

## EFFECTS OF ANEMIA ON THE OUTCOME IN ELDERLY ADMITTED TO THE ICU

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### Keywords:

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### Abstract

**Background:** In critically ill patients, the increase in metabolic demands overwhelms the compensatory mechanisms for tolerating anemia, leading to increased morbidity and mortality.

**Objectives:** Assess the effect of anemia on the outcome of elderly patients in -----  
- intensive care unit (ICU)

**Methodology:** prospective study, 100 critically ill elderly patients. They were subjected to comprehensive geriatric assessment, complete blood count, evaluation of Acute Physiological and Chronic Health Evaluation Score (APACHE II) on the first day of admission and Sequential Organ Failure Assessment Score (SOFA) score on admission and daily.

**Results:** 61% anemic, no statistically significant difference between anemic and non anemic critically ill elderly as regards mortality, length of stay, complications and APACHE II score ( $P>0.05$ ) while SOFA scores were significantly higher among anemics ( $P<0.05$ ). SOFA scores were significantly higher among patients with microcytic anemia than those with normocytic anemia and non anemic patients ( $P<0.05$ ). SOFA on admission, maximum SOFA, mean SOFA and APACHE II scores were significantly higher in patients with moderate anemia ( $P<0.05$ ).

**Conclusion:** Anemia is considered an important parameter in critically ill elderly patients. Anemia affects the evaluation scoring of ICU patients and should be well considered in management and follow up.

### Introduction

Elderly patients make up between 26% and 51% of Intensive Care Unit (ICU) admissions<sup>(1)</sup>. Different studies have studied the association of age with the outcome in geriatric patients. An age-related increase in mortality was reported in a multihospital study of 38 ICUs. They concluded that the adjusted odds of death increased with each 5-year age increment<sup>(2)</sup>.

On the other hand anemia is associated with increased of death in the ICU<sup>(3)</sup>. In critically ill patients, the increase in metabolic demands overwhelms the compensatory mechanisms for tolerating anemia, leading to increased morbidity and mortality<sup>(4)</sup>. Also lower hemoglobin levels are associated with higher Sequential Organ Failure Assessment Score (SOFA) scores, longer ICU length of stay and increased in-hospital mortality<sup>(5)</sup>.

The short-term prognosis after intensive care is most likely the result of the interplay between illness severity, baseline patient characteristics (comorbidities, performance status) and the quality of care<sup>(6,7)</sup>.

Accurate prognosis predictions in critically ill elderly patients may help to decrease morbidity, improve therapeutic strategies and increase patients' quality of life<sup>(8)</sup>.

An important role of information derived from validated scores will help in guiding physician decision making in the future<sup>(9)</sup>.

This article was aimed at studying the effects of anemia on the outcome in elderly admitted to the ICU.

## Materials and methods

A prospective study performed among 100 critically ill elderly ( $\geq 60$  years) admitted to the ----- intensive care unit in ----- hospitals. Each participant was subjected to; Comprehensive Geriatric assessment, which include detailed history taking, complete medical, psychological and functional assessment. Examination was done on admission, including recording of vital data, assessment of conscious level and recording of the worst parameters during the first 24 hours of admission. Patients admitted to the ICU for less than 48 hrs were excluded.

Complete blood count (CBC) was done on admission for all patients including hemoglobin level (Hb), hematocrit (HCT) and mean corpuscular volume (MCV) in the central laboratory of ----- University hospitals. Anemia was defined according to WHO classification as a hemoglobin concentration less than 12 g/dl in women and 13 g/dl in men<sup>(10)</sup> and was graded according to WHO grading of anemia into; mild (Anemia Hb:10 g/dl - cutoff point ), moderate Anemia: 7-10 g/dl and severe anemia: Hb <7 g/dl <sup>(10)</sup>. Furthermore, Anemia was divided according to MCV into; normocytic (MCV 80-100 fl), microcytic (MCV less than 80 fl) and macrocytic anemia (MCV more than 100 fl) <sup>(11)</sup>.

Assessment of severity of illness was performed on admission within 24 hours using Acute Physiological and Chronic Health Evaluation Score (APACHE II)<sup>(12)</sup>. SOFA score was recorded on admission and daily thereafter <sup>(13)</sup>. Mean SOFA score was calculated and maximum SOFA (SOFA max) score was recorded. Assessment of the patient outcome: in the form of mortality or discharge and length of stay (LOS). Any complications were also recorded.

