www.jhas-bhs.com

Journal of Hematology and Allied Sciences

Systematic Review

Usage of blood components in obstetric practice

Kanjaksha Ghosh[1], Prakas Kumar Mandal[2]

[1]National Institute of Immunohematology, KEM Hospital, Mumbai, Maharashtra, [2]Department of Hematology, N.R.S. Medical College and Hospital, Kolkata, West Bengal, India.

***Corresponding author:**
Prakas Kumar Mandal, Department of Hematology, N.R.S. Medical College and Hospital, Kolkata, West Bengal, India.

pkm.hem@gmail.com

Received: 30 November 2023
Accepted: 20 December 2023
Published: 07 February 2024

DOI
10.25259/JHAS_51_2023

Quick Response Code:

ABSTRACT

Transfusion of blood and its components form an important component in obstetric care. Almost 5% of pregnant mothers require some sort of red cell and/or component transfusion as part of their obstetric management. Although red cell usage in large parts of developed countries are coming down, its usage in obstetric care is increasing. About 27% of maternal deaths in the world are due to hemorrhage. There are many causes where transfusion with different blood components is required in obstetric practice; to name a few are – accidental hemorrhage, placenta previa, hemoglobinopathies, pre-eclamptic toxemia, postpartum hemorrhage, amniotic fluid embolism, disseminated intravascular coagulation, malaria, etc. Certain complications and challenges of transfusion such as transfusion related acute lung injury, microangiopathy, Thrombotic thrombocytopenic purpura, isoimmunization, and transfusion-associated cardiac overload occur with increased frequency in pregnant mothers. Transfusion requirement around peripartum period is uncertain and sometimes could be massive. Hence, both obstetrician and transfusion experts should remain prepared for this eventuality. Transfusion of blood products even though has never been safer than it is today; yet, this procedure carries with it many immunological, infectious, and other complications, hence, should be used judiciously and very cautiously. Several procedures such as apheresis and intraoperative cell salvage are being increasingly used nowadays for various facets of management and obstetric care. Present review condenses on the knowledge of usage of blood and blood products in obstetric care.

Keywords: Obstetric care, Blood, Components, Usage

INTRODUCTION

Transfusion of red cells and various components of blood has substantially reduced the maternal mortality and morbidity across the globe. Hemorrhage is now responsible for substantial proportion of maternal mortality and morbidity across the world being responsible for 27% of 78,000 deaths during childbirth across the world annually.[1] In fact, there is a trend of increase in blood product transfusion in obstetric care even in developed countries.[2] Present review focuses on main indications of transfusion in obstetric practice and challenges to meet them in developing countries.

MATERIAL AND METHODS

The present review was built on PubMed search between 2000 and 2018 with key words like "pregnancy," "anemia in pregnancy," "obstetric practice," "obstetric complications," "hemoglobinopathies in pregnancy," "blood transfusion," "red cell transfusion," "component therapy," complications of transfusion in pregnancy," "disseminated intravascular coagulation

(DIC)," "amniotic fluid embolism," antepartum hemorrhage," and "postpartum hemorrhage," transfusion medicine. We mainly focused and reviewed these topics and also relevant guidelines published by learned obstetric societies across the globe. Case reports were excluded, though few case series were considered that studied the complications of transfusion in obstetric practice. A total of 3573 published articles were available in the PubMed; 3375 were excluded on the basis of title of the paper. Out of the remaining 198 papers, 157 were excluded due to duplication of data and similar findings compared to more recent papers (all read by both the authors). Thus, 44 papers were finally selected and used in this review. In addition, a national database, that is, IndMed (National Databases of Indian Medical Journals) and recent review articles were also evaluated for the review. Reviews were classified into groups of papers such as – (I) Anemia in obstetrics, (II) Hemoglobinopathies in obstetrics practice, (III) Hemorrhage in obstetrics, (IV) Situation requiring massive transfusion (Massive Transfusion Protocol), and (V) Other hematological and non-hematological disorders not necessarily related to obstetrics but required transfusion therapy as demanded by the patient condition. [Tables 1- 9] summarize the various indications, available blood products, classification, guidelines, scores, etc., for transfusion therapy in obstetric practice.

Table 1: Common indications of blood transfusion in obstetric practice.

RBC transfusion	
Severe anemia (common causes)	Nutritional anemia Hemoglobinopathies Other hematological disorder
Hemorrhage	Antenatal Perinatal Abortion associates
DIC	Septic abortion Accidental hemorrhage Dead fetus Amniotic fluid embolism
Platelet and other blood components	
1. Severe thrombocytopenia 2. Hypofibrinogenemia	DIC, liver disease, and amniotic fluid embolism.
Plasmapheresis and erythrocytapheresis	(i) Thrombotic thrombocytopenic purpura, (ii) Severe alloimmunization, (iii) Severe *Plasmodium falciparum* malaria, (iv) Several complications and delivery in SCA patients.
Intraoperative cell salvage	During cesarean delivery.
Blood substitutes (research products)	
	Various types of blood substitutes as ready-made oxygen carriers.

