

Research Article

## Relationship between Mortality and Albumin, Alkaline Phosphatase, Phosphorus and Calcium Values that May Change with Renal Function and Nutrition in Intensive Care Setting

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### Abstract

#### Objective

To investigate the relationship between mortality and laboratory values that may change with renal function and nutrition, namely creatinine, ALP, albumin, phosphorus and calcium, in patients admitted to the intensive care unit (ICU).

#### Method

A total of 2549 patients older than 18 years of age,

who were followed up in the ICU of our hospital between 2015-2018, had no history of malignancy or pregnancy, had a length of ICU stay longer than 24 hours, and had laboratory values available at the time of admission to ICU, were included in the study.

#### Results

The results of our study showed that advanced age and prolonged length of stay are associated with mortality ( $p < 0.001$ ). Low albumin and calcium values and high creatinine and ALP values at the time

of ICU admission were a risk factor for mortality ( $p < 0.001$ ). Phosphorus value was not an important risk factor for mortality ( $p: 0.753$ ).

### Conclusion

In ICU patients, the relationship between mortality and renal function and laboratory values that may change with renal function and nutrition, namely creatinine, albumin, calcium, and ALP has been shown while no such relationship was observed between phosphorus values and mortality.

**Keywords:** Albumin; Alkaline phosphatase (ALP); Calcium; Creatinine; Intensive care unit (ICU); Phosphorus

### 1. Introduction

The mortality rate is the most reliable indicator of performance in intensive care unit (ICU). ICUs serve a seriously ill patient population exposed to a large number of complex interventions. Therefore, ICUs have the highest mortality compared to other departments of any given hospital [1]. Elderly patients admitted to ICU constitute a complicated patient group. More often than not, elderly patients are hospitalized for acute exacerbations of comorbidities as well as underlying chronic diseases and nutritional disorders. Therefore, an increased risk of mortality is expected in older patients [2,3]. In addition, ICU stays tend to be longer and mortal in the elderly. Furthermore, malnutrition, renal dysfunction and electrolyte disorders are common in this group of patients. In the present study, we aimed to investigate the effects of renal function and

alkaline phosphatase (ALP) values, which may change with renal dysfunction as well as the effects of albumin, phosphorus and calcium values, which may change with nutrition, on mortality in patients admitted to the ICU.

### 2. Methods

Our study was conducted among the patients admitted to the Internal Medicine ICU of our hospital between 2015 and 2018. Patients older than 18 years of age were enrolled in the study. Patients, who were pregnant, had a history of malignancy and did not have laboratory data available, were excluded. A total of 2549 patients were included in the study by retrospectively retrieving data from the electronic registry system.

### 3. Results

Of the 2549 patients included in our study, 48.3% ( $n=1231$ ) were female while females accounted for 47.3% ( $n=320$ ) of those with a fatal outcome. Regardless of gender, there was a statistically significant difference between the mean age of the deceased group ( $76 \pm 16$  years) and that of survivors ( $66 \pm 36$  years) ( $p < 0.001$ ). Again, a statistically significant difference was observed between the deceased ( $6 \pm 12$  days) and the survivors ( $3 \pm 5$  days) in terms of length of stay ( $p < 0.001$ ). The association of albumin levels showed a statistically significant difference between the group of deceased patients ( $2.6 \pm 0.8$  g/dL) and those who survived ( $3 \pm 0.9$  g/dL) ( $p < 0.001$ ) (Table 1). ALP values were significantly higher in the deceased group ( $86 \pm 57$ ;  $p < 0.001$ ). Creatinine values were significantly lower in the

group of survivors (0.8±0.3; p<0.001). There was no significant difference between the deceased group and the survivors in terms of phosphorus levels

(p=0.753). Calcium levels were lower with a statistically significant difference in the deceased group (8.6±1; p<0.001) (Table 1).

