Albumin Levels as Prognostic Markers in ICU Mortality

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ABSTRACT

Objective: To evaluate the association of serum albumin levels with short-term mortality in ICU patients, including ICU and 28-day mortality.

Study Design: Observational study.

Place and Duration of the Study: Intensive Care Unit, Izmir Tepecik Training and Research Hospital, Izmir, Turkiye, from January to July 2023.

Methodology: The study included 60 patients aged above 18 years who had stayed in the ICU for at least two days. Exclusion criteria were massive transfusion within the last 48 hours, septic shock with fluid resuscitation, liver failure at admission, end-stage renal disease, proteinuria, and BMI <18.5. The primary outcome included ICU mortality and 28-day mortality. Normality was assessed using the Shapiro-Wilk's test. A comparison between the quantitative data of the two studied groups was made with the independent samples t-test for normal distribution and for skewed data using the Mann-Whitney U test. A p-value of <0.05 was considered statistically significant.

Results: There was a significant association of both APACHE-II scores with ICU and 28-day mortality besides age and serum albumin level. In the binary logistic regression analysis, a statistically significant correlation was found between the albumin level at 48-hour and 28-day mortality (p <0.001).

Conclusion: Serum albumin levels at 48 hours post-admission were independent predictors of 28-day mortality.

Key Words: *Albumin, Critical care, Mortality*.

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INTRODUCTION

Albumin is the most prevalent protein found in plasma.[1] It performs a function by which it modulates microvascular permeability, maintains oncotic pressure, and carries out buffering and other physiological functions.[2] Serum albumin levels determine the nutritional status and provide valuable information in acute and chronic states of malnutrition.[3] Albumin binds some medicines in circulation, so their half-lives and effective doses are altered.[4] Albumin levels are highly important in the intensive care setting for the reasons mentioned above. Additionally, previous studies in the literature have also investigated the relationship between albumin levels and intensive care mortality.[5] Albumin decrease 48-hour after the hospital admission may exhibit the severity of disease and the value of prediction of mortality in critical disease settings such as the acute phase of infections among other stress factors.

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The objective of this study was to compare ICU mortality and 28-day mortality with albumin levels at ICU admission and albumin levels 48-hour post-admission. Establishing a relationship between serum albumin levels and mortality can be beneficial, as serum albumin is an inexpensive and readily accessible test.

METHODOLOGY

Ethical approval was obtained from the Non-Interventional Research Ethics Committee (No: 2023/06-11) on July 13 2023. The study included patients who were treated between January and July 2023. All the patients who were included in the study were over 18 years and spent at least two days in the ICU.

Exclusion criteria were massive transfusion in the first 48 hours, defined as requiring ≥10 units of red blood cell concentrates (RBCs) within 24 hours, or needing transfusion of half the blood volume within 4 hours, or experiencing blood loss at a rate of more than 150 mL per minute.[6] Other criteria were septic shock with fluid resuscitation, known or diagnosed liver failure on admission, end-stage renal disease, proteinuria in complete urine tests, and BMI less than 18.5kg/m^2.

The invalidity of hypoalbuminaemia had been evaluated by the ROC curve analysis. The two primary outcome measures analysed were the ICU mortality and the 28-day mortality. Secondary outcome measures included transferring patients to another ICU or other hospitals.

Based on the referenced study, the odds ratio (OR) for patients with moderate and severe hypoalbuminaemia was calculated as 22. Using this, a logistic Wald test was conducted, and a sample size of 68 was determined.[7] The national intensive care mortality rate was determined to be approximately 40% and was used in the formula.[8] The patients' data were recorded retrospectively in a digital format. The analyses were performed using a software programme, SPSS for Windows, version 26. Normality was assessed using the Shapiro-Wilk's test. Values of categorical data were analysed by the descriptions in frequencies and percentages, along with their 95% confidence interval. Values for continuous data were reported as mean and standard deviation for normally distributed data, and median and interquartile range for non-normally distributed data. A comparison between the quantitative data of the two studied groups was made for data with normal distribution using the independent samples t-test, and for data with non-normal distribution using the Mann–Whitney U test. A p-value of <0.05 was considered statistically significant.

