0	18-54
White blood cells (/mm3)	20 845 +/- 17624.5	2 862-63000
Platelets (/mm3)	120.814 +/- 84.431	80-490 000
Lactates	5.67+/- 2.54	1.08-8.5
GOT(UI/l)	305.45 +/- 701	14-4014
GPT(UI/l)	150.96 +/- 353.03	5-1742
PAL (UI/L)	151.3 +/- 76.5	74-382
Total bilirubin (µmol/l)	23.36+/- 25.2	2-104

IV. Aetiological diagnosis

- Uterine atony was found in 38 patients, or 38% of cases.
- Anomaly inserted placenta were found in 21 patients, or 21% of cases, including 3 retained placentae.
- 4 placenta accreta and 14 placenta previa.
- Trauma to the genital tract were found in 29 patients, or 29% of cases including 12 uterine ruptures, 15 cervical-vaginal lesions and 2 perineal lesions.
- Finally, in 11 cases, several aetiologies were associated.
- Figure 11 shows the distribution of cases according to the aetiology of the bleeding.

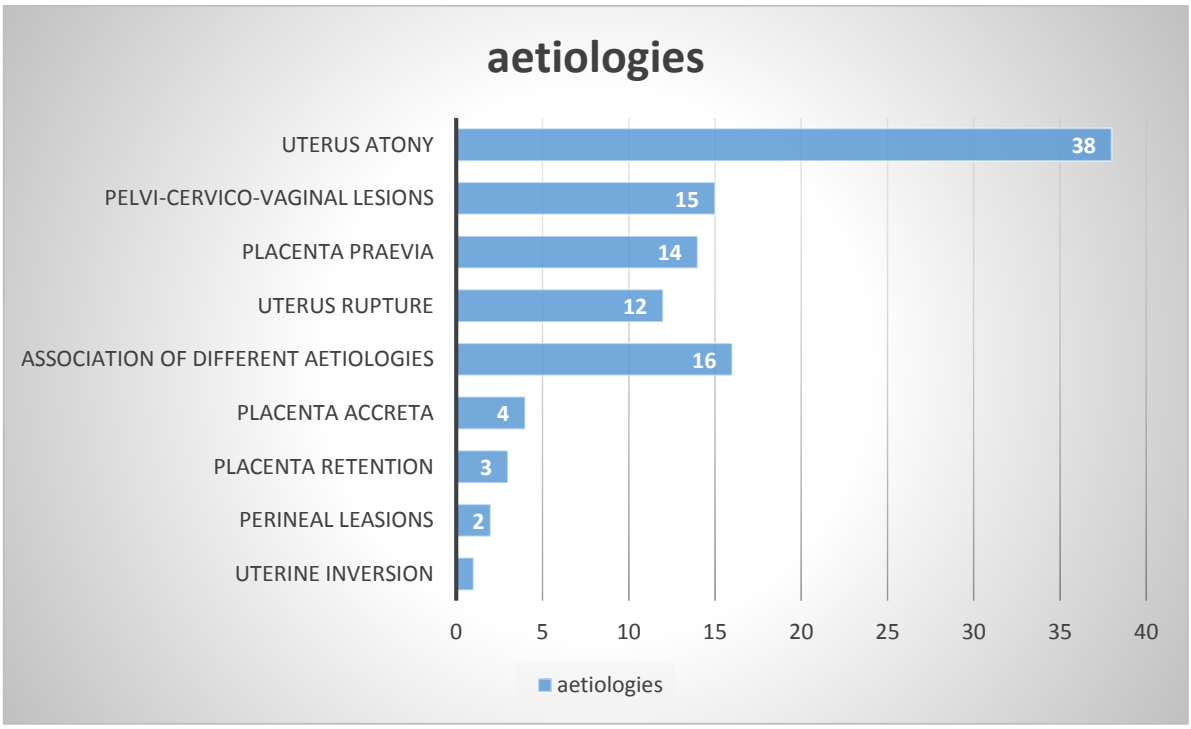


Figure 11: Breakdown by aetiologies of PPH.

Table 6 shows the different associations of aetiologies found in 16 patients

table 6: illustrates the distribution of associated aetiologies in patients that presented with PPH.

Associated aetiologies	percentage
Placenta retention + cervical lesions	8%
Placenta retention+ perineal lesions	3%
Uterus rupture + cervical-vaginal lesions	3%
Perineal lesions + cervical-vaginal lesions	2%

V. POST PARTUM HAEMORHAGE MANAGEMENT

V.1 Resuscitation measures

All of our patients benefited from the first resuscitation measures, namely:

- the taking of two peripheric Intra veinous lines.
- heart monitoring.
- oxygen therapy.
- bloodwork for assessment.
- The rest of the management is presented in the following results.

V.1.1 Stay in intensive care:

The average hospital stay was 7 days, with extremes ranging from 1 day to 33 days.

V.1.2 Invasive devices used in intensive care:

The majority of patients had at least one invasive device:

- 68% of patients were on mechanical ventilation of which 43% were admitted already intubated and 15% were intubated after hospitalisation. The average duration of this ventilation was 6 days.
- All had a urinary catheter, with an average duration of use of 3 days.
- 70% had a central venous catheter. The average duration of its use was
- of 2 days.
- 42% had an arterial catheter to measure blood pressure more accurately.

Table 7: shows the different types of invasive devices used on our patients during their hospitalisation

Type of device	Number/percentage
Tracheal intubation	16 patients -68%
Urinary catheter	24 patients- 100%
Central veinous catheter	17 patients- 70%
Arterial catheter	10 patients- 42%

V.1.3 vascular Filling

All of our patients received vascular filling by crystalloids with either normal saline or ringer's lactate.

V.1.4 vasoactive drugs

67% of our patients received vasoactive drugs either in the operating room or in the resuscitation ward. The table below shows which drugs were given and the number of patients who benefited from it. Only two (2) patients benefited from dobutamine due to cardiac insufficiency.

Table 8: vasoactive drugs administered in patients in our study cohort.

Type of drug	Number of patients/percentages
noradrenaline	56%
Dobutamine +noradrenalin	2%
Adrenalin + noradrenalin	9%

V.2 blood transfusion

89 patients or 89% received a blood transfusion.

The transfusion was done with red blood cells, fresh frozen plasma, or both and platelets.

The distribution of patients according to their transfusions is shown in Table 9.

Table 9: Distribution by transfusion status of patients with presented with severe postpartum haemorrhage.

Substance transfused	Number of cases
Not transfused	11
Red blood cells	28
Fresh frozen plasma+ red blood cells+ platelets	61

Table 10 illustrates the breakdown of the quantities of substances transfused.

Table 10: distribution by quantity of substances transfused in patients that presented with sever post-partum haemorrhage

Substance transfused	Mean+/- standard deviation	extremes
RBC pallet	3.85 +/-2.3	3-18
Fresh frozen plasma	4.5+/- 2.7	1-16
Platelets	4.45+/-2.4	1-10

V.3. Medical patient care

V.3.1. Antibiotic therapy

All of the patients in our case study received antibiotic prophylaxis based on amoxicillin and clavulanic acid.

V.3.2 Uterotonics

- Oxytocin was administered in 98% of our cases, with an average dose of 26.5 IU +/- 7 of syntocinon. With an exception of 2 (two) women who had home deliveries.
- The only Prostaglandin we have available in our ICU is misoprostol and was administered to patients either vaginally or through the rectum.
- 76% of our patients received both products except in cases where the prostaglandin was out of stock.
- Figure 12 shows the distribution of uterotonics administration

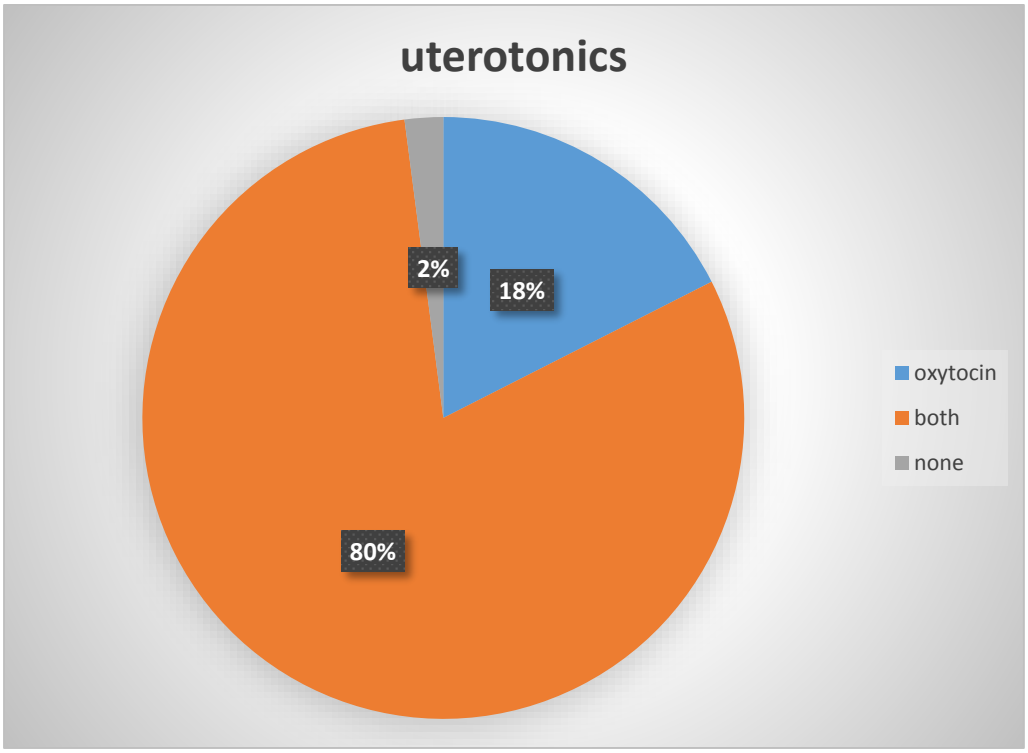


Figure 12: breakdown of administration of uterotonics in patients who presented with severe postpartum haemorrhage.

V.3.3. Tranexamic acid

- 1g of Exacyl was administered to 83% of our study population and was not administered only when out of stock.
- Tranexamic acid reduces death due to bleeding in women with post-partum haemorrhage with no major adverse effects. When used as a treatment for postpartum haemorrhage, tranexamic acid should be given as soon as possible after bleeding onset.

V.3.4 fibrinogen

32% of our patients received fibrinogen. It was administered to all who presented a fibrinogen level of <2g/l and in cases of clinical coagulopathy. This was highly dependent on its Availability.

Taking into account the high level of physiological fibrinogen levels in pregnant women, the early and rapid drop in this level in the event of PPH, the link between a fibrinogen level <2 g / L and the risk of severe PPH, it is recommended to prescribe fibrinogen supplementation if the fibrinogen level is <2 g / L during worsening PPH. [74]

V.3.5 haemodialysis and Hemofiltration

kidney failure was noted in 28 patients of which extra renal purification was initiated in 8 patients. It consisted of intermittent haemodialysis of six (6) patients and only two (2) patients underwent hemofiltration secondary to acute kidney failure with one (1) patient that benefited from both procedures. The mean number of (Renal Replacement Therapy) RRT sessions was 3.8 sessions/patient (range 1-9 sessions). The main indications for RRT were:

- Metabolic acidosis (pH≤ 7.15) in 3 cases.
- Hyperkalaemia (≥ 7 mmol/l) in 3 cases.
- fluid overload in 2 cases

V.3.6. other medical treatments

Table 11 shows a distribution of the medical treatments received by our patients all through their admission from the delivery room, operating room and the intensive care unit.

Table 11: breakdown of medication received by patients who had PPH.

medication	Number of patients
Anti-hypertensive	26
Analgesic	100
Anticoagulation	46
Diuretics	23
Gastric protection	57

V.4. Obstetrical patient care

V.4.1. delivery of placenta.

The table below outlines the distribution of different forms of placenta delivery received by the patients in our case study.

Table 12: breakdown of placenta delivery in patients with severe PPH.

Type of delivery	Percentage/number of cases
spontaneous	4
Active management	61
Manual removal	35

V.4.2. Other non-surgical obstetrical technics

72% of our patients benefitted from a uterus revision while 45% got a uterus massage.

60% got a vulva pelvic exam. Most of the patients who benefitted from at least two of the above-mentioned technics.

Table 13: breakdown of non-surgical obstetrical technics performed on patients with severe PPH.

Technic	Percentage/number
Uterine massage	45%
Uterine revision	13%
Vulva pelvic exam	60%

V.5. Surgical patient care.

V.5.1. hysterectomy

- A total of 56 hysterectomies were performed.

-24 of our patents received immediate hysterectomies while 32 were performed after failure of haemostasis.

-13 caused by uterus atony 8 caused by accreta and percreta placenta insertion only 3 caused by uterus rupture.

Figure 8 illustrates the percentages of patients that received immediate hysterectomies and the aetiologies associated.

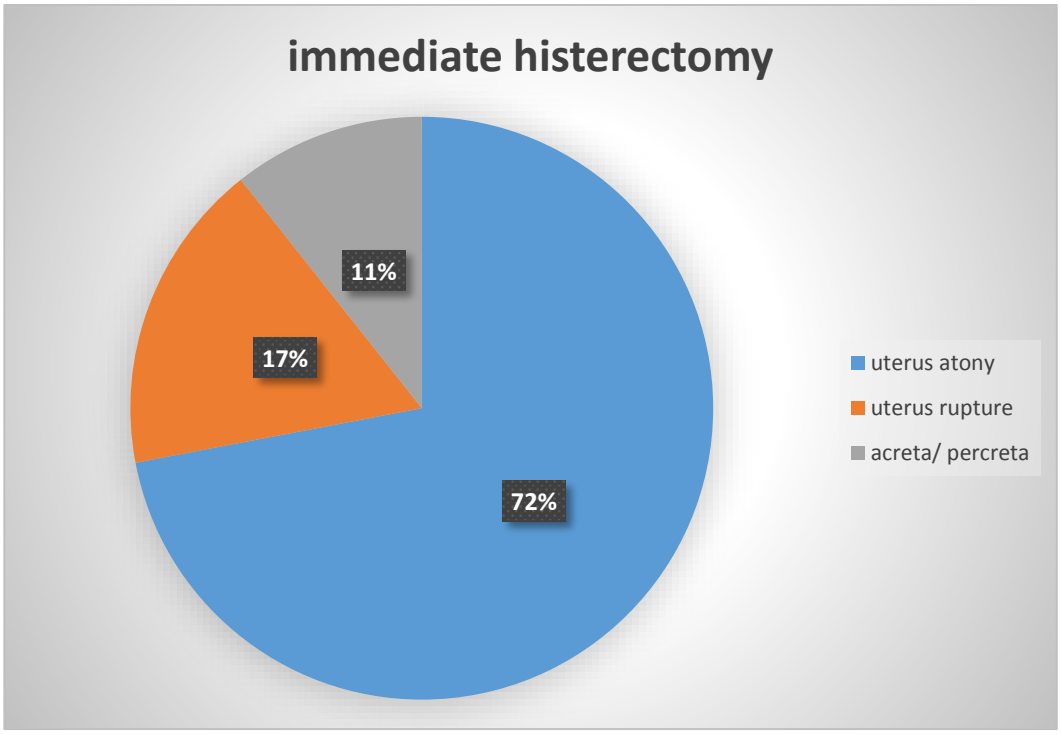


Figure 13: breakdown of patients that received immediate hysterectomies after PPH.

V.5.2. *other surgical technics performed.*

Most of the patients in our case study underwent more than one surgical procedure after an unsuccessful procedure. For example, 32% of the hysterectomies performed were done after the failure of a b-lynch or hypogastric ligature. Below is an illustration of the cumulation of all surgical procedures performed in total.

Table 14: breakdown of all surgical procedures performed on patients with severe PPH coagulopathies.

Surgery performed	Percentage /number of patients
Hysterectomy	56
B-lynch	16
Hypogastric ligation	35
Triple ligation	16
Uterus suture	6
Suture or vaginal tears	11

VI. Maternal morbidity

There was a total of 46 complicated cases figure 14 represents the different complications found.

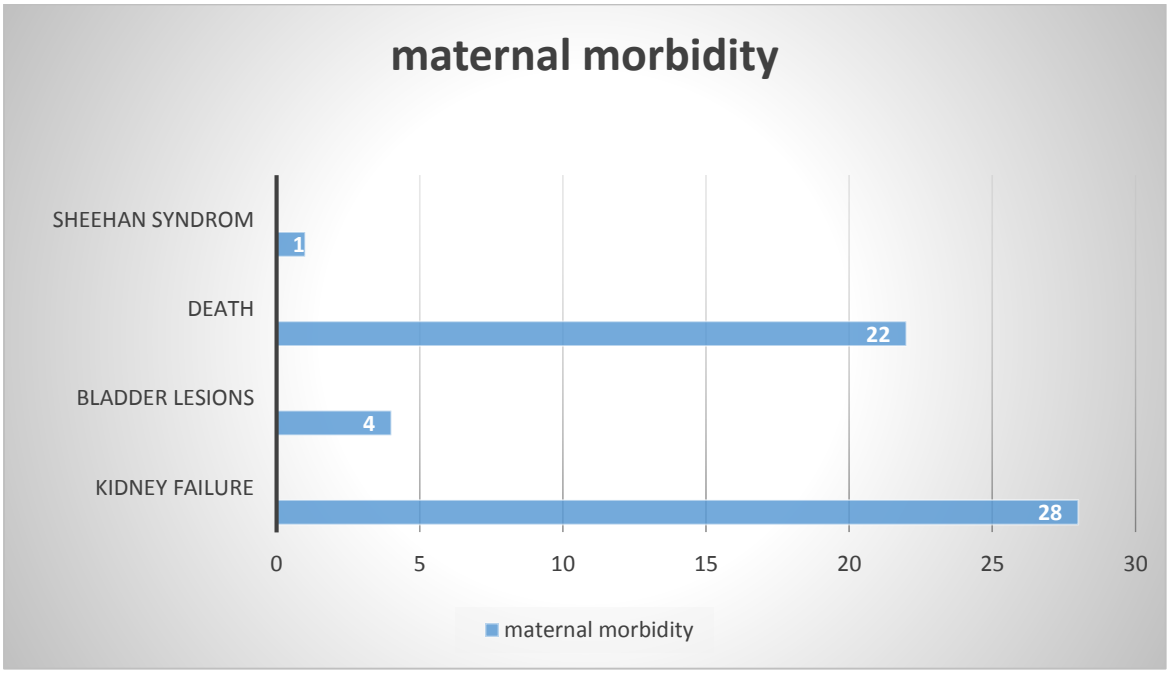


Figure 14: breakdown of maternal morbidity in patients with PPH.

Graph illustrates that we have one (1) case of amniotic embolism and one (1) case of Sheehan's syndrome. With the highest morbidity being secondary to kidney failure.

VII. Maternal mortality

A total of 22 deaths were recorded. figure 15 represents the number of deaths related to each aetiology in our case study.

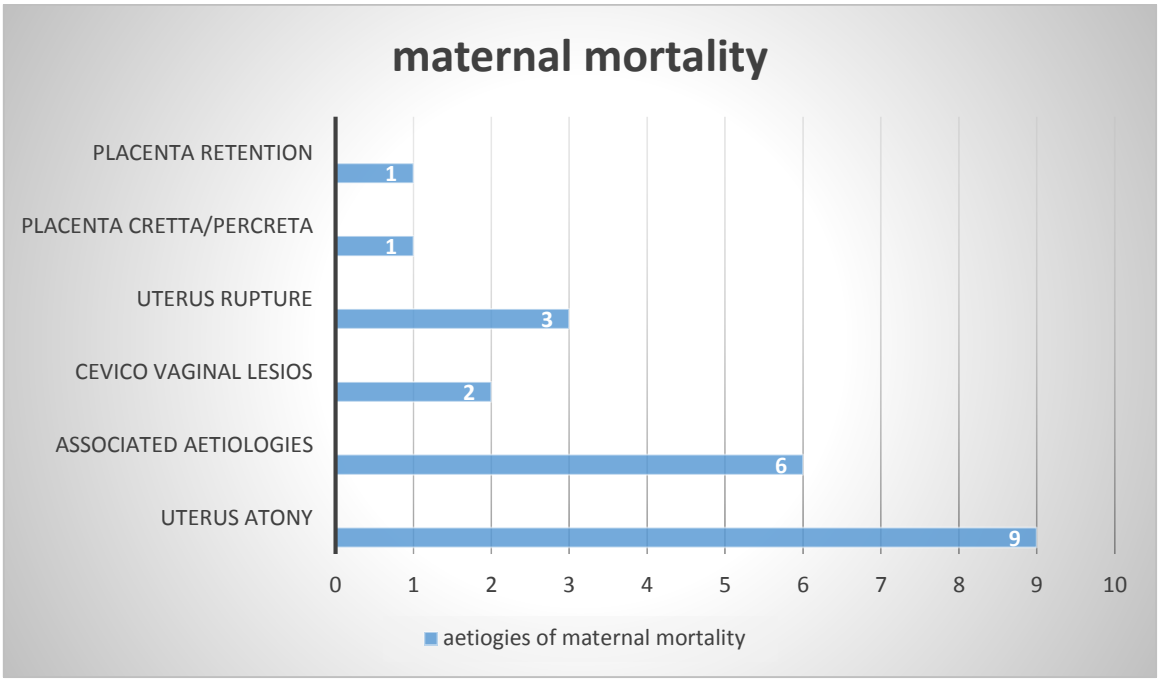


Figure 15: breakdown of maternal mortality in relation to sever PPH aetiologies.

VIII. coagulopathies in PPH

Coagulopathy refers to an abnormality in the blood coagulation system that Increases the tendency for bleeding and may be due to hereditary or acquired factors.

In the context of our study, coagulopathy is most likely to arise as a consequence of massive PPH and hence, would be 'acquired'. This occurs due to the consumption of clotting factors or due to the dilutional effects of massive blood loss on clotting factors, platelets and fibrinogen ('washout phenomenon').

Massive PPH may also occur, albeit less commonly, in the context of a patient predisposed to bleeding by an underlying coagulopathy (e.g., von Willebrand's disease, abnormally functioning platelets or patients receiving treatment with anticoagulants) [6].

Acquired coagulopathy is likely once 2L of the blood volume has been lost; this equates to an incidence record of 23% as recorded by journal of obstetric anaesthesiology. [7] no heredity was noted in our study cohort.

VIII.1. Epidemiology

From our study cohort of 100 patients 24 patients fit the below-mentioned parameters of coagulopathies secondary to post-partum haemorrhage outside of or in addition to obstetric cause.

The inclusion criteria for coagulopathy were:

i) Patients that presented with a PT >1.5 and/or an aPTT >1.5

ii) Fibrinogen levels <2

iii) Clinical evidence of coagulopathy

Below is a pie chart illustrating the percentages of patients presenting with PPH without coagulopathy and those who presented with coagulopathy.

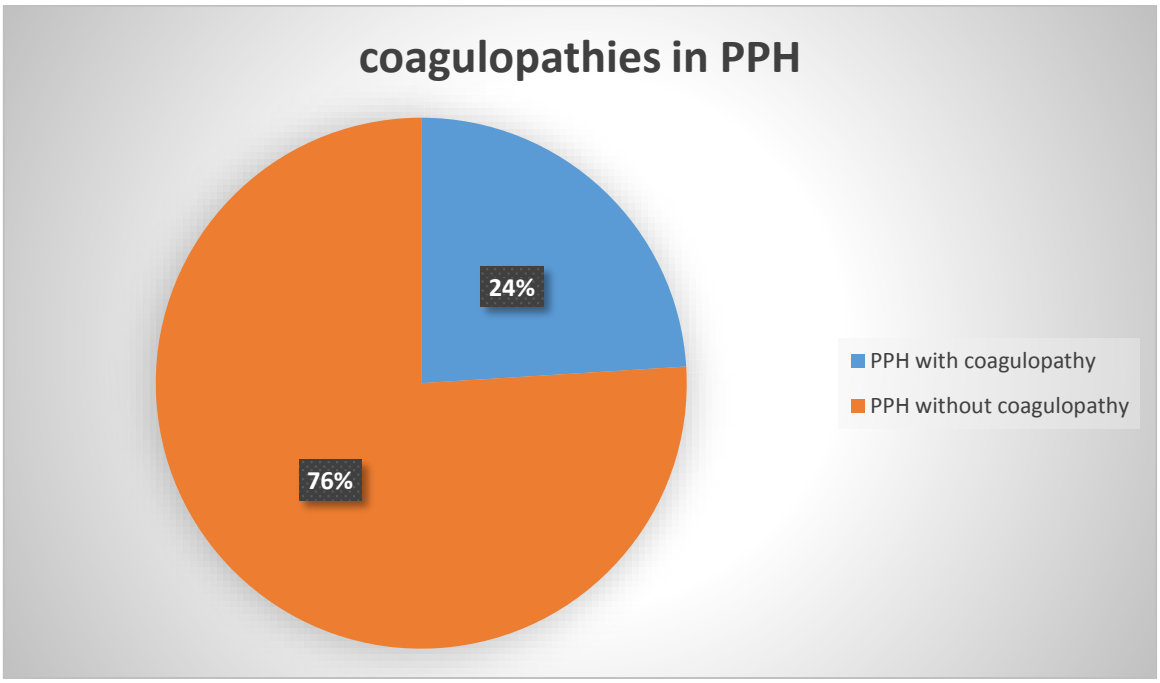


Figure 16: percentage of patients who presented with coagulopathy among those who had PPH.