RBC: Red blood cell, DIC: Disseminated intravascular coagulation, SCA: Sickle cell anemia

ANEMIA IN OBSTETRIC PRACTICE

Anemia is not uncommon in pregnancy. According to National Family Health Survey–IV (2015–16), the prevalence of anemia among women in the reproductive age was 53.1%; being 5th highest globally; 63–70% of pregnant ladies are anemic,[3,4] The prevalence in India is much higher than the global scenario as per the World Health Organization fact sheet (37% of pregnant women and 30% of women 15–49 years of age are affected by anemia)[5,6] Good antenatal care starting with the diagnosis of pregnancy is the best way to control anemia in pregnancy. In normal pregnancy, though red cell production increases by 30%, still there is hemodilution due to the fact that in addition plasma volume also increases by 50%, leading to hemodilution in the face of increased red cell mass.[7] Hence, the cutoff value of hemoglobin under which a pregnant lady in considered to have anemia is 110 g/L and severe anemia, that is, <70–80 g/L of hemoglobin. Severe anemia affects a small number of normal pregnancies in developed countries, but, in developing countries, this number is substantial. A patient with severe anemia and pregnancy is predisposed to many pregnancy related complications including peripartum hemorrhage. Hence, whatever may be the cause (from iron/Vitamin B12/folate deficiency, traits/carriers of some common hemoglobinopathy such as – sickle cell, hemoglobin E (HbE) or beta-thal trait, symptomatic hemoglobinopathies, antepartum blood loss, and other hematological disorders) of severe to moderate anemia in pregnancy, it needs correction as soon as possible and definitely before the patient goes to labor. During labor, even a small amount of blood loss (which is unavoidable) may precipitate cardiac failure, hypoxia, and various other complications leading to shock and death if the patient has severe anemia from the antenatal period itself.

HEMOGLOBINOPATHIES

There is a large increase in maternal mortality in sickle cell anemia (SCA) varying from 0.07% to 9.2%.[8] Asymptomatic carrier status of beta thalassemia and carrier state of sickle cell disease is very common in many parts of the world. Although majority of these carriers have normal or slightly lower hemoglobin with progress of pregnancy, their hemoglobin level may drop, significantly more so with thalassemia-intermedia (NTDT), HbE thalassemia, SCA, and various combinations of sickle cell gene along with other hemoglobinopathies. Usually, these conditions (except severe iron loaded transfusion-dependent thalassemias) do not interfere with fertility and pregnancy (Except severe iron loaded transfusion dependent states) and these patients very quickly drop in Hb with progress of pregnancy. They will

Table 2: Various blood products available for transfusion.

Products	Description	Volume.	Dose
Red cell concentrate/PRBC	Plasma removed from whole blood with final PCV >60	180–200 mL	Each unit increase Hb by 3% or 16 g/L.
FFP	Contains all coagulation factors as well as anticoagulants, that is, protein C and S, antithrombin, ADAMTS-13.	200–250 mL	15 mL/kg as the done volume Overload is a problem
Whole blood	Contains all the plasma elements and red cells. (Factor V and factor VIII being labile may not be present)	400–460 mL	Each unit will increase hemoglobin by 10 g/L. This product is usually recommended where PRBC are not available or in special circumstances.
Cryo precipitate	Concentrated levels of factors VIII, VWF, Fibrinogen, FXIII	10–15 mL	Six pack should increase fibrinogen 1.0–1.5 g/L.
A six pack pool of RDP	--	30–50 mL	total six packs improve platelet counts be 30–50×10^9/L
Single donor platelets	Also to be matched with ABO antigen of recipient	150 mL	One unit improve platelet counts be 30–50×10^9/L
Coagulation Proteins	Freeze-dried from plasma or Recombinant proteins.		
MTP			
1: 1: 1 Protocol or 2: 1: 1 Protocol or 4: 1: 1 Protocol; Then, as per Protocol i.e., 1: 1: 1, 2: 1: 1 or 3: 2: 1	Stat 4-6 units of red cell, 4 FFP. 24 RDPs, Then, 1–2 g of calcium gluconate in IV route for every 4-6 units of RBC transfused and serum potassium should also be checked.		

PRBC: Packed red blood cell, RBC: Red blood cell, FFP: Fresh frozen plasma, RDP: Random donor platelets, MTP: Massive transfusion protocol, FFP: Fresh frozen plasma, VWF: von Willebrand factor, PCV: Packed cell volume, Hb: Hemoglobin, ADAMTS: A Disintegrin and Metalloproteinase with Thrombospondin motifs

Table 3: Risk factors for postpartum hemorrhage.

A. Uterine tone
- a. Uterine distension (multiple gestation and polyhydramnios fetal macrosomia)
- b. Grand multipara
- c. Uterotonics
- d. Quick or prolonged labor
- e. Uterine inertia
- f. Long oxytocin exposure
- g. Chorioamnionitis.
- h. Uterine myoma

B. Trauma:
- a. Valvovagonal injury
- b. Uterine rupture
- c. Inversion of uterus
- e. Cervical tear
- f. Episiotomy/perineal injury

C. Thrombin (coagulation defect)
- a. Gestational (Thrombocytopenia/HELLP syndrome)
- b. DIC (Pre-eclampsia, Intrauterine fetal death, abruptio placentae, and amniotic fluid embolism)
- c. Coagulation defects (Congenital and acquired)
- d. Plasmatic defect (A/Hypo/Dysfibrinogenemia, Von Willebrand disease)
- e. Platelet defects (Severe ITP, Glanzmann's thrombasthenia etc.)

