

Clinical Prognostic Value of Serum Albumin in Patient Recovery Outcomes

Marufkhanov Kh.M.

Tashkent State Medical University, Tashkent, Uzbekistan

Isroilov A.G'

Tashkent State Medical University, Tashkent, Uzbekistan

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Abstract: Serum albumin is increasingly recognized as a prognostic biomarker reflecting systemic inflammation, disease severity, and physiological reserve. This review summarizes evidence on the clinical significance of hypoalbuminemia in hospitalized and critically ill patients and across cardiovascular, renal, oncologic, and autoimmune diseases. Reduced albumin levels at admission are consistently associated with increased mortality, prolonged hospitalization, and higher complication rates. In intensive care settings, severe hypoalbuminemia predicts short-term mortality and organ dysfunction. Dynamic changes in albumin during hospitalization and albumin-based indices further enhance risk stratification. Serum albumin remains a simple, cost-effective marker for predicting clinical outcomes and monitoring recovery.

Keywords: Serum albumin, hypoalbuminemia, prognosis, inflammation, critical illness, cardiovascular disease, chronic kidney disease, oncology, autoimmune diseases, biomarker.

Introduction: Albumin is the main protein in the plasma. It is produced in the liver and serves several important functions; these it does by contributing to oncotic pressure, providing transport for endogenous and exogenous compounds, and providing antiinflammatory defenses [3, 8]. The albumin concentration reflects the balance between the processes of synthesis/catabolism, distribution and loss of albumin, each of which can be influenced by a number of factors, including nutritional status, hormonal status, systemic inflammation, organ dysfunction and acid-base status [2, 8]. In the setting of both acute and chronic inflammation, albumin acts as a negative acute phase reactant, with the alteration of hepatic protein synthesis directed by cytokines and the resulting increase in capillary permeability leading to decreased levels of circulating albumin [6, 19]. As a result, it is now apparent that hypoalbuminemia should not only be considered an indicator of malnutrition but should also serve as an integrated biomarker of systemic inflammation, severity of illness and reduced physiological reserve. Although there are some studies

to support this hypothesis, hypoalbuminemia may still lack the sensitivity (e.g., due to its slower rate of change) in terms of being able to detect short-term changes in nutritional status, as compared to other markers/biomarkers. Because of this, there is an increasing body of evidence that suggests that shorter-term changes in albumin during hospitalization are more strongly correlated with the overall decline in inflammatory response and clinical trajectory than with strictly nutritional interventions. These findings further support the idea that both baseline albumin levels and their dynamic changes can provide independent prognostic information.

Critical Levels of Albumin in Hospitalized and Intensive Care Unit (ICU) Patients

Thresholds of serum albumin have been studied widely as predictors of adverse outcomes for in-hospital or critically ill patients. In general medical populations, hypoalbuminemia is typically defined as serum albumin <3.5 g/dL (35 g/L), whereas serum albumin <3.0 g/dL (30 g/L) is usually defined as having clinically significant

risk and will typically result in an increased risk for mortality [8, 19]. Multiple observational studies have demonstrated that having an albumin level <3.0 g/dL at admission is independently associated with a higher risk for in-hospital mortality, longer lengths of stay, and increased complication rates, after adjusting for the effects of age and comorbidities [21, 22]. In the ICU population specifically, lower thresholds of serum albumin are generally associated with worse outcomes. An albumin level of <2.5 g/dL (25 g/L) has been linked to substantially higher short-term mortality, especially in patients with sepsis, cardiogenic shock and multiorgan failure [1, 3]. For instance, in patients with cardiogenic shock, having an albumin level at admission <30 g/L was independently associated with higher 30-day mortality than patients with an albumin level ≥ 30 g/L; a further decline in albumin levels during the ICU stay additionally increased the risk of 30-day mortality [14]. Critically ill patients with persistent hypoalbuminemia within the first week of their ICU stay were determined to exhibit higher rates of organ dysfunction and mortality when compared to critically ill patients with stable or improving albumin levels [2].

Albumin in Cardiovascular Diseases

Serum albumin is increasingly used as a universal predictor of cardiovascular disease (CVD) around the world because it represents the combined effects of inflammation and oxidative stress and endothelial dysfunction, as well as a measure of total physiological reserve [1, 13].

Population and clinical studies have shown repeatedly that low levels of albumin are associated with poor cardiovascular outcomes regardless of comorbidities and other factors that may affect an individual's condition.

In heart failure (HF) hypoalbuminemia (defined as an albumin concentration of <3.5 g/dL) is associated with an increased risk for both death and readmission to the hospital due to HF. A recently published large study ($>5,836$) showed that among patients hospitalized with HF, those who had an increase in serum albumin during their hospitalization had a better long-term survival rate compared to those whose serum albumin levels did not improve (54.5% vs. 45.4% respectively, $p < 0.005$). There was also evidence of worse prognoses (poor outcomes) for those with even small decreases in albumin while hospitalized [7].

Hypoalbuminemia, or low levels of the protein albumin in the blood, also has an association with increased mortality risk in patients experiencing acute myocardial infarction (AMI) and acute coronary syndromes (ACS). Among a total of 6,283 AMI survivors, 22.7% had an albumin level of less than 3.5 g/dL; low levels of

albumin were an independent predictor of mortality during the long term [17]. Additionally, ACS patients undergoing percutaneous coronary intervention (PCI) have statistically significantly longer lengths of stay if they have low oxygen or low levels of albumin [12]. Therefore, these studies demonstrate that measuring albumin may be useful in identifying high-risk patients early in inpatient care.

