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Survey on Pattern and Determinants of Blood Transfusion in Benha Neonatal Intensive Unit

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ABSTRACT
Background: Blood transfusion is used to replenish lost blood components in a number of medical situations. **Objective:** To identify blood transfusion indications, complications and frequency in Benha neonatal intensive care (NICU). **Patients and Methods:** This research was carried out on all neonates attended to NICU in Benha University Hospital between January 2022 and July 2022. A number of 173 neonates were admitted to NICU during the study period, 51 (29.5%) of them needed blood transfusion.
Results: Neonates who had blood transfusion consisted of 27 males (52.9%) and 24 females (47.1%); their mean gestational age was 32.7±3.1 weeks. The most common causes of blood transfusion in the studied group were anemia of prematurity (29.4%), followed by neonatal sepsis (16.9%). Most cases (49%) received blood transfusion at 7 to 14 days. Neonates who had blood transfusion had statistically higher frequency of mortality and longer duration of hospital stay compared to neonates who didn't have blood transfusion. Multiple linear regression analysis revealed that gestational age, weight, and need of oxygen support are potential predictors for blood transfusion.
Conclusion: Rate of transfusion in the newborn unit was 29.5%. The most common causes of blood transfusion in the studied group are anemia of prematurity (29.4%), followed by neonatal sepsis (16.9%). Efforts are required to prevent preterm labour and sepsis, in order to decrease the need for transfusions in neonatal units.
Keywords: Blood transfusion, NICU, Preterm, Neonatal.

INTRODUCTION

Blood transfusion is a vital method of medical therapy, especially in pediatrics, where prevalent diseases are often associated with blood loss or destruction. The treatment restores the blood's volume and particular components, that have distinct functions in oxygen transport, immunity, and coagulation. By improving cardiac output and oxygen supply to tissues, and by eliminating toxins such as bilirubin from the body, blood transfusions are necessary to sustain life [(1)].

Neonatal transfusions may be necessary for physiological or pathological reasons. Anemia of prematurity is a physiological condition associated with insufficient maternofetal iron transfer and inadequate postnatal synthesis of endogenous erythropoietin in newborns. In sections of developing world, where recombinant erythropoietin is accessible, blood donation is a widespread procedure, but replacement treatment using manufactured erythropoietin is prevalent in the developed world[(2)].

In the developing world, the primary causes of newborn morbidity and death are mechanical and chemical birth traumas, jaundice and infections. These problems may be related to hemolysis, coagulation abnormalities, or the buildup of potential poisons [(3)]. Frequently, neonatal bleeding issues need blood transfusions. In such cases, blood transfusion is necessary to avoid mortality due to sudden circulatory collapse or serious hypoxemia [(4)].

In most regions of the poor world, the practice of using blood and its derivatives in newborn care is riddled with the issue of an ineffective blood banking infrastructure, despite the high demand. Furthermore, facilities for rigorous blood screening before transfusion are very restricted; thus, danger of transmitting illnesses such as hepatitis, CMV, syphilis, and HIV is elevated [(5)]. Despite the inadequate blood storage system, neonatologists in this region of the globe are faced with the clinical necessity of transfusing a high number of critically sick infants with blood. This renders precise compliance with international criteria for the use of blood and its derivatives challenging in underdeveloped nations [(2)].

Many NICUs have adopted packed red blood cells (RBCs) transfusion protocols to reduce transfusions number given to severely unwell neonates. Neonatal patients maintained without reference for transfusion guidelines are twice as likely to require a blood transfusion as neonates handled according to recommendations [(2)]. It has been determined that strict adherence to rules reduces exposure of extremely low birth-weight neonates to donor products of blood; as a result, our institution and others have adopted guidelines. In addition to recommendations, the choice to transfuse often depends on the clinical situation of the patient (i.e. increasing apnea and desaturations). These symptoms may also be caused by infection, gastroesophageal reflux, respiratory distress, prematurity apnea, or necrotizing enterocolitis [(6)].

