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The Predictive Value of Serum Albumin Concentration and Nutritional Risk Index for Clinical Outcomes in Non-Critically Ill Hospitalized Patients

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ABSTRACT

Introduction: Previous studies have identified serum albumin level as a key factor associated with various clinical outcomes in hospitalized patients. This study aims to evaluate the relationship between serum albumin levels, nutritional risk index, and hospital clinical outcomes, including long-term hospital stay and hospital mortality, in non-critical patients.

Methods: Serum albumin levels and patient weight were measured within the first 24 hours of hospital admission. Usual weight was recorded, and the Nutritional Risk Index (NRI) for adults and the Geriatric Nutritional Risk Index (GNRI) for elderly patients were calculated. The hospital information system recorded the length of hospital stay and the occurrence of clinical outcomes. Cox regression analysis assessed the relationship between low serum albumin levels, malnutrition risk, and clinical outcomes.

Results: The results showed no significant relationship between low serum albumin levels at admission or a moderate-to-severe risk of malnutrition and clinical outcomes. Furthermore, no significant differences between these groups were found in in-hospital mortality or prolonged hospital stays. However, the length of hospital stay was significantly longer in patients with low serum albumin levels compared to others.

Conclusions: This study revealed that low serum albumin levels or moderate-to-severe malnutrition risk at admission may not be reliable predictors of in-hospital mortality or prolonged hospital stays, independently. However, conducting larger studies is necessary to reach a definite conclusion.

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Introduction

Albumin is a protein synthesized by the liver that serves as a regulator of colloidal osmotic pressure (1). It also plays an essential roles in modulating inflammatory processes (2), antioxidant activity (3), and inhibition of platelet aggregation (4). Recent studies have highlighted the protective effects of serum albumin against carotid atherosclerosis (5), cardiovascular diseases (6), and hypertension (7). Additionally, serum albumin levels are commonly used as an indicator of nutritional status in both chronic and critically ill patients (8). Hypoalbuminemia refers to a condition where serum albumin levels fall below 3.5 g/dL (9). The prevalence of hypoalbuminemia at the time of admission in hospitalized patients is reported to be 21% (10). This condition is

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prevalent in patients with malignancies, renal disease (11, 12), hip fractures (13), heart failure (14), stroke (15-17), and acute myocardial infarction (18). Numerous studies have documented the relationship between hypoalbuminemia and poor clinical outcomes. For example, a meta-analysis demonstrated that each 2.5 g/L decrease in serum albumin concentration increases mortality risk by 24% to 56% across various patient populations (19). Furthermore, Akirov et al. found that low serum albumin levels were significantly associated with longer hospitalization and increased mortality risk in hospitalized patients (20).

The Nutritional Risk Index (NRI) was developed by the Veterans Affairs Total Parenteral Nutrition Cooperative Study Group as a tool to assess the nutritional status of hospitalized patients (21). One of the main advantages of the NRI is its reliance on objective variables, such as changes in weight and albumin levels, rather than subjective measurements (22, 23). In addition to its simplicity and ease of use, the NRI has been significantly associated with mortality and clinical outcomes in some previous studies (24). These studies have highlighted a significant relationship between the NRI and clinical outcomes, further underscoring the importance of monitoring serum albumin levels (24). However, there is still no consensus on the predictive value of serum albumin levels, the NRI, and GNRI indexes for clinical outcomes. This longitudinal study investigates the relationship between low serum albumin levels, NRI, and GNRI values with clinical outcomes in non-critically ill hospitalized patients.

Materials & Methods

We conducted this longitudinal pilot study from May to December 2023 at two large hospitals (Imam Reza and Qaem hospitals) in Mashhad, Iran. The study was approved by the ethics committee of Mashhad University of Medical Sciences. The inclusion criteria were adult (18 years old ≤) hospitalized patients who provided informed consent to participate in the study. The exclusion criteria were: a) being hospitalized in the ICU, b) receiving an albumin infusion within the past month, c) receiving anabolic steroids or growth hormone, and d) using insulin.

