Review Article

Patient blood management in India - Review of current practices and feasibility of applying appropriate standard of care guidelines. A position paper by an interdisciplinary expert group

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Abstract

In a developing country like India, with limited resources and access to healthcare facilities, dealing with massive hemorrhage is a major challenge. This challenge gets compounded by pre-existing anemia, hemostatic disorders, and logistic issues of timely transfer of such patients from peripheral hospitals to centers with adequate resources and management expertise. Despite the awareness amongst healthcare providers regarding management modalities of bleeding patients, no uniform Patient Blood Management (PBM) or perioperative bleeding management protocols have been implemented in India, yet. In light of this, an interdisciplinary expert group came together, comprising of experts working in transfusion medicine, hematology, obstetrics, anesthesiology and intensive care, to review current practices in management of bleeding in Indian healthcare institutions and evaluating the feasibility of implementing uniform PBM guidelines. The specific intent was to perform a gap analysis between the ideal and the current status in terms of practices and resources. The expert group identified interdisciplinary education in PBM and bleeding management, bleeding history, viscoelastic and platelet function testing, and the implementation of validated, setting-specific bleeding management protocols (algorithms) as important tools in PBM and perioperative bleeding management. Here, trauma, major surgery, postpartum hemorrhage, cardiac and liver surgery are the most common clinical settings associated with massive blood loss. Accordingly, PBM should be implemented as a multidisciplinary and practically applicable concept in India in a timely manner in order to optimize the use the precious resource blood and to increase patients' safety.

Keywords: Bleeding, blood transfusion, coagulopathy, hemorrhage, hemostasis testing, patient blood management, patient safety, point-of-care testing, thromboelastometry

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Introduction

The prognosis of excessive bleeding patients, particularly during the perioperative or periprocedural period, is dependent on the clinical situation, patient's hemostatic ability and the clinician's experience with bleeding management. The utility of the pre-operative evaluation,[1] the clinical and diagnostic assessment during bleeding, and the accessibility to and availability of procedures, pharmacologic agents or blood components to arrest bleeding, are the most crucial aspects of management of abnormal bleeding.

Clinical history of bleeding diathesis and family history of same is the first step that can predict abnormal bleeding.[2] Most centers rely on standard laboratory tests to predict bleeding during surgical interventions[3] despite their proven limited utility in elective and acute settings.[4] The medical/health education curriculum is structured on stratified disciplines, and there is a conspicuous absence of a multidisciplinary approach model; The basic medical education still needs to define and incorporate the principles and protocols of patient blood management. While there is a non-uniform adoption of blood component therapy, the use of point-of-care viscoelastic testing[5-8] in diagnosing as well as guiding the management of such cases, also, is limited to, mostly, private healthcare facilities based in large cities.

This interdisciplinary expert group evaluated all challenges and current practices and attempted to address them in a structured manner based on a detailed *questionnaire* designed and developed by the group itself. This expert group aims to provide consensus statements towards identifying steps which can uniformly predict abnormal and excessive bleeding and, at the same time, minimizing perioperative blood loss by rational use of blood products and hemostatic agents as an essential part of a Patient Blood Management program. In this first step of the exercise, a consensus was developed, the focus of which is on assessing the competence of patient's hemostasis as well as the availability of resources at various levels of healthcare facilities in India. Some broad consensus statements on managing an unexpected case of abnormal bleeding in select clinical settings have also been made. The consensus from this expert group is expected to pave the way for concerned medical disciplines and associations towards developing specific algorithms for the management of perioperative bleeding in various clinical settings, particularly customized for India, as an essential part of a Patient Blood Management and patient safety programs in India.

Methods

Establishment of an interdisciplinary expert group

The unmet needs and poorly understood protocols of managing perioperative bleeding led to a group of experts, belonging to different disciplines from across the country, working in government and private healthcare institutions, to come together and discuss, evaluate and strategize the modus operandi to deal with such clinical situations. This expert group first met on November 21st, 2018 in New Delhi, India, with the agenda based on common clinical situations encountered, challenges faced, and resources required to manage them.

