ORIGINAL ARTICLE

Pattern and determinants of blood transfusion in a Nigerian neonatal unit

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Abstract

Objective: To determine the pattern and determinants of blood transfusion in a Nigerian neonatal unit.

Materials and Methods: Newborn babies who required blood transfusions between January and December, 2008, were studied. The sex, age, and weight at the first transfusion, clinical conditions, indications for transfusion, and the outcome were analyzed with bivariate and multivariate methods.

Results: A total of 402 neonates were hospitalized and 112 (27.9%) had blood transfusion; 61.9% had exchange transfusion, 66.1% had red cell transfusion, and 8% had plasma transfusion. There were 251 transfusions with a rate of 4.8 transfusions per week. Blood transfusions were done for severe jaundice (55.4%), severe anemia (40.2%), and bleeding disorders (4.4%). Weight < 2.5 kg, outside delivery, and jaundice were independent determinants of neonatal transfusion.

Conclusion: The blood transfusion rate in this facility was remarkably high. Improved standard of newborn care and infrastructural support are required to reduce the transfusion rate.

Key words: Bleeding, exchange transfusion, hemolysis, neonatal jaundice, plasma transfusion

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Introduction

Blood transfusion is an essential form of medical treatment, particularly in pediatric practice, where common illnesses are usually related to blood destruction or blood loss.[1] The procedure replaces the volume and the specific constituents of blood, which play specific roles in oxygen carriage, immunity, and clotting. Therefore, blood transfusion is required to maintain life, by increasing the cardiac output and oxygen delivery to tissues, and removing toxins like bilirubin from the body.[2]

The need for transfusion in the neonate may occur due to physiological or pathological causes.

Anemia of prematurity is a physiological phenomenon, which is related to the inadequate maternofetal transfer of iron and poor postnatal production of endogenous erythropoietin in infants. Although, replacement therapy with synthetic erythropoietin is a common practice in the developed world,[3] blood transfusion is commonly used in parts of the developing world, where recombinant erythropoietin is unavailable.

The leading causes of neonatal morbidities and mortality in the developing world include mechanical and chemical birth injuries, infections, and jaundice.[4] These conditions may be associated with hemolysis, disorders of coagulation or accumulation of potential toxins.

Bleeding disorders in neonates often require blood transfusion.[5] In such instances, blood transfusion is required to prevent death from acute circulatory collapse or severe hypoxemia.

Top-up transfusion with red cells is done for anemic cases, while exchange blood transfusion (EBT) is

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recommended for hyperbilirubinemia. In some cases of severe hyperbilirubinemia, EBT is required to rapidly remove the excess bilirubin from the blood, to prevent irreversible brain damage known as bilirubin encephalopathy. Interestingly, recent studies have shown that while the newborn exchange blood transfusion rate in some health facilities in the developing world like Nigeria remains very high, the procedure has become very rare in most parts of the developed world.[6]

Despite the huge requirement for the use of blood and its products in neonatal care, the practice in most parts of the developing world is fraught with the problem of an inefficient blood banking system.[7] In addition, facilities for the extensive screening of blood prior to use are highly limited, hence, the risk of transmission of infections like hepatitis, cytomegalovirus, syphilis, and HIV is high.

Yet, neonatologists in this part of the world are confronted with the clinical need to transfuse a large number of critically ill babies with blood, in spite of the inefficient blood banking system.

This makes strict adherence to universal guidelines on the use of blood and its products difficult in the developing parts of the world.

Therefore, as a step toward improving the safety and efficiency of blood transfusion therapies in under-resourced settings, it is essential to generate data on the prevailing situation of the pattern of use of transfusion among newborn babies. These data can then be used to devise measures useful for improving transfusion services in Nigeria and other poor-resource settings. The present study is the first report from this Nigerian Newborn Unit, which was established more than two decades ago. The objective of the study is to examine the pattern and clinical determinants of blood transfusion among Nigerian newborn infants.

Materials and Methods

This study was retrospectively carried out over the period of January to December, 2008, at the Neonatal Unit of the Olabisi Onabanjo University Teaching Hospital, Sagamu, Nigeria.

This is a tertiary hospital located in the Ogun State, southwest Nigeria, and provides general and specialized neonatal care services to babies delivered in the Maternity Unit of the hospital as well as babies referred from other parts of the Ogun, Lagos, and Ondo States of Nigeria.

The subjects were consecutive admissions who required transfusion with blood and any blood product. Babies who required blood transfusion at the point of admission as well as babies who required transfusion days after admission were included in the study. The referred babies who had been transfused from places of referral were excluded.

