Are Albumin and Lactate Predictive Indicators for Mortality in Critically Ill Patients with Acute Kidney Injury?

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Abstract

Introduction: The aim of this study was to assess the effect of age, gender, estimated glomerular filtration rate, albumin and lactate on mortality on critically ill patients admitted to intensive care unit due to acute kidney injury.

Methods: The study included 54 critically ill patients over the age of 18, who were admitted to our Level 3 intensive care unit with the diagnosis of acute kidney injury. Patients were divided into two groups as those who did not develop mortality (Group 1) and those who developed (Group 2). Both groups were compared in terms of age, gender, estimated glomerular filtration rate, albumin and lactate levels in the first 24 hours of admission. In addition, patients were divided into two groups according to both albumin levels (<2.5 g/dL and ≥2.5 g/dL) and lactate levels (<2 mmol/L and ≥2 mmol/L) and examined in terms of 30-day mortality.

Results: The patients' total mortality was 68.5% (37 patients). There was no statistically significant difference between the two groups (Group 1 and Group 2) in terms of age, sex, estimated glomerular filtration rate, albumin and lactate levels (p-values, respectively: 0.13; 0.39; 0.32; 0.83; 0.52). In addition, there was no statistically significant difference between the groups in terms of 30-day mortality (p-values: 0.625; 0.127).

Conclusion: Age, gender, estimated glomerular filtration rate, albumin and lactate levels did not affect 30-day and total mortality in our patients who were hospitalized in our intensive care unit with acute kidney injury diagnosis, and that albumin and lactate levels during admission were not a predictor of mortality in this patient group.

Keywords: Critically ill patients; Acute kidney injury; Albumin; Lactate; Mortality

Introduction

Acute kidney injury (AKI) is a growing medical problem associated with mortality and morbidity. AKI has a reported incidence of 22% in hospitalized patients worldwide [1]. Several studies investigating risk factors for AKI have shown that age, gender, race, basic renal function, and underlying diseases are associated with the development of AKI [2]. Studies investigating AKI-dependent mortality rate have reported a wide range of mortality, 23% to 75% [3-5].

Albumin is an acute phase protein synthesized by the liver. It has many physiological functions including protection of osmotic pressure, binding of various compounds and ensuring plasma antioxidant activity [6,7].

Hypoalbuminemia is considered not only as an indication of inflammation and malnutrition but also as a risk factor for AKI development and mortality in critically ill patients [1]. Several studies have reported that hypoalbuminemia is associated with mortality in various patient groups such as patients with acute coronary syndrome, chronic kidney disease, AKI, cancer, and hip fracture [8,9]. Hypoalbuminemia has been associated with short-term mortality, the duration of hospital stays, and increased complications [6].

Renal function is currently best assessed by eGFR as serum creatinine is an unreliable marker of kidney function [10].

Hyperlactatemia, which is mostly described and investigated in critically ill patients, is caused by anaerobic glycolysis caused by tissue hypoxia, increased aerobic glycolysis or decreased clearance [11]. Hyperlactatemia is a risk classification tool in septic patients because high lactate levels are highly correlated with in-hospital mortality [12]. Hyperlactatemia have been found to be associated with increased mortality in critically ill patients with sepsis, acute heart failure or cardiac arrest, acute liver failure, AKI, trauma and surgical patients[11,13,14]. It has been shown that the initial serum lactate level can be used as an indicator of the mortality of septic patients in the emergency department [12]. In the 'Surviving Sepsis Campaign:International Guidelines for Management of Sepsis and Septic Shock: 2016', the 4 mmol/L threshold for serum lactate level was reported to be associated with poor outcome [15].

Kawarazaki et al. have associated the elevated serum lactate and low serum albumin values in Intensive care unit (ICU) patients with AKI to 48-hour mortality [16].

We think that the effects of age, sex, estimated glomerular filtration rate (eGFR), albumin and lactate on 30-day and total mortality in patients who are hospitalized in Level 3 ICU due to AKI are not similar to those who do not develop AKI.

The aim of this study was to assess the effect of age, gender, eGFR, albumin and lactate on mortality on critically ill patients admitted to ICU due to AKI.

Methods

This prospective observational study was performed in Level 3 ICU of the anesthesiology and reanimation department of our hospital. The study included 54 critically ill patients over the age of 18, who were admitted to our ICU with the diagnosis of AKI between January 2018 and December 2018. Written and signed informed consent forms were obtained from the relatives of the patients included in the study.

Exclusion criteria:

- Patients under 18 years of age
- Patients who do not grant research permission,
- Patients with Chronic kidney disease (CKD)
- Patients with End stage renal disease (ESRD)

Our study protocol was approved by the ethics committee and the study was carried out in accordance with the 2008 Helsinki Declaration criteria.

