Albumin A Utilitarian Marker in Acute Febrile Illness

Medical Science

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ABSTRACT

Background: Acute illness has profound effect on the body milieu. Of interest is the serum albumin level which gets affected in severe illness and in turn may affect the disease outcome.
Objectives: To assess the correlation of serum albumin with severity of acute febrile illness and with other markers of disease severity like hypotension, acute kidney injury, need for ventilation, live function tests and haematological parameters and finally with disease outcome.
Materials and methodology: The present study was conducted on 100 patients of acute febrile illness of more than seven days duration regardless of aetiology admitted at Government Medical College, Amritsar. Serum albumin levels and other markers of organ failure like hypotension, kidney failure, need for ventilatory support, deranged liver function tests, thrombocytopenia, leucocytosis, ESR, duration of hospital stay and overall mortality were recorded and their correlation was analysed statistically.
Summary and conclusion: Mean serum albumin was low in severely ill patients at presentation (<3.5g/dl) which improved with recovery of the patient indicating that hypoalbuminemia was the result of the illness. Albumin levels showed statistically significant correlation with hypotension, acute kidney dysfunction and the requirement of ventilator support. It failed to show significant association with the presence of thrombocytopenia, length of hospital stay and mortality.

INTRODUCTION

Serum albumin levels are one of the several clinical parameters used to assess status of general health. Hypoalbuminemia frequently occurs in acute medical illness but its clinical significance is not well known. A decrease in serum albumin concentration is almost inevitable finding in severe diseased states and albumin concentration may be a marker for subclinical disease in elderly patient. Large community based studies have shown a link between serum albumin and an increase in morbidity and mortality.[1] Further hypoalbuminemia is associated with increase in length of hospital stay, higher complication rates and higher mortality, increased length of stay in ICU and ventilator dependcy.[2,3,4] The purpose of the study was evaluate a similar relationship.

MATERIAL AND METHODS

This study was conducted on 100 patients, between the age group of 18 to 60 years with an acute febrile medical illness admitted in various medical wards of Guru Nanak Dev Hospital and Government Medical College, Amritsar. Only patients with an acute febrile illness of not more than 7 days duration along with organ dysfunction were included in the study. Serum albumin levels and various markers of organ dysfunction were recorded at the time of admission and in recovered patients. Serum albumin was repeated at their first follow up visit within 21 days.

EXCLUSION CRITERIA

Patients with age <18 years and 60 years and with pre-existing co-morbid conditions like chronic liver disease, congestive heart failure, chronic kidney disease, malabsorption, malnutrition, pregnancy, chronic infections like tuberculosis, burns, and known malignancy were excluded from the study. Those who received albumin/plasma transfusions were not included.

Criteria Used To Define Organ System Involvement Was As Follows

CARDIOVASCULAR SYSTEM

Systolic blood pressure <90 mmHg despite adequate fluid resuscitation or need for vasopressor to maintain systolic BP >90 mm of Hg

RENAL SYSTEM

Urine output <0.5ml/kg or <30ml/hour or serum creatinine >2mg/dl.

HEPATOBILIARY SYSTEM
Serum bilirubin >2mg/dl or
Raised AST and ALT >2 times upper limit of normal.
Prolonged prothrombin time >6 secs
RESPIRATORY SYSTEM

PaO2 70mm of Hg or O2 saturation <90% pulse oximetry in room air or PaO2/FiO2 >250

In all the patients satisfying the above mention criteria following parameter were determined: symptoms and clinical signs, serum albumin, haemoglobin, hematocrit, total leukocyte count, ESR, serum creatinine, serum bilirubin, aspartate aminotransferase (AST/SGOT) and alanine aminotransferase (ALT/SGPT). Patient were monitored for development of hypotension, renal failure, need for ventilator support, increased serum bilirubin, increased AST/ALT, thrombocytopenia, leukocytosis, duration of stay in hospital and the final outcome or mortality. Patients were divided into three severity groups based on admission level of serum albumin:

Group 1   -   < or 2.4 gm/dl
Group 2   -   2.5 to 2.9 gm/dl
Group 3   -   > 3gm/dl

Clinical and laboratory data was then compared among these groups. In patients with complete recovery serum albumin was repeated at the first outpatient follow up within 21 days.

The parameters representing severity of acute illness included in our study was hypotension, acute renal failure, need for ventilator support, increased bilirubin, increased AST/ALT, thrombocytopenia, leukocytosis, ESR, duration of stay in hospital and overall mortality.

OBSERVATIONS

The following results were observed from the prospective study study of 100 patients suffering from acute febrile illness, regardless of etiology of the disease. Patients were categorized on the basis of serum albumin levels and time admission and were evaluated for any organ system dysfunction. After discharge patient's serum albumin was also checked after 21 days of follow up.

Mean age of study population was found to be 33.78 years. 66 patients were between 18-40 years of age 19 were between 41-50 years and 15 were between 51-70 years. 71 were males and 39 were females in study group.