Development of the questionnaire

Following the meeting, and a series of communications around the summary of the discussions held, a *questionnaire* was developed as a systematic approach to cover a broad spectrum of clinical, scientific, technical, and referential aspects. The expert group thoroughly validated the questionnaire. The questionnaire was sent to all the experts and all of them responded with their inputs within the given timeline.

Consensus statements and manuscript development

Basis inputs to the questionnaire received, a subcommittee started summing up the responses. Following a series of communications, several virtual and one physical meeting, the opinions, suggestions, and recommendations were summarized in the final manuscript. Some of the terminology used is as follows:

Expert group "agrees/suggests"—when more than 50% of members agreed to a statement.

Expert group "recommends" —when more than 75% of members agreed to a consensus statement.

No consensus—when less than 50% of members agreed.

Negative recommendation—when the expert group recommended against a practice.

Evidence and references

This is a consensus statement based on the experience and expertise of the members of the interdisciplinary expert group. The expert group members have quoted appropriate references from literature to support their opinions and statements.

Results, Consensus and Discussions

Abnormal bleeding

Abnormal bleeding is defined as any perioperative or peri-procedural bleeding exceeding the usual (expected) average for a given surgery or procedure based, either on surgeon's subjective opinion or, as in some cases, pre-defined established criteria. Such a bleeding may require (massive) transfusions adversely affecting hospital course and patient outcomes. The common conditions associated with perioperative abnormal bleeding are listed in Table 1.

Bleeding history assessment

Bleeding and medication history is an essential tool to evaluate the risk of abnormal bleeding before a surgical procedure or intervention.[9-12] Ideally, any laboratory screening should only be done if bleeding history is indicative.[13,14] However, minor bleeding disorders could be missed even with an elaborate history.[15] Globally, the International Society of Thrombosis and Haemostasis (ISTH) Bleeding Assessment Tool (BAT) score is the most commonly used tool.[16]

Adequacy and reliability of the bleeding history

Bleeding history (or medical history, per se) is limited by inadequacy in standardization and evaluation as well as, to some extent, non-reliability of the patient; the expert group *agrees* that there is a need to understand the utility of ISTH-BAT score from that perspective. The expert group *suggests* assessing the confidence intervals for ISTH-BAT score. The expert group *recommends* designing a bleeding score that could aid in quick bedside evaluation of hemostatic challenges like platelet disorders and clotting factor deficiency, leaving aside the ones that evaluate connective tissue factors. The expert group *recommends* that there should *not* be an attempt to supplement the history by standard laboratory tests. The expert group consensus on medical history for assessing patient's bleeding risk are presented in Table 2.

Laboratory screening tests for perioperative abnormal bleeding

The aim of preoperative screening is to predict the risk of bleeding before surgery or invasive interventions. Traditionally, the usual pre-operative screen includes bleeding time (BT), platelet count (PLC) or complete blood count (CBC), prothrombin time (PT) and activated partial thromboplastin time (APTT).[17] However, the positive predictive value of these tests is limited.[18,19] Only a few follow up the abnormal screen test with mixing studies for further evaluation although these studies could miss minor factor deficiencies. Some centers go for platelet function testing since BT is not very reliable or reproducible.[20] The expert group *recommends against* the use of BT as a pre-operative test. Notably, the most common causes of bleeding, platelet function defects and Von Willebrand disease (vWD) are not depicted by these standard lab tests.[21] Also, a common reason for a prolonged APTT in children with infection, e.g., tonsillitis, is positive transient lupus anticoagulant.[22,23] There is growing consensus,[24] and the expert group *agrees* that a collaborative and cost-effective strategic approach is required to identify patients with high

Table 1: Conditions associated with abnormal bleeding

Bleeding disorder (potential bleeder)
Hereditary
Acquired
Iatrogenic
Comorbid conditions
Ante/Postpartum hemorrhage
Chronic Liver disease
Chronic Renal disease
Procedure/external injury related
Surgery - Liver transplant/Cardiac (including redo) surgery
Trauma
Snake bite
Complex mechanism
DIC
Dilutional coagulopathy
Patient's clinical condition
Thrombocytopenia
Hypothermia
Acidosis
Low Haematocrit/Haemoglobin
Hypocalcaemia
Drugs (anti-platelet drugs, anticoagulants)
Evolutionary
Inappropriate blood component transfusion
Inadequate blood component transfusion
Massive trauma

