Frequency of Anemia and Blood Transfusion in Critically Ill Patients

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Abstract

Background: Anemia in adults is defined as, hemoglobin of <13.5 g/dl in males and <12 g/dl in females, with a hematocrit of <41% and <36% in males and females respectively. Most patients admitted to critical care units become anemic within the first 3 days of ICU stay due to a number of reasons, and almost half of the patients receive blood transfusion and the number of transfusion increases proportionately with the duration of stay of patient in critical care unit.

Objective: To determine the frequency of blood transfusion due to anemia in critically ill patients.

Subject and Method: This cross-sectional study was conducted at Medical ICU of Liaquat National hospital Karachi from 26th July 2016 to 25th January 2017. Total 196 patients from critical care unit were included. The data collection technique applied is non-probability consecutive sampling. Demographic data along with co morbidities recorded and value of hemoglobin is recorded on daily basis.

Results: Out of 196 patients 65.8% were anemic at the time of admission in ICU with mean hemoglobin of 10.85 ± 1.14 mg/dl. 84.7% of patients developed anemia during their ICU stay and their mean hemoglobin was 9.51±1.65 mg/dl. 13.8% patients were transfused Packed red blood cells, 9.7% were transfused once, while only single patient was given 4PRBCs. The mean pre-transfusion hemoglobin was 7.57 ± 0.60 mg/dl.

Conclusion: Anemia is very frequent and multifactorial in critically ill patients. The study has helped to gauge the burden of blood transfusion in critically ill patients. It has highlightened the fact that blood transfusion has become an important component in the critical care units for the management of worsening anemia during ICU stay.

Keywords:

Anemia; Hemoglobin; Hematocrit; Transfusion

Introduction

Anemia in adults is defined as hematocrit of <41% and hemoglobin of <13.5 g/dl in males and hematocrit of <36% and hemoglobin of <12 g/dl in females [1]. Among the many causes of anemia in critically ill, some of the most important are production of endogenous erythropoietin and immune associated functional iron deficiency [2]. Iron status is rapidly altered in critically ill patients, especially in septic patients [3]. These alterations persist during the course of disease and are associated with decreased erythropoises [3]. The bone marrow is still capable of incorporating iron and responds to treatment with recombinant human erythropoietin (rh-epo) [4]. 60% of patients admitted to ICU are anemic and 20 to 30% have first Hemoglobin <90 g/l [5]. After 7 days 80% of ICU patients have an Hemoglobin <90 g/l [5]. On average, hemoglobin concentrations decreased by 0.66 g/dl/day for the first 3 days and by 0.12 g/dl/day thereafter [6]. Almost 50% of patients admitted to ICU receive red blood cell transfusion during their ICU stay [7]. In those patients with an ICU length of stay of >1 week, proportion of patients transfused increases to 85% [8].

Anemia is a very common problem in critically ill patients being managed in intensive care units (ICU) setups [9]. Many factors contribute to anemia in critically ill patients, including sepsis [10], overt or occult blood loss, and frequent phlebotomies for blood sampling, functional iron deficiency that is immune associated [11] as well as decreased production of erythropoietin. As anemia is generally not well tolerated by critically ill patients [12] therefore PRBC transfusions are being used to augment oxygen delivery to tissues and to avoid the deleterious effects of tissue hypoxia [13]. Therefore, PRBC transfusions remain a cornerstone of critical care practice [14] but there is still a point of concern to look for risk versus benefit in blood transfusion and anemia tolerance in individual patients on clinical basis. Studies have suggested that anemia increases the risk of death after surgery in patients with cardiac disease and in critically ill patients [15].

Critically ill patients are thought to be at an increased risk for the immunosuppressive [16,17] and microcirculatory [18,19] complications of PRBC transfusions.

