

PROGNOSTIC SIGNIFICANCE OF SERUM ALBUMIN IN ACUTE ISCHEMIC STROKE**^{1*}Fnu Sandeep, ²Poonam Bai, ³Roopa Kumari, ⁴Sheena Shiwani, ⁵Sateesh Kumar and ⁶Fnu Poonam**^{1,3}MBBS, Dow University of Medical and Health Sciences.²MBBS, MD, Peoples University of Medical and Health Sciences.⁴MBBS, ISRA University.⁵MBBS, Jinnah Postgraduate Medical Center.⁶MBBS, Peoples University of Medical and Health Sciences.***Corresponding Author: Fnu Sandeep**

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ABSTRACT

Objective: Evaluating the prognostic significance of serum albumin in acute ischemic brain stroke (AIS) in comparison to NIH stroke scale and modified Rankin score. **Study Design:** Observational study. **Study setting & Duration:** Department of Medicine, Liaquat University of Medical and Health Sciences Hospital Hyderabad/Jamshoro from February 2016 to October 2016. **Subjects & Methods:** A sample of 135 diagnosed cases of acute ischemic brain stroke (AIS) was selected. Inclusion and exclusion criteria were strictly exercised. National Institute of Health Stroke Scale (NIHSS) and modified Rankin scale (mRS) score was noted. Albumin was estimated from blood sera by ELISA kit. Statistical SPSS 22.0 software and Microsoft excel were used for statistical analysis ($P \leq 0.05$). **Results:** Correlation showed the serum albumin was negatively correlated with NIHSS score ($r = -0.724$, $P = 0.0001$) and mRS score ($r = -0.774$, $P = 0.0001$). ROC area under curve was 0.901 (90.1%), revealing strong predictive value of serum albumin as a prognostic factor ($P = 0.0001$). Specificity 90.8% and sensitivity 79.8% was noted (albumin cut off value 2.01 g/dl). **Conclusion:** Low serum albumin was associated with poor prognosis in acute ischemic stroke patients, hence it is concluded that it may be used as simple, easy, inexpensive and rapid technique in clinical practice.

KEYWORDS: Serum Albumin, Acute ischemic brain stroke, Prognosis.**INTRODUCTION**

Ischemic brain stroke is caused by sudden cessation of blood supply to the brain, resulting in corresponding neuronal cell death and neurological loss of function.^[1] Acute Ischemic stroke (AIS) is caused either by a thrombus or an embolus resulting in complete occlusion of cerebral vessel. Occlusion and vascular cessation damages the concerned brain areas.^[1,2] AIS is more common than the hemorrhagic brain stroke. Brain stroke is a cause of morbidity and mortality. WHO estimates show the brain stroke is second most leading cause of mortality next to the ischemic heart disease in the developed countries, whereas in poor countries it ranks sixth leading cause.^[2] It is crucial to diagnose the acute brain stroke at the earliest as the available drug therapy reduces the morbidity and mortality and improves the patient prognosis. Currently, the neuroimaging is the best available method of diagnosis.^[3] But the neuroimaging is costly and expensive in particular for the low income countries, and also are not freely available in remote areas of developing countries. Hence, interest is growing in the cost effective and easy biomarkers for its diagnosis. Various biochemical indicators are analyzed

for the acute stroke but none merited for clinical use.^[4,5] Albumin is a simple monomeric protein synthesized by hepatocytes. It functions as carrier protein and exerts plasma oncotic pressure (plasma colloid osmotic pressure).^[5] Previous researches had reported on the diagnostic and prognostic evaluation of serum albumin for the brain stroke.^[6,7] A previous study reported the small ischemic cerebral infarcts were independently correlated with serum albumin levels.^[8] They reported the low serum albumin is one of the predictive factors for a first-ever non-embolic stroke in old age patients. Experimental studies have suggested the albumin exerts neuroprotective effects by reducing brain edema^[9] or by reducing oxidative stress and apoptosis.^[10] It is proved that sufficient serum albumin levels improve the plasma viscosity, microcirculation and oxygen transport capacity.^[11] Immune functions are positively influenced by the serum albumin.^[12] It was reported that the low dose, cold albumin infusion locally in the ischemic areas exerted neuroprotective effects. Serum albumin increases the collateral perfusion in the ischemic areas has been suggested as one of neuroprotective mechanism.^[11,12] The present study is the first research being reported

from our tertiary care hospital analyzed the prognostic significance of serum albumin in acute ischemic brain stroke. It was hypothesized that the serum albumin has no effect on the prognosis of acute ischemic brain stroke.