Table 2: Expert group recommendation for assessment of patient's bleeding risk

History of bleeding:
Bleeding during infancy (e.g., umbilical stump bleeding) and childhood (e.g., bleeding with loss of deciduous teeth);
Bleeding during adolescence and adulthood (menstruation and pregnancy);
Any bleeds severe enough to require surgical intervention, nasal packing or cautery, a visit to the emergency department, or transfusion.
Any history of unusual bleeding or spontaneous bleeding into mucosa or muscles even with minimal cuts/bruises/brushing.
Dark stools/blood in sputum/hematemesis
History of iron deficiency or iron-responsive anemia
Family history relevant to risk of bleeding disorder
Past/currently used drugs & medication
Low dose aspirin
Antiplatelet drugs
Anticoagulants
Consanguinity in family

bleeding risk in the form of an adequate and appropriate medical and bleeding history along with laboratory tests, where needed.

Predicting the likelihood of bleeding or identifying "abnormal" bleeding

Not all bleeding tendencies will be evident on history, nor will laboratory tests pick up all cases of abnormal bleeding. The expert group *recommends* a structured and collaborative approach as given in Table 3. As depicted in Table 3, none of the tests, by itself, is sensitive or specific to predict the risk of bleeding or identify the abnormal one during an episode. Most often, abnormal bleeding is based on a combination of haemostasis issues. Furthermore, not all the tests are available at all levels of health care, particularly in primary health care facilities in developing countries. Often, the "ideal best" test is supplemented by the "available best" test. The expert group *agrees* that there is a need to fill the gap between the "ideal best" and the "available best". There was *no consensus* formed in the expert group on whether the "ideal best" is a true or a surrogate replacement of the "available best". The expert group *recommends* that whenever and wherever possible, the appropriate tests should be done at the baseline. They may be repeated as per other validated protocols or depending on the patient's clinical condition.

Stratifying resources based on health-care facilities

The expert group *suggests* the minimum infrastructure which must be available at a health care center to manage cases with or at high risk of perioperative abnormal bleeding. Health care facilities in most developing countries are primarily of three categories. Primary health-care facility means either a government primary healthcare center or a nursing home or a very small hospital with limited health care services. Secondary health-care facility means a government community health center (CHC) or a small hospital in a non-metro city. Tertiary health-care facility means a medical university hospital or a large private hospital or an apex governmental institute or national reference hospital. The expert group *recommended* resources for dealing with cases of abnormal bleeding are given in Table 4.

Blood components and other products available (*Not in order of preference or prevalence*) in India are:

A. Packed red blood cells (PRC)
B. Fresh frozen plasma (FFP)
C. Platelet concentrate (Random Donor/Single Donor)
D. Cryoprecipitate
E. Fibrinogen concentrate
F. Recombinant factor VIIa
G. Tranexamic acid (TXA)/Epsilon Aminocaproic Acid (EACA)
H. Prothrombin complex concentrate (PCC)
I. Antidotes - Protamine, PCC, Idarucizumab
J. Desmopressin.

Medical/Health education curriculum

The medical/health education system of India is very elaborate and is updated continuously. However, the expert group *agrees* that there is a scope of improvement. The expert group *suggests* revising the medical or health education curriculum to a more organized, multi-disciplinary and resourceful in dealing with perioperative abnormal bleeding. A transition from traditional laboratory methods towards viscoelastic testing in managing bleeding patients, wherever feasible, could shift clinical practice from fixed-ratio-driven massive transfusion protocols (MTPs) to goal-directed therapy and patient blood management. Many of the patient blood management concepts and protocols adopted globally are relevant and available in countries like India; however, many hospitals may need educational and logistic support in implementation.