The following data were obtained: age and weight at first transfusion, indication for transfusion, and specific clinical disorders like seizure, apnea, dyspnea, jaundice or obvious bleeding. Others included type of blood component and type of transfusion done. The babies were clinically classified into preterm, term or post-term.

In our unit, decisions to transfuse babies are usually taken by the resident physicians and the consultants in the unit. Generally, the indications for blood use in our unit include severe anemia, severe hemorrhage, severe hyperbilirubinemia, overwhelming sepsis, severe thrombocytopenia, and patent ductus arteriosus. Whole blood is transfused at 20 ml / kg in cases of bleeding. Double volume exchange transfusion with 160 ml / kg is done for severe hyperbilirubinemia or overwhelming sepsis, while single volume exchange transfusion with 80 ml / kg is done for severe anemia within the first week of life. Due to lack of facilities for packing red cells, we transfuse 15 ml / kg of partially packed cells for cases of severe anemia after the first week of life. Severe anemia is defined, in our unit, as Packed Cell Volume (PCV) $< 30\%$, and this is used along with clinical details like features of systemic hypoxia, to decide on the need for transfusion.

For double volume exchange transfusion, indications include serum bilirubin $>$ 10 mg / dl / kg for babies weighing < 2 kg or $>$ 18 mg / dl for babies weighing > 2 kg. Early clinical features of bilirubin encephalopathy are also indications for exchange transfusion. Fresh plasma is serially transfused at 10 ml / kg / day in the presence of sepsis or when double volume exchange transfusion for severe hyperbilirubinaemia is impossible. Grouping and cross-matching according to standard principles precede all transfusions, although we lack facilities for irradiation. In addition to transfusion, other important therapies like medications, fluid therapies or respiratory supports with oxygen are also used during the treatment.

Data were managed with SPSS 15.0 software using descriptive statistics. The means were compared with Student's t-test, while the proportions were compared using the Chi-Square (χ^2) test and Odds Ratio (OR). Bivariate analysis was used to compare babies who required or did not require transfusions for specific clinical parameters. Variables having a significant association with blood transfusion by bivariate analysis were subjected to multivariate analysis using a binary logistic method, to determine independent relationships with the requirement for blood transfusion.

Statistical significance was established when *P* values were < 0.05 or 90% Confidence Interval (CI) excluded unity.

Results

A total of 402 babies were admitted over a period of one year and 112 (27.9%) of these had blood transfusion. Overall, 251 transfusions were done and the overall rate of transfusion was 4.8 per week or 20.9 per month. The subjects comprised of 80 (71.4%) males and 32 (28.6%) females, with a male-to-female ratio of 2.5 : 1. The mean weight of the subjects on admission was 2.0 ± 0.9 kg, while the babies who did not require transfusion had a mean weight of 2.7 ± 0.9 kg. The difference was statistically significant (t = 6.99; *P* < 0.0001). Sixty-three babies (56.2%) had transfusions at the point of admission, while the remaining 49 (43.8%) required blood after admission.

Seventeen (15.2%) babies who had transfusion were in-born, while the remaining 97 (84.8%) were referred. The reasons for blood transfusion included jaundice in 62 (55.4%), severe anemia in 42 (37.5%), PDA with anemia in three (2.7%), and bleeding disorders in five (4.4%) babies.

Types of blood transfusion

Overall, 75 (66.7%) babies had EBT, 74 (66.1%) had top-up transfusion, and six (8.0%) had fresh plasma transfusion. Some babies had more than one type of transfusion. Sixty-three (56.2%) babies actually had multiple transfusions, while 49 (43.8%) had only one transfusion. Of the 75 EBT, 13 (17.3) were single volume procedures, while 62 (82.7%) were double volume procedures. All the double volume EBTs were done for severe jaundice; none was done for severe sepsis. Thirty-eight (33.9%) had only EBT, 37 (33.0%) had only top-up transfusion, 31 (27.7%) had EBT with top-up transfusion, and the remaining six (5.4%) had EBT, top-up transfusion, and plasma transfusion. The EBT rate was 1.4 per week or 6.2 per month. Thirty-seven (49.3%) of the 75 babies who had EBT subsequently developed anemia requiring top-up transfusion.

Table 1 describes the age of the babies at the first transfusion. The peak age for blood transfusion was between 97 and 168 hours of life. Most babies had EBT between 97 and 168 hours of life, while most babies had top-up transfusion after the tenth day of life. These observations were statistically significant in each case (*P* < 0.0001 and < 0.0001, respectively).