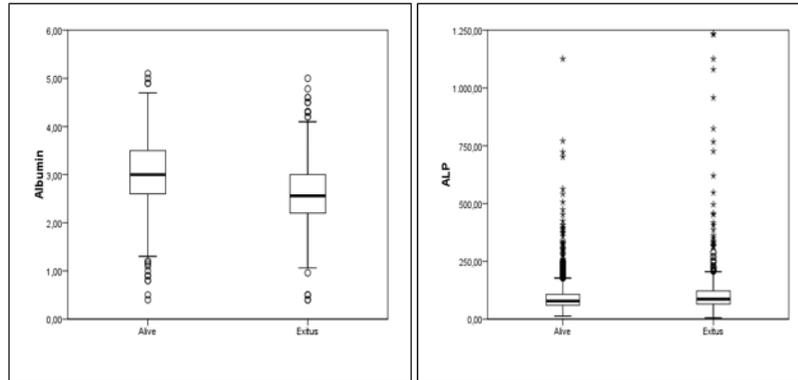
	Total	Alive	Exitus	P
	(n=2549)	(n=1872 %73.45)	(n=677 %26.55 )	
	n (%)	n (%)	n (%)	
<b>Gender</b>				
Female	1231 (48,3)	911 (48,7)	320 (47,3)	<b>0,560<sup>p</sup></b>
Male	1318 (51,7)	961 (51,3)	357 (52,7)	
	<b>n (Median±IQR)</b>	<b>n (Median±IQR)</b>	<b>n (Median±IQR)</b>	
<b>Age</b>	2549 (70±28)	1872 (66±36)	677 (76±16)	<b>&lt;0,001<sup>u</sup></b>
<b>Time of stay hospital</b>	2549 (3±6)	1872 (3±5)	677 (6±12)	<b>&lt;0,001<sup>u</sup></b>
<b>Albumin</b>	2082 (2,9±1)	1599 (3±0,9)	483 (2,6±0,8)	<b>&lt;0,001<sup>u</sup></b>
<b>ALP</b>	1860 (80,5±49)	1393 (78±47)	467 (86±57)	<b>&lt;0,001<sup>u</sup></b>
<b>Creatinine</b>	1704 (0,8±0,5)	1287 (0,8±0,3)	417 (0,9±0,8)	<b>&lt;0,001<sup>u</sup></b>
<b>Phosphorus</b>	1465 (3,5±1,2)	1092 (3,5±1,2)	373 (3,5±1,3)	<b>0,753<sup>u</sup></b>
<b>Calcium</b>	1881 (8,8±1)	1418 (8,9±1)	463 (8,6±1)	<b>&lt;0,001<sup>u</sup></b>
<sup>p</sup> Pearson Chi-Square Test(Exact), <sup>u</sup> Mann whitney U test(Monte Carlo), IQR: Interquartile Range				

**Table 1:** Association of mortality with gender, age and laboratory values (normal ranges of the lab:phosphorus, 2.6-5.5 mg/dL; urea, 10-50 mg/dL; calcium, 8.4-10.8 mg/dL; ALP, 30-128 U/L)

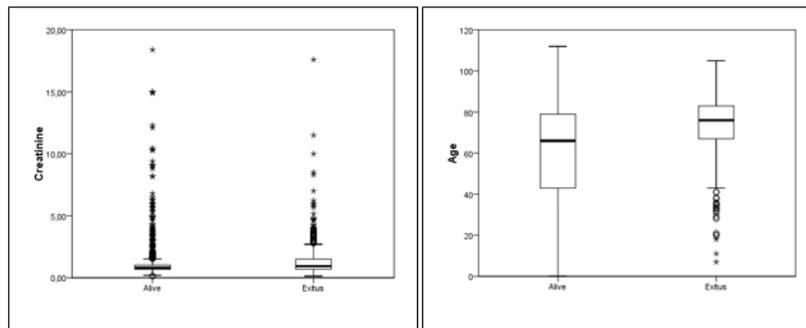
Dependent Variable is Mortality	B	SE	P	OdssRatio	95,0% CI forOdssRatio	
					Lower	Upper
Albumin (↓)	-0,37169	0,12382	0,003	1,450	1,138	1,848
ALP	0,00025	0,00042	0,553	1,000	0,999	1,001
Creatinine (↑)	0,20821	0,04826	<0,001	1,231	1,120	1,354

Calcium	0,08041	0,06430	0,211	1,084	0,955	1,229
1 / 2 / 3 / 5 – year survival rates (SE): 68,8 (0.025) / 39,7 (0.037) / 21,1 (0.037) / 6,2 (0,026) - Base Line Hazard: 0,040 Cox Regression-Enter Model, C.I. :Confidence interval B: regression coefficients SE: Standard error						

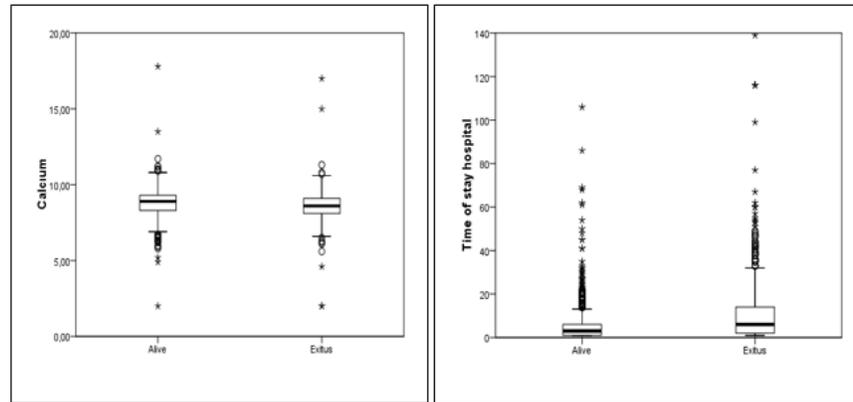
**Table 2:** Laboratory values associated with mortality



