Prediction of Outcome in Anemic Critically ill Patients in Intensive Care Unit: A Retrospective Observational Study

Marwa Elsayed*, Samah Mohamed Mahmoud, Lamia Hamed Mohamed, Walid Omar, Kamel Abdelaziz

Department of Critical Care, Cairo University, Cairo, Egypt

Abstract

AIM: Anemia is a universal finding in critically ill patients which add to the risk of poor outcomes. We aimed to evaluate the prevalence of anemic critically ill patients and to detect predictors of outcome.

METHODS: A retrospective study was from 5-year data in the electronic medical record of the critical care department at Cairo University. All medical ICU patients that were admitted with or developed anemia during their ICU stay were included in the study. All data of admission, ICU stay, and APACHE II were recorded and their association with the final outcome was determined.

RESULTS: The study included 301 patients. Anemia was detected in 84.6% of patients. Blood transfusion was given to 61.8% of patients while not given to 38.2% and was not significantly associated with outcome. Non-survivors were 37.5%. Non-survivor was associated with higher APACHE II score than survivors (20.88 ± 7.647 vs. 12.61 ± 5.809, p = 0.0001). Only DM, IHD, and CKD were associated with poor outcome (p = 0.045, 0.026, and 0.001, respectively). Need for MV or vasopressors were also associated with poor outcome (p 0.0001 for both). The multi-variate analysis detected that these variables (need for MV, vasopressors, and Hb at the 14th day e 7.3 g/dl) could correctly detect outcome with sensitivity 91.6%, specificity 73.6%, PPV 76.7%, and NPV 90.3%, and total accuracy 82.4%.

CONCLUSIONS: Anemia in critically ill patients is common and associated with poor outcomes. Blood transfusion was not associated with a better outcome. Combination of MV need and vasopressors with persistent anemia at day 14 was the best predictors of poor outcomes.

Introduction

Anemia is a frequent problem that faced clinicians in intensive care units' patients (ICU) and according to the WHO, anemia is clinically diagnosed by hemoglobin (Hb) level <12 gm/dl in females and 13 gm/dl in males [1]. Nearly, 60% of ICU patients are anemic on admission [2] and between 70 and 95% develop anemia on the 3rd day of admission [3], [4].

The causes of anemia in critically ill patients are diverse and the most frequent ones are sepsis syndromes [5], [6], blood loss due to bleeding or frequent sampling [7], impaired production, or immune-mediated process [8], [9]. However, the accurate impact of anemia on the outcome of critically ill patients is undefined properly and also the target hemoglobin level needs further evaluation.

As Hb is the main source of oxygen delivery to the tissues, anemia is potentially harmful and could impair tissue oxygenation in critically ill patients with high metabolic demand. Patients with anemia in ICU usually had longer ICU stay and a higher incidence of worse outcome [2].

Blood transfusion is the most frequent treatment choice for anemia besides other forms of anemia management (supplements and erythropoietin). Around 27% of patients in post-operative ICUs and 16% in medical ICUs receive blood transfusions during their ICU stay [3].

We aimed to determine the prevalence, impact of anemia on critically ill medical patients in ICU, and also to determine the predictors of worse outcome.

Patients and Methods

This retrospective observational study included that any patients admitted to ICU and discovered to be anemic. Data were collected from the existing data on electronic medical records (EMR) in the critical care department at Cairo University hospitals for 5-year period, from January 2011 to December 2015 for different medical causes.

Inclusion criteria

All patients above 18 years with medical indications for ICU admission and had anemia during their ICU course which either on admission or developed

during the ICU course were included in the study. Anemia was considered if hemoglobin level <12 gm/dl [1].

Exclusion criteria

We excluded any patient who had anemia as the primary cause of ICU admission, surgical causes, and missing data in the EMR.

Data collection

From the EMR system of the critical care department, all patients data were taken as follows:

All data related to history taking, clinical examination, ICU course (particularly, medications given, ICU stay, and clinical management), clinical scoring systems (APACHE II), all laboratory, and imaging results was also recorded. Blood transfusions were given if the Hb level below 7 gm/dl.