SUBJECTS AND METHODS

The present observational study took place at the Department of Medicine, Liaquat University of Medical and Health Sciences Hospital Hyderabad/Jamshoro from February 2016 to October 2016. A sample of 135 cases of acute ischemic brain stroke was selected through non-probability (purposive) sampling. Acute ischemic brain stroke was defined as sudden loss of blood circulation to an area of the brain, resulting in a corresponding loss of neurologic function. CT scan was mandatory for the diagnosis of AIS. Inclusion criteria were; focal neurological symptoms not exceeding 12 hours, CT scan diagnosis of ischemic brain area and age 40-60 years of both gender. Hemorrhagic brain stroke, Diabetes mellitus, Ischemic heart disease, cardiac failure, chronic kidney disease and chronic liver disease qualified for exclusion. Neurological examination was performed at the time of admission based on the National Institute of Health Stroke Scale (NIHSS).^[13] Modified Rankin scale (mRS) was used to quantify the disability of patient. The mRS included scale ranges from 0-6.^[14] Low serum albumin were defined as <3.5 g/dl.^[15] Willing volunteer subjects were interviewed and were informed about the purpose of study. Volunteers were informed that the study will benefit the acute brain stroke patients. Consent form was essential to be signed voluntarily. Physical examination was performed. Printed NIHSS and mRS proforma were used for severity of ischemic stroke ranking. 5ml venous blood was taken by venesection from antecubital fossa. 3 ml blood was stored in EDTA containing tubes. Remaining blood was allowed to clot, centrifuged and sera were separated out. Albumin was estimated from sera by ELISA kit (Cell Biolabs, Inc., San Diego, CA). Sera were diluted with 1:10⁶ PBS (Phosphate buffered saline) before biochemical analysis.

Albumin was estimated by the albumin decrease index (ADI). Biochemical analysis was performed on the Cobas analyzer (e 411), Roche Diagnostics (GmbH, Mannheim, Germany). Study protocol was approved by the ethical review committee. A structured proforma was used for data entry. SPSS 22.0 (IBM, Incorporation, Chicago, Illinois, USA) and Microsoft were used for statistical analysis. Student's t-test, Chi square tests and Spearman's rho rank correlation were used for the continuous data, categorical data and correlation respectively. Significance was defined at 95% confidence interval ($P \leq 0.05$).

RESULTS

The present observational study was conducted to analyze the prognostic value of serum albumin in acute ischemic stroke patients. Age (mean \pm SD) was noted as 55.71 \pm 5.76 and 59.31 \pm 7.81 for male and female respectively (0.026). Of 135, 105 (77.7%) were male and 30 (22.2%) were female ($P=0.0001$). Male to female ratio was 3.5:1. Systemic blood pressure, blood complete counts, serum albumin ($P=0.0001$), NIH stroke scale ($P=0.0371$) and mRS score ($P=0.010$) are shown in table 1. Of 135, 13 (9.6%) patients of AIS died and 122 (90.3%) survived (table 2). Serum albumin, NIH Stroke scale and mRS score in dead and survived patients of acute ischemic stroke were noted as 2.85 \pm 0.39 & 3.71 \pm 0.69 ($P=0.0001$), 36.51 \pm 4.19 & 15.85 \pm 9.56 ($P=0.0001$) and 5.13 \pm 0.3 & 3.25 \pm 1.12 ($P=0.0001$) respectively (table 2). Spearman's rho rank correlation revealed serum albumin was significantly negatively correlated with NIHS score ($r= - 0.724$, $P=0.0001$) and mRS score ($r= - 0.774$, $P=0.0001$) (table 3, Graphs 1 & 2). The ROC curve shows the prognostic significance of serum albumin for the acute ischemic stroke. Area under curve (AUC) of 0.901 (90.1%) showed strong predictive value of serum albumin as a prognostic factor as shown in graph 3. Specificity 90.8% and sensitivity 79.8% was noted (albumin cut off value 2.01 g/dl).