Clinical conditions with high bleeding risk

Many clinical conditions are associated with a higher bleeding risk, example—von Willebrand Disease, hemophilia, liver/kidney diseases, specific medications—aspirin, antiplatelet drugs, NSAIDs, oral anticoagulants (vitamin K antagonists and direct oral anticoagulants (DOACs)). Furthermore, certain procedures are associated with excessive bleeding such as major orthopedic surgery (e.g., total hip/knee arthroplasty), major abdominal surgery (e.g., liver resection and transplantation, tumor resection, pancreatic surgery), cardiovascular-thoracic surgery, etc., Such procedures, along with pre-existing hemostatic disorder or those acquired during the procedure, may cause massive bleeding. In such cases, the effectiveness of bleeding risk assessment tools decreases. The expert group *recommends* that, in all such cases, adequate and appropriate diagnostic screening tests must be performed. Here, standard laboratory tests (SLTs) or, preferably, viscoelastic testing (VET) are more appropriate. VET provides a comprehensive picture with shorter turn-around time. Patients with or at risk of abnormal bleeding must be referred to an appropriate health care facility to ensure optimal management and allow for improved patient outcomes.[25-30]

Massive transfusion protocols and the need for "shock packs"

Various definitions of massive blood transfusion (MBT) have been published in the medical literature.[31-38] The principles of management of any acute/massive blood loss involve the management of intravascular blood volume and loss of blood components and management strategies specific to the

Table 3: Tests recommended for predicting bleeding or identifying abnormal bleeding (NOT in order of preference)

Abnormal bleeding condition	Utility of clinical history	Recommended test	Best lab based test	Best POC test
Hereditary bleeding disorders				
Hemophilia	Effective	Single factor assays	APTT and Mixing	INTEM; Kaolin-TEG
VWD	Effective	VWF: RCo/VWF: Ag	PFA-100/200/Multiplate	Multiplate
Platelet dysfunction	Effective	Aggregometry/Flow cytometer	Light transmission aggregometry	Multiplate/ROTEM platelet/Verify now/TEG platelet mapping
Acquired bleeding disorders				
Factor deficiency (Fibrinogen, II, VII, VIII, X, XIII)	Not always	Factor assay and inhibitor assays	PT/APTT and Mixing	EXTEM, INTEM and FIBTEM; Kaolin-TEG, TEG-FF
Thrombocytopenia	No	Platelet count with histogram	Platelet count	EXTEM and FIBTEM; Kaolin-TEG and TEG-FF
Iatrogenic Bleeding	No	Hb and platelet count	Hb and platelet count	EXTEM, INTEM, FIBTEM and ROTEM platelet to exclude other reasons for bleeding
Liver condition				
Cirrhosis	Unlikely	Factor assays (Fib and FV) D-Dimer	PT/APTT and Mixing	EXTEM and FIBTEM
Liver Transplant	No	Factor assays (Fib and FV) D-Dimer	PT/APTT and Mixing	EXTEM, FIBTEM, INTEM and HEPTEM
Renal disease	No	HCT and PFA	PT/APTT and Mixing	EXTEM and FIBTEM
Peri- or post-partum	No	Fibrinogen	Fibrinogen	EXTEM and FIBTEM; rapid-TEG and TEG-FF
Cardiac procedures	No			
Aortic dissection	No	EXTEM, FIBTEM, INTEM, HEPTEM; Kaolin-TEG, Heparinase-TEG, Rapid-TEG, TEG-FF/Multiplate/ROTEM platelet/Verify Now/TEG platelet mapping; ACT	Fibrinogen/Platelet count/PT/APTT and Mixing	EXTEM, FIBTEM, INTEM and HEPTEM; Kaolin-TEG, Heparinase-TEG, raid-TEG and TEG-FF/Multiplate/ROTEM platelet/Verify now/TEG platelet mapping; ACT/blood gas analysis
CABG	No	EXTEM, FIBTEM, INTEM, HEPTEM; Kaolin-TEG, Heparinase-TEG, Rapid-TEG, TEG-FF/Multiplate/ROTEM platelet/Verify Now/TEG platelet mapping; ACT	Fibrinogen/Platelet count/PT/APTT and Mixing	EXTEM, FIBTEM, INTEM and HEPTEM; Kaolin-TEG, Heparinase-TEG, raid-TEG and TEG-FF/Multiplate/ROTEM platelet/Verify now/TEG platelet mapping; ACT/blood gas analysis
ECMO	No	EXTEM, FIBTEM, INTEM, HEPTEM; Kaolin-TEG, Heparinase-TEG, Rapid-TEG, TEG-FF/Multiplate/ROTEM platelet/Verify Now/TEG platelet mapping; ACT; anti-Xa	Fibrinogen/Platelet count/PT/APTT and Mixing. anti-Xa	EXTEM, FIBTEM, INTEM and HEPTEM; Kaolin-TEG, Heparinase-TEG, raid-TEG and TEG-FF/Multiplate/ROTEM platelet/Verify now/TEG platelet mapping; ACT/blood gas analysis
Heparin effect	No	Anti-Xa	Anti-Xa/ACT	INTEM/HEPTEM CT-ratio/ Kaolin-TEG; Heparinase-TEG/ACT
Protamine overdose	No	INTEM/HEPTEM CT-ratio	NA	INTEM/HEPTEM CT-ratio
Trauma	No	EXTEM and FIBTEM; Rapid-TEG and TEG-FF	Fibrinogen/Platelet count/PT/APTT and Mixing	EXTEM and FIBTEM; Rapid-TEG and TEG-FF/blood gas analysis
DIC	No	Fibrinogen, platelet count, D-dimer	PT/APTT and Mixing	EXTEM, FIBTEM and NA-HEPTEM; Multiplate/ROTEM platelet
Dilutional coagulopathy	No	Fibrinogen and Platelet count	Fibrinogen/PT/APTT and Mixing	EXTEM and FIBTEM; Rapid-TEG and TEG-FF
Hypothermia	No	Test devices that adjust temperatures	VET adjusted to patient temperature	VET adjusted to patient temperature

