# Prognostic Significance Of Serum Albumin Levels In Acute Ischemic Stroke

**Gaurav Kasundra*, Isha Sood****

*DM Neurology Resident, Department of Neurology, ** Senior Resident, Department of Medicine, Dr. S. N. Medical College, Jodhpur.

**Abstracts**: **Objectives**: Recent studies in acute ischemic stroke (AIS) have brought to light newer risk factors like serum levels of high sensitivity-C-Reactive Protein (hs-CRP), procalcitonin, homocysteine and albumin. Aim of our study is to objectively determine the short term prognostic value of serum albumin levels in AIS by correlating its levels with the clinical outcome. **Methods:** A cross-sectional study was carried out in Shri Sayajirao General Hospital, Vadodara over a period of 2 years where-in 108 cases of AIS were screened and 50 patients who met the inclusion criteria were studied. Patients presenting within 72 hours of onset and aged≥ 40 years were included in this study. Apart from routine investigations, serum albumin levels were done in all the patients. **Results and Interpretation:** Patients with a lower NIHSS score on admission had higher levels of serum albumin, and those with a higher National Institute of Health Stroke Scale (NIHSS) score had a lower level of albumin [P value <0.001]. Similarly, patients with a higher score on Barthel index after 1 week of admission had a higher serum albumin level, while those with lower score had lower albumin levels [P value <0.001]. Thus serum albumin level has a direct correlation with short term prognosis. [ Kasundra G NJIRM 2014; 5(2) :1-4]

**Key Words**: albumin, Acute ischemic stroke, NIHSS score, Barthel index

**Author for correspondence:** Dr Gaurav Kasundra, A-702, Merigold, Ram Mandir Road, Vazira Naka, Borivali west, Mumbai- 400092, E- mail: gauravkasundra@gmail.com

**Introduction:** A stroke, or cerebrovascular accident, is defined by an abrupt onset of a neurologic deficit that is attributable to a focal vascular cause. Thus, the definition of stroke is clinical, and laboratory studies including brain imaging are used to support the diagnosis. Major risk factors identified in India are hypertension, hyperglycemia, tobacco use, and low hemoglobin levels (<10 gm %). As our knowledge about the various risk factors for stroke increases day-by-day, more and more therapeutic interventions for prevention of stroke in various high risk groups have come into practice.[1] Recent studies have shown prognostic role of serum albumin level in cases of Acute Ischemic Stroke [AIS], a higher level of which correlate with a better prognosis as shown in some western studies.[1,2,3] However these finding have not been validated sufficiently in the Indian population. Therapeutic interventions in murine models of acute ischemic strokes have shown a better prognosis with albumin infusions alone, as also when given in combination with tissue-plasminogen activator (tPA) as it decreased tPA induced vascular and Blood-Brain- barrier damage.[4] Thus there is a rising interest in the correlation of albumin levels with clinical severity of acute stroke as there underlies an opportunity for a medical intervention.

**Material and Methods:** In the present study 108 cases presenting with all vascular events (including hemorrhagic strokes, ischemic strokes, venous sinus thrombosis and subarachnoid hemorrhage irrespective of interval between onset and presentation to our hospital) were screened, of which 50 cases of acute ischemic cerebrovascular accidents were studied. Consent of the patients or their next-of-kin and approval of institutional review board was taken. All cases were admitted to the medical wards of Shri Sayajirao General Hospital, Baroda, Gujarat.

Patients aged ≥ 40 years and diagnosed as having acute ischemic cerebrovascular stroke within previous 72 hours by clinical examination and confirmed by either a CT scan or by a MRI Scan were included. Patients aged <40 years, presenting with hemorrhagic stroke/ subarachnoid hemorrhage/ cerebral venous sinus thrombosis, presenting with ischemic stroke after 72 hours of onset were excluded from study.