Data were collected from the institutional electronic medical record system and patient files. Demographic information, inpatients' serum albumin, eGFR and lactate levels in the first 24 hours of admission to the ICU, length of stay in ICU and mortality were recorded. Serum albumin levels were analyzed using a bromocresol green dye-binding method (ROCHE c702-502 modular analyzer). The estimated glomerular filtration rate (eGFR; mL/min/1.73 m^2) was calculated from serum creatinine concentrations using the Chronic Kidney Disease Epidemiology Collaboration formula. Creatinine was analyzed by kinetic colorimetric assay (Jaffe) method (ROCHE c702-502 with modular analyzer). Lactate levels were analysed using an amperometric method (SIEMENS Rapid Point 500 blood gas analyzer). The effects of age, gender, eGFR, albumin and lactate levels on mortality were investigated. Patients were divided into two groups as those who did not develop mortality (Group 1) and those who developed (Group 2). Both groups were compared in terms of age, gender, eGFR, albumin and lactate levels. In addition, patients were divided into two groups according to both albumin levels (<2.5 g/dL and ≥2.5 g/dL) and lactate levels (<2 mmol/L and ≥2 mmol/L) and examined in terms of 30-day mortality.

Statistical Analysis

SPSS 16.0 for Windows program was used for statistical analysis. Statistically, numerical data was expressed in the form of mean and standard deviation while categorical data was expressed in the form of frequency and percentage. The comparison of categorical data obtained from groups was performed by chi-square test and the results were expressed as n (%). Kolmogorov-Smirnov test was used to determine whether non-categorical data follows the normal distribution. Student-t-test was used to evaluate the data following the normal distribution and the results were expressed as mean ± SD. The Mann-Whitney U test was used to compare data that did not follow the normal distribution, and the results were expressed as median ± minimum-maximum. p < 0.05 was considered significant in all comparisons.

Results

54 patients who were admitted to the intensive care unit with AKI diagnosis were included in the study. The patient's mean age was 63.95 ± 18.23, mean eGFR value was 36.8 ± 25.6 ml/min/1.73 m^2, mean albumin level was 2.68 ± 0.68 g/dL, mean lactate level was 3.54 ± 2.9 mmol/L, and mean length of stay in ICU duration in the intensive care unit was 30.6 ± 47.34 days. The patients' total mortality was 68.5% (37 patients) **(Table 1)**.

Table 1 Baseline characteristics of the study patients.

Variables	Mean ± SD[a]
Age	63.95 ± 18.23
eGFR[b] (m^l/min/1.73 m^2)	36.8 ± 25.6
Albumin (g/dL)	2.68 ± 0.68
Lactate (mmol/L)	3.54 ± 2.9
LOS (ICU)[c] (day)	30.6 ± 47.34
Variables	**n (%)**
Gender	
Female	30 (55.6)
Male	24 (44.4)
Mortality	
-	17 (31.5)
+	37 (68.5)

a: Standard Deviation; b: Estimated Glomerular Filtration Rate; c: Length of Stay in Intensive Care Unit

There was no statistically significant difference between the two groups in terms of age, sex, eGFR, albumin and lactate levels (p-values, respectively: 0.13; 0.39; 0.32; 0.83; 0.52) **(Table 2)**.

The patients were divided into two groups according to both albumin levels (<2.5 g/dL and ≥2.5 g/dL) and lactate levels (<2 mmol/L and ≥2 mmol/L) and examined in terms of 30-day

mortality. There was no statistically significant difference between the groups in terms of 30-day mortality (p-values: 0.625; 0.127) **(Table 3).**

Table 2 The effect of age, gender, eGFR1, albumin and lactate on mortality.

Variables	Group 1	Group 2	p-value
Age	54.05 ± 25.08	67.08 ± 15.61	0.13
eGFR[a] (ml/min/1.73 m^2)	48.05 ± 24.39	40.43 ± 26.65	0.32
Albumin (g/dL)	2.68 ± 0.84	2.63 ± 0.65	0.83
Lactate (mmol/L)	2.94 ± 1.87	4.6 ± 3.19	0.52
Variables	**n (%)**	**n (%)**	**p-value**
Gender			
Female	8 (47.1)	22 (59.5)	0.39
Male	9 (52.9)	15 (40.5)	
Total	17 (100)	37 (100)	
eGFR1: Estimated Glomerular Filtration Rate			

Table 3 The effect of albumin and lactate on 30-day mortality.

Variables	Survive	Mortal	p-Value
	n (%)	n (%)	
Albumin (g/dL)			0.625
<2.5	9(40.9)	11(34.4)	
≥2.5	13(59.1)	21(65.6)	
Lactate (mmol/L)			
<2	4(18.2)	12(37.5)	0.127
≥2	18(81.8)	20(62.5)	
Total	22(100)	32(100)	

Discussion

A wide range of mortality rates of 23% to 75% has been reported in AKI-related mortality studies [3-5]. The variation in mortality rates observed in these studies is related to differences in study populations, reasons for ICU admission and underlying diseases, and non-standard criteria for diagnosing AKI [17]. Also, as the number of organ failure increases, mortality increases as well [5]. The reason for our high mortality rate may be that our patient population consists of critically ill patients.

