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ORIGINAL ARTICLE

Serum Albumin Level as a Prognostic Tool: A Clinico-Biochemical Study

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Abstract

Background: The correlation between hypoalbuminemia and Acute Febrile Medical Illness has not been extensively investigated in prospective controlled studies and only a few studies are available in the world literature. Seeing paucity of such a research in India, especially in North India, the present study was undertaken. **Methods**: In this study 60 patients suffering from Acute Febrile Medical Illness having fever of 38°C or higher and of less than seven days duration were taken. As per criteria, study patients who besides having Acute Febrile Medical Illness also had at least two organ dysfunctions while those with pre-existing co- morbidities were excluded. On admission, investigation for serum albumin and other markers of organ dysfunction were done and the results recorded. Patients were divided on the basis of baseline serum albumin level into group I (d" 2.4 g/dl) and Group II (e"2.5 g/dl). On recovery, serum albumin was again estimated at their first follow up. **Results:** Hypoalbuminemia (Serum albumin d"3.5 g//dl) was seen in 90% of the study population with 2.99± 0.52 g/dl of Mean S. Albumin on admission. All the survivors, on the first follow up showed an appreciable improvement in albumin levels with a mean serum albumin level of 3.73 ± 0.31g/dl with a statistically highly significant p-value ($p<0.001$). Group I patients compared to Group II showed significant differences in hypotension, renal dysfunction and mean Hemoglobin values. However, the difference between group I and II regarding the need for ventilatory support, mean duration of hospitalization and mortality was appreciable but not significant statistically. **Conclusions**: Hypoalbuminemia, invariably, is an accompaniment to Acute Febrile Medical Illness and the level of serum albumin is inversely proportional to the severity of this illness.

Key words: Hypoalbuminemia, Acute Febrile Medical Illness, Predictor, Prognostic Tool

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Introduction

It is observed that hypo-albuminemia, a decrease in serum albumin concentration, is consistently found to accompany severe diseased conditions. Review of literature shows that estimation of serum albumin alone in diseased conditions could act as predictor of mortality in many clinical conditions [1]. A link has been shown to exist between low serum albumin level and an increase in morbidity and mortality [2]. Serum albumin estimation in elderly patients could be an indicator of subclinical disease. Hypo-albuminemia is found to be associated with higher complication rates, increased length of hospital stays and higher mortality in studies of hospitalized patients [3]. Serum albumin estimation have prognostic value also in critically ill patients [4,5]. Hypo-albuminemia is associated with ventilator dependency, increased length of hospitalization and development of new infection [6].

The purpose of this study was to evaluate if serum albumin level could also serve as another marker of disease severity as well as a prognostic tool in patients suffering from Acute Febrile Medical Illness.

Materials and Methods

In this study 60 patients suffering Acute Febrile Medical Illness admitted from time to time in Medical Wards as well as ICU of SGT Medical college and Hospital, Gurugram were taken up for study**.** Only those patients who fulfilled the study criteria were chosen and admitted.

Selection of Patients

Selection of the patients was done as per the study criteria for inclusion and exclusion which was as follows:

Inclusion Criteria

1. Patients included were in the age group of 18-60 years
2. Patients with fever e" 38°C
3. Febrile duration < 7 days
4. Acute Febrile Medical Illness patients having at least two organ dysfunctions as well.

Criteria used to define organ system involvement were as follows:

Cardiovascular System

Systolic BP<90 mm Hg and Diastolic Pressure < 60 mm Hg despite requisite measures to maintain blood pressure.

Respiratory System

PaO2 < 70mm of Hg or oxygen saturation < 90% on pulse oximetry in room air or PaO2 / Fi O2 < 250.

Renal System

Urine output <0.5ml/kg or <30 ml / hour despite requisite measures or Serum Creatinine >2 mg dl.

