ORIGINAL RESEARCH

Serum Albumin as a Marker of Metabolic Response to Injury and its Role with Calorie Intake Regarding Length of Stay, Readmission Rates and Hospital Survival

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ABSTRACT

Background: Studies have shown a relationship between albumin level & hospital mortality, but none have looked at low serum albumin, calorie intake and survival.

Aim: To evaluate the relationship between serum albumin level, calorie intake, length of hospital stay (LOS), readmission rates and hospital mortality in a large population of disadvantaged and underinsured patients at a County of Los Angeles Medical Center.

Design: Prospective observational study using data collected over a 6-year period of hospital survival, LOS and readmission rate in 11,441 patients. Calorie intake in those 400 patients with serum albumin <1.5 g/dL was collected. Our hypothesis was to test if the relationship of admission serum albumin to mortality was linear or exponential. In addition, in those with a serum albumin <1.5 g/dL, we evaluated calorie intake and hospital survival.

Methods: A total of 11,441 patients were included in the dataset. ANOVA and regression analysis were performed. Calorie intake was extracted from dietary and intravenous intake data of each of the 400 patients with an albumin <1.5 g/dL.

Results: Serum albumin was obtained within the first 7 days of admission in all patients. Mortality increased in patients with admission serum albumin <3.5 g/dL (8.8% vs 2.3%, $p<0.05$). Serum albumin was exponentially related to mortality (mortality = 32 / albumin^2; $p <0.01$). The group of patients with albumin <1.5 g/dL had the greatest mortality rate (18%), approximately seven times that of patients with normal serum albumin levels. These patients also had an average LOS of 14.7 days ($p<0.05$), twice that of patients with normal albumin values. 30-day admission rates for this group were three times greater (6.3% vs. 1.9%, $p<0.05$). Calorie intake was associated with a dose response curve with regards to hospital mortality.

Conclusion: A single measurement of serum albumin identifies patients who are at high risk for prolonged hospital stay, readmission and mortality. Calorie intake may modify mortality risk, but prospective studies are needed.

INTRODUCTION

Hypoalbuminemia is emerging as a valuable indicator in predicting a patient's chance of mortality. Certain studies have concluded the existence of a dramatic rise in mortality rates or surgical complications directly corresponding to a decrease in albumin.[1-4] Serum albumin levels are easy to obtain, relatively cost-effective, and may provide the physician with a single measurement prediction of mortality. Serum albumin has not only proven itself a valuable marker of mortality, but it has shown itself to be more effective in predicting length of stay and readmission rates than other data such as age.[1]

This specific study, conducted at Harbor-UCLA Medical Center, is based on 11,441 separate admissions of patients with varying albumin levels measured within the first seven days of admission.

METHODS

This IRB-approved study was part of a student-driven summer project. Data was collected and analyzed by ANOVA with significance at $p<0.05$. The data was collected from Harbor-UCLA Medical Center for 6 years before June of 2000. 14,000 separate albumin test results were used, along with patient identification numbers, date of admission, date of test administration, date of discharge, and status of discharge. From these 14,000, all albumin tests on the same patient within the same admission were extracted, treating second admissions as different patients. Table 1 shows enrollment numbers. Most commonly, the albumin was tested on the day of admission to the hospital, but the first date may be as late as seven days from admission. The overall average albumin was 2.8 g/dL (Figure 1). The data was set up extracting all primary albumin tests done after the first seven days and removing multiple albumin values for a patient during the same admission. Mortality of the patient was determined by a discharge status of "expired," while all other discharges, including transfers to another hospital, were left in our calculations as assumed survivors.

In calculating the data, five separate groups were used: albumin <1.5 g/dL, 1.5-1.9 g/dL, 2.0-2.4 g/dL, 2.5-2.9 g/dL, and all normal values 3.0-5.0 g/dL. Group #1 had an average albumin of 1.2 g/dL, group #2 had an average of 1.7 g/dL, group # 3 had an average of 2.2 g/dL, group #4 had an average of 2.7 g/dL, and group #5 averaged 3.5 g/dL. It was from these five groups that average albumin values were obtained, and mortality percentages were calculated. A Multiple Organ Dysfunction Score (MODS) was calculated on all patients' admission labs. 53.6% of the patients had abnormal albumin levels (<3.0 g/dL) as seen in Figure 1. The smallest group with serum albumin <1.5 (Group 1) had only 400 patients.