Table 1. Demography, physical and laboratory findings of study subjects (n=135)

	Male	Female	P-value
Age (years)	55.71 \pm 5.76	59.31 \pm 7.81	0.026
Systolic BP (mmHg)	157.44 \pm 22.09	148.97 \pm 27.14	0.085
Diastolic BP (mmHg)	83.62 \pm 15.5	87.59 \pm 12.58	0.210
Haemoglobin (g/dl)	12.93 \pm 1.57	12.44 \pm 1.54	0.138
Hematocrit (%)	41.19 \pm 6.46	40.04 \pm 6.07	0.393
RBC (10 ⁹ / μ L)	3.03 \pm 0.55	3.01 \pm 0.51	0.862
WBC (μ L)	6128.8 \pm 3120.0	6589.2 \pm 2735.4	0.472
Platelet (10 ⁹ / μ L)	283.2 \pm 84.5	251.7 \pm 83.1	0.077
S. Albumin (g/dl)	3.74 \pm 0.75	3.19 \pm 0.44	0.0001
NIH Stroke Scale	18.03 \pm 11.73	20.17 \pm 10.05	0.0371
Modified Rankin Scale	3.44 \pm 1.23	4.10 \pm 1.11	0.010

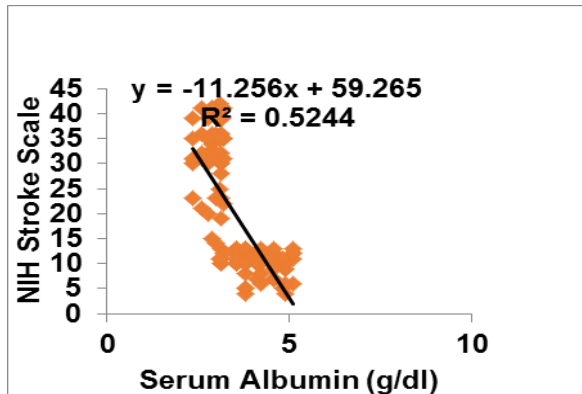
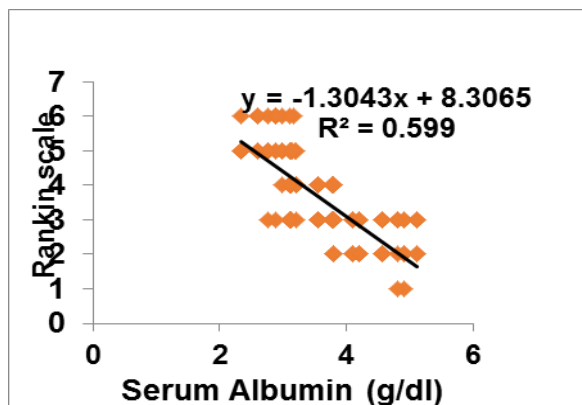
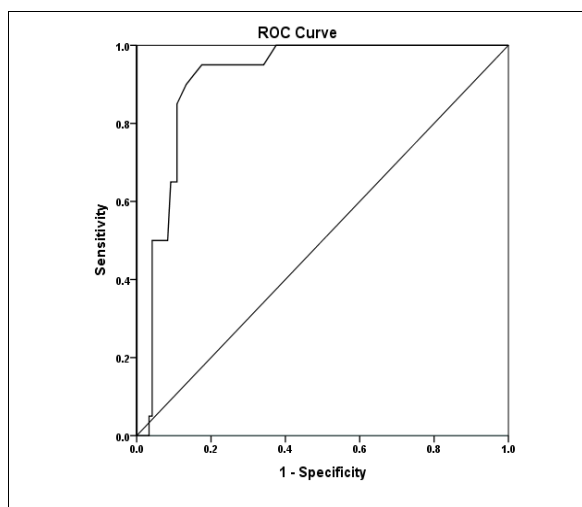
Table 2: Serum albumin, NIHS Stroke scale and modified Rankin Scale

	Dead	Survived	P-value
Serum Albumin	2.85 \pm 0.39	3.71 \pm 0.69	0.0001
NIHS stroke scale	36.51 \pm 4.19	15.85 \pm 9.56	0.0001
Modified Rankin scale	5.13 \pm 0.3	3.25 \pm 1.12	0.0001

Table 3: Correlation of serum albumin with NIHs and mRS

	r-value	p-value
NIH Stroke Scale	- 0.724**	0.0001
Modified Rankin Scale	- 0.774**	0.0001