Material and Methods

This cross-sectional study was conducted in Medical ICU of the Liaquat National Hospital Karachi, Pakistan, from 26th July 2016 to 25th January 2017 (6 months duration), using Non-probability consecutive sampling. 196 patients were included in the study. The sample size was calculated by using WHO software taking P=50% [7], d=7% and 95% confidence interval. All patients of both genders and age 20-70 years, admitted and managed in ICU settings after being diagnosed as sepsis, coronary artery disease, malignancy and chronic liver disease were included in the study. All those patients with active or major bleeding (trauma, variceal bleed, any surgery, bleeding or clotting disorder), patients with hemolysis, chronic renal failure and patients with Hemoglobin <9 g/l at the time of admission were excluded from the study. All those patients admitted in Medical ICU of LNH who fulfilled the inclusion criteria were included in the study. An approval from the ethical committee of LNH was taken prior to conducting the study. The purpose, procedure and risk benefits ratio of the study were explained and informed consent was taken from patient or attendant. Patient's demographics and comorbidities were recorded. Patients were labeled as anemic if hemoglobin <12 g/dl and hematocrit <36% in females and hemoglobin <13.5 g/dl and hematocrit <41% in males. Patient's hemoglobin and hematocrit were recorded on daily basis during ICU stay. Total numbers of units transfused were recorded. Outcome variables were measured in terms of anemia and blood transfusion due to anemia.

Confounding variables and biasness were controlled by strictly following inclusion and exclusion criteria. All the demographic data were entered into the predesigned proforma. Data was analyzed using statistical software package SPSS version 20. Mean and standard deviation were calculated for quantitative variable like age and number of blood transfusions. Frequency and percentages were calculated for categorical data like gender, comorbidity (i.e. CLD, CAD, and Malignancy), anemia (yes/no), transfusion (yes/no). Stratification was done on gender and age to see the effect of modifiers on outcome using chi square test considering P<0.05 as significant.

Results

A total of 196 patients of either gender diagnosed as sepsis, coronary artery disease, malignancy, and chronic liver disease were evaluated to determine the frequency of anemia and blood transfusion due to anemia in ICU patients. Descriptive statistics were calculated using SPSS version 21. Stratification was done and post stratification Chi square test was applied to observe the effect of modifiers on outcome. Mean difference was compare by using independent t-test. P value ≤ 0.05 was considered as significant.

The results showed that there were 102 male and 94 female patients. Mean age of patients was 54.90 ± 16.82 years. Mean hemoglobin level at admission was 12.10 ± 2.20 g/l while mean hemoglobin level at onset of anemia was 10.02 ± 2.08 g/l. Most of the patients 115(58.7%) was found with no complication/co morbid.65 (33.2%) were presenting with CKD, 5(2.6%) with CLD and 11(5.6%) with Malignancy. 129(65.8%) were found Anemia at Admission while 166(84.7%) were develop Anemia during ICU stay. 27(13.8%) patients were received blood transfusion. Demographic and Clinical characteristics are presented in Table 1. Number of transfusion received by patients is presented in Figure 1.

Significant mean difference of anemia during hospital stay was found for Hemoglobin level at admission (p=0.021) and Hemoglobin

level at onset of anemia (p=0.000) while significant association was found with anemia at admission (p=0.021) and transfusion of blood (p=0.017). Detailed results of comparison and association with anemia during hospital stay are presented in Table 2.

Parameters	N(%)
Age(years)±	54.90±16.82
Hemoglobin level at admission (g/dL)	12.10 ±2.20
Hemoglobin level at onset of anemia	10.02±2.08
Gender	
Male	102(52)
Female	94(48)
Comorbids	
None	115(58.7)
CAD	65(33.2)
CLD	5(2.6)
Malignancy	11(5.6)
Anemia at admission	
Yes	129(65.8)
No	67(34.2)
Anemia during ICU stay	
Yes	166(84.7)
No	30(15.3)
Transfusion of Blood	
Yes	27(13.8)
No	169(86.2)
± Mean ± SD	

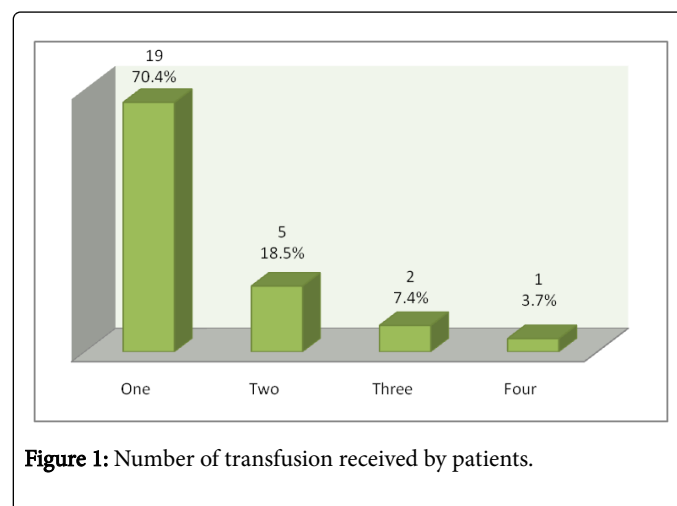**Table1:** Demographic and clinical characteristics.

