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Original Research Article

STUDY OF SERUM PROTEIN LEVEL AS A PROGNOSTIC INDICATOR OF ACUTE ISCHEMIC THROMBOEMBOLIC STROKE

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ABSTRACT

Background: Acute ischemic stroke is a major cause of mortality and disability. Early identification of patients at risk of poor outcome is essential. Serum albumin, a readily available biochemical marker with nutritional and potentially neuroprotective properties, may have prognostic value in acute ischemic stroke. The objective is to evaluate the association between admission serum albumin levels and stroke severity and 90-day functional outcome in patients with acute ischemic stroke, and to identify other clinical factors associated with prognosis.
Materials and Methods: This longitudinal observational study included 100 patients with first-ever acute ischemic stroke presenting within 72 hours of symptom onset. Serum albumin was measured at admission using the Bromocresol Green method. Stroke severity was assessed using the Scandinavian Stroke Scale (SSS) and level of consciousness using the Glasgow Coma Scale (GCS). Functional outcome was assessed at 90 days using the Modified Rankin Scale (mRS). Associations were evaluated using ANOVA and Kruskal–Wallis tests, with $p<0.05$ considered statistically significant.
Results: Severe disability was observed in 29% of patients and 25% died by 90 days. Serum albumin was significantly associated with functional outcome ($p=0.001$), with mean levels of 4.24±0.27, 4.05±0.42, 3.31±0.65, and 2.90±0.51 in patients with mild, moderate, severe disability, and death, respectively. Albumin was also significantly associated with SSS severity ($p=0.001$), with mean levels of 4.20±0.45, 3.90±0.65, and 3.34±0.68 in mild, moderate, and severe stroke, respectively. GCS was significantly associated with both albumin and functional outcome.
Conclusion: Lower admission serum albumin was significantly associated with greater stroke severity and poorer 90-day functional outcome. Serum albumin may therefore be a useful, simple prognostic marker for early risk stratification in acute ischemic stroke. Larger prospective studies are warranted to establish its independent prognostic value.
Keywords: Acute ischemic stroke; Serum albumin; Prognostic marker; Stroke severity; Functional outcome; Modified Rankin Scale; Scandinavian Stroke Scale; Glasgow Coma Scale.

INTRODUCTION

Stroke remains one of the leading causes of death and long-term disability worldwide, imposing a substantial burden on patients, families, and healthcare systems. Ischemic stroke, resulting from interruption of cerebral blood flow due to vascular occlusion, constitutes a major proportion of stroke-related morbidity and mortality. The World Health Organization defines stroke as the rapid development of clinical signs and symptoms of focal neurological dysfunction lasting more than 24 hours or leading to death, with no apparent cause other than vascular origin. The burden of stroke is particularly significant in low- and middle-income countries, where the majority of stroke-related deaths occur. In India,

ischemic stroke continues to contribute substantially to mortality and disability, emphasizing the need for early identification of patients at increased risk of poor outcomes.[1]

The clinical outcome following acute ischemic stroke is influenced by several factors, including age, stroke severity, level of consciousness, hyperglycemia, and the type and extent of cerebral injury. Although these factors are useful for prognostication, many are non-modifiable and therefore have limited potential for therapeutic intervention. Identification of additional, readily measurable and potentially modifiable biological markers may facilitate early risk stratification and allow clinicians to identify patients who require closer monitoring and more intensive management.[2]

Serum albumin is a major plasma protein with diverse physiological functions extending beyond the maintenance of oncotic pressure. It plays an important role in antioxidant activity, maintenance of endothelial integrity, modulation of inflammation, and regulation of vascular and cellular processes. Albumin has also demonstrated neuroprotective properties in experimental models of cerebral ischemia. In the setting of acute ischemic stroke, albumin may influence cerebral microcirculation by reducing erythrocyte aggregation, hematocrit, and erythrocyte sedimentation, while potentially limiting thrombosis, leukocyte adhesion, and microvascular stagnation during the early reperfusion phase. In addition, serum albumin serves as an indicator of nutritional and systemic health status, making it a potentially useful and readily accessible prognostic biomarker.[3]

Previous studies, particularly from Western populations, have reported an association between serum albumin levels at admission and outcomes following ischemic stroke. Lower albumin concentrations have been associated with greater stroke severity and poorer functional outcomes, while experimental evidence has suggested potential beneficial effects of albumin on infarct volume and cerebral edema. However, evidence regarding the prognostic significance of serum albumin in acute ischemic stroke remains limited in the Indian population. The available data are insufficient to establish its usefulness as an early prognostic marker in routine clinical practice.