Hepatobiliary System

Serum total bilirubin > 2mg/dl or AST > 80 U/L (>twice the upper limit of normal) and / or ALT > 112 U/L (> twice the upper limit of normal) or Prothrombin Time > 6 seconds

Hematological System

WBC < 4,000/cumm or >12,000/cumm or ESR >15mm / Ist hr. or Platelet count <1,00,000/cumm

Exclusion Criteria

Patients excluded were those who had any of the pre-existing co-morbidities like Chronic liver disease, Chronic kidney disease, Chronic infection, Malabsorption, Malnutrition, Burns and Pregnancy.

On admission written consent for the study was taken from the family, a detailed history of the patients taken, thorough clinical examination and laboratory investigations done and findings recorded on the Clinical Proforma.

Laboratory investigations included Hemoglobin estimation, Haematocrit values, Platelet and Leucocyte counts, Prothrombin time, Serum albumin, Serum total bilirubin, Blood urea, Serum creatinine, AST & ALT. Reports of the laboratory investigations were recorded on the proforma.

Monitoring was then done by watching the signs of disease-severity on the basis of the altered laboratory values as mentioned with the disease .We monitored Anaemia (Hemoglobin level < 13g/dl in men and < 12gdl in women), Leucocytosis (> 12000 /ml WBCs) , Thrombocytopenia (< 100,000 / ml platelets) , Prolonged Prothrombin time (> 6 seconds), Increased Total Bilirubin (> 2 mg/dl), Increased AST / ALT (AST > 80 U /L , ALT > 112 U/L), Hypotension (Systolic Pressure < 90 mmHg , Diastolic Pressure < 60mm Hg) , Renal Dysfunction (Urine output < 0.5ml/Kg or <30ml/hour &/or Serum creatinine > 2 mg / dl) , Need for Ventilatory Support , mean duration of Hospitalization and Mortality if any. For the purpose of evaluation, study population was divided into two severity groups based on their serum albumin levels at the time of admission:

Group I d” 2.4 g/dl

Group II e”2.5 g/dl

On recovery, serum albumin estimation was repeated on the first follow up within 21 days. On completion of the Clinico-Biochemical study, all the data so obtained were then compared among these two groups and statistically analyzed.

Statistical Analysis:

The results were initially assessed with mean, range and standard deviation measures. Suitable percentage and proportion expression were also recorded. The parametric variables were analyzed using Student “t” test (independent for different groups) and paired t test (for dependent variables) and the results were expressed as significant if p value was less than 0.05.

Study Outcome Measure

Outcome measure was assessed in terms of difference in serum albumin levels at the time of admission as well as at the time of discharge and between group I and group II.

Ethical Consideration

An informed written consent was taken from the attendants of the patients selected for this study after explaining them the purpose and procedure of the study. They were told that their participation was entirely voluntary and even if they choose not to participate, they will still get the same treatment. They were told that they were free to stop participating even if they change their mind later. They were apprised that the outcome of the study may be of benefit to them and other patients with alike disease. The participating subjects were ensured that their identity would not be shared and the information so collected about them during the study would be kept confidential. They were also informed that data so generated from the study would only be published without divulging their identity.

Results

Hypoalbuminemia (Serum albumin d”3.5 g /dl) was seen in 90% of the study population with 2.99± 0.52 g /dl of Mean S. Albumin on admission while only 6 patients had a serum albumin more than 3.5gm /dl. Only 25% of study population was found to have d” 2.4 g /dl serum albumin (Group I) while rest of the 75% study population had e” 2.5 g /dl serum albumin (Group II). Forty-two patients (70% of study population) were in the age group of 18-40 years and eighteen patients (30% of study population) were in the age group of 41-60 years. Sex distribution showed 73.4% males and 26.6% females. The causes of acute febrile medical illness in the study population were Systemic Viral Illness in 23.33 %, Dengue in 20%, Sepsis in 16.67%, Enteric fever and Malaria in 10% each, UTI in 8.33%, Pneumonia in 6.67% and Meningitis in 5%.