Figure 1: Number of transfusion received by patients.

Significant mean difference of transfusion of blood was found for Hemoglobin level at admission (p=0.000) and Hemoglobin level at onset of anemia (p=0.000) while significant association was found with anemia at admission (p=0.006) and anemia during ICU stay (p=0.017). Detailed results of comparison and association with blood transfusion are presented in Table 3.

Parameters	Anameia during hospital stay n(%)		
	Yes (n=66)	No(n=30)	P-Value
Age(years)±	55.29 ± 16.56	52.77 ± 18.33	0.451[*]
Hemoglobin level at admission (g/dL)±	11.89 ± 1.99	13.22 ± 2.89	0.021
Hemoglobin level at onset of anemia(g/dL)±	9.51 ± 1.65	12.81 ± 2.06	0
Gender			
Male	83(50)	19(63.3)	0.179[*]
Female	83(50)	11(36.7)	
Comorbids			
None	94(56.6)	21(70)	
CAD	58(34.9)	7(23.3)	0.484[*]
CLD	5(3)	0(0)	
Malignancy	9(5.4)	2(6.7)	
Anemia at Admission			
Yes	115(69.3)	14(46.7)	0.021
No	51(30.7)	16(53.3)	
Transfusion of Blood			
Yes	27(16.3)	0(0)	0.017
No	139(83.7)	30(100)	

± Mean ± SD; Independent t-test applied; Chi Square test was applied; P-value ≤ 0.05 considered as significant; [*] Not Significant at 0.05 level.

Table2: Anemia during hospital stays with demographic and clinical characteristics.

Discussion

Anemia is a very common entity among critically ill patients. This is a cross sectional study being carried out in a developing country, Pakistan. Total 196 patients were enrolled in this study, with an average age of 20-70 years and with different comorbidities like Coronary artery disease, Chronic liver disease and Malignancy. Our results found that out of 196 patients 65.8% were anemic at the time of admission in ICU with mean hemoglobin of 10.85 ± 1.14 mg/dl. 84.7% of patients develop anemia during their ICU stay and they were found to have mean hemoglobin of 9.51 ± 1.65 mg/dl.

These results are comparable to previous studies as well, the CRIT study by Howard L. Corwin et al in USA stated that 70% patients develop anemia within 48 hours of hospital stay while 95% become anemic in 72 hours [8]. According to a prospective, multicenter, observational cohort study done in USA, almost 50% of patients receive RBC transfusion during their ICU stay and the number increased to 85% with a length of stay for greater than 1 week in ICU [20].

Parameters	Transfusion of Blood n(%)		
	Yes (n=66)	No(n=30)	P-Value
Age(years)±	55.29 ± 16.56	52.77 ± 18.33	0.451[*]
Hemoglobin level at admission (g/dL)±	11.89 ± 1.99	13.22 ± 2.89	0.021
Hemoglobin level at onset of anemia (g/dL) ±	9.51 ± 1.65	12.81 ± 2.06	0
Gender			
Male	83(50)	19(63.3)	0.179[*]
Female	83(50)	11(36.7)	0
Comorbids			
None	94(56.6)	21(70)	0.484[*]
CAD	58(34.9)	7(23.3)	0
CLD	5(3)	0(0)	0
Malignancy	9(5.4)	2(6.7)	0
Anemia at Admission			
Yes	115(69.3)	14(46.7)	0.021
No	51(30.7)	16(53.3)	0
Transfusion of Blood			
Yes	27(16.3)	0(0)	0.017
No	139(83.7)	30(100)	0

± Mean ± SD; Independent t-test applied; Chi Square test was applied; P-value ≤ 0.05 considered as significant; [*] Not Significant at 0.05 level.

Table 3: Blood transfusion with Demographic and clinical characteristics.