Binary logistic regression based on multivariate analysis was applied, considering it measures how the tested risk factors may have effects. The model included age, APACHE II score, and albumin levels taken at admission and 48-hour. The ROC curves were plotted to the discriminatory threshold level of the serum albumin level corresponding to that best-predicted ICU mortality, optimised concerning the Youden's index (Youden's index = Sensitivity + Specificity − 1), combining sensitivity and specificity.[9,10]

RESULTS

The mean age was 60.65 (50.5 – 73) years, which was significantly associated with the mortality in the ICU ($p = 0.026$) and the 28-day mortality ($p = 0.018$). APACHE-II score was 14.78 ± 7.504 in relation to ICU mortality ($p = 0.010$) and 28-day mortality ($p = 0.039$). The level of albumin on admission (2.97 ± 0.64 g/dL) was significant with both ICU ($p <0.001$) and hospital ($p <0.001$) mortality. Other information is shown in Table I.

The area under the ROC curve using the Youden's index presented the following: The optimal albumin value for 28-day mortality was 2.95 g/dL, with a sensitivity of 80% and a specificity of 72.5%. For ICU mortality, the same value (2.95 g/dL) showed a sensitivity of 73.1% and a specificity of 76.5%. When evaluating ICU mortality using 48-hour albumin levels, the optimal value was 2.85 g/dL, with a sensitivity of 73.1% and a specificity of 79.4%. Similarly, for 28-day mortality, the optimal value at 48-hour albumin levels was 2.85 g/dL, with a sensitivity of 85% and a specificity of 77.5%. ROC curves are presented in Figure 1.

Age, APACHE II score, and albumin levels at admission and at 48 hours, which were found statistically significant using Student's t-test and Mann-Whitney tests, were evaluated in a binary logistic regression model. The results of the model are presented in Table II.

The OR for age, APACHE-II score, albumin at admission, and albumin levels at 48 hours were evaluated to determine their association with mortality outcomes in the ICU setting. The OR for age was 1.033 (95% CI: 0.985 - 1.082), with a p-value of 0.179. Age is not a significant predictor of mortality in this model. The OR for the APACHE-II score was 1.036 (95% CI: 0.942 - 1.140) with a p-value of 0.470. APACHE-II scores are not statistically significant predictors of mortality within this dataset. The OR for albumin levels at admission was 6.1 (95% CI: 0.257 - 144.761) with a p-value of 0.263. Albumin at admission is not a statistically significant predictor. Notably, albumin levels measured at 48 hours post-admission showed an OR of 0.010 (95% CI: 0.000 - 0.314) with a p-value of 0.009. Albumin levels at 48 hours are a statistically significant predictor of mortality, highlighting the prognostic value of albumin after the initial ICU admission. Specifically, a decrease in albumin levels at 48-hour by 1 g/dL was associated with an approximately 90% increase in the odds of mortality, underscoring the critical role of monitoring albumin levels as part of patient management in the ICU.

Table I: Patient characteristics at admission and outcome.