Contd...

Table 3: Contd...

Abnormal bleeding condition	Utility of clinical history	Recommended test	Best lab based test	Best POC test
Acidosis	No	Blood gas analysis	Blood gas analysis VET adjusted to patient temperature	Blood gas analysis
Low Hb/Hct	No	Hemoglobin	Hemoglobin	POC Hb devices/Blood gas analysis Blood gas analysis

EXTEM - Tissue factor-activated ROTEM assay with heparin neutralization; FIBTEM - Tissue factor-activated ROTEM assays with elimination of platelet contribution and heparin neutralization; HEPTEM -Ellagic acid-activated ROTEM assay with heparin neutralization; INTEM - Ellagic-acid-activated ROTEM assay; NA-HEPTEM - non-activated ROTEM assay with heparin neutralization; Heparinase-TEG - Kaolin-activated TEG with heparin neutralization; Kaolin-TEG - kaolin-activated TEG assay; Rapid-TEG - TEG assay activated by kaolin and tissue factor; TEG-FF - TEG functional fibrinogen; PT - Prothrombin Time; APTT - Activated partial thrombin time; DIC - Disseminated intravascular coagulation; NA - not applicable; VET - Viscoelastic Testing; PFA-100/200 - Platelet Function Analyzer 100/200; ACT - Activated Clotting Time; VWF: RCo/VWF Ag: VWF Ristocetin Cofactor/Antigen ratio; Hb - hemoglobin; Hct - hematocrit

Table 4: Recommended resources for management of abnormal bleeding (NOT in order of preference)

Resources/Tool	Primary HCF	Secondary HCF	Tertiary HCF
Protocol/Procedure*	Yes	Yes	Yes
Blood bank and component center†	Storage	Storage with freezers/Blood bank with components	Blood bank with cryoprecipitate and platelet concentrate and fibrinogen concentrate
Pharmacological agents‡	Tranexamic Acid	Tranexamic Acid	Tranexamic Acid, PCC, rVIIa
Haemostaseology Team§	May/May not	May/May not	Yes
Lab based screening tests‖	Hemoglobin/Platelet count	Fibrinogen/PT/APTT/D Dimer	Factor assays/Aggregometer/Verify now
POC investigations¶	May/May not	Hb/VET	Hb/VET/Verify Now/Multiplate/ROTEM platelet
Triggers for hospital transfer	4 red cells on top of blood order schedule	8 red cells on top of blood order schedule	10 red cells on top of blood order schedule