RESULTS

Length of Stay: Using the admission and discharge dates, we calculated the average stay in the hospital for each of the five groups. Patients with normal albumin values averaged 7.8 days in the hospital and those with the lowest albumin levels had nearly twice the average stay at 14.7 days (Figure 2). This data roughly coincides with a three-day increase in hospital stay for every decrease of 1 g/dL of albumin observed. The distribution is skewed and arbitrarily truncated at ninety days (33 outliers spanned from 91 to 254 days in the hospital).

Hospital Readmission Rates: In this study, the term readmission applies to the admission of one patient at the same hospital within thirty days of a previous admission there. In procuring the readmission data, all patients with more than one admission were tagged and separated. Using the admission dates, the length between admissions was calculated and patients with readmissions were separated from the rest. The patients were then sorted according to their very first serum albumin level. In this manner, the percentage of each group that was readmitted within one month was determined. For further comparison, the percentage of each group that either expired or was readmitted was calculated (Figure 3). The same was also done to readmissions within one year. As seen in Figure 3, there was a significantly higher chance of readmission for patients with hypoalbuminemia. For patients with initial albumin values falling into the lowest group, there was a 6.3% 30-day readmission rate. This is a 16.3% readmission rate if one looks at the readmission over the period of 365 days. Patients with albumin between 1.5-1.9 g/dL have a 3.4% chance of readmission, those with albumin 2.0-2.4 g/dL have a 2.3% chance, patients with albumin of 2.5-2.7 g/dL have a 2.0% chance, and those with normal albumin have a 1.9% chance. The statistics for readmission within one year are unusually high due to site-specific reasons.

Second albumin values were measured on 14.9% of the patients on roughly the third day after admission (two days after the first albumin testing). These results were separated from the rest and effectively document one's health throughout their hospital stay.

Albumin and Mortality: The mortality rate drastically rises as the serum albumin level of the patient decreases (Figure 4). The percent mortality for the group with normal albumin levels was 2.3%, whereas the group from 2.5-2.9 g/dL was 5.2%, the group from 2.0-2.4 g/dL was 9.2%, the group from 1.5-1.9 g/dL was 13.5%, and the group <1.5 had a mortality rate of 18%. The overall mortality rate for the entire patient population was 5.8%.

In attempt to find a direct correlation between the two sets of values, it was necessary to detect any hidden trends among the data points. Upon graphing the square root of the mortality rate vs. the albumin levels, a nearly straight line was obtained (data not shown). This observation directs us towards various types of equations such as power equations, polynomials and exponential equations in search of a simplistic method for roughly determining the mortality rate from the albumin level. The most concise equation comes from the power equation and is $32/(\text{albumin})^2$. However, its accuracy is distorted as the serum albumin values approach zero. The most accurate equation is, $\text{Mortality}=1.7(\text{albumin})^2-15(\text{albumin}) + 33.8$. The exponential equation had the next best fit. The power equation was the simplest to use and to remember: % Hospital Mortality = $32/(\text{albumin})^2$.

Secondary Albumin: Secondary albumin values were taken in some cases. The data for this implies that patients with initially low albumin levels would show improvement whereas patients with normal values showed a decrease in albumin during their hospital stay (data not shown). The average change in albumin values over the period of approximately three days was -0.10 g/dL. The increase or decrease in serum albumin during one's hospital stay also shows a relationship on mortality rates. If the patient's albumin stayed the same or increased, then they had a mortality rate of 7.6% (n=792), while those whose albumin levels dropped had an 11.7% mortality rate (n=908).

Caloric Intake: As part of this exploratory research, those with a serum albumin <1.5 g/dL had their calorie intake estimated from chart review and were categorized into 5 groups <20%, 20-40%, 40-60%, 60-80% and 80-100% of meals provided during the last 30 days of hospital stay (Figure 5). There was an increase in observed mortality in albumin <1.5 g/dL group if the caloric intake was <770 calories (<40% of daily needs).