The prognostic value of albumin may vary by severity of illness. For example, patients diagnosed with cardiogenic shock and admitted to the intensive care unit (ICU) with an albumin ≤ 30 g/L had statistically significantly higher rates of death at 30 days postadmission. Additionally, patients whose albumin dropped $\geq 20\%$ during the first 3 days were also at an increased risk of mortality [14]. This highlights the need to pay attention to the trend of albumin rather than just individual measurement.

Albumin in Nephrology

Lower serum albumin levels have been independently associated to increased cardiovascular and all-cause mortality in chronic kidney disease (CKD). CKD patients that have serum albumin levels below 3.5 g/dL have significantly higher risks of being hospitalized or dying than those who have normal levels. The relationship between low serum albumin and increased risk of both hospitalization and death remain significant after adjusting for estimated glomerular filtration rate (eGFR), comorbidities, and inflammatory markers [22]. Hypoalbuminemia in CKD is frequently associated with chronic inflammation, protein-energy wasting, and increased risk for vascular disease.

In patients receiving hemodialysis, serum albumin level is one of the best predictors of survival. Large dialysis registries have shown that each 1 g/dL drop in serum albumin level significantly increases risk of death. Patients with serum albumin levels below 3.5 g/dL are often identified as being at high-risk for mortality in the dialysis setting. The presence of persistently low serum albumin during the course of a follow-up period has also been associated with poor long-term outcomes, including complications due to infection and cardiovascular events [21, 22].

Albumin in Oncology

Research shows a correlation between low albumin levels and an increased likelihood of death among cancer patients. In one large cohort study that utilized NHANES data as its source, it was found that cancer patients with lower albumin levels were nearly twice as likely to die than those with higher levels after controlling for age or other risk factors [20].

In addition to determining long-term outcomes,

albumin can also help predict short-term outcomes for hospitalized cancer patients. For instance, one recent cohort study involving more than 5,000 cancer patients, found that for every 1 g/L increase in serum albumin, the associated reduction in risk of death was approximately 45%, while the duration of hospitalization was shortened [24].

Combined with inflammatory markers, albumin can provide additional clinical utility. Particularly, many studies have assessed C-reactive protein (CRP) to albumin ratio (CAR) as a prognostic marker in patients with cancer. A large study that included several studies showed that patients with CAR values greater than 0.7 had a 1.8-2.0 times greater chance of death compared to those with lower CAR values [4]; thus, utilizing CAR provides a way for physicians to determine the interplay between nutritional reserves and inflammation.

Low albumin at diagnosis has also been associated with poorer treatment response and lower survival in patients with blood cancers such as acute myeloid leukemia (AML) [15].

Albumin in Rheumatologic Autoimmune Diseases

Serum Albumin functions as a "negative acute phase reactant" in the field of rheumatology; Low levels of serum albumin imply failure of recovery after systemic autoimmune exacerbations. In patients with rheumatoid arthritis (RA), it is useful to measure long-term recovery and "biological aging" using the Neutrophil % to Albumin Ratio (NPAR). Each unit increase in NPAR correlates with an increase of 1.32 years of biological age over chronological age, showing the protective effects of albumin against oxidative damage hindering physiological recovery. [16]

A low albumin concentration in Systemic Lupus Erythematosus (SLE) is an indicator of poor prognosis and outcomes. For example, below 20 g/L of serum albumin, patients have higher rates of venous thromboembolism; thus, prophylactic anticoagulant therapy should be provided [5]. Additionally, lower albumin at initial diagnosis correlates with increased disease activity and is an early predictor of renal recovery [18]. In ANCA-associated vasculitis, the CRP-to-albumin ratio (CAR) is a sensitive indicator of how well patients respond to treatment with immunosuppressive therapies.

Patients with a CAR greater than or equal to 0.98 have significantly greater Birmingham Vasculitis Activity Scores (BVAS) and a higher incidence of severe kidney involvement than patients with CAR 0.97 or less. Therefore, the CAR is an excellent tool for distinguishing between patients who have entered remission from those who require heightened

immunosuppressive therapy [10].

CONCLUSIONS

The role of serum albumin as a "negative acute-phase reactant" is becoming more widely recognized in regard to the clinical prognostic value of serum albumin in how well a patient will recover. Low serum albumin levels are viewed across the spectrum of both oncology and rheumatology as important predictors of poor long-term survival, prolonged hospital stays, and accelerated biological aging. In oncology, every 5 g/L increase in serum albumin reduced mortality risk by 45%, and in autoimmune diseases, such as SLE, falling below the 20 g/L threshold places individuals at a significantly higher risk of developing life-threatening vascular complications [18, 9]. Serum albumin can be incorporated into composite ratios (i.e., CAR and NPAR) and provide a more comprehensive view of the relationship between systemic inflammation and the body's physiologic reserve. Serum albumin represents one of the most cost-effective and reliable biomarkers for assessing a patient's likelihood of recovery or worsening, whether predicting chemotherapy success in AML or evaluating the adequacy of immunosuppression in vasculitis [10, 11].

In summary, serum albumin is a readily accessible clinical marker, and stabilization or increase in serum albumin is the primary indicator of successful therapeutic intervention and a favorable trajectory for patient recovery in a variety of disease states.

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