The study population showed mean values of age (in years) as 33.55 ± 12.32, Mean S. Albumin on admission (g /dl) as 2.99± 0.52 and on follow up as 3.73 ± 0.31, Hemoglobin (gm %) as 12.26 ± 2.66, TLC (/cumm) as 13251.67 ± 12, Platelet Count (/cumm) as 162350 ± 103807, ESR as 23.60 ± 15.44, S. Bilirubin (mg/dl) as 1.71 ± 3.02, AST (IU/L) as 275.88 ±613.46, ALT (IU/L) as 257.05 ± 655.11, Total Protein (g/dl) as 6.37 ± 0.83, Hypotension as 33.3%, Renal Dysfunction as 16.7%, Ventilatory Support as 15 %, Mean number of days in hospital as 7.18 ± 6.62and Mortality as 3.3 %.

All the survivors, on the first follow up showed an appreciable improvement in S. Albumin level which rose from Mean S. Albumin of 2.99 g /dl on admission to 3.67 g /dl on follow up with a statistically highly significant p-value (p<0.001). In Group I mean serum albumin rose from 2.22 g /dl to 3.65 g /dl and in Group II from 3.25 g /dl to 3.76g /dl. Here again p-value being (p<0.001) was highly significant statistically (Table1 and Figure 2).

On comparative analysis of the two groups with other parameters showing disease severity, Group I patients as compared to Group II showed statistically significant differences in Hypotension as 73.33% vs. 20%, p- 0.001(Figure 3) and renal dysfunction as 40% vs. 8.88 %, p- 0.005 (Figures 3 & 4). The difference between the

mean Hemoglobin values among group 1 and 2 was also found to be statistically significant with p value of <0.001. However, the difference in mean values of TLC, platelet count, S Bilirubin, AST/ ALT was not found to be significant statistically (Table 2 and Figure 5).

However, the difference between group I and II regarding the need for ventilatory support was 33.33% % vs.8.88 % p-0.022, for mean duration of hospitalization in days was 9.53 vs. 6.40, p-value 0.113 and for mortality was 6.66 % vs. 2.22% & p-value 0.406 was appreciable but not statistically significant.

Table 1: Graph showing Group wise Albumin Levels on Admission & Follow-up.

Group	Mean S. Albumin at admission (g/dl)	Mean S. Albumin at follow-up (g/dl)	P-value
I	2.22	3.65	
II	3.25	3.76	<0.001
Total	2.99	3.67	

Statistical Test applied: Student t test

Table 2: Relationship between serum albumin groups and Median values of Haematological and Biochemical parameters.

	Group I	Group II	p-value
Hemoglobin (gm%)	9.987	13.013	<0.001
TLC (/cumm)	16600.00	12135.56	0.211
Platelet Count (/cumm)	127600.00	173933.33	0.136
S. Bilirubin (mg/dl)	1.5533	1.7669	0.815
AST (IU/L)	207.00	298.84	0.620
ALT (IU/L)	106.67	307.18	0.309