Table 1. Study Enrollment

14,000 (serum albumin measured)
-1,500 (second serum albumin measured)
-1,059 (>2 serum albumin levels measured)
11,441 (patients in study)

Fig 1: Distribution of Serum Albumin Levels

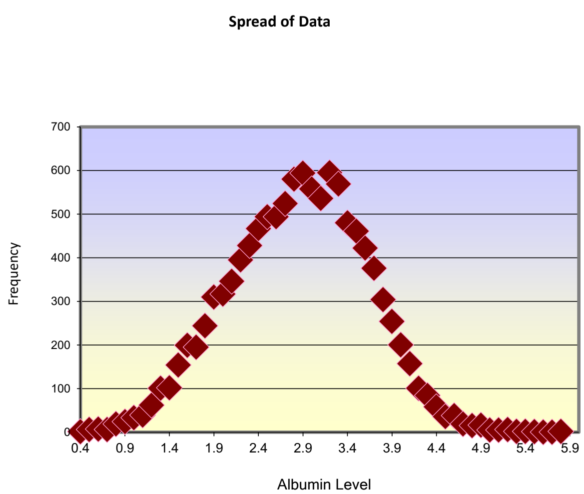


Fig 2: Relationship between Admission Serum Albumin and Length of Stay

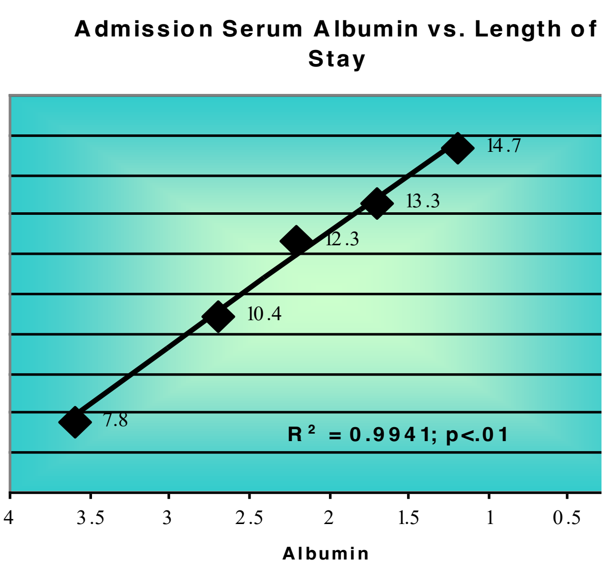


Fig 3: Readmission Rates Related to Serum Albumin Groups (g/dL)