*HCF: Health care facility, VET: Viscoelastic Testing, Hb: Hemoglobin. * - Depicts Standard Operating Procedure or commonly accepted and validated protocol or algorithm. †Blood bank that makes blood components like packed red cells, fresh frozen plasma, platelet concentrate (PC) and cryoprecipitate available for patient use. ‡Pharmacological agents include tranexamic acid (TXA), epsilon aminocaproic acid (EACA), prothrombin complex concentrate (PCC), fibrinogen concentrate, single factor concentrates (e.g., factor VIII, IX, XIII, rFVIIa - recombinant factor VIIa) and antidotes for certain drugs that may cause bleeding (e.g., protamine, PCC - prothrombin complex concentrate). §Haemostaseology team including anesthetists, intensivists, transfusion medicine and surgeons as mandatory and preferred presence of a lab hematologists and/or a clinical hematologist. ‖Lab based screening test include blood cell count (Hb & PLC), PT, APTT, Fibrinogen, D-Dimer, single factor analysis and platelet function testing. ¶POC investigations include ACT, viscoelastic testing (global coagulation tests) and platelet function testing. Timely and appropriate transfer of patient to health care centers which are capable of and experienced in dealing with patients suffering from abnormal bleeding*

underlying clinical setting.[39] With the better understanding of the pathophysiology of hemorrhagic shock, resuscitation of patients with massive hemorrhage has advanced from reactive, supportive treatment (crystalloid, packed red cells, laboratory tests-based use of coagulation factors) to use of proactive standardized protocols called massive transfusion protocols (MTP). MTPs aim at curbing or eliminating the potential threat of acidosis, hypothermia and coagulopathy that eventually appears in these settings.

Shock packs have a predefined ratio (1:1:1 or 2:1:1) of RBCs, FFP/cryoprecipitate and platelet units (random donor) for transfusion.[40,41] Currently, 1:1:1 ratio (1 unit each of packed red cells, Fresh Frozen Plasma and Platelet (Single donor)) is the most commonly adopted MTP concept in India. However, it must be considered that, fixed-ratio MTPs have certain limitations. First, they are not standardized, i.e., the trigger for initiating or stopping the protocol as well as the optimum ratio of blood components is non-uniform. Second, if an MTP is triggered for a non-massive blood loss situation, it may lead to wastage of blood products and over-transfusion resulting in transfusion-associated circulatory overload (TACO), which is a major reason for transfusion-associated morbidity and mortality.[42-46] The expert group *agrees* that the trigger for initiating an MTP should be defined and standardized. The obligation of developing such triggers of transfusion is on respective medical associations dealing with different clinical fraternities.

One significant limitation of standard coagulation tests in the management of massive hemorrhage is the long turn-around-time of 45-90 minutes;[47-49] also, efficacy of MTPs is assessed by means that are not standardized or validated. Shock packs gain importance in the early phase of massive hemorrhage when point-of-care viscoelastic testing results are not available.[5,50] The expert group *agrees* that waiting for POCT results until the blood loss is 1-1.5 liters (like in case of PPH) could avoid unnecessary and irrational administration of shock packs early and wouldn't further complicate the coagulopathy.[51-53] However, since there is no POCT available for goal-directed bleeding management in most Indian hospitals to replace empirical transfusion, the expert group *recommends* defining the composition and triggers of shock packs for centers with no availability of or

access to viscoelastic testing. The stop criteria for an MTP should also be predefined in case of bleeding control based on physiological criteria (hemodynamic status and/or laboratory values) or a decision that further resuscitation is likely to be futile.