The aim of this research was to identify blood transfusion indications, complications and frequency in Benha NICU.

PATIENTS AND METHODS

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This research included all newborns hospitalized to NICU at Benha University Hospitals between January and July 2022.

Inclusion criteria: All neonates admitted at Benha neonatal intensive unit during the duration of the study.

Exclusion criteria:

- Patients who had been referred from neonatal intensive unit in Benha University to other hospitals.
- Patients whose parents refused to be included in the study.

173 newborns were admitted to the NICU and these neonates were divided according to need to blood transfusion into 2 group:

- **Group 1:** included 51 neonates who needed blood transfusion.
- **Group 2:** included 122 neonates who didn't need blood transfusion.

All neonates were subjected to:

- Full history taking.
- Clinical examination.
- Admission diagnosis, co-morbidities.
- Blood transfusion.

Laboratory investigations:

- Complete blood count (CBC).
- CRP and blood culture if needed in cases of sepsis.
- Bilirubin in cases of jaundice.
- ABG and chest X-ray in case of RDS.
- Electrolytes for complication.

In blood transfusion group; blood transfusion indications, kind of transfused blood products and frequency, clinical indicators prior, throughout, and then after transfusion, and Hb level at first transfusion time were studied extensively. Consent was received from the parents of neonates who were recruited. Blood transfusion was administered on a clinical basis and in accordance with Manual of Neonatal Care's transfusion standards [7]**.** Prior to transfusion, all blood products were prewarmed, and 1 ml of calcium gluconate per 100 mL of blood was supplied. The newborns were monitored to detect any difficulties.

Ethical approval:

The study was done after being approved by the Ethical Scientific Committee of Benha Children's Hospital (MS approval date: 13/1/2022), and informed permission was acquired from the parents, who were properly informed about all study procedures. The study was conducted according to the Declaration of Helsinki.

Statistical analysis

Using IBM's 2017-released Statistical Package for the Social Sciences Using IBM SPSS Statistics for Windows, Version 25.0 (Armonk, NY: IBM Corp.), the obtained data were inspected, classified, and tabulated, and then they were analyzed, categorized, and tabulated. Based on the kind of data gathered for each variable, the results were displayed and examined. The Shapiro test was used to determine whether the data distribution was normal. Median and range were used for nonparametric numerical data. Mean± Standard deviation (SD) were used for parametric numerical data. Percentage and frequency were used for non-numerical data. The Mann Whitney Test (U test) was used to determine the statistical significance of a difference between two nonparametric research groups. Utilizing the Chi-Square test, the connection between two qualitative variables was evaluated. Multiple linear regression was also performed. P-value less than 0.05 was considered statically significant.

RESULTS

This research was conducted on all newborns hospitalized in NICU, Benha University Hospital between January 2022 and July 2022. A number of 173 neonates were admitted to NICU during the study period, 51 of them needed blood transfusion.

Neonates who had blood transfusion consists of 27 males and 24 females; their mean gestational age was 32.7±3.1 weeks. Neonates who had blood transfusion had statistically lower gestational age and statistically higher frequency of preterm compared to neonates who didn't have blood transfusion, while no critical change was seen among groups concerning sex. The most common causes of blood transfusion in the studied group were anemia of prematurity (29.4%), followed by neonatal sepsis (16.9%) (Table 1).

Table (1): Sociodemographic data of the studied neonates

		Blood transfusion			
		Yes		No	
		N=51	%	N=122	%
Sex	**Male**	24	47.1%	63	51.6%
	Female	27	52.9%	59	48.4%
Gestational age/weeks	**Mean ±SD**	32.7±3.1		35.1±2.8	
	Range	28-39		28-40	
Gestational age	**27-29 weeks**	15	29.4%	7	5.7%
	30-33 weeks	10	19.6%	15	12.3%
	34-36 weeks	6	11.7%	20	16.4%
	>37 weeks	20	39.3%	80	65.6%
Indication of blood transfusion	**Jaundice**	5	9.8%		
	Severe anemia at term	6	11.8%		
	Disseminated intravascular coagulation	6	11.8%		
	Anemia of prematurity	15	29.4%		
	Neonatal sepsis	10	19.6%		
	Vitamin K def.	1	2.0%		
	Intraventricular hemorrhage	2	3.9%		
	Twin to twin transfusion	1	2.0%		
	Necrotizing enterocolitis	2	3.9%		
	Congenital anomalies	2	3.9%		
	Pre-operative	1	2.0%		

