

## The Frequency of Packed Red Blood Cells Transfusion in Preterm Infants Admitted to NICU of Shahid Sadoughi Hospital During 2016

Mohamad Hosein Lookzadeh MD<sup>1</sup>, Fateme Adhami MD<sup>1\*</sup>, Mahmood Nouri Shadkam MD<sup>1</sup>, Seyyed Reza Mirjalili MD<sup>1</sup>, Elnaz Sheikhpour PhD<sup>2</sup>

1- Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

2- Hematology and Oncology Research Center, Shahid Sadoughi Hospital, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

\*Corresponding author: Dr Fateme Adhami, Mother and Newborn Health Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran. Email: Omid\_ddo@yahoo.com.

Received: 24 November 2018

Accepted: 20 February 2019

### Abstract

**Background:** Red blood cells transfusion is a useful practice for preterm infants. Large amount of blood is usually wasted in the infants. Considering that few studies have been carried out on infants, the aim of current study was to investigate the frequency of packed red blood cells transfusion in preterm infants admitted to NICU of Shahid Sadoughi Hospital in Yazd during 2016

**Materials and Methods:** This retrospective descriptive-analytical study was conducted on infants admitted to Neonatal intensive care unit (NICU) of Shahid Sadoughi Hospital, Yazd, Iran during 2016. Variables including fetal age, sex, birth weight, delivery method, Apgar score, infant status, premature birth complications and transfusion information were extracted from medical records of patients.

**Results:** Current study was conducted on 335 premature infants. Among them, 85 cases were received packed red blood cells transfusion (25.4%). Of the infants receiving packed red blood cells, 59 cases (69.4%) were alive and 26 (30.6%) dead. Distribution of preterm complications in infants including respiratory distress syndrome, sepsis, respiratory failure and Pneumothorax was observed in 66 (77.6%), 19(22.4%), 52(61.2%) and 14 patients (16.5%), respectively. There was significant difference between mean age and mean Apgar score in terms of transfusion ( $p < 0.01$ ). The mean volume of consumed blood was  $34.20 \pm 27.44$  ml. The mean volume of wasted blood was  $488.39 \pm 355.88$  ml. Minimum and Maximum volume of wasted blood was 220 and 1873 ml.

**Conclusion:** According to results of current study, the mean age and mean Apgar score in patients undergoing transfusion was lower than those did not have transfusion. Moreover, total volume of wasted blood was 14.2 times more than consumed blood. Therefore, optimal usage of blood products and the use of smaller blood bags are proposed in order to improve the health of infants in intensive care units and lessen complications of blood transfusion in newborns.

**Keywords:** Blood cell transfusion, Infant, Preterm, Prevalence

### Introduction

Packed red blood cells (PRBC) transfusion is a usual procedure in preterm infants hospitalized in neonatal intensive care units (NICUs)(1-6). It is a beneficial practice for preterm infants (7-12) by replenishing low circulating blood volumes, improving tissue oxygenation, increasing circulatory hemoglobin, and reducing the cardiac output to retain the same level of oxygenation (13). Potential advantage of red blood cell transfusion for anemic preterm infants involves

prevention of apnoeas (14) and promotion of weight gain (15).

Infants with very low birth weight (VLBW) are considered as a patients group with high transfusion requirement. Actually, 40% of neonates at 1,000–1,500 g and 90% of them at 1,000 g birth weight may need transfusion. Preterm infants may receive a mean number of five red blood cells (RBC) transfusions during their hospitalization (16). Transfusion of RBC in infants is associated with many risks (16). RBC transfusion leads to overload of iron in liver in VLBW infants (17).

Moreover, a relationship between RBC transfusion and risk of intra-ventricular haemorrhage, bronchopulmonary dysplasia, and retinopathy of prematurity was observed (18). The incidence of adverse outcome following RBC transfusion in UK is estimated 12.3 per 10,000 individuals (16). Among 3453 RBC transfusion cases with side effects, 110 ones were in children less than 18 years and 21 cases in newborns (16). RBC transfusion is associated with mortality in VLBW preterm infants. The risk of mortality was higher in patients receiving more than two transfusions within first 28 days of their life (19). Therefore, it is necessary to decrease the frequency of transfusion in critically sick neonates using residual cord blood for initial laboratory investigations, decreasing phlebotomy losses, determining guidelines of transfusion, confirming the most suitable nutrition with supplementation of iron, vitamin, and folic acid, and clamping the umbilical cord. Most of the demands for PRBC supplies are routine and the requested blood is not used (20). Other study also has reported that usually large amount of blood is wasted because infants need low amount of blood supply (21). Considering that few studies have been carried out in this field, current study decided to investigate the frequency of PRBC transfusion in preterm infants admitted to NICU of Shahid Sadoughi Hospital, Yazd, Iran. If the frequency of PRBC transfusion in preterm infants is too much, this issue should be considered and done with more caution to lessen the complications of blood transfusion in newborns.

### Materials and Methods

This retrospective descriptive-analytical study was approved by Ethical Committee of Shahid Sadoughi University of Medical Sciences (IR.SSU.MEDICINE.REC.1396.38) before initiation. Then, all infants admitted to NICU of Shahid Sadoughi Hospital, Yazd, Iran, during 2016 were selected.

After obtaining the necessary permissions to access archival files, the list of all newborns hospitalized during 2016 was extracted from medical records (n= 863 cases). Of 863 cases, 335 infants were included based on our defined inclusion criteria and the rest were excluded from the study.

Patients' data, including fetal age, sex, birth weight, delivery method, Apgar score, infant status, premature birth complication, and transfusion information were extracted from medical records of patients.

The population of current study was all patients under the age of 28 days (infancy) and fetal age below 37 weeks (preterm) admitted to NICU of Shahid Sadoughi Hospital.

Patients with incomplete medical records and neonatal jaundice were excluded from the study. Moreover, patients admitted to hospital for a second or third transfusion were excluded.

### Statistical analysis

Data were entered SPSS (version 19) and analyzed by Independent T test, Chi square, and Tukey Test. P-value < 0.01 was considered statistically significant.

### Results

Current study was conducted on 335 premature infants. Among them, 85 cases were received blood (25.4%). Moreover, of the 85 infants undergoing transfusion, 37 (43.5%) were girls and 48 (56.5%) boys. The mean neonatal age at first transfusion was  $18.84 \pm 16.35$  days and the mean fetal age was  $28.88 \pm 2.92$  weeks. Normal vaginal delivery and caesarean section were seen in 24 (28.2%) and 61 cases (71.8%), respectively. Mean Apgar score in infants was  $6.0 \pm 2.5$  (0-9). Of the infants receiving PRBC, 59 (69.4%) were alive and 26 (30.6%) dead. Distribution of preterm complication in infants, including respiratory distress syndrome, sepsis, respiratory failure, and pneumothorax was shown in 66 (77.6%), 19(22.4%),

52(61.2%), and 14 cases (16.5%), respectively. Frequency distribution of patients in terms of weight showed that 39(45.9%), 34(40%), 4(4.7%), and 8(9.4%) patients have birth weight less than 1000 g, 1000-1500 g, 1500-2000 g, and more than 2000 g, respectively. The frequency of blood transfusion in patients showed that 42, 16, 15, 6, 3, 1, and 85 patients received blood once, twice, three times, four times, five times, six times, and eight times; respectively. The mean volume of consumed blood was  $34.20 \pm 27.44$  ml. Minimum and maximum volume of blood was 7 and 153 ml, respectively. The mean volume of wasted blood was  $488.39 \pm 355.88$  ml. Minimum and maximum volume of wasted blood was 220 and 1873 ml. The total volume of blood consumed was about 2907 cc and the total volume of wasted blood was 41713 cc. Table I shows frequency distribution of pregnancy complications in mothers with preterm infants. As shown in Table I, the most complications in mothers were premature rupture of

membranes and Preeclampsia. The mean age and mean Apgar score in terms of transfusion are shown in Table II. As Table II shows, there was significant difference between mean age of patients and mean Apgar score in terms of transfusion ( $p < 0.01$ ). Table III shows frequency distribution of Apgar score in infants undergoing transfusion. Table IV shows Classification of prematurity complication, mortality, and weight in terms of transfusion. According to results of current study, there was significant difference between prematurity complications groups with respect to transfusion ( $p < 0.01$ ). Moreover, significant difference was seen between mortality groups in terms of transfusion ( $p < 0.01$ ). Furthermore, significant difference was observed between weight groups regarding transfusion ( $p < 0.01$ ). Table V shows the mean volume of consumed blood in terms of weight. As shown Table V, there is significant relation between weight and mean volume of consumed blood ( $p < 0.01$ ).

Table I: Frequency distribution of pregnancy complications

Complications	Number
Preeclampsia	15
Asphyxia	5
Premature rupture of membranes	22
Gestational diabetes mellitus	15
Hypothyroidism	7
Oligohydroamnios	5
Polyhydroamnios	3
Hypertension	3
Intrauterine growth restriction	10
Total	85

Table II: The mean age and Apgar score in terms of transfusion

Parameters	Transfusion	Number	Mean $\pm$ SD	p-value
Mean age	Yes	85	$28.8 \pm 2.92$	0.001
	No	250	$32.42 \pm 2.7$	
Mean Apgar	Yes	85	$6 \pm 2.57$	0.001
	No	250	$7.6 \pm 2.18$	

Table III: Frequency distribution of Apgar score in infants undergoing transfusion

Apgar	Number	Percent
0	2	2.35%
1	5	5.88%
2	3	3.52%
3	6	7.05%
4	8	9.41%
5	5	5.88%
6	16	18.82%
7	11	12.94%
8	10	11.76%
9	19	22.35%
<b>Total</b>	85	100%

Table IV: Classification of prematurity complication, mortality, and weight in terms of transfusion

Parameters		Without transfusion	With transfusion	Total number	p-value
<b>Prematurity complication</b>	RDS	138(67.6%)	66(32.4%)	204(100%)	0.001
	Sepsis	12(38.7%)	19(61.35)	31(100%)	
	Respiratory failure	49(48.5%)	52(51.5%)	101(100%)	
	Pneumothorax	7(33.3%)	14(66.7%)	21(100%)	
<b>Mortality</b>	Dead	229(68.33%)	59(17.63%)	47(14.04%)	0.001
	Alive	21(6.27%)	26(7.77%)	288(85.9%)	
<b>Weight</b>	Less than 1000 g	16(4.77%)	39(11.65%)	55(16.42%)	0.001
	1000-1500 g	55(16.42%)	34(10.15%)	89(26.47%)	
	1500-2000 g	104(31.03%)	4(1.2%)	108(32.23%)	
	More than 2000g	75(22.38%)	8(2.4%)	83(24.87%)	

RDS: Respiratory distress syndrome

Table V: The mean volume of consumed blood in terms of weight

Weight	Number	Mean	Standard deviation	Min	Max
<b>Less than 1000 g</b>	39	12.94	3.64	7	27.5
<b>1000-1500 g</b>	34	17.68	4.46	10	30
<b>1500-2000 g</b>	4	19.75	0.5	19	20
<b>More than 2000 g</b>	8	27.36	4.3	18.33	30.6
<b>Total</b>	85	16.51	5.8	7	30.6
<b>p-value</b>			0.001		

## Discussion

This study was conducted to evaluate the frequency of receiving PRBC transfusion in preterm infants admitted to NICU of Shahid Sadoughi Hospital. Multiple complications of transfusion and immune system disorders in infants may be related to the blood transfusion. In the current

study, the mean birth weight of Apgar was significantly lower in neonates with transfusion. It seems that this may be due to the effect of hypoxia on functional dysfunction of various organs. Other factors, including increased risk of coagulation disorder and consequently

increased need for transfusion in these infants may also play a significant role. Complications such as sepsis, respiratory failure, and pneumothorax were significantly higher in patients undergoing transfusion. Perciaccante et al., (22) reported that RBC transfusion increased the incidence of necrotizing enterocolitis. RBC transfusion induces a pro-inflammatory answer which may confirms the pathogenesis of transfusion related necrotizing enterocolitis (13). Dani et al. evaluated 20 premature infants and measured the level of several cytokines before and after transfusion. The findings showed the increase of interleukins, namely IL-1 $\beta$ , IL-17 and IL-8 (23). A study showed that transfusion was related to developing of retinopathy of prematurity (24). Dani et al., also reported that RBC transfusion volume was associated with ROP in infants with a birth weight of < 1,250 g (23). Wang et al., reported that red blood cell transfusion was associated with intraventricular hemorrhage (24). Early RBC red blood cell transfusion suppresses production of erythropoietin (25). Hirano et al., reported that after blood transfusion, plasma non-transferrin bound iron (ferrous form) was significantly higher in preterm infants due to the reduction of ferric iron (Fe<sup>3+</sup>) by ascorbic acid and the low ferroxidase activity. Moreover, Hirano et al., reported that most preterm infants developed retinopathy of prematurity and/or chronic lung disease (26). According to results of these studies, it seems that transfusion is associated with serious complications. Borna et al. assessed the frequency and risk factors of blood transfusions in newborns. In their study, 19.98% of patients needed transfusion. Moreover, significant relation was seen between frequency of blood transfusion with using of ventilator and during hospital stay. They reported that decreasing length of hospital stay and duration of mechanical ventilation led to reduction of the frequency and complications of blood transfusions.

