Blood and Blood product Transfusion in sick Neonate: an Observational study at a Tertiary Care Hospital

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Abstract

Background: Blood and blood product transfusions are common among hospitalized neonates in this advanced era at NICU, particularly in those of preterm low birth neonates.

Objective: In this study we try to find out the types of transfusion in a neonatal intensive care unit among the sick neonates.

Methods: Neonates who required blood or blood product transfusion between 1st Jan 2013 to 31st March 2014 at the neonatal intensive care Unit (NICU) of Ad- Women's Medical college Hospital were included in this prospective observational study. Total 86 inborn and out-born babies with regular maternal antenatal care (ANC) check up with ANC book and other papers with good documentation were selected for the study. A structured questionnaire was used to obtain medical data i.e maternal and neonatal medical problems, indications for blood or other types of transfusion, type of blood products transfused and the frequency of transfusion during the hospital stay. We also observed maternal illnesses during pregnancy and neonatal demography as well as illnesses during the time of admission. Written consent was obtained from the parents or caregiver each time of blood and blood product transfusion as well as for the inclusion in the study. Statistical analysis was done with computer software SPSS version 16 (Statistical Package for Social Sciences). All data were processed and analyzed. Analyzed data were presented in the form of tables, charts, and graphs with due interpretation.

Results: Out of 743 neonates who were admitted during the study period, 86 (10.9%) were studied who required one or more episode of blood or blood product transfusion. Five (5.80%) neonates required whole blood for the double volume exchange transfusion. Neonates required packed red blood cell (PRBC) for anemia was in 40(46.51%), fresh frozen plasma (FFP) for abnormal coagulation profile (with/ without active bleeding) in 64 (74.41 %), platelet for thrombocytopenia in 44(51.16%),albumin for hypoalbuminemia in 23(26.73%) and intravenous immunoglobulin (IVIG) in 9(11%) for severe thrombocytopenia. Four types of transfusion FFP+ PRBC +Albumin+ PLT required in 7(8.10%) neonates, 3 types of transfusion FFP+ platelet+ PRBC in 11(12.79%), FFP+ PLT+albumin in 3(3.48%) neonates, 2 types of transfusion FFP+PRBC in 9(10.46%), FFP+ albumin in 6(6.90%), FFP+ Platelet in 10(11.62%). Single type of transfusion in the form of Platelet or PRBC or FFP or whole blood in 7(8.12%), 10(11.62%), 11(12.79%) and 5(5.80%) respectively. So multiple transfusions were required in 53(61.62%) neonates.

Conclusion: In this study we found that the Fresh frozen plasma transfusion was highest and the IVIG was the lowest number of transfusions in a neonatal intensive care unit.

Keywords: Neonate, Neonatal intensive care unit, blood, and blood product transfusion.

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Introduction

Transfusion therapy in neonate poses specific challenges, requiring consideration of issues not found in older children and adults. Sick neonates are one of the most heavily transfused groups of patients in modern medicine. In modern day practice apart from whole blood, variety of blood components like packed red blood cell (PRBC), platelet or fresh frozen plasma are used. In the last few decades, the hazards of blood and blood product transfusion have been recognized. For that reason, risks and benefits of transfusion as well as the disease being treated, and the condition of the baby must be considered before transfusion.

PRBC transfusion in the neonate is huge because of reduced marrow activity in the neonatal period,[1] which is further suppressed in premature neonate with septicemia. Other indications include replacement of losses with

significant anemia due to repeated venipuncture for taking blood sample for various tests during hospital stay. Whole blood is needed for exchange transfusion when bilirubin at kernicterus level, removal of antibodies and replacement of red cells.

Blood products such as platelets concentrate, and fresh frozen plasma are also transfused in septicemic neonates with DIC and neonates with bleeding diathesis.[2] However, despite considerable research, most neonatal transfusion practice remains opinion based rather than truly evidence based. In spite of wide use of blood and blood products in the neonatal period, there is paucity of local data on the pattern, indications of blood and blood product transfusions. This study evaluates the indications of blood and blood product transfusion in neonates admitted into the neonatal intensive care unit in a tertiary care hospital.