**Correlation is significant at the 0.01 level (2-tailed).

**Graph 1: Scatter plot showing negative correlation of serum albumin and NIH Stroke Scale.****Graph 2: Scatter plot showing negative correlation of serum albumin and modified Rankin scale.****Graph 3: Receiver Operating Characteristic (ROC) curve showing AUC of 0.901 (90.1%), specificity 90.8% and sensitivity 79.8% (cut off value 2.01 g/dl).****DISCUSSION**

The present observational study was conducted to analyze the prognostic significance of serum albumin in acute ischemic stroke (AIS) patients. We are the first to report our clinical experience of prognostic significance of serum albumin in AIS patients in association to NIHs stroke scale and modified Rankin scale. Mean age reveals patients were in their fifth decade (55.71 ± 5.76 and 59.31 ± 7.81 for male and female respectively). The old age of AIS patients of present study is in agreement with previous studies,^[16-19] but another study reported low mean age of 47 years.^[20] Of 135, 105 (77.7%) were male and 30 (22.2%) were female ($P=0.0001$). Male predominated in the present study (M:F ratio 3.5:1.) which matches to previous studies.^[16,21,22] Male dominance of present study is consistent with these studies.^[16,21,22] A previous study^[23] reported female dominance which is incomparable to the present and previous studies.^[16,21,22] Of 135, 13 (9.6%) patients of AIS died and 122 (90.3%) survived. Serum albumin, NIH Stroke scale and mRS score in dead and survived patients of acute ischemic stroke were noted as 2.85 ± 0.39 & 3.71 ± 0.69 ($P=0.0001$), 36.51 ± 4.19 & 15.85 ± 9.56 ($P=0.0001$) and 5.13 ± 0.3 & 3.25 ± 1.12 ($P=0.0001$) respectively. These findings are in agreement with previous studies.^[1,5,24-26] Of 13 dead patients, 11 (8.14%) male and 2 (1.48%) female died in the present study. These findings are in keeping with previous studies.^[1,5,24-26] Our findings of NIHs and mRS score conforms to the findings of a previous study.^[27] They reported better prognosis of AIS patients with high serum albumin decreasing the mortality. Suggested mechanisms of beneficent effects of serum albumin include the; anti thrombosis effects, decreases leukocyte adherence, and endothelial stasis of cells.^[28] The above mechanisms facilitate the early reperfusion phase of AIS offering neuroprotective effect.^[29] Neuroprotective effects of albumin are also contributed through the improved venular perfusion and microcirculation, maintaining endothelial integrity, and anti oxidant & anti lipid peroxidant activity. Low serum albumin adversely affects the prognosis of cardiac and kidney diseases.^[30,31] A previous study^[32] reported the serum albumin improves sub- occlusive microcirculation, vascular integrity, mitigates cerebral edema and prevents microvascular re-occlusion. Alvarez-perez et al^[33] reported positive association of cardio-embolic brain stroke and reduced serum albumin. They further reported mean serum albumin was low in AIS patients. The finding supports the present research work. In present study, the Spearman's rho rank correlation revealed serum albumin was significantly negatively correlated with NIHs score ($r= - 0.724$, $P=0.0001$) and mRS score ($r= - 0.774$, $P=0.0001$). This is in agreement with previous studies,^[1,5,33] but contradicts to Idicula et al^[34] as they reported no association. The ROC area under curve (AUC) of 0.901 (90.1%) showed strong predictive value of serum albumin as a prognostic factor (albumin cut off value 2.01 g/dl) with specificity and sensitivity of 90.8% and 79.8% respectively. The findings are

consistent with previous studies.^[1,5,21,22] Small sample size, ethnicity, and particular geographical segment are few of the limitations of the present study. However, the its strength lies prospective design, inclusion and exclusion criteria and comparison with NIS stroke scale and modified Rankin scale scores. The serum albumin as a prognostic biomarker for acute ischemic stroke patients is a worth finding which needs further large scale studies.

CONCLUSION

Low serum albumin was associated with poor prognosis in acute ischemic stroke patients, hence it is concluded that it may be used as simple, easy, inexpensive and rapid marker in clinical practice. Serum albumin was negatively associated with NIHSS stroke and modified Rankin scale. However, further future large sample size prospective studies are recommended.

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