Statistical Test applied: Student t test

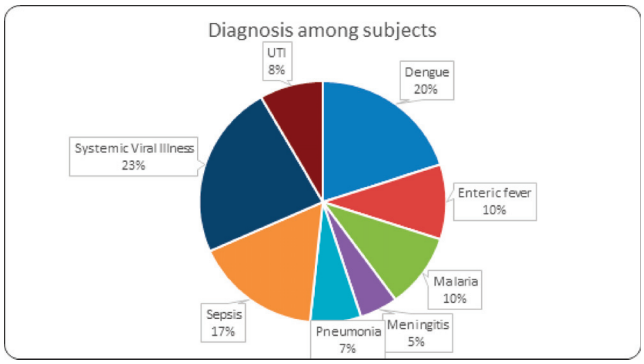

Fig.1: Pie graph showing diagnosis percentage in study population

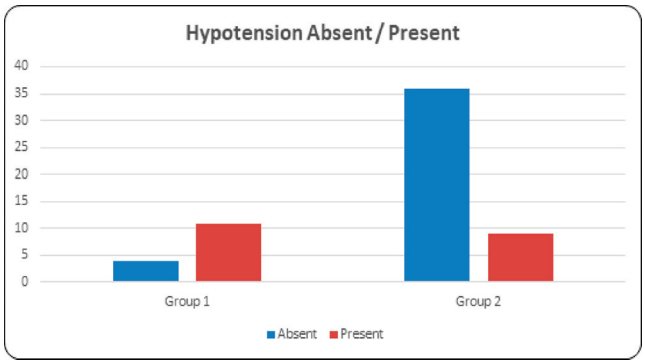

Figure 3: Relationship between serum albumin groups and Hypotension

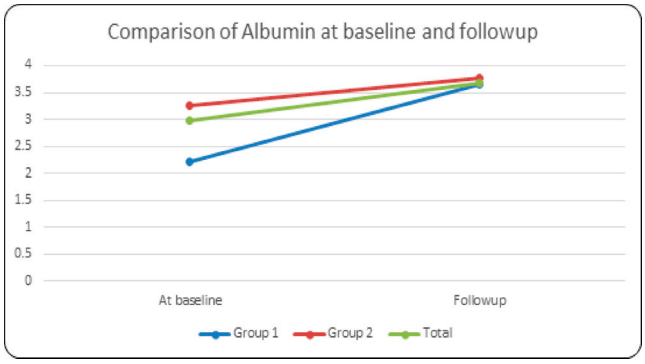

Fig. 2: Line graph showing group wise improvement in Albumin level on recovery in Group I, Group II and total study population

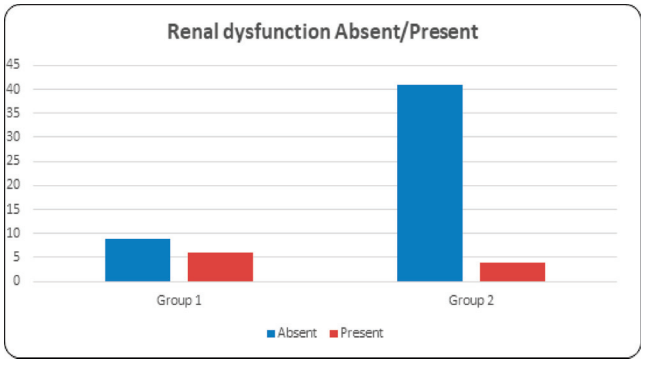

Fig. 4: Relationship between serum albumin groups and Renal Dysfunction

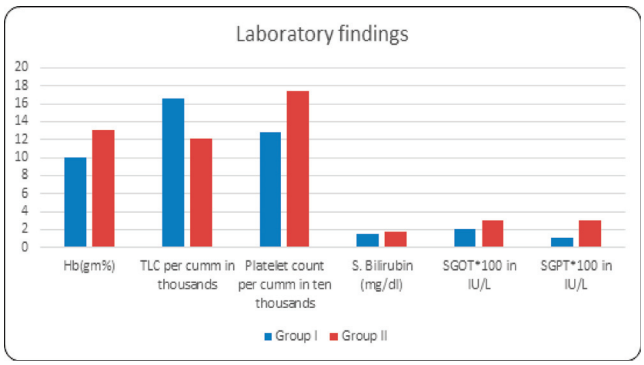

Fig. 5: Relationship between serum albumin groups and Median values of Hematologicaland Biochemical parameters

Discussion

Hypoalbuminemia is found to be related to complications and mortality in cases of acute infectious diseases [7]. Likewise, hypoalbuminemia was seen in about 25%-69.2 % of patients suffering from scrub typhus [8,9]. A similar study in scrub typhus patients by Chang-Seop Lee et al [10,11] showed a close relation between hypoalbuminemia and a higher rate of complications which required more efficient medical management and a longer hospital stay and thus raising the treatment cost. A study on cases of Hanta virus renal syndrome, revealed statistically significant correlation between hypoalbuminemia and parameters of morbidity like liver enzymes, length of hospital stays and mortality. However, in these cases kidneys were diseased and hence hypoalbuminemia could have been due to proteinurea and not because of the severity of systemic illness [12]. However, we excluded the patients having co-morbidities from our study population to evade the interference of factors which could affect the serum albumin levels.