Data Collection

Patients were included in this study within 24 hours of admission, provided they gave informed consent. Demographic information, disease diagnosis, and medical records—including biochemical analyses such as serum albumin levels and other relevant laboratory tests—were extracted from the patient's files. Specific dates for each patient's analysis were recorded to ensure accuracy. The patient was then asked to stand on a Seka scale (with an accuracy of 0.1 kilograms) at the nursing station, wearing light clothing and no shoes. Additionally, the patient was asked about their usual weight over the past 6 months. A registered nurse collected Fasting venous blood samples from all patients according to hospital protocol. Plasma was separated from serum by centrifugation at 3000 RPM. To minimize any potential impact on biochemical markers, such as serum albumin, the time from blood sample collection to centrifugation was kept under 30 minutes. Post-centrifugation, the samples were stored at -80°C until analysis. Serum albumin levels were measured using an albumin assay kit (Pars Azmoon, Tehran, Iran, licensed by DiaSys Diagnostic Systems, Germany).

NRI was calculated using the following formula for adults: NRI = (1.519 × serum albumin (g/L) +41.7× (present weight/usual weight). NRI score >100 indicated no risk group, 97.5–100 mild risk, 83.5–97.5 moderate risk, and < 83.5 denoted severe risk groups.

In the geriatric population, the Geriatric Nutritional Risk Index (GNRI) was calculated using the following formula: GNRI = 1.489 × serum albumin (g/L) + 41.7 × (present body weight / ideal body weight). The inclusion of both the Nutritional Risk Index (NRI) and GNRI was based on the diverse characteristics of our patient population, which consisted of both younger adults and elderly patients. This approach allowed for a comprehensive nutritional risk assessment across different age groups. A GNRI > 98 indicated no nutritional risk, 92 ≤ GNRI ≤ 98 was considered low risk, 82 ≤ GNRI ≤ 91 was identified as moderate risk, and a GNRI < 82 indicated major risk. The duration of patients' hospital stay and hospital mortality were evaluated using the hospital information system (HIS).

Statistical Analysis

The sample size for the in-hospital mortality outcome was calculated based on the findings of the study by Akirov et al. (2017) using the G Power software version 3.1.9.7 (Kiel University, Germany) based on z tests (logistic regression) and considering the two-tailed test, odds ratio (OR) of 0.0677 (normal albumin level and

mortality), and type I and II errors of 0.05 and 0.2, respectively (25). The primary sample size was 23 patients. Sample size for Considering the possible confounders, the sample size was increased to 53. The sample size was increased to 64 considering 20% dropout. Sample size for the length of stay outcome was calculated based on the findings of the study by Marinella et al. (1998) considering the mean length of stay in hypoalbuminemia and normal albumin patients (6.74 ± 4.79 and 3.85 ± 2.55 days, respectively) using the following equation and considering the type I and II errors of 0.05 and 0.2, respectively (26, 27).

$$n_1 = \frac{(\delta_1^2 + {\delta_2^2}/{k})(Z_{1-\alpha/2} + Z_{1-\beta})^2}{\Delta^2}$$

The sample size for length of stay was 56 patients. The largest calculated sample size was considered for the study and the sample size was increased to 68 patients considering 20% dropout rate.

All statistical analyses were performed using SPSS version 24. A two-sided P-value < 0.05 was considered statistically significant. Qualitative data were reported as numbers (%), and proportions between the two groups were compared using the chi-square or Fisher's exact test. The normality of quantitative data was assessed using the Kolmogorov-Smirnov test. Quantitative variables with a normal distribution were presented as mean ± SD, while variables with a non-normal distribution were reported as median (IQR). Student's t-test was used to compare normally distributed variables between two groups, and the non-parametric Mann-Whitney U test was used for comparing quantitative variables with a non-normal distribution. Multivariable analysis (COX regression) was conducted to assess the relationship between low serum albumin levels or moderate to severe risk of malnutrition and the risk of clinical outcomes.