Average transfusion age was 14.2±3.8 days. Most cases (49%) received blood transfusion at 7-14 days. Three cases had exchange transfusion. Regarding element blood transfusion, the most common type was packed red blood cells (49%). The mean total amount of blood transfusion was 55.4±10.7 ml (Table 2).

Table (2): Criteria of blood transfusion

		Blood transfusion group	
		N=51	%
Element blood transfusion	**Packed red blood cells (RBCs)**	25	49.0%
	Fresh frozen plasma	17	33.3%
	Platelets	6	11.8%
Exchange transfusion		3	5.9%
Blood volume per time	**15 ml / kg**	20	80.0%
	10 ml / kg	5	20.0%
Total amount of RBCs (ml)	**Mean ±SD**	55.4±10.7	

Neonates who had blood transfusion had statistically higher frequencies of maternal diseases, twins, compared to neonates who didn't have blood transfusion, whereas no critical change among groups was seen concerning delivery mode (Table 3).

Table (3): Perinatal history of the studied neonates

		Blood transfusion				Test	P value
		Yes		No			
		N=51	%	N=122	%		
Maternal Diseases	**None**	24	47.1%	102	83.6%	X^2=30.7	**<0.001***
	DM	3	5.9%	5	4.1%		
	HTN	11	21.6%	9	7.4%		
	UTI	5	9.8%	5	4.1%		
	SLE	3	5.9%	0	0.0%		
	DM and HTN	5	9.8%	1	0.8%		
	PROM	37	72.5%	54	44.3%		
Singleton	**Single**	40	78.4%	113	92.6%	X^2=7.1	**0.008***
	One of twins	11	21.6%	9	7.4%		
Mode of delivery	**CS**	25	49.0%	62	50.8%	X^2=0.05	0.83
	NV	26	51.0%	60	49.2%		

X^2: Chi square test, *: significant, DM: diabetes mellitus, HTN: hypertension, UTI: urinary tract infection, SLE: systemic lupus erythematosus, PROM: premature rupture of membrane, CS: cesarean section, NVD: normal vaginal delivery.

Regarding complications; 11.8% of cases had sepsis, 5.9% had hyperkalemia, 3.9% had hypocalcemia, 3.9% had fever, 3.9% had thrombocytopenia and 2% had hypothermia, 3.9% had hypersensitive reaction (rigor and rash). 68.6% of cases didn't have complication after blood transfusion (**Figure 1).**

