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Evaluation of C - reactive Protein, Albumin and the C - reactive Protein/Albumin Ratio as Prognostic Markers in Trauma Patients Admitted to Intensive Care Unit

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Authors' contributions

This work was carried out in collaboration between all authors. Author FS designed the study, wrote the protocol and wrote the first draft of the manuscript. Author MRP managed the literature searches and analyses of the study performed the spectroscopy analysis. Author MR and other authors managed the experimental process. All authors read and approved the final manuscript.

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ABSTRACT

Background and Objectives: Deaths, injuries and disabilities resulting from Road traffic injuries (RTIs) are considered as the major concerns in public health and they are the second highest cause of mortality in Iran. Traumatic injury accounts for approximately one of six hospital admissions and almost 20% of the cases include admission to intensive care units (ICU). Laboratory diagnostic tests can help predict the clinical outcome of these patients. This study aimed to determine the ability of C-reactive protein (CRP), albumin and the CRP/albumin ratio to predict the outcome of

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trauma patients admitted to ICU.
Methods: We evaluated 76 patients with traumatic injury admitted to ICU for more than 48 h. CRP, albumin and the CRP/albumin ratio were measured on day one and three after admission to ICU and analysed with regard to predictability of mortality and survival.
Results: There was a significant association between CRP, albumin and the CRP/albumin ratio on the first and the third day upon admission (t-test, *p=0.03*). The mortality rate was correlated with an increase in the CRP/albumin ratio, and patients with a ratio of 4.01–9 had a poorer clinical outcome in comparison with other patients. High mortality and a poor outcome were seen in patients with a CRP concentration more than 12 mg/dl and an albumin level less than 3 g/dl in our study.
Conclusion: Albumin, CRP and the CRP/albumin ratio are simple and reliable prognostic markers in ICU patients with traumatic injury.

Keywords: ICU; prognostic marker; CRP/albumin ratio.

1. INTRODUCTION

Motor vehicle collision is the leading cause of traumatic death worldwide and accounts for 45% of all hospital admissions attributed to trauma [1]. The World Health Organization (WHO) estimated that more than 1.3 million people are killed in motor vehicle collisions every year with up to 50 million non-fatal injuries [2]. The mortality rate for males is three times higher than for females and more than 50% of the mortality caused by motor vehicle collisions occurs in adults aged 15–44 years [3]. The global economic cost of road traffic injuries, including medical treatment and loss of productivity, is estimated to US$ 518 billion per annum. For each country, this typically represents between 1—3% of the gross national product per annum [4].

However, the pattern of road traffic accidents and deaths differs in developed and developing countries and therefore require specific approaches and strategies [5,6]. Deaths caused by road traffic accidents should be of particular concern in Iran, where in 2007, 27,567 people, mainly young adults and children, lost their lives and 276,762 were injured [6,7]. Hence, reducing mortality due to road traffic accidents should be among the most important priorities for the government and health care system in particular [8]. Traumatic injury accounts for approximately one of six hospital admissions, and almost 20% of the cases include admission to intensive care units (ICU) [9]. Therefore crucial for intensivists to be familiar with the care of trauma patients [10]; however, many of the principles used to treat other critically ill patients apply. In addition to therapeutic procedures, laboratory diagnostic tests can predict the outcome of critically ill patients [11]. Multiple biochemical markers are associated with the outcome of critical illness, including C-reactive protein (CRP), procalcitonin, some cytokines (e.g. interleukin 6 (IL-6) and tumour necrosis factor α (TNF-α) [12,13]. CRP, an acute-phase protein, markedly increases upon infection or inflammation. Numerous studies have demonstrated an increase of this protein in critically ill patients with multiple organ dysfunction [14]. Serum albumin, commonly measured in the laboratory, has been proposed as a reliable predictor of the outcome in critically ill patients with various diseases [15]. In additionto serum CRP and albumin level, many studies demonstrated a correlation between the CRP/albumin ratio with the severity of organ dysfunction and clinical outcome [16]. The objective of this study was to evaluate CRP, albumin and the CRP/albumin ratio as biochemical markers of mortality and clinical outcome in trauma patients admitted to ICU, hypothesising that the CRP/albumin index would be of prognostic value for such patients.

