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Research Article

The Association Between Albumin Level and Mortality in Patients Hospitalised in Internal Medicine Clinic, Large Patient Population

Ali Kaan Güren,[1] Refik Demirtunç[2]

[1]Department of Medical Oncology, Marmara University Pendik Training and Research Hospital, Istanbul, Türkiye
[2]Department of Internal Medicine, University of Health Sciences, Haydarpasa Numune Training and Research Hospital, Istanbul, Türkiye

Abstract

Objectives: Albumin, an essential structural protein, performs numerous critical functions throughout the body. Its serum level is low in several disorders that decrease production and increase consumption and loss. We investigated the relationship between serum albumin (SA) levels measured within 24 hours of hospitalization and in-hospital mortality, duration, and recurrent hospitalizations within one year in all Internal Medicine clinic patients, regardless of diagnosis or comorbidities.

Methods: The data of the patients were recorded retrospectively. Patients were divided into 4 groups according to SA level as severe hypoalbunemia (< 2.5 g/dl), mild hypoalbunemia (2.5-3.5 g/dl), normal albumin (3.5-4.5 g/dl) and hyperalbunemia (>4.5 g/dl). In-hospital mortality, duration of hospitalisation, recurrent hospitalisation and time to mortality were compared between the groups.

Results: A total of 2164 patients, 51% of whom were female, aged 66.15±18.05 years, participated in the study. Among the patients, 220 (10.2%) had severe hypoalbuminemia (Group 1), 1054 (48.7%) had mild hypoalbuminemia (Group 2), 863 (39.9%) had normal albumin (Group 3) and 27 (1.2%) had hyperabuminemia (Group 4). In-hospital mortality rate was 41.4% in Group 1, 12.9% in Group 2, 3.1% in Group 3 and 0% in Group 4 ($p<0.001$; $p<0.05$). Median hospital stay was 4 days in hyperalbuminemia group, 6 days in normoalbuminemia group, 8 days in mild albuminemia group and 12 days in severe hypoalbuminemia group ($p<0.001$; $p<0.05$).

Conclusion: Hypoalbuminaemia increased in-hospital mortality and poor prognosis in Internal Medicine clinic patients. Serum albumin levels predict in-hospital mortality, length of stay, and repeat hospitalizations independently.

Keywords: Hypoalbuminemia, serum albumin, in-hospital mortality, hospitalisation

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Serum albumin is a structural protein synthesised in the liver and involved in many vital functions in the body and a negative acute phase reactant that can be used as a marker in inflammatory conditions.[1]

Hypoalbuminaemia is a very common condition in hospitalised patients. Although the conditions in which it occurs are well defined, there is no clear consensus about its mechanism of occurrence. In acute cases, it is thought to

Address for correspondence: Ali Kaan Güren, MD. Department of Medical Oncology, Marmara University Pendik Training and Research Hospital, Istanbul, Türkiye
Phone: +90 216 625 45 45 **E-mail:** alikaanguren@gmail.com

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occur as a result of increased outflow of serum albumin out of the vein with increased vascular wall permeability due to inflammation.[2] In chronic conditions, it is known to occur as a result of malnutrition and decrease in albumin synthesis in the liver.[3]

Decrease in serum albumin levels will lead to disruption in fluid distribution balance by causing changes in osmotic pressure of plasma, disruption in microvascular circulation by increasing leakage in capillaries, disruption in the distribution of drugs by decreasing the binding of drugs, emergence of hypercoagulable states by decreasing the anticoagulant effect of albumin, and increase in circulating free oxygen radicals due to decreased antioxidant effect of albumin. It is thought that hypoalbuminaemia has negative effects on vital functions with such effects.[4–6]

The relationship between serum albumin level and mortality is known.[7–10] According to our current knowledge, there is no study in the literature including only patients hospitalised in the Internal Medicine clinic and independent of the diagnosis of the patients. In this study, we aimed to determine the relationship between serum albumin levels measured within the first 24 hours of hospitalisation and in-hospital mortality, length of hospital stay, time to mortality, need for intensive care unit(ICU) follow-up and recurrent hospitalisations within one year in all patients hospitalised in the Internal Medicine clinic, regardless of their hospitalisation diagnosis and comorbidities.

Methods

Our study was conducted in patients hospitalised in the Internal Diseases Clinic of Health Sciences University Haydarpaşa Numune Health Practice and Research Centre between 01.06.2018-01.06.2019.