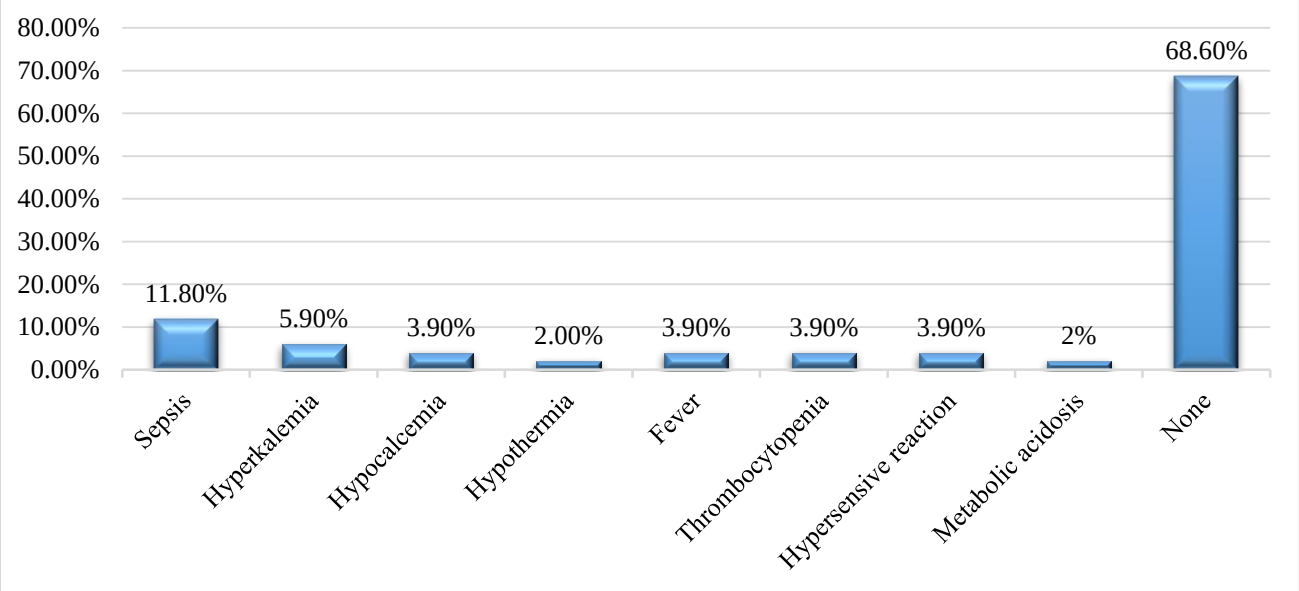

Figure (1): Complication of blood transfusion.

Neonates who had blood transfusion had statistically higher frequency of mortality and longer duration of hospital stay compared to neonates who didn't have blood transfusion (Table 4).

Table (4): Comparison between the studied groups regarding outcome

		Blood transfusion				Test	P value
		Yes		No			
		N=51	%	N=122	%		
Mortality	**Yes**	13	25.5%	18	14.8%	X^2=3.53	**0.02***
	No	38	74.5%	104	85.2%		
Length of hospital stay (days)	**Median**	14		7		U=5.1	**0.006***
	Range	8-45		2-36			

X^2: Chi square test, U: Mann-Whitney test, *: significant

Analysis of multiple linear regression was conducted to identify blood transfusion predictors; it revealed that gestational age, weight, and need of oxygen support were potential predictors for blood transfusion (Table 5).

Table (5): Multiple linear regression analysis for predictors of blood transfusion

	B	Standardized Coefficients		*P*
		Lower	Upper	
Gestational age (weeks)	-0.098	-0.161	0.022	**0.003***
Sex	0.030	-0.021	0.091	0.32
Weight/ gram	-0.109	-0.233	0.043	**<0.001***
Maternal Diseases	0.005	-0.058	0.103	0.08
PROM	0.136	0.011	0.255	0.31
Jaundice	0.017	-0.091	0.114	0.077
Hemoglobin on admission (gm/dl)	0.058	0.108	0.218	0.22
Platelets on admission (10^3/l)	0.082	0.040	0.174	0.14
Positive culture	0.034	-0.005	0.103	0.21
Need of oxygen support	0.078	0.046	0.189	**<0.001***

*: significant, PROM: premature rupture of membrane.

DISCUSSION

The procedure of injecting blood and blood products into a patient's circulatory system is known as transfusion. Early in the nineteenth century, the discovery of different blood types led to the mixing of donor and recipient blood prior to surgery [(5)].

In a number of medical contexts, blood transfusion is used to replace lost blood components. Component treatment has replaced blood transfusion, in which prescription blood components such as fresh frozen plasma, red cell concentrate, cryoprecipitate, and platelet concentrate are administered [(8)].