Detailed history and examination of the patients included in the study was done. The National Institute of Health Stroke Scale (NIHSS) score of all the patients at admission (baseline) and Barthel score [which tests functional independence objectively] of all patients after 1 week of initial assessment were calculated. All routine

investigations including complete hemogram, fasting sugar, renal function test, liver function test, lipid profile and serum proteins with albumin, Electrocardiograph, Fundus examination, C.T./ M.R.I. Scan examination, X-ray chest PA view, 2D-ECHO and USG- KUB in certain cases was done

**Results:** In our study, out of 50 patients, 58 percentage (%) were males and 42% were females. Thus, the ratio of males to females was 1.38: 1. Maximum patients were in 55-64 years age group.

**Table1. Age and sex distribution in study population:**

| AGE GROUP | MALES | FEMALES | TOTAL |
|---|---|---|---|
| 40-44 | 3 | 1 | 4 |
| 45-54 | 7 | 3 | 10 |
| 55-64 | 10 | 9 | 19 |
| 65-74 | 7 | 6 | 13 |
| 75-84 | 2 | 1 | 3 |
| ≥85 | 0 | 1 | 1 |
| TOTAL | 29 | 21 | 50 |

**Table2. Presenting symptoms in study population:**

| SYMPTOM | No.of patients | % |
|---|---|---|
| Headache | 4 | 8 |
| Vomiting | 4 | 8 |
| Motor weakness | 47 | 94 |
| Unconsciousness | 8 | 16 |
| Dysarthria | 46 | 92 |
| Vertigo | 4 | 8 |
| Tingling | 6 | 12 |
| Diplopia | 1 | 2 |
| Convulsions | 1 | 2 |

**Table3. Past medical history of study population:**

| | Male | Female | Total | % |
|---|---|---|---|---|
| CVA | 6 | 1 | 7 | 14% |
| DM | 4 | 0 | 4 | 8% |
| HTN | 10 | 6 | 16 | 32% |
| IHD | 2 | 0 | 2 | 4% |
| TOTAL | 22 | 7 | 29 | 58% |

**Addiction history in study population:** In our study, a positive history of alcoholism was obtained in 10% while that of smoking was obtained in 14% of the patients.

**Table4. Distribution according to systolic blood pressure (SBP) on admission:**

| SBP | MALE | FEMALE | TOTAL | % |
|---|---|---|---|---|
| ≤138 | 7 | 6 | 13 | 26% |
| 140- 158 | 11 | 3 | 14 | 28% |
| 160- 178 | 5 | 5 | 10 | 20% |
| 180- 198 | 4 | 5 | 9 | 18% |
| ≥200 | 2 | 2 | 4 | 8% |
| TOTAL | 29 | 21 | 50 | 100% |

**Table5. Distribution according to diastolic blood pressure (DBP) on admission:**

| DBP | MALE | FEMALE | TOTAL | % |
|---|---|---|---|---|
| <78 | 0 | 3 | 3 | 6% |
| 80- 88 | 8 | 5 | 13 | 26% |
| 90- 98 | 11 | 8 | 19 | 38% |
| 100- 108 | 4 | 5 | 9 | 18% |
| ≥110 | 4 | 2 | 6 | 12% |
| TOTAL | 29 | 21 | 50 | 100% |

**Distribution according to findings on fundus examination in study population:**

16% had hypertensive retinopathy, 6% had diabetic retinopathy, 78% had normal fundus examination while one patient had papilloedema.

**Distribution according to Electrocardiographic findings in study population:**

In our study, 52% had a normal ECG, 14% had ischemic heart disease on ECG, 20% had stroke related changes while 24% of the patients had left ventricular hypertrophy on ECG.

**Table6. Distribution according to serum Cholesterol levels in study population:**

| Chol mg/dL | MALE | FEMALE | TOTAL | % |
|---|---|---|---|---|
| <100 | 2 | 2 | 4 | 8% |
| 100-149 | 11 | 8 | 19 | 38% |
| 150-199 | 14 | 6 | 20 | 40% |
| ≥200 | 2 | 5 | 7 | 14% |