In general, indications for PRBC transfusion were due to severe anemia, where 20 ml/kg PRBC was given to the patient. The whole blood was used for exchange transfusion in case of severe hyperbilirubinemia, double volume exchange transfusion was done with 160 ml /kg.

Indications of PRBC transfusions[3] (based on American Task Force). Transfuse PRBC with 20 ml/kg, not to exceed hematocrit of 0.45 nor hemoglobin of 15g/dl.

1) Hematocrit 0.20 or hemoglobin 7g/dl, and reticulocyte count <4% of RBC count. (i.e. approximately $80*10^9$/ L).
2) Hematocrit 0.25 or hemoglobin 8g/dl and any of the following conditions :
   a) Episode of apnea/bradycardia 10 episodes/24 h or 2 episode requiring bag- mask ventilation.
   b) Sustained tachycardia(180 beats per minute) or sustained tachypnoea(80 breaths per minute).
   c) Cessation of adequate weight gain for 4 days (10 g/d despite 100 Kcal/kg/d).
   d) Mild RDS and FiO_2 0.25 -0.35 or nasal cannula 0.1 to 0.25L/min or NCPAP with Paw 6cm mbar.
3) Hematocrit 0.30 or hemoglobin 10g/dl, with moderate RDS and FiO_2 35% or nasal cannula O_2 or intermittent mandatory ventilation with Paw 6-8 mbar.
4) Hematocrit 0.35 or hemoglobin 12g/dl, with severe RDS requiring mechanical ventilation with Paw 8 cm mbar and FiO_2 (50% or severe congenital heart disease associated with cyanosis or heart failure.

Thrombocytopenia (< 1,50,000/ cu mm)[4] has been observed in 1 to 5% of newborn at birth.[5] Severe thrombocytopenia defined when platelet (PLT) count less than 50,000/cu mm may occur in 0.1 to 0.5% of newborn[6] and risk of bleeding increased in neonates with platelet count less than 50,000 cu mm. Significant proportion of these bleeding episodes (20%) are severe, specially in babies who require intensive care.[7] In neonate non-immune mediated thrombocytopenia is more common than immune thrombocytopenia. It occurs at less than 72 hours of age and mostly due to placental insufficiency, maternal pregnancy induced hypertension (PIH), early onset neonatal sepsis (EOS), and peri-natal asphyxia. After 72 hours of age thrombocytopenia is due to necrotizing enterocolitis (NEC). Inborn error of metabolism, intrauterine infection like TORCHS and congenital defect in platelet production are other infrequent cause of thrombocytopenia in neonate.[9] Neonatal alloimmune thrombocytopenia and neonatal autoimmune thrombocytopenia are responsible for immune thrombocytopenia. Alloimmune thrombocytopenia is a self-limiting condition and resolves within two weeks. Occasionally thrombocytopenia persists for eight weeks. Several transfusions of compatible platelet may be required if there is bleeding, or a platelet count less than 30,000 cu mm. Administration of IVIG is effective in about 75% of cases which reduces the frequency of platelet transfusion. Neonatal autoimmune thrombocytopenia occurs due to maternal ITP. Indications for platelet transfusion in non-immune thrombocytopenia depend on the level of sickness of newborn.[10]

1. Platelet count less than 30,000/cu mm - transfuses all neonates, even if asymptomatic.
2. Platelet count less than 30,000/cu mm to 50,000 cu mm, consider transfusion in following conditions.
   a) Sick or bleeding neonate
   b) Neonates less than 1000gm or less than 1 week of age.
   c) Newborn with concurrent coagulopathy.
   d) Requiring surgery or exchange transfusion.
3. Platelet count more than 50,000 to 99,000 cu mm, transfuse only when actively bleeding.