VIII.1.1. Risk factors and aetiologies.

The following is a table showing the distribution of risk factors the 24 patients presented with some patients presented with more than 1 risk factor

Table 15: risk factors from patients who presented with coagulopathies secondary to PPH.

Risk factors	Number / percentage
Placenta abruption	9 - 37.5%
HELLP syndrome	6 - 25%
Fatty liver disease	4 - 16.7%
Massive bleeding >2l	9 - 37.5%
Amniotic embolism	1 - 4.1%

VIII.1.2. Gravidity:

The average gravida from our study cohort was 4.2 with a minimum of 1 and a maximum of 6. In WHO recommendations, high multigravida is still considered a risk factor for bleeding.[3]

VIII.1.3 Gestational age:

The average gestational age in our stud group was 38.5 weeks with the minimum of 35 weeks and a maximum of 42 weeks.

VIII.1.4 method of delivery

Out of the 24 patients in our study cohort 18 gave birth through c-section while the rest of the 6 were delivered vaginally of which all were instrumental extractions.

VIII.2. PATIENTS CHARATERISTICS

VII.2.1 clinical symptoms,

clinical symptoms of patients that presented with coagulopathy is variable, it's represented essentially by: pallor, tachycardia, polypnea, hypotension and alteration of consciousness.

Table 16: clinical characteristics of patients that presented with coagulopathies.

variables	Number of cases/ percentages	extremes
Breathing rate (c/min)	28.5 +/- 11.4	10-50
Heart rate (b/min)	115.7 +/- 16.3	56-140
Systolic BP (mmHg)	105	Undetectable-200
Diastolic BP (mmHg)	62.4	Undetectable-70
Glasgow score	12+/- 1.2	3-12

VIII.2.2 Biological tests

Table 17: the average laboratory results in our study cohort

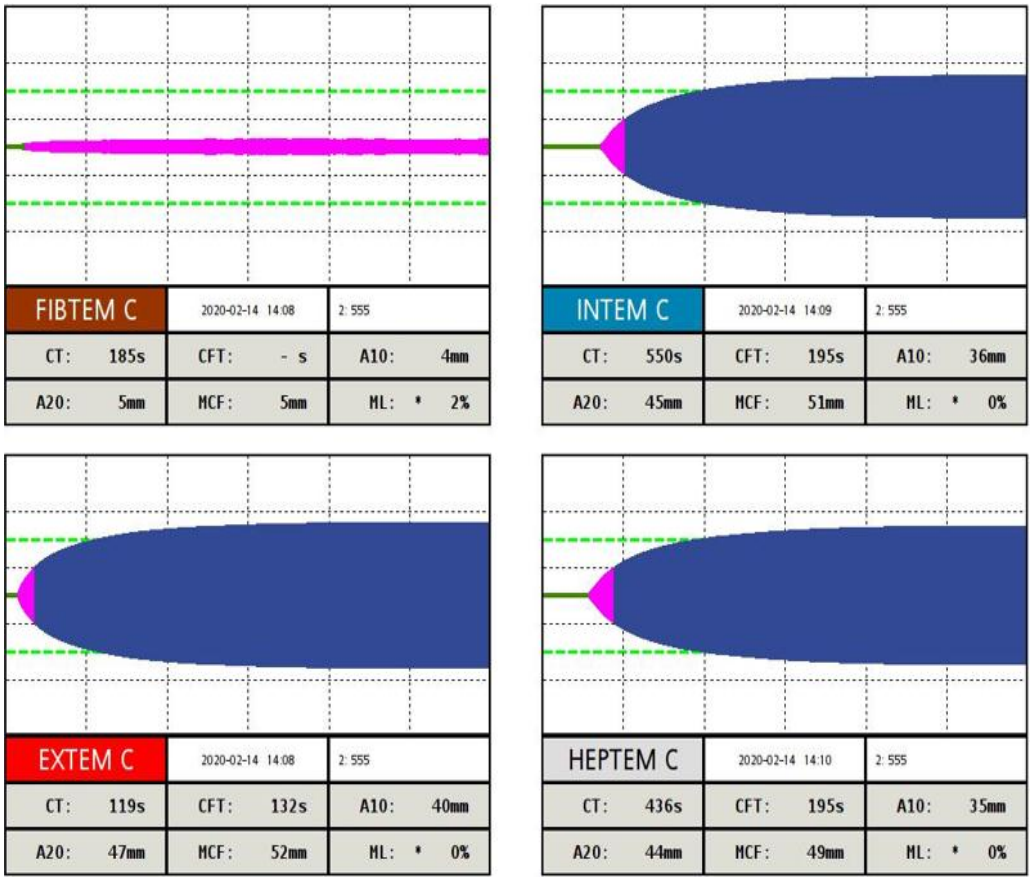
Laboratory results	Average +/- standard deviation	extremes
PT (%)	53 +/- 22.45	16- 80
aPPT (s)	47 +/- 10.6	30- 48.8
Fibrinogen (g/l)	1,5 +/- 0.45	0.31-2.8
Platelets (/mm3)	90.34 +/- 75.63	10 000-230 000

VIII.2.3 point of care testing (POCT): viscoelastic haemostasis assay

VHAs analyze the viscoelastic properties of whole blood and charts the entire process of clot formation from clot initiation through termination to fibrinolysis. In this way, VHAs have an advantage over common coagulation tests (CCTs) in that they assess the cumulative contribution of all components of the blood throughout the entire formation of a clot. [8]

since 2019 our ICU has benefitted from POC testing based on thromboelastometry ROTEM® below are 5 cases that were performed in our ICU.

Case 1: diagnosis of coagulopathy



Coagulopathy secondary to SHAG

Thromboelastometry results:

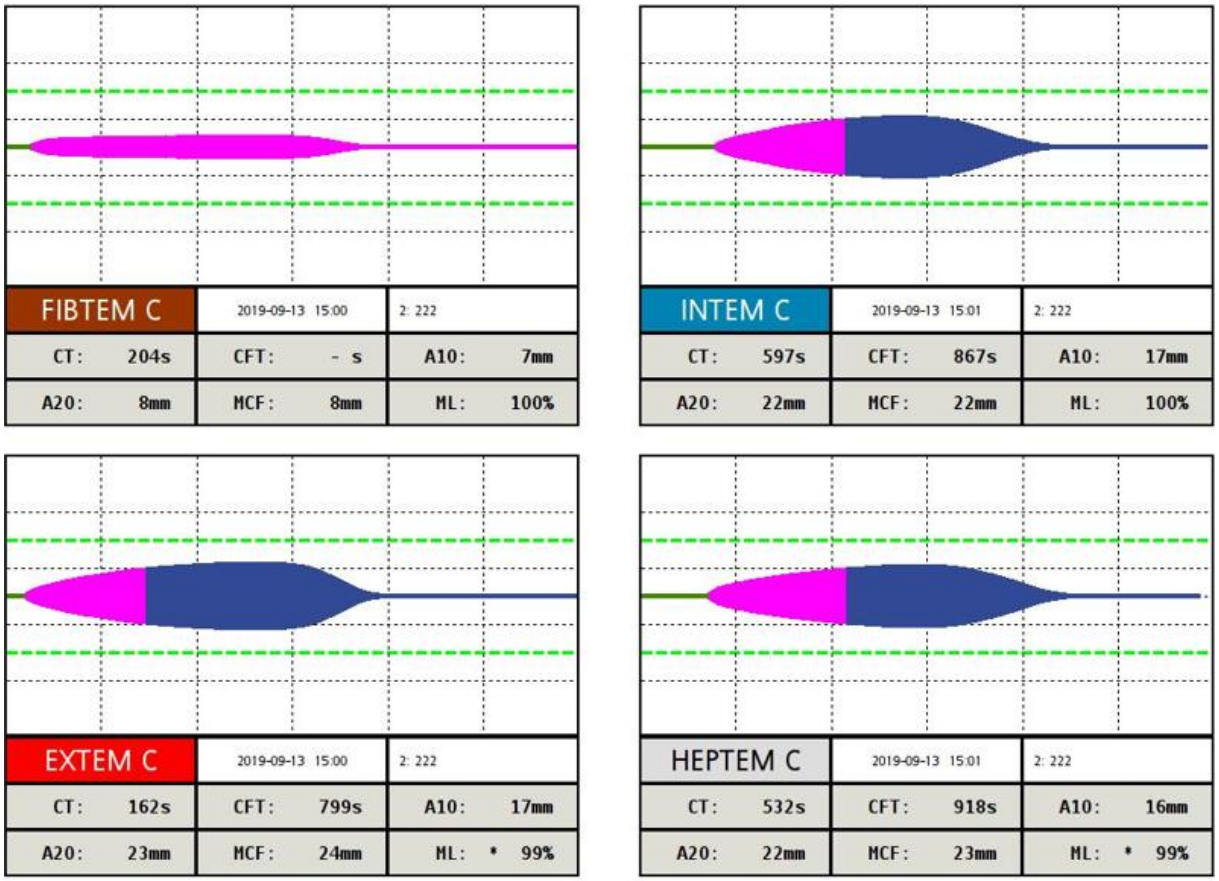
- prolonged CT in EXTEM 119 s (NR: 38-79) and INTEM 550 s (NR: 100-240).
- Amplitude of A10: below normal range in FIBTEM A10: 4 mm (NR: 7-23 mm) and in
  EXTEM A10: 40 mm (NR: 43-65 mm)

Conclusion: Deficit in fibrinogen and coagulation factors.

Management: transfusion of FFP and fibrinogen. After that, if EXTEM A 10 and FIBTEM A

10amplitudes are respectively low and normal: indication to transfuse platelets

Case 2: diagnosis of coagulopathy



Massive PPH referred from another structure

Case summary: massive PPH referred from a peripheral medical structure

Thromboelastometry results:

- prolonged CT in both EXTEM 162 s (NR: 38-79) and INTEM 597 s (NR: 100-240).
- Amplitude of MCF: low in both FIBTEM A10: 8 mm (NR: 9-25 mm) and EXTEM: 24 mm (NR: 50-72 mm).
- Maximum lysis in INTEM: 100%

Conclusion: Deficit in coagulation factors, fibrinogen, probably platelets and hyperfibrinolysis

Management: transfusion of FFP, fibrinogen, platelets, tranexamic acid.

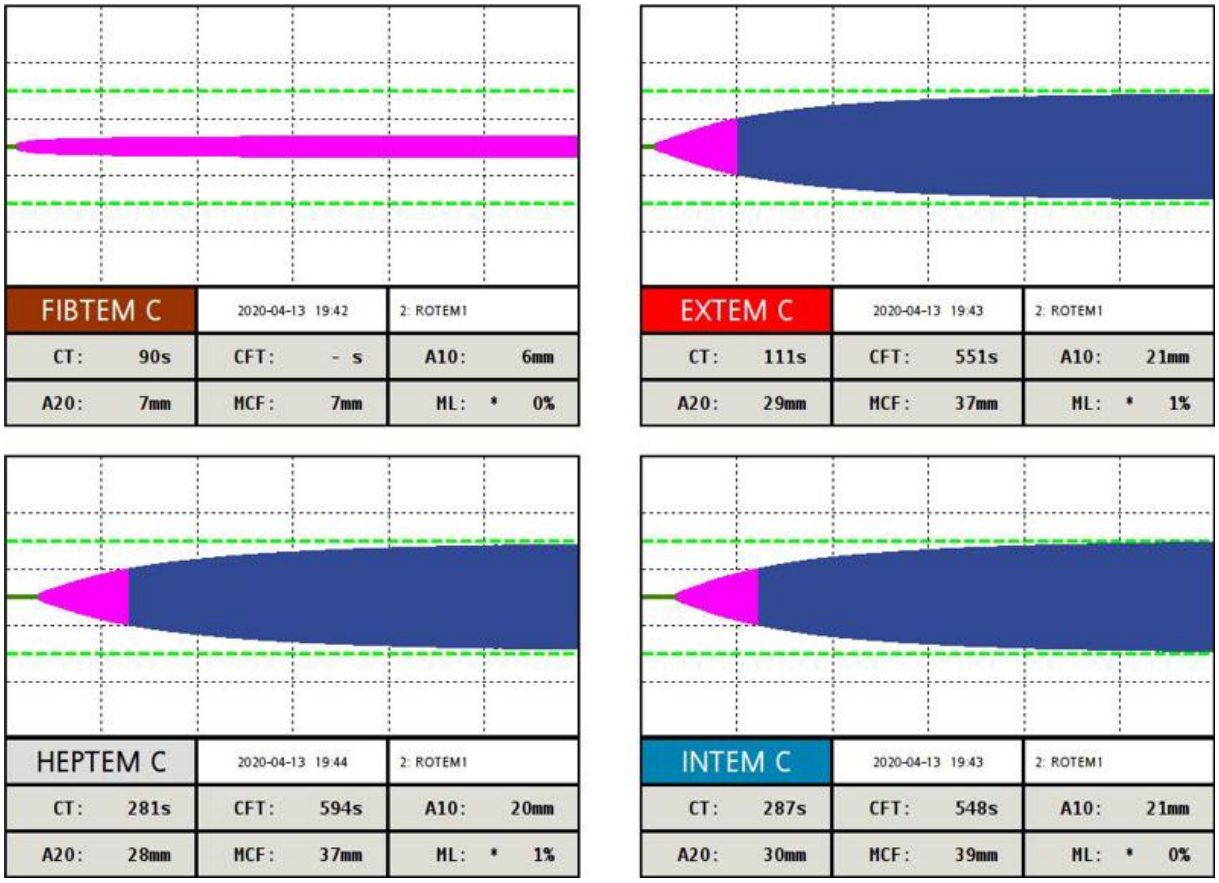
Case 3: management of coagulopathy

Retroplacental hematoma + HELLP syndrome:

Surgical management: hypogastric ligature + B lynch:

Transfusion: 7 CP, 5 PFC, 3g of fibrinogen

Thromboelastometry 1:



Thromboelastometry 1 results:

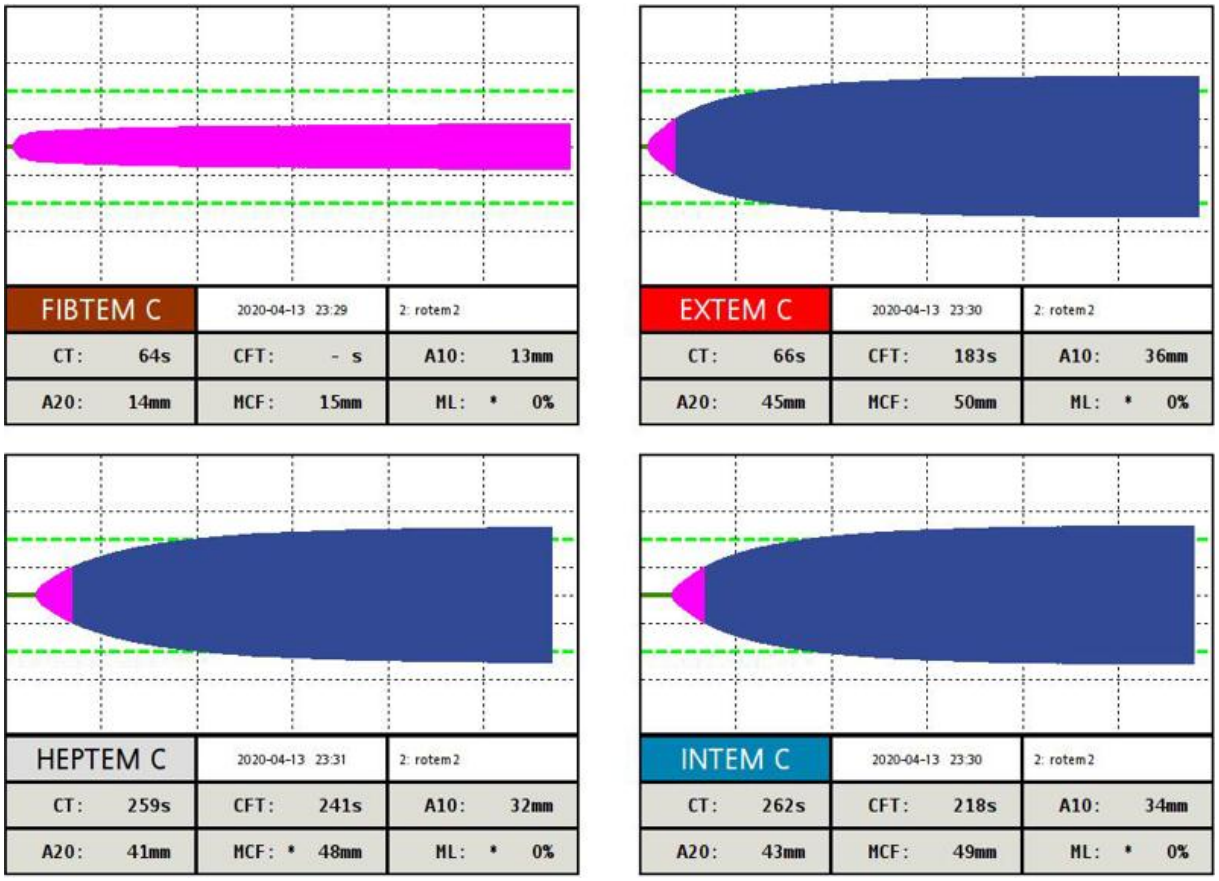
- prolonged CT in EXTEM 111 s (NR: 38-79) and INTEM 287 s (NR: 100-240).
- Amplitude of A10: below normal range in FIBTEM A10: 6 mm (NR: 7-23 mm) and
  in EXTEM A10: 21 mm (NR: 43-65 mm)

Conclusion: Deficit in fibrinogen, platelets (thrombopenia in blood assay) and coagulation

factors.

Management: transfusion of 5 CP, 3 FFP and 3g of fibrinogen. After that, if EXTEM A 10

and FIBTEM A10amplitudes are respectively low and normal: indication to transfuse platelets



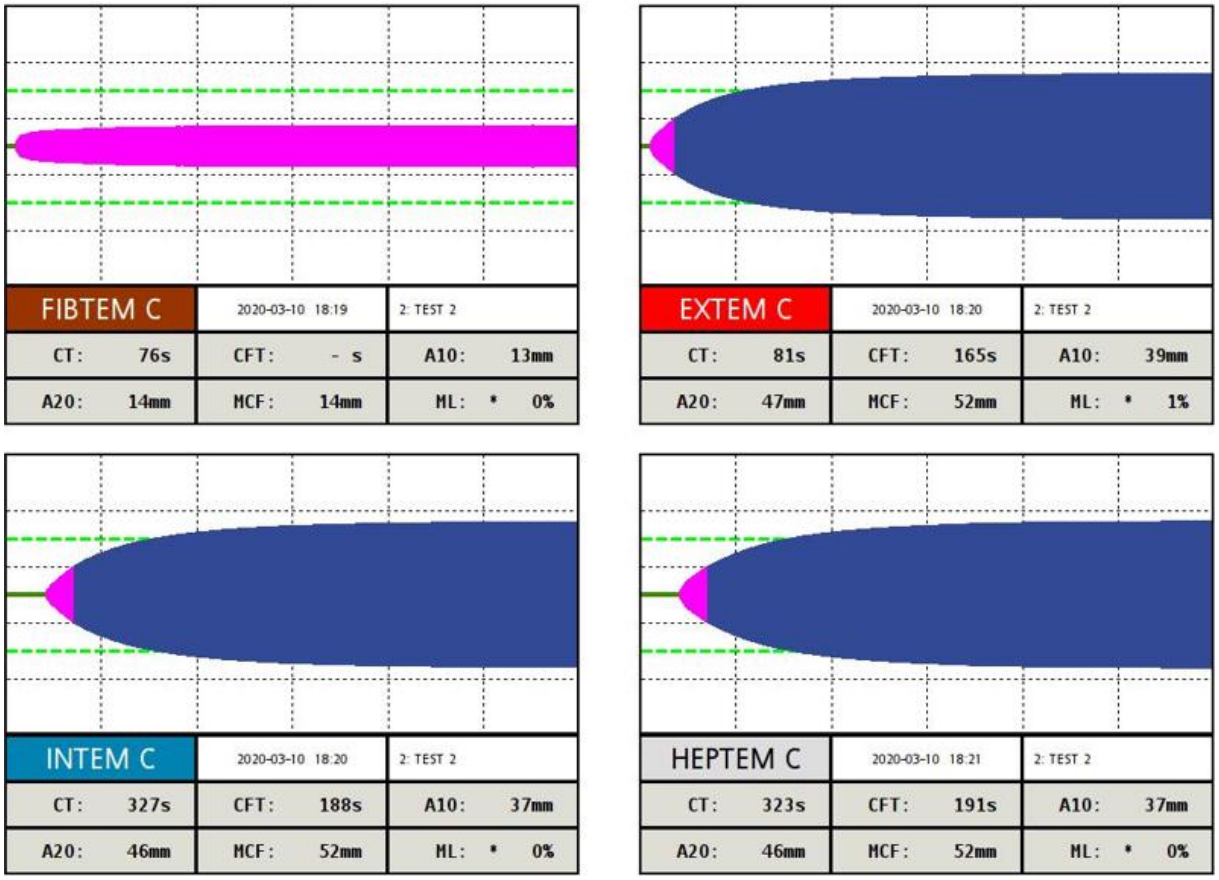
Thromboelastometry 2 results :

- Normal CT in EXTEM 66 s (NR: 38-79) and prolonged CT IN INTEM 262 s and HEPTEM
  259 s (NR: 100-240).
- Amplitude of A10 : normal in FIBTEM A10: 13 mm (NR: 7-23 mm) and low in EXTEM
  A10: 36 mm (NR: 43-65 mm)

Conclusion: Deficit in platelets and mild deficit in coagulation factors.

Management: transfusion of 3 CP, 2 FFP

Case 4: management of coagulopathy



Case summary: Coagulopathy secondary to SHAG and PPH (uterine atonia)

Management: Arteriography+ initial massive transfusion RBC+ FPP + platelets + fibrinogen

Thromboelastometry results:

- prolonged CT in EXTEM 81 s (NR: 38-79) and INTEM 327 s (NR: 100-240).
- Amplitude of A10: normal in FIBTEM A10: 13 mm (NR: 7-23 mm) and diminished in
  EXTEM A10: 39 mm (NR: 43-65 mm)

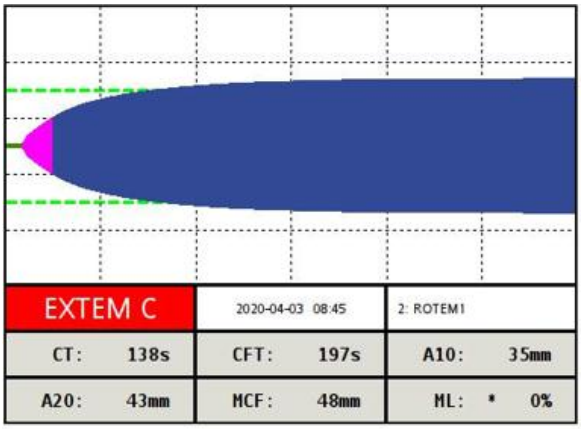
Conclusion: Deficit in platelet and coagulation factors.