D. Tissue (Retained tissues)
- a. Abnormal placental implantation
- b. Vascular malformation of placenta.
- c. Placenta previa (more of antepartum hemorrhage)
- d. Retained placenta.

DIC: Disseminated intravascular coagulation, HELLP: Hemolysis, elevated liver enzymes, low platelets, ITP: Immune thrombocytopenic purpura

Table 4: Summary of primary PPH definition in current use globally.[18]

Guidelines	Definition
Australian Guidelines 2008	Blood loss of >500 mL after vaginal delivery and >750 mL after cesarean section
Austrian Guidelines 2008	Blood loss of 500–1000 mL and clinical signs of hypovolemic shock or blood loss >1000 mL
German Guidelines 2008	Blood loss of >500 mL within 24 hours after birth severe PPH is blood loss of >1000 mL within 24 hours
UK Royal College of Obstetricians and Gynecologists 2009	Primary PPH-estimated blood loss of 500–1000 mL in the absence of clinical signs of shock Severe PPH-estimated blood loss of >1000 mL or clinical signs of shock or tachycardia with a smaller estimated loss
WHO definition	>1000 mL within 24 hours.

PPH: Postpartum hemorrhage

need red cell transfusion as and when required to keep their hemoglobin >100 g/L. Patient who has sickle cell disease or double heterozygous state of sickle cell gene may need close follow-up during pregnancy. Their red cell transfusion should be carefully calibrated to use Hb level between 80 and 100 g/L; as Hb >100 g/L may precipitate sickling events. Some of these patients may need red cell exchange.[9] Detailed accounts of transfusion management in SCA[8,10-12] and in other hemoglobinopathies[9,13] during pregnancy are available elsewhere and beyond the scope of discussion here. Patients

Table 5: Guidelines from National and International Obstetric Societies for use of blood products in postpartum hemorrhage.

	ACOG (USA)	SOGC (Canada)	RCOG (UK)	RANZ COG (Australia and NZ)	DACH (Germany Austria and Switzerland)	International Expert Panel	NPMS	CNGOF (France)
Indication	Significant and continuous blood loss with unstable vital sign	Not discussed	Loss >IL clinical shock continued blood loss	Should be considered early to improve O_2 Carrying Capacity	According to Clinical picture often blood loss underestimated	Blood loss >1L To maintain Circulating blood volume and tissue Oxygenation	Not discussed	Indication for specific blood components for PPH management after vaginal delivery
RBC	Replacement for O_2 Carrying Capacity not volume	Not discussed	Goal Hb >80 g/L In emergency can use O RhD- blood If ABO RhD group known use ABO RhD group compatible uncross matched blood	Order 4.0 RBC or other locally agreed volume consider Group Specific or O (RhD)-blood early	No Specific recommend Goal HB between 80 and 100 g/L	Not discussed.	Protocol for emergency release of blood	Based on clinical sign of PPH severity Maintain HB. 80 g/L. Goal <1.5* PT Normal. 1 unit FFP for every 6 unit RBC, if PT. >1.5*Normal
Plasma	Not discussed.	Not discussed	Goal <1.5×Normal 4 unit FFP for every 6 unit RBC, if PT >1.5×Normal	Goal PT/APTT <1.5 mean. if, INR >1.5.; then FFP 15 mL/kg	FFP 20-30 ml/kg to correct coag deport	Not discussed	AB plasma in emergency fixed Ratio RBC: Plasma and use of POC Coagulation TEG.	Severe PPT FFP can be given without Labht
Platelets	Not discussed.	Not discussed.	Platelet >75×10^9/L Transfuse if <50*10^9/L	Goal >50×10^9/L Transfuse if <50.	Goal >50×10^9/L	Not discussed Give with Intrinsic defect	Not dis cussed	Manual Plt >50×10^9/L

N.B.:- Guidelines accessed and composite chart prepared from National and International society Guidelines as depicted above. PPH: Postpartum hemorrhage, TEG: Thromboelastograph, RBC: Red blood cell, Hb: Hemoglobin, POC: Point-of-care, FFP: Fresh frozen plasma, APTT: Activated partial thromboplastin time, PT: Prothrombin time, ACOG:American College of Obstetricians and Gynecologists, INR : International Normalised Ratio, SOGC: The society of Obstetricians and Gynaecologists of Canada, RANZ COG: Royal Australian and New Zealand College of Obstetricians and, Gynaecologists, DACH: Germany(D), Austria(A), and Switzerland(CH), NPMS: National partnership for maternal safety, CNGOF: Collège national des gynécologues et obstétriciens français.

Table 6: Classes of hemorrhagic shock.[25]

	Class I	Class II	Class III	Class IV
Blood loss (mL)	<750 mL	750–1580 mL	1500–2000 mL	>2000 mL
Blood loss as % blood loss	<15%	15–30%	30–40%	0.40%
Pulse rate	<100	100–120	120-140	>140
Blood pressure	Normal	Normal	Decreased	Decreased
Pulse presons	Normal	Normal	Decreased	Decreased
Respiratory rate	14–20	20–30	30–40	>35
Urine output (mL/L)	>30	20–30	5–15	Negligible
Mental status	Slightly anxious	Mildly anxious	Anxious confused	Confused lethargic
Fluid replacement	Crystalloid	Crystalloid	Crystalloid+Blood	Crystalloid+Blood

Table 7: Current indications for use of intraoperative cell salvage for cesarean section.