2. MATERIALS AND METHODS

2.1 Study Design

During 12 months (from March 2012 to February 2013), we studied 86 traumatic injury patients admitted to ICU for >48 h. All patients were admitted to ICU within 24 h of injury. Collected clinical information such as age, sex and chronic diseases including diabetes mellitus and cardiac, liver, renal and malignant diseases. Patients were excluded if they were younger than 16 years, had been transferred or discharged from another hospital, were suffering from immunosuppressive disease, including human immunodeficiency virus infection, had active pulmonary disease, or were receiving blood or blood products like fresh frozen plasma, or had been given intravenous albumin. Ten patients died during the course of the study and were excluded; thus, 76 patients were evaluated. In

addition to the previous criteria, Sequential Organ Failure Assessment (SOFA) scores were calculated on admission and throughout the study, and only patients with a SOFA score of 6–8 were included in the study [17]. All patients were evaluated on the first and third day after admission in terms of biochemical parameter status.

This research has research ethic code (ajums.REC.1393.21) from research ethic center of Ahvaz Jundishapur University of Medical Sciences.

2.2 Blood Collection and Processing

Blood samples were collected on day one and three after admission. Samples were transported to the hospital laboratory where serum was extracted and stored at –80℃. Serum albumin and CRP levels were measured using an immunochemistry analyser (Hitachi, Tokyo, Japan). Serum CRP was quantified by turbidimetric method (Roche Diagnostics, Mannheim, Germany) and albumin by colorimetry using bromocresol green. Concentrations were expressed as mg/L and g/dl, respectively.

2.3 CRP/Albumin Ratio

The CRP/albumin ratio provides a prediction of the inflammatory prognosis of the patient and was calculated by dividing the serum CRP by the albumin. The ratio was calculated for both days (first and third day after admission) as described previously.

2.4 Statistical Analysis

Serum CRP, albumin, the CRP/albumin ratio and patient outcome were the primary variables. Categorical variables were analysed using the Chi square test or Fisher's exact test, and continuous variables were analysed using the Student's t-test. A p-value<0.05 was considered statistically significant. Statistical comparison for prognosis was calculated between two CRP/albumin ratios. All statistical tests were performed using SPSS 19.0 for Windows (Chicago, Illinois, USA).

3. RESULTS

A total of 86 patients from the general ICU were included. Ten patients died during the study and were excluded; therefore, 76 patients were included in the evaluation. Mean (SD) age was 39 (21.53) years; 61 patients (80.2%) were males.

3.1 CRP, Albumin and the Crp/Albumin Ratio

Plasma concentration of CRP, albumin and their ratio for the both days were calculated and compared. Mean (SD) CRP1, Alb1 (first day of admission) and CRP2, Alb2 (third day of admission) are presented in Table 1. A significant association was reported between CRP1, CRP2 and also Alb1 and Alb2 via *t test* (p=0.03). Comparison of mean values of CRP, albumin and the CRP/albumin ratio in first and third day are presented in Fig. 1. As shown in Fig. 2, the highest mortality was reported on the third day, and the CRP concentration of these patients ranged 12–18 mg/dl. A significant association existed between the CRP/albumin ratio for both days (p=0.03). Mean CRP concentration was significantly increased on the third day (10.92) compared to the first day (9.5). In contrast, the mean albumin level was significantly decreased on the third day (3.11) compared with the first day (3.32). The difference between CRP/albumin 1 (2.98) and CRP/albumin 2 (3.68) was significant (p=0.03).

We categorised patients in three clusters to evaluate these data in terms of outcome prediction. As shown in the Table 2, increase in mortality rate was correlated with an increase in the CRP/albumin ratio. The mortality rate/percentage increase from first cluster (1/6.7%) to third cluster (11/73.3%). Hence, patients in third cluster (ratio: 40.1–9) had poorer outcome in comparison with other patients.