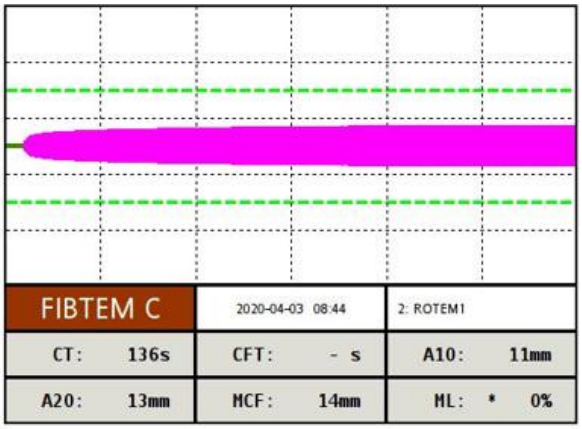
Management: transfusion of FFP and platelets.

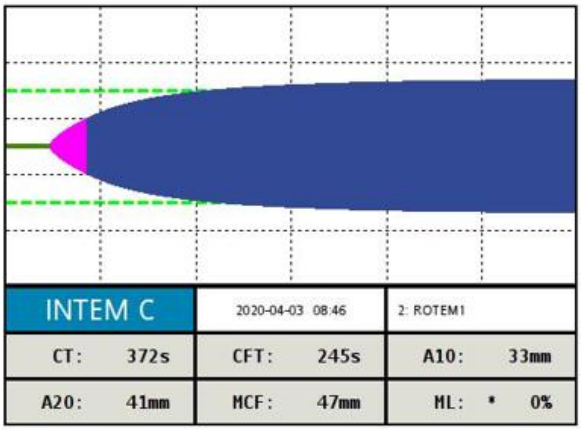
Case 5: management of coagulopathy

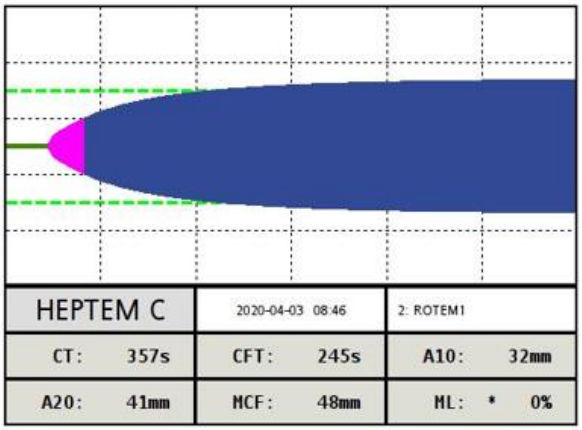
Retroplacental hematoma + HELLP syndrome:
Surgical management: hysterectomy and abdominal packing.
Massive transfusion: 10 platelets, 8 FPP, 6g of fibrinogen, tranexamic acid 1g

Thromboelastometry 1 :









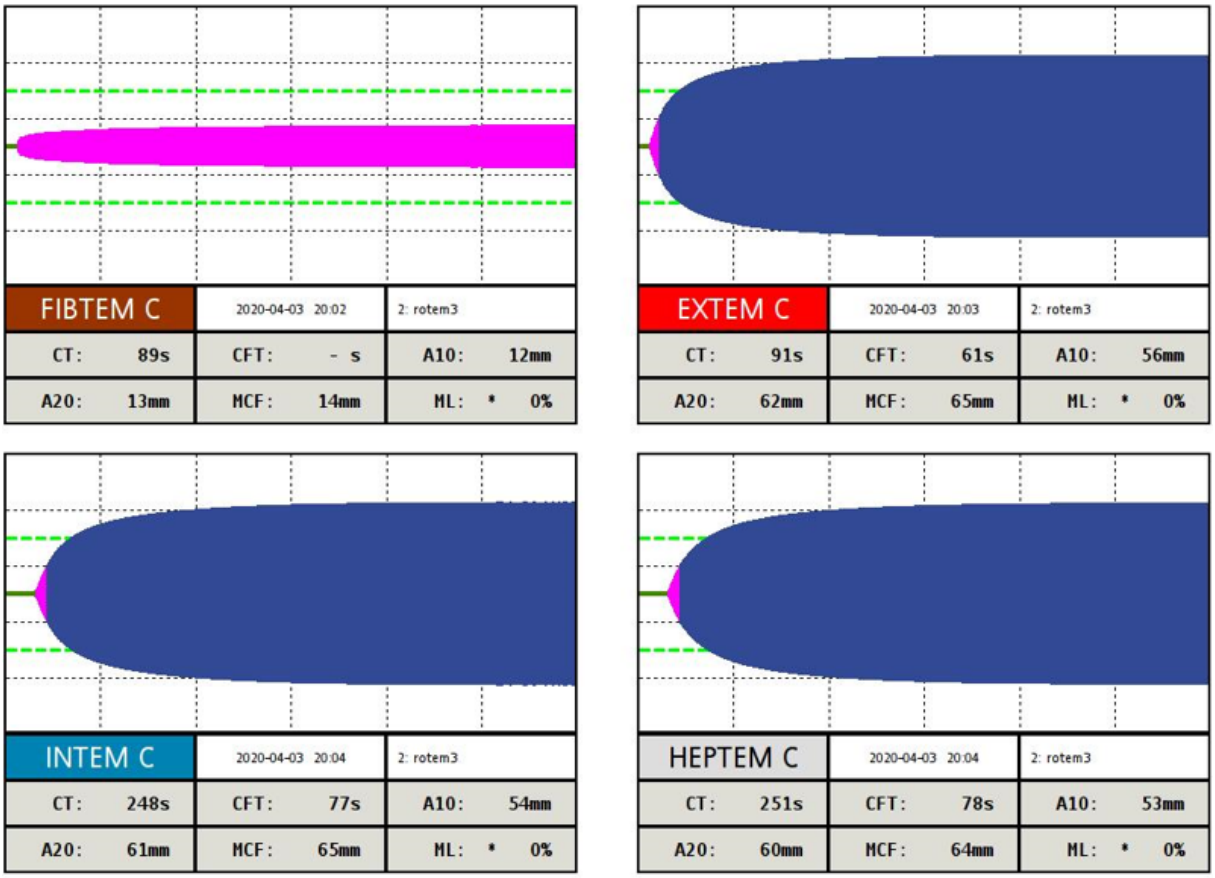
- prolonged CT in both EXTEM 138 s (NR: 38-79) and INTEM 372 s (NR: 100-240).
- Normal FIBTEM A10: 11 mm (NR: 9-25 mm) and low EXTEM A10: 35 mm (NR: 50-72 mm).
- Maximum lysis in all channels: 0%

Conclusion: Deficit in coagulation factors, low platelet count

Normal fibrinolysis and fibrinogen level

Management: transfusion of FFP and platelets

Thromboelastometry2:



- prolonged CT in both EXTEM 91 s (NR: 38-79) and INTEM 248 s (NR: 100-240).
- Normal FIBTEM A10: 12 mm (NR: 9-25 mm) and normal EXTEM A10: 56 mm (NR: 50-72 mm).
- Maximum lysis in all channels: 0%

Conclusion: Deficit in coagulation factors. No Fibrinogen or platelets deficit and normal fibrinolysis.

Management: transfusion of FFP.

VIII Management of coagulopathy in PPH

VIII.3.1 Blood Transfusion.

All 24 patients (100%) benefited from transfusion of labile blood products as illustrated in the table below:

Table 18: illustrates the distribution of labile blood products in coagulopathy patients.

Substance transfused	Percentage / number of patients
Fresh frozen plasma + RBC	11 patients- 45.8%
FFP+RBC+PLT	13 patients - 54.2%

All patients were transfused with fresh frozen plasma.

Table below illustrates the breakdown of quantities of products transfused.

Table 19: distribution by quantity of substance in patients that presents PPH coagulopathy

Substance transfused	Mean +/- standard deviation	extremes
Fresh frozen plasma	6.1 +/- 2.3	3-18
Red blood cells	6.45+/- 2.7	1- 16
platelets	6.5+/- 2.4	1- 10

VIII.3.2 Fibrinogen

17 patients or 70.8% received fibrinogen concentrate but its administration to patients was highly dependent on its availability in stock at the ICU.

VIII.3.3 Tranexamic acid

All patients received tranexamic acid as follows:

- 14 patients or 58.3% received 2 doses of 1g each during their hospitalisation
- 10 patients or 41.7% only received one dose of 1g.

VIII.3.4 Factor vii

Only 3 patients or 12.5% received factor vii.

VIII.3.5 Patient mortality

We had a total of 9 deaths or 37.5% reported in our study.

DISCUSSION

I) Background and pathophysiology

I.1 definition

PPH is defined by the world health organisation (WHO) [3] as blood loss >500 ml in the first 24 hours following childbirth, often developing minutes after childbirth, but can also be secondary if occurring after the first 24 hours up to 6 weeks postpartum [5]. For women undergoing caesarean section the cut-off is higher and usually defined as >1,000 ml [9]. However, not all countries or studies agree on these definitions, creating not only confusion but also conflicting results [77]. Further inconsistency is found when it comes to defining severe PPH, where there is variation in not only the cut-off used to define it, but also no uniform agreement of whether to use the term severe, major or moderate PPH (78,10,11). In our study PPH between 500-1000 ml was classified as moderate and 1000-2000ml was classified as major while anything >2000ml was quantified as severe. Estimation of blood loss can be assessed in many ways depending on the equipment available. Visual estimation is the easiest method, but also the method that is most inaccurate as large quantities of blood loss are often underestimated and small quantities of blood loss overestimated compared to blood collection bags or weighing of drapes etc [12,5,13.]

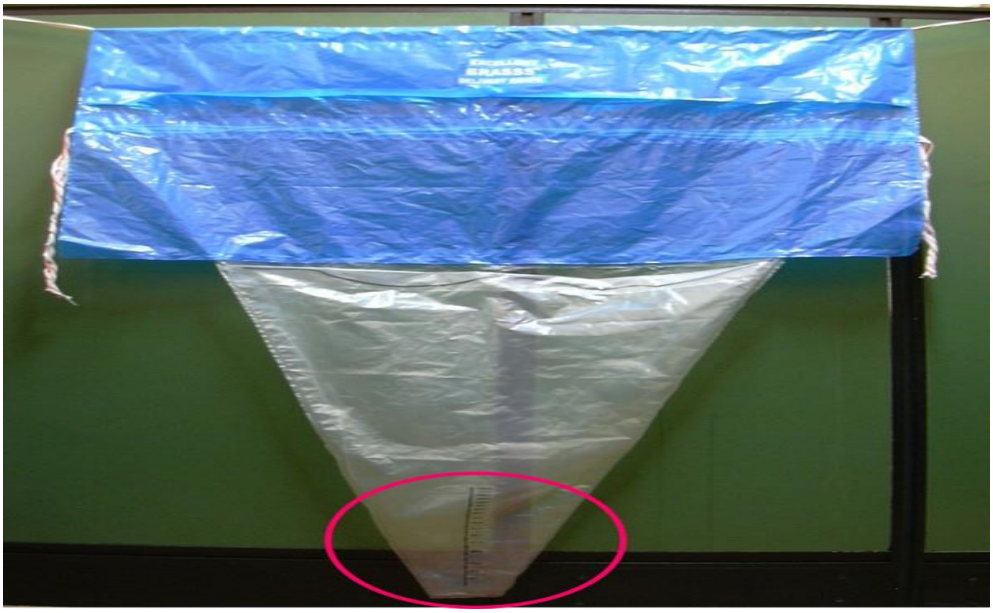


Image 1: blood collection bag [13]

I.2 Pathophysiology of Haemostasis in pregnancy and postpartum

Haemostasis is the process that maintains equilibrium between coagulation and fluidity of blood in damaged blood vessels through the actions of the coagulation cascade, platelets, and fibrinolysis [14,15]. The purpose of the coagulation cascade is to stop bleeding by forming a clot, through a cascade of processes initiated after the exposure of tissue factor primarily after vascular damage [16,17]. The coagulation system is comprised of clotting factors in an inactive state that become activated through a cascade of processes, and culminates with conversion of large amounts of thrombin from prothrombin. Thrombin converts fibrinogen into fibrin fibres, which together with activated platelets and von Willebrand factor create the blood clot [15,18]. Fibrinogen is a glycoprotein synthesized in the liver and is indispensable in formation of the clot not only through conversion to fibrin fibres but also for platelet aggregation. [19] There are several regulators of the coagulation cascade including the anticoagulation factors: antithrombin, protein C, and protein S that limit the formation of clots in healthy vessels [46,48]. In addition, simultaneous activation of fibrinolysis dissolves the clot in a highly regulated process, preventing excessive clot formation [17,18].

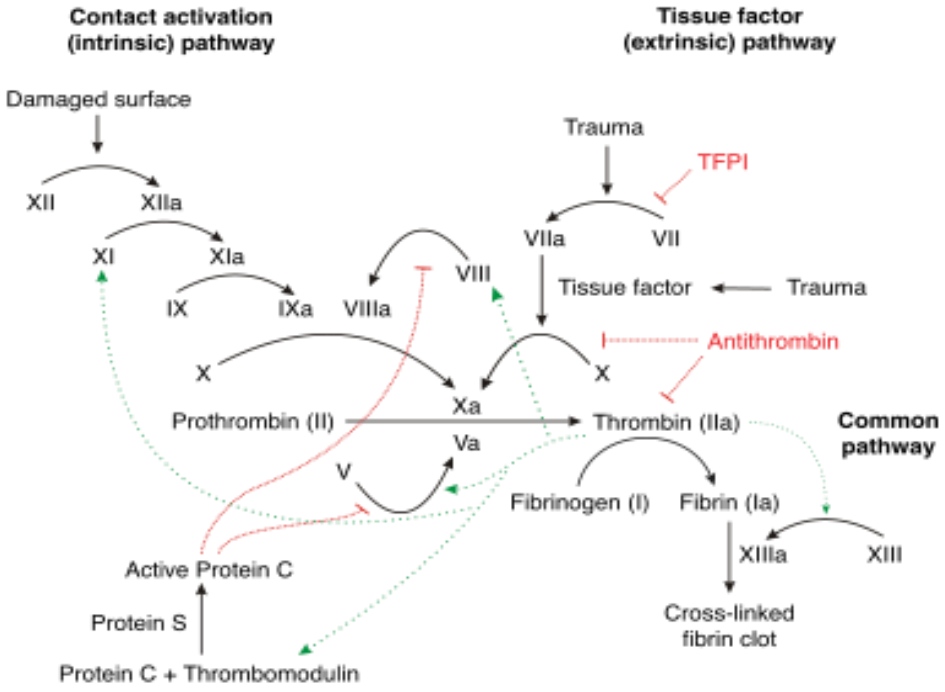


Image 2: coagulation cascade [20]

During pregnancy blood volume and coagulation increase while anticoagulants and fibrinolysis decrease, all part of the prophylactic measures to prepare for blood loss and placental separation after childbirth [14,17]. This change in haemostasis involves a rise in some of the coagulation factors including prothrombin, fibrinogen, and von Willebrand factor, but also a decrease in platelet count due to haemodilution and presumed consumption at the placental site [14,21,22]. However, this hypercoagulable state in pregnancy leads to an up to six-fold increase in the risk of thromboembolic complications including pulmonary embolisms and deep vein thrombosis [22,23]. Additional increase in coagulation factors including fibrinogen takes place during labour and delivery. Coagulation factors are activated through release of abundant amounts of tissue factor upon placental separation leading to formation of clots. Increased levels of fibrinogen and platelets postpartum are also a result of inflammation [14]. An unimpaired coagulation system will together with

sufficient contraction of the uterus result in minimal blood loss after delivery [14,21,22]. However, a high consumption of coagulation factors and platelets in formation of clots at the placental site can potentially lead to depletion if haemorrhage is ongoing [22,24]. Under normal circumstances coagulation factors remain high the first few days after delivery with fibrinolysis rising to normal levels within 1-2 days postpartum and normal coagulation attained within 4-6weeks postpartum.

Coagulopathy should be considered early on in the events of progressing PPH, with simultaneous focus on both transfusions and surgical control as neither can stand alone [25,26]. As the rate of transfusion in obstetrics is relatively low at 0.5-2.0%, research into the optimal ratio of RBCs, FFP and PLTs is scarce [27,28-30]. A few retrospective studies have shown that a high FFP:RBC ratio was associated with a reduced risk of interventions and a higher success rate of hysterectomy, but none of the studies were in relation to PPH requiring massive transfusion [31,32]. The methods used to monitor coagulopathy in severe PPH are the same as in other patients with severe haemorrhage. The WHO guideline for PPH recommends traditional laboratory tests including platelet count, international normalized ratio (INR), activated partial thromboplastin time (APTT) and fibrinogen early on in the course of events, or if available point-of-care viscoelastic assays [33]. Laboratory tests do not give rapid results, and the haemostasis of the patient can have changed substantially before it is possible to react to the results [34]. It is therefore of great importance to be continuously aware of formation of clots in the operating field.

II) Epidemiology of PPH

II.1 incidence

Table 13 summarizes the different incidences found in the literature reported in the study by different diverse case studies worldwide [4]

Table 20: The various incidences found in the literature reported in the study by Deneux-t et al. [4]

study	country	year	Incidence of PPH	Incidence of severe PPH
Althabe et al	Argentina	2005	10.8%	1.9%
Deneux-T et al	France	2006	6.4%	1.6%
Scottish confidential audit of severe maternal morbidity	Scotland	2011	-	0.6%
Caroli et al	International	2006	10.6%	3.0%
Calvert et al	international	2009	10.8%	2.8%

Because our study is retrospective and descriptive, we were unable to calculate the incidence. And the total number of births was not clearly recorded from 2014-2020 at the CHU Hassan II hospital. We only got 128 cases of which 100 had records that could be used and analysed.

II.2. Age

The mother's age is recognized as one of the factors most linked to maternal mortality, regardless of parity. When studied by increasing age group, the frequency of death from PPH follows exactly the same trend as the frequency of death from other causes [3].

Table 14 summarizes a comparison of female all-cause mortality versus postpartum haemorrhage by age in the United States (per 100,000 births). The 95% confidence interval is given in square brackets. [3]

Table 21: Comparison of Female All-Cause Mortality vs. Postpartum Haemorrhage by Age in the United States of America

Age	Female all-cause mortality (100 000)	RR [CI 95]	PPH mortality	RR [CI 95]
-20	7.2	1.1 [0.97-1.3]	0.8	1.0 [0.7-1.4]
20-24	6.5	(Referent rate)	0.8	(Referent rate)
25-29	7.1	1.2 [1.1-1.3]	1.2	1.6 [1.2-1.9]
30-34	11.8	1.8 [1.6-2.0]	2.1	2.8 [2.3-3.6]
35-39	23.0	3.6 [3.1-4.1]	4	5.2 [4.0-6.6]
40-49	55.9	8.6 [7.1-10.5]	10	12.9 [9.2-17.9]

The average age in our study is 31.55 years +/- 6.0, this agrees with the data in the literature which were 30.2 years +/- 4.8 according to F. Reyal [35] and 33.2 years according to G. Ducarme [36].

II.3. Gravidity

In more recent studies carried out in countries with a high level of resources, great multigravidity is generally no longer noted because of its rarity, and it is primigravida that is now identified as a risk factor for PPH [4].

In WHO recommendations, high multigravida is still considered a risk factor for bleeding. [3]

Table 22: Comparison of the mean Gravidity with data from the literature.

study	Mean Gravidity
Ducarme et al [94]	2.4
Reyal et al [93]	1.8 +/- 1.14
m. lahlou et al [99]	2.8+/- 1.2
Our study	3.14 +/- 1,5

II.4. Place of birth

The rate of medicalised deliveries reached a total 86% in our series, which corresponds to the rate given by the Ministry of Health and which was 72.7% in 2011 [5].

Of which 65% of cases gave birth outside the UTH in rural health centres and birthing clinics and were referred to the UTH for further management of PPH. This can be explained by the difference in socio-economic levels and by a lack of infrastructure in rural areas allowing transport to an adequate health structure.

II.5.antenatal surveillance

In Morocco, the Ministry of health has set an objective in its 2012-2016 plan of action to increase the rate of prenatal consultations from 77% to 90%. [5]

In our study, we found that only 32% of patients were followed up during their pregnancies, this remains extremely low and may be closely linked to PPH due to the lack of screening for high-risk pregnancies.

II.6. Term of pregnancy

In our series, delivery took place at term in 61% of cases. *Reyal et al* found a significant number of premature births with a frequency of 36% [35].

But according to *Decargues*, gestational age does not seem to have an impact on the occurrence of PPH [2].

II.7. risk factors

- The time from the delivery of the baby to the delivery of the placenta is known as the third stage of labour [37]. The uterus will under normal circumstances contract and expel the placenta within 10 minutes [38-40], efficiently cutting off the blood flow to the placenta [9]. The placenta will in some circumstances need manual removal if it is not delivered spontaneously. If the duration of the third stage of labour exceeds 30 minutes there is an increased risk of PPH [37,41,42].
- Recent studies have questioned the 30-minute threshold and have suggested that the risk of PPH is increased after only 15 to 20 minutes [38–40,43,44]. An active management of the third stage of labour has been shown to reduce the risk of PPH. This includes administration of oxytocin (a uterotonic that stimulates contraction of the uterus), controlled cord traction and uterine massage [22].

- If the placenta is not delivered spontaneously; several conditions should be considered:
    - The placenta could be detached from the uterine wall but still trapped inside the uterus due to a closed cervix: ***an entrapped placenta***;
    - the placenta is not detached but there are no signs of invasive growth in the uterine wall: ***an adherent placenta.***
    - or there is abnormal invasive growth into or through the uterine wall: ***an abnormal invasive placenta (AIP)*** [46,47].

AIP has an incidence of approximately 0.2-3 per 1,000 deliveries [48 -51]. Depending on the depth of attachment AIP is termed:

- *placenta accreta (*placenta attached to the myometrium);
- *placenta increta* (placenta invades the myometrium);
- or *placenta percreta* (placenta invades through the myometrium) [48,52].

AIP often leads to severe PPH requiring blood transfusions and in more severe cases even the need for hysterectomy, complications that can be minimized if diagnosed before labour [51]. Currently, up to 50% of AIP cases are identified antenatally through ultrasound screening of women with a prior caesarean section and placenta praevia [48,53].

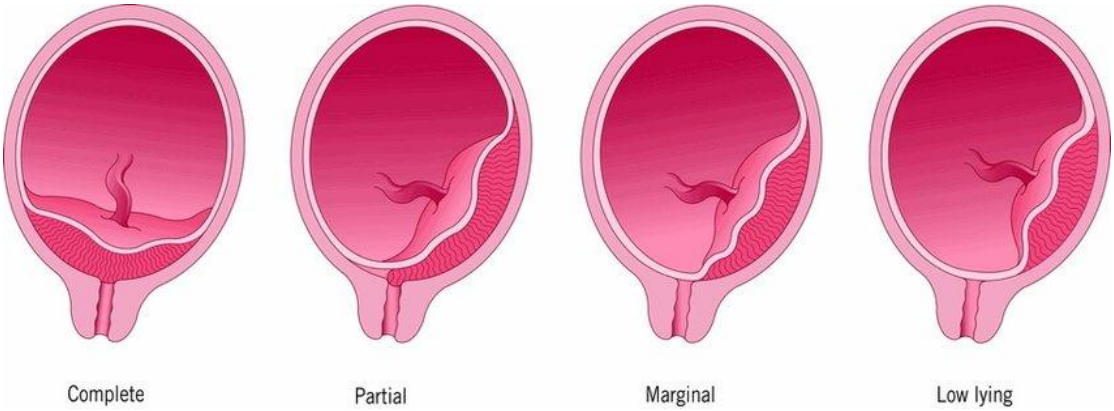


Image 3: types of placentae praevia [54]

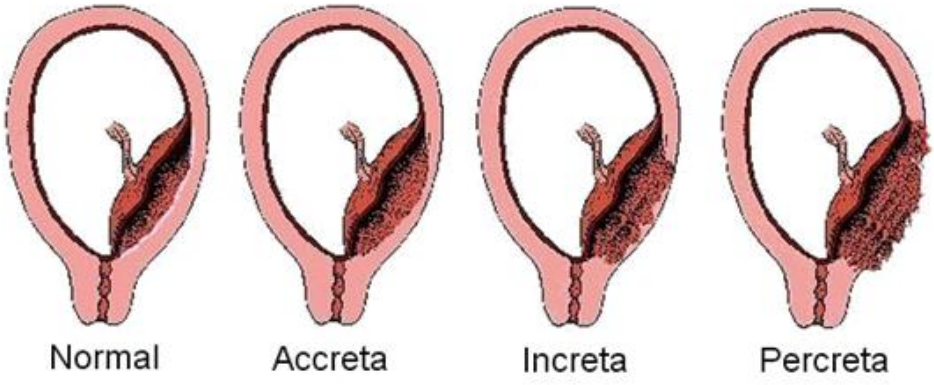


Image 4: placenta accreta increta percreta [55]

Numerous epidemiological studies have been performed to try and identify women at risk of developing PPH, in the hope of initiating sufficient preventive measures [42,56–58].