**Table7. Distribution according to Serum Albumin and NIHSS score on admission in study population:**

| Albumin g/dL | NIHSS ≤10 | NIHSS>10 | TOTAL |
|---|---|---|---|
| <2.5 | 0 | 1 | 1 |
| 2.5 – 2.9 | 0 | 1 | 1 |

| | | | |
|---|---|---|---|
| 3- 3.4 | 1 | 13 | 14 |
| 3.5- 3.9 | 13 | 2 | 15 |
| 4- 4.4 | 10 | 0 | 10 |
| ≥4.5 | 6 | 3 | 9 |
| TOTAL | 30 | 20 | 50 |

Thus in our study, 2% of patients each had serum albumin level ≤ 2.5 g/dl and between 2.5 to 2.9, 28% had it between 3 to 3.4, 30% had between 3.5 to 3.9, 20% between 4 to 4.4 and 18% had a value of 4.5 g/dl or above.

**Table8. Distribution according to levels of Serum Albumin and Barthel score after one week of initial evaluation in study population:**

| Albumin g/dL | Barthel > 60 | Barthel ≤ 60 | TOTAL |
|---|---|---|---|
| <2.5 | 0 | 1 | 1 |
| 2.5 – 2.9 | 0 | 1 | 1 |
| 3- 3.4 | 1 | 13 | 14 |
| 3.5- 3.9 | 12 | 3 | 15 |
| 4- 4.4 | 10 | 0 | 10 |
| ≥4.5 | 6 | 3 | 9 |
| TOTAL | 29 | 21 | 50 |

Thus in our study, 2% of patients each had serum albumin level ≤ 2.5 g/dl and between 2.5 to 2.9, 28% had it between 3 to 3.4, 30% had between 3.5 to 3.9, 20% between 4 to 4.4 and 18% had a value of 4.5 g/dl or above.

**Discussion:**

**Table9. Distribution according to levels of Serum Albumin and NIHSS score on admission:**

| Serum Albumin | NIHSS ≤10 | NIHSS>10 |
|---|---|---|
| <3.5 g/dl | 1 | 15 |
| ≥3.5g/dl | 29 | 5 |

Thus, most patients with a better prognosis as determined by their lower NIHSS score had a higher serum albumin level, and most with a worse prognosis as per their higher NIHSS score had a lower serum albumin level. The p value was <0.001. Thus, there was a highly significant correlation between serum albumin level and a better prognosis at the time of admission. This correlates with most of the previous studies.

**Table10. Comparision of albumin level with previous studies**

| STUDY | No. of patients | Mean albumin | P value |
|---|---|---|---|
| Sharma et al[6] | 120 | 3.73 | <0.001 |
| Idicula et al[3] | 444 | 3.76 | <0.05 |
| Dziedzic et al [7,8] | 759 | 3.55 | <0.01 |
| Alvarez-Perez et al[9] | 200 | | 0.053 |
| Present study | 50 | 3.81 | <0.001 |

**Table11. Distribution according to levels of Serum Albumin and Barthel score after one week of initial evaluation:**

| Serum Albumin g/dL | Barthel > 60 | Barthel ≤ 60 |
|---|---|---|
| <3.5 g/dl | 1 | 15 |
| ≥3.5g/dl | 28 | 6 |

Thus, most patients with a better prognosis as determined by their higher Barthel score had a higher serum albumin level, and most with a worse prognosis as per their lower Barthel score had a lower serum albumin level. The p value was <0.001. Thus, there was a highly significant correlation between serum albumin level and a better prognosis at one week after the onset of symptoms. This correlates with most of the previous studies which included either Barthel index or modified Rankin scale after one week of initial examination.

**Table12. Comparision of albumin level with previous studies**

| STUDY | No. of patients | Mean albumin | P value |
|---|---|---|---|
| Sharma et al[6] | 120 | 3.73 | significant |
| Idicula et al[3] | 444 | 3.76 | <0.05 |
| Dziedzic et al[7,8] | 759 | 3.55 | <0.01 |
| Present study | 50 | 3.81 | <0.001 |