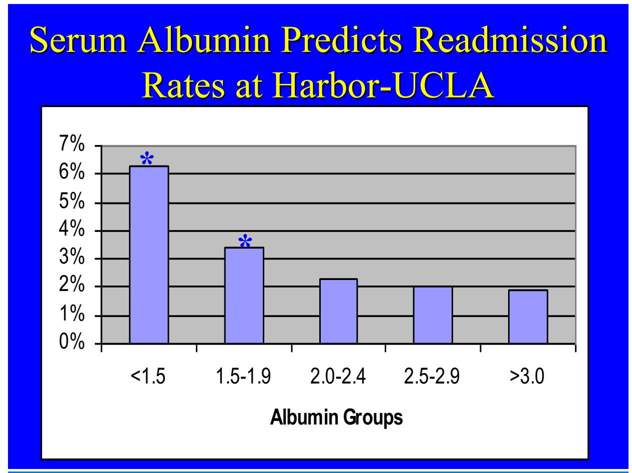


Fig 4: Hospital Mortality by Serum Albumin Level

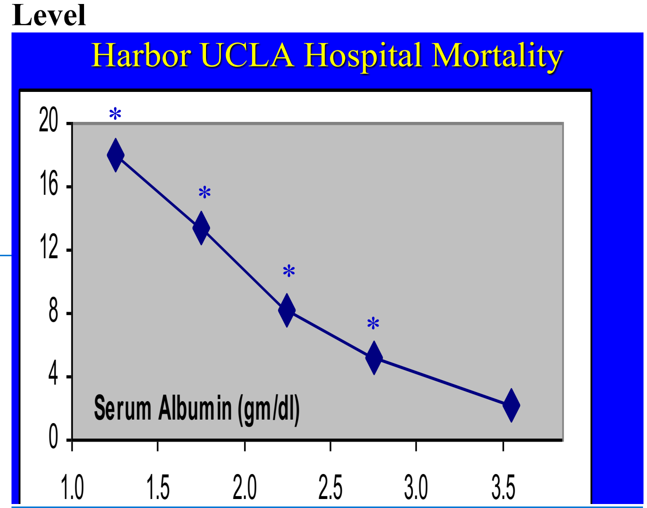
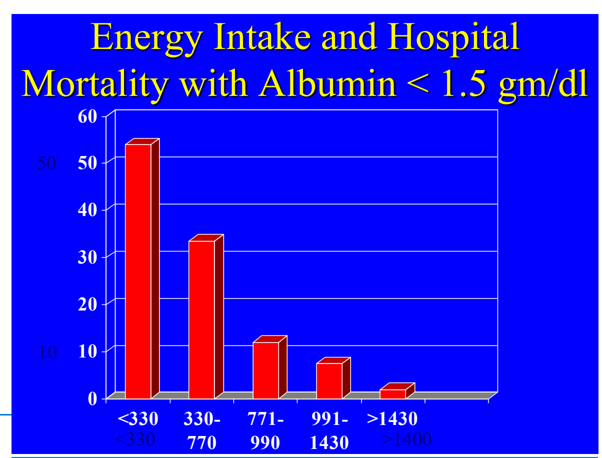


Fig 5: Caloric Intake and Hospital Mortality



DISCUSSION

Albumin concentrations have been associated with hospital mortality.[1-5] The largest study looked at 52,215 non-cardiac surgical patients admitted to the Veterans Affairs (VA) Medical Centers,[1] and surgical mortality was exponentially increased as albumin decreased. The overall 30-day mortality was 3.9%, and this increased to 28% for albumin below 2.1 g/dL.[1] Using an expanded data set, n=343,352, mortality was 21.6% in patients with albumin less than 2.1 g/dL (Personal Communications, J Gibbs). Mortality in our center was lower. This difference may be attributed to the fact that Gibbs' study was based solely on surgical patients coming from VA Medical Center, making his patient population composed of predominantly 60-year-old males. More similar to our study, Herrmann's study found a 14% mortality rate in patients with albumin below 3.4 g/dL compared to a 4% mortality rate in patients with normal albumin.[4]

Overall mortality of our population can be explained as a power function between albumin and mortality (Figure 4). Mortality was correlated with an R-squared value of 0.923 ($p<0.01$), where mortality is equal to $32/\text{albumin}^2$. When albumin equals one, mortality is 32%, when albumin is 3, the mortality is 3.6%, and when albumin is 4.5, mortality is 1.58%. Gibbs' data on surgical mortality also demonstrated a power relationship between mortality and albumin where mortality equals $66/\text{albumin}^2$. In this surgical population, the mortality is approximately two times that which we observed. This is likely due to our data comprising only 30% surgical patients.

Serum albumin was directly associated with length of stay (Figure 3). Herrmann also reported an association between albumin concentration and length of stay.[3] Consistent with our results, the length of stay increased in patients with low serum albumin values. Their study separated the data according to albumin and age, hence making it difficult to compare our overall calculations with theirs. The Herrmann study grouped the data in such a way as to combine all albumin values <3.0 g/dL and to go into more detail of values of between 3.4-4.5 g/dL. Between the 3.4-3.9 g/dL and the <4.5 g/dL groups, the length of stay increased by 3.2 days.[4] It was found that for every 1 g/dL decrease in albumin, the length of stay increased by 3 days.