Our study was designed to estimate the frequency of anemia in Asian population, among those patients admitted to ICU, at the time of admission in ICU and during their ICU stay as no figures are found and no work has been done so far in an Asian country on this ground. The high frequency of anemia is multifactorial, decreased endogenous erythropoietin production; frequent phlebotomy and functional iron deficiency are the major contributing factors [2, 21,22]. Other factors involved in pathogenesis include coagulopathies, pathogen-associated hemolysis, hypoadrenalism, and nutritional deficiencies [23,24], including deficiencies of iron, B12, and folate can lead to ineffective erythropoiesis with resultant anemia [25,26].

There is an important role of decreased erythropoietin production and impaired bone marrow response to erythropoietin in the development of anemia [27]. The inflammatory cytokines such as Interleukin-1 (IL-1) and tumor necrosis factor-α (TNF-α) inhibit erythropoietin (EPO) production, while IL-1, IL-6, and TNF-α suppress erythropoiesis by direct inhibitory effects on bone marrow [28]. The inflammatory cytokines IL-6 and interferon-γ (IFN-γ) are

released in hyper-adrenergic states following severe injury and they inhibit the differentiation and proliferation of erythroid precursor cells [29].

The most common causes of Anemia of Chronic Disease are acute or chronic inflammatory conditions such as infections, cancer, autoimmune diseases, and chronic kidney disease (CKD) [30]. In anemia of chronic disease there is sequestration of iron in macrophages and iron-restricted erythropoiesis.

Its association with elevated levels of inflammatory cytokines, including IL-1, IL-6, and IFN-γ [31] induce excess hepcidin production, which in turn down regulate ferroportin, an iron export protein on the cell surface of duodenal enterocytes, macrophages, and hepatocytes [25, 32]. That is how high serum levels of hepcidin decrease intestinal iron absorption and block iron export from tissue stores, resulting in functional iron deficiency [33,34].

In our study, we found that 13.8% patients were transfused PRBC, 9.7% received only single PRBC transfusion, only single patient was given 4PRBCs. The mean pre-transfusion hemoglobin recorded was 7.57 ± 0.60 mg/dl. Our transfusion trigger of 7.6 mg/dl approaches the threshold proposed by TRICC of 7.0 g/l, although significant variability exists. This may reflect increasing comfort over time with lower transfusion threshold suggested by TRICC trial results [35]. The guidelines proposed by AUTRALIAN NATIONAL HEALTH & MEDICAL RESEARCH COUNCIL in Dec, 2012 for blood transfusions were followed [36].

We have further stratified patients on the basis of age, gender and comorbid, no significant association of age and gender with anemia and blood transfusion was found. Most patients with comorbidities were found to be anemic and were transfused blood. 58 patients with CAD out of 65 were found to be anemic, 9 out of 11 patients with Malignancy and all 5 CLD patients were transfused blood. All these results were comparable to the results of the CRIT study [8].

Strengths and limitations of the study

Although multiple studies have been done so far on the frequency of anemia and blood transfusion internationally, this is the first study in a developing country, Pakistan, which has estimated frequency of anemia in critically ill patients at the time of admission and during the ICU stay.

This study has highlightened the fact that patients with chronic illnesses like chronic liver disease, malignancy and coronary artery disease are mostly anemic and they require frequent blood transfusion at a lower threshold, once they become critically ill and being managed in an ICU setup. Other comorbidities are yet to be addressed as our study is limited to these three comorbid conditions.

Current data regarding frequency and low transfusion threshold for PRBC transfusion in today's world that actually shows an obvious change over the last decade is shown in our study. However further study is required to more fully explore the risk of anemia, optimal hemoglobin level and the risk and efficacy of PRBC transfusion in the critically ill.

Conclusion

The study results showed that 166 patients developed anemia during their ICU stay or had further worsening of anemia with mean hemoglobin recorded as 10.02 mg/dl, and the minimal value of hemoglobin was found to be 6 mg/dl. 27 patients were transfused blood, and 19 among them received only single PRBC transfusion.

To conclude; Anemia is very frequent and multifactorial in critically ill patients. The study emphasizes the fact that the practice of frequent blood transfusion has been changed drastically over the last decade, yet it is found to be an important component of management in critically ill patients.

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