Correlation Of Hematological And Radiological Parameters With Functional Outcome In Patients Of Acute Ischemic Stroke

Saman Fatima*, Ruhi Khan**

* MD, Junior Resident, ** MD, Assistant Professor, Department Of Medicine, J N M C, AMU Aligarh UP, India

Abstract: Background: Stroke in developing countries is reported to have a younger mean age at onset as compared to developed countries. Objectives: To correlate hematological and radiological parameters with functional outcome in patients of acute ischemic stroke. Material & Methods: This study was undertaken in the Department of Medicine in collaboration with the Departments of Radio diagnosis and Pathology, Jawahar Lal Nehru Medical College and Hospital, AMU, Aligarh from January 2017 to November 2018. By convenience method for sampling, 102 patients who were admitted with the diagnosis of acute ischemic stroke to IPD of JNMCH, Aligarh, on clinical as well as radiological grounds were taken into study. Results: There was a positive correlation between serum cortisol and functional outcome according to m RS. As serum cortisol increased, m RS grade also increased with a correlation coefficient of 0.812 and the result was statistically significant ($p < 0.01$). There was a negative correlation between serum albumin and functional outcome according to m RS. As serum albumin increased, m RS grade decreased with a correlation coefficient of -0.659 and the result was statistically significant ($p < 0.01$). There was no correlation between CCA-IMT and functional outcome ($r=0.091$) and neither was the result statistically significant. Conclusion: Serum cortisol level was found to have a significant positive correlation with radiological parameter and worsening functional outcome. Serum albumin was found to have a neuroprotective effect. [Saman F Natl J Integr Res Med, 2020; 11(3):1-6]

Key Words: Serum albumin, Serum cortisol, functional outcome, correlation coefficient, m RS grade, Radiological parameter

Author for correspondence: Dr. Ruhi Khan, D/o Mr. Masoom Ali, E-5, Abdullah Apartment, Girls College Road Civil Lines, Aligarh, UP, India 202002 E-Mail: drruhi5@gmail.com Mobile: 9267522882

Introduction: Studying long-term stroke outcomes including body functioning (neurologic and neuropsychological impairments) and activity limitations and participation is essential for long-term evidence-based rehabilitation and service planning, resource allocation, and improving health outcomes in stroke.[1]

Functional outcome after stroke is subject to complex interactions with multiple factors, including age, gender, ethnicity, pre-existing morbidity, stroke severity, acute interventions, and post stroke care. Other important predictors of outcome include causal type of stroke, sedentary lifestyles, alcoholism and cigarette smoking, hypertension, diabetes, dyslipidemia, coronary artery disease, atrial fibrillation, and previous history of stroke or TIA. However, the need to identify better biomarkers as predictors of outcome in acute ischemic stroke still exists. This study was conducted to study the prognostic significance of serum cortisol and serum albumin in patients of ischemic stroke.

In cerebral ischemia, derangements of the HPA axis are one of the first measureable changes. Stroke acts as a stressor and stimulates the HPA axis to increase serum levels of cortisol. Hypercortisolism has been suggested to exacerbate ischemia induced neuronal injury in addition to causing immune dysregulation leading to an increased rate of adverse events. Increased levels of serum cortisol at presentation have been shown to be an independent predictor of poor functional outcome in a number of studies.[2]

Serum albumin is another biomarker that has a neuroprotective effect that is mediated by its multitude of actions including anti-oxidant properties, modulation of endothelial functions and venular perfusion. Albumin ameliorates brain swelling, enhancing blood flow to sub-occlusive microvascular lesion, maintaining vascular patency and preventing re-occlusion. Relatively high albumin levels at presentation in patients of acute ischemic stroke have been shown to be a predictor of good outcome.[3] This study was conducted with the objective to correlate of blood level of serum cortisol, serum albumin and radiological findings at doppler ultrasonography with functional outcome.

Material & Methods: This hospital based observational cohort prospective study was undertaken in the Department of Medicine in collaboration with the Departments of Radio diagnosis and Pathology, Jawahar Lal Nehru Medical College and Hospital, AMU, Aligarh, during the period lasting from January 2017 to

November 2018. By convenience method for sampling, 102 patients who were admitted with the diagnosis of acute ischemic stroke to Inpatient department of JNMCH, Aligarh, on clinical as well as radiological grounds were taken into study.

Inclusion Criteria: All patients age ≥ 18 years presenting with acute ischemic stroke.

Exclusion Criteria: Age < 18 years, Hemorrhagic stroke,Previous TIA/ischemic attack, Hyper uricemia, Known patients of gout, Fever at presentation. Patients who had surgery within last 3 weeks, Patients on immunosuppressive agents or steroids. Only patients who presented with a focal or global disturbance of cerebral function within 48 hours were considered. A detailed clinical history was taken and examination findings were recorded.

Complete blood counts, RFT, Blood sugar levels, lipid profile, ESR, TSH, chest X-ray, ECG, and brain imaging (NCCT head/ MRI brain) were done in all the patients. Besides these investigations, serum albumin, serum cortisol were done. At baseline, demographic data (age and sex) and history of conventional vascular risk factors (hypertension, diabetes mellitus, atrial fibrillation, coronary artery disease, smoking and alcohol abuse) were obtained.

Measurement Of Outcome: Neurological and functional outcome was assessed by Modified Rankin Scale at day 90. We defined poor outcome as mRS 2 or more (m RS >2), because it was suggested that using this cut off point makes it easier to define poor outcome. [4]

Biochemical Parameters Used In Study: The investigations were carried out in Central lab 1 of JNMCH, Aligarh and Chemical lab, department of pathology, medical central and renal lab of department of medicine, JNMCH, AMU, Aligarh.
COMPLETE BLOOD COUNTS: By automated machine (NIKOH KOHDEN Celltac hematology analyser)

Serum Cortisol: Using VIDAS (Vitek Immuno Diagnostic Assay System). The technology used, which is adaptable to a wide range of assays, combines the EIA method with a final fluorescence reading: this technology is known as ELFA (Enzyme Linked Fluorescent Assay) The enzyme used in the VIDAS range is alkaline phosphatase.

Serum Albumin: Quantitative estimation of serum albumin was done using BeneSphera semiauto-analyser.

ECG: Resting 12-lead ECG recorded at a speed of 25 mm/second was done in all patients.

Carotid Doppler: CCA-IMT was determined by colour Doppler studies of the carotid artery using Toshiba Aplio XG Doppler equipment using a linear array transducer (5-12MHz) at the department of radio diagnosis, JNMCH. Mean values of the left and right CCA-IMT were taken up for statistical analyses.

CT Scan Head: CT Scan Head was done by SOMATOM Emotion eco at the Department of Radiodiagnosis, JNMCH by a qualified radiologist.
MRI Brain: MRI Brain was done by the Magnetom Avanto with Tim+ Dot Fit model of Siemens with 48 channels, the most updated of 1.5 Tesla MRI scanners.

Echocardiography: Echocardiographic studies of these patients was performed in Echo lab of Centre of cardiology.

Statistