Original Article

Access this article online

Quick Response Code:

Website: www.ijhonline.org

DOI: 10.4103/ijh.ijh_19_20

Prevalence of anemia among pediatric critical care survivors and impact of restrictive transfusion strategy on it: A study from North India

Manideepa Maji, Saikat Mandal[1], Nowneet Kumar Bhat, Gita Negi[1], Sarika Agarwal[1]

Abstract:

BACKGROUND: Anemia occurs frequently in critically ill patients and it can impact on long-term outcome more so after a critical illness. Very little data are available about anemia in pediatric critical care survivors. Recent randomized control trials in children support the use of restrictive transfusion strategy in critically ill children.

OBJECTIVES: This study aims to estimate the prevalence of anemia in pediatric critical care survivors, its causative factors and impact of restrictive transfusion strategy on its resolution.

PATIENTS AND METHODS: In this retrospective observational study, patients who got discharged from pediatric intensive care unit (PICU), their clinical course, serial hemoglobin (Hb) level, and transfusion history were collected. Patients were divided into two groups according to transfusion strategy (restrictive and liberal group). Patients with anemia were followed up and persistence of anemia was noted monthly.

RESULTS: In 54 cases enrolled in the study, 35 children had anemia (prevalence 35/54 = 64.8%). Statically significant difference between anemic and nonanemic groups was found in terms of duration of PICU stay and development of infection and no significant difference in age, gender, diagnosis, and requirement of mechanical ventilation. Among the 35 anemic children, restrictive transfusion strategy was followed in 21 and in 14 children liberal transfusion strategy was followed. Ten children were lost to follow-up. Anemia got resolved in 18 children (18/25 = 72%) and 7 children (7/25 = 20%) had persistent anemia. Among 25 children, 4 children in restrictive group (4/15 = 26.6%) and 3 children in liberal group (3/10 = 30%) had persistent anemia (statistically not significant; $P > 0.05$).

CONCLUSIONS: A large proportion of PICU survivor children is anemic at discharge, this could be due to long duration PICU stay or acquired infection during hospital stay or following restrictive transfusion strategy but on a long-term follow-up no statistically significant difference was noted between two groups.

Keywords:

Anemia, intensive care units, pediatric emergency medicine, pediatrics, transfusion

Departments of Pediatrics and [1]Transfusion Medicine, All India Institute of Medical Sciences, Rishikesh, Uttarakhand, India

Address for correspondence:
Dr. Saikat Mandal, Gopal Residency, 3rd Floor, Flat No - C2, Aam Bag, Rishikesh - 249 201, Uttarakhand, India.
E-mail: saikatmandal500@gmail.com

Submission: 19-04-2020
Revised: 31-5-2020
Accepted: 22-06-2020
Published: 10-11-2020

Introduction

Anemia occurs frequently in critically ill patients and it can impact on improvement from acute disease state as well as long-term outcome after a critical illness as it hampers delivery of oxygen to tissues.[1,2] There are very little data available about anemia in pediatric critical care survivors. Packed red blood cell (PRBC) transfusions in critically ill patients have multiple risks and are associated with worsened clinical outcomes.[3]

Recent randomized control trials in children supports the use of restrictive transfusion strategy in critically ill children.[4,5] Studies suggest that children with normal cardiac

How to cite this article: Maji M, Mandal S, Bhat NK, Negi G, Agarwal S. Prevalence of anemia among pediatric critical care survivors and impact of restrictive transfusion strategy on it: A study from North India. Iraqi J Hematol 2020;9:97-100.

output can maintain tissue oxygenation despite fall in hemoglobin (Hb) level to 7 gm/dl.[6] Adherence to the restrictive transfusion strategy may have some impact on occurrence of anemia in these pediatric critical care survivors. From Indian scenario, there is no data available on the development of anemia in pediatric critical care survivors. In developing countries, safety, and efficacy of restrictive transfusion among pediatric population have not been studied.

Hence, it was planned to study the prevalence of anemia in pediatric critical care survivors, its causative factors and impact of restrictive transfusion strategy on its resolution.

Materials and Methods

It was a retrospective observational study conducted at the Department of Paediatrics of All India Institute of Medical Sciences, Rishikesh, India, from March 2019 to June 2019, and their follow-up details were mentioned till the next 3 months' postdischarge. Infants, children aged 1 month to 18 years and admitted to pediatric intensive care unit (PICU) for >24 h and successfully discharged were included in the study. Patients with diagnosis of chronic hemolytic anemia, leukemia, malignancy, severe acute malnutrition (SAM), any child suffering from malabsorption, short gut syndrome were excluded from the study. Data related to age of the children, detailed history, examination findings, anthropometric measurements, investigations, final diagnosis, clinical course during hospital stay, serial Hb level, and transfusion history were collected. Anemia was defined as per the WHO guidelines.[7] Hb level was measured using SYSMEX automated analyzer.

Anemic children were divided into two groups as per transfusion strategy, i.e., restrictive strategy group – Hb threshold for transfusion was set at 7 g/dl and liberal strategy group-here threshold for transfusion was 9.5 g/dl.[4,5] Postdischarge all anemic children's data were collected monthly from follow-up register of outpatient department (OPD). Persistence of anemia was followed up in each specific group.

Data were expressed as means ± standard deviation. Normally distributed continuous variables were compared between two groups using unpaired *t*-test and Fisher's exact test was used for categorical variables. $P < 0.05$ was considered statistically significant. The associations were analyzed using the Statistical package for social science (SPSS) version 23.0. software.

Results

A total of 54 cases who got discharge from pediatric critical care unit during the study period were enrolled in the study. Thirty-five children had anemia at the time of discharge (prevalence 35/54 = 64.8%) [Table 1]. Among 54 participants, 28 children belonged to <5 years of age group and rest were from the age group of 5–18 years. Five out of these 28 children (<5 years age group) had moderate acute malnutrition (17.8%) and 3 out of these 5 malnourished children (60%) had anemia at discharge.

A comparison was made between two groups (anemic and nonanemic) in terms of age, gender, duration of stay in PICU, systemic diagnosis, requirement of mechanical ventilation, development of infection during the hospital stay, pre-admission anemia, and PRBC transfusion in PICU. There were no statistically significant difference between anemic and nonanemic groups in terms of age, gender, receiving PRBC transfusion in PICU, preadmission anemia, and requirement of mechanical ventilation. Statistically significant difference between these two groups was noted in terms of Hb level postdischarge, duration of stay in PICU, and development of infection during PICU stay [Table 1].

In 54 children, during PICU stay in 26 children, restrictive transfusion strategy was followed and for 28 children liberal transfusion strategy was followed. There was a statistically significant difference between anemic and nonanemic group in terms of following restrictive blood transfusion strategy (Fisher's exact test $P < 0.05$) [Table 2].

Among the 35 anemic children, restrictive transfusion strategy was followed in 21 (21/35 = 60%) and in 14 (14/35 = 40%) children liberal transfusion strategy was followed. Ten children (6 in restrictive group and 4 in liberal group) were lost to follow-up. On OPD-based follow-up, it was noted that among 25 children (after excluding lost to follow-up) who had anemia on discharge in 18 children anemia got resolved after 3 months (18/25 = 72%) and 7 children (7/25 = 28%) had persistent anemia. Among 25 children, 4 children in restrictive group (4/1 5 = 26.6%) and 3 children in liberal group (3/10 = 30%) had persistent anemia (statistically not significant; $P = 0.601$, Fisher's exact test) [Table 3].

Discussion

This study showed anemia was prevalent in pediatric critical care survivors which correlates with other studies. A study done by Demaret *et al*. showed that anemia is frequently observed at pediatric critical care discharge (around 57.4% children were found anemic).[3]

Patients who developed infection and had longer duration of stay in critical care unit were more prone to

Table 1: Comparison between participants of two subgroups (anemic and nonanemic) in terms of age, gender, duration of PICU stay, systemic diagnosis, requirement of mechanical ventilation, development of infection, pre-admission anemia, and PRBC transfusion (*n* = 54)

	Anemic (%)	Nonanemic (%)	*P*
Number (*n*)	35 (64.8)	19 (35.2)	
Mean age (years)	6.5714	6.4737	0.47*
Gender			
Male (*n*)	19	12	0.57**
Female (*n*)	16	7	
Mean Hb±SD (g/dl) after discharge	9.75±1.4	13.48±1.16	<0.05*
Systemic diagnosis at admission			
Respiratory disease (*n*)	4	2	0.89*
Infective etiology (*n*)	6	2	
Surgical complications (*n*)	3	2	
Hepatobiliary disease (*n*)	4	2	
Shock (*n*)	2	3	
Gastroenterological dysfunction (*n*)	3	1	
Cardiovascular disease (*n*)	5	2	
Poisoning (*n*)	1	2	
Neurological disease (*n*)	7	3	
Preadmission anemia (*n*)	15 (42.9)	5 (26.3)	0.27**
Mean PICU stay (days)	10.97	5.1	<0.05*
PRBC transfusion in PICU (*n*)	10	3	0.34**
Infection during stay (*n*)	18	4	<0.05**
Mechanical ventilation required (*n*)	9	5	0.60**

*Unpaired *t*-test, **Fisher's exact test. SD=Standard deviation, PICU=Pediatric intensive care unit, PRBC=Packed red blood cell, Hb=Hemoglobin

Table 2: Comparison between participants of two subgroups (anemic and nonanemic) in terms of transfusion strategy (*n*=54)

	Anemic	Nonanemic	Fisher's exact test (two-tailed) (*P*)
Restrictive transfusion	21	5	0.0240
Liberal transfusion	14	14	

Table 3: Comparison between two subgroups of different transfusion strategies in terms of persistence of anemia (*n*=25 excluding, 10 patients lost to follow up)

	Restrictive transfusion	Liberal transfusion	Fisher's exact test (one-tailed) (*P*)
Resolved anemia	11	7	0.6014
Persistent anemia	4	3	

have anemia. It may be due to frequent blood sampling[8] for arterial blood gas, serum electrolyte monitoring and other relevant investigations or due to suppression of erythropoiesis[9] caused by reduction in erythropoietin production[10] related to underlying disease causing prolonged inflammation or bone marrow suppression[11] or may be due to underlying conditions like malnutrition. Inflammation causes increase production of inflammatory cytokines like interleukin 1 (IL-1), IL-6 which leads to increased production of hepcidin which hampers iron absorption from the intestine.[12,13] As it is a retrospective study findings could not be confirmed by analyzing red cell indices and hepcidin level. Bateman *et al*. showed in their multicenter observational study that around 73% of patients had blood loss from blood draws accounted for the majority of total blood loss during the intensive care unit stay in all age groups.[8] Studies show for nonbleeding patients frequent blood sampling in critical care unit may cause fall in Hb level by >0.5 g/dL/day during the first 3 days.[14] This effect may be aggravated in children <5 years of age and infants due to less blood volume. Although in our study SAM was excluded, in children with moderate acute malnutrition of age group <5 years anemia was prevalent.

Children for whom restrictive transfusion strategy was followed during PICU stay developed prolonged anemia in spite of improving from underlying disease and receiving supplementation.

Furthermore, 72% patients with anemia on discharge from the PICU recovered their Hb to normal levels within 3 months. Ngo *et al*. also got similar findings in his study.[15]

Although anemia is more common in restrictive transfusion strategy group, on follow-up no statistically significant difference on resolution of anemia was noted between two transfusion strategy groups. Simultaneously, it should also be mentioned that transfusion has multiple hazards of infection, transfusion reactions, immunomodulation, and many more.[16] As in terms of resolution of anemia restrictive transfusion is not inferior to liberal group, keeping the hazards of

transfusion in mind restrictive transfusion strategy can be followed in pediatric age group[17] even in critical care.[4,5]

Limitations

The study was conducted in small number of samples with wide range of age group and cases were included only for 4 months. Hb on the day of PICU, discharge was not available for all patients, and we considered that an Hb level collected 3 to 4 days after PICU discharge should be a good surrogate of the Hb on the day of PICU discharge. Some cases were lost to follow-up. Correlation between anemia and socioeconomic status could not be evaluated. Patients who were already anemic and those who developed anemia during PICU stay could not be compared.

Conclusions

A large proportion of PICU survivor children are anemic at discharge. This could be related to long duration of PICU stay, acquired infection during hospital stay and following restrictive transfusion strategy. However, on long-term follow-up no statistically significant difference on resolution was observed between two transfusion strategy groups. Hence, restrictive transfusion may be beneficiary for pediatric age group also.

This study is the first from India to examine the incidence and time to resolution of anemia among children discharged from the PICU and impact of transfusion strategy on the resolution of anemia. It also puts a question on transfusion practices followed in critical care that despite of significant medical evidence pediatricians still prefer to follow liberal transfusion strategy. Hence, prospective studies with larger sample size from India and South East Asian region are needed to confirm these findings.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. McLellan SA, Walsh TS. Oxygen delivery and haemoglobin. Continuing Education in Anaesthesia. Critical Care Pain 2004;4:123-6.
2. Kanmaz HG, Sarikabadayi YU, Canpolat E, Altug N, Oguz SS, Dilmen U. Effects of red cell transfusion on cardiac output and perfusion index in preterm infants. Early Hum Dev 2013;89:683-6.
3. Demaret P, Karam O, Tucci M, Lacroix J, Behal H, Duhamel A, *et al*. Anemia at pediatric intensive care unit discharge: Prevalence and risk markers. Ann Intensive Care 2017;7:107.
4. Lacroix J, Hébert PC, Hutchison JS, Hume HA, Tucci M, Ducruet T, *et al*. Transfusion strategies for patients in pediatric intensive care units. N Engl J Med 2007;356:1609-19.
5. Akyildiz B, Ulgen Tekerek N, Pamukcu O, Dursun A, Karakukcu M, Narin N, *et al*. Comprehensive analysis of liberal and restrictive transfusion strategies in pediatric intensive care unit. J Trop Pediatr 2018;64:118-25.
6. Weiskopf RB, Viele MK, Feiner J, Kelley S, Lieberman J, Noorani M, *et al*. Human cardiovascular and metabolic response to acute, severe isovolemic anemia. JAMA 1998;279:217-21.
7. World Health Organization. Haemoglobin Concentrations for the Diagnosis of Anaemia and Assessment of Severity. Vitamin and Mineral Nutrition Information System. Geneva: World Health Organization; 2011.
8. Bateman ST, Lacroix J, Boven K, Forbes P, Barton R, Thomas NJ, *et al*. Anemia, blood loss, and blood transfusions in North American children in the intensive care unit. Am J Respir Crit Care Med 2008;178:26-33.
9. Hayden SJ, Albert TJ, Watkins TR, Swenson ER. Anemia in critical illness: Insights into etiology, consequences, and management. Am J Respir Crit Care Med 2012;185:1049-57.
10. Chasis JA, Mohandas N. Erythroblastic islands: Niches for erythropoiesis. Blood 2008;112:470-8.
11. Faquin WC, Schneider TJ, Goldberg MA. Effect of inflammatory cytokines on hypoxia-induced erythropoietin production. Blood 1992;79:1987-94.
12. Nemeth E, Rivera S, Gabayan V, Keller C, Taudorf S, Pedersen BK, *et al*. IL-6 mediates hypoferremia of inflammation by inducing the synthesis of the iron regulatory hormone hepcidin. J Clin Invest 2004;113:1271-6.
13. Lee P, Peng H, Gelbart T, Wang L, Beutler E. Regulation of hepcidin transcription by interleukin-1 and interleukin-6. Proc Natl Acad Sci U S A 2005;102:1906-10.
14. Nguyen BV, Bota DP, Mélot C, Vincent JL. Time course of hemoglobin concentrations in nonbleeding intensive care unit patients. Crit Care Med 2003;31:406-10.
15. Ngo QN, Matsui DM, Singh RN, Zelcer S, Kornecki A. Anemia among pediatric critical care survivors: Prevalence and resolution. Crit Care Res Pract 2013;2013:684361.
16. Stainsby D, Jones H, Wells AW, Gibson B, Cohen H, SHOT Steering Group. Adverse outcomes of blood transfusion in children: Analysis of UK reports to the serious hazards of transfusion scheme 1996-2005. Br J Haematol 2008;141:73-9.
17. Markham C, Small S, Hovmand P, Doctor A. Transfusion Decision Making in Pediatric Critical Illness. Pediatr Clin North Am 2017;64:991-1015.