The collected data was revised, coded, tabulated and introduced to a PC using SPSS statistical software package and suitable analysis was done according to the type of data obtained for each parameter. Data was presented as mean $\pm$  standard deviation ( $\pm$  SD) for numerical data, frequency and percentage of non-numerical data. The distribution of qualitative variables was evaluated by Chi-Square test or Fisher's exact test, as indicated. Means of normally distribute variables were compared by Students' test or analysis of variance, as appropriate.

## Results

The sample enrolled (100) consisted of 54 males and 46 females, most of them were in the 60-65 age group (49%) and the larger number of the sample were non-smokers (58%). Among the 100 studied subjects, the most prevalent comorbidity was hypertension (62 subjects) and the least prevalent was dementia (10 subjects). The most prevalent causes of ICU admission in our study were cerebrovascular stroke (CVS) and disturbed conscious level (DCL) due to causes other than stroke mainly due to delirium secondary to acute medical problem.

Among the 100 studied patients 39% were non anemic, 28% had mild anemia, 27% had moderate anemia and 6% had severe anemia. The mean ( $\pm$ SD) hemoglobin level on admission was 11.2 ( $\pm$ 2.7) g/dl. As regards types of anemia, 34% of the studied group had normocytic anemia and 27% had microcytic anemia. Mild anemia was more common in the older age.

There was no statistical significance between anemia per se or its different grades and different causes of ICU admission. But it was found that the variable distribution of types of anemia among different causes of ICU admission shows significance. For example, microcytic anemia was significantly more common in patients admitted to the ICU because of septic shock or DCL.

As regards the outcome of the studied cases 54% were discharged, 53% developed ICU complications with mean length of ICU stay 5.5 $\pm$ 2.8 days. The mean APACHE II score was 19.22 $\pm$ 5.8, mean SOFA score on admission was 5.1 $\pm$ 2.3, mean maximum SOFA score was 7 $\pm$ 4 and the mean of the mean SOFA score was 5.3 $\pm$ 2.7.

Table 1 shows the relation between the presence of anemia and ICU outcome. Although non significant still mortality and morbidity were more among anemic patients.

Table 2 shows the relationship between grades of anemia and ICU outcome and revealed significantly higher APACHE II and SOFA scores among patients with moderate anemia. No other significant relation was evident.

Similarly, there was no significant relation between types of anemia with either mortality or length of ICU stay nor complications.

On the other hand, there was a statistically significant relation between types of anemia and SOFA admission score, maximum SOFA score and the mean SOFA score. No significant difference was elicited when comparing the types of anemia and APACHE II score (table 3).

**Table 1: Relation between anemia and ICU outcome**

		Anemic N=61	Nonanemic N=39	P value
ICU outcome N (%)	Discharge (N=54)	30(49.2%)	24(61.5%)	0.23
	Death (N=46)	31(50.8%)	15(38.5%)	
ICU complications N (%)	Yes (N=53)	32(52.5%)	21(53.8%)	0.89
	No (N=47)	29(47.5%)	18(46.2%)	
Length of ICU stay (days) Mean(±SD)		5.3(±2.8)	5.7(±2.9)	0.47
APACHE II total score Mean(±SD)		19.8(±5.8)	18.2(±5.7)	0.163
SOFA admission Mean(±SD)		5.6(±2.6)	4.3(±1.6)	0.004*
Maximum SOFA Mean(±SD)		7.79(±4.3)	5.7(±3.2)	0.014*
Mean SOFA Mean(±SD)		5.9(±3)	4.2(±2)	0.002*

**Table 2: Relation between grades of anemia and the ICU outcome (qualitative variables: ICU outcome and ICU complications), (quantitative variables: length of stay, APACHE II, SOFA)**

		Non anemic N=39	Mild anemia N=28	Moderate Anemia N=27	Severe Anemia N=6	P value
ICU outcome N (%)	Discharge (N=54)	24 (61.5%)	15 (53.6%)	12 (44.4%)	3 (50%)	0.58
	Death (N=46)	15 (38.5%)	13 (46.4%)	15 (55.6%)	3 (50%)	
ICU complications N (%)	Yes (N=53)	21 (53.8%)	15 (53.6%)	15 (55.6%)	2 (33.3%)	0.79
	No (N=47)	18 (46.2%)	13 (46.4%)	12 (44.4%)	4 (66.7%)	
Length of ICU stay (days) Mean(±SD)		5.7 (±2.9)	5.1 (±3.1)	5.7 (±2.7)	4.6 (±1.2)	0.7
APACHE II total score Mean(±SD)		18.2 (±5.7)	17 (±5.2)	22.5 (±5.3)	20.5 (±6.2)	0.003*
SOFA admission Mean(±SD)		4.3 (±1.6)	4.8 (±2.5)	6.3 (±2.4)	5.8 (±3.2)	0.005*
Maximum SOFA Mean(±SD)		5.7 (±3.2)	6.2 (±3.4)	9.7 (±4.5)	6.1 (±3.4)	0.001*
Mean SOFA Mean(±SD)		4.2 (±2)	4.9 (±2.5)	7.2 (±3)	5.3 (±3.4)	0.001*