Recommendations for specific clinical settings

Obstetric hemorrhage

Obstetric hemorrhage is one of the most common causes of maternal mortality in developing countries, including India.[54,55] Obstetric hemorrhage most often occurs in the peripartum, particularly in the postpartum period. In most institutions, severe postpartum hemorrhage (PPH) is defined as blood loss of more than 1500 ml, or a fall in hemoglobin more than 4 g/dl after acute blood loss in a parturient.[56] Current concepts of bleeding management in military hemorrhage have been transferred to PPH, where the tendency is to use PRBCs and FFP in the ratio of 1:1 with early use of platelets.[57] It is arguable whether FFP transfusion is reasonable at all in PPH due to a higher fibrinogen plasma concentration in pregnant women compared to the blood donors.[58] The 2016 ISTH guideline on the management of coagulopathy associated with PPH recommends not to transfuse FFP if POC or laboratory tests of hemostasis are normal. A massive bleeding protocol should be present and implemented in all obstetric departments and delivery rooms.[59] This protocol/algorithm should be adapted to local expertise and the availability of diagnostic tools and therapeutic interventions. The massive transfusion 'pack' consisting of four units of O-negative PRBCs, four units of AB FFP, and one apheresis platelets should ideally be available. Here, fibrinogen concentrate, and prothrombin complex concentrate could replace FFP in these transfusion packs and may improve bleeding management in PPH, significantly.[51-53] The expert group *agrees* that the two most important reasons for obstetrics hemorrhage-related morbidity and mortality are, first, the absence of blood banks in rural areas or the delay in/inability to transfer bleeding parturient to centers with a blood bank and second, the unavailability of coagulation testing facilities around the clock for guiding bleeding management with appropriate blood components. The expert group *recommends* that bleeding management protocols or guidelines need to be developed in a manner to address all issues of suboptimal treatment and outcome of bleeding parturient. A PPH management flowchart[60-62] is presented in Figure 1.

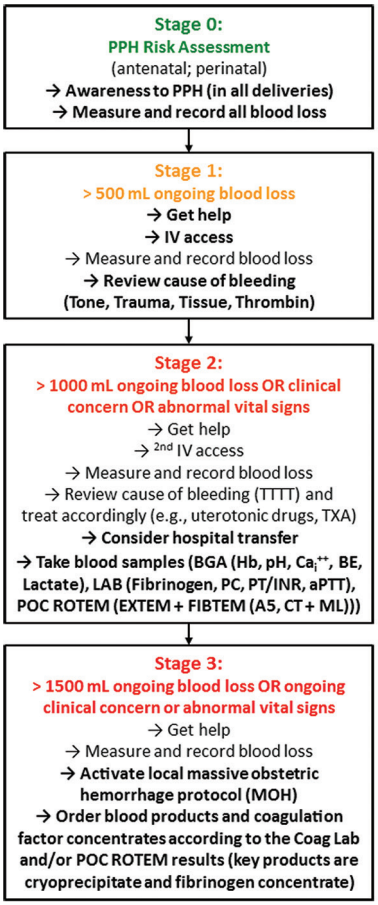

Figure 1: Postpartum Hemorrhage (PPH) Management Flowchart adopted from OBS CYMRU quality improvement project Wales, UK. [References mentioned in the text]. TXA – tranexamic acid; BGA – blood gas analysis; Hb – hemoglobin; Cai++ – ionized calcium; BE – base excess; Coag – coagulation; LAB – laboratory; PC – platelet count; PT – prothrombin time; INR – international normalized ratio; aPTT – activated partial thromboplastin time; POC – point-of-care; ROTEM – rotational thromboelastometry; EXTEM – tissue factor-activated ROTEM assay with heparin neutralization; FIBTEM – tissue factor-activated ROTEM assays with elimination of platelet contribution and heparin neutralization; A5 – amplitude of clot firmness 5 minutes after CT; CT – coagulation time; ML – maximum lysis in % of maximum clot firmness (MCF); MOH – massive obstetric hemorrhage

Liver surgery and transplantation

Liver surgery and transplantation has been associated with large amounts of blood loss in the past.[63] However, with increased expertise, refined surgical skills and improved hemostatic management, the blood loss and subsequent transfusion requirements are decreasing worldwide.[64-68] In India, liver transplant programs are evolving at most centers.[69] There are high transfusion requirements and transfusion-associated complications.[70-77] based on in-house blood bank and appropriate facilities for coagulation testing. There is a general awareness regarding the usefulness of POC viscoelastic testing devices.[78] to monitor and guide hemostasis and bleeding management in these patients. The expert group *recommends* that it should be mandatory to have POC viscoelastic testing devices in or near the operating room and ICU for such patients. Furthermore, validated bleeding management algorithms should be followed during surgery and post-operatively.