Primary outcome was the outcome at the end of ICU stay which either improvement and discharge or death. Secondary outcomes included ICU stay, rate of complications in anemic critically ill patients, and predictors of outcome.

Statistical methods

Data were verified and coded before analysis. All quantitative data were expressed as mean ± SD. All qualitative data were expressed as frequency and percentage tables.

Chi-square test to confirm the presence of an association between different categorical data. Student t-test to compare quantitative data were used. Univariate and multivariate regression analysis for all variables to test for factors associated with poor outcome. P < 0.05 considered significant. Analysis has been performed using SPSS 20 (Statistical Package for the Social Science).

Results

This retrospective cohort included 7900 patients that were recorded on the EMR system. All patients admitted just for interventions (coronary interventions, pacing, and electrophysiologic studies) and surgical patients were excluded from the study. The flow chart of our cohort is shown in Figure 1.

Demographic and clinical data of included patients

Out of 301 patients, 134 were males (44. 5%) with a mean age of 54.9 ± 21.1. The most common
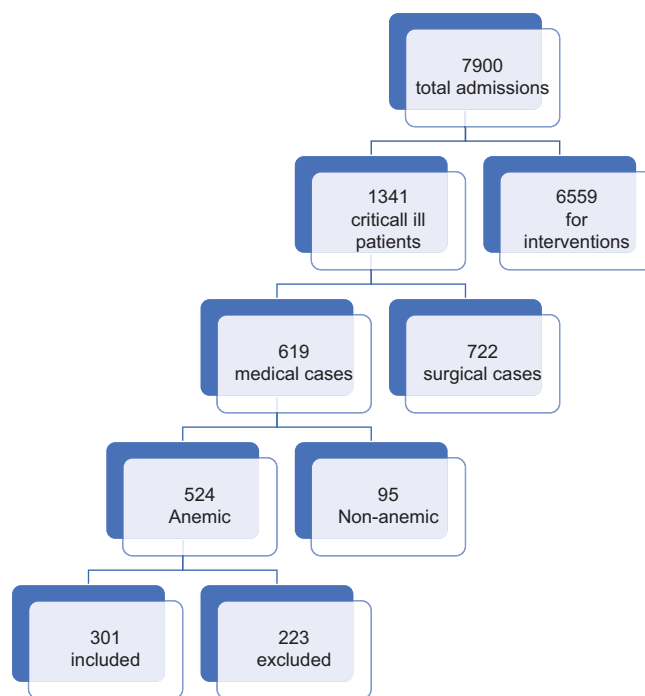

Figure 1: The flow chart of included patients

comorbid conditions were HTN (52.5%), chronic renal failure (47.5%), and DM (41.9%). Cardiac causes for admission were 47.8%. APACHE II was 17.5 ± 6.2 and 113 patients were died (37.5%).

Out of the total medical critically ill patients, 84.6% were anemic. Of the included patients (301), 30.9% received iron supplementation and 38.2% received blood transfusions (Table 1).

Figure 2: Mortality in different causes of admission
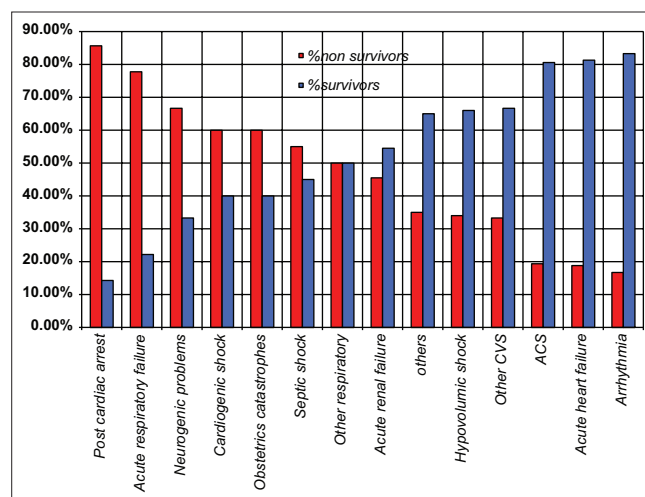
Outcome analysis