Parameters	General	Died in ICU		p-value	28-day mortality n (%)		p-value
		Yes	No		Yes	No	
All	60	26 (43.3%)	34 (53.3%)		20 (33.3%)	40 (66.7%)	
Age median (IQR) (years)[b]	62 (50.5 – 73)	70.5 (56.25 – 77.25)	59 (48 – 68)	0.026	71 (61.00 - 77.75)	59 (48.00 - 68.75)	0.018
APACHE-II[b]	14.78 ± 7.504	17.58 ± 8.631	11 (8 – 18)	0.010	17.30 ± 8.543	11.50 (9-18)	0.039
Males (n)[a]	36	17 (47%)	19 (53%)	0.57	13 (36%)	23 (64%)	0.78
Females[a] (n)	24	9 (37%)	15 (63%)		7 (29%)	17 (71%)	
Sodium median (IQR) (mEq/dL)[b]	137.5 (135.25 – 139)	138 (135.75 – 139)	137 (135 - 139)	0.409	138 (135.25 - 139.00)	137 (135.25 - 139.00)	0.538
Potassium[c] (mEq/dL)	4.02 ± 0.63	3.99 ± 0.78	4.04 ± 0.51	0.784	4.16 ± 0.76	3.95 ± 0.56	0.249
ALT median (IQR) (IU/L)[b]	24 (15.25 – 60.5)	25.5 (15.75 – 79.5)	21.5 (15 – 35.75)	0.429	23 (12.75 - 66.75)	24 (17.25 - 42.75)	0.451
AST median (IQR) (IU/L)[b]	37 (19 – 101.75)	37 (20.5 – 191.5)	37 (17.75 – 60.75)	0.303	32 (37.50 - 198.50)	37.5 (18.25 - 78.75)	0.730
Creatinine median (IQR) (mg/dL)[b]	1.1 (0.9 – 1.9)	1.35 (0.9 – 2.575)	1 (0.7 – 1.5)	0.103	1.35 (1.350 - 2.050)	1.05 (0.700 - 1.500)	0.172
Albumin[c] (g/dL)	2.97 ± 0.64	2.63 ± 0.59	3.22 ± 0.56	<0.001	2.54 ± 0.52	3.188 ± 0.59	<0.001
Albumin at*48 hours median[c]	2.9 ± 0.64	2.4 (2.075 – 2.925)	3.135 ± 0.52	<0.001	2.345 ± 0.52	3.125 ± 0.52	<0.001

The Shapiro-Wilk's test was used to assess normality ($p >0.05$ normal distribution). [a]The p-value for categorical variables was calculated using the Chi-square test. [b]One of the subgroups did not show normal distribution, and therefore the Mann-Whitney test was used to determine the p-value. [c]Subgroups followed a normal distribution, the independent samples t-test was used to determine the p-value.

Table II: Binary logistic analyses for the studied variables.*

Factor	OR (%95 CI)	p-value
Age	1.033 (0.985 - 1.082)	0.179
APACHE-II	1.036 (0.942 - 1.140)	0.470
Albumin at admission	6.1 (0.257 - 144.761)	0.263
Albumin levels at 48-hour	0.010 (0.000 - 0.314)	0.009

**Age, APACHE II score, and albumin levels at admission and at 48-hour were evaluated in a binary logistic regression model.*

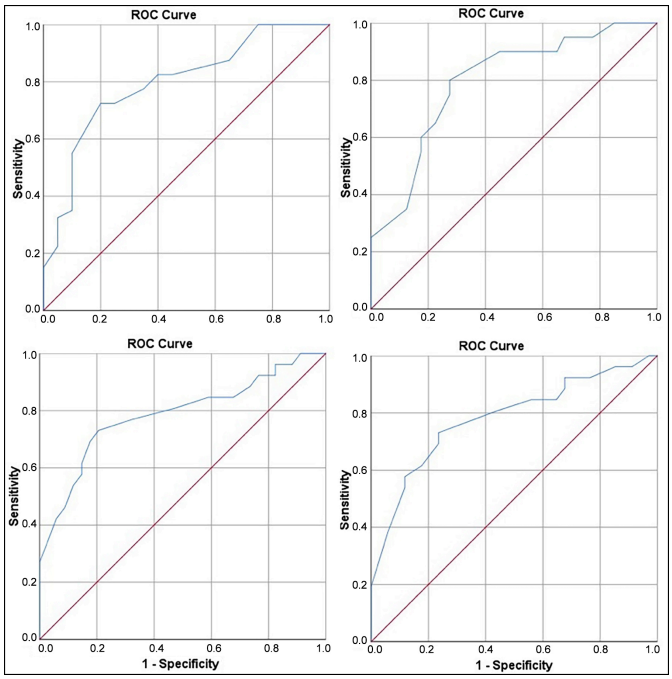

Figure 1: ROC Curves.