Some of the risk factors identified include:

- previous caesarean section
- hypertensive disorders,
- macrosomia
- previous PPH
- previous RPH
- induction of labour
- augmentation of labour,

- operative vaginal delivery
- caesarean section and
- placenta praevia [59,60].

Some of the risk factors have a higher risk of PPH than others, but women with high risk or multiple low risks can still have a completely uncomplicated delivery [57]. Furthermore, 22-39% of women that develop PPH have no risk factors, making it extremely difficult to predict which women will in fact develop PPH [64,61-63].

There are a wide range of complications following PPH. Mild cases of PPH can lead to anaemia, fatigue, depression and feelings of separation or anxiety [9,40,41]. In more severe cases the complications are often critical and involve blood transfusions, open surgery, organ failure, treatment in an intensive care unit, thromboembolic complications, hysterectomy and in worst case even death [64,67-69.]

In our case study, 52% of cases presented with more than 1 one risk factor, which corresponds to the results reported by M. Lahlou et al, which was 52.59% [70].

III. Diagnosis of PPH

- Anticipating obstetric coagulopathy is important when obstetric anaesthesiologists are involved in the clinical management of women with postpartum haemorrhage. Although the incidence of coagulopathy in women with postpartum haemorrhage is low, significant hypo-fibrinogenaemia is associated with major haemorrhage-related morbidity and thus early identification and treatment is essential to improve outcomes.

III.a clinical observation,

- Regardless of known pathologies, any woman who has given birth must be monitored for at least 2 hours following childbirth. This monitoring takes into account the pulse, BP, assessment of skin pallor, assessment of the safety globe, and quantification of bleeding.
- Quantification of blood loss should be done with a collection bag placed immediately after expulsion. This method allows objective quantification of blood loss and therefore better prevention of the effects of such loss.
- A visual estimate without a collection bag is too inaccurate, and this method of evaluation has been shown to lead to almost 45% errors, in the sense of underestimation. (2) PPH is defined as blood loss greater than 500 ml. The serious nature of this loss is defined by a volume greater than 1000ml, an alteration in the patient's hemodynamic function or the need for a red blood cell transfusion. [71]
- In our hospital, collection bags are not readily available. The quantification of blood loss was visually estimated and subjectively divided into minimal bleeding, moderate bleeding, and heavy bleeding.

- In the results of our study, we found 63% of cases with unstable hemodynamic states. This can be explained by a diagnostic delay linked to a lack of quantification of the lost blood, but also by the fact that in 65% of cases, the patients were referred to us from a health-care establishment outside the UTH, which could be the cause of a delay in medical care.

III. b Laboratory evaluation

- Coagulopathies may evolve rapidly and repeated testing and observation of trends is more useful than single measurements. Laboratory tests are widely available and have well-regulated quality control but are often too slow to be useful in acute and rapidly evolving bleeds and inevitably reflect past haemostatic status.
- Serial tests are useful, however, for following trends in an evolving clinical scenario. Clauss fibrinogen should always be measured as part of the routine coagulation screen because it falls early and may be reduced to a clinically significant level despite adequate levels of other procoagulant factors. Derived fibrinogen assays (indirectly measured) may be misleading and should not be used [72].

III.C point of care testing (POCT): viscoelastic haemostasis assays

- Point-of-care viscoelastic haemostatic assays, including thromboelastography and rotational thromboelastometry, provide granular information about alterations in clot formation and hypo-fibrinogenaemia, allow near-patient interpretation of coagulopathy, and can guide goal-directed treatment.
- If these assays are not available, anaesthesiologists should closely monitor the maternal coagulation profile with standard laboratory testing during the active phase of postpartum bleeding in order to rule coagulopathy 'in or out', decide

if pro-haemostatic therapies are indicated, and assess the response to haemostatic support.

- Sebastian D. Sahli et al in their article on Point-of-Care Diagnostics in Coagulation Management [73] wrote that:
- Viscoelastic tests are initiated with citrated whole blood and defined activators or inhibitors. The thromboelastographic system (TEG®) is in use more often in America, and the rotational thrombelastic system (ROTEM®) in Europe. Different from standard coagulation assays, viscoelastic methods display clot formation and clot stability in real time.
- They permit detection of a delayed initiation of coagulation, a reduced fibrinogen level, an increased fibrinolytic activity and of the platelets' contribution in whole blood. Viscoelastic assays are fast and give first results within 5–10 m.
- Viscoelastic tests are of an advantage in acute situations such as trauma-induced coagulopathy, transfusions management, intra- and postoperative bleeding and targeted haemostatic therapy. Using guidance by viscoelastic tests, superior outcomes in trauma patients, cardiac surgery and postpartum haemorrhage are proved. Further, they allow the detection of a delayed coagulation initiation, diminished fibrinogen level, an increased fibrinolytic activity and of the platelet level in whole blood. They may also indicate the presence of anticoagulants, and give additional information in patients with hypercoagulability or substitution therapy in hemophiliacs.
- Below is an extract from the ROTEM ® analysis-09-2016 *for targeted treatment of acute haemostatic disorders* [74]. Written and edited by Andreas Calatzis et al:

ROTEM® thromboelastometry detection method

In the ROTEM® system, the sample is placed into a cuvette and a cylindrical pin is immersed. Between pin and cuvette remains a gap of 1mm, which is bridged by the blood or the blood clot. The pin is rotated by a spring alternating to the right and the left. As long as the blood is liquid, this movement is unrestricted. As soon as the blood clots, the clot restricts the rotation of the pin increasingly with rising clot firmness. Thus, the rotation of the pin is inverse proportional to the clot firmness.

It is detected optically. An integrated computer calculates the ROTEM® curve as well as its numerical parameters.

The parameters of ROTEM® thromboelastometry analysis

For historical reasons, the curve is plotted two-sided, expressed in mm.

- **CT** (clotting time): time from start of the measurement until initiation of clotting **initiation of clotting, thrombin formation, start of clot polymerization**
- **CFT** (clot formation time): time from initiation of clotting until a clot firmness of 20 mm is detected **fibrin polymerization, stabilization of the clot with thrombocytes and FXIII**
- **MCF** (maximum clot firmness): firmness of the clot **increasing stabilization of the clot by the polymerized fibrin, thrombocytes as well as FXIII**
- **ML** (maximum lysis): reduction of clot firmness after MCF in relation to MCF **stability of the clot (ML< 15%) or fibrinolysis (ML > 15% within 1h)**

ROTEM® thromboelastometry detection method

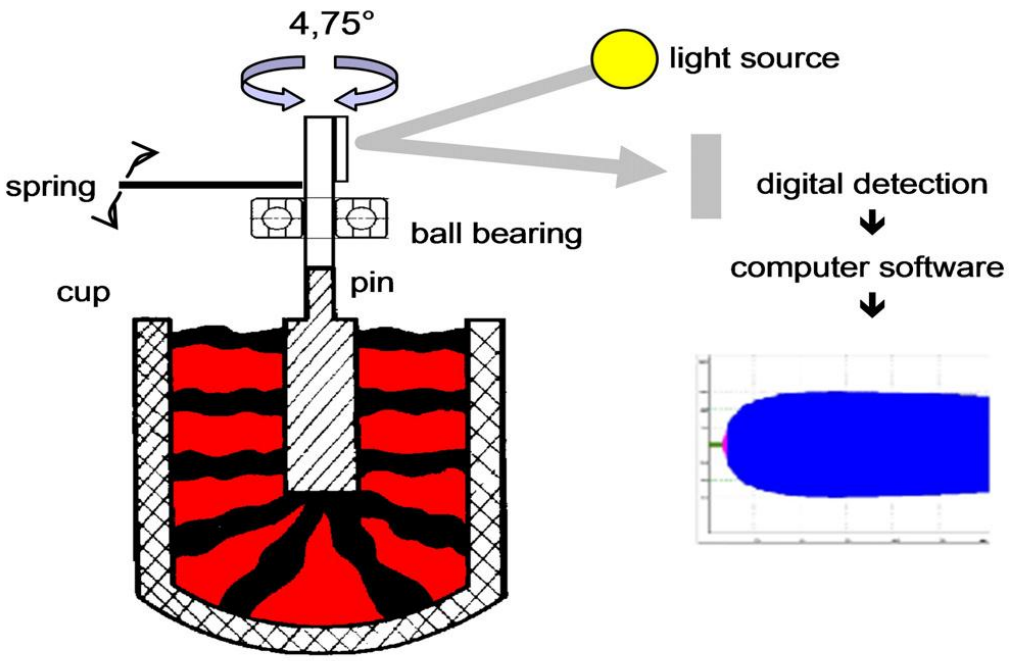


Image 5: illustrates the thromboelastometry detection method [74]

ROTEM® thromboelastometry tests

- In the past, "the thrombelastogram" was analyzed using freshly drawn blood without the addition of any citrate / calcium and without any activators. The measurements were therefore very time consuming (45 – 60 min.) and quite unspecific.
- With the ROTEM®, activated determinations are usually performed. As in the laboratory coagulation analysis, various activators or inhibitors are added to the sample, in order to represent different processes of hemostasis. For the analysis, citrated blood is usually used. In **EXTEM,** coagulation is activated by a small amount of tissue thromboplastin (tissue factor). This typically leads to the initiation of clot formation within 70 seconds. Thus, clot formation can be assessed within 10 minutes.

- In **INTEM,** coagulation is activated via the contact phase (as in the aPPT and ACT). The INTEM is therefore sensitive for factor deficiencies of the intrinsic system (e.g. FVIII) and for the presence of heparin in the sample.
- In **FIBTEM,** coagulation is activated as in EXTEM. By the addition of cytochalasin D, the thrombocytes are blocked. The resulting clot is therefore only depending on fibrin formation and fibrin polymerization.
- In **APTEM,** coagulation is also activated as in EXTEM. By the addition of aprotinin or tranexamic acid in the reagent, fibrinolytic processes are inhibited *in vitro*. The comparison of EXTEM and APTEM allows for a rapid detection of fibrinolysis. Furthermore, APTEM enables the estimation if an antifibrinolytic therapy alone normalizes the coagulation or if additional measures have to be taken (e.g. administration of fibrinogen).
- In **HEPTEM,** coagulation is activated as in INTEM. The addition of heparinase in the reagent degrades heparin present in the sample and therefore, allows the ROTEM® analysis in heparinized samples.

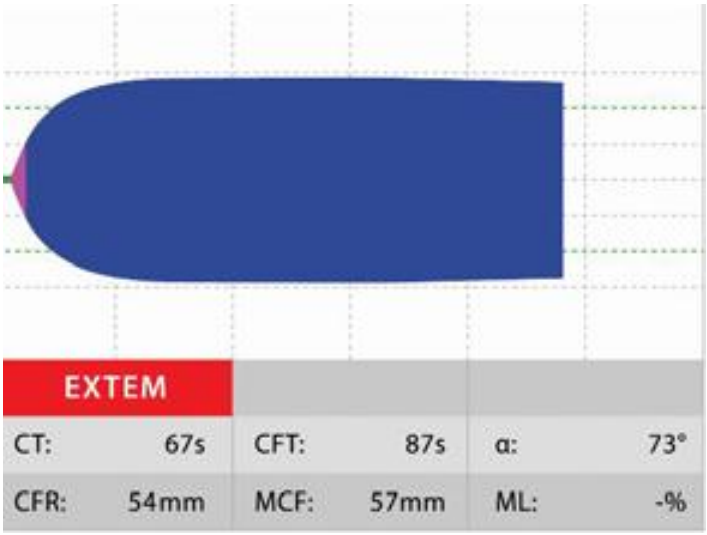
Table 23: breakdown of reagents used in ROTEM®

Reagent type	Test name for each reagent type				
Single Use	EXTEM S	FIBTEM S	APTEM S	INTEM S	HEPTEM S
Liquid	EXTEM (L)	FIBTEM	APTEM	INTEM	HEPTEM
Cartridge	EXTEM C	FIBTEM C	APTEM C	INTEM C	HEPTEM C

ROTEM® thromboelastometry tests

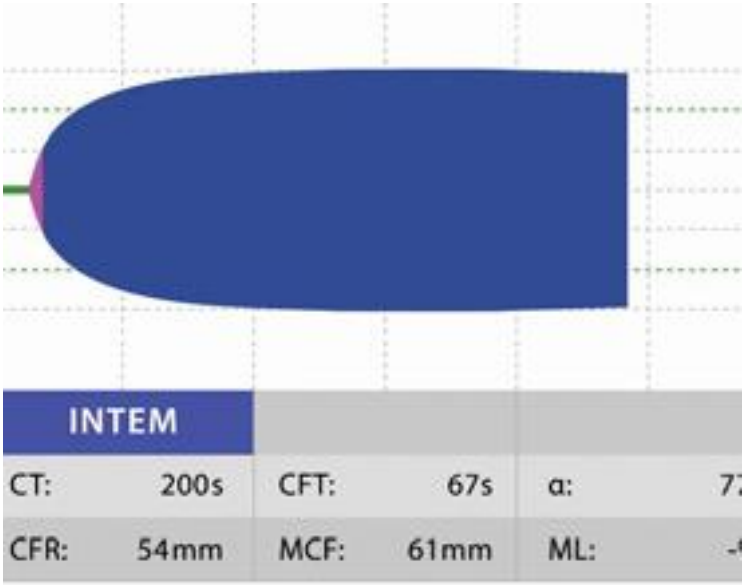
EXTEM (L, S, C): activation of clot formation by thromboplastin (tissue factor).

Assessment of factors VII, X, V, II, I, platelets, Fibrinolysis

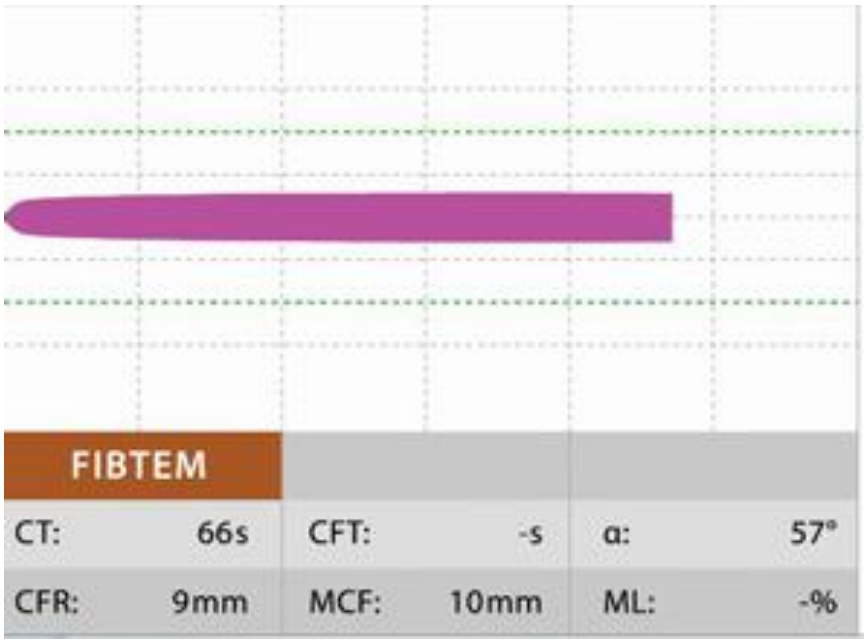


INTEM (S, C): activation of clot formation via the contact phase.

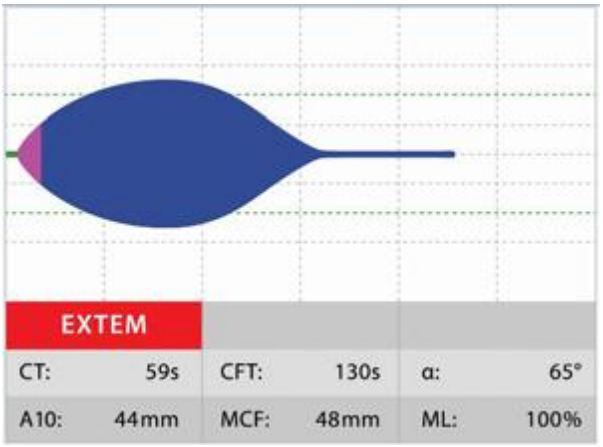
Assessment of factors XII, XI, IX, VIII, X, V, II, I, platelets, fibrinolysis

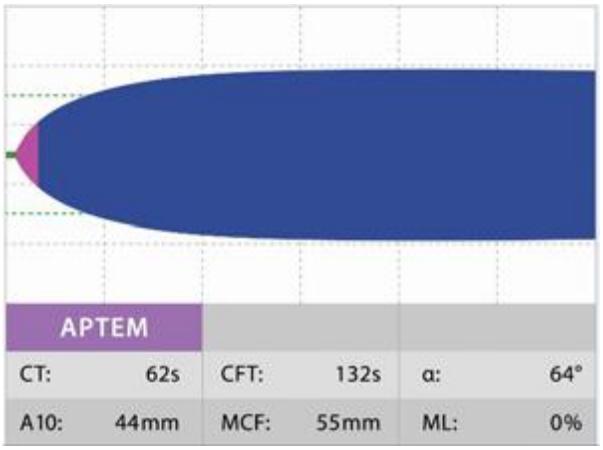


FIBTEM (S, C): activation as in EXTEM with the addition of cytochalasin D, a platelet blocking substance. In the FIBTEM assay, fibrinogen levels and fibrin polymerization can be assessed in a functional way.

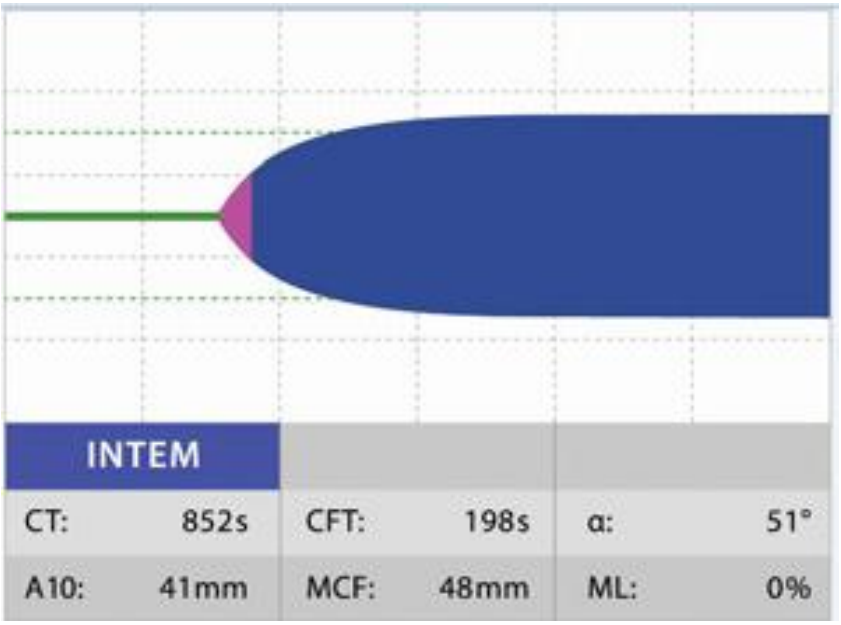


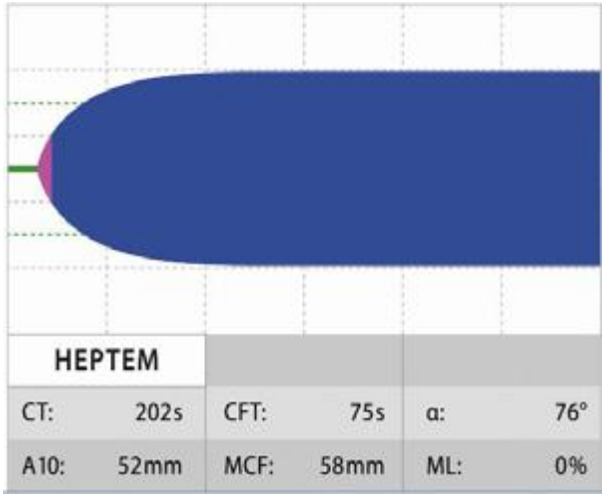
APTEM (S, C): activation as in EXTEM with the addition of aprotinin or tranexamic acid, fibrinolysis inhibitors. In an assay comparing APTEM to EXTEM, fulminant hyperfibrinolysis can be recognized within 10-20 minutes.





HEPTEM (S, C): activation as in INTEM with the addition of heparinase. Heparinase degrades heparin. When HEPTEM results are compared to INTEM, heparin related coagulation disturbances can be specifically detected.





Interest of POC testing in obstetrics

The use of ROTEM-based algorithms to guide transfusion for PPH leads to a reduction in overall blood component transfusions, consumption of FFP, incidence of transfusion-associated circulatory overload and cost of care. [75]

in the *Four years' experience of ROTEM®_-guided algorithm for treatment of coagulopathy in obstetric haemorrhage** [76] written by H. McNamara et al, it was discovered that obstetric patients who suffered major haemorrhage demonstrated improved clinical outcomes by the selective use of fibrinogen concentrate to treat coagulopathy identified using ROTEM.

Use of an algorithm with point-of-care testing allowed individualised treatment, focusing on fibrinogen as one of the main factors in obstetric haemorrhage, while avoiding the use of unnecessary blood products with the associated morbidity and mortality.

below Is the proposed ROTEM® protocol for use in PPH in obstetrics.

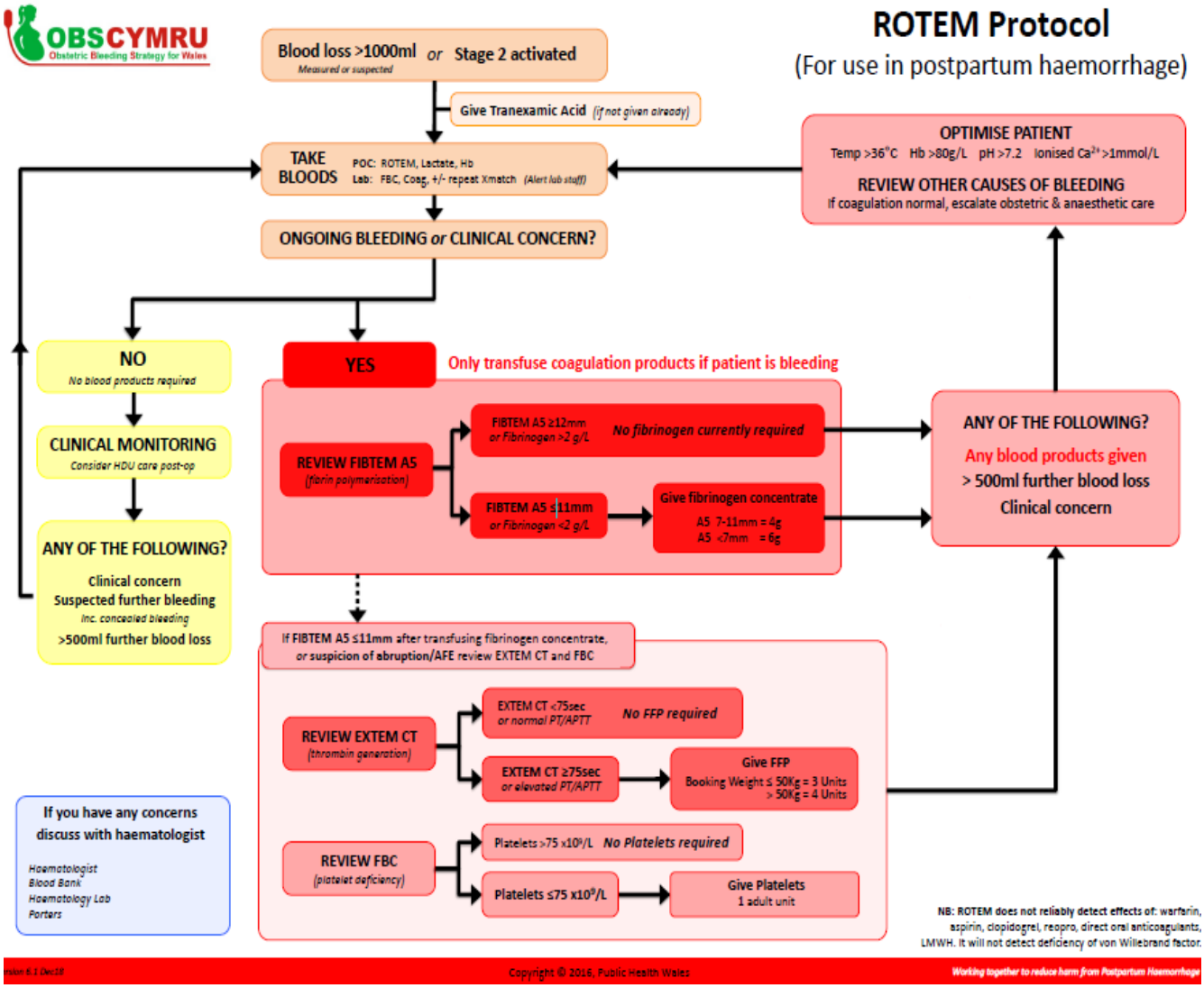


Image 6: ROTEM® protocol for PPH. [76]

Below is another algorithm proposed for managing abnormal bleeding using ROTEM® as a therapeutic guide.