Mortality was recorded in 113 (37.5%) of included cases. An independent t-test was used to compare age, ICU stay, APACHE II score, and blood transfusions between survivors and non-survivors groups. All were non-significant except a significantly higher value of APACHE II which was found in non-survivors (20.88 ± 7.647 vs. 12.61 ± 5.809, p =.0001).

Table 1: Data of all study group

Variable	Mean or Percentage
Age	54.9 ± 21.1
Male	134 (44.5)
Length of stay	12.1 ± 11.9
Comorbid conditions	
HTN	158 (52.5)
CRF	143 (47.5)
DM	126 (42)
IHD	100 (33.2)
Others	80 (26.6)
Causes of admission	
Cardiac causes	144 (47.8)
Respiratory causes	24 (8)
Neurological causes	18 (6)
Septic shock	20 (6.6)
Acute renal failure	11 (3.7)
Obstetric emergencies	10 (3.3)
Post-CPR	7 (2.3)
Others	67 (22.3)
Anemia management	
No blood transfusion	115 (38.2)
Blood transfusions	186 (61.8)
Iron supplement	93 (30.9)
MV	141 (46.8)
Vasoactive drugs	149 (49.5)
Survivors	188 (62.5)
Non-survivors	113 (37.5)

HTN: Hypertension, CRF: Chronic renal failure, DM: Diabetes mellitus, IHD: Ischaemic heart disease, CPR: Cardio-pulmonary resuscitation, MV: Mechanical ventilation.

Post-CPR state, acute respiratory failure, neurological complications, acute heart failure, sepsis with shock states, acute kidney injury, and obstetrics complications were associated with a higher incidence of mortality among the total number of each reason (85.7%, 77.8%, 66.7%, 60%, 55%, 45.5%, and 60%), respectively (Figure 2).

Univariate analysis

For all comorbid conditions, only DM, CRF, and IHD were associated with mortality (p values are 0.045, 0.026, and 0.001), respectively. For the management of anemia either by iron supplement or blood transfusion, there is no significant association with outcome. For medications given during ICU stay, the significant association with outcome is the use of vasoactive drugs (p value = 0.0001). The need for MV was also significantly associated with worse outcome (p = 0.0001) (Table 2).

Laboratory investigations that were significantly associated with the outcome are white blood count (WBC) and platelets on admission, Hb level at day 14, Hb level at the final outcome, ALT, aPTT on admission,

Table 2: Association of qualitative variables with the outcome

	Survivors		Non-survivors		p-value
	No. (%)	% in outcome	No. (%)	% in outcome	
DM	87/126 (69)	46.3	39/126 (31)	34.5	0.045
No DM	101/175 (57.7)	53.7	74/175 (42.3)	65.5	
CRF	80/143 (55.9)	42.6	63/143 (44.1)	55.8	0.026
No CRF	108/158 (68.4)	57.4	50/158 (31.6)	44.2	
IHD	77/100 (77)	41	23/100 (23)	20.4	0.0001
No IHD	111/201 (55.2)	49	90/201 (44.8)	79.6	
Blood transfusion	115/186 (61.9)	61.2	71/186 (38.1)	62.8	0.123
No blood transfusion	73/115 (63.5)	38.8	42/115 (36.5)	37.2	
Iron supplement	61/93 (65.6)	32.4	32/93 (34.4)	28.3	0.453
No iron supplement	127/208 (61.1)	67.6	81/208 (38.9)	71.7	
Vasoactive drugs	53/149 (35.6)	28.8	96/149 (64.4)	85	0.0001
No vasoactive drug	135/152 (88.8)	71.8	17/152 (11.2)	15	
MV	42/141 (29.8)	22.3	99/141 (70.2)	87.6	0.0001
No MV	146/160 (91.2)	77.7	14/160 (8.8)	12.4	

DM: Diabetes mellitus, CRF: Chronic renal failure, MV: Mechanical ventilation.

serum creatinine on day 3, and creatinine at the final outcome (p = 0.014, 0.002, 0.001, 0.0001, 0.049, 0.001, 0.001, and 0.0001), respectively (Table 3).