ROC curves: The top-left corner (AUC 0.79) shows the relationship between albumin levels at ICU admission and 28-day mortality. The top-right corner (AUC 0.78) illustrates the relationship between albumin levels at ICU admission and ICU mortality. The bottom-left corner (AUC 0.85) demonstrates the relationship between albumin levels at 48-hour and 28-day mortality. The bottom-right corner (AUC 0.78) indicates the relationship between albumin levels at 48-hour and ICU mortality.

DISCUSSION

Intensive care patients may experience a decrease in albumin levels due to malnutrition or metabolic stress. Studies in the literature indicate that low albumin levels can lead to prolonged ICU stays and increased complications. Another study in the literature found that each 1 g/dL decrease in albumin levels in ICU patients increased the likelihood of mortality by 1.37 times.[11]

The age of the patient was (median: 62, IQR 50.5 - 73), which is consistent with the literature.[7] Age was also identified as a risk factor for both ICU and 28-day mortality, in line with existing studies.[12] As expected, the APACHE-II scores predicted both ICU and 28-day mortality.[13-15] Sodium, potassium, ALT, and AST levels were not found to be significantly different. The exclusion of patients with advanced renal and liver failure might explain this finding.[10]

The main focus of the study, albumin, was measured at 2.97 ± 0.64 g/dL upon ICU admission. Admission albumin levels were found to be significant for both ICU mortality and 28-day mortality. This result is consistent with studies in the literature.[7,16-21] The optimal admission albumin value for determining ICU mortality was 2.95 g/dL. In the literature, the optimal admission albumin values ranged between 1.85 g/dL and 2.92 g/dL. The found value was close to the upper limit of this range. The albumin level at 48 hours was 2.9 ± 0.64 g/dL. This value was also significant for both ICU and 28-day mortality. A study found a relationship between albumin levels measured between days one and seven in ICU patients and mortality, with an albumin level of 2.57 g/dL on three days and 48-hour observed in patients who did not survive. Unlike this study, a research calculated mortality over the entire ICU stay rather than at 28 days. In this respect, the results of the present study are consistent with the literature.[11]

In the logistic regression analysis, the admission albumin level, age, and APACHE II scores were found to be statistically insignificant in explaining the model. However, the albumin level at 48 hours significantly explained 28-day mortality. It is particularly interesting that the admission albumin level was insufficient in explaining 28-day mortality, while the albumin level at 48 hours was significantly associated with 28-day mortality. The findings may be related to excessive fluid administration during the first days of ICU admission, warranting further analysis.[22]

The limitations of the study include its single-centre nature, small sample size, and retrospective design. Therefore, it remains unclear whether the decline in albumin at 48-hour is related to disease severity or fluid resuscitation. In the future, these limitations could be addressed through a prospective study design.

CONCLUSION

Serum albumin level at 48-hour post-admission was an independent predictor of 28-day mortality. From these findings, albumin may be used as a general prognostic marker in a critical care area. Further prospective studies should be conducted.

ETHICAL APPROVAL:

Ethical approval was granted by the Izmir Tepecik Education and Research Hospital, Non-Interventional Research Ethics Committee (No: 2023/06-11) on July 13, 2023.

PATIENTS' CONSENT:

Patient consent was waived as per the guidelines of the Non-Interventional Research Ethics Committee.

COMPETING INTEREST:

The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

YO: Designed the study and performed the data analysis.
HY: Contributed to data collection and manuscript preparation.
KR: Reviewed the final manuscript.

All authors approved the final version of the manuscript to be published.

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