Herrmann's study also researched hypoalbuminemia's relevance to the remittance rate of a patient.[5] This study considered readmission as the return of a patient within one year. Patients tested for albumin levels were compared to patients whose serum albumin values were not taken (26% vs. 15% readmission, $p<0.0001$). They found an increase readmission rate for patients with albumin <3.4 g/dL (29% vs. 26%, $p<0.0001$). When we look at our readmissions at one year, we have a readmission rate of 16.3% for patients with albumin <1.5 g/dL compared to 6.9% for patients with albumin >3.0 g/dL ($p<0.01$). When we look only at the 30-day readmission rate, there is a significant relationship based on serum albumin (Figure 3). The lower the serum albumin values, the greater risk of readmission.

Change in serum albumin after the initial value was also a predictor of hospital survival. If the patient's albumin stayed the same or increased, then they had a mortality rate of 7.6% (n=792), while those who dropped the albumin level had an 11.7% mortality rate (n=908, $p<0.05$).

In addition, comparison with other recent data suggests that the exponential relationship between admission serum albumin level and hospital mortality are similar between Mayo Clinic Hospital and Harbor-UCLA Medical Center for the County of Los Angeles (Figure 4).[11] The likely relationship between albumin and mortality suggest that the level of reduction in serum albumin may reflect the severity of metabolic injury (infection and/or inflammation).

Recently, the American Society of Parenteral and Enteral Nutrition (ASPEN) recommended that serum albumin not be used as marker of malnutrition. The classic case of this is seen in patients with anorexia nervosa where a 40lb weight loss will not reduce serum albumin levels with severe weight loss and malnutrition. This author suggests that a 1 g/dL drop in serum albumin likely reflects a single major injury (i.e. community acquired pneumonia or acute inflammation response as seen in a lupus flare). A larger drop in serum albumin may reflect longer duration of infection or inflammation, or occult cirrhosis, nephrotic range proteinuria or a yet unknown inflammatory process.

In an additional study, we prospectively tested if baseline serum albumin levels in interstitial lung patients awaiting lung transplant would predict survival at Harbor-UCLA Medical Center. This study concluded that reduced serum albumin increased mortality rates by 54% with each 0.5 g/dL decrease in serum albumin concentration.[11] The lower albumin levels likely identified those patients with more lung inflammation.

Lastly, calorie intakes in those with a serum albumin <1.5 g/dL appear to vary widely and may provide the clinician insight to survival in those who have severe hypoalbuminemia. We have recently demonstrated that ingesting >500 calories-per-day in patients with acute respiratory distress syndrome was associated with an improved survival, similar to what we see in the 440-calorie group in Figure 5.[12] Prospective clinical trials in patients with severe metabolic injury, illness and/or inflammation reflective of a serum albumin <1.5 g/dL should be conducted to identify the risks and benefits of enteral nutrition in this group of seriously ill patients.

CONCLUSION

Serum albumin, a commonly obtained hospital lab measurement, provides important information for the clinicians in three areas: hospital survival, length of stay and readmission rates. Low serum albumin levels indicate a higher chance of mortality, which can be due to metabolic injury, inflammation, illness and/or underlying diseases. Calorie ingestion in those with the lowest serum albumin may also be a predictor of a poor outcome.

This study roughly follows the equation of the Mayo Clinic Hospital study. (Mortality = $42/\text{albumin})^2$ [Our more recent unpublished data is similar 40/albumin).[2] In the preoperative patients, this risk appears to double (mortality = $66/\text{albumin})^2$ compared to what we observed in a large group of hospitalized patients ($32/\text{albumin})^2$. As serum albumin levels drop approximately 1 g/dL, there is an increase of about three days added on to the length of stay. Patients with the lowest albumin values (<1.5 g/dL) had the longest length of stay.

Patients with severe hypoalbuminemia are more than three times as likely to need readmission within one month than those with normal serum albumin values (6.3% vs. 1.9%). The readmission rates quickly lower as the albumin values approach normal. Earlier data demonstrated that repletion of serum albumin to normal levels does not change the clinical outcome for most medical illnesses. Combined, the readmission rates and the mortality rates show the extent of complications infringed upon one's health that can be easily determined by one test.

Conflict of Interest: None declared.
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