A. Medical Indication	B. Obstetric Indication
Thrombocytopenia	Placenta previa
Severe anemia	Placenta accreta
Rare blood type	Prior uterine rupture
Difficult cross match	Placental abruption
Jehovah's witness	Abnormal placental insertion
Refused of allogeneic blood	Ruptured ectopic pregnancy

of sickle cell disease who due to previous complications (e.g., stroke) require regular exchange transfusion need to continue the same during pregnancy. Normally, if cesarean section is required in these patients, a regional anesthesia is preferred as general anesthesia can predispose to additional complications of sickling crisis if hemoglobin S (HbS) levels are very high.

Conventionally, during delivery or surgery, HbS level in SCA patients was lowered to ≤40% by exchange transfusion, as this is the level usually found in carriers of sickle cell gene (sickle cell trait) who normally has uneventful pregnancy, delivery, and postpartum recovery. However, this contention is now debatable and with improvement of antenatal care and care at various stages of delivery, red cell exchange program may not be needed. One of the major challenges of red cell transfusion in multi-transfused beta thalassemia or SCA during pregnancy is prior alloantibody formation due to isoimmunization against one or multiple red cell antigens. In countries where alpha-thalassemia in cis mutation (both alpha 1 and alpha 2 genes in cis are involved in carriers) is common in the general population, hydrops fetalis is not uncommon. These cases of non-immune hydrops will need close monitoring like isoimmune hydrops and needs to be differentiated from the immune form of hydrops by serological and other tests. These patients may develop the problem very early in pregnancy and will need intrauterine exchange transfusion[14] which needs to be irradiated for prevention of transfusion-associated graft versus host disease. Although most of the non-immune hydrops have very bad prognosis, survival is possible with Hb Barts hydrops if early diagnosis and regular intrauterine transfusion therapy with irradiated packed red cells is initiated.

Although prevalence of pregnancy in even well-chelated multitransfused beta-thalassemia major patients is rare, alloantibodies in these patients could be a challenge in providing properly cross matched blood for such patients. The situation in cases of pregnancy with SCA is very different as the prevalence of significant alloantibodies in such patients could be very high, even it may go up to 12–50% of such transfused patients.[15,16] Hence, these patients needs to be screened and red cells should be fully phenotyped so that matched red cell concentrates can be made available when they are needed in an emergency.

HEMORRHAGE

Hemorrhage in obstetrics is an important cause of maternal mortality across the world.[17-19] It is the major cause of maternal mortality in developing countries. To reduce this cause of maternal mortality, Government of India has developed a concept of blood storage centers in remote areas of the country where blood is made readily available for transfusion in small hospitals where quick saline spin ABO and Rh grouping is done and blood is given.[20] The definition of postpartum hemorrhage (PPH) and the important causes of it are shown in [Tables 3 and 4], respectively. PPH requiring red cell transfusion is defined differently by different national and international bodies [Table 5], but any blood loss above 700 mL or continuous blood loss or symptomatic blood loss requires attention. Hb of <8 g/dL has been agreed on by most of the expert bodies as the transfusion threshold for these complications. Hemorrhagic shock has been classified in trauma or other situations into four categories for quick clinical identification and management [Table 6]. Of the four categories, Class III and Cass IV definitely need transfusion support so also a large proposition of patients in Class II.

As hemorrhage in antepartum or peripartum state may have several causes, commoner among them being antepartum hemorrhage (namely, placenta previa Grades III and

Table 8: Thromboelastographic interpretation of blood component requirement.[25]

Parameter	Definition	Normal value	Abnormal value	Blood component deficiency	Transfusion product
R time	Time to develop maximum clot	5–10 min	>10 min	Coagulation factors	Fresh frozen plasma
K time	Speed of fibrin formation	1–3 min	>3 min	Fibrinogen	Cryoprecipitate or fibrinogen concentrate
X angle	Speed of fibrin formation	>53–72°	<50°	Fibrinogen	Cryoprecipitate or fibrinogen concentrate
Maximum amplitude	Highest vertical distance in shortest time	50–70 mm	<50 mm	Platelets	Platelets concentrate
Lysis of clot at 30 min	% of maximum amplitude	0–8%	>8%	Increased Fibrinolysis	Tranexamic acid or aprotinin

Table 9: Laboratory parameters in DIC (ISTH Score and pregnancy modified ISTH score).[28]

ISTH score	Points	Pregnancy modified ISTH score	Weight
Platelet count		<50*	1
100×10^9/L	0	50–100	2
50–100×10^9/L	1	100–185	1
<50×10^9/L	2	>185	0
PT prolonged			
<3 s of Normal	0	<0.5 s	0**
3–6 s of Normal	1	0.5–1 s	5
>6 s of Normal	2	1–1.5 s	12
		>1.5 s	25
Fibrinogen		<3.0 g/L	25
>100 mg/dL	0	3.0–4.0 g/L	6
<100 mg/dL	1	4.0–4.5 g/L	1
		>4.5 g/L	0
D-Dimer			
No increase	0		
Moderate increase	2	Not applicable	
Strong increase	3		
Overt DIC if total score >5		Assigned weight >26 diagnostic of DIC	
D-Dimer in FEU 0.4 ugm/mL		*Platelet count weight is less due to gestational thrombocytopenia is not uncommon	
		**PT difference in Scores	