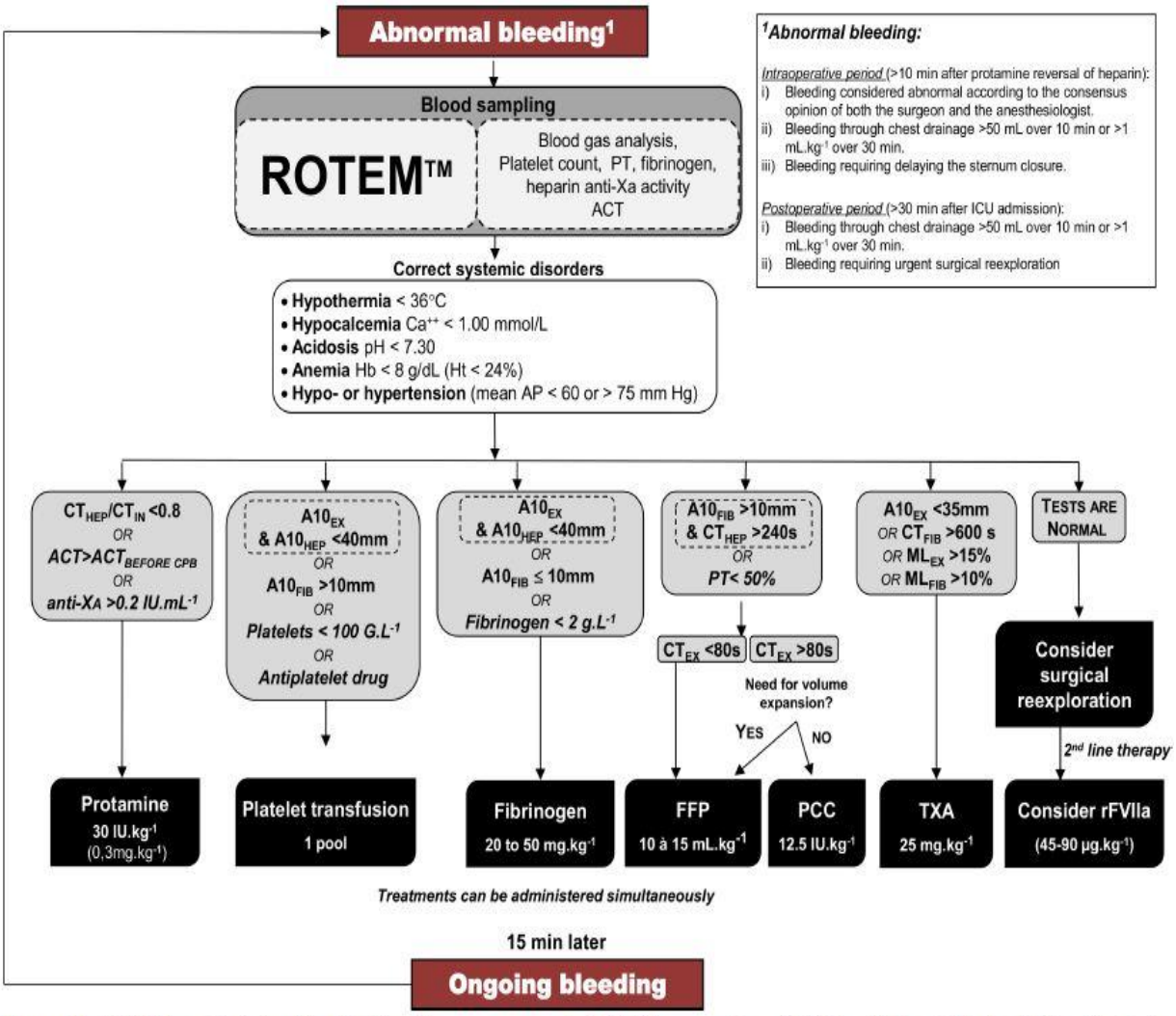


Figure 1 ROTEM-guided algorithm for bleeding management. ROTEM parameters: A10, Amplitude at 10 min; ACT, activated clotting time; AP, arterial pressure; CPB, cardiopulmonary bypass; CT, clotting time; EX, EXTEM; FFP, fresh frozen plasma; FIB, FIBTEM; HEP, HEPTEM; ML, maximum lysis; PCC, prothrombin complex concentrate; PT, prothrombin time; rVIIa, recombinant factor VII; TXA, tranexamic acid.

Image 7: management of abnormal bleeding based on ROTEM® [73]

IV.Aetiologies

The aetiologies of PPH are classically divided into four different categories, known as the four

T's – Tone, Trauma, Tissue, and Thrombin [9]. ***Tone*** refers to atony, which is insufficient contraction of the uterus during and after delivery of the placenta, leading to extensive bleeding from the placental bed. ***Trauma*** refers mainly to lacerations of the vagina and perineum, graded from first to fourth degree depending on their depth and extent, but can also include vulva and vaginal haematomas or uterine rupture, all of which will need surgical repair. ***Tissue*** refers to retained placenta or fragments of placenta inhibiting contraction of the uterus. *Thrombin* refers to coagulopathies, that can be defects known prior to childbirth or developed during or after childbirth due to other complications such as amniotic fluid embolism [6,8]. The majority of cases are traditionally attributed to atony [8]

Table 16 shows the frequency of the four main aetiologies and the comparison of the results with the data in the literature.

Table 24: Comparison of the main aetiologies found with data from the literature

aetiology	Our study	w.sanbi [79]	Deneux-T [4]	Panbou [81]	m. Lahlou [70]
Atony	38%	38.9%	50-80%	23.9%	30.27%
Placenta retention	3%	22.2%	10-3-%	17%	20.54%
Uterus tear	12%	8.3%	2%	4.54%	15.13%
Cervical-vaginal lesions	15%	22.1%	20%	-	13.51

IV.1 TONE

Uterine atony

Uterine atony is the leading cause of PPH In up to 2 to 5% of all deliveries worldwide. Several factors predispose to atony: exhaustion of the myometrium after prolonged labour, uterine over-distension (twin pregnancies, hydramnios, macrosomia, etc.), fibrous degeneration of the myometrium in elderly multigravida women, decrease in contractility of a fibromatous or malformed uterus, and certain drug interactions such as: betamimetics, abruptly stopping the use of oxytocin after childbirth, anaesthesia or deep analgesia ... [82]

IV .2 TISSUE

2 Placental insertion anomalies

2.1. Placental retention

There are two types of retained placenta:

o *Partial retention*: where the placenta has not been fully delivered and fragments of membranes or placentae persist in the uterus. Its diagnosis is simple and is based on immediate examination of the delivered placenta.

O *Complete retention*: we speak of complete placental retention when 30 minutes after the expulsion of the new-born, the delivery of placenta has still not been made.

-There are factors predisposing to placental retention, among them we can note lesions of the endometrial mucosa due to infections or trauma, abnormalities of uterine contraction, uterine hypotonia, placental abnormalities, and finally premature delivery of baby.

2.2. The placenta accreta

Placenta accreta is defined by the insertion of the placental chorionic villi directly in contact with the muscle fibres of the myometers. It is said to be increta if it is confined to the myometrium alone, and percreta if it goes beyond it and invades the serosa and sometimes the bladder or other neighbouring organ. [83]

The incidence of placenta accreta has increased tenfold in the past fifty years and is estimated to be 1/2,500 deliveries. It is more common in women who have a scarred uterus from one or more caesarean sections, myomectomy, or surgery for uterine malformation. It is more common if the scar is associated with an anterior placenta previa located on it. In this case the risk increases with the number of scars, going from 24% in the woman who had a caesarean section to 67% in the one who had three or more caesarean sections. [83]

In our case study, we collected 4 cases of placenta accreta diagnosed after postpartum haemorrhage. All 4 required haemostatic hysterectomy.

Radical caesarean section-hysterectomy treatment remains the gold standard in the latest 2002 recommendations from the American College of Obstetricians and Gynaecologists. Based on the 2004 clinical practice guidelines of the French National College of Obstetricians and Gynaecologists, conservative treatment with the placenta left in place can be considered in the absence of bleeding. [84]

It is necessary to have a policy of screening by Ante-Natal care (ANC) with ultrasound in order to be able to refer patients to level 3 maternity hospitals and to limit the mortality and morbidity linked to this pathology. Antenatal diagnosis is necessary in order to be able to refer such patients to these structures.

2.3. Placenta previa

The term placenta previa means the implantation of the placenta is in the lower segment of the uterus. Placenta previa is classified into 4 categories: low, marginal, partial and fully covering. [85]

The main complications of placenta previa are bleeding during pregnancy, prematurity, and postpartum haemorrhage. [86]

In our case study, 14 patients presented with placenta previa. 5 of those patients were not diagnosed antenatally or followed up so labour and delivery took place at home, the diagnosis of placenta previa was made during the management of PPH at the UTH after referral.

TRAUMA

3. Trauma of the genital tract

3.1. Uterine rupture/abruption

Uterine rupture usually secondary to labour dystocia, its occurrence is more common in scarred uteri, but it can be spontaneous in a weakened uterus.

Most often, a uterine rupture is diagnosed during childbirth with acute foetal distress or severe "stabbing" pain that persists outside of the contraction. In this case, externalized vaginal bleeding is rare. The diagnosis can also be made after childbirth when performing a uterine revision.

In our series, the frequency of uterine ruptures was 12%, which is very high and worrying in comparison with the data in the literature. This could be explained by an increasing number of caesareans with a lack of patient follow-up in present.

3.2. Lesions of the birth canal

One of the known causes of PPH is damage to the birth canal. Their management is rarely discussed in the literature and thus little evaluated despite their potential seriousness. Lesions of the genital tract can affect and involve all levels of the chain: vaginal, vulvar and perineal tears, vaginal hematoma, and tears of the uterine cervix.

Although in the majority of cases the bleeding is controlled by surgical suture and / or vaginal packing, to date the only recommendation regarding the management of HPP on genital tract wound is the systematic assessment of lower genital tract

through visual inspection. This revision allows the diagnosis and management by suturing the lesion. The latter being sometimes insufficient, the bleeding worsens requiring intensive and invasive management, which is sometimes complex.

IV.4 Thrombin

If findings are abnormal in conjunction with ongoing bleeding or oozing from puncture sites, mucous surfaces, or wounds, additional blood products are required. Infuse fresh frozen plasma (FFP), beginning with 4 U and following with additional units to normalize the coagulation test findings. Many authorities recommend the addition of 1 U of FFP for every 5 U of PRBCs for patients who require continued transfusion. [87]

Thrombocytopenia is likely after 1.5-2 times the blood volume has been replaced. Keep the platelet count more than 50 X 10^9/L by using platelet transfusion. Each unit of platelets increases the platelet count by approximately 10 X 10^9/L. (Platelets are usually given in packs of 5-6 U.) If bleeding is continuing and the platelet count is less than 50 X 10^9/L, administer 10-12 U initially. If surgical intervention is necessary, maintain the platelet count at more than 80-100 X 109/L. Platelet preparations contain some RBCs, and the administration of anti-D immunoglobulin (RhoGAM, WinRho) is recommended for Rh-negative women after the crisis has passed. [87]

Congenital or acquired clotting disorders (e.g. factor VIII or factor IX deficiency, Von Willebrand's disease) can cause or contribute to PPH; therefore, identification and correction of any coagulopathy can help improve the outcome. Coagulopathy may be diagnosed by:

- Clinical observation;
- Laboratory-based clotting studies and platelet counts;

- Point-of-care testing – with the advantage of prompt availability of results.

Local transfusion policies on the use of blood and other blood-related products should be sought alongside expert advice from hematologists in cases of ongoing bleeding caused by coagulopathy.

V) management of patient with PPH

There are wo important concepts in the management of severe postpartum haemorrhages:

The multidisciplinary approach (resuscitation measures, medical treatment and obstetrical management) + **The chronology** with which the care is administered.

V.1 Algorithm of management of PPH

This patient management algorithm should be done within the first 30mins

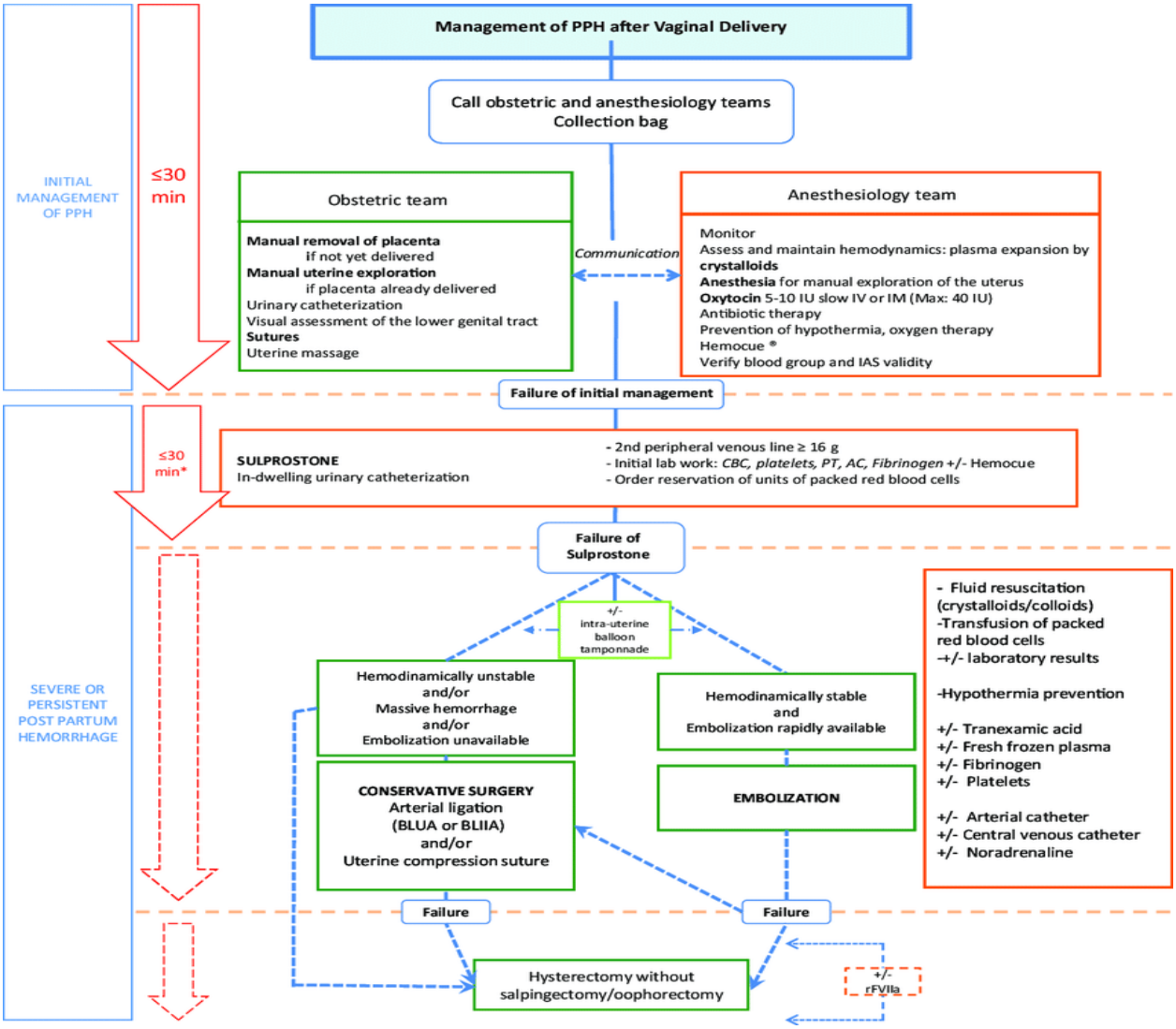


Image 8: Algorithm of patient care during and after a vaginal delivery [88]

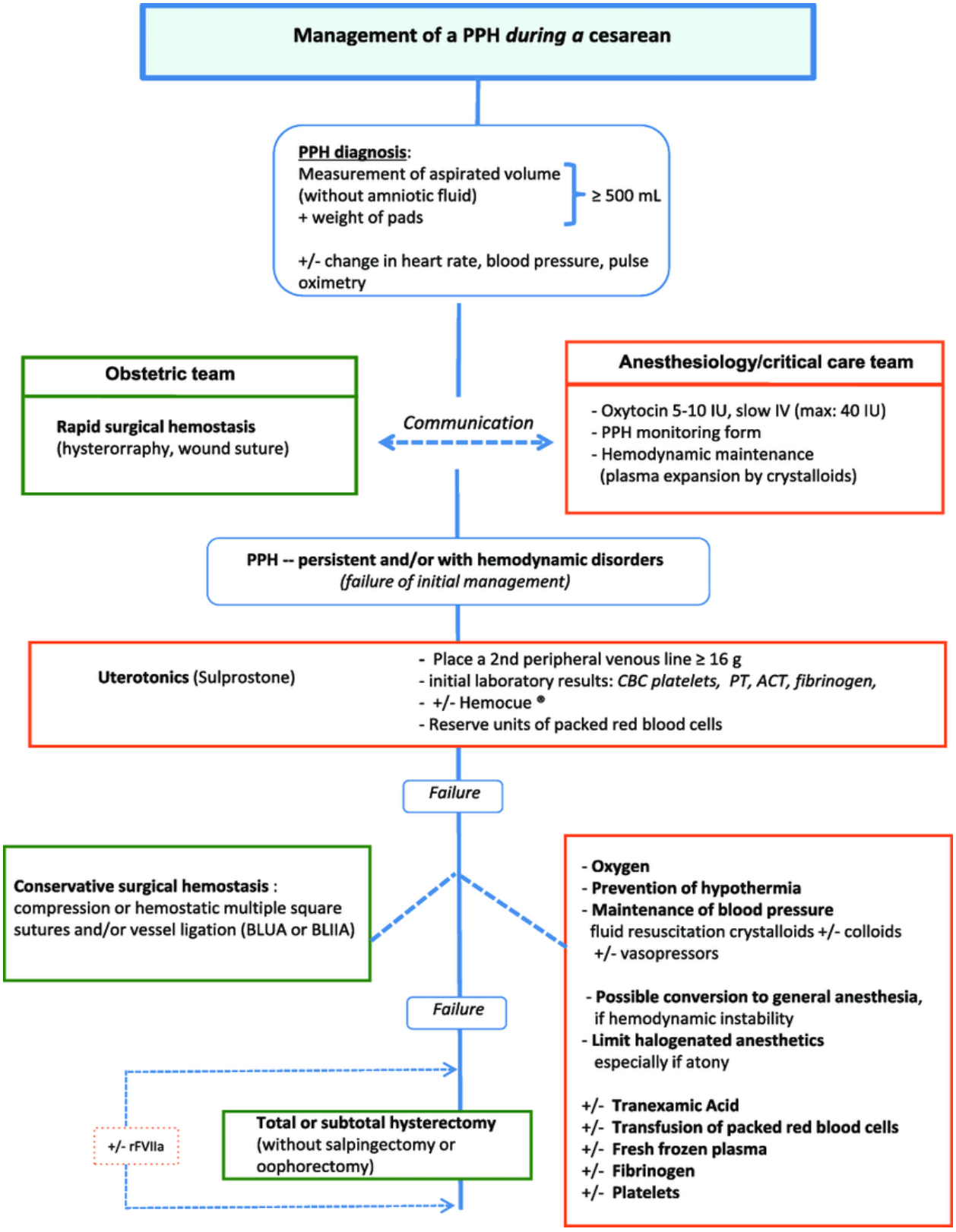


Image 9: Algorithm of patient care after caesarean section [88]

Below is the proposed Moroccan protocol for the management of PPH for vaginal delivery

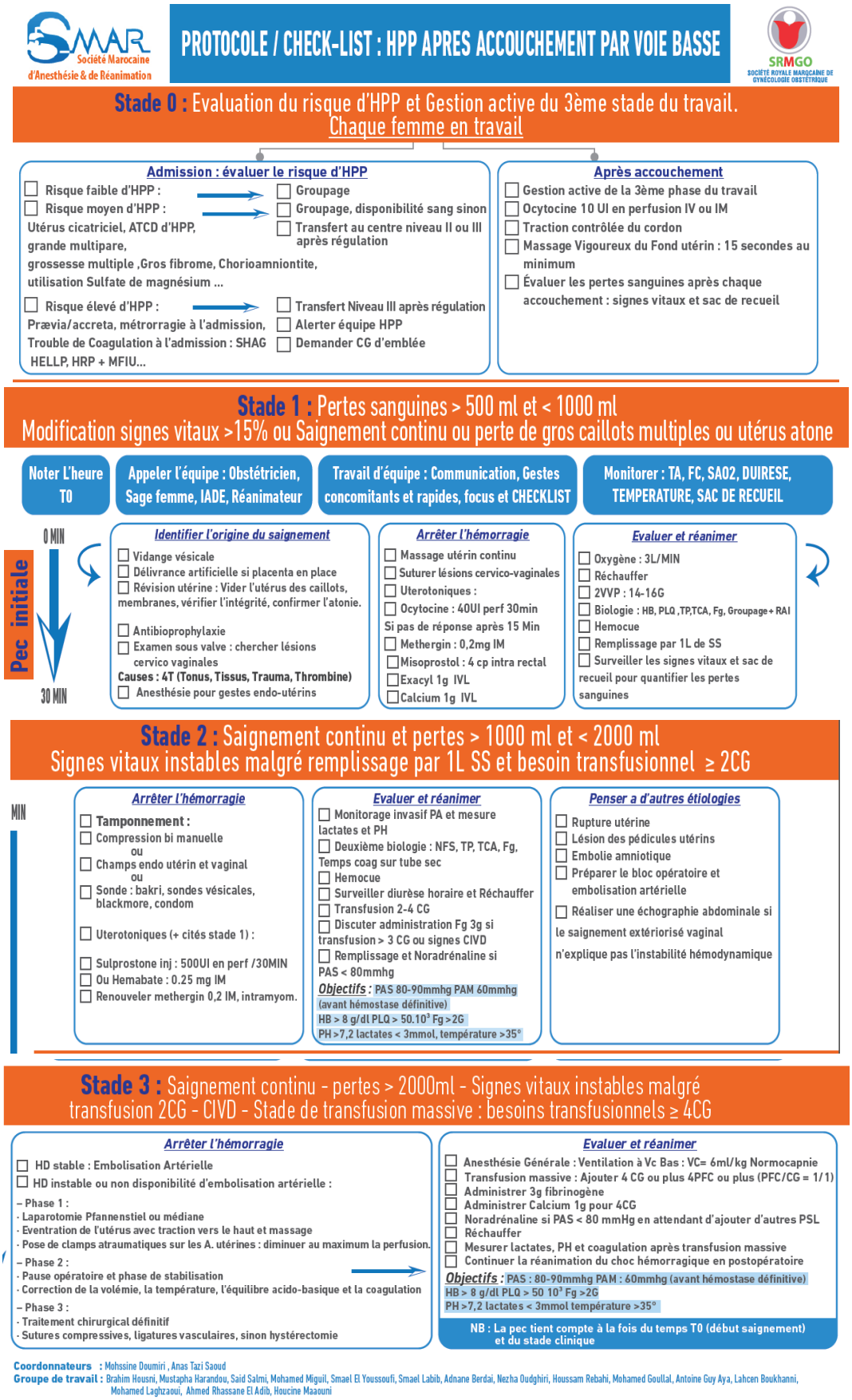


Image 10: proposed Moroccan protocols for PPH in obstetrics. [89]

V.2. Resuscitation measures.