Trauma and ICU

The expert group *agrees* that management of bleeding trauma patients needs to be improved in India. Both central and state governments in India are developing dedicated trauma centers in various states. Accordingly, it would be easy and worthwhile at the time of formation of these centers to implement protocoled, guideline-concordant management of trauma-induced coagulopathy and bleeding management in these centers.[49,79,80] This could include the blood banks/blood storage facilities, coagulation testing facilities and availability of point-of-care viscoelastic testing devices.

Cardiothoracic and vascular surgery/ Cardiovascular ICU

Postoperative bleeding is a common and severe complication in cardiac surgery, resulting in emergency re-exploration in about 5% of cases.[81] The risk factors for abnormal bleeding in cardiovascular procedures include age, anemia, thrombocytopenia, complex procedures (redo-coronary artery bypass graft surgery, redo-valve replacement thoracic aortic procedures), medications (antiplatelet/anticoagulant), and comorbidities. Pre-operative interventions aimed to reduce the bleeding risk include treating anemia, opting off-pump or less invasive surgical techniques, discontinuation of antiplatelet drugs and treatment of co-morbidities. The expert group *suggests* that Aspirin should be continued throughout CABG. Stopping aspirin should be considered in patients at high risk of bleeding or those refusing blood transfusion. For patients taking P2Y12 receptor antagonists, postponing non-emergent surgery for 3 days after discontinuation of ticagrelor, 5 days after clopidogrel, and 7 days after prasugrel should be considered.[82] Modifications in CPB, like the use of minimally invasive extracorporeal circuit (MiECC), cell salvage, heparin level-guided anticoagulation, modified ultrafiltration, autologous priming and normothermia reduce the risk of bleeding. In bleeding patients with coagulation factor deficiency, FFP, PCC, cryoprecipitate or fibrinogen concentrate administration may be considered.[83] Viscoelastic testing, particularly TEG and ROTEM, provide real time quantitative global assessment of clotting function, and have led to the development of algorithms to diagnose and treat coagulopathy during and after cardiac surgery.[68]

Conclusions

The multidisciplinary expert group evaluated the current practices and protocols of management of abnormal bleeding, in various clinical settings, across India. Owing to the diverse healthcare facilities, it is difficult to implement the international guidelines for the management of massive blood loss in India. In this first phase of the exercise, all experts developed a skeleton framework of guidelines for different levels of health care. Some of the key consensus statements could be summarized as follows:

A. The health education curriculum needs to incorporate holistic, multidisciplinary approach for management of abnormal bleeding.
B. A quick, representative clinical history is a very effective tool for predicting risk of abnormal bleeding before a surgical intervention.
C. Bleeding Time (BT) is an ineffective screening tool for pre-operative risk assessment.
D. Platelet function alterations are common and need to be picked up adequately and appropriately
E. The role of coagulation laboratories and the timely use of POC Viscoelastic testing is vital.
F. The availability of resources to deal with a case of perioperative abnormal bleeding should be based on the level of health care facility.
G. The triggers for transfer from rural hospitals to appropriate centers must be predefined and standardized.
H. Shock packs and MTPs need a uniform, widely available and acceptable definition from the developing countries' perspective.
I. Specific clinical settings, like trauma, obstetric hemorrhage or cardiac and liver surgeries, must be dealt as per validated protocols. Such protocols need to be designed in a manner so as to have a wider incorporation of inputs and better acceptability thereby ensuring uniform, validated practices across all geographical domains and clinical settings.
J. Perioperative bleeding management should be implemented in a timely manner in order to increase patients' safety.

Development, adoption, and implementation of Patient blood management guidelines in a standardized and uniform manner is the pressing priority for a developing country like India and all the stakeholders must work towards it collectively.

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Conflicts of interest

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