DIC: Disseminated intravascular coagulation, ISTH: International society of thrombosis and hemostasis, FEU: Fibrinogen equivalent unit, PT: Prothrombin Time

IV), accidental hemorrhage, amniotic fluid embolism and uterine atony, trauma, retained placenta, DIC, etc. Management of all these conditions requires a specific approach to address the cause along with transfusion support to maintain adequate tissue oxygenation, blood coagulation, and to some extent volume replacement along with crystalloids. Various specialist bodies have addressed their therapeutic approach for bleeding in obstetric practice [Table 5].[21]

In any obstetric hemorrhage, transfusion of specific/required blood products should be initiated early rather than initiate red cell transfusion when it is too late. Specific challenges of getting proper blood products in adequate amount require screening for ABO and Rh blood groups and atypical antibody screening in the antenatal stage. Quick ABO and RhD matching in emergency in the absence of alloantibodies and in dire emergency with unknown ABO status of the mother, RhD negative "O" blood could be released without any delay. Patients having alloantibodies should be specially cared for with proper blood units and stand by donors for possible emergencies.

When blood loss is substantial, that is, loss of more than 200 mL/kg/h or loss of 50% of the blood volume in 4 h and/or patient need replacement of whole blood volume in 24 h, massive transfusion protocol needs to be implemented either with 3: 2: 1 (RBC: FFP: Platelet) or 2: 1: 1 or 1: 1: 1 or similar such protocol keeping an eye on fluid overload.[21,22] In obstetric hemorrhage, there is uncertainty of it as regards the amount and speed with which blood may be lost in a given condition so the management team should be ready with massive transfusion protocol [Table 2] if the situation on ground so demands.[22-24] Hemorrhagic shock has been classified [Table 6] depending on amount of blood loss and symptoms that it produces; obviously prior anemia compounds this problem.[25]

If the patient is undergoing cesarean section, then the obstetrician has the additional advantage of tackling the problems, that is, uterine stitches, artery ligation, hysterectomy, etc., can be easily undertaken where applicable. In addition in a well set up facility and under certain circumstances, intraoperative red cell salvage technique may be applied when the blood from the operative field may be collected, washed, and transfused through manual macroaggregate blood filter in a transfusion set, etc. There are various indications where autologous blood through red cell salvage can be used in the operation room [Table 7].

However, having a point of care instrument to assess the global coagulation parameter such as thromboelastography[26] or similar such machine is helpful and can rationally direct blood product management [Table 8] and also can suggest at what point rationally tranexamic acid or similar fibrinolytic

inhibitor therapy may be given. Blood substitute, that is, artificial O_2 carrier or bioengineered Hb molecules is still some distance away from routine use and is unlikely to be used in obstetric practice unless its safety and efficacy has been unequivocally demonstrated in trauma and other cases. However, when available they can be used along with intraoperative blood salvage to prevent exposure of allergenic/immunogenic blood products with their associated side effects.

Hypofibrinogenemia is an important cause of PPH.[27] This has to be attended early during the course using fibrinogen concentrate or cryoprecipitate. During pregnancy, normal fibrinogen levels are very high (4–6 g/L). Hence, fibrinogen levels of 2 g/L or less should be considered as hypofibrinogenemia threshold in need of replacement therapy.[27] Management of coagulopathy associated with PPH has been well described in International Society of Thrombosis and Hemostasis guidelines.[23]

DIC

Some of the severe causes of peripartum hemorrhage (i.e., accidental hemorrhage) can develop into DIC as also patients with intrauterine fetal death, sepsis, malaria, amniotic fluid embolism, etc. The management of DIC involves management of the primary cause and then replacement of critically altered blood products.[21-24] to correct hemoglobin and deranged coagulation system. Platelets are to be infused cautiously in this situation only if platelet count is below 30×10^9/L and the patient is bleeding. Prothrombin time should be kept at <1.5 times of mean reference range and fibrinogen level should be replaced when below 2 g/L by cryoprecipitate or fibrinogen concentrate. International Society of Thrombosis and Hemostasis (ISTH) developed a DIC score for diagnosis and follow-up of DIC cases.[28,29] ISTH-DIC score and its parameters need some modification for pregnancy as fibrinogen level in normal pregnancy is very high and a fall below 2 g/L is indicative of low fibrinogen level, similarly, D-dimer level lose most of it diagnostic value in pregnancy unless serial measurements are available to compare and gestational thrombocytopenia being common, the impact of platelet count is also minimized. Considering all these factors a modified DIC score applicable during pregnancy has been proposed.[29] Both the ISTH-DIC score[28] and pregnancy modified score[29] are presented here as a composite chart in [Table 9]. Good assessment of peripheral smear for fragmented RBC along with thrombocytopenia will help in diagnosis of microangiopathic hemolysis in this condition.