V.2.1Monitoring:

Monitoring parturients in the minutes following birth is essential. In situations where no monitoring has been instituted during labour and delivery, detection of bleeding should lead to its onset.

- Knowing that non-invasive monitoring alone can detect hypovolaemia secondary to PPH is essential.
- Searching for signs such as, a tachycardia with malaise or a severe hypotension refractory to vascular filling signal the installation of hypovolemia. [90]

Appropriate monitoring and investigation should be guided by clinical judgement, but in all cases of PPH, should, at a minimum, include the recording of observations at regular intervals, (not monitoring and already done by now) and repeating, as indicated, in an appropriate time frame the haematological investigations:

- Pulse rate
- blood pressure
- oxygen saturation and
- urinary output measurement should be instigated for any significant (>1000ml) or ongoing PPH.
- invasive monitoring **of arterial blood pressure or central venous** pressure may be necessary depending upon the clinical situation. Consideration must be given to the most appropriate place of care in women with severe PPH; this may be a high dependency care or intensive care unit in some instances. Where patients need to be transferred to a more highly equipped facility for management of PPH, the need for transfer should be anticipated and initiated early. In the meantime, aggressive resuscitation should continue and regular communication with the receiving unit is essential. Appropriate prophylaxis for venous thromboembolism should also be instituted once the acute situation has been controlled.[91]

V.2.2Peripheric and central venous lines:

The existence of at least one venous route of good functional calibre should be verified, a second **peripheral venous** route can be taken in the event of poor quality peripheral venous routes or severe bleeding from the onset.

A **central venous** line either femoral or jugular may be taken in cases where emergency venous access for patients in which peripheral access cannot be obtained it can also deliver fluids and medications into a larger vein, and that it can stay in the body for a longer period of time than a usual, shorter IV.

Special care is to be taken when these blood access routes are inserted as they can also be a port of entry for infection.

- when no assessment prior to childbirth is available, a biological laboratory assessment is taken on this occasion including a full blood count with a platelet count, an initial assessment of haemostasis (PT, aPTT, fibrinogen) and a test for irregular agglutinins (IA) if these are not up to date. [90] these blood samples can be collected through the veinous lines already inserted.

V.2.3 bladder catheterization:

at the initial stage of PPH does not appear to be mandatory (professional consensus). It can help maintain bladder emptiness and hourly monitoring of urine output. -However, ensuring the absence of a full bladder can rule out an associated cause of poor uterine retraction. It should be considered permanently if you have very severe early onset or persistent PPH. [90] in our study cohort 76% of our patients had permanent bladder catheters in order to monitor urine output.

V.2.4Oxygenation:

Oxygen is delivered through a nasal cannula (2—4 L / min), a venturi mask (8—12 L / min), or even a high concentration oxygen mask with reservoir in spontaneously ventilated women.

-In the event of impaired consciousness or general anaesthesia, oxygenation is provided by mechanical ventilation after tracheal intubation. [91]

In our study cohort 68% of our patients received tracheal intubation of which 43% where admitted already intubated while 15% were admitted already intubated.

V.2.5Position:

The venous return can be improved by placing patient in Trendelenburg position / or the elevation of the lower limbs placed in stirrups.

V.2.6Hypothermia:

In practice, the most effective strategy for preventing and treating hypothermia is through the combined use of several methods, especially warming infusion fluids and blood products, and warming the patient's skin.

- Warming the body to normal temperature during resuscitation dramatically improves cardiac contractility and hepatocellular function. [92]

V.2.7Antibiotic prophylaxis:

In these acute bleeding situations, the risk of a pre-existing or secondary infection is very high [93]. Apart from acute bleeding, several more or less invasive obstetric procedures are often performed, and very often in an emergency context. This justifies broad spectrum antibiotic coverage at least during the initial 24/48 hours. In our study cohort all patients benefited from antibiotic prophylaxis of amoxicillin and clavulanic acid.

starting a patient monitoring form is essential, in order to detect the various physiological crises and the time of onset of such disturbances

V.2.8 Vascular Filling

Vascular filling is the first treatment for haemorrhagic shock in order to maintain effective blood volume and prevent early organ failure including cardiac arrest. However, until the bleeding is controlled, filling should be limited to strictly maintaining recommended blood pressure targets to limit dilution of clotting factors. [94]

There are no data regarding uncontrolled PPH, but it is possible that a MAP goal of between 60 and 80 mmhg, without necessarily aiming for normal MAP, could limit the bleeding and the consequences of massive filling. [90]

For fluids used, it is recommended to use crystalloids (ringer-lactate or normal saline) as a first-line treatment during initial stages, due to their clinical efficacy, moderate toxicity and low cost. [95]

Vascular reactivity in response to hypovolemia is a depleting phenomenon, which justifies the use of vasopressors when bleeding is prolonged. They are also useful for maximising blood supply while waiting for a transfusion. [93]

In our case study all patients benefited from filling with crystalloids.

V.2.9 Vaso-active drugs

The use of vasoconstrictors in the management of PPH is poorly documented. In obstetric anaesthesia-resuscitation, these agents are mainly prescribed for the prevention and treatment of hypotension during locoregional anaesthesia, spinal anaesthesia in particular.

In this instance, two substances are used: ephedrine, and phenylephrine. In the management of PPH, the pathophysiological bases for choosing between these two molecules or for giving preference to other agents (dopamine, norepinephrine, adrenaline, vasopressin) are unclear. In the management of shock, the effects of norepinephrine make it a preferred substance and is thus recommended. [91]

In our study cohort however 67% of our patients received vasoactive drugs either in the operating room or in the resuscitation ward. The table below shows which drugs were given and the number of patients who benefited from it. Only two (2) patients benefited from dobutamine due to cardiac insufficiency.

Table 25: vasoactive drugs given and percentage of patients.

Type of drug	Number of patients/percentages
noradrenaline	56%
Dobutamine + noradrenalin	2%
Adrenalin + noradrenalin	9%

V.2.10Prevention of thromboembolic complications

Clinical and epidemiological studies draw attention to the risk of thromboembolic events in the aftermath of PPH [71], and the existence of transfusions during childbirth is a strong risk factor for venous thromboembolism in the postpartum period [4]. This risk is the result of several factors, including the existence of lesions of the genital tract, the existence of an inflammatory syndrome, the activation of the haemostasis inherent in the bleeding and the use of pro-coagulant therapy, it is recommended to prescribe thromboprophylaxis after severe PPH, the volume of which is> 1000 ml, especially in the case of multiple transfusion. It will be started 12 to 24 hours after the bleeding, preferably with an LMWH, preventive dose, for 7 to 14 days. Of course, the existence of additional thromboembolic risk factors may cause the duration of thromboprophylaxis to be re-evaluated. [32]

V.3 Transfusion of labile blood products.

The transfusion of labile blood products is an essential element in the management of PPH. Its precocity and its adequacy condition the maternal prognosis. The establishment of emergency procedures within the maternity unit must make it possible to quickly obtain LBPs in good conditions: have vital emergency depots available, rapid means of communication with the transfusion centre and optimize blood flow procedures.

During PPH, the purpose of LBP transfusion is to maintain or restore circulating blood volume and oxygenation, but also to prevent and treat coagulopathy. There are no data on which to base a transfusion strategy during PPH. Despite the similarities that may exist, it does not seem justifiable to generalise the strategies of PPH to those proposed in the context of traumatic shock. [32]

The prescription of RBCs is considered mainly during large volume haemorrhages, or on the basis of the clinical signs of severity of PPH i.e.: tachycardia, hypotension resistant to vascular filling, significant externalized haemorrhage, paleness of the mucous membranes and integuments, oligo-anuria.

A laboratory-obtained Hb concentration can aid in the diagnosis, but should not be a prerequisite for prescribing LBP. Furthermore, in the event of a discrepancy between the clinical signs and the Hb concentration, the clinic signs should take precedence. Priority is given to RBC transfusion, with the objective of maintaining a Hb concentration> 8 g / dL. It is agreed that the first order must include 3 RBC pellets. After the transfusion of these 3 RBCs, if the bleeding persists, as well as the clinical signs, an additional order of 3 RBCs should be made, associated with 3 FFPs. The time of prescribing of PFC based on the aetiology of the PPH is at the discretion of the clinician. [32]

In our series, and concerning all PPH with or without PPH, the transfusion of red blood cells alone was indicated in 28% of cases with an average RBC transfused of 38.85 +/- 2.3. As for the transfusion of RBC and FFP, it was indicated in 45% of cases

Table 26: patients who were transfused with FFP and RBC and platelets.

substance	Our study	Lahlou et al [70]	Panbou et al [81]	Tarik et al [97]
Red blood cell pallet	28%	85.40%	58%	36.4%
RBC + FFP + PLT	61%	84%	36.4%	69.7%

Regarding platelets, the results of a meta-analysis suggest that a high platelets / RBC ratio is associated with a reduction in mortality in trauma patients [92]. These were retrospective observational studies, however, so the optimal ratio remains to be determined. In practice, it is desirable to maintain a platelet count> 50G / L. [91]

Image 11: fresh frozen plasma, red blood cell pallet and platelets [98]

VI) MANAGEMENT OF COAGULOPATHY IN PPH.

VI.1 massive transfusion.

Massive haemorrhage is defined as loss of total blood volume within 24 hours, 50% within 3 hours, or a rate of blood loss of 150 ml/min [99]. Blood loss of this quantity can be difficult to assess during an emergency situation, which is why massive haemorrhage can also be defined as haemorrhage requiring massive transfusion of 10 units of red blood cells (RBC) within 24 hours [100].

In obstetrics there is no well-defined consensus for massive haemorrhage, with the terms major and massive PPH being used at random for blood loss of more than 1,000 ml to blood loss of more than 2500 ml [101-103].

Massive haemorrhage following trauma, surgery or childbirth may lead to coagulopathy a state of impaired haemostasis. In all three circumstances the abundant release of tissue factor leads to activation of the coagulation cascade and consequent consumption of coagulation factors and platelets [106,105]. The simultaneous systemic hypoperfusion causes *hypothermia and acidosis, inhibiting coagulation and activating anticoagulation factors and fibrinolysis,* which complicate coagulation further [100,105].

At the same time transfusion with RBCs, crystalloids or colloids are given in an effort to re-establish perfusion causing additional dilutional coagulopathy. The combination of consumptive and dilutional coagulopathy, acidosis and hypothermia, known as the lethal triad will result in further haemorrhage [104,105,107]. Therefore, treatment involving not only volume resuscitation and surgical control of haemorrhage, but also correction of coagulopathy is necessary [107,108].

Identifying patients with low levels of specific coagulation factors is possible through conventional laboratory testing. However, these tests can be time consuming and they do not assess the general functionality of coagulation, which is why point-of-care viscoelastic assays are being used more and more. These assays can be performed bedside and give an assessment of clot formation and fibrinolysis, thereby providing vital information on the development of coagulopathy [100,109]. Prevention and treatment of coagulopathy in patients with massive haemorrhage is also possible with early transfusion of RBCs, FFP and PLTs. Furthermore, studies from both trauma and non-trauma have shown a reduction in mortality when a fixed ratio of 1:1:1 of PLTs, FFP and RBCs is used during massive haemorrhage [110–112].

Due to the high risks associated with blood transfusions, all strategies that can reduce blood transfusions are essential. Today the risk of transmission of infection through blood transfusions is low; instead, the risks are related to non-infectious reactions including haemolytic, allergic, and immunological reactions that occur in approximately 1% of all transfusions [113–115]. Transfusion related acute lung injury (TRALI) is an immunological reaction and the leading cause of transfusion related morbidity and mortality with an incidence of 0.08–15% [116].

TRALI evolves within 6 hours of transfusion and is mainly associated with plasma transfusions. Symptoms include dyspnoea, hypoxaemia and hypotension due to pulmonary oedema and up to 70% will need respiratory support [113]. Additional complications are seen in patients requiring massive transfusions, including metabolic complications due to haemolysis and high levels of citrate, and transfusion associated circulatory overload [100].

Below is a table showing the number of cases in our work compared to other studies:

Table 27: showing the percentage of coagulopathies in post-partum haemorrhage

aetiology	Our study	W. sanbi [79]	Panbou [81]	Lahlou [70]
coagulopathy	24%	25%	58.9%	14%

VI.2 Fibrinogen concentrate

Fibrinogen is the first coagulation factor known to drop to critical levels during massive haemorrhage, and as the normal level of fibrinogen is 2.0-4.5 g/L in healthy adults, low levels are difficult to substitute with FFP alone, where the concentration is 1-3 g/L [19,117].

Additional substitution is, however, possible through cryoprecipitate and fibrinogen concentrate. Cryoprecipitate contains high concentrations of fibrinogen (approximately 15 g/L), von Willebrand factor and other coagulation factors. However, cross matching and thawing is

necessary before administration. Fibrinogen concentrate on the other hand only contains fibrinogen (15-20 g/L), and comes as a powder that only requires dissolving in sterile water before administration [19,118].

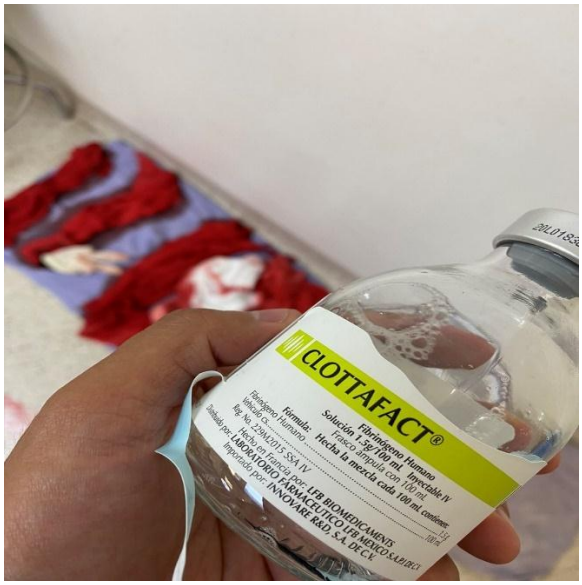


Image 12: fibrinogen concentrate powder *Clottafact* used in our institution (19)

Fibrinogen plays a central role in forming a solid clot. It is produced by the liver and its plasma concentration (2-4.5 g / L) is the highest of all coagulation proteins. The level of fibrinogen rises during pregnancy, so the range of normal concentrations (4.4-7.2 g / L) is significantly higher than outside pregnancy. [91]

Hypofibrinogenemia can be primary, congenital, or secondary, and only the latter will be considered in this paragraph. Secondary hypofibrinogenemia may be due to dilution during refilling or blood transfusion, or consumption following bleeding. Consumption coagulopathy appears early in severe PPH and is accompanied by dilution coagulopathy due to certain therapeutic measures. In a cohort study,

Charbit et al analysed haemostatic data from 128 women who had samples taken at the time of prescribing sulprostone for PPH and over the next 24 hours. Based on clinical and therapeutic data, the authors identified 2 groups of women according to the severity of PPH. The study showed that a fibrinogen level <2 g / L (11 women) predicted the progression to severe PPH with a positive predictive value of 100%, and that a level> 4 g / L had a negative predictive 79%.[119]

Taking into account the high level of physiological fibrinogen level in pregnant women, the early and rapid drop in this level in the event of PPH, the link between a fibrinogen level <2 g / L and the risk of severe PPH, as well as on the basis of European recommendations, it is recommended to prescribe fibrinogen supplementation if the fibrinogen level is <2 g / L during worsening PPH. The current evidence does not justify a systematic prescription of fibrinogen without prior determination of the plasma fibrinogen level. However, if physicians managing PPH deem it necessary to administer fibrinogen without waiting for laboratory results, this administration is possible (professional consensus). [119]

VII.3 Tranexamic acid (TA)

There is a lot of literature on the prescription of TA in the treatment of haemorrhagic syndromes in various medical situations (menometrorrhagia, subarachnoid haemorrhages...) Or surgical (orthopaedic surgery, cardiac surgery, hepatic surgery, neurosurgery...), In prevention or in treatment of perioperative haemorrhage or trauma.

In the obstetrical context, several studies have been devoted to the evaluation of TA and have been the subject of a recent review. TA has been used preventively to reduce bleeding, mainly after caesarean delivery at a dose of 1 g or 10 mg / kg, or 2 g before caesarean section. Despite methodological limitations, these studies consistently show a reduction in the volume of peri-partum bleeding, and in some cases, a reduction in the incidence of PPH. There was no thromboembolic complication reported. [91]

Administration of these large doses was accompanied by notable side effects: nausea, vomiting, dizziness, tinnitus. Regarding these adverse effects, it should be noted a warning recently issued by the NMSA (National Medicines Safety Agency) on accidents of cortical necrosis with acute renal failure encountered in the context of PPH. This risk must be weighed against the benefit strongly suggested by comparing the results of different studies carried out outside the obstetrical context, in terms of reduction of bleeding and transfusion needs, and of reduction in the risk of worsening. [91]

When using TA in PPH, two practical questions remain unanswered: when to initiate treatment and under what protocol. Regarding when to prescribe TA, an objective trigger could be failure of treatment with sulprostone. As to the method of administration, no range of potentially relevant doses has really been established. However, taking into account the pharmacovigilance alert, it seems important to limit the doses of TA in the event of administration in the management of PPH resistant to sulprostone. The NMSA proposes as part of the summary of product characteristics, a slow intravenous injection of 0.5 to 1 g every 6 to 8 hours in the event of localized fibrinolysis, the dose being increased to 1 g (or 15 mg / kg) in cases of generalized fibrinolysis. [91]

VI.4 rFVIIa factor

rFVIIa was initially used (and received Marketing Authorization) for the treatment of bleeding episodes and the prevention of perioperative bleeding in patients with haemophilia A or B with inhibitors directed against FVIII and FIX, those with congenital FVII deficiency, and those with Glanzmann's thrombasthenia with anti-GPIIbIIIa antibody rendering platelet transfusion ineffective. [91]

More recently, various haemorrhagic situations have been approved as off-label indications, and several publications report the use of rFVIIa for the treatment of haemorrhagic syndromes due to anticoagulant drugs. Over the past decade, several clinical cases, case series, and registry results have been published on the use of rFVIIa in the management of PPH. In most cases, this is a last resort use on bleeding that persists despite conventional treatment measures. In the majority of publications, rFVIIa was effective in reducing the volume or stopping bleeding and reducing the need for transfusion. [46]

Regarding the dose of rFVIIa in PPH, there are no dose-response studies of rFVIIa in PPH. While a wide range of doses has been reported in clinical case records and series, the 90 g / kg dose is most often used. It corresponds to that prescribed for haemophiliac patients, and is also what is recommended in Europe and by the temporary therapeutic protocol of ASNM (French Agency for the safety of health products) in the context of treatment of severe haemorrhages. Further studies would nevertheless be necessary to clarify the impact on the hysterectomy rate and on maternal mortality. [91]

The efficacy of rFVIIa depends on the availability of haemostasis effectors and metabolic conditions. The following thresholds are those from the European recommendations: fibrinogen> 1 g / L, platelet count> 50,000 G / L, haematocrit> 24%, pH> 7.2, normal plasma calcium level, and body temperature as close to normal as possible. [91]

With regards to side effects, a few cases of thromboembolic events have been published in pregnant women who have received rFVIIa for the treatment of PPH. These are exclusively deep vein thrombosis, and sometimes non-fatal pulmonary embolism. The relevance of the thrombotic risk justifies a benefit / risk approach in the decision to prescribe rFVIIa during PPH, and particular attention to thromboprophylaxis in the postpartum period. [91]

Overall, the data available in the literature show that the use of rFVIIa is associated with stopping of bleeding. However, there are no formal arguments to recommend its systematic or early prescription for the prevention or treatment of severe PPH. Prescription should therefore only be considered for the time being in uncontrolled bleeding, after failure of conventional therapies, and after having undertaken the correction of effectors and other haemostasis parameters.

VI.5 Prothrombin complex concentrate (PCC) Prothrombin

complex concentrate is occasionally used during PPH. A study is currently investigating its role in combination with fibrinogen concentrate during PPH 2000-3000 ml. PCCs are associated with thrombotic events in the non-obstetric population. A deficiency of factor (F) II, VII,IX or X assayed directly or assumed because of an abnormal PT/aPTT is uncommon during PPH. [120]

VII. the obstetric management of PPH.

VII.1 initial management.

VII.1.1 Uterotonics

a.1. Oxytocin:

Etymologically the word oxytocin means rapid delivery (from the Greek 'oxus': rapid and 'tokos': childbirth), it is a hormone that has been used for several decades in obstetrics, whether for the activation or the direction of labour. [121]

Compared with physiological delivery without recourse to uterotonics, prophylactic administration by IV or IM route halves the risk of developing a PPH of more than 500ml and of more than 1000ml of blood loss. Preventive administration of oxytocin is recommended for all vaginal deliveries to decrease the incidence of PPH. [122]

In the treatment of PPH secondary to uterine inertia, it is recommended to administer 5 to 10 IU of oxytocin by a slow IV bolus followed by maintenance treatment with an infusion of 20 IU in 250 ml of 5% glucose serum with a flow rate from 5 to 10 IU per hour for 2 hours. [123]. The rate of 10 IU / h and the cumulative dose of 40 IU should not be exceeded, especially that after 30 minutes of ineffectiveness, a second-line treatment should be started. If PPH is stopped after these initial measures, the venous route should be kept for 12 hours after the bleeding diagnosis. [128]

Direct intravenous flash injection of oxytocin produces drops in blood pressure with flushing and transient tachycardia due to the presence of oxytocin receptors on endothelial cells, which leads to a slow IV bolus being preferred in about a minute. Oxytocin has properties similar to those of the antidiuretic hormone, explaining that administration of large amounts (much greater than those recommended here) can lead to water poisoning with headache and nausea. [124]

Uterotonics were administered in 98% of patients in our case study, this rate is almost similar to the data in the literature, and Ducarme [69] reported in his case study of 16 patients who presented a severe haemorrhage during the delivery of which 93.8% of them received oxytocin.

a.2. Prostaglandins:

If after 15 to 30 minutes of using oxytocin, the bleeding is not stopped, prostaglandins should be used. After this 30-minute period, the risk of ineffectiveness increases.

Sulprostone: it is a synthetic prostaglandin E2 (1 ampoule of 500 µg in 50 ml of isotonic saline with an electric syringe). The infusion is started at a rate of 10ml / hr which will be increased in 10ml / hr increments every 15 minutes until clinical improvement. The effective flow should be maintained for 2 hours. Without exceeding a maximum flow rate of 50 ml / h and a total of 3 ampoules. The infusion is then gradually stopped over 12 hours. [125]

Misoprostol: analogue of prostaglandin E1, it is a potently uterotonic prostaglandin which has no marketing authorisation in obstetrics even if it is commonly used, in particular to induce labour in foetal deaths in utero and in interruptions voluntary or medical pregnancy [122]. According to two studies carried out in 2014 [124,126], the use of misoprostol should only be considered when oxytocin is not available for the treatment of PPH in uterine atony. Which is the case in developing countries that cannot use oxytocin because of thy lack efficient cold chain delivery. A single dose of 800 µg (4 tablets of 200 µg) sublingually or intrarectally is effective after childbirth. The co-use of misoprostol and oxytocin in the treatment of PPH has not been shown to be effective. [126]

The contraindications for these prostaglandins are: cardiac pathologies, a history of asthma, severe liver function disorders, decompensated diabetes and a history of epilepsy. [127]

VII.1.2 Artificial delivery

It involves the introduction of the hand into the birth canal to access the uterine cavity and then detach the placenta. It is the only guarantor of obtaining a firmly contracted uterus fundus [128]

After the artificial delivery, it is recommended to practice a uterine massage which consists of applying, repeatedly, manual compression movements of the uterus in order to generate reactive uterine contractions. Postnatal, these contractions aim to fight against the uterus atony (120). Uterine massage is very often performed after endo-uterine procedures as indicated by the French recommendations of 2004 [129] as well as Canadian [130] and American [131] societies.