Dose of platelet transfusion is generally 10 to 15 ml/ kg. Platelet can be pooled from random donor or from single donor. Single donor platelet is required only when prolonged and severe thrombocytopenia and multiple transfusion is anticipated to prevent alloimmunization.

Plasma derivatives, fresh frozen plasma (FFP) is indicated in neonatal age group is due to disseminated intravascular coagulation, vitamin K deficiency bleeding and inherited deficiencies of coagulation factors. FFP is not used for simple volume replacement in polycythemia. Other indications are afibrinogenemia, von Willebrand factor deficiency, congenital antithrombin III, protein C and protein S deficiency when

specific factors are not available. The conventional dose of FFP is from 10 to 20 ml/kg. FFP should be group AB, or compatible with recipient's ABO red cell antigen.

Human albumin solution (HAS) is used as a primary volume replacement solution for sick newborns. However, HAS is not superior to other colloid or crystalloid solutions as a volume replacement solution in standard neonatal practice.[11]

Concentrated HAS solutions (20%) are sometimes administered to hypoalbuminemic neonates with clinically significant peripheral oedema to correct the hypoalbuminemia, ameliorate the oedema, and hasten clinical improvement. However, there is no convincing evidence to support this practice,[12] and, as the underlying cause of the hypoalbuminemia in this situation is inadequate nutritional support, optimizing nutrition by early initiation of trophic feed, if needed total parenteral nutrition is the preferred option.

Normal human immunoglobulin (NHI) or IVIG is standard treatment for both alloimmune and autoimmune neonatal thrombocytopenia and is generally administered to neonates in both clinical situations at platelet counts below 30,000/l. Platelet counts will usually rise promptly after NHI at a dose of 1 g/kg on two consecutive days (in single or divided doses). Further courses may be required in refractory or relapsing cases.

Methods

This study was carried out at the Neonatal Intensive Care Unit (NICU) at Ad- Women's Medical college Hospital and it was a prospective observational study. Study period was from 1st Jan 2013 to 31st March 2014. A total of 86 admitted neonates who required blood or blood product transfusion in course of treatment during their hospital stay. Both the inborn and out-born babies with regular maternal antenatal (ANC) check up with ANC book and other papers with good documentation were selected for the study. A structured questionnaire was used to obtain medical data like maternal and neonatal medical problems, indications for blood transfusion, type of blood products transfused and the frequency of transfusion during the period of the hospital stay. Written consent was obtained from the parents or the caregiver during the 1st transfusion (including blood and blood products) for inclusion of the neonate in the study.

All donor blood and the blood product were screened against HBsAg, VDRL, Anti HCV, Anti-HIV and the malarial parasite, screening for cytomegalovirus were done only in few cases because of lack of facilities in all centers and for the high cost.

Also, a cross matched against the baby's blood was done. Grouping and cross-matching of all blood and blood products were done according to standard principles preceding all transfusions.

Results

A total of 743 neonates were admitted during the study period, out of which 86 neonates (10.9%) received one or more episode of blood or blood product transfusion during their hospital stay.

Out of 86 neonates, 5 neonates required whole blood for the double volume exchange transfusion and the rest 81 neonates needed 1 or more than 1 episode of blood (PRBC) and blood products (FFP, PLT) transfusions, also needed albumin and IVIG. All these 86 neonates were included in the study.

In this study male baby were 47 and female were 39 with male: female distribution was (M:F = 1.18:1) Fig.:1.

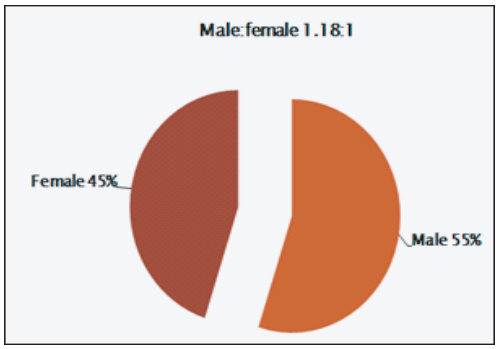

Fig.: 1 Gender distribution

Inborn were 65(75.5%) and out born babies were 21(24.41%). Thirty-nine (44.44%) were delivered by normal vaginal delivery and rest 47(55.55%) were delivered by lower uterine caesarian section.

