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ACUTE ISCHEMIC STROKE;

CLINICAL AND PROGNOSTIC SIGNIFICANCE OF SERUM ALBUMIN IN ACUTE ISCHEMIC STROKE.

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ABSTRACT… Objectives: Analysis of Clinical and Prognostic significance of Serum Albumin in Acute Ischemic Stroke and its correlation with National Institute of Health Stroke Scale (NIHSS) and modified Rankin scale (mRS). **Study Design:** Case control study. **Setting & Period:** Department of Medicine, Liaquat University of Medical and Health Sciences Hospital Hyderabad/Jamshoro from March 2016 to June 2017. **Subjects & Methods:** A sample of 100 cases of acute ischemic brain stroke (AIS) and 100 controls were selected according to inclusion and exclusion criteria. Clinical criteria of NIHSS and mRS were calculated. Blood samples were taken for biochemical analysis. Albumin was analyzed between 2 groups and its correlation with NIHSS and mRS was estimated by Pearson`s correlation. Data was analyzed on Statistical Package *SPSS 22.0* software and Microsoft excel sheet ($P \leq 0.05$). **Results:** Serum albumin was found low in AIS cases 3.86±0.68 g/dl compared to controls 5.16±0.34 g/dl (P=0.0001). Of 100 AIS cases, 23% patients died and 77.0% survived. Bivariate analysis shows serum albumin was inversely associated with NIHS score and mRS (r= -0.596, P=0.0001) (r= -0.720, P=0.0001) respectively. **Conclusion:** Low serum albumin adversely affects the prognosis of acute ischemic stroke patients.

Key words: Acute Ischemic Stroke, Serum Albumin, NIHSS, mRS, Prognosis.

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INTRODUCTION

Brain stroke is a medical problem of vascular occlusion which results in non-functioning of a part of neuronal tissue. Pathophysiology of acute ischemic brain stroke (AIS) suggests it is caused by sudden loos of blood supply (ischemia) to the brain. Ischemia results in neuronal necrosis that casues paralysis of affected body part.[1] Vascular occlusion of brain artery is caused by thrombo- embolic phenomena.[1,2] Brain ischemia is commoner than brain haemorrhage. Brain ischemic stroke accounts for a large number morbidity form muscle paralysis and also the mortality. Now the brain stroke is considered as second most common cause of mortality next to the ischemic cardiac catastrophes in developed countries, this has been reported by World Health Organization (WHO). In developing the brain stroke accounts for mortality but ranks as sixth leading cause.[2] Timely institution of drug therapy helps decrease morbidity and mortality and improves the clinical prognosis and patient outcome. Neuroimaging is available one of easy and reliable method of diagnosing the AIS, but it is costly.[3] Developing countries have meager facilities of neuroimaging particularly in the remote rural areas of these countries where majority of population is residing. These problems are faced by developing countries which in turn begets financial loss due to morbidity from physical disability caused by brain stroke. Nowadays, interest has been on rise in validating cost effective blood testing for prognosis of various disease to overcome the problems of modern imaging. Similarly, much interest has grown in the inexpensive blood testing of prognostic value

for the acute brain stroke.[4,5] Albumin is one such ray of light which is being researched for the prognosis of acute brain stroke. Albumin is one of major plasma proteins synthesized by liver and circulates in the blood. Previous studies[6,7] have reported on the diagnostic and prognostic aspects of serum albumin in AIS patients. A previous study[8] concluded the serum albumin is independently correlated with AIS. They suggested low serum albumin is of prognostic significance in the first-ever non-embolic brain stroke in elderly. Previous studies[9,10] concluded albumin improves ischemia mediated adverse neuronal activity through improving blood viscosity, vascular integrity, neuronal oxygen supply and the microcirculation.[9] The present case control study was designed to study the clinical and prognostic significance of serum albumin in Acute Ischemic Stroke and its correlation with clinical severity of brain stroke as assessed by National Institute of Health Stroke Scale (NIHSS) and modified Rankin scale (mRS) severity scale at our tertiary care hospital.

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 March 2016 to June 2017. A sample of 100 cases of acute ischemic brain stroke and 100 age and gender subjects (controls) were selected through non-probability (purposive) sampling. Sudden cessation of blood supply to a part of brain resulting in clinically evident neurological deficit and confirmed by computer tomography scanning was defined as acute ischemic stroke. CT scan was ordered for all acute ischemic stroke patients. Inclusion criteria were; age 40- 60 years, both genders, focal neurological deficit (not exceeding 12 hours) confirmed as ischemia by CT scanning. Brain stroke due to brain hemorrhage were strictly excluded. Acute ischemic stroke patients suffering from coronary artery disease, valvular cardiac disease, atrial fibrillation, cardiac failure, chronic kidney disease, chronic pulmonary disease were also excluded. Severity of acute ischemic stroke was determined by the National Institute of Health Stroke Scale (NIHSS).[11] Modified Rankin scale (mRS) was used for stroke disability. Range of mRS was taken 0-6 as referenced.[12] Low serum albumin were defined as <3.5 g/dl.[13] AIS patients and legal heirs/attendants were communicated and those who showed willingness were interviewed and negotiated about the purpose of study. Volunteer subjects qualified for the study protocol. Written signed consent form was mandatory for study purpose. Patient biodata, clinical history and physical examination were performed. Acute ischemic was established clinically added by CT scanning.