CONGENITAL BLEEDING DISORDERS

In the event of congenital bleeding disorders of the mother associated with pregnancy, concentrates for deficient coagulation factor should be used whenever they are available in adequate quantity and frequency under the care of a trained hematologist.[30,31] For hereditary platelet defects, platelet concentrates needs to be transfused even if the platelet counts are high and the patient is bleeding. Not infrequently these patients have antiplatelet antibodies making platelet transfusion relatively ineffective; hence, in those cases, larger amounts of cross-matched platelets in continuous infusion or recombinant activated factor VII (rFVIIa) needs to be used. rFVIIa has increasingly been used to treat hemorrhages due to congenital platelet defected or when PPH has not slopped in spite of replacing the coagulation factors and platelets in adequate amount.[31]

THROMBOTIC THROMBOCYTOPENIC PURPURA (TTP) AND OTHER MICROANGIOPATHIES

Although rare, TTP in pregnancy is a serious complication and often comes in differential diagnosis of hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome, severe pre-eclampsia, atypical hemolytic uremic syndrome, or other rare causes associated with microangiopathic hemolytic anemia. The condition in acquired state is caused by development of autoantibody to ADAMTS-13 metalloproteinase that is involved in cleaving ultra-high molecular weight von Willebrand factor.[32] Treatment for this complication is regular plasmapheresis and replacement with cryo deficient plasma. More often the thrombotic microangiopathy is due to HELLP syndrome where delivery of the baby is curative; supportive measures including blood transfusion may be required in all of them.

Similarly, severe *Plasmodium falciparum* infected patients with pregnancy may need erythrocytapheresis with replacement of packed red cell coupled with antimalarial therapy when high levels of parasitemia affects the patient (>10% parasitemia). Erythrocytapheresis could be life-saving in this condition.[33]

OTHER COMPLICATIONS AND CHALLENGES OF TRANSFUSION IN OBSTETRIC PRACTICE

Usually, common non-hemolytic transfusion reactions are also common in obstetrics and gynecological practice too. However, reactions have substantially reduced after universal prestorage leucodepletion has become the norm of blood collection. The presence of alloantibody to red cell antigen is more frequent in obstetric practice and most of the time, they are directed against RhD antigen, but other important red cell antigens may also be involved.[15,34-36] Transfusion management of this condition broadly follows that of RhD isoimmunization.[35] Sometimes mother may have alloantibodies due to past transfusion, past

pregnancies or may have developed autoimmune hemolysis. In that case providing compatible, red cell concentrates may be challenging to the transfusion service. Delayed hemolytic transfusion reaction due to evanescent antibodies (e.g., anti-Jk) could be missed during pretransfusion screening and may cause delayed hemolytic transfusion reaction.

Two other more serious reaction to transfusion which is more likely to occur is transfusion-associated cardiac overload (TACO)[37] and transfusion-related acute lung injury (TRALI).[38,39] TACO is most likely to happen during implementation of massive transfusion protocol or during third stage of labor when uterus is contracting and sending a large part of the blood sequestered within to systemic circulation. This could be avoided by judicious control of rate of transfusion and use of diuretics along with careful patient monitoring. TRALI more often happens in obstetric practice because transfusion of blood products particularly whole blood, platelet concentrates, and plasma products containing anti-human leukocyte antigen antibodies or anti-neutrophil antibodies may react with recipient neutrophils or in those places where leucodepletion is not routinely used a reverse mechanism involving residential leukocytes in blood products (neutrophils) may interact with alloantibodies circulating in the blood of pregnant ladies may cause infiltration of these cells in the lung interstitium. TRALI can also occur in the absence of antibodies where lipid peroxides in donor blood components may activate recipient neutrophils. TRALI is a serious complication of blood transfusion and has high mortality.[38] Incidence of antibody mediated TRALI has been drastically reduced after avoiding plasma/cryo/buffy coat platelets from multiparous donors.[40]

CHALLENGES FOR THE DEVELOPING COUNTRIES

Major challenges in preventing obstetric hemorrhage, anemia, and its dire consequences on fetal morbidity and mortality in developing countries stems from a combination of factors such as – availability and access of adequate antenatal care, endemic malaria and hemoglobinopathies along with presence of anemia in large number of pregnant women, lack of timely availability of red cells, and other blood products and lack of communication and expertise. In India, these challenges have recently been partly solved by improved road connectivity and ambulance access and ensuring availability of blood at blood storage centers[20] and antenatal care for the remote areas are being administered through multipurpose health workers.

Several studies have shown two doses of tranexamic acid can reduce maternal deaths due to hemorrhage and may reduce requirement of blood.[41-44] while there are debates about magnitude of this effect and some complications related to this therapy.[42,45] However, generally, it was recognized safe, inexpensive, and at least moderately effective in reducing blood loss and should be given.[41,43] Autologous collection of blood for future transfusion in complicated cases and erythrocyte salvage using simple devices has also been suggested to improve blood availability.[46,47] Other challenges for transfusion service for obstetric care in developing countries have been described elsewhere.[47,48] Obstetric practice requires almost all types of blood components in different scenarios and judicious use of these components in adequate amounts[40] taking cognizance of the complications can save lives and improve maternal mortality rate in a country.

Ethical approval

The Institutional Review Board approval is not required.

Declaration of patient consent

Patient's consent was not required as there are no patients in this study.

Financial support and sponsorship

Nil.

Conflicts of interest

Kanjaksha Ghosh and Prakas Kumar Mandal are members of the Editorial board of the journal.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using the AI.