In case study, artificial delivery was performed in 45 of cases, which corresponds to the data from studies carried out at the university hospitals of Fez and Casablanca and which report respective rates of 23.6% and 29% of artificial delivery performed. [132.133]

VII.1.3 Uterine revision

The technique is similar to that of artificial delivery, with the hand introduced into the uterine cavity, it perceives the placental fragment which has remained stuck to the uterus, detaches it and evacuates it. Often, the revision only brings up a few pieces of membrane debris, the retention of which could be the cause of haemorrhages and infections in the aftermath of childbirth. It is imperative to perform a careful examination, allowing to fully explore the entire uterus and in particular the left angle of the uterine scar, looking for a uterine rupture [128]

In our case study, uterine revision was performed in 14% of cases. It has sometimes been performed on several occasions in patients referred to the UTH from peripheral facilities. following a lack of communication between the different care structures it was not recorded. Considering the risk of postpartum infection, this practice must be corrected.

VII.1.4 Vulva and pelvic exam

After making sure the uterus is empty, the birth canal should be systematically checked, looking for cervical, vaginal or vulvar lesions. Certain elements of the delivery process should point to a traumatic aetiology of PPH: very rapid expulsion of the child, foetal macrosomia, instrumental extraction, antecedent of intervention on the uterine cervix.

In our series, this examination made it possible to diagnose and suture 11 cervical-vaginal lesions, which is between that mentioned by the study carried out at Al Ghassani hospital, the rate of which is 20.58%. [134] and that of the study carried out at the Lariboisière hospital in Paris, the rate of which was 9.3% [135].

VII.1.5 Bakri balloon tamponade

Apart from uterine embolization or laparotomy allowing haemostatic sutures or uterine vascular ligation, uterine balloon tamponade is increasingly developing technic for stopping PPH. Several types of balloons have been used, the principle being to compress the uterine vessels against the uterine wall and stop the bleeding. We can list the "Sengstaken Blakemore tube", the Foley probe or the Bakri balloon.

Bakri's balloon is currently the most used. A few studies with limited numbers have shown a tendency to the stop bleeding, mainly after vaginal or caesarean delivery, but the results remain contradictory [136] and the use of uterine balloon tamponades is not yet common practice. [136] In a study by Alouini S. et al, the Bakri balloon placed as a first line stopped the bleeding in 93% of cases after vaginal delivery and in 80% of cases after caesarean section [136]. In our case study, this method was not used.

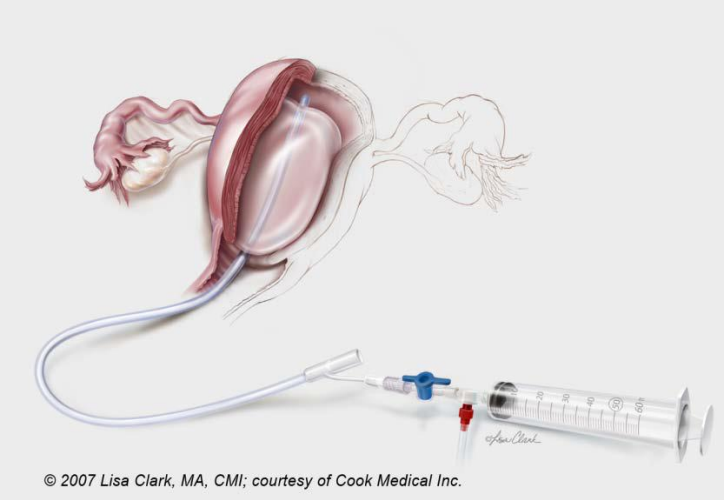


Image 13: shows a Bakri balloon placed in the uterine cavity. [137]

Image 11 represents an algorithm summarizing the course of action to be taken in the event of PPH up to the pre-surgical stage. .

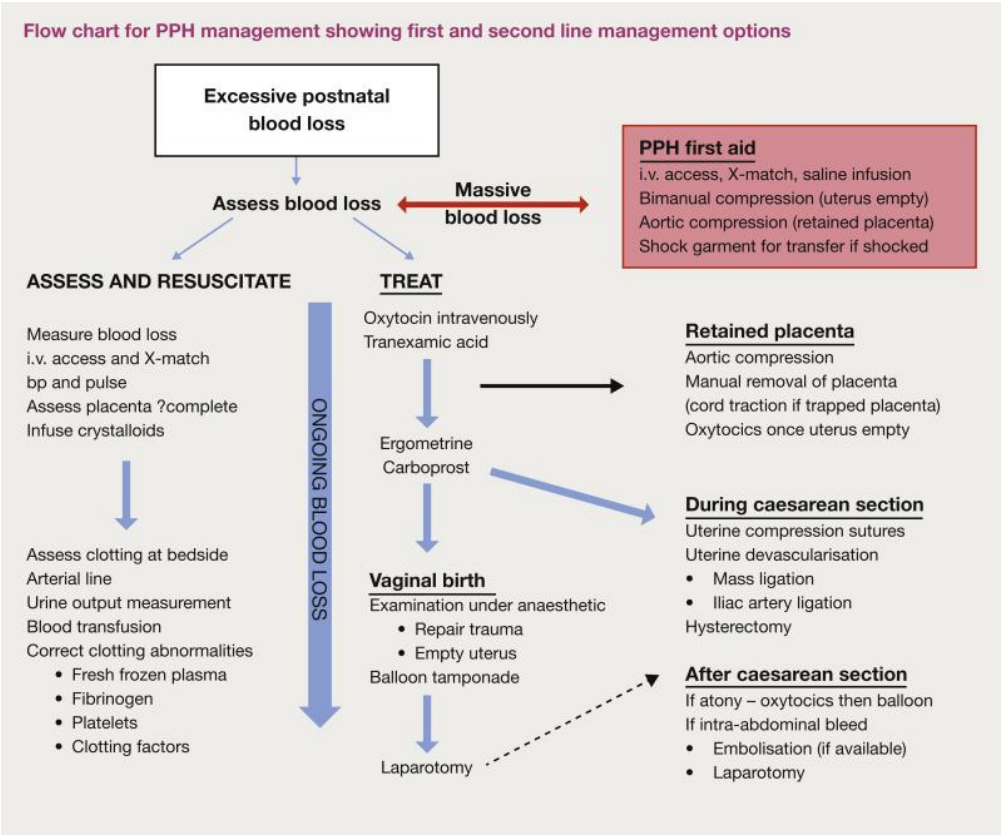


Image 14: flow chart for PPH first and second line management options.

VII.2. Secondary management

If these measures fail and if the patient's hemodynamic state allows it and depending on the technical platform, embolization of the uterine arteries may then be considered. In the event of an unstable patient or embolization failure, surgical treatment will then be decided. Although many advances have been made in conservative surgical treatments (vascular ligatures, uterine plication and padding using various techniques), radical surgical treatment (haemostatic hysterectomy) remains the last step in the event of bleeding from the delivery. massive uncontrollable [138].

VII 2.1. Embolization of the uterine arteries

Pelvic embolization has been used for haemostasis for nearly 30 years to control uncontrollable bleeding after severe trauma to the pelvis or in connection with inoperable gynaecological or urological cancers. Haemostasis uterine embolization was first used successfully in 1979 in a woman with severe immediate postpartum haemorrhage persisting after vascular ligation and hysterectomy. Its use as an alternative to surgical treatment in the management of severe immediate postpartum haemorrhages is currently enjoying renewed interest. [139]

Selective embolization of both uterine arteries should be performed in patients with uterine atony. If arterial vasospasm is present or if catheterization is difficult, non-selective embolization of the anterior dividing trunk of the hypogastric artery may be offered. Anterior trunk embolization is effective in shortening the procedure time and pelvic irradiation. The rate of effectiveness of this strategy appears satisfactory and the rate of complications comparable to that observed during selective embolization of the uterine arteries [140].

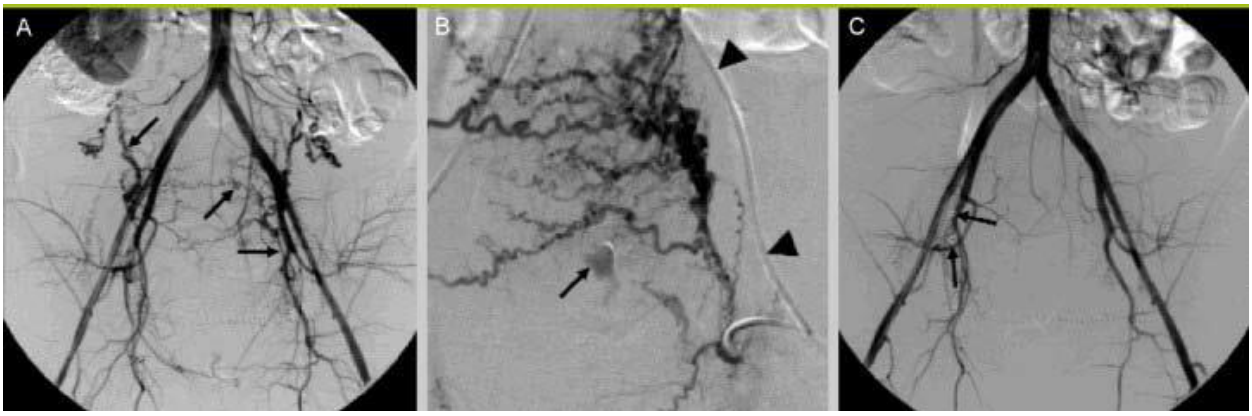


Image 15: Angiography with successful uterine artery embolization in a 31-year-old patient with severe PPH. [141]

A: the initial pelvic angiogram identifies the two uterine arteries (black arrows)

B: after selective catheterization of the left uterine artery (black arrowhead), evidence of extravasation of contrast product at the level of a terminal branch (black arrow), indicating bleeding.

C: The final angiographic check shows complete occlusion of the uterine arteries.

In the event of cervical-uterine haemorrhage, vaginal thrombus, or a tear in the sutured birth canal, additional exploration and embolization of the cervicovaginal pedicles is most often necessary [142].

In our study, no patient was able to benefit from an embolization because of the lack of technical platform in our training.

VII.2.2. Vascular ligation

a. Bilateral hypogastric artery ligation (LBAH)

The surgical technique consists in approaching the iliac vessels, in individualizing the internal iliac arteries which will be linked to the absorbable thread. Performing the surgical procedure in good conditions requires perfect exposure of the small pelvis which passes through the exteriorization of the uterus outside the abdomen and its maintenance pressed forward against the pubic symphysis and laterally in relation to the side concerned as well as the upward repression of the digestive loops by the intestinal fields.

bilateral ligation of the hypogastric arteries does not appear to impair fertility and the subsequent obstetric prognosis of the patients. Although limited data are currently available, the pregnancies described after a history of hypogastric artery ligation were unremarkable and resulted in the delivery of eutrophic infants at term. [143]

Image 16: Ligation of the right and left hypogastric arteries [144].

b triple ligation

This technique presents the same risks of ureteric complications as ligation of the uterine arteries in the event of a technical error.

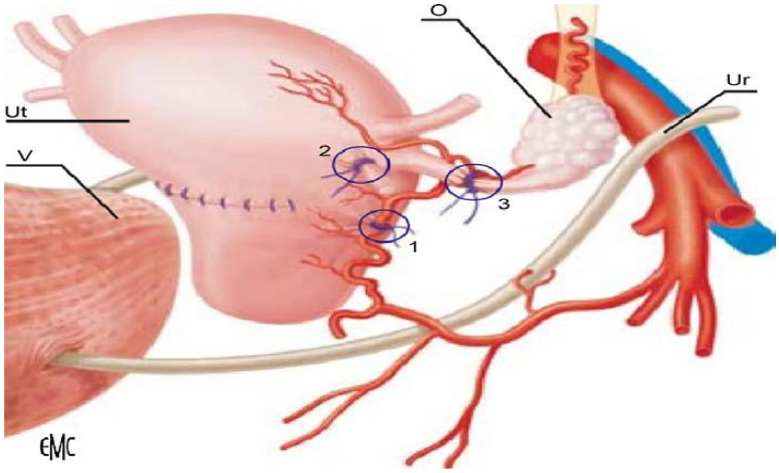


image 14: Triple vascular ligation according to Tsirulnikov. [145]

V: bladder; Ut: uterus; O: ovary; Ur: ureter; 1: ascending branch of the uterine artery; 2: round ligament; 3: utero-ovarian ligament.

In our study, this technique was used in 16 patients. It was judged effective in seven cases, in association with uterine plication, and in the other nine cases required additional management by hysterectomy. Which gives us an efficiency rate of 43%. In the literature, Tsirulnikov reported a success rate of 100%. [143]

C.B Lynch's technique

Lynch has described a mass ligation that aims to counteract uterine inertia by compressing the uterine body [146]. With an open stomach, with a needle set with 70 mm of absorbable suture 0 or 1, he punctures the lower segment 3 cm below the hysterotomy (or at this level if there has been no caesarean). The needle comes out 3 cm above the incision then goes around the uterine fundus and goes back down inside the uterine horns to perforate the posterior lower segment again, go up on the other side on the posterior face, step over the fundus and go back down to the anterior face where it re-enters the lower segment as on the opposite side. After compressing the uterus, the operator tightens the threads and knots to maintain the compression.

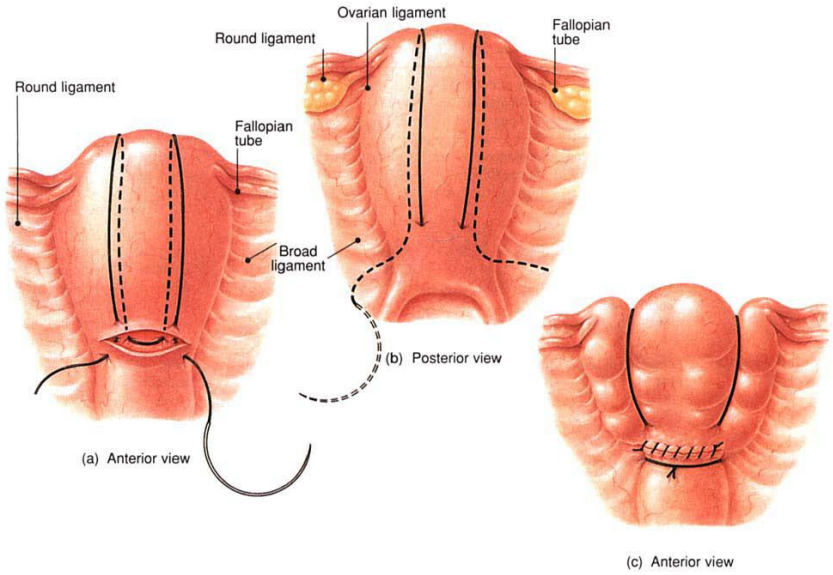


image 17: Images a and b represent an anterior and posterior view of the uterus using the B. Lynch technique. Image c shows the anatomical appearance after applying the technique. [147]

VII.2.3. Radical treatment: haemostatic hysterectomy

A haemostatic hysterectomy is the last resort if obstetric treatments, ligation or padding have failed. It can be total (uterus with the cervix) or subtotal.

As this is a procedure performed in a haemorrhagic emergency context, the important thing is to be quick and efficient. The benefits of subtotal hysterectomy are clear, especially if cervical dilation is initiated. Ureteral and bladder wounds are always something to beware of; accidents occur mainly during total hysterectomies, and in almost all cases during difficult bladder detachments on a scarred uterus. Caution therefore encourages the preference for subtotal hysterectomy. However, there are cases where total hysterectomy is unavoidable such as: placenta previa, placenta accreta, complex rupture of the lower segment, associated severe cervical tear. [148]

We are witnessing a parallel evolution in the frequency of hysterectomies for postpartum haemorrhage, and frequency of caesarean deliveries. The uterine scar being a factor favouring placentation abnormalities, the latter are the most common cause of haemostatic hysterectomy during caesarean section (the increase in placenta

previa rates is thus linked to an inflation of caesarean sections), next comes uterine atony, a much less frequent cause of haemostasis hysterectomy due to changes in its management, in particular by arterial embolization or conservative surgery. The indications for hysterectomy for severe postpartum haemorrhage are ultimately failure of conservative treatment, uterine collapse (uterine rupture), and placentation abnormalities [149].

In our study, haemostasis hysterectomy was used in 56 patients of which 70% of the 56 led to haemostasis, the latter being higher than those mentioned by the results of the literature, especially in France with the study by F. Reyal [152] and D. castiel [150] with 6.8% and 1.96% respectively. This rate is also high compared to a study carried out in Togo by N. Sitti [151] which found a rate of 6.3%

Our rate of 56% hysterectomy remains very high. This could be explained by the high number of patients referred for PPH. In developed countries, the low rate of this intervention is explained by the better conditions of patient care, in particular by the use of new therapeutic methods. It is not the same in other African countries, with which we share the same socio-sanitary conditions. A better policy to prevent bleeding during delivery is therefore essential in our country.

Our study on HPP was carried out within our teaching hospital over a period of 5 years from January 2015 to December 2020. The comparison of our results with those reported by Sanbi et al [79] in Casablanca and Lahlou et al [70] in Marrakech are summarized in Table 20. We note that haemostatic hysterectomies are used at the expense of management with conservative surgery techniques.

Table 28: shows the comparison of our results at the UTH in fez with that of Marrakech and Casablanca for the management of persistent HPP after initial stage.

Surgery performed	Our study	Lahlou et al [70]	Sanbi et al [79]
Hysterectomy	56	35 - 18.9%	18 - 25%
B-lynch	16	6 - 3.24%	-
Hypogastric ligation	35	12 - 6.48%	9 - 12.5%
Triple ligation	16	10 - 5.4%	6 -8.3%
Uterus suture	6	21 - 11.35%	-
Suture or vaginal tears	11	-	-

VIII. Severe postpartum haemorrhage – prevention and treatment

Active management of the third stage of labour and removal of a retained placenta can reduce the risk of PPH. Further preventive measures include minimizing avoidable risk factors or giving additional uterotonics to high-risk women [35,10,153]. Once PPH has developed treatment options relate to the cause of haemorrhage: uterotonics for atony, surgical repair of lacerations, removal of retained tissue, and correction of diagnosed coagulopathy [9]. However, progression in severity is not always avoidable, and has therefore led to increased focus on early warning signs and treatment of severe PPH. Risk factors associated with progression to a more severe PPH include instrumental delivery, augmentation of labour, multiple pregnancy, polyhydramnios and hypertensive disorders [56,154]. As these risk factors are not always preventable or directly treatable, recent studies have tried to identify more specific predictors of severity related to coagulopathy The main focus has been on fibrinogen since Charbit et al in 2007 showed that a fibrinogen concentration 2 g/L was 100% predictive of severe PPH [154]. The study included 128 women with PPH of which 50 (39%) developed severe PPH (defined as haemoglobin decrease 4 g/dl,

transfusion of 4 RBCs, embolization, arterial ligation, hysterectomy or death). Women were enrolled if they had PPH requiring IV prostaglandin infusion (uterotonics). A fibrinogen level of 2 g/L at enrolment was identified in 11 of the 50 women (22%) that developed severe PPH. A number of other studies have confirmed the association between low levels of fibrinogen and blood loss in PPH [155,156,157]. However, association is not always the same as causation. The results from Charbit et al have therefor led to recent studies investigating the impact of fibrinogen substitution on development of a more severe PPH [158-160]. However, as the normal level of fibrinogen at delivery is higher than in the non-pregnant woman (3.5-6.5 g/L vs. 2.0-4.5g/L), the exact threshold for intervention is unclear [161,117,34].

Intensive treatment and care becomes the main focus once PPH has progressed, involving a close collaboration between obstetricians, gynaecologists, anaesthetists and sometimes also coagulation experts. Atony is mainly treated with additional uterotonics, but other causes of PPH should be considered if haemorrhage is refractory to first-line uterotonics [45,162]. Further treatment of all causes of ongoing PPH mainly takes place in the operating room involving all of the multidisciplinary team. Surgical repair of lacerations, removal of placental tissue and intrauterine balloon tamponade can be performed from a vaginal approach. Additional surgical interventions require laparotomy, with uterine haemostatic suturing (e.g. B-lynch suture) or artery ligation being attempted before hysterectomy [10,162,163]. Even though hysterectomy is often considered last option in uncontrollable PPH, it does not necessarily lead to haemostasis perhaps due to untreated coagulopathy [69,164,25].

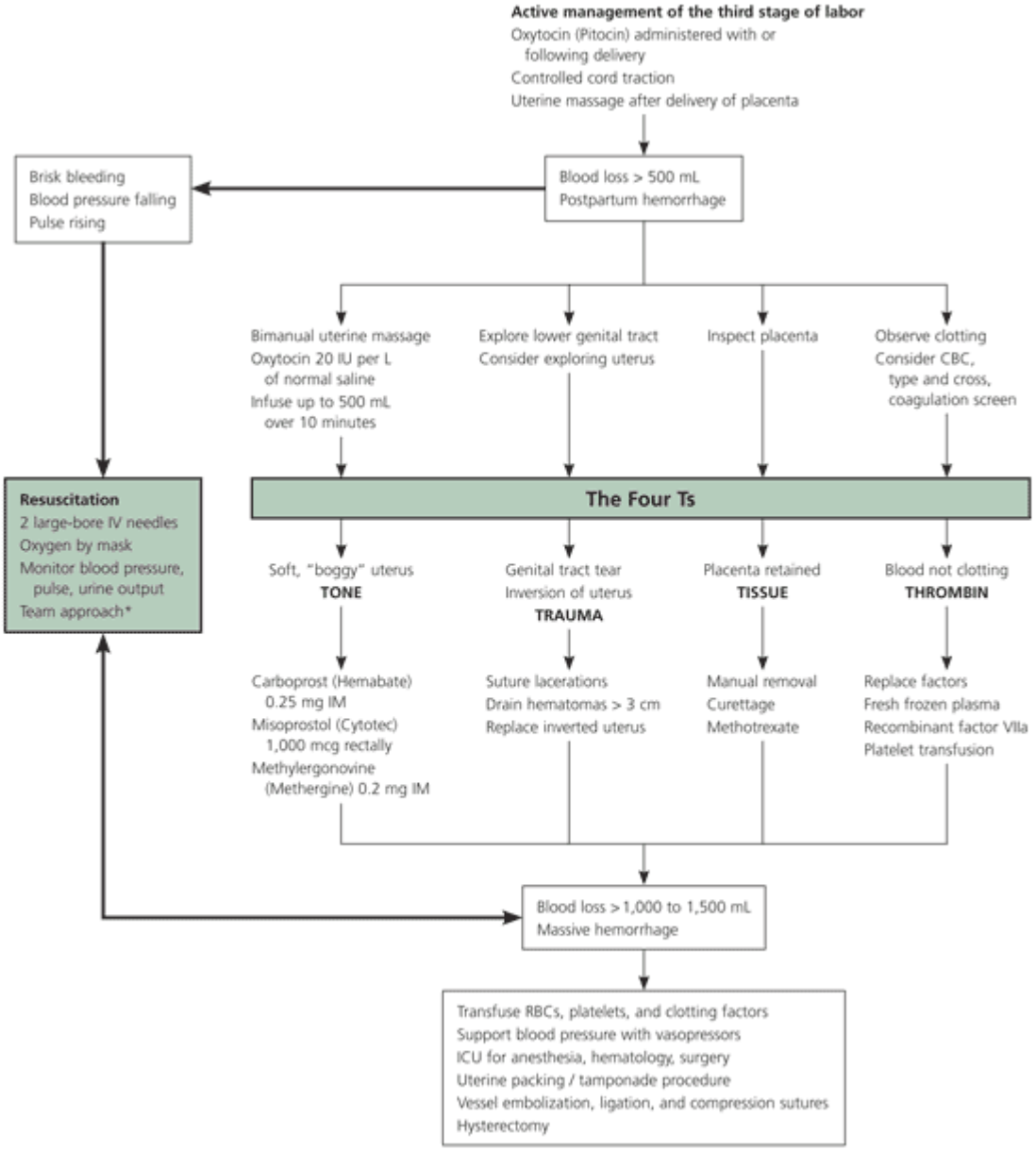


Image 18: Management algorithm according to the aetiology of PPH. [165]