This study was carried out on a total of 173 neonates who were admitted to NICU during the study period, 51 (29.5%) of them needed blood transfusion. Neonates who had blood transfusion consisted of 27 males (52.9%) and 24 females (47.1%). The prevalence of blood transfusion was similar to what reported by **Ayede and Akingbola,** [(8)] who reported 27.9% and **Ogunlesi and Ogunfowora** [(2)] who reported 30.8% and higher than that of **Joel-Medewase *et al.*** [(9)] who reported a prevalence of 11.7%.

In the current work, there was an insignificantly difference between neonates who had and who didn't have blood transfusion groups regarding their sex. This was in agreement with **Ayede and Akingbola[(8)] and Kusfa *et al.*[(10)],** who didn't find statistical difference between males and females regarding blood transfusion need. In contrast, **Ogunlesi and Ogunfowora** [(2)], studied determinants and pattern of blood transfusion in a Nigerian neonatal unit, and they declared that blood transfusion group had substantially increased proportions of male neonates (P-value less than 0.001).

In the current study, neonates who had blood transfusion had statistically lower gestational age and statistically higher frequency of preterm compared to neonates who didn't have blood transfusion. In addition, neonates who required blood transfusion, their gestational age was 27-29 weeks in 29.4%, 30-33 weeks in 19.6%, and 34-36 weeks in 11.7%. Came with our findings, **Said Conti *et al.*** [(11)], documented that the most heavily transfused neonates were between 24 and 29 weeks of gestation. Similarly, **Liao *et al.*** [(12)] found that children who received blood transfusion had considerably lower gestational age of 30.6±2.2 weeks, compared to neonates without blood transfusion 32.9±2.5 weeks, p< 0.001.

Premature children born before 32 weeks gestation are prone to develop excessive physiological anemia between 4 and 6 weeks of life. Frequently, this is a case of normocytic, non-deficient anemia. Other reasons of anemia in preterm neonates include their vulnerability to infections (septicemia, etc.) and the ensuing problems, as well as iatrogenic damage from the frequent phlebotomies necessary by thorough examinations. The repeated small blood losses during phlebotomy convert into water droplets to build a large ocean. Inadequate bone marrow response to anemia also contributes to the severity of the anemia. Therefore, the abnormal decline of hematocrit and reticulocytes, hypoplasia of the bone marrow, and inadequate endogenous erythropoietin production all contribute to the onset or development of anemia [(13)].

In the current work, the most common causes of blood transfusion in the studied group were anemia of prematurity (29.4%), followed by neonatal sepsis (16.9%), severe anemia at term (11.8%), DIC (11.8%), IVH (3.9%), NEC (3.9%), congenital anomalies (3.9%), vitamin K deficiency (2%), twin to twin transfusion (2%), and pre-operative (2%). Similarly, **Kusfa *et al.*** [(10)], reported that neonatal anemia 30 (50%), neonatal sepsis (3, 5%), neonatal jaundice (25, 41.7%), and surgery preparation (2, 3.3%) were the indications for blood transfusion. While the study by **Ayede and Akingbola** [(8)], showed that the main indications for transfusion were disseminated intravascular coagulopathy 24%; neonatal sepsis 46%; and neonatal Jaundice 14%.

In the current work, the mean age at transfusion was 14.2±3.8 days. Most cases (49%) received blood transfusion from 7 to 14 days. Our results were in agreement with **Essabar *et al.*** [(14)], who reported that the

age at transfusion ranged from 1 to 30 days with mean value of 13 days, while 30% of their patients were aged ≥21 days.

Our results showed that three cases had exchange transfusion (5.9%) and 48 neonates had element blood transfusion (94.1%); the most common type was packed red blood cells (49%), and the mean total amount of blood transfusion was 55.4±10.7 ml. 17 neonates (33.3%) received fresh frozen plasma and 6 neonates (11.8%) received platelets transfusion. Our results are in accordance with **Ayede and Akingbola [8],** where the most common element blood transfusion was packed RBCs in 46%, followed by fresh frozen plasma in 24%. In the same way, **Hameed *et al.* [15],** reported that (62.9%) received packed red blood cells (PRBCs) followed by (18.6%) received exchange transfusion, (11.4%) received fresh frozen plasma and (7.1%) received platelets. In contrast to **Amrutiya *et al.* [16],** out of a total of 1002 transfusions, 37.82% consisted of fresh frozen plasma, 31.34 percent consisted of red cell concentrate, 28.14 percent consisted of platelet concentrate, and 2.70 percent consisted of whole blood.