Moreover, given the wide range of differences between different communities for choosing the type of product, the time, and correct dose of consumable products, physicians should consider transfusion guideline to prevent unnecessary consumption of blood products (19).

In the current study, there was significant relation between blood transfusion and birth weight of infants. Mosayebi et al., reported that there was a significant relationship between birth weight and blood volume (27). Strauss et al., reported significant relation between birth weight and the need for blood, which is consistent with findings of our study. However, Rafati et al., demonstrated inverse relation between blood transfusion and birth weight (19). This difference can be due to different blood transfusion protocols in hospitals and different guidelines used in different parts of the world.

In total, the mean blood transfusion for each infant was 16.51 cc /kg. Bednarek et al., suggested that the mean blood transfusion was 24 cc/kg per baby (28). In another study by Patterson et al., transfusion rates in infants were reported 29% (33). Moreover, 55.9% of patients received at least one RBC transfusion in Brazil (29). The mean volume of wasted blood in current study was 488.39 ml. It seems that this difference may be due to different blood transfusion protocols in different hospitals. Rafiei et al., found that the pattern of blood transfusion in the Besat hospital was not ideal. They also observed that excessive demand for blood did not only reduce the quality of blood, but also imposed additional financial burdens on health centers (30). Contrary to the current study, most studies did not investigate the amount of wasted blood, which was a hallmark of this study.

## **Conclusion**

According to results of current study, the mean age and mean Apgar score in patients undergoing transfusion was lower than those who did not have transfusion.

Moreover, total volume of wasted blood was 14.2 times more than consumed blood. Therefore, optimal usage of blood products by providing accurate protocols and the use of smaller blood bags are proposed in order to improve the health of infants in intensive care units and lessen the complications of blood transfusion in newborns.

### Conflict of interest

There is no conflict of interest.