Whenever acute cerebral infarction occurs, dysfunction of the sodium (Na+)-potassium (K+) ATPase pump causes marked ATP depletion, increase in extracellular $K^+$, increase in intracellular $Ca^{++}$, and cellular acidosis, invariably leading to histologic signs of necrosis. Cellular depolarization also causes glutamate release from synaptic terminals; excess extracellular glutamate produces neurotoxicity by activating postsynaptic glutamate receptors that increase neuronal calcium influx. Free radicals are produced by membrane lipid degradation and mitochondrial dysfunction. Free radicals cause catalytic destruction of membranes and likely damage other vital functions of cells. The cells swell up due to a process called cellular or

cytotoxic edema. Vascular endothelial growth factor (VEGF) is known to be an important stroke-related pathogenic factor for the formation of brain edema. In studies on animal models, the therapeutic effect of human serum albumin on VEGF expression in acute ischemic stroke has been proved.[2] Extrapolating these results in humans, it was believed that maintaining the serum albumin at a higher level by intravenous infusion of human albumin, and attenuating endogenous VEGF expression, may lead to the protective effects of albumin on reduction of brain edema and thus better prognosis. However, the recent ALIAS [Albumin in Acute Ischemic Stroke] part 2 trial was terminated prematurely after interim analysis due to non-superiority of albumin infusions compared to saline infusions in acute ischemic stroke patients, but still the investigators of the trial were reluctant to give up upon albumin given its excellent results in rat models of stroke.[10]

**Conclusion:** Our results indicate that higher levels serum albumin is associated with a better short term prognosis. Thus, they may act as indicators of short term prognosis. These results reinforce the available evidence, and point towards a potential therapeutic approach for patients presenting with acute ischemic cerebrovascular stroke, in the form of therapeutic correction of the hypoalbuminemia in a bid to improve the outcome for the patients. Though results of ALIAS part 2 trial are not encouraging, further studies are needed to test the role of albumin on a larger scale, at a different dose, and over a longer duration of follow-up.

**References:**


1. Natural History of stroke in Rochester-Minnesota, 1955 through 1969: Matsumoto N., et al, stroke, vol.2, pg 11, 1969.
2. Cho YM, Choi IS, Bian RX, Kim JH, Han JY, Lee SG. Serum albumin at admission for prediction of functional outcome in ischaemic stroke patients. Neurol Sci. 2008; 29: 445-449.
3. Idicula TT, Waje-Andreassen U, Brogger J, Naess H, Thomassen L. Serum albumin in ischemic stroke patients: the higher the better. The Bergen Stroke Study. Cerebrovasc Dis. 2009; 28: 13-17.
4. Tang J, Li YJ, Mu J, Li Q, Yang DY, Xie P. Albumin ameliorates tissue plasminogen activator-mediated blood-brain barrier permeability and ischemic brain injury in rats. Neuronal Res. 2009; 31: 189-194.
5. Appel SA, Molshatzki N, Schwammenthal Y et al. Serum Calcium Levels and Long-Term Mortality in Patients with Acute Stroke. Cerebrovasc Dis. 2010; 16: 31: 93-99.
6. Sharma V, Giri S,agarwal MP. Correlation of Serum Albumin levels with Neurological Severity and Short term Outcome in Acute Ischemic troke. J Assoc Physicians India 2009; 74:115.
7. Dziedzic T, Pera J, Slowik A, Gryz-Kurek EA, Szczudlik A. Hypoalbuminemia in acute ischemic stroke patients: frequency and correlates. Eur J Clin Nutr. 2007; 61: 1318-1322.
8. Dziedzic T, Slowik A, Szczudlik A. Serum albumin level as a predictor of ischemic stroke outcome. Stroke. 2004; 35: 156–158.
9. Alvarez-PerezFJ, Castelo-Branco M, Alvarez-Sabin J. Albumin Level and Stroke. Potential Association Between Lower Albumin Level and Cardioembolic stroke. Int J Neuroscience. 2011; 121(1): 25-32.
10. Ginsberg MD, Palesch YY, Hill MD, Martin RH, Moy CS, Barson WG, et al. High-dose albumin treatment for acute ischaemic stroke (ALIAS) part 2: a randomised, double-blind, phase 3, placebo-controlled trial. The Lancet Neurology 2013; 12(11): 1049-1058.



| |
|---|
| Conflict of interest: None |
| Funding: None |