Clinical severity of AIS was established by grading of NIHSS and mRS proforma. Volunteers were informed that the study will cause no harm or financial burden. They were asked for 5 ml blood sample. Area was cleaned and sterilized with alcohol swab. 5 ml blood was collected from a peripheral vein by venesection preferably from antecubital fossa. 2 ml was centrifuged to separate out sera and 3 ml was stored in the EDTA bottles. Sera were diluted with Phosphate buffered saline ($1:10^6$ PBS) prior to biochemical analysis. Cobas analyzer (e 411), Roche Diagnostics (GmbH, Mannheim, Germany) was used for biochemical estimation of albumin. EDTA blood was analyzed on Sysmex analyzer for the blood parameters. Study protocol was applied for ethical issue and unanimously approved by the ethical review committee.

Biodata, physical examination and biochemical findings were noted in a pre- structured proforma. Data was entered on Microsoft excel sheet and copied to the SPSS SPSS 22.0 (IBM, Incorporation, Chicago, Illinois, USA) for statistical analysis. Student`s t-test (e.g.; age, systolic and diastolic BP), Chi square test (e.g.; gender) and Bivariate Pearson`s correlation used for the data analysis. Results of statistical significance were considered at 95% confidence interval ($P \leq 0.05$).

RESULTS

The present case control study was conducted to analyze the clinical and prognostic significance of serum albumin in acute ischemic stroke patients in correlation with the NIHSS and mRS. Age of control and cases was noted as 52.41 ± 5.08 and 56.72 ± 7.12 respectively ($P=0.002$). Male to

female ratio was 1.88:1 (Table-I). Serum albumin was found low in cases 3.86±0.68 g/dl compared to controls 5.16±0.34 g/dl (P=0.0001). NIH stroke scale 35.7±5.13 and mRS score 7.33± 1.3 was noted in cases (P=0.0001) (Table-II). Of 100 AIS cases, 23% patients of AIS died and 77.0% survived (Table-III). Serum albumin, NIHS and mRS showed statistically significant differences between AIS who died and AIS who survived as shown in table 3. Bivariate analysis shows serum albumin was inversely associated with NIHS score and mRS (r= -0.596, P=0.0001) (r= - 0.720, P=0.0001) respectively as shown in (Table-IV) (Figure-1 and 2).

	Controls	Cases	P-value
Age (years)	52.41±5.08	56.72±7.12	0.002
Male	64.0	64.0%	0.0001
Female	36.0	36.0%	
Systolic BP (mmHg)	147.75±21.15	155.3±23.3	0.057
Diastolic BP (mmHg)	79.65±11.51	89.15±14.1	0.002
Haemoglobin (g/dl)	13.39±1.44	12.57±1.56	0.0138
Hematocrit (%)	43.63±6.14	39.81±6.19	0.0031
S. Albumin (g/dl)	5.16±0.34	3.86±0.68	0.0001

Table-I. Demography, physical and laboratory findings of study subjects (n=200)

	Mean	SD	P-value
NIHS	35.7	5.13	0.0001
mRS	7.33	1.3	0.0001

National Institute of Health Stroke Scale, modified Rankin Scale

Table-II. NIH and modified Rankin scale in cases (n=100)

	Mortality		P-value
	Yes (n=23)	No (n=77)	
Serum Albumin	2.15±0.27	4.11±0.59	0.0001
NIHS	35.7±5.13	14.15±7.16	0.0001
mRS	7.33±1.3	3.25±0.52	0.0001

National Institute of Health Stroke Scale, modified Rankin Scale

Table-III. Serum albumin, NIHS and mRS Stroke scale

	Correlation Co-efficient	Statistical Significance
NIH Stroke Scale	- 0.596**	0.0001
Modified Rankin Scale	- 0.720**	0.0001