The data of the patients were retrospectively analysed using patient files and the electronic system of the hospital. Patients' age, gender, hospitalisation dates, length of hospital stay, number of repeated hospitalisations, hospitalisation diagnoses, chronic diseases, ICU needs, mortality, serum albumin, protein, haemoglobin, leukocyte and neutrophil counts, C-reactive protein (CRP) levels were recorded using Health Information System.

Patients were divided into 4 groups as those with SA value <2.5g/dl (Group 1), SA value between 2.5-3.5g/dl (Group 2), SA value between 3.5-4.5g/dl (Group 3) and SA value >4.5g/dl (Group 4). In-hospital mortality, duration of hospitalisation, time to mortality, number of repeat hospitalisations within one year, and ICU needs were compared between the groups.Patients who had an SA value within the first 24 hours of hospitalisation were included.

Patients who received blood, blood product transfusion or albumin replacement in the last 3 months or during hospitalisation were excluded. Patients who were interned for routine drug treatment, pregnant patients, patients who were transferred to other departments within 1 day after hospitalisation, patients who were interned for pre-operative medication, patients who were transferred from other clinics and patients who left the hospital on their own accord were excluded from the study.

Comorbidity scores of the patients were calculated using the Charlson Comorbidity Index (CCI).

IBM SPSS Statistics 22 (IBM SPSS) programme was used for statistical analyses. The conformity of the parameters to normal distribution was evaluated by Shapiro Wilks test. In addition to descriptive statistical methods (mean, standard deviation, frequency), Oneway Anova test was used for the comparison of quantitative data between groups for parameters showing normal distribution. Kruskal Wallis test was used for intergroup comparisons of parameters that did not show normal distribution and Mann Whitney U test was used to determine the group causing the difference. Mann Whitney U test was used in comparisons between two groups of parameters that did not show normal distribution. Fisher Freeman Halton test was used for comparison of qualitative data. Significance was evaluated at $p<0.05$ level.

Results

A total of 3391 patients hospitalised in the internal medicine clinic were screened. We excluded 1195 patients due to exclusion criteria and 32 patients due to missing data. The study included 2164 patients.

The mean age of the patients was 66.15±18.05 years and 1114 (51%) of the patients were female. The mean duration of hospitalisation was 9.37±7.43 days. 203 (9.4%) patients needed ICU. The total number of mortality was 254 (11.7%) and the mean time to mortality was 15.08±11.61 days (Table 1).

Table 1. Baseline characteristics

	Min-Max	Mean±SD
Age (years)	18-104	66.15±18.05
Length of stay (days) (median)	1-56	9.37±7.43 (7)
Number of Hospitalizations (median)	1-5	1.15±0.6 (1)
Charlson score (median)	0-15	4.71±2.75 (5)
Time to mortality (days) (median)	1-56	15.08±11.61 (12)
	n	**%**
Gender		
Male	1050	49
Female	1114	51
Need for ICU	203	9.4
Mortality	254	11.7

The study participants were analysed in 4 groups as follows: 220 (10.2%) with albumin value <2.5 g/dl (Group 1), 1054 (48.7%) between 2.5-3.5 g/dl (Group 2), 863 (39.9%) between 3.5-4.5 g/dl (Group 3) and 27 (1.2%)>4.5 g/dl (Group 4).

The most common hospitalization reasons were pneumonia (16.3%), acute kidney disease (15.1%), gastrointestinal hemorrhage (9.5%), and acute heart failure (8.8%) (Table 2).

Comorbidities included diabetes mellitus (36%), chronic kidney disease (15.6%), heart failure (24.1%), coronary artery disease (22.3%), and chronic obstructive pulmonary disease (15.5%). The mean CCI was 4.71 (Table 3).

In-hospital mortality rate was 11.7% in all patients. In-hospital mortality rate was 41.4% in group 1, 12.9% in group 2, 13.1% in group 3 and 0% in group 4. This difference between the groups was statistically significant (p<0.001; p<0.05). ICU requirement was 32% in group 1, 10.6% in group 2, 2.5% in group 3 and 0% in group 4, and this difference between the groups was statistically significant (p<0.001; p<0.05). The duration of hospitalisation was 4 days in the hyperalbuminaemia group, 6 days in the normoalbuminaemia group, 8 days in the mild hypoalbuminaemia group and 12 days in the severe hypoalbuminaemia group and this difference between the groups was statistically significant (p<0.001; p<0.05).