Results

Participant Characteristics

A total of 74 eligible hospitalized patients were included in this study. The mean age of the patients was 58.33 years, and 35.1% of them aged ≥65 years. Additionally, 51.5% of the participants were male. The most common comorbidities among the patients were hypertension (28.4%), diabetes (25.7%), previous surgery (17.6%), cancer (17.6%), cerebrovascular accident (CVA) (8.1%), and chronic kidney disease (CKD) (8.1%). The median length of hospital stay was 8 days. Also, 35 patients (47.3%) experiencing prolonged hospital stays (i.e., staying >8 days). Furthermore, the mean serum albumin level was 3.14 g/dL, and the hospital mortality rate in the studied population was 12.2% (Table 1).

Table 1. Baseline characteristics, comorbidities, and prevalence of clinical outcomes according to serum albumin levels.

	All	Low serum albumin levels (<3.5 g/dL)	Normal serum albumin levels (3.5 g/dL≤)	Pvalue
Number	74	50 (67.6%)	24 (32.4%)	
Age	58.33 ± 16.13	60.02 ± 16.08	54.83± 16.00	0.19[b]
Males	38 (51.5%)	26 (52.0%)	12 (50.0%)	0.87[a]
Age ≥65 years	26 (35.1%)	20 (40.0%)	6 (25.0%)	0.20[a]
BMI (kg/m²)	23.00 ± 5.35	22.82 ± 5.33	23.37 ± 5.48	0.68[b]
Serum albumin (g/dl)	3.14 ± 0.75	2.74 ± 0.56	3.96 ± 0.25	<0.001[b]
Past medical history				
HTN	21 (28.4%)	15 (30.0%)	6 (25.0%)	0.65[a]
DM	19 (25.7%)	16 (32.0%)	3 (12.5%)	0.09[d]
Surgery	13 (17.6%)	10 (20.0%)	3 (12.5%)	0.52[d]
Cancer	13 (17.6%)	8 (16.0%)	5 (20.8%)	0.74[d]
CVA	6 (8.1%)	5 (10.0%)	1 (4.2%)	0.65[d]
CKD	6 (8.1%)	4 (8.0%)	2 (8.3%)	1.00[d]
Other PMH	21 (28.4%)	19 (38.0%)	2 (8.3%)	0.01[d]
Clinical outcomes				
LOS (days)	8.0 (6.0, 13.0)	9.0 (6.0, 13.2)	7.0 (4.5, 11.7)	<0.001[c]
Prolonged hospital stays	35 (47.3%)	26 (52.0%)	9 (37.5%)	0.24[a]
Hospital mortality	9 (12.2%)	8 (38.0%)	1 (38.0%)	0.25[d]

Abbreviations: *BMI, Body mass index; HTN, Hypertension; DM, Diabetes Mellitus; CVA, cerebral vascular accident; PMH, Past medical history; LOS, Length of hospital stay.*

a) Chi-squared test, b) Student t test, c) Mann_Whitney, d) test Fisher test.

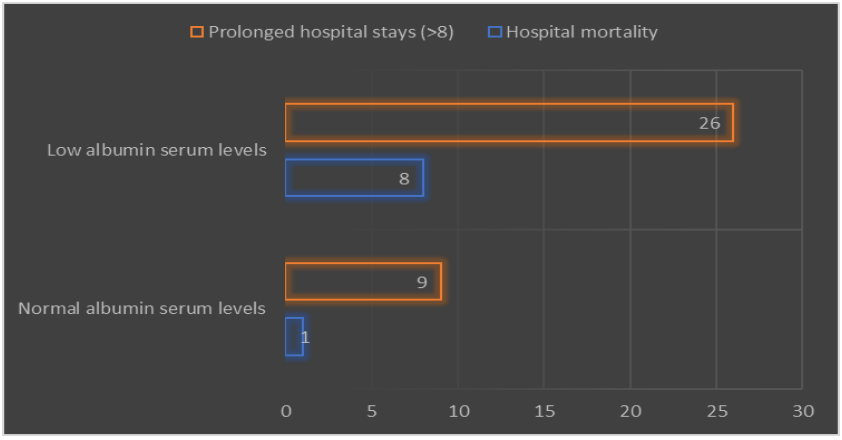

Figure 1. There was no significant difference in prevalence of hospital mortality and prolonged hospital stays (8<) between patients with normal and low serum albumin levels (P>0.05).

The Relationship between Serum Albumin Levels and Clinical Outcomes

Among the included patients, 24 (32.4%) had normal serum albumin levels, while the remaining patients had low serum albumin levels (<3.5 g/dL). Furthermore, 14 patients (18.9%) had very low serum albumin levels (<2.5 g/dL), and 36 patients (48.6%) had low serum albumin levels (2.5 ≤ x < 3.5 g/dL) (Supplementary Table 1). There was no significant difference in age, age category, gender, BMI, or primary comorbidities between patients with normal and low serum albumin levels. This study found that the length of hospital stay for patients with low serum albumin levels was significantly longer than for those with normal serum albumin levels. However, no significant difference was observed between these groups in the incidence of prolonged hospital stays or hospital mortality (P > 0.05) (Table 1 & Fig. 1). Cox regression analysis showed no significant relationship between low serum albumin levels and the incidence risk of prolonged hospital stays or hospital mortality (P > 0.05) (Table 2).

Table 2. Predictive validity of low serum albumin levels for malnutrition diagnosis: multivariate analysis

Dependent variable	HR** (CI 95%)	P-Value
Prolonged LOS (>8 days) *		
Crude	0.64 (0.24, 1.69)	0.37
Model I[a]	0.57 (0.19, 1.73)	0.32
Model II[b]	0.57 (0.19, 1.66)	0.30
Hospital mortality*		
Crude	1.41 (0.17, 11.72)	0.74
Model I[a]	1.44 (0.15, 13.60)	0.75
Model II[b]	1.18 (0.12, 10.93)	0.88

a) Model was adjusted based on Charlson Comorbidity Index (CCI)
b) Model was adjusted based on gender, age, Age ≥65 years, and history of cancer

The Relationship between the Nutritional Risk Index and Clinical Outcomes

Among the patients involved, 17 (23.0%) had no risk (11 patients, 14.9%) to mild risk (6 patients, 8.1%) of malnutrition, while 57 (77.0%) had moderate (29 patients, 39.2%) to severe (28 patients, 37.8%) risk of malnutrition based on the nutritional risk index scoring (Supplementary Table 3). There was no significant difference in age, gender, age category, primary comorbidities, or BMI between patients with no to mild malnutrition risk and those with moderate to severe malnutrition risk (P > 0.05). Additionally, there were no significant differences in the length of hospital stays, prevalence of prolonged hospital stays, or hospital mortality between these groups (Table 3 & Fig. 2). Furthermore, no significant relationship was observed between the risk of prolonged hospital stays or hospital mortality and moderate to severe malnutrition risk based on the nutritional risk index (Table 4).

Table 3. Baseline characteristics, comorbidities, and prevalence of clinical outcomes according to nutritional risk index.

	All	No to Mild risk	Moderate to severe risk	Pvalue
Number	74	17 (23.0%)	57 (77.0%)	
Age	58.33 ± 16.13	53.17 ± 14.27	59.87 ± 16.45	0.13[b]
Males	38 (51.5%)	7 (41.2%)	31 (54.4%)	0.33[a]
Age ≥65 years	26 (35.1%)	3 (17.6%)	23 (40.4%)	0.14[d]
BMI (kg/m²)	23.00 ± 5.35	24.85 ± 4.77	22.45 ± 5.43	0.10[b]
Serum albumin (g/dl)	3.14 ± 0.75	4.04 ± 0.27	2.87 ± 0.63	<0.001[a]
Past medical history				
HTN	21 (28.4%)	4 (23.5%)	17 (29.8%)	0.76[d]
DM	19 (25.7%)	2 (11.8%)	17 (29.8%)	0.20[d]
Surgery	13 (17.6%)	3 (17.6%)	10 (17.2%)	1.00[d]
Cancer	13 (17.6%)	1 (5.9%)	12 (21.1%)	0.27[d]
CVA	6 (8.1%)	1 (5.9%)	5 (8.8%)	1.00[d]
CKD	6 (8.1%)	2 (11.8%)	4 (7.0%)	0.61d
Other PMH	21 (28.4%)	2 (11.8%)	19 (33.3%)	0.12[d]
Clinical outcomes				
LOS	8.0 (6.0, 13.0)	7.0 (5.0, 10.0)	9.0 (6.0, 15.0)	0.09[c]
Prolonged hospital stays	35 (47.3%)	5 (29.4%)	30 (52.6%)	0.10[d]
Hospital mortality	9 (12.2%)	1 (5.9%)	8 (14.0%)	0.67[d]