In Table 2, a significantly higher proportion of term infants had only one top-up transfusion, while a significantly higher proportion of preterm babies had three sessions of top-up transfusions.

Although a higher proportion of preterm babies also had two sessions of EBT, the difference was not significant.

Factors related to the use of blood transfusion

Table 3 shows that significantly higher proportions of male babies (*P* < 0.0001), preterm babies (*P* = 0.001), and referred babies (*P* < 0.0001) had blood transfusion. Similarly, higher proportions of babies with jaundice (*P* < 0.0001), apnea (*P* = 0.001), and seizure (*P* = 0.001) had blood transfusion. However, there was no significant difference in the proportion of babies with and without respiratory distress or babies with and without bacterial isolates on blood culture, who also had blood transfusion. A multivariate analysis [Table 4] showed that male sex (*P* < 0.0001), preterm birth (*P* = 0.001), referred status

Table 1: Age of subjects at the first transfusion

Age (Hours)	Total (n = 112)	Top-up (n = 37)	EBT (n = 75)	*P* values
≤ 24	13 (11.6)	3 (8.1)	10 (13.3)	NS*
25 – 96	15 (13.4)	5 (13.5)	10 (13.3)	NS
97 – 168	56 (50.0)	5 (13.5)	51 (68.0)	< 0.0001
169 – 240	7 (6.2)	3 (8.1)	4 (5.3)	NS
> 240	21 (18.8)	21 (56.8)	0 (0.0)	< 0.0001

KEY: Figures in parentheses are percentages of the respective total, *Not Significant, EBT = Exchange blood transfusion

Table 2: Number of transfusions distributed according to maturity of subjects

Type	Number	Preterm	Term	*P* values
EBT				
	1	34 (54.0)	29 (46.0)	
	2	6 (50.0)	6 (50.0)	NS*
Top-up transfusion				
	1	3 (15.8)	16 (84.2)	< 0.0001
	2	17 (58.6)	12 (41.4)	NS
	3	20 (86.9)	3 (13.1)	0.001
	4	3 (100.0)	0 (0.0)	NS

KEY: Figures in parentheses are percentages of the respective total, *Not Significant, EBT = Exchange blood transfusion

Table 3: Bivariate analysis of factors related to blood transfusion requirement

Factors	Transfused (n = 112)	Not transfused (n = 290)	*P* values
Male sex	80 (71.4)	145 (50.0)	0.0001
Preterm	57 (50.9)	96 (33.1)	0.001
Weight < 2.5 kg	75 (66.9)	102 (35.2)	< 0.0001
Multiple birth	28 (25.0)	53 (18.3)	NS*
Referred	95 (84.8)	157 (54.1)	< 0.0001
Jaundice	86 (76.8)	133 (45.9)	< 0.0001
Apnea	35 (31.2)	48 (16.6)	0.001
Seizure	33 (29.5)	42 (14.5)	0.001
Respiratory distress	36 (32.1)	74 (25.5)	NS
Positive culture	31/58 (53.4)	81/144 (56.2)	NS

KEY: Figures in parentheses are percentages of the respective total, *Not Significant, **Positive Blood Culture

Table 4: Multivariate analysis of possible determinants of blood transfusion

Independent variables	OR* (CI**)	*P* values
Male sex	3.59 (2.046 – 6.304)	< 0.0001
Preterm birth	0.19 (0.076 – 0.516)	0.001
Weight < 2.5 kg	9.33 (3.607 – 24.170)	< 0.0001
Referred status	4.68 (2.401 – 9.140)	< 0.0001
Severe jaundice	5.90 (3.222 – 10.803)	< 0.0001
Apnea	1.83 (0.971 – 3.437)	0.062
Seizures	1.43 (0.743 – 2.788)	0.281

KEY: Dependent variable: Blood transfusion requirement, *Odds Ratio, **Confidence Interval

($P < 0.0001$), and presence of jaundice ($P < 0.0001$) were independent determinants of blood transfusion requirement in this cohort of babies. On the other hand, the presence of apnea and seizures was not independently associated with blood transfusion use.

Outcome

Twenty-nine (34.1%) of the 85 babies who died during the hospitalization had blood transfusion, as compared to 72 (25.7%) of the 280 babies who were discharged home in good condition. The difference was statistically insignificant ($\chi^2 = 2.301$; $P = 0.129$). Eight of the 75 (10.7%) babies who had EBT died within 24 hours of the procedure compared to six of the 37 (16.2%) babies who had only top-up transfusion. The difference was not statistically significant ($\chi^2 = 0.698$; $P = 0.404$).