REFERENCES

1. Say L, Chou D, Gemmill A, Tunçalp Ö, Moller AB, Daniels J, *et al.* Global causes of maternal death: A WHO systematic analysis. Lancet Glob Health 2014;2:e323-33.
2. Knight M, Callaghan WM, Berg C, Alexander S, Bouvier-Colle MH, Ford JB, *et al.* Trends in postpartum hemorrhage in high resource countries: A review and recommendations from the International Postpartum Hemorrhage Collaborative Group. BMC Pregnancy Childbirth 2009;9:55.
3. International Institute for Population Sciences (IIPS) and ICF. National Family Health Survey (NFHS-4), India, 2015-16; 2017.
4. Sappani M, Mani T, Asirvatham ES, Joy M, Babu M, Jeyaseelan L. Trends in prevalence and determinants of severe

and moderate anaemia among women of reproductive age during the last 15 years in India. PLoS One 2023;18:e0286464.
5. WHO global database on anaemia. Geneva, Switzerland: WHO; 2023. Available from: https://www.who.int/news-room/fact-sheets/detail/anaemia [Last accessed on 2023 May 01].
6. Global health metrics. Anaemia-level 1 impairment. Lancet; 2019. p. 393. Available from: https://www.healthdata.org/results/gbd_summaries/2019/anemia-level-1-impairment[Last accessed on 2023 Nov 23].
7. Chandra S, Tripathi AK, Mishra S, Amzarul M, Vaish AK. Physiological changes in hematological parameters during pregnancy. Indian J Hematol Blood Transfus 2012;28:144-6.
8. Mortara M, Turay MS, Boyle S, Caracciolo C, Bah S, Kargbo H, *et al.* Impact and burden of sickle cell disease in critically ill obstetric patients in a high dependency unit in Sierra Leone-a registry based evaluation. BMC Pregnancy Childbirth 2023;23:580.
9. Naik RP, Lanzkron S. Baby on board: What you need to know about pregnancy in the hemoglobinopathies. Hematology Am Soc Hematol Educ Program 2012;2012:208-14.
10. Malinowski AK, Shehata N, D'Souza R, Kuo KH, Ward R, Shah PS, *et al.* Prophylactic transfusion for pregnant women with sickle cell disease: A systematic review and meta-analysis. Blood 2015;126:2424-35.
11. Vianello A, Vencato E, Cantini M, Zanconato G, Manfrin E, Zamo A, *et al.* Improvement of maternal and fetal outcomes in women with sickle cell disease treated with early prophylactic erythrocytapheresis. Transfusion 2018;58:2192-201.
12. Howard J, Oteng-Ntim E. The obstetric management of sickle cell disease. Best Pract Res Clin Obstet Gynaecol 2012;26:25-36.
13. Cassinerio E, Baldini IM, Alameddine RS, Marcon A, Borroni R, Ossola W, *et al.* Pregnancy in patients with thalassemia major: A cohort study and conclusions for an adequate care management approach. Ann Hematol 2017;96:1015-21.
14. Jatavan P, Chattipakorn N, Tongsong T. Fetal hemoglobin Bart's hydrops fetalis: Pathophysiology, prenatal diagnosis and possibility of intrauterine treatment. J Matern Fetal Neonatal Med 2018;31:946-57.
15. Jariwala K, Mishra K, Ghosh K. Comparative study of alloimmunization against red cell antigens in sickle cell disease and thalassaemia major patients on regular red cell transfusion. Indian J Med Res 2019;149:34-40.
16. da Cunha Gomes EG, Machado LA, de Oliveira LC, Neto JF. The erythrocyte alloimmunisation in patients with sickle cell anaemia: A systematic review. Transfusion Med 2019;29:149-61.
17. O'Brien KL, Shainker SA, Lockhart EL. Transfusion management of obstetric hemorrhage. Transfus Med Rev 2018;32:249-55.
18. Abdul-Kadir R, McLintock C, Ducloy AS, El-Refaey H, England A, Federici AB, *et al.* Valuation and management of postpartum hemorrhage: Consensus from an international expert panel. Transfusion 2014;54:1756-68.
19. Vaught AJ. Critical care for the obstetrician and gynecologist Obstetric haemorrhage and disseminated intravascular coagulopathy. Obstet Gynecol Clin N Am 2016;43:611-22.
20. Panchal Y, Jariwala K, Ghosh K. Utilization of red cell concentrate from storage centers of South Gujarat. Asian J Transfus Sci 2021;15:157-9.
21. Shaylor R, Weiniger CF, Austin N, Tzabazis A, Shander A, Goodnough LT, *et al.* National and international guidelines for patient blood management in obstetrics: A qualitative review. Anesth Analg 2017;124:216-32.
22. Chay J, Koh M, Tan HH, Ng J, Ng HJ, Chia N, *et al.* A national common massive transfusion protocol (MTP) is a feasible and advantageous option for centralized blood services and hospitals. Vox Sang 2016;110:36-50.
23. Collins P, Abdul-Kadir R, Thachil J, Subcommittees on Women' s Health Issues in Thrombosis and Haemostasis and on Disseminated Intravascular Coagulation. Management of coagulopathy associated with postpartum hemorrhage: Guidance from the SSC of the ISTH. J Thromb Haemost 2016;14:205-10.
24. Collis R, Guasch E. Managing major obstetric haemorrhage: Pharmacotherapy and transfusion. Best Pract Res Clin Anaesthesiol 2017;31:107-24.
25. ATLS Subcommittee, American College of Surgeons' Committee on Trauma, International ATLS Working Group. Advanced trauma life support (ATLS®): The ninth edition. J Trauma Acute Care Surg 2013;74:1363-6.
26. Karlsson O. Experience of point-of-care devices in obstetrical care. Semin Thromb Hemost 2017;43:397-406.
27. Ducloy-Bouthors AS, Mignon A, Huissoud C, Grouin JM, Mercier FJ. Fibrinogen concentrate as a treatment for postpartum haemorrhage-induced coagulopathy: A study protocol for a randomised multicentre controlled trial. The fibrinogen in haemorrhage of DELivery (FIDEL) trial. Anaesth Crit Care Pain Med 2016;35:293-8.
28. Soundar EP, Jariwala P, Nguyen TC, Eldin KW, Teruya J. Evaluation of the International Society on Thrombosis and Haemostasis and institutional diagnostic criteria of disseminated intravascular coagulation in pediatric patients. Am J Clin Pathol 2013;139:812-6.
29. Erez O, Novack L, Beer-Weisel R, Dukler D, Press F, Zlotnik A, *et al.* DIC score in pregnant women-a population based modification of the International Society on Thrombosis and Hemostasis score. PLoS One 2014;9:e93240.
30. Shahbazi S, Moghddam-Banaem L, Ekhtesari F, Ala FA. Impact of inherited bleeding disorders on pregnancy and post partum haemorrhage. Blood Coagil Fibrinolysis 2012;23:603-7.
31. Demers C, Derzko C, David M, Douglas J. No. 163-Gynaecological and obstetric management of women with inherited bleeding disorders. J Obstet Gynaecol Can 2018;40:e91-103.
32. Scully M. Thrombotic thrombocytopenic purpura and atypical hemolytic uremic syndrome microangiopathy in pregnancy. Semin Thromb Hemost 2016;42:774-9.
33. Riddle MS, Jackson JL, Sanders JW, Blazes DL. Exchange transfusion as an adjunct therapy in severe *Plasmodium falciparum* malaria: A meta-analysis. Clin Infect Dis 2002;34:1192-8.
34. Urbaniak SJ, Greiss MA. RhD haemolytic disease of the fetus and the newborn. Blood Rev 2000;14:44-61.
35. Pahuja S, Gupta SK, Pujani M, Jain M. The prevalence of irregular erythrocyte antibodies among antenatal women in Delhi. Blood Transfus 2011;9:388-93.