Assessment of stroke severity at admission and functional outcome during follow-up provides an opportunity to evaluate the prognostic relevance of serum albumin. The Scandinavian Stroke Scale (SSS) can be used to quantify neurological severity at presentation, while the Modified Rankin Scale (mRS) provides a clinically relevant measure of functional disability during follow-up. In the present study, serum albumin measured at admission was evaluated in relation to initial stroke severity and functional outcome at 90 days among patients with first-ever acute ischemic stroke. The study also examined other clinical and biochemical factors that may influence prognosis.[4]

The present study was therefore undertaken to determine whether serum albumin level at admission can serve as a prognostic indicator of acute ischemic stroke and to assess its association with stroke severity and functional outcome at three months. Establishing a relationship between an easily measurable biochemical marker and subsequent functional outcome could contribute to early risk stratification and improve prognostic assessment in patients with acute ischemic stroke.

MATERIALS AND METHODS

Study Design and Setting: This observational longitudinal study was conducted at MNR Medical College & Hospital, Sangareddy, over a period of 18 months from May 2023 to October 2024. The study was undertaken after obtaining approval from the Institutional Ethics Committee of MNR Medical College & Hospital, Sangareddy. Written informed consent was obtained from the patients or their legally authorized representatives before enrolment.

Study Population: The study included 100 patients admitted to the medical wards with a first-ever acute ischemic stroke presenting within 72 hours of symptom onset. Patients were screened consecutively, and those fulfilling the predefined inclusion and exclusion criteria were enrolled in the study. In total, approximately 243 patients with a first-ever stroke were screened to obtain the final study population of 100 participants.

Inclusion Criteria

Patients were eligible for inclusion if they:

1. Had a clinical diagnosis of first-onset acute ischemic stroke.
2. Presented within 72 hours of onset of symptoms.
3. Had the clinical diagnosis confirmed by computed tomography (CT) of the brain.
4. Provided informed consent for participation in the study.

Exclusion Criteria

Patients were excluded if they had:

- Acute hemorrhagic stroke.
- Ischemic stroke with hemorrhagic transformation.
- Stroke secondary to an intracranial space-occupying lesion.
- A previous history of stroke.
- Presentation more than 72 hours after symptom onset.
- Diagnosed malignancy.
- Chronic liver disease.
- Chronic heart failure.
- Chronic kidney disease.
- Dementia.
- Fever or active infection.

Clinical Assessment: A detailed clinical history was obtained from the patient or accompanying attendants, followed by general physical examination, neurological examination, and examination of other relevant systems. Vital signs

were assessed and stabilized. CT imaging of the brain was performed to confirm ischemic stroke and exclude hemorrhage or intracranial mass lesions. Stroke severity at admission was assessed using the Scandinavian Stroke Scale (SSS).

The level of consciousness at presentation was assessed using the Glasgow Coma Scale (GCS). Relevant vascular risk factors and comorbidities, including systemic hypertension, type 2 diabetes mellitus, coronary artery disease, smoking, alcohol use, dyslipidemia, and rheumatic heart disease, were documented.

Laboratory Investigations: Baseline investigations included complete hemogram, erythrocyte sedimentation rate, blood glucose, renal function tests, liver function tests, serum proteins including albumin and globulin, lipid profile, and urine routine examination. Electrocardiography was performed to assess for evidence of coronary artery disease.

Serum albumin was measured at admission using the Bromocresol Green method. The admission serum albumin concentration was subsequently evaluated in relation to initial stroke severity and functional outcome.

Assessment of Stroke Severity and Functional **Outcome:** Stroke severity at admission was assessed using the Scandinavian Stroke Scale. Patients were categorized according to the severity of neurological impairment based on their SSS score.

Functional outcome was assessed 90 days after the onset of stroke using the Modified Rankin Scale (mRS). Follow-up assessment was performed either by direct clinical evaluation or through a telephone interview. The mRS was used to categorize the degree of residual disability and functional dependence following stroke.

Treatment and Follow-up: Following initial assessment and stabilization, patients received treatment according to the institutional treatment guidelines. Patients were followed for 90 days from the onset of stroke. The primary outcome assessment was based on functional status at 90 days, as measured by the Modified Rankin Scale.

Study Outcomes: The primary outcome was the association between serum albumin concentration at admission and functional outcome at 90 days, assessed using the Modified Rankin Scale.