There was no statistically significant difference between the groups in terms of hospitalisation time until mortality (p:0.791; p>0.05) (Table 4).

The mean age was 61.2±19.21 years in the normal albumin group (group 3), 70.13±25.86 years in group 2 and 71.14±13.32 years in group 1. The difference in age distribution between the groups was statistically significant (p<0.001; p<0.05). As the SA level decreased, haemoglobin level also decreased, while leukocyte, neutrophil, CRP level and Charlson score increased. These differences between the groups were statistically significant (p<0.001; p<0.05). These findings are summarised in Table 5.

Discussion

In our study, as SA levels decreased in patients hospitalized in the Internal Medicine clinic, in-hospital deaths, hospitalization procedures, and recurrent hospitalizations increased. This relationship demonstrated that SA level can be used as a stand-alone parameter independent of the pa-

Table 2. Reasons for admission to the ınternal medicine clinic

Reason for Hospitalization	n	%
Pneumonia	353	16.3
Acute Kidney Injury	323	15.1
Gastrointestinal Hemorrhage	205	9.5
Acute Decompenseted Heart Failure	189	8.8
Malignancy Examination	119	5.5
Acute Pancreatitis	109	5
Anemia Etiology Study	95	4.4
Electrolyte Disorder	95	4.4
Diabetes Regulation	94	4.3
Ürinary System Infection	88	4.1
Palliation	84	3.9
Other	60	18.7

Table 3. Distribution of additional diseases

	n	%
Additional diseases (n=3633)		
Diabetes Mellitus	780	36
Heart Failure	521	24.1
Coronary Artery Disease	483	22.3
Kidney Failure	338	15.6
Chronic Obstruktive Pulmonery Disease	335	155
Solid Tumor	318	14.7
Dementia	186	8.6
Cerebrovascular Disease	173	8
Charlson score (median)	0-15	4.71±2.75 (5)

Table 4. Mortality by albumin level, need for ICU, length of stay, time to mortality

	Group 1 (n=220) Mean±SD (median)	Group 2 (n=1054) Mean±SD (median)	Group 3 (n=863) Mean±SD (median)	Group 4 (n=27) Mean±SD (median)	p
Length of stay (days)	14.33±10.07 (12)	10.48±7.52 (8)	6.9±5.37 (6)	4.52±2.47 (4)	[1]0.000*
RH	1.29±0.63 (1)	1.19±0,76 (1)	1.07±0.3 (1)	1±0 (1)	[1]0.000*
T.t.M. (days)	15.76±12.33 (13)	14.45±10.91 (11.5)	15.96±12.75 (11)	-	[1]0.791
	n (%)	n (%)	n (%)	n (%)	
Mortality	91 (41.4)	136 (12.9)	27 (3.1)	0 (0)	[2]0.000*
Need for ICU	70 (32)	111 (10.6)	22 (2.5)	0 (0)	[2]0.000*

[1]Kruskal Wallis Test; [2]Chi-Square Test; *p<0.05; RH: Recurrent Hospitalizations; T.t.M.: Time to Mortality.

Table 5. Group comparisons of age, laboratory data, and CCI score

	Grup 1 (n=220) Mean±SD (median)	Grup 2 (n=1054) Mean±SD (median)	Grup 3 (n=863) Mean±SD (median)	Grup 4 (n=27) Mean±SD (median)	p
Age (years)	71.14±13.32 (72)	70.13±25.86 (73)	61.2±19.21 (65)	38.34±19.02 (31)	[1]0.000*
Total Protein (g/dl)	5.21±1.12 (5.2)[a]	5.79±1.12 (5.7)[b]	6.58±0.7 (6.6)[c]	7.46±0.65 (7.5)[d]	[1]0.000*
Hemoglobin (g/dl)	9.23±1.85 (9.1)[a]	10.07±2.82 (10)[ab]	11.73±2.45 (11.5)[b]	12.06±2.5 (12.35)[b]	[1]0.001*
Leukocytes (/mm^3)	12269±7768 (12245)	10482±7687 (8940)	9206±5450 (8280)	8433±3138 (8035)	[2]0.000*
Neutrophil (/mm^3)	10406±7437 (8900)	8206±6436 (6680)	6649±4101 (5550)	5891±3048(4530)	[2]0.000*
CRP (mg/dl)	11.38±7.77 (9.6)	7.84±7.82 (5.3)	3.6±5.1 (1.2)	1.42±2.72 (0.3)	[2]0.000*
Charlson Score	6.87±2.39 (7)	5.15±2.42 (5)	3.71±2.66 (4)	1.31±1.91 (1)	[2]0.000*