In the literature, there are studies reporting that mortality increases as age increases in AKI patients [18-20] and also studies reporting that age has no effect on mortality [17]. In our study, we concluded that age has no effect on mortality in patients with AKI. In different studies investigating mortality in patients with AKI, different results have been reported about the effect of gender on mortality. In some studies, mortality has been reported to be more common in male patients

[5,18,21,22], while in some other studies, it has been reported to be more common in women [23,24]. In a similar study, Saxena et al. [17] reported that gender did not affect mortality in patients with AKI. In our study, we found that there was no gender difference.

Albumin is a protein synthesized by the liver. Serum albumin level is controlled by albumin synthesis, albumin distribution, fractional catabolic rate and loss of albumin [1]. Albumin levels reflect nutritional status, organic function or patients' previous physical activity [25]. Albumin appears to play an important role in maintaining renal function, preserving renal perfusion and protecting kidneys from toxic agents [1,2].

Hypoalbuminemia may be a combined result of inflammation, malnutrition, oxidative stress, colloid oncotic pressure and liver dysfunction [1]. Previous studies have reported a correlation between hypoalbuminemia and mortality in critically ill patients, patients in emergency departments and patients with cancer, stroke, myocardial infarction or hip fracture [6,26-30]. Jellinge et al. [6] found that hypoalbuminemia was associated with 30-day mortality and serum albumin level was a good predictor of mortality. Albumin is a binding protein. Especially in the elderly, the concentration of unbound drugs in the circulation increases, and this increased bioavailability may have adverse effects on hypoalbuminemia. In this study, hypoalbuminemia as a strong predictor of 30-day mortality is linked to this condition [6]. Hypoalbuminemia is an independent risk factor for mortality in patients with AKI [1,2,6,25,30,31]. In their study, Yu et al. [1] found that patients with hypoalbuminemia had a higher 30-day, 90-day and 1-year mortality rate than patients with normal albumin levels. In addition, in this study, it was shown that mortality is highest when hypoalbuminemia and AKI coexist. In patients with AKI, the protection of renal functions decreases due to low albumin levels, which makes patients more susceptible to AKI. AKI may worsen with inflammation and hypoalbuminemia caused by high catabolism. These results may be a potential explanation of the synergistic interaction between hypoalbuminemia and AKI [1]. In their study of AKI patients, Thongprayoon et al. [3] found that patients with serum albumin levels >4 g/dL had the lowest mortality. AKI was found to be less severe and had lower mortality rates in patients with serum albumin level >4.5 g/dL than patients with serum albumin levels < 2.4 g/dL [3].

The level of serum lactate is closely related to tissue hypoxia and anaerobic metabolism. In addition, mechanisms other than tissue hypoxia, such as mitochondrial dysfunction, pyruvate dehydrogenase deficiency, drugs and intoxications, may also explain hyperlactatemia [13]. There are many studies investigating the effect of serum lactate levels on mortality in different patient groups. In 2 studies on trauma patients, increased mortality was reported in patients with lactate >2.5 mmol/L [32,33]. When we look at the studies performed in patients hospitalized for hip fracture, Jonsson et al. [34] found no correlation between the initial plasma lactate concentration and 30-day mortality or morbidity in contrast to previous studies [35,36].

Recently, in many studies on sepsis patients, it has been suggested that lactate is not an independent predictor of prognosis [37,38]. The basal lactate concentration in an unstressed individual is 1.0 ± 0.5 mmol/L. Lactate level in critically ill patients is considered to be within the reference range of ≤ 2 mmol/L and therefore lactate level >2 mmol/L is considered as hyperlactatemia. High lactate is frequently seen in critically ill patients and is mainly a result of insufficient oxygen delivery associated with significant cardiopulmonary compromise, as seen in cardiogenic, hypovolemic and septic shock [14]. The Surviving Sepsis Campaign Guideline proposed lactate > 4 mmol/L (even if there is no hypotension) as one of the criteria for initiating early-targeted treatment [15]. In many studies on critically ill patients, it has been reported that hyperlactatemia is an independent predictor of both hospital and ICU mortality [14,15,39,40]. In a recent study, it was suggested that lactate increase (lactate >4.0 mmol/L) was not associated with mortality in initial evaluations in the emergency department [41].

In our study, patients were divided into two groups as those who did not develop mortality (Group 1) and those who developed (Group 2). There was no statistically significant difference between the two groups in terms of albumin and lactate levels (p-values, respectively: 0.83; 0.52). In addition, patients were divided into groups according to albumin (<2.5 g/dL and ≥2.5 g/dL) and lactate (<2 mmol/L and ≥2 mmol/L) levels and examined in terms of 30-day mortality. There was no statistically significant difference between the groups in terms of 30-day mortality (p-values, respectively: 0.625; 0.127).

Conclusion and Limitations

According to the findings of our study, we concluded that age, gender, eGFR, albumin and lactate levels did not affect 30-day and total mortality in our patients who were hospitalized in our intensive care unit with AKI diagnosis, and that albumin and lactate levels during admission were not a predictor of mortality in this patient group.

Our study has some limitations. Our study is single-centered, and our study population is small. Since our patients were critically ill patients, they could be standardized by scoring systems such as Apache 2. These limitations reduce the generalizability of our findings.

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