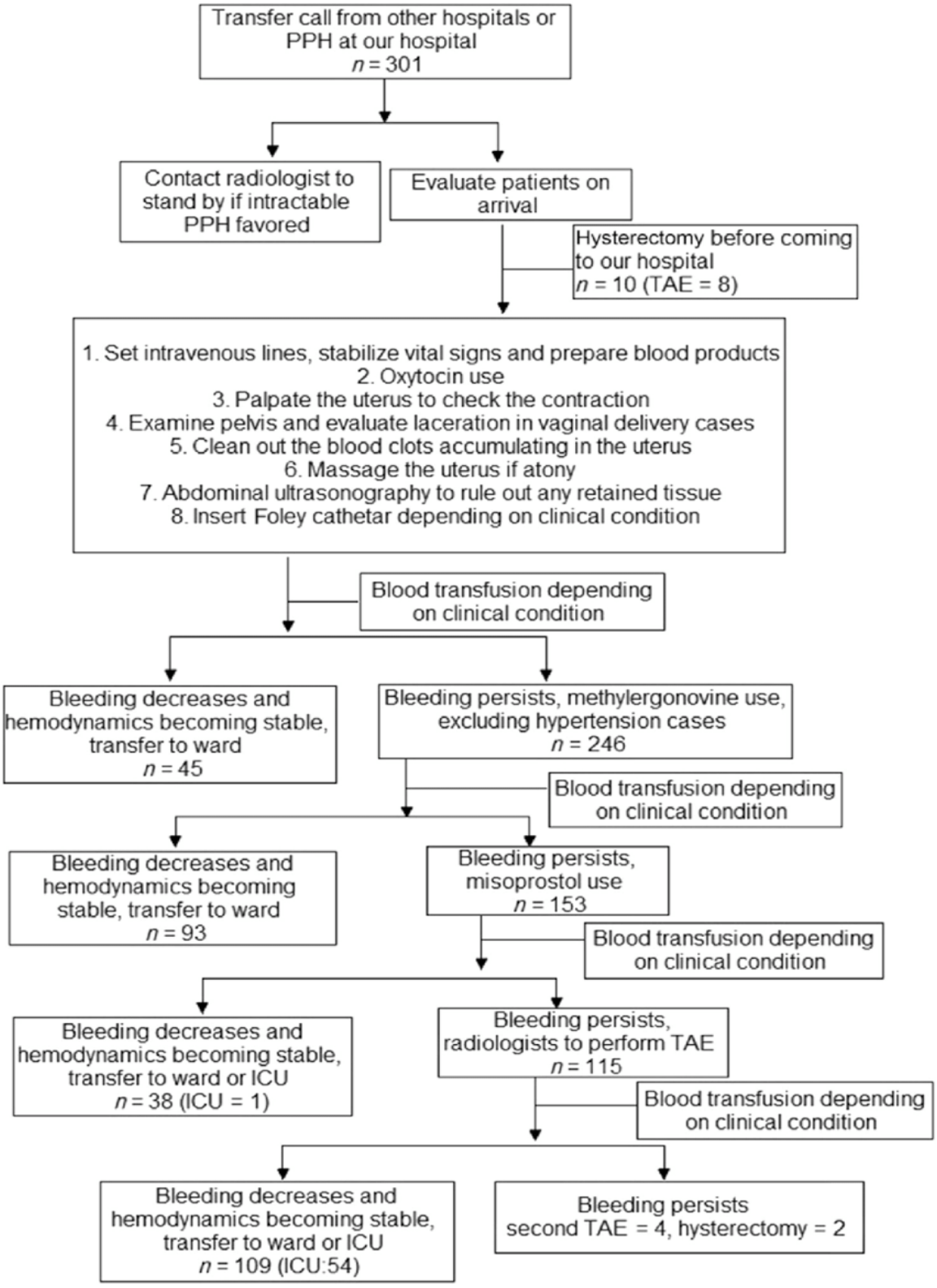


image 19: flow chart for the management of a persistent PPH after initial care.

[166]

IX. Maternal morbidity

IX.1. Kidney failure

Renal failure in PPH is linked to hypoperfusion of the kidneys following blood loss. In our series, we found 28 cases of renal failure, ie a rate of 28%. In the series by Ducarme et al, the rate of renal failure was 6.2%. [36] which was less than our study.

IX.2. Bladder lesions

We counted 4 bladder lesions or 4% of cases, including 4 secondary to uterine rupture and 1 other accidental during caesarean section. In the literature, urological lesions are found in 4 to 16% of cases. This is most often the spread of a rip line to the bladder. [167]

IX.3. Venous thrombosis

An increased risk of venous thrombosis in the postpartum period has been reported in women who have had PPH. This association could be explained by the activation of coagulation processes caused by blood loss, which is even more marked in the context of tissue damage. In the absence of a study with both a sample of sufficient size and detailed data on the treatments administered, it is difficult to know whether this increased risk is directly related to PPH and / or to a pro-thrombotic effect of the treatments received. Fresh frozen plasma (PFC), synthetic fibrinogen and tranexamic acid all potentially have a pro-thrombotic effect, but this remains to be characterized in the context of PPH. [4]

IX.4. Risk of transfusion

PPH exposes women to the immunological and infectious risks of transfusion. Complications of transfusion are linked to the intrinsic quality of the product itself, to genetic diversity, to the disease of the recipient, to human errors combined with organizational flaws, or to the conjunction of several of the above factors. [79]

Immunological risks	- Erythrocyte incompatibility: ABO error, "Dangerous" donor O, Immune or natural alloantibodies - Leuko-platelet incompatibility; post-transfusion purpura - Allergy / anaphylaxis - Graft versus host reaction (GVH) - Immunomodulation - Transfusion inefficiency
Infectious risks	- Viral: (HIV, HBV, HCV, HTLV I / II, CMV, parvovirus B19, EBV, West Nile virus) - Bacterial, syphilis - Parasitic (malaria, American trypanosomiasis) - Unconventional transmissible agents
Overload complications	- Pulmonary oedema - Hemochromatosis

IX.5 nosocomial Infections

An often mentioned but ultimately very little documented complication of PPH is infection. In a retrospective cohort study from a California hospital database including 1.5 million parturients between 2005 and 2007, PPH did not modify the risk of non-severe sepsis but was significantly associated with the risk of severe sepsis (OR adjusted around 4). However, it is difficult, in the absence of prospectively collected data, to establish the temporality between the onset of sepsis and that of PPH. In addition, it is not easy to know whether this associated potential risk is linked to the blood loss itself, or to the invasive procedures used for the treatment of PPH, especially in severe forms. [4]

IX.6 Hysterectomy and permanent sterility

The use of haemostatic hysterectomy is both a marker of acute severity of PPH, but also an element of morbidity in itself, since it induces permanent infertility. The population incidence of haemostatic hysterectomy reported in resource-intensive countries is generally around 3 to 5 per 10,000 deliveries, or 1 case per 2,000 to 3,500 deliveries. [4] in our study cohort out of 100 patients 56% underwent hysterectomies and thus permanent sterility.

IX.7.Sheehan syndrome

PPH with haemorrhagic shock can be responsible for the classic Sheehan syndrome, corresponding to ischemic necrosis of the pituitary gland resulting in more or less complete pituitary insufficiency (mainly ante-pituitary), and the diagnosis of which can be delayed. [4] in our study cohort only one (1) patient presented with Sheehan syndrome.

IX.8.Breastfeeding

A less serious consequence but concerning more women is that of the potential impact on breastfeeding, but this aspect remains poorly studied. In an Australian multicentre study of 206 women who had PPH, two-thirds of women who wanted to breastfeed immediately in postpartum were able to do so, and the proportion of women breastfeeding at 4 months decreased with increasing importance of the loss of blood; however, in the absence of a comparison group, the conclusions are weak. The hypotheses put forward to explain this possible negative impact on breastfeeding are the difficulty of immediate breastfeeding in the context of PPH, the psychological and hormonal repercussions of the stressful event and the physical fatigue related to the anaemia. [4]

X.)Maternal mortality

The latest synthesis of causes of maternal mortality produced by WHO using data from 115 countries for the period 2003-2009 estimates that 27% of maternal deaths worldwide are due to obstetric haemorrhage, ranking it first position. The proportion of deaths attributable to obstetric haemorrhage varies by region of the world, and is 16% for all developed countries, 2/3 of which are related to PPH. [4]

The number of maternal deaths in our series was 22 cases. The main aetiology found was uterine atony followed by associations of aetiologies.

In a study carried out in Antananarivo Madagascar by Fenomanana et al in 2009 [168], the risk factors for mortality related to a PPH found were: maternal age greater than 35 years, parity greater than 4, more work from 1 p.m., a transfusion of less than one red blood cell, a treatment delay of more than one hour and the presence of uterine inertia or uterine rupture.

Recommendations

According to the *Journal of Thrombosis and Haemostasis [72]* the following recommendations were given with regarding PPH coagulopathies:

- If POC or laboratory tests of haemostasis are normal, then no FFP is required.
- if PPH is ongoing, 15 mL kg^-1 FFP should be infused if the PT/aPTT is prolonged to prevent progression to a ratio 1.5 x normal.
- if PT/aPTT is >1.5 x normal larger volumes of FFP may be required to correct haemostasis.
- blood-product replacement based on POCTs supported by a local algorithm is likely to be at least as efficacious as replacement based on laboratory testing.
- if no coagulation results are available and bleeding is ongoing, then, after 4 units of RBC, 4 units of FFP should be infused and 1: 1 RBC: FFP transfusion maintained until haemostatic test results are known.
- FFP should not be used before haemostatic tests are available in PPH caused by trauma or uterine atony until 4 units RBC have been infused because haemostatic impairment is unlikely. FFP before haemostatic tests are available may be justified for placental abruption, AFE or if recognition of PPH has been delayed.
- fibrinogen of at least 2 g L^-1 should be maintained during ongoing obstetric bleeding, even if PT and aPTT are normal. Either cryoprecipitate or fibrinogen concentrate may be used.
- the use of fibrinogen concentrate in an unmonitored or pre-emptive manner is not recommended.
- platelets should be transfused when the platelet count is < 75 x 109 L^_1 based on laboratory monitoring and against 1: 1: 1 RBC : FFP : platelet transfusion ratios.

- In cases of massive ongoing bleeding where women have been given 8 units of RBCs and 8 units of FFP and no coagulation results or platelet count are available then two pools of cryoprecipitate and one pool of platelets may be given.
- women experiencing ongoing PPH should be considered for treatment with 1gm intravenous tranexamic acid.
  - 60 kg^-1 rFVIIa can be considered for ongoing PPH unresponsive to standard treatment or to prevent hysterectomy. We suggest that the fibrinogen should be > 2 g L^-1 and platelets > 50 x109 L^-1. If two doses of rFVIIa have not arrested bleeding, further doses are unlikely to work.
- the use of PCC outside of clinical trials is not recommended. [72]
  - WHO has presented recommendations for the management of postpartum haemorrhage for low-income countries which include Morocco. Some of the important messages contained in this guidance text include:

- The adoption by health centres of official protocols for the prevention and treatment of PPH, as well as official protocols for the referral of women to a higher level of care.
- The use of uterotonics to prevent PPH during delivery and in case of caesarean section is recommended for all deliveries, especially oxytocin (10 IU IV / IM).
- If the placenta does not come out spontaneously, additional administration of 10 IU oxytocin IV or IM combined with controlled cord traction is recommended
- Assessment of uterine tone by abdominal palpation after childbirth for the early identification of uterine atony is recommended in all women.
- Oxytocin administered intravenously is the uterotonic recommended for the treatment of PPH.

- The administration of isotonic crystalloids by the intravenous route is recommended, in preference to colloids, for the fluid resuscitation of women with PPH
- Tranexamic acid is recommended for treatment of PPH if oxytocin and other uterotonics fail to stop the bleeding.
- In women who do not respond to uterotonics or if they are not available, the practice of external uterine massage and intrauterine balloon tamponade is recommended for the treatment of PPH due to uterine atony
- If bleeding continues despite administration of uterotonics and other conservative procedures (such as uterine massage and balloon tamponade), surgical intervention is recommended. [33]

CONCLUSION

Postpartum haemorrhage is a major obstetric emergency, which despite an awareness of the risk associated with its occurrence, remains the leading cause of maternal death in our country and in the world.

Its management must be carried out according to a therapeutic escalation involving medical resuscitation, clinical exploration, and surgical treatment. This, associated with an optimal and systematic treatment delay, determines the success of the treatments.

Coagulopathy in PPH is the single most important predictor for massive transfusion and hysterectomy, and is related to maternal morbidity.

The transfusion ratio of RBC:FFP: PLT should be $\leq$ 2:1:1.

Fibrinogen concentrate is indicated if fibrinogen levels are $<$2g/l or in case of clinical diagnosis of coagulopathy.

Tranexamic acid is indicated at the dose of 1g after the diagnosis of PPH.

The techniques of vascular ligation and uterine plication seem to be promising surgical techniques.

Embolization seems to be the treatment of choice with more than 90% efficiency, but presents as a major inconvenience the need for the presence of a suitable technical platform and nearby, an interventional radiologist available and a patient who's haemodynamic are poor. stable. Unfortunately, these conditions are rarely met.

Haemostatic hysterectomy, despite its drawbacks, remains the ultimate and most effective surgical technique. It is performed immediately when maternal haemodynamic are unstable, or secondarily following failure of conservative treatments.

Preventing postpartum haemorrhage primarily involves raising public awareness and continuing training for professionals involved in childbirth: doctors, midwives, nurses. This is to decrease the prevalence of this entity which predisposes our parturients to an increased risk of death.

ABSTRACT

Abstract :

Introduction:

In our context, Postpartum haemorrhage (PPH) remains the first cause of maternal mortality. Coagulopathy is one of the serious complications of PPH; it nevertheless remains difficult to explore and treat. Lack of early diagnosis or adequate management of coagulopathy worsens the PPH and precipitates the maternal prognosis.

Materials and methods:

We conducted a retrospective, descriptive and analytical, non-interventional study of 100 cases with postpartum haemorrhage and requiring hospitalization in the mother and child intensive care unit of the CHU Hassan II in Fez, during the period from January 2014 to December 2020. This study focused particularly on a cohort of 24 patients who presented with coagulopathy in the context of postpartum haemorrhage.

Results:

The average age of our patients was 31.55 years +/- 6.0. Uterine atony was the most common aetiology and was observed in 38% of patients. Transfusion of labile blood products was performed in 89% of parturients. Tranexamic acid and fibrinogen concentrates were administered in 83% and 32% of cases respectively. Fibrinogen was administered when the fibrinogen level was below 2 g/l or in the presence of clinical signs of coagulopathy.

Oxytocin and misoprostol were administered in 98% and 76% of cases respectively. Vascular ligation was performed in 35% of patients and haemostasis hysterectomy in 56% of cases. The average duration of hospitalization in intensive

care was 7 days with a minimum of 1 day and a maximum of 33 days. 28% of patients in our study had renal failure; including 8 patients who underwent haemodialysis. The mortality rate was 22% in the entire study.

Coagulopathy accounted for 24% of all PPH cases. Retroplacental hematoma and massive bleeding each accounted for 37.5% of the causes of this coagulopathy. All patients with coagulopathy received a transfusion of red blood cells and fresh frozen plasma, including 54.1% who also received platelet concentrates. Fibrinogen concentrates were used in 70.8% of cases. Mortality in the coagulopathy subgroup was 37.5%.

Discussion and conclusions

The management of PPH during pregnancy requires a multidisciplinary and codified approach. The treatment of PPH coagulopathy has seen major advances with the use of fibrinogen concentrates and tranexamic acid, as well as the improvement of massive transfusion practices. Our results show that the absence of early diagnosis or adequate management of coagulopathy worsens PPH and precipitates maternal prognosis. The causes of coagulopathy in our context are dominated by retro-placental hematoma in a context of pre-eclampsia and by massive bleeding, which highlights the major role of pregnancy monitoring in order to detect risk situations. and anticipate the occurrence of coagulopathy. The management of PPH coagulopathy should also benefit from viscoelastic tests of haemostasis, in particular thromboelastometry, which allows rapid assessment of haemostasis and continuous adaptation of management.

Résumé

Introduction :

L'hémorragie du post-partum (HPP) reste dans notre contexte la première cause de mortalité maternelle. La coagulopathie est l'une des complications graves de l'HPP ; elle reste néanmoins difficile à explorer et à traiter. L'absence de diagnostic précoce ou de prise en charge adéquate de cette coagulopathie aggrave l'HPP et précipite le pronostic maternel.

Matériels et méthodes :

Nous avons mené une étude rétrospective, descriptive et analytique, non interventionnelle de 100 cas présentant une hémorragie du post-partum et nécessitant une hospitalisation dans la réanimation mère et enfant du CHU Hassan II de Fès, durant la période allant de janvier 2014 à décembre 2020. Cette étude s'est particulièrement concentrée sur une cohorte de 24 patientes ayant présenté une coagulopathie dans un contexte d'hémorragie du post-partum.

Résultats :

L'âge moyen de nos patientes était de 31,55 ans +/- 6,0. L'atonie utérine était l'étiologie la plus fréquente et a été observée chez 38 % des patientes. La transfusion de produits sanguins labiles a été réalisée chez 89 % des parturientes. L'administration de l'acide tranexamique et des concentrés de fibrinogène a été effectuée respectivement dans 83 % et 32% des cas. Le fibrinogène a été administré quand le taux de fibrinogène était inférieur à 2 g/l ou en présence de signes cliniques de coagulopathie.

L'ocytocine et le misoprostol ont été administrés respectivement dans 98 % et 76% des cas. Une ligature vasculaire a été réalisée chez 35% des malades et l'hystérectomie d'hémostase dans 56 % des cas. La durée moyenne d'hospitalisation

en réanimation était de 7 jours avec un minimum de 1 jour et un maximum de 33 jours. 28 % des patientes de notre étude avaient une insuffisance rénale ; dont 8 patientes ayant bénéficié d'une hémodialyse. Le taux de mortalité était de 22 % dans l'ensemble de l'étude.

La coagulopathie représentait 24 % de l'ensemble des cas de l'HPP. L'hématome retro-placentaire et les hémorragies massives représentaient chacun 37,5% des causes de cette coagulopathie. Toutes les patientes ayant une coagulopathie ont reçu une transfusion de culots globulaires et de plasma frais congelé, dont 54,1% qui ont reçu en plus des concentrés plaquettaires. Les concentrés de fibrinogène étaient utilisés dans 70.8% des cas. La mortalité du sous-groupe de la coagulopathie était de 37,5%.

Discussion et conclusions

La prise en charge de l'HPP durant la grossesse nécessite une approche multidisciplinaire et codifiée. Le traitement de la coagulopathie de l'HPP a connu des avancés majeurs avec l'utilisation des concentrés de fibrinogène et de l'acide tranexamique, ainsi que par l'amélioration des pratiques de transfusion massive. Nos résultats montrent que l'absence de diagnostic précoce ou de prise en charge adéquate de la coagulopathie aggrave l'HPP et précipite le pronostic maternel. Les causes de la coagulopathie dans notre contexte sont dominées par l'hématome rétro-placentaire dans un contexte de prééclampsie et par les hémorragies massives, ce qui met en évidence le rôle majeur du suivi de la grossesse afin de dépister les situations à risque et d'anticiper la survenue de la coagulopathie. La prise en charge de la coagulopathie de l'HPP doit aussi bénéficier des tests viscoélastiques de l'hémostase, notamment la thromboélastométrie qui permet une évaluation rapide de l'hémostase et une adaptation continue de la prise en charge.

ملخص :

مقدمة:

يظل النزف التالي للوضع السبب الرئيسي لوفيات الأمهات في سياقنا .يعتبر تجلط الدم أحد المضاعفات الخطيرة للنزف التالي للوضع .ومع ذلك يظل من الصعب استكشافها وعلاجها .يؤدي غياب التشخيص المبكر أو الإدارة الكافية لهذا الاعتلال الخثاري إلى تفاقم النزف التالي للوضع ويعجل تشخيص الأم.

المواد والأساليب:

أجرينا دراسة استعادية وصفية وتحليلية غير تدخلية لـ 100 حالة مصابة بنزيف ما بعد الولادة وتتطلب دخول المستشفى في وحدة العناية المركزة للأم والطفل في CHU الحسن الثاني في فاس ، خلال الفترة من يناير 2014 إلى ديسمبر .2020 هذه الدراسة ركز بشكل خاص على مجموعة من 24 مريضًا تعرضوا لاعتلال التخثر في سياق نزيف ما بعد الولادة.

نتائج:

كان متوسط عمر مرضانا 31.55 سنة .6.0 -/+ ونى الرحم كان أكثر المسببات شيوعا ولوحظ في38 ٪ من المرضى .تم إجراء نقل منتجات الدم القابلة للشفاء في 89 ٪ من المخاض .تم إعطاء مركزات حمض الترانيكساميك والفيبرينوجين في83 ٪ و32 ٪ من الحالات على التوالي .تم إعطاء الفيبرينوجين عندما كان مستوى الفبرينوجين أقل من 2 جم / لتر أو في وجود علامات سريرية لاعتلال التخثر.

تم إعطاء الأوكسيتوسين والميزوبروستول في98 ٪ و76 ٪ من الحالات على التوالي .تم إجراء ربط الأوعية الدموية في35 ٪ من المرضى واستئصال ارقاء الرحم في56 ٪ من الحالات .كان متوسط مدة الاستشفاء في العناية المركزة 7 أيام بحد أدنى يوم واحد وبحد أقصى 33 يومًا28 .٪ من المرضى في دراستنا يعانون من الفشل الكلوي .بما في ذلك 8 مرضى خضعوا لغسيل الكلى .كان معدل الوفيات22 ٪ في الدراسة بأكملها.

يمثل تجلط الدم24 ٪ من جميع حالات النزف التالي للوضع .كان الورم الدموي خلف المشيمة والنزيف الهائل مسؤولاً عن37.5 ٪ من أسباب هذا الاعتلال الخثاري .تلقى جميع المرضى الذين يعانون من تجلط الدم نقل خلايا الدم الحمراء والبلازما الطازجة المجمدة ، بما في ذلك 54.1 ٪ ممن تلقوا أيضًا تركيزات الصفائح الدموية .تم استخدام مركزات الفيبرينوجين في70.8 ٪ من الحالات .كان معدل الوفيات من المجموعة الفرعية لتجلط الدم 37.5 ٪.

المناقشة والاستنتاجات

يتطلب تدبير النزف التالي للوضع أثناء الحمل منهجًا متعدد التخصصات ومقننًا .شهد علاج تجلط النزف التالي للوضع تطورات كبيرة مع استخدام مركزات الفيبرينوجين وحمض الترانيكساميك ، بالإضافة إلى تحسين ممارسات نقل الدم على نطاق واسع .تظهر نتائجنا أن غياب التشخيص المبكر أو الإدارة الكافية لاعتلال التخثر يفاقم النزف التالي للوضع ويعجل تشخيص الأم .تهيمن أسباب اعتلال التخثر في سياقنا على الورم الدموي خلف المشيمة في سياق تسمم الحمل والنزيف الهائل ، مما يسلط الضوء على الدور الرئيسي لمراقبة الحمل من أجل اكتشاف حالات الخطر وتوقع حدوث اعتلال التخثر .يجب أن تستفيد إدارة اعتلال تخثر الدم في النزف التالي للوضع أيضًا من اختبارات المرونة اللزجة للإرقاء ، ولا سيما قياس التخثر البطني ، الذي يسمح بالتقييم السريع للإرقاء والتكيف المستمر للإدارة.

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Coordonnateurs : MohssineDoumiri , Anas Tazi Saoud

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FACULTÉ DE MÉDECINE, DE PHARMACIE ET DE MÉDECINE DENTAIRE

سنة 2022 أطروحة رقم 22/115

نزيف ما بعد الولادة :
إدارة تجلط الدم و جوانب العلاج في وحدة العناية المركزة للولادة

الأطروحة

قدمت و نوقشت علانية يوم 2022/03/14

من طرف

السيدة إديث نجاوا إنغالاندي

المزدادة في 1993/11/06 بزامبيا

لنيل شهادة الدكتوراه في الطب

الكلمات الأساسية

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