[1]ANOVA; [2]Kruskal Wallis Test; *p<0.05.

tient's age, comorbidities and reason for hospitalisation in predicting in-hospital mortality, length of hospital stay and recurrent hospitalisations.

In the meta-analysis by Vincent J.L. et al.,[8] patients with hypoalbuminemia (SA<3.4 g/dl) were 21% of all hospitalised patients. In the study conducted by Akirov A. et al.[9] with patients hospitalised in all departments in their hospital, 29% of the patients were shown to have hypoalbuminemia. Mortality was reported to be 6% in all patients. In our study, 58.7% of the patients had hypoalbuminaemia (SA<3.5 g/dl) and the mortality rate was found to be 11% in all patients. This difference showed that patients hospitalised in the Internal Medicine clinic had lower SA levels and a more mortal prognosis compared to patients hospitalised in other departments and throughout the hospital.

Hermann F.R. et al.[11] reported that patients with hypoalbuminemia (SA<3.4) were hospitalised longer and had more recurrent hospitalisations compared with patients with normal SA level (SA≥3.5 g/dl). In our study, the duration of hospitalisation and recurrent hospitalisations within one year were significantly higher in the groups with low SA levels compared to the groups with normal or high SA levels.

Previous studies have shown a relationship between low serum albumin level and high mortality and morbidity in patients with acute decompensated heart failure,[12] sepsis,[13] colorectal cancer,[14] acute non-ischemic heart failure,[15] ischaemic stroke[16] and renal failure.[17] However, we included all patients hospitalised in the Internal Medicine clinic in our study, not a specific patient group. After the comorbidities of the patients were calculated by CKI, when the comorbidity scores were compared with SA, we found that SA levels decreased as the comorbidity scores increased. However, the comorbidities of the patients varied. In this study, we found that the SA level was associated with comorbidities, but this was not specific to a single diagnosis and could be found to be low in all comorbid diseases.

Previous studies have shown that mortality increased with decreased haemoglobin levels and increased leukocyte count and CRP values.[18,19] In our study, we found a significant correlation between decreased haemoglobin levels, increased leukocyte count and CRP values and increased mortality. It has long been known that serum albumin level decreases with age.[20,21] In our study, when the ages were compared according to SA level, it was found that the mean age of the groups with low SA level was significantly higher than the mean age of the groups with normal or high SA level.

The most important limiting factor of our study was the lack of post-discharge data. We could not record the in-hospital mortality of patients who were interned by another hospital some time after discharge, if they were readmitted or if they died in that hospital. Since some of our patients were interned after admission to the emergency department, hydration, diuresis or other treatments that may affect the SA level in the emergency department could not be taken into consideration.

Our study is different from other studies in that it was performed only in patients hospitalised in the Internal Medicine clinic, it included all age groups, it addressed acute and chronic conditions together, it included all patient groups instead of patient groups with a specific disease or hospitalisation diagnosis, and it examined the SA level in 4 groups, not only in 2 groups as low and normal-high.

Conclusion

In our study, a significant correlation was found between low SA levels measured at hospital admission and increased in-hospital mortality, increased length of hospitalisation and increased recurrent hospitalisations in patients hospitalised in the Internal Medicine clinic.

Hypoalbuminaemia is very common in patients hospitalised in Internal Medicine clinics. Hypoalbuminaemia is a sign of poor prognosis for patients and can be used as an

independent factor in predicting prognosis and mortality during hospitalisation.

However, there is a need for studies showing the effect of changes in SA levels on prognosis in more detail by serial SA measurements during hospitalisation and showing the effects of SA replacement or SA raising therapies on prognosis in patients with hypoalbuminemia.

Disclosures

Ethics Committee Approval: Our study was conducted in patients hospitalised in the Internal Diseases Clinic of Health Sciences University Haydarpaşa Numune Health Practice and Research Centre between 01.06.2018-01.06.2019.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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