Their age on admission was from 0 days to 28 days and their weight ranged between 864 gm to 3083 gm with a mean weight of 1064 gm.

The distribution of neonates according to age groups 0-7, 8-14, 15- 21, 22-28 days and their number were 63(73.2%), 14(16.3%), 5(5.8.2%) and 4(4.6%) respectively Fig.: 2.

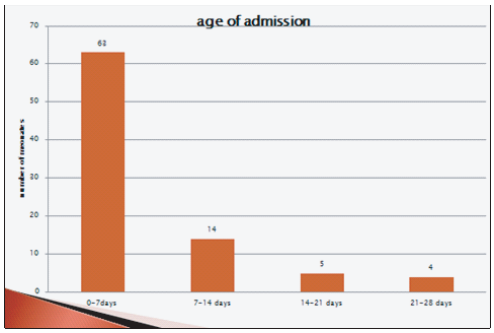

Fig..: 2 Age distribution on admission

The gestational age of the neonates ranged from 26 weeks to 41 weeks and the mean gestational age was 35 ± 4 weeks. Majority of the patients were preterm 60(69.76%) <37 weeks,

22(28%) were <34 weeks, 38 (44.18%) 34 to <37 weeks, Rest 26(30.23%) were > 37 weeks gestation Fig. 3.

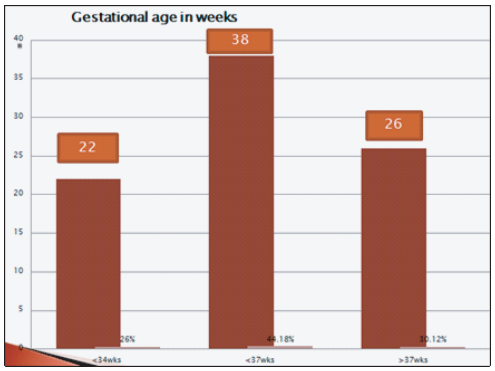

Fig. 3: Gestational age on admission

Maternal illnesses, neonatal problems either single or in combination, were documented from history and ANC papers were as follows- (Table I, Table II)

Table I : Maternal condition during pregnancy

Maternal illnesses	No. (%)
Less Fetal Movement	30(37%)
Meconium stained amniotic fluid (MSAF)	8(9.8%)
Premature rupture of membrane (PROM)	18(22.22%)
Urinary tract infection (UTI)	12(14.8%)
Maternal Hypothyroidism	6(7.4%)
Prolapse hand / cord around the neck/ cord prolapse	4(4.9%)
Diabetes Mellitus (DM) /GDM	18(22.22%)
Oligohydramnios	15(18.5%)
Hypertensive disorder in pregnancy (HDP)	30(37%)
Reduced/ absent / reversed diastolic flow	5(6.1%)
Multiple pregnancy	7(8.6%)

Table II : Neonatal clinical profile on admission

(Gestational age, Birth weight and Clinical conditions of neonates)

Clinical conditions	No.(%)
Term AGA >37 weeks	19(22%)
Term LBW <2.5 kg	9(11.5%)
Term Very LBW <1.5 kg/ IUGR	3(3.4%)
PTLBW < 37wks/ <2.5 kg	41(47.67%)
PTVLBW < 34wks/ <1.5 kg	14(12.27%)
IUGR	12(14%)
PNA	10(11.6%)
Seizure	21(24.4%)
Respiratory failure need resp. support	6(6.9%)
Respiratory distress	29(33.8%)
Jaundice	10(11.6%)
Apnea	11(13%)
Early onset sepsis	35(40.69%)
Late onset sepsis	6(6.9%)

In this study we found the types of transfusion needed for the neonates were whole blood, PRBC, FFP, PLT, albumin and IVIG Fig.: 4.