Table 3: Association of quantitative variables with the outcome

	Survivors		Non-survivors		p value
	No.	M ± SD	No.	M ± SD	
WBC at admission	188	11.53 ± 6.3	113	14.34 ± 11.1	0.014
Platelets at admission	188	230 ± 133.7	113	182.4 ± 125.5	0.002
Hb at day 14	43	8.56 ± 1.2	31	7.7 ± 0.9	0.001
Hb at outcome	188	9.3 ± 1.1	113	8.1 ± 1.8	0.0001
aPTT at admission	188	34.4 ± 15.3	113	41.9 ± 19	0.001
ALT at admission	188	65 ± 105	113	223 ± 840	0.049
Creatinine at day 3	183	1.88 ± 1.7	97	2.6 ± 1.9	0.001
Creatinine at outcome	188	1.7 ± 1.5	113	2.8 ± 1.7	0.0001

WBC: White blood cell counts, Hb: Hemoglobin, aPTT: Activated partial thromboplastin time, ALT: Alanine aminotransferasa

Multivariate analysis and outcome prediction

Multivariate analysis has been used to choose the best predictors of outcome from all variables that were detected by the previous univariate analysis to have a significant association with outcome.

The need for mechanical ventilation or vasopressors and hemoglobin level at the 14th day £7.3 g/dl was the best predictors of prognosis. These variables could correctly detect outcome with sensitivity 91.6%, specificity 73.6%, PPV 76.7%, and NPV 90.3%, and total accuracy 82.4% (Table 4).

Table 4: Predictors of outcome for patients stayed for at least 14 days

Total	Predicted group mortality by the need for MV or vasopressor and Hb at day 14th		Outcome
	Non-survivors	Survivors	
43 (100)	10 (23.3)	33 (76.7)	Survivors
31 (100)	28 (90.3)	3 (9.7)	Non-survivors
44	38	36	Total

Discussion

During 5-year analysis of EMR, 7900 patients were recorded at Cairo University hospitals, 6559 were admitted for interventional procedures as coronary interventions (diagnostic or therapeutic), pacing, or electrophysiologic studies. Patients admitted for surgical causes were 722 patients. Medical reasons represented 619 patients, 524 of them were anemic, and 301 of them fulfilled our inclusion criteria. Hence, 84.6% of the patients admitted for medical reasons had anemia during their ICU stay.

Many reports have confirmed that anemia is highly prevalent on admission to critical care units and during ICU stay. The ABC study involved 3534 patients that were admitted to around 146 European hospitals detected the mean hemoglobin level at ICU admission to be 11.3 gm/dl, with 29% having Hb level <10 gm/dl [10].

In another USA study (the CRIT), which included 4892 patients, the mean Hb level was 11 gm/dl at ICU admission [11].

In a study at 10 Scottish ICUs which included 1023 patients, they detected that the median Hb level was 10.5 gm/dl on admission to ICU with 25% of ICU patients which had Hb level <9 gm/dl [12]. In our retrospective cohort study, 301 patients were included, males represented 44.5%, while females were 55.5% with a mean age 54.9 ± 21.1, and a mean ICU stay 12.1±11.9. One hundred and eighty-eight patients were survived, while 113 (37.5%) died. The mean Hb level was 8.28 ± 1.96 gm/dl for the survivor group and 8.27 ± 2.36 gm/dl for the non-survivor group, which is less than the mean Hb level in the ABC study (11.3g/dl) [10], and in the CRIT study (11.0g/dl) [11], but nearly matched with the Scottish study mean Hb level < 9g/dl.