36. Liu S, Ajne G, Wikman A, Lindqvist C, Reilly M, Tiblad E. Management and clinical consequences of red blood cell antibodies in pregnancy: A population-based cohort study. Acta Obstet Gynecol Scand 2021;100:2216-25.
37. Roubinian NH, Hendrickson JE, Triulzi DJ, Gottschall JL, Michalkiewicz M, Chowdhury D, *et al.* Contemporary risk factors and outcomes of transfusion-associated circulatory overload. Crit Care Med 2018;46:577-85.
38. Teofili L, Bianchi M, Zanfini BA, Catarci S, Sicuranza R, Spartano S, *et al.* Acute lung injury complicating blood transfusion in post-partum hemorrhage: Incidence and risk factors. Mediterr J Hematol Infect Dis 2014;6:e2014069.
39. Andreu G, Boudjedir K, Muller JY, Pouchol E, Ozier Y, Fevre G, *et al.* Analysis of transfusion-related acute lung injury and possible transfusion-related acute lung injury reported to the french hemovigilance network from 2007 to 2013. Transfus Med Rev 2018;32:16-27.
40. Lee AI, Kaufman RM. Transfusion medicine and the pregnant patient. Hematol Oncol Clin North Am 2011;25:393-413, ix.
41. Hibbs SP, Roberts I, Shakur-Still H, Hunt BJ. Post-partum haemorrhage and tranexamic acid: A global issue. Br J Haematol 2018;180:799-807.
42. Novikova N, Hofmeyr GJ, Cluver C. Tranexamic acid for preventing postpartum haemorrhage. Cochrane Database Syst Rev 2015;6:CD007872.
43. Shakur H, Roberts I, Fawole B, Chaudhri R, El-Sheikh M, Akintan A, *et al.* Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN): An international, randomised, double-blind, placebo-controlled trial. Lancet 2017;389:2105-16.
44. Franchini M, Mengoli C, Cruciani M, Bergamini V, Presti F, Marano G, *et al.* Safety and efficacy of tranexamic acid for prevention of obstetric haemorrhage: An updated systematic review and meta-analysis. Blood Transfus 2018;16:329-37.
45. Ker K, Shakur H, Roberts I. Does tranexamic acid prevent postpartum haemorrhage? A systematic review of randomised controlled trials. BJOG 2016;123:1745-52.
46. Priuli G, Darate R, Perrin RX, Lankoande J, Drouet N. Multicentre experience with a simple blood salvage technique in patients with ruptured ectopic pregnancy in sub-Sahelian West Africa. Vox Sang 2009;97:317-23.
47. Schantz-Dunn J, Nawal M. The use of blood in obstetrics and gynecology in the developing world. Rev Obstet Gynecol 2011;4:86-91.
48. Oladapo OT, Adetoro OO, Ekele BA, Chama C, Etuk SJ, Aboyeji AP, *et al.* When getting there is not enough: A nationwide cross-sectional study of 998 maternal deaths and 1451 near-misses in public tertiary hospitals in a low-income country. BJOG 2016;123:928-38.

How to cite this article: Ghosh K, Mandal PK. Usage of blood components in obstetric practice. J Hematol Allied Sci. 2023;3:93-102. doi: 10.25259/JHAS_51_2023