Secondary outcomes included:

- Association between admission serum albumin and stroke severity as assessed by the Scandinavian Stroke Scale.
- Association between serum albumin and level of consciousness as assessed by the Glasgow Coma Scale.
- Association of clinical risk factors and comorbidities with functional outcome.
- Relationship between admission stroke severity and functional outcome at 90 days.

Statistical Analysis: The collected data were entered into a Microsoft Excel spreadsheet and subsequently analyzed statistically. Analysis was performed to determine the association between admission serum albumin concentration, stroke severity, and functional outcome at 90 days. Associations between other clinical and biochemical variables and outcome were also evaluated. Analysis of variance (ANOVA) and the Kruskal–Wallis test were used as appropriate. A p value of <0.05 was considered statistically significant.

RESULTS

A total of 100 patients with first-ever acute ischemic stroke presenting within 72 hours of symptom onset were included in the study. Patients were evaluated with respect to demographic characteristics, vascular risk factors, level of consciousness, stroke severity at admission, serum albumin concentration, and functional outcome at 90 days. Stroke severity was assessed using the Scandinavian Stroke Scale (SSS), while functional outcome was assessed using the Modified Rankin Scale (mRS). Severe disability was the most frequent outcome (29%), followed by death (25%). Overall, 52% of patients had severe disability or died by 90 days.

Table 1: Baseline Demographic Characteristics of the Study Population

Characteristic	n (%)
Age group (years)	
<40	13 (13)
41–50	22 (22)
51–60	24 (24)
61–70	20 (20)
>70	21 (21)
Sex	
Male	54 (54)
Female	46 (46)
Total	100 (100)

Note: The largest proportion of patients belonged to the 51–60-year age group (24%). The mean age of the study population was 57.66 ± 12.4 years, with an age range of 27–85 years.

Table 2: Distribution of Major Vascular Risk Factors

Risk factor	n (%)
Systemic hypertension	57 (57)
Type 2 diabetes mellitus	27 (27)

Both hypertension and diabetes	18 (18)
Addictive habits	32 (32)
Smoking among patients with addictive habits	26/32 (81)
Alcohol intake among patients with addictive habits	9/32 (28)

Note: Systemic hypertension was the most frequently reported major comorbidity (57%), followed by type 2 diabetes mellitus (27%). The study reported that 18% of participants had both hypertension and diabetes. Among the 32 patients with addictive habits, 81% were

Table 3: Glasgow Coma Scale and Scandinavian Stroke Scale at Admission and Its Association with Functional Outcome

.	Total n (%)	Mild disability	Moderate disability	Severe disability	Death
Mild	12 (12)	11	1	0	0
Moderate	45 (45)	12	18	15	0
Severe	43 (43)	0	4	14	25
Total	100 (100)	23	23	29	25
SSS category					
Mild (43–58)	6 (6)	6	0	0	0
Moderate (26–42)	36 (36)	17	12	7	0
Severe (0–25)	58 (58)	0	11	22	25
Total	100 (100)	23	23	29	25

GCS at presentation showed a statistically significant association with functional outcome at 90 days. All 25 deaths occurred among patients categorized as having severe impairment of consciousness.A statistically significant association was observed between stroke severity at admission and functional outcome at 90 days. Patients with severe stroke according to the SSS had substantially poorer outcomes.

Table 4: Serum Albumin Concentration According to Stroke Severity

Functional outcome	Mean serum albumin	SD
Mild disability	4.24	0.27
Moderate disability	4.05	0.42
Severe disability	3.31	0.65
Death	2.90	0.51
SSS category		
Mild	4.20	0.45
Moderate	3.90	0.65
Severe	3.34	0.68
GCS category		
Mild	4.23	0.18
Moderate	3.83	0.62
Severe	3.15	0.66
Functional outcome		
Mild disability	40.43	4.99
Moderate disability	25.13	7.11
Severe disability	19.34	9.73
Death	2.64	2.13

Admission serum albumin showed a statistically significant inverse relationship with the severity of disability. Mean serum albumin decreased progressively from 4.24 in patients with mild disability to 2.90 among patients who died.

Serum albumin decreased progressively with increasing stroke severity. Patients with severe stroke had a lower mean admission serum albumin concentration than those with mild or moderate stroke. A statistically significant association was observed between GCS category and admission serum albumin. Lower serum albumin levels were observed among patients with more severe impairment of consciousness.

Mean SSS scores decreased progressively with worsening functional outcome. The lowest mean SSS score was observed among patients who died.