Abbreviations: BMI, Body mass index; HTN, Hypertension; DM, Diabetes Mellitus; CVA, cerebral vascular accident; PMH, Past medical history; LOS, Length of hospital stay.
a) Chi-squared test, b) Student t test, c) Mann_Whitney, d) test Fisher test.

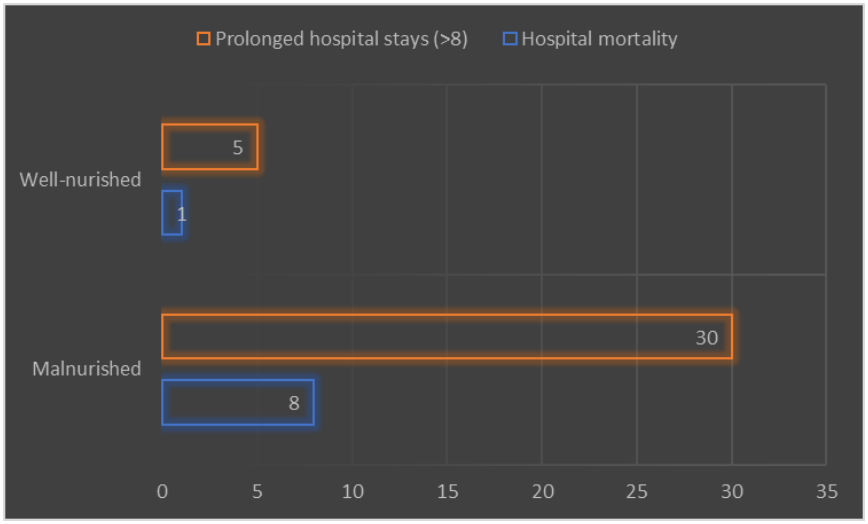

Figure 2. There was no significant difference in prevalence of hospital mortality and prolonged hospital stays (8<) between malnourished and well-nourished patients (P>0.05).

Table 4. Predictive validity of moderate to severe risk of malnutrition for malnutrition diagnosis: multivariate analysis

Dependent variable	HR**(CI 95%)	P-Value
Prolonged LOS (>8 days) *		
Crude	1.08 (0.49, 2.33)	0.84
Model I	1.08 (0.49, 2.34)	0.84
Model II	0.99 (0.44, 2.25)	0.99
Hospital mortality*		
Crude	2.89 (0.35, 23.57)	0.32
Model I	2.96 (0.35, 24.73)	0.31
Model II	2.87 (0.31, 26.00)	0.34

a) Model was adjusted based on Charlson Comorbidity Index (CCI)
b) Model was adjusted based on gender, age, Age ≥65 years, and history of cancer

Discussion

The present study revealed that the length of hospital stay was significantly longer in patients with low serum albumin levels within the first 24 hours of hospital admission compared to other patients. However, no significant differences were found in the incidence of prolonged hospital stays (defined as >8 days) or hospital mortality between patients with low and normal serum albumin levels at admission. Additionally, Cox regression analysis showed no significant relationship between low serum albumin levels and the risk of prolonged hospital stays or hospital mortality.