Table 1. Serum CRP and albumin levels on day one and three after admission to ICU

Variable	N	Minimum	Maximum	Mean	Std. Deviation	*P value*
CRP1	76	0.75	16	9.50	5.873	0.03
CRP2	76	1.2	18	10.92	5.689	
Alb1	76	2.2	5.6	3.328	.5712	0.03
Alb2	76	2.0	4.7	3.111	.5773	
Total	76					

CRP1, Alb1: CRP and albumin level in first day; CRP2, Alb2: CRP and albumin level in third day

4. DISCUSSION

Trauma is one of the main causes of ICU admissions and correlates with high morbidity and mortality rates, particularly in Iran. Most studies have focused on prognostic outcome in critically ill patients using biomarkers and a scoring system [18]. Biochemical and inflammatory markers with scoring systems enable critical care physicians to measure illness severity in ICU patients accurately and reliably. Several studies demonstrated that SOFA score assessment during ICU admission is a good indicator of prognosis in critically ill ICU patients [19].

Table 2. CRP/albumin ratio categories and patients' outcomes

Cluster (ratio amount)	Outcome		
	Survivor	Deceased	Total
1.00 (0.01-2)	22	1	23
	36.1%	6.7%	30.3%
2.00 (2.01-4)	24	3	27
	39.3%	20.0%	35.5%
3.00 (4.01-9)	15	11	26
	24.6%	73.3%	34.2%
Total	61	15	76
	100%	100%	100%

Lobo et al. [17] reported that an increase in SOFA score during the first 48 h in ICU predicts a mortality rate of at least 50%, while a decreasing SOFA score is associated with a decrease in mortality rates from 50 to 27%. In order to analyse the primary variables selected in the study, it was necessary to keep SOFA scores constant; therefore, only patients scoring between 6 and 8 were included in this study.

Based on our data, a significant association between CRP increase and albumin decrease on the first and third day of ICU admission could be identified. Increased serum CRP represents an independent predictor of poor clinical prognosis and a low survival rate of these patients. Previous studies have reported CRP levels to be a prognostic factor in different situations [20]. In our study, patients with a CRP level higher than 12 mg/dl had a poor clinical outcome. Sung et al. [21] reported that CRP levels higher than 10 mg/dl were predictive of a poor clinical outcome after hematopoietic stem cell transplantation in children. Lobo et al. [17] reported that CRP levels higher than 10 mg/dl were associated with a mortality rate of 60.9% in critically ill patients. In contrast, Silvestre et al. [18] reported that no differences in CRP levels at ICU discharge could be found among surviving and deceased surgical and medical patients. Therefore, at ICU discharge serum CRP concentration was a poor marker of post-ICU prognosis. In addition to CRP, serum albumin may be an important short and long term marker for prognosis [18]. Serum albumin is a negative acute phase protein; therefore, CRP and serum albumin levels should diverge during an inflammatory response.

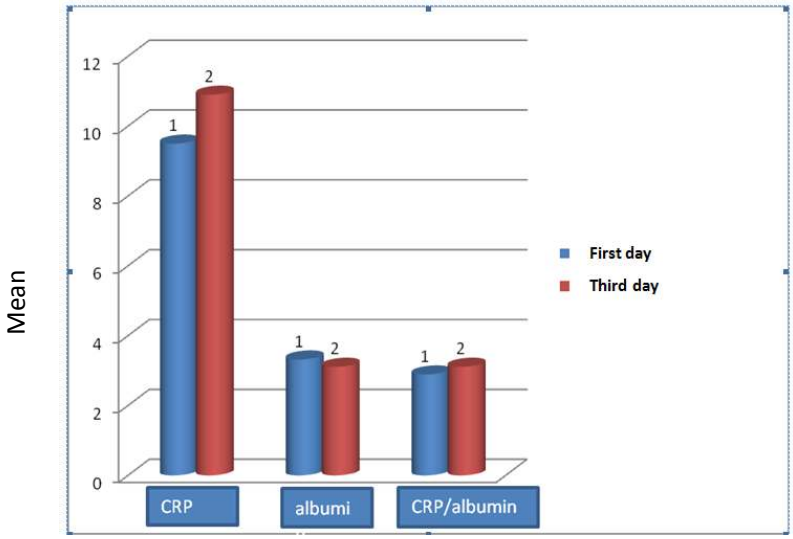

Fig. 1. Mean comparison of CRP, albumin and CRP/albumin ratio level in first and third day after admission

CRP1, albumin1 and CRP/albumin1: data from first day after admission; CRP2, albumin2 and CRP/albumin2: data from third day after admission