### References

1. Chirico G. Red blood cell transfusion in preterm neonates: current perspectives. *Neonatology* 2018;114: 7–16.
2. Strauss RG, Widness JA. Is there a role for autologous/placental red blood cell transfusions in the anemia of prematurity? *Transfus Med Rev* 2010; 24(2):125–129.
3. Christensen RD. Identifying neonates likely to benefit from a red blood cell transfusion. *Transfusion* 2012;52(2):217–218.
4. Christensen RD, Henry E, Jopling J, Wiedmeier SE. The CBC: reference ranges for neonates. *Semin Perinatol* 2009; 33(1): 3–11.
5. La Gamma EF. Introduction to transfusion practices in neonates: risks, benefits, and alternatives. *Semin Perinatol* 2012; 36(4):223–224.
6. Bishara N, Ohls RK. Current controversies in the management of the anemia of prematurity. *Semin Perinatol* 2009;33(1): 29–34.
7. Keramati R, Tafazoli M. Blood transfusion and its products usage in Emam Reza hospital, 2003. *J Mashhad Univ Med Sci* 2006; 92:199-208.
8. Garehbaghian A, Jalilzadeh Kohi M, Honarkaran N, Davoodi F. Estimation and comparison of the production cost of blood and blood products in IBTO centers in 2002. *J Blood Res* 2004; 2:61-69.
9. Marziehbeigohm Kh. Prevalence of blood transfusion in cesarean section Khvosar hospital, 2000-2001. *Intensive care Congress* 2005; 181-182.
10. Keramati R, Tafazoli M. Blood transfusion and its products usage in Emam Reza hospital, 2003. *J Mashhad Univ Med Sci* 2006; 92:199-208.
11. Kiasari A, Mirzade A, Hashemi M. The rate of blood transfusion and its components in Emam Khomeini hospital in Sari. *Med Sci Univ Mazandaran* 2008; 67: 91-95.
12. Entezari M, Amani F, Khorasani S. The rate of unnecessary blood transfusion and its components in hospitalized patients in Dr. Kazemi hospital in Ardabil. *Ardabil J Univ Med Sci* 2006; 4: 345-350.
13. Howarth C, Banerjee J, Aladangady N. Red Blood Cell Transfusion in Preterm Infants: Current Evidence and Controversies. *Neonatology* 2018;114: 7–16.
14. Ross MP, Christensen RD, Rothstein G, Koenig JM, Simmons MA, Noble NA. A randomized trial to develop criteria for administering erythrocyte transfusions to anemic preterm infants 1 to 3 months of age. *J Perinatol* 1989; 9: 246–253.
15. Meyer J, Sive A, Jacobs P. Empiric red cell transfusion in asymptomatic preterm infants. *Acta Paediatr* 1993; 82: 30–34.
16. Bolton-Maggs PHB, Poles D, Watt A, Thomas D, Cohen H. Serious Hazards of Transfusion (SHOT) Steering Group. Annual Shot Report 2013;1-9.
17. Ng PC, Lam CW, Lee CH, To KF, Fok TF, Chan IH. Hepatic iron storage in very low birthweight infants after multiple blood transfusions. *Arch Dis Child Fetal Neonatal Ed* 2001; 84:F101–F105.
18. Baer VL. Red blood cell transfusion of preterm neonates with a Grade 1 intraventricular hemorrhage is associated with extension to a grade 3 or 4 hemorrhage. *Transfusion* 2011; 51: 1933–1939.
19. Borna H, Rafati S, Tehrani FHE, Gadimii S. The prevalence and assessment of blood transfusions in newborns. *Tehran J Med Sci* 2017;75(3):200-207.

20. Nadri S. Frequency of blood transfusion and its products in the Khorramabad medical center.  *Lorestan J Med Univ Med Sci* 2013;9:1-9.
21. Zamani Kiasary A. Evaluation of blood transfusion in Imam Khomainsi Hospital during 2007.  *Mazandran J Univ Med Sci* 2008; 18(7):91-97.
22. Perciaccante JV. Necrotizing enterocolitis associated with packed red blood cell transfusions in premature neonates.  *E-PAS* 2008; 58298-58313.
23. Dani C, Poggi C, Gozzini E, Leonardi V, Seregni A, Abbate R. Red blood cell transfusions can induce proinflammatory cytokines in preterm infants.  *Transfusion* 2017; 57: 1304–1310.
24. Wang YC, Chan OW, Chiang MC, Yang PH, Chu SM, Hsu JF. Red blood cell transfusion and clinical outcomes in extremely low birth weight preterm infants.  *Pediatr Neonatol* 2017; 58: 216–222.
25. Dos Santos AM, Guinsburg R, De Almeida MF, Procianoy RS, Leone CR, Marba ST, et al. Red blood cell transfusions are independently associated with intra-hospital mortality in very low birth weight preterm infants.  *J Pediatr* 2011; 159: 371–376.
26. Hirano K, Hiroi M, Ban R, Sogawa S, Ogihara H, Tamai H. Blood transfusion increases radical promoting non-transferrin bound iron in preterm infants.  *Arch Dis Child Fetal Neonatal Ed* 2001;84:F188–F193.
27. Mosayebi Z, Movahedian A, Mousavi SG, Toluee F. The prevalence of different blood derivatives consumption in neonates admitted to Kashan Shahid Beheshti Hospital (2000-2001).  *Razi J Med Sci* 2005;12(45):147-154.
28. Bednarek FJ, Weisberger S, Richardson DK, Frantz III ID, Shah B, Rubin LP, et al. Variations in blood transfusions among newborn intensive care units.  *J pediatrics* 1998;133(5):601-617.
29. Patterson JA, Bowen JR, Francis S, Ford JB. Comparison of neonatal red cell transfusion reporting in neonatal intensive care units with blood product issue data: a validation study.  *BMC pediatrics* 2018;18(1):86-91.
30. Rafieimehr H. The Status of Packed Red Blood Cell Transfusion in Besat Hospital of Hamadan in 2009- 2010.  *Med Laboratory J* 2010; 4(2):26-30.