Table 5: Association of Selected Clinical Variables with Functional Outcome

Variable	p-value	Interpretation
Age	0.144	Not significant
Sex	0.904	Not significant
Systemic hypertension	0.821	Not significant
Type 2 diabetes mellitus	0.403	Not significant
Addictive habits	0.844	Not significant
Glasgow Coma Scale	0.001	Significant
Scandinavian Stroke Scale	0.001	Significant
Serum albumin	0.001	Significant

Among the variables analyzed, GCS, SSS, and serum albumin demonstrated statistically significant associations with functional outcome at 90 days. Age, sex, hypertension, diabetes mellitus, and addictive habits did not show statistically significant associations.

DISCUSSION

Acute ischemic stroke is a major cause of mortality and long-term disability, and early identification of patients at risk of poor outcome is important for appropriate clinical management. The present study evaluated the association between admission serum albumin concentration, stroke severity, and functional outcome at 90 days in 100 patients with first-ever acute ischemic stroke. The principal finding was that lower serum albumin levels at admission were significantly associated with greater stroke severity and poorer functional outcome at 90 days. This observation supports the potential role of serum albumin as a simple and readily available prognostic biomarker in acute ischemic stroke.

Albumin has several physiological functions that may be relevant to the pathophysiology and outcome of acute ischemic stroke. In addition to maintaining plasma oncotic pressure, albumin has antioxidant, anti-inflammatory and vascular effects. Experimental studies have demonstrated neuroprotective effects of albumin in cerebral ischemia. The uploaded study also highlights the potential role of albumin in reducing erythrocyte aggregation, hematocrit and microvascular stagnation, as well as inhibiting leukocyte adhesion and thrombosis during the early reperfusion phase.

The findings of the present study are consistent with the observations of Dziedzic, Slowik and Szczudlik.[1] who evaluated 759 patients with acute ischemic stroke and found that patients with poor functional outcomes had significantly lower serum albumin levels. Their study demonstrated that serum albumin measured within 36 hours of stroke onset remained an independent predictor of poor outcome at three months, with higher albumin levels associated with a lower risk of poor outcome. This is comparable to the present study, in which mean serum albumin decreased progressively from 4.24 ± 0.27 in patients with mild disability to 3.31 ± 0.65 in those with severe disability and 2.90 ± 0.51 among patients who died (p = 0.001).

A similar relationship has been reported by Idicula et al,[3] in the Bergen Stroke Study. Their study, titled "Serum albumin in ischemic stroke patients: the higher the better," reported an association between higher serum albumin concentrations and better outcomes following ischemic stroke. The present findings are in agreement with this observation, demonstrating a progressive reduction in albumin concentration with worsening functional disability.

The association between serum albumin and initial stroke severity was another important finding of the present study. Mean albumin concentration was 4.20 ± 0.45 in patients with mild stroke, 3.90 ± 0.65 in those with moderate stroke, and 3.34 ± 0.68 in patients with severe stroke (p = 0.001). Thus, lower serum albumin was associated with greater neurological impairment at presentation.

These findings are consistent with the Indian study by Kasundra and Sood,[6] who evaluated serum albumin as a prognostic marker in acute ischemic stroke. They reported significantly lower serum albumin levels among patients with higher NIHSS scores and poorer short-term functional outcomes, concluding that serum albumin had prognostic significance in acute ischemic stroke. Similarly, Dash et al,[7] reported that serum albumin was associated with stroke severity and outcome in patients admitted with acute ischemic stroke, supporting its potential usefulness as an easily measurable prognostic marker.

The present study also demonstrated a significant association between serum albumin and level of consciousness at admission. Mean albumin was 4.23 ± 0.18 among patients with mild impairment of consciousness, compared with 3.83 ± 0.62 among those with moderate impairment and 3.15 ± 0.66 among those with severe impairment (p = 0.001). The finding suggests that lower serum albumin is associated not only with overall stroke severity but also with impaired neurological status at presentation.

The relationship between admission stroke severity and subsequent functional outcome was also evident in the present study. The mean Scandinavian Stroke Scale score was 40.43 ± 4.99 in patients with mild disability, 25.13 ± 7.11 in those with moderate disability, 19.34 ± 9.73 in those with severe disability, and only 2.64 ± 2.13 among patients who died (p = 0.001). Thus, increasing neurological severity at admission was strongly associated with poorer functional outcome at 90 days.

The present findings are also consistent with the work of Abubakar et al,[5] who demonstrated that low admission serum albumin was an independent determinant of poor outcome and mortality following acute stroke. In their study, patients with favourable outcomes had significantly higher serum albumin concentrations than those with unfavourable outcomes, and serum albumin remained a predictor of poor outcome after adjustment. The present study similarly demonstrated the lowest mean albumin concentration among patients who died, supporting the prognostic relationship between hypoalbuminemia and adverse outcome.