Discussion

The findings in the present study showed that most transfusions in our unit involved the use of whole blood, partially packed cells, and plasma, as we presently lack facilities to administer concentrates of leucocytes or platelets. The implication of this is that we are constrained to use whole blood in situations where cell concentrates would have been most ideal. This should form a basis for advocacies to get health planners and policy makers make provision for such facilities in designated centers.

About one out of every four babies admitted to our newborn unit required at least one transfusion. This was relatively higher than the rate of one out of every six, reported earlier from Jos, Nigeria.[8] Similarly, the rate of 4.8 transfusions per week observed in the present study was high indicating a great utilization of blood and transfusion services in our unit. The transfusion rate in our unit was also double the rate of 2.4 transfusions per week previously reported from Jos, Nigeria.[8] It is not certain why we recorded double the rate of Jos at our center, but we speculate that it might be due to the fact that most of the babies studied in our center were referred. Previous studies had shown that referred babies were at a higher risk for morbidities.[9] In the absence of regular training, Traditional Birth Attendants are likely to lack the appropriate, but simple skills, which could prevent bleeding during delivery of babies.

Half of the transfusions in our unit took place during the first week of life, thus, indicating the role of perinatal events in the conditions warranting transfusion. In the same vein, EBT was most commonly carried out toward the end of the first week of life. Thus, jaundice was obviously the most prominent indication for transfusion in this study. This implied that aggressive prevention of severe hyperbilirubinemia using effective phototherapy would prevent the bulk of EBT.[6] Half of the babies who had EBT in the present study subsequently had anemia, requiring top-up transfusion. This is most likely related to the ongoing hemolysis from the primary causes of jaundice such as blood group incompatibilities. Invasive bacterial infection following umbilical cannulation during EBT may also predispose a baby to hemolysis. It is also plausible that poor mixing of blood used for the procedure may cause sedimentation of cells, as also part transfusion of plasma instead of whole blood. Some practitioners routinely commence prophylactic antibiotics following EBT, to prevent secondary invasive bacterial infection, but this practice remains controversial.[10] Therefore, aside from adequate mixing of blood during EBT, there may be very little that can be done to prevent post-EBT anemia, especially when it is due to ongoing hemolysis.

More than half of the babies studied in the present report had multiple transfusions, unlike 29% previously reported from Jos, Nigeria.[8] Further to this is the observation that preterm babies often require multiple transfusions compared to term babies. This might be related to the greater physiological predisposition of preterm babies to anemia compared to term babies.[11] However, repeated transfusions of preterm infants depresses endogenous erythropoietin production and further suppresses the bone marrow.[12]

Unfortunately, the scarcity of recombinant erythropoietin in our part of the world leaves practitioners with no other option apart from multiple transfusions and the persistence of anemia, among these babies. The higher number of transfusions in the present study might also be due to our practice of transfusing anemic babies serially, usually in two or three stages, depending on the PCV at the outset. This is far from the ideal, but we are constrained to do this because of the hindrances we encounter in getting blood from the blood bank every time we need it. Therefore, it is important to suggest a review or modification of the existing guidelines on neonatal transfusion, in consonance with the peculiarities of the under-resourced parts of the world.

Bivariate analysis shows that the presence of jaundice, apnea, and seizures are significantly associated with the need to transfuse blood. The relationship between seizures, apnea, and transfusion may be explained in terms of their characteristics as possible manifestations of systemic hypoxemia. As a matter of fact, transfusion would increase the partial pressure of oxygen, and in turn, oxygen delivery to the tissues, in such dire emergencies. Therefore, attention should be focused on the prevention of common clinical conditions associated with newborn seizures[13] and apnea, as a way of minimizing the need for transfusion. In addition, in the present study, the independent contribution of the presence of jaundice to the need for neonatal transfusion agrees with the earlier submission that jaundice is the leading indication for transfusion. This may also be related to the role of male sex, as severe hyperbilirubinemia has been reported to be more common among males, in our center.[14]

Conclusions

The transfusion rate in our newborn unit was high and most transfusions take place within the first week of life. In addition, we only transfuse whole blood, partially packed cells, and plasma, but more blood products would be used as laboratory facilities improve with time. Efforts are required to prevent severe hyperbilirubinemia as well as conditions that may cause seizures and apnea, so as to reduce the requirement for transfusions in newborn units. The retrospective nature of this study is acknowledged as a limitation. Therefore, larger prospective studies are definitely desirable. This study has formed a basis for conducting an audit of blood use in newborn units in the developed world.

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