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

Table-IV. Bivariate analysis of serum albumin

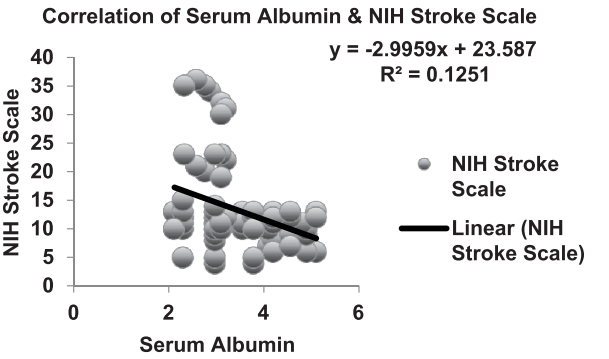

Figure-1. Scatter plotting shows inverse association of serum albumin and NIHSS

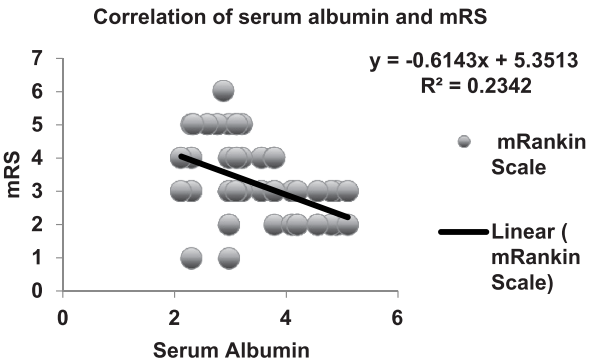

Figure-2. Scatter plotting shows inverse association of serum albumin and mRS

DISCUSSION

The present research is a case control study, conducted to analyze the clinical and prognostic significance of serum albumin in acute ischemic stroke (AIS) patients and its correlation with the NIHSS and mRS at our tertiary care hospital. Age of control and AIS cases was noted as 52.41±5.08 and 56.72±7.12 respectively (P=0.002). Mean age shows elderly study population, this is consistent with previous studies,[14-16] which have reported similar age category. Mean age finding of sixth decade is in contrast to a previous study[17] that reported mean age of fifth decade. In the present study, majority of male comprised the

study population. Male to female ratio was 1.88:1 (64% male and 36% female) (Table-I). These findings of gender discrimination are in keeping with previous studies.[14,18,19] However, a previous study has reported conflicting result of female gender being dominant in their research. This is in contradistinction to present and previous studies.[14,18,19] Most probable reason of such controversy could be an incidental findings because of by chance presentation of female population at the time of study was being conducted. The present study included 100 cases of AIS, of that 23% patients and 77.0% survived (Table-III). Serum albumin was found low in AIS cases compared to controls i.e. 3.86±0.68 g/dl versus 5.16±0.34 g/dl (P=0.0001). NIH stroke scale and mRS were raised in AIS cases. NIHSS and mRS were noted as 35.7±5.13 and 7.33± 1.3 (P=0.0001) respectively. As regards prognostic significance of serum albumin the statistical analysis shows its poor prognostic value in acute ischemic stroke cases. Serum albumin, NIHS and mRS showed statistically significant differences between AIS who died and AIS who survived (P=0.0001) (Table-III). These findings of low serum albumin adversely affects the prognosis of AIS cases is consistent with previous studies.[1,5] Such findings of low albumin as marker of poor prognosis in AIS has been reported by other studies also.[20,21]

The findings of elevated NIHS and mRS is in confirmation with a previous study.[22] This previous study[22] reported better prognosis in AIS cases with upper normal serum albumin levels and mortality was reported with low serum albumin. This is highly supporting the observations of the present study. Mechanisms of neuroprotective effects of albumin are because of its anti- thrombotic activity, maintenance of endothelial integrity, and inhibition of leukocyte adherence and stasis onto the vascular endothelium.[23] A previous study[24] reported the albumin offers neuroprotective effects during the early reperfusion phase of AIS.

Other proposed mechanism of neuroprotective effects of albumin suggested are the anti-oxidant and anti- lipid peroxidant activity of albumin that helps maintain vascular endothelial integrity thus improving the venular perfusion and microcirculation.[23-25] Previous studies[25,26] concluded low albumin levels in circulation of AIS patients adversely affects prognosis in renal and cardiac disease patients. Another previous study[27] suggested the circulating albumin mitigates cerebral edema, prevents microcirculation thrombosis and maintain vascular integrity. Present study observed positive correlation of serum albumin with worsening NIHSS and mRS which are clinical markers of mortality. This is agreement with Alvarez-perez et al.[28] This previous study[28] reported low mean serum albumin in AIS patients similar to observed in the present study. In present study, the Bivariate analysis shows serum albumin was inversely associated with NIHS score and mRS (r= -0.596, P=0.0001) (r= -0.720, P=0.0001) respectively. These findings are supported by previous studies.[1,5,21,22] The findings of present study in view of above literature review concludes low serum albumin is a risk of poor prognosis in acute ischemic stroke patients and they should be managed cautiously to prevent mortality.

CONCLUSION

Low serum albumin was found in acute ischemic stroke with poor prognosis and mortality. Serum albumin showed negative correlation with National Institute of Health Stroke Scale (NIHSS) and modified Rankin scale (mRS) this shows its prognostic significance. Further nationwide studies are suggested to validate these findings with large sample size.

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It is **better** to offer no excuse than a **bad** one.

"George Washington"

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2	Suresh Kumar	Literature reivew, material statictis analysis.	
3	Dileep Kumar Artwani	Concept, Introduction, Lab Investigation.	
4	Nathumal Maheshwari	Manuscript, hand up material.	
5	Rewachand	Material hand up profreading.	
6	Bilawal Hingorjo	Material, Handup Proof reading.	