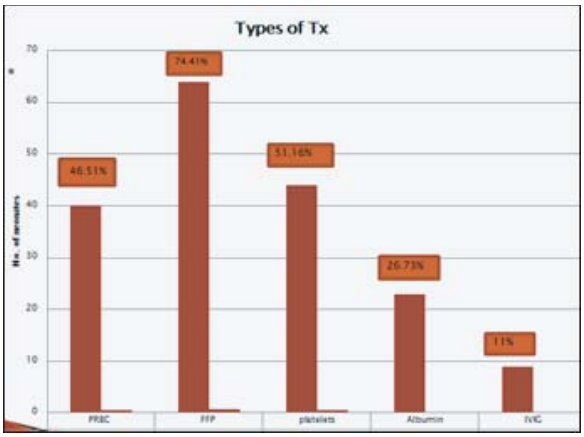

Fig. 4 : Types of transfusion needed

Whole blood needed for 5(5.80%), PRBC for 40(46.51%), FFP for 64(74.41%), platelets for 44(51.16%), albumin required for 23(26.73%) and immunoglobulin needed in 9(11%) neonates Table III .

Table III: Indications and the types of blood product transfusion

Name of the products	No of neonates (%)	Causes of transfusions
PRBC	40 (46.51%)	Anaemia, Anaemia of prematurity, anaemia with apnoea of prematurity, With delay / difficulty in withdrawal from respiratory support, Failure to gain desired weight.
FFP	64(74.41%)	Abnormal coagulation profile with bleeding manifestations, Abnormal coagulation profile without bleeding manifestation on respiratory support .
PLT	44(51.16%)	Thrombocytopenia,
Albumin	23(26.73%)	Hypo albuminaemia, Hyperbilirubinaemia,
IVIG	9(11%)	Thrombocytopenia,< 10000, refractory or relapsing cases,
Whole blood transfusion	5(5.80%)	Double volume exchange transfusion

We found multiple types of transfusion has needed for the study population which were as follows-

- **4 types of transfusion** FFP+ PRBC +Alb+ PLT required in 7(8.1%) with IVIG for 2 neonates.
- **3 types of transfusion** FFP + PRBC+ PLT required in 11 (12.79%) with IVIG for 2 neonates.

- **3 types of transfusion** FFP+ PRBC + Alb required in 3 (3.48%) neonates.
- **3 types of transfusion** FFP + PLT+ Alb. required in 7 (8.1%) neonates
- **2 types of transfusion** FFP + PRBC required in 9 (10.46%) neonates
- **2 type of transfusion** FFP+ Alb. for 6 (6.90%) neonates
- **FFP+PLT** only in 1 (11.62%) with IVIG for 4 neonates.
- **FFP** in 11 (12.79%) neonates.
- **PLT** in 7(8.13%) with IVIG for 3 neonates and
- **PRBC** only in 10 (11.62%) neonates,
- **Whole blood** in 5 (5.8%) neonates shown in Fig:5.

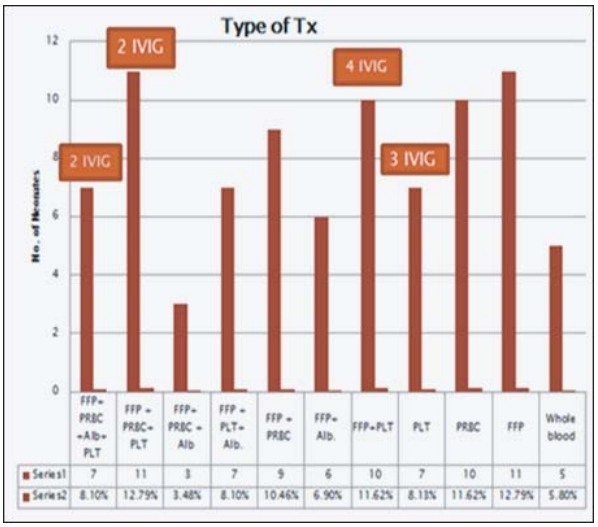

Fig. 5: Multiple types of transfusion

Discussion

Transfusion of blood and blood product is very important and lifesaving in neonatal intensive care unit. These practices vary according to the birth weight, gestational age and severity of illness.[13,14] Among them premature infants are the most frequently transfused group of patients[13,14]