Even though relation between hypoalbuminemia and many diseases has been studied but its correlation with fever, such a commonly presenting complaint, has not been extensively studied, more so in North India. Hence, the study was conducted on individuals suffering from fever and to be more precise on individuals suffering from Acute Febrile Medical Illness. It has been postulated that hypoalbuminemia occurs as a result of decreased synthesis of albumin due to hepatic dysfunction, increased catabolism of protein, decreased intestinal absorption of protein due to poor oral intake, extensive vascular leakage of serum protein due to increased capillary permeability and albuminuria [13]. Hypoalbuminemia is quite commonly seen in critically ill patients where it appears to be due to increased albumin losses through bleeding from the gastrointestinal tract [14], a redistribution of albumin from the intravascular to the interstitial space due to increased capillary permeability [15] and dilution owing to intravenous fluid administration. As we excluded co-morbidities and the factors that could influence the intake and metabolism of albumin, the mechanism that results hypoalbuminemia in Acute Febrile Medical Illness appears to be the result of vascular changes like increased vascular permeability and impaired vascular tone which is accomplished by inflammatory mediators and endotoxins as also reported by Moshage et al [11]. To evade the influence of variables like insufficient food intake which could impact the albumin levels, patients suffering from Acute Febrile Medical Illness of less than 7 days duration only were taken up for study. Another ground for choosing patients of short duration fever was the fact that half-life of albumin is 19 days [16-18]. To nullify the effect of age on serum albumin levels, study was carried out on patients between the age group of 18-60 years only because serum albumin levels decrease by 9.7 % for each decade after 60 years of age [19,20]. Seventy percent of patients in our study were in the age group of 18-40 years where we could anticipate good albumin levels. As per study criteria patients suffering from Acute Febrile Medical Illness with at least two organ dysfunctions were included and those with pre-existing co- morbidities were excluded from the study.

In our study 25% patients had serum albumin d" 2.4 g/dl, 65% had albumin 2.5-3.5 g/dl and 10% had albumin > 3.5 g/dl. Hypoalbuminemia (Serum albumin d"3.5 g//dl) was seen in 90% of our study population while only 6 patients had a serum albumin level more than 3.5gm/dl. Such a high prevalence of hypoalbuminemia in patients with short duration of Acute Febrile Medical Illness unaccompanied by any pre-existing co-morbidity was indicative of severe nature of the disease under study. Prevalence of hypoalbuminemia in as high as 90% of our study population suffering from Acute Febrile Medical Illness prompted us to investigate if hypoalbuminemia is an accompaniment to Acute Febrile Medical Illness. To prove our observation, serum albumin estimation was repeated in the recovered patients on their first post-hospitalization follow up within 21 days. It was quite surprising to find that serum albumin level had appreciably increased in all the recovered patients from their baseline levels irrespective whether they were hypo- albuminic or normo-albuminic. On recovery, the mean baseline serum albumin level of 2.22 g / dl rose to mean serum albumin level of 3.65 g /dl in group I study population and likewise in the group II study population it rose from 3.25 g /dl to 3.76 g /dl. Thus, all the patients showed a significant increase in albumin levels on recovery with a statistically highly significant p-value p<0.001). Prevalence of hypoalbuminemia in majority (90%) of patients of the study population which disappeared on recovery proves that hypoalbuminemia, invariably, is an integral accompaniment to Acute Febrile Medical Illness.