In the present study, regarding need of oxygen: 31.7 of cases needed MV, 27.3 needed CPAP, 27.4 needed nasal prongs, while 13.7 didn't need oxygen support. Which supports our findings; **Gomaa and Abdelkhalik [17]** found a moderately positive link between the quantity of transfusions and the length of mechanical ventilation as well as a moderately negative correlation between the quantity of transfusions and the length of CPAP. A strong negative correlation existed between the amount of transfusions received in the first month, birth weight, and gestational age.

In the present study, regarding complication after blood transfusion; 11.8% of cases had sepsis, 5.9% had hyperkalemia, 3.9% had hypocalcemia, 3.9% had fever, 3.9% had thrombocytopenia, 2% had hypothermia, and 3.9% had hypersensitive reaction (rigor and rash). While 68.6% of cases didn't have complication after blood transfusion. Parallel to our findings, **Abdelghaffar *et al.* [18],** reported that serum electrolytes were affected by blood transfusions, and compared to those who didn't receive blood transfusion there was a considerable increase of serum K^+ (4.48 ± 1.19 mmol/l vs 5.83 ± 1.37 mmol/l; P<0.001), and a considerable decrease of Ca^{+2} (1.33 ± 0.09 mmol/l vs 1.30 ± 0.09 mmol/l; P<0.001). Six (15%) of infants developed hyperkalemia following the RBC transfusion. In contrast, there was no indication of rigidity, rash, jaundice (post transfusion), oliguria, or a reduction in hematocrit in the research undertaken by **Ayede and Akingbola [8]**. Nonetheless, 5% of patients suffered fever (temperatures not exceeding 2°C above the prior temperature) following transfusion. The urine of four patients with DIC contained hemosiderin and blood.

Decades ago, clinical hyperkalemia owing to RBC transfusion was identified as a result of transfusion. Not only is transfusion-related hyperkalemia reliant on the K^+ concentration of the RBCs, but also on the volume and rate of RBC transfusion [19].

In the present work, neonates who had blood transfusion had statistically higher frequency of mortality (25.5% and 14.8, respectively) and longer duration of hospital stay (median 14 days and 7 days respectively) compared to neonates who didn't have blood transfusion. Similarly, **Liao *et al.* [12],** found that time of hospital stay in observation group was (41±16.9) days, and in control group was (18±7.4) days. RBC transfusion in the first week was essentially related to death in preterm neonates as shown in the study of **Gomaa and Abdelkhalik [17] and Wang *et al.* [20]. Vamvakas and Blajchman [21]** suggested that transfusion may be associated with multi-organ system failure, pro-inflammatory mechanisms, and transfusion-related immunomodulation. Furthermore, the cause of mortality in relation to transfusion in the first week is unknown and may be related to prematurity itself.

In the current study, multiple linear regression analysis was conducted to identify the predictors of blood transfusion; it revealed that gestational age, weight, and need of oxygen support are potential predictors for blood transfusion.

CONCLUSION

Our newborn unit had a rate of 29.5% for transfusions. Given that the bulk of hospitalizations and blood transfusions occurred within two to three weeks of delivery, greater attention should be placed on the perinatal period, particularly immediately after birth. Anemia of prematurity (29.4%), followed by newborn infection, was the most prevalent cause of blood transfusion in the examined population (16.9%). Preterm labor and sepsis must be prevented in order to limit the need for blood transfusions in neonatal units.

Limitation of the study: It was single center study with a relatively small sample size and the results may differ elsewhere. We excluded patients who had been referred from neonatal intensive unit in Benha University to other hospitals and patients whose parents refused to be included in the study.

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