Hypotension was found in 8% of patients. In hematological parameters, mean hemoglobin was found to be 11.12gm%, mean TLC was 7,764/mm3 and mean platelet count was found to be 97662/mm3. In biochemical parameters, mean serum bilirubin was 2.13mg/dl, SGOT and SGPT were 160 & 143 IU/L respectively. Total serum protein and albumin were 6.16 and 3.78 g/dl respectively. 16% of total patients had deranged renal function. 5% of patients required ventilator support during hospital course and 4% of patients from study group died. Mean hospital stay was of 6.56 days and follow up serum albumin of survivors was 3.56g/dl

Patients were divided into various groups according to serum albumin levels (g/dl) as depicted in table 1.

Group	S. Albumin [gm/dL]	No. of patients
I	< 2.4	16
II	2.5-3.0	28
III	> 3.0	66

Out of 100 patients of acute febrile illness, 16 patients had albumin levels < 2.4 g/dl, 28 had level between 2.5-2.9 g/dl and 66 patients had levels > 3.0 g/dl.

Maximum number comprised of dengue with half of the study population suffering from it. Eight had malaria with one such patient developing superadded infection in the form of pneumonia and eventually sepsis. Nine patients had enteric fever, 15 suffered from systemic viral illness in whom diagnosis was made after reasonably excluding common bacterial, viral and parasitic illness by appropriate testing. Total 19 patients suffered from bacterial infection out of which 13 had evidence of septicemia.

On follow up all patients showed a significant increase in albumin levels with a statistical significant p-value of 0.029. Thus a drop in serum albumin is almost an invariable accompaniment of a severe acute febrile illness. [Table-2]

Table 2 – Mean serum albumin at admission and on follow up.			
Group	Mean serum albumin at admission	Mean serum albumin on follow up	P value
I	2.24	2.57	
II	2.78	3.26	
III	3.58	3.85	0.029
Total	3.22	3.56	

Serum albumin levels at admission were correlated with the following variables to see whether these correlate with morbidity and mortality.

1. Hypotension
2. Renal dysfunction
3. Need for ventilator support
4. Mortality
5. Mean duration of illness
6. Other hematological and biochemical parameter.

There was a statistically significant correlation of lower se-

rum albumin levels with the presence of hypotension (p value <0.001), renal dysfunction (p value <0.001) and the need for ventilator support (p value 0.018).

However albumin levels did not show a direct statistical correlation with duration of hospital stay (p value 0.11) and mortality (p value 0.12). However the percentage of patients who died were higher in group I, who had the lowest serum albumin.

Table 3 – Relationship of serum albumin with various laboratory parameters				
	Group I	Group II	Group III	P value
Hb (gm/dL)	8.7	11.0	12.0	<0.001
TLC (/mm³)	15600	4450	4250	<0.001
Platelet count (/mm³)	81000	90000	73500	0.994
S. bilirubin (mg/dL)	2.35	2.08	2.03	<0.001
SGOT (IU/L)	151	140	130	0.069
SGPT (IU/L)	141	129	137	0.165

Table 3 shows relationship between serum albumin groups and median values of Hb, TLC, platelet count, serum bilirubin, SGOT and SGPT. Low serum albumin was associated with lower Hb, higher TLC and higher serum bilirubin and the correlation was statistically significant. However no correlation was found when albumin groups were compared with platelet count, SGOT and SGPT.

DISCUSSION

This study was done as it has been noted that hypoalbuminemia was not an uncommon occurrence in individuals with a short febrile illness without pre-exiting disease. In the study only febrile illness of < 7 days were included to decrease any confounding variable like decreased food intake which could affect albumin levels. 7 days was chosen as half-life of albumin is normally 19 days.5,6,7

Study population included was between 18-60 years in order to avoid influence of age on albumin levels. Albumin levels are known to decrease by 9.7% for each decade after 60 years of age.8,9 The majority of patients in our study were in 18-40 years group (66%). The data shows that hypoalbuminemia frequently occurred in acute febrile medical illness and was seen in 74% of the study population, in whom serum albumin was found to be < 3.5 g/dl. This is much higher evidence that one would usually expect and probably reflects the severe nature of the disease they had.

To prove that hypoalbuminemia has occurred as part of acute febrile illness the patients were followed up after discharge from hospital when they had there repeat albumin checked. This showed statistically significant increase from low albumin levels. Mean albumin at admission was 3.22 g/dl and at follow up was 3.56 g/dl (p<0.029). Even patient who had normal albumin levels during admission showed an increase on follow up. This again suggests that the significant decrease in albumin levels is a common occurrence in severe acute febrile illness.10,11,12,13

Hemodynamic alterations leading to hypotension and shock have been well characterized in patients with acute illness. These alterations appear to be the consequence of widespread vascular dysfunction; including impaired vascular tone and increased vascular permeability.14 Marked capillary congestion and episodes of hypotension reflect the impairment of vascular tone, while retroperitoneal edema, pleural effusion, ascites and pericardial effusions reflect vascular leakage due to increased vascular permeability. Beside these direct factors acute renal failure, leucocytosis, anemia, abnormal liver functions are well known abnormalities seen in acute febrile illness.