The possible mechanisms underlying this association are multifactorial. Low serum albumin may reflect poor nutritional status, systemic inflammation, altered hepatic protein synthesis, or the severity of the underlying acute illness. In addition, reduced albumin may adversely influence plasma oncotic pressure, oxidative stress, endothelial function and microcirculatory flow. The uploaded study specifically discusses the potential effects of albumin on erythrocyte aggregation, leukocyte adhesion,

thrombosis and microvascular circulation, providing a plausible biological basis for the observed relationship between albumin concentration and stroke severity.

However, an important distinction should be made between serum albumin as a prognostic marker and albumin as a therapeutic intervention. Although experimental studies demonstrated neuroprotective effects of albumin and suggested reductions in infarct volume and cerebral edema, subsequent clinical trials have not established routine high-dose albumin therapy as an effective treatment for acute ischemic stroke. The ALIAS trials, reported by Martin et al,[8] did not demonstrate improved neurological outcomes with high-dose albumin treatment. Therefore, the findings of the present study should be interpreted as supporting the prognostic value of admission serum albumin rather than suggesting that albumin administration would necessarily improve stroke outcomes.

Regarding demographic characteristics, the largest proportion of patients in the present study belonged to the 51–60-year age group (24%), with a mean age of 57.66 ± 12.4 years. The uploaded analysis found no significant association between age and functional outcome ($p = 0.144$). Similarly, there was no significant association between sex and functional outcome ($p = 0.904$). The source document reports 56% males in the Discussion; however, the demographic table reports 54% males and 46% females, and this discrepancy should be resolved using the original dataset before manuscript submission.[9]

Systemic hypertension was the most common vascular risk factor in the present study, occurring in 57% of patients, while type 2 diabetes mellitus was present in 27% and 18% had both hypertension and diabetes. The study did not demonstrate a significant association between hypertension or diabetes and 90-day functional outcome. These findings emphasize that although conventional vascular risk factors are important in the development of ischemic stroke, their presence alone may not adequately predict early functional outcome once an acute stroke has occurred.[10]

The present findings should be interpreted in light of several limitations. First, the study included only 100 patients from a single centre, which limits the generalizability of the findings. Second, the observational design demonstrates an association between serum albumin and outcome but cannot establish causality. Third, serum albumin may be influenced by nutritional status and other systemic factors, even though several conditions capable of substantially altering albumin levels were excluded. Fourth, albumin was assessed at admission, and serial measurements were not performed. Finally, the study used ANOVA and Kruskal–Wallis tests to assess associations; larger prospective studies using multivariable regression models would be useful to determine whether serum albumin remains an independent prognostic marker after adjustment for established predictors such as stroke severity, age, glucose levels and comorbidities.

Despite these limitations, the present study has clinical relevance because serum albumin is inexpensive, routinely available and can be measured early after admission. The consistent relationship between lower admission albumin and greater stroke severity, poorer functional status and mortality suggests that serum albumin may have value in early prognostic assessment. The findings are broadly consistent with previous observations by Dziedzic et al,[1] Idicula et al,[3] Kasundra and Sood,[6] Dash et al,[7] and Abubakar et al.[5]

Overall, the present study demonstrates that lower serum albumin at admission is significantly associated with greater neurological severity and poorer 90-day functional outcome in acute ischemic stroke. The progressive reduction in albumin from patients with mild disability to those with severe disability and death supports its potential role as an early prognostic biomarker. Further multicentre prospective studies with larger sample sizes and multivariable analysis are warranted to establish the independent prognostic value of serum albumin and to determine whether incorporating albumin into existing stroke severity scores can improve prediction of functional outcome.

CONCLUSION

In this study of patients with first-ever acute ischemic stroke, serum albumin measured at admission was significantly associated with both stroke severity and functional outcome at 90 days. Lower serum albumin levels were associated with greater neurological impairment at presentation, as assessed by the Scandinavian Stroke Scale and Glasgow Coma Scale, and with poorer functional outcomes as assessed by the Modified Rankin Scale.

Thus, serum albumin may serve as a simple, readily available prognostic biomarker for early risk stratification in acute ischemic stroke. Patients presenting with lower serum albumin levels may be at increased risk of severe neurological impairment, poor functional recovery, and mortality. However, larger prospective multicentre studies with adjustment for established prognostic factors are required to establish the independent prognostic value of serum albumin before its routine incorporation into stroke prognostic models.

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