Further, to investigate if any correlation exists between levels of serum albumin and disease-severity , the study population was divided on the basis of baseline serum albumin levels, into two groups and both the groups were compared with disease severity parameters namely hypotension, renal dysfunction, liver dysfunction, need for ventilatory support, mean duration of hospitalization, haematological and biochemical investigations like haemoglobin, TLC , platelet count , serum bilirubin, AST, ALT and mortality.

In our study, Group I patients compared to Group II patients showed significant differences in hypotension (73.33% vs. 20%, p< 0.001) and renal dysfunction (40% vs. 8.88%, p- 0.005). The difference between the mean Haemoglobin values among group I and II (9.99 vs. 13.01, p<0.001) was also found to be highly significant statistically with p value of<0.001. However, the difference between group I and II regarding need for Ventilatory Support (33.33% % vs. 8.88% p- 0.022), mean duration of hospitalization (9.53 vs. 6.40, p- 0.113) and mortality (6.66 % vs. 2.22%, p-o.406) was appreciable but not statistically significant.

In our study hypotension, renal failure and hemoglobin level correlated statistically with the severity of hypoalbuminaemia. Though the relationship of serum albumin level with the need for ventilatory support, mean days of hospitalization and mortality was not statistically significant but grossly the incidence was higher in Group I which had the lowest serum albumin levels. Our study also did not show statistically significant correlation with other parameters of morbidity like raised liver enzymes and low platelet counts. This could possibly be due to the fact that our study

population was not debilitated enough to have baseline serum albumin level as low as which could have statistically significant influence on parameters like ventilatory support, mean duration of hospitalization, mortality and parameters of morbidity like raised liver enzymes and low platelet counts.

Our study differs in regard to need for ventilatory support which was lesser and the mean duration of hospitalization again was shorter than the results of a nearly similar study from South India by Vijapur and Varghese [21]. This difference seems to be due to comparatively lower baseline serum albumin levels of the patients of the above study reported which resulted in more severity of disease in them necessitating higher need for ventilatory support and longer hospitalization and this very well corroborates with our observations that level of serum albumin is inversely proportional to severity of illness. Our study also gets reinforced from another study done on indoor patients of medical and surgical ICUs wherein hypoalbuminemia showed a good outcome predictor at admission and the level of serum albumin correlated with other conventional markers of severity [12].

Limitation of our study is that it was conducted on a group of heterogeneous diseases presenting with Acute Febrile Medical Illness. Had the study been conducted separately on individual disease, there could have been better overall interpretations of these individual parameters. A similar study on individual diseases with Acute Febrile Medical Illness is recommended. However, authors have already started a retrospective study on individual diseases.

To sum up, hypoalbuminemia in our study significantly correlated with parameters of morbidity like hypotension, renal dysfunction and parameter of disease severity like Anaemia. Though not significant statistically, still the incidence of need for ventilatory support, mean duration of hospitalization and mortality was much higher in group I than in group II. We infer from our study that hypoalbuminemia, invariably, is an integral accompaniment to Acute Febrile Medical Illness and its level correlates with severity of disease and thus it can predict the severity of disease and can also serve as a prognostic tool to gauge the severity of disease in Acute Febrile Medical Illness and our observations are in consonance with many other studies [11,12,22-25].

Conclusion

From our observations of high prevalence of hypoalbuminemia in Acute Febrile Medical Illness at the start of illness and its disappearance on recovery, we conclude that hypoalbuminemia, invariably, is an integral accompaniment to Acute Febrile Medical Illness and there undoubtedly, exists a correlation between level of serum albumin and severity of disease. The level of serum albumin is inversely proportional to the severity of this illness The serum albumin level thus, can serve as another marker of disease severity as well as a prognostic predictor like conventional markers of disease severity in patients suffering from Acute Febrile Medical Illness. From our study we infer that a simple test like serum albumin estimation on the outset of the disease can serve as a predictor as well as a prognostic tool to anticipate the severity of disease.

Conflict of Interest:	Author declare no COI
Ethics:	There is no ethical violation as it is based on voluntary anonymous interviews
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