The study looked at the relationship of the levels of serum albu-

min and altered clinical & biochemical parameters representing the severity of disease. To evaluate this, patients were grouped into 3 groups. These were compared regarding morbidity parameters like hypotension, renal dysfunction etc. Group 1 had greater incidence of hypotension, need for ventilator support, renal dysfunction and mortality than groups 2 and 3.this simply suggests that morbidity of illness as manifested by parameters like hypotension (p<0.001), need for ventilator support (P=0.018) had statistical correlation with severity of hypoalbuminemia.

A similar conclusion was reached in a Corchrane meta-analysis done in ICU patients that had collected data from 291,433 patients in medical and surgical ICUs and showed that hypoalbuminemia at admission was a good outcome predictor.15 However this Cochrane meta-analysis was done on a heterogeneous group of patients and the only criteria was the need for ICU admission. Patients with coexisting diseases like renal failure, liver failure and others were also not excluded.

Study from South Korea in patients with Hanta Virus renal syndrome which showed statistical correlation of hypoalbuminemia with morbidity, length of hospitalization, liver enzymes and mortality.16 The problem with Hanta virus renal disease is that it is a condition which primarily involves the kidneys and therefore it would not be surprising that the serum albumin levels were more likely to be a reflection of proteinuria rather than the severity of systemic illness.

In our study hypotension, need for ventilator support and renal failure correlated statistical with the severity of hypoalbuminemia. There was no good correlation with mortality but in crude terms the incidence was higher in Group 1 which had the lowest serum albumin levels. The overall mortality in the entire group was 12.5%.It is possible that if series were larger a statistical correlation with mortality might also have been detected. Similar findings were obtained from a study done in southern part of Indian subcontinent where also hypotension, need for ventilator support and renal failure were statistical correlated with severity of hypoalbuminemia.17

Our study did not show correlation with other parameters of morbidity like length of hospitalization (p=0.11), raised liver enzymes (p=0.165) and low platelet counts (p=0.994). This could partly be due to the fact that, the study population was a miscellaneous bag of illness, ranging from viral illness like dengue to bacterial sepsis and severe malaria. Each of these diseases is likely to have different presentations that predominate and could have affected the overall interpretations of these individual parameters. This finding of ours were in correlation with those done by Vijapur et al.17

Studies have shown that serum concentration of less than 3.4 gm/dl was associated with 30 day mortality rate of 24.6% which increased further to 62% when serum albumin fell below 2gm/dl or less.4 Hypoalbuminemia at admission was important marker for outcome and found to be strong predictor of poor outcome.15,18,19

Serum albumin level at the onset of fever and the reduction rate in serum albumin level from the baseline to day eight after onset of febrile illness were predictive of mortality with 30 day of fever. When examining febrile, elderly patients, checking serum albumin level is useful for determining which patients are at high risk.20

Study conducted in India on 121 patients where prevalence of hypoalbuminemia in acute febrile illness was found to be 97.5% (albumin< 3.5 gm/dl) at admission with a mean admission albumin level of 2.7gm/dl the patient with low albumin level had more incidence of hypotension, renal failure & requirement of

ventilator support during hospital stay and all showed improvement in albumin level with a mean albumin 3.5 gm/dl on follow up.17

SUMMARY AND CONCLUSION

74% of the patients with an acute severe illness as manifested by hypotension or dysfunction of organ systems had hypoalbuminemia < 3.5 g/dl at presentation. Mean albumin level at admission was 3.22g/dl. All patients who came for follow up showed good improvement in their albumin levels compared to their baseline admission values. This recovery to normal albumin levels clearly indicates that the hypoalbuminemia was the result of acute febrile illness. The serum albumin levels at admission showed a statistical correlation with important markers of morbidity like hypotension, renal dysfunction and need for ventilator support. There was less direct correlation with other indicators of disease severity like thrombocytopenia, transaminases levels, and length of hospitalization or mortality. Admission serum albumin appears to be a simple marker of disease severity in patients with acute febrile illness.

Ideally it would have been better to look and see if hypoalbuminemia correlated with some of these indices in each individual disease. This was not done, as the numbers for each individual disease was small once the strict exclusion criteria were applied. It therefore appears that a simple test like an albumin level at admission is a good indicator of severity of disease in individual with short febrile illness and could be a useful prognostic marker. It is a reflection of the extent of the disease process and the pathological effects seen in severe disease. It is clearly the effect of disease and not the cause as is shown by prompt improvement on recovery. Recovery to normal albumin levels is also probably a good indicator of patient's recovery from acute illness.

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