In this regard, a study by Nicolau et al. surveyed patients admitted for SARS-CoV-2 infection and found that the length of hospitalization was significantly longer in patients with low serum albumin levels and obesity upon admission compared to other patients (28). Furthermore, this study observed no significant difference in hospital mortality between these groups (28). Additionally, Marinella et al. reported that low serum albumin levels upon admission were significantly associated with prolonged hospital stays (29). This suggests that while low serum albumin levels may warrant closer monitoring during hospitalization, they do not necessarily correlate with mortality rates or prolonged hospitalization in every patient. Similarly, our findings indicate that the length of hospital stay in patients with low serum albumin levels upon admission was significantly longer than in other hospitalized patients. However, in a retrospective study conducted by Akirov et al. involving 30,732 hospitalized patients, in-hospital mortality was significantly higher in those with low serum albumin levels compared to other patients (30). Additionally, low serum albumin levels within 48 hours of admission were significantly associated with hospital mortality (30). Notably, this study found that normalizing serum albumin levels before discharge, compared to discharging with low serum albumin levels, was significantly associated with lower mortality (30). This highlights the importance of monitoring serum albumin as a potential indicator of patient risk. Furthermore, a study by Ling et al. involving 3,398 critically ill patients with COPD showed a significant negative relationship between serum albumin levels within 24 hours of ICU admission and hospital mortality (31). Similarly, another study on ICU patients found that low serum albumin levels at admission and 48 hours after admission were significantly associated with increased ICU mortality (32).

In the present study, no significant differences were found in the length of hospital stays, prolonged hospital stays, or hospital mortality between patients with no to mild risk of malnutrition compared to those with moderate to severe risk of malnutrition based on the nutritional risk index. This finding is particularly noteworthy as it contrasts with the literature suggesting a link between malnutrition and clinical outcomes. Specifically, moderate to severe malnutrition risk had no significant relationship with prolonged hospital stay or mortality risks. In this regard, Gärtner et al. found a significant positive relationship between higher nutritional risk based on the GNRI and length of stay (LOS). However, no significant relationship was observed between higher-risk GNRI and in-hospital mortality (33). Additionally, Zhang et al. identified GNRI as an independent factor for postoperative major complications in elderly rectal cancer patients who underwent surgical treatment following neoadjuvant therapy (34).

The nutritional risk index (NRI) did not significantly correlate with prolonged hospital stays or mortality in our study, primarily due to its inability to fully capture the complexities of patient health or other influencing factors, such as illness severity (21, 23, 24). Despite this, low serum albumin levels remain a critical indicator of nutritional status and overall patient health, suggesting that while the NRI may not directly predict outcomes, it can still help identify patients who might benefit from dietary interventions (23, 24). This study also emphasized the importance of understanding post-discharge outcomes, as these can provide insights into ongoing risks related to low serum albumin levels that may not be reflected during hospitalization. Future research should include post-discharge follow-ups to better assess the long-term relationship of low serum albumin and nutritional risk indexes (NRI and GNRI) at admission on patient clinical outcomes.

Yet, to our knowledge, this is one of the first studies to calculate a nutritional risk index using a formula for adults and elderly individuals, independently. Other strengths of this study include its prospective design, the exclusion of

critically ill patients, and survival analyses adjusting for confounding variables.

However, this study had several limitations, including limited sample size, the lack of data on clinical outcomes after patient discharge, and insufficient information on the causes of death. Given the relatively low incidence of hospital mortality (12.2%), we suggest that future studies involve a larger cohort or a multi-center design to enhance statistical power and provide more robust findings regarding the association between baseline serum albumin levels or nutritional risk with clinical outcomes in hospitalized patients.

Conclusion

This longitudinal study showed that low serum albumin levels and moderate to severe risk of malnutrition within the first 24 hours of admission were not significantly associated with clinical outcomes, including prolonged hospital stay and in-hospital mortality. However, the length of hospital stays was significantly longer in patients with lower serum albumin levels during the first 24 hours of admission than others. It seems that more high-sample size studies are necessary to obtain conclusive results regarding the clinical outcome predictive value of serum albumin levels and nutritional risk indexes in non-critically ill patients.

Declaration

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Availability of Data

Due to ethical concerns, the datasets gathered and/or processed for this study are not publicly available; however, upon reasonable request, the corresponding author may make the datasets available.

Conflicts of Interest

This study was carried out without any conflicts of interest.

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