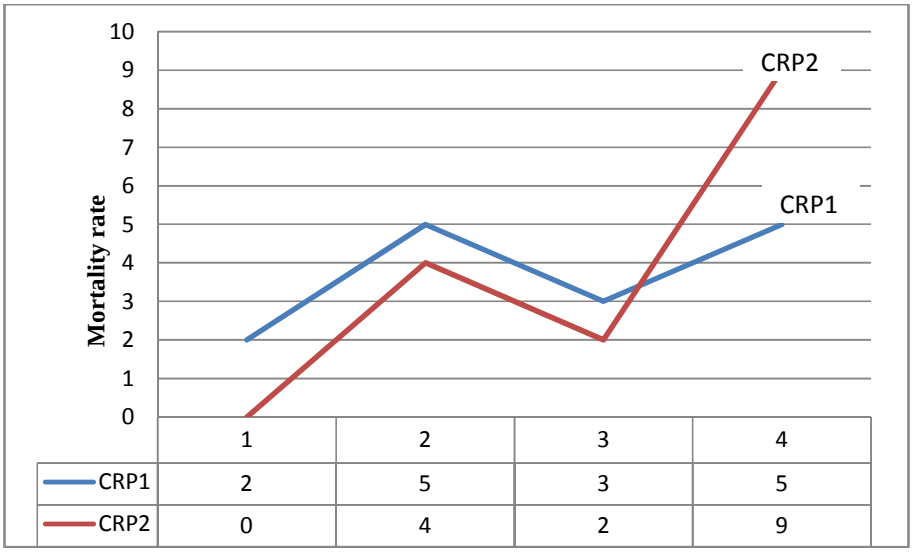

Fig. 2. Mortality rate on the first and third day of ICU admission upon CRP concentration 1; 1-5 mg/dl, 2; 5.01-6 mg/dl, 3; 6.01-12 mg/dl, 4; 12.01-18 mg/dl

Albumin levels after critical illness were also prognostic. There is a paucity of data evaluating serum albumin on admission as a predictor of outcome in adult trauma patients. Several studies have focused on albumin level on admission, during critical illness and in clinical prognosis in different entities [19].

Al-subaie et al. [20] found that ICU re-admission unexpectedly had a high correlation with hypoalbuminemia. In another study, Sung et al. [21] reported that a serum albumin level of <2.6 g/dl was a significant independent predictor of morbidity and mortality in trauma patients. The combination of increased age and low albumin level was most predictive of infection and mortality. Yap et al. [22] showed that serum albumin had low sensitivity and specificity for predicting hospital mortality; however, medical patients had higher admission albumin levels than surgical patients.

In a systemic review, Gupta et al. [23] reported that pretreatment serum albumin levels provide useful prognostic significance in cancer patients. Accordingly, serum albumin levels could be used in clinical trials to better define the baseline risk in cancer patients.

The use of the CRP/albumin ratio would provide a variable capable of merging the information provided by CRP and albumin into an index that correlated positively with infection, a higher ratio indicating higher inflammatory status.

Based on our findings, there was a significant correlation between an increase in CRP/albumin ratio and poor prognosis. Notably, the highest mortality was reported in patients who had the highest CRP/albumin ratio.

Ranzani *et al.* also reported that CRP and the CRP/albumin ratio were associated with a poor outcome on ICU admission and discharge [16]. They hypothesised that the CRP/albumin ratio could be more consistent than CRP alone. Some authors employed other ratios such as CRP/prealbumin as a severity index in comparison with CRP/albumin [24]. CRP and albumin may not be routinely monitored in all ICU patients; therefore, the validity of these tests may be dismissed in clinical studies. Our study indicated the importance of these simple but valuable tests as prognostic marker in trauma patients.

Limitations of this study are due to the small patient sample size, the control group, and ROC curve analysis. Thus, future clinical studies with larger sample size and ROC curve analysis with sensitivity and specificity of the serum CRP and albumin are recommended.

5. CONCLUSIONS

Accurate prognostic markers for patient survival in ICU are important and helpful to guide clinical decision making. CRP, albumin and the CRP/albumin ratio can be valuable markers in critically ill patients with trauma.

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CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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