Cardiac causes for ICU admission represented nearly 50% of the total patients in the study and their related deaths represented 31.2% of the total mortality outcome. While those who were admitted due to respiratory causes represented 8% of the total admissions and their related deaths represented 15.1% of the total mortality outcome. Furthermore, 6% of the total admissions were due to neurogenic problems, 15.6% were due to hypovolemic shock, 6.6% had septic shock, and 6.6% had obstetric catastrophes.

Regarding the association of chronic diseases and comorbidities on the outcome, there were significant associations between the presence of DM, chronic renal failure, ischemic heart diseases, and outcome with p values 0.045, 0.026, and 0.0001, respectively.

Our result agreed with many papers that discussed the association of anemia and other chronic diseases. In a retrospective analysis of nearly 100,000 patients undergoing hemodialysis, Hb level ≤8 gm/dl had almost doubling of the odds of mortality, in comparison with Hb levels of 10–11 gm/dl [13].

In our study, there was no significant difference in the relation of blood transfusion and the outcome. There were 115 patients out of 301 who had no blood transfusion, 42 patients of them not survived (37.2%), while there were 186 patients who had a blood transfusion during their ICU stay, 71 patients of them not survived (38.1%). In the transfusion requirements in critical care (TRICC) [14], 838 patients were randomized to either a restrictive or non-restrictive transfusion strategy (7 vs. 10 gm/dl). There was no statistically significant difference in the all-cause 30-day mortality between the two groups.

Regarding the effect of transfusing blood as a therapy for correction of anemia on mechanically ventilated patients in our study, there was no significant difference in death rate between ventilated patients who received a blood transfusion and those who did not received it. Although ventilation need was affecting the outcome and had high mortality, blood transfusion did not improve the outcome in ventilated patients.

This result disagreed with another study which concluded that blood transfusion to target Hb > 11 gm/dl had lowered ventilation and work of breathing [15]. Furthermore,

in the TRICC study with 713 patients on MV, about 219 patients out of them were ventilated for > 7 days. There was no difference in duration of MV nor deaths between restrictive and liberal groups [14]. In our trial, there were 74 patients admitted for >2 weeks, around 40% of them died with mean hemoglobin 7.7 gm/dl which was significantly lower than its mean level in survivors 8.56 gm/dl. This finding agreed with the large study, conducted in many European ICUs, which detected that lower Hb levels are associated with longer ICU stay and higher in-hospital mortality [10].

The variables that have been chosen on multiple variate analysis as best predictors of prognosis in anemic patients in our study were the need for mechanical ventilation or vasopressors and hemoglobin level at the 14th day £7.3 g/dl was the best predictors of prognosis. These variables could correctly detect outcome with sensitivity 91.6%, specificity 73.6%, PPV 76.7%, and NPV 90.3%, and total accuracy 82.4%.

Conclusions

Anemia in critically ill patients is highly prevalent and associated with a poor outcome. Blood transfusion was not associated with a better outcome. There were many predictors of the poor outcome, but the combination of MV need and vasopressors with persistent anemia at day 14 was the best predictors of poor outcome. The main limitation of our study comes from its retrospective observational data with the absence of a controlled group with normal hemoglobin level for comparison. Furthermore, it was a single-center study that recruited a limited number of medical ICU patients.

Recommendations

Based on this retrospective study, categorization of anemic critically ill patients admitted to ICU as high-risk patients with poor prognosis that needs intensified medical management. Try to avoid any sources of blood loss in the ICU. Liberal blood transfusion for correction of anemia is not recommended.

Source of Funding

Conflicts of Interest

The authors have no conflicts of interest to declare.

Ethics Approval

The study was approved by the Local Ethical Committee of the critical care department of Cairo University for the registry and retrospective nature of the study but not given approval number that was only for interventional trials. Informed oral consents were taken from available telephone numbers of first-degree relative on medical records.

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