**Figures 1,2:** Association of albumin and ALP values with mortality.



**Figures 3,4:** Association of creatinine and age with mortality rates



**Figures 5,6:** Association of calcium and length of stay with mortality rates.

#### 4. Discussion

Mortality rates in the ICU have been reported to vary between 22.5% and 61.5% across different studies [4,5]. The mortality rate in our ICU was 26.55%, which is consistent with the literature (Table 1). The parameters investigated as risk factors for ICU mortality in our study were reported, in general, as risk factor in the studies investigating advanced age as a variable [6,7]. In the present study, the mortality rate was statistically significantly higher in patients aged 76 ( $\pm 16$ ) years or older ( $p < 0.001$ ) (Table 1, Figure 4). Studies investigating the length of hospital stay have reported that length of stay is another parameter associated with mortality [8,9]. In our study, increased mortality was observed with increasing number of in-hospital days ( $p < 0.001$ ) (Table 1, Figure 6). A number of factors, including age, diet, exercise, stress, pregnancy and kidney disease, may affect serum creatinine levels. Both low creatinine values [10] and high creatinine levels are an independent risk factor for mortality [11] in hospitalized patients. Although it was shown in our

study cohort that high creatinine values were an independent risk factor in the deceased group for mortality, consistent with the literature (Tables 1,2 Figure 3), we could not form a different group to demonstrate the effect of low creatinine values on mortality, due to the limited number of patients. Calcium is the most abundant mineral in the human body and has several essential functions. This mineral is involved in vital events such as muscle function, nerve conduction, intracellular signaling and vascular mediation, including contraction and vasodilation [12,13]. In addition, intracellular calcium concentration has an effect on cardiac contractility [14,15]. Abnormal calcium irregularities and changes in serum calcium levels have a prevalence of 88% in clinical practice, especially among critically ill patients [16]. Decreased serum calcium levels correlate with the severity of disease and nutrition [16-18]. Previous studies have shown the effect of serum calcium levels, including hypocalcemia and hypercalcemia, on in-hospital mortality [19]. In our study, calcium levels were

lower in the deceased group compared to the survivors; however, the ratio of low calcium values was not at a level to support this parameter as an independent risk factor for mortality (Table 1, Figure 5). The low calcium levels may be due to renal dysfunction as well as malnutrition. Phosphorus is the main substrate of mineralization. Serum phosphorus levels correlate with age and various nutritional markers [20] and it is known that young patients tend to consume more phosphorus [21] while elderly patients are usually hypophosphatemic due to their intake of less phosphorus, often associated with malnutrition [22]. In our study, the effect of hypophosphatemia on mortality decreased after adjusting for nutritional markers [23] and this may explain how the relationship between serum phosphorus values and mortality changes with age. However, studies have shown that both hyperphosphatemia ( $\geq 7.0$  mg/dL) and hypophosphatemia ( $< 3.0$  mg/dL) increase mortality rates through a bidirectional effect of serum phosphorus levels on mortality [24]; and it has been reported that low phosphorus levels are an important risk factor for increased morbidity and mortality in ICU patients [25]. Phosphorus level was not an independent risk factor for mortality in our patients (Table 1). While we would expect the patients in the deceased group to be hypophosphatemic resulting from malnutrition due to the advanced age, we believe that the reason for the normal phosphorus levels of the patients is the hyperphosphatemia expected in relation to the renal dysfunction in this group, which balances the serum phosphorus levels. Alkaline Phosphatase (ALP) is particularly abundant in the liver, bone, kidney, and placenta [26]. High

serum ALP levels are associated with increased mortality in the general population. It is estimated that the pathogenesis between serum ALP values and mortality includes not only high-turnover bone diseases, but also vascular calcification, myocardial contractility disorders, and valvular calcification [27-29]. In our study, ALP values were significantly high in the deceased group ( $p < 0.001$ ); however, it was not an independent risk factor for mortality (Tables 1,2; Figure 2). In our study, we believe that this may be due to high-turnover bone disease due to high creatinine or malnutrition. Albumin, the main component of plasma proteins, maintains microvascular permeability, oncotic pressure, acts as a buffer, transports cations, and plays a role in preventing platelet aggregation [30,31]. In addition to publications showing that serum albumin level has a high sensitivity in predicting ICU mortality, there are publications reporting a low sensitivity in this regard [32-34]. In our study, albumin levels were an independent risk factor for mortality (Table 2) and albumin values were significantly lower in the deceased group compared to survivors ( $p < 0.001$ ) (Table 1, Figure 1). We believe that the hypoalbuminemia in our patients may be related to the severity of disease, renal dysfunction and inadequate nutritional level. In our study investigating the association of mortality with phosphorus, albumin, calcium, and ALP values that can change with renal function and nutrition, we observed albumin and creatinine to be independent risk factors for mortality. In the deceased group, ALP levels were high, while calcium values were low. Consistent with the literature, we concluded that calcium and albumin values, which are related to the

nutritional level in ICU patients, are both important parameters for mortality in these patients.

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