**Table3: Relation between types of anemia and the ICU outcome (quantitative variables)**

	Non anemic N=39	Normocytic anemia N=34	Microcytic anemia N=27	ANOVA	
				F	P
<b>Length of ICU stay</b>	<b>5.7</b>	<b>5.2</b>	<b>5.4</b>	<b>0.28</b>	<b>0.753</b>
<b>Mean (±SD) (days)</b>	<b>(±2.9)</b>	<b>(±2.9)</b>	<b>(±2.7)</b>		
<b>APACHE II total score</b>	<b>18.2</b>	<b>19.3</b>	<b>20.4</b>	<b>1.2</b>	<b>0.163</b>
<b>Mean (±SD)</b>	<b>(±5.7)</b>	<b>(±5.8)</b>	<b>(±5.9)</b>		
<b>SOFA admission</b>	<b>4.3</b>	<b>5.4</b>	<b>5.8</b>	<b>3.8</b>	<b>0.025*</b>
<b>Mean (±SD)</b>	<b>(±1.6)</b>	<b>(±2.5)</b>	<b>(±2.8)</b>		
<b>Maximum SOFA</b>	<b>5.7</b>	<b>7.3</b>	<b>8.3</b>	<b>3.5</b>	<b>0.033*</b>
<b>Mean (±SD)</b>	<b>(±3.2)</b>	<b>(±3.8)</b>	<b>(±4.8)</b>		
<b>Mean SOFA</b>	<b>4.2</b>	<b>5.8</b>	<b>6.1</b>	<b>5</b>	<b>0.008*</b>
<b>Mean (±SD)</b>	<b>(±2)</b>	<b>(±3)</b>	<b>(±3)</b>		

## Discussion

Age is generally thought to be strongly associated with intensive care outcomes, but this relationship may be confounded by acute physiological impairment, age-related changes (lower functional reserve, co-morbidity) and differences in intensive care practice<sup>(14,15)</sup>.

Anemia is one of the most common medical complications encountered in critically ill patients. About two-thirds of patients have hemoglobin concentrations less than 12 g/dl at the time of ICU admission, with a subsequent decrement of about 0.5 g/dl per day<sup>(16,17)</sup>.

As will be shown below there has been great conflict between studies regarding the effect of anemia on critically ill patients. Despite the established consequences of anemia many studies have shown no effect on the outcome. Both aspects of the debate will be presented in correlation with the results of this study which was aimed specifically to assess the outcome in critically ill elderly given their decreased homeostatic reserve and multiple comorbidities.

Deleterious effects of anemia include increased risk of cardiac-related morbidity and mortality<sup>(18,19)</sup> as well as a generalized decrease in oxygen-carrying capacity. However, the specific impact of anemia on ICU patient morbidity and mortality is poorly defined, as is the optimal hemoglobin level for this population<sup>(5)</sup>.

The current study aimed to assess the effect of anemia on the outcome of elderly patients admitted to ----- ICU in ----- . A prospective study was carried out to assess the relationship between anemia at ICU admission and the ICU outcome in the form of ICU mortality, complications, LOS and severity of illness that was assessed on admission using APACHE II score and organ failure was followed during ICU stay daily using SOFA score.

As regards the relation between anemia and admission demographics, there was a significant relationship between age and grade of anemia where mild grade of anemia was more common at older age. This agrees with Patel (2008) who found that the far majority of anemia among older community-dwelling adults were mild, with less than 1% of them having hemoglobin concentration below 10 g/dl and less than 3% were below 11 g/dl (according to NHANES III, National Health And Nutrition Examination Survey). This can be explained that causes of severe anemia probably shorten life expectancy<sup>(20)</sup>.

As regards ICU outcomes in our study, among the 100 patients 54 were discharged and 46 died. The mean APACHE II score was 19.2±5.8 reflecting severity of illness at ICU admission. Mean admitting SOFA score was 5.1(±2.3), mean maximum SOFA score was 7(±4), mean value of mean SOFA score was 5.3(±2.7) and mean LOS was 5.5(±2.8).

We found that there was no statistically significant relationship between presence of anemia or its grade or type and ICU outcome as regards discharge or death, ICU complications and LOS, however, mortality among anemic group was higher (50.8%) and discharge was higher among non anemic group (61.5%).

Vincent et al, (2002) reported that anemia is common in critically ill patients and is associated with considerable morbidity and worse outcome. However, when they did hierarchical logistic regression to determine the associations between various patient characteristics and death in the ICU, the associations of transfusion, APACHE II, SOFA, and age with mortality were statistically significant but admitting hemoglobin level was not<sup>(5)</sup>.

Vincent et al. (2002) also found in their study that hemoglobin patterns over the 28-day period of ICU admission, revealing a convergence of hemoglobin levels over time, irrespective of the admitting hemoglobin level either high or low, which can affect the interpretation of the relation between the admitting hemoglobin and the ICU outcomes. This could also be why both groups in this study had comparable outcomes<sup>(5)</sup>.

On the other hand, Walsh et al., (2006) reported that anemia is well tolerated by critically ill patients and a hemoglobin of 7-9 g/dl does not adversely affect outcome as regards ICU mortality in comparison with maintaining a value >10 g/dl<sup>(21)</sup>.

Moreover, Hébert et al. (1999) found that anemia in critical illness is not necessarily harmful, with particular reference to acute anemia<sup>(22)</sup>. A major confounder to interpretation to the effect of anemia on the ICU mortality is transfusion practice. The TRICC (Transfusion Requirements In Critical Care) trial compared a transfusion trigger of <7 g/dl, with a target level of 7-9 g/dl during ICU admission, with a trigger <10 g/dl and target of 10-12 g/dl in patients whose hemoglobin concentration had a value of 9 g/dl during the first 3 days in ICU. The 30 and 60 day mortality were similar for these groups and significantly lower with the restrictive strategy among younger (<55 yr) and less ill (APACHE II score <20) patients<sup>(23)</sup>. Studies carried out after publication of this landmark trial continue to show variation in transfusion triggers. As a result, the prevalence and incidence of anemia among populations of critically ill patients needs to be placed in context by a description of the associated transfusion practice<sup>(21)</sup>.

Also we found that the relation between the presence of anemia and APACHE II score was statistically insignificant, however, APACHE II score was higher among the anemic group (19.8±5.8) than the non anemic group (18.2±5.7). This can be explained by the effect of the ICU practice on the predictive value of APACHE II scores which is calculated on admission, especially with prolonged ICU stay<sup>(24)</sup>.

Moreover, this score does not take into account the many factors that can influence patient outcome during the course of an ICU stay, so proper evaluation of changes in patient status over time is also important<sup>(8)</sup>.

Hence, the study by Peres and colleagues, 2002 revealed that in patients with septic shock, the SOFA score has been shown to have better predictive power than the APACHE II score<sup>(25)</sup>.

As regards the relation between grade of anemia and APACHE II score it was statistically significant, it was found that APACHE II score was higher in patients with moderate anemia than patients with mild anemia (P=0.001) and non anemic patients (P=0.002), also APACHE II score was higher in patients with normocytic anemia and microcytic anemia than non anemic patients.

This agrees with Nguyen et al. (2003) who found that hemoglobin concentrations were inversely related to the severity of the disease, as reflected by the APACHE II and SOFA scores<sup>(17)</sup>.

On the other hand, there was a statistically significant relation between presence of anemia, its grade and type and SOFA score on admission, SOFA maximum score and mean SOFA score, it was found that presence of anemia was related to higher SOFA scores. Moreover, SOFA scores were higher in patients with moderate anemia than patients with mild anemia and non anemic patients (P values 0.017, 0.001 respectively). It was also found that SOFA scores were higher among patients with normocytic and microcytic anemia than non anemic patients (P values 0.043, 0.012 respectively).

This agrees with Vincent et al., (2002) that performed a large, epidemiologic study in European ICUs that validated the common occurrence of anemia in critically ill patients and also reported that lower mean hemoglobin levels were associated with higher SOFA scores and longer lengths of stay<sup>(95)</sup>.

An important point to be considered in the current study is that this is a single-center study, so caution should be taken when applying our results to other ICUs due to differences in the ICU policies. Another point to be considered in this study is the transfusion practice which can affect the interpretation of the relation between the admitting hemoglobin and the ICU outcomes.

Moreover, our analysis focused only on ICU mortality, and we did not examine post discharge mortality or long-term prognosis. Therefore, to validate these results we recommend further studies involving critically ill elderly, taking into consideration different transfusion policies and hemoglobin level throughout the admission period.

**Conclusion:** Anemia is considered an important parameter in critically ill elderly patients. Anemia affects the evaluation scoring of ICU patients and should be well considered in management and follow up.



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