In our study majority of the patients 55 (67.9%) were preterm (<36±6 weeks) who received different types of blood product transfusion.

The findings in the present study showed that most transfusions in our unit were fresh frozen plasma, platelets, packed red blood transfusion but no WBC as we presently lack facilities to administer concentrates of leucocytes. 53(61.62%) neonate that is more than 50% of our neonates required multiple transfusions.

In our NICU platelet transfusion required in 44 (45.51%) neonates, that is platelet transfusion required in 5.92% of the total admitted neonates which corresponds to other studies.[15]

Traditionally fresh frozen plasma (FFP) has been administered to neonates for a variety of reasons,[16] for treatment of proven or suspected disseminated intravascular coagulation (DIC), prevention of IVH, volume replacement, during sepsis, during episodes of thrombocytopenia, to "correct" indices of coagulation. Except for the treatment of DIC, there is no evidence to support the use of FFP in the other clinical situations listed above.[17]

In different studies DIC was present only 10% of episodes of neonatal thrombocytopenia.[18] "Blind" administration of FFP to thrombocytopenic neonates is not indicated unless there is good clinical or laboratory evidence of concurrent DIC.

In our study FFP was transfused in clinically suspected and laboratory proven disseminated intravascular coagulation (DIC) and to "correct" prolonged indices of coagulation (unaccompanied by clinical signs of bleeding or other laboratory findings consistent with DIC—for example, thrombocytopenia or RBC fragmentation).[5] In this study 64 (74.4%) neonates required FFP transfusion.

Concentrated HAS solutions (20%) are sometimes administered to hypoalbuminemia neonates with clinically significant peripheral oedema to correct the hypoalbuminemia, ameliorate the oedema, and hasten clinical improvement. However, there is no convincing evidence to support this practice,[19] and, as the underlying cause of the hypoalbuminemia in this situation is almost always inadequate nutritional support, optimizing nutrition is the preferred option like total parenteral nutrition. Cochrane review shoed transfusion of albumin is not free of risk.[20]

In this study 23(26.73%) neonates required concentrated albumin transfusion that is 3% neonates out of total 743 admitted neonates. Causes of albumin transfusion in this study were edema with hypo-albuminemia.

Normal human immunoglobulin (NHI) or IVIG is standard treatment for both alloimmune and autoimmune neonatal thrombocytopenia and is generally administered to neonates in both clinical situations at platelet counts below 30000. But in our study NHI/ IVIG was transfused when platelet count was less than 10000 and difficult to increase the platelet level even after platelet transfusion. The count usually rises promptly after NHI will give at a dose of 1 g/kg for 2 consecutive days (in single or divided doses). Further courses may be required in refractory or relapsing cases. Cochrane reviews of both situations suggest that prophylactic NHI is not protective against neonatal sepsis,[21]and in our study we never used NHI as an adjuvant therapy in neonatal sepsis. Recent systematic reviews have found that treatment of neonates with alloimmune hemolysis with NHI does reduce the need for exchange transfusion.[22]

Conclusion

Blood and blood product transfusions are common among hospitalized neonates, particularly in those of preterm birth. In this study we found that Fresh frozen plasma transfusion was highest, after that of the platelets and the lowest was IVIG transfusion in a NICU.

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Editorial Note

This study was conducted and accepted for publication nearly a decade ago but was not published due to an administrative oversight. We sincerely regret this error and are now publishing the article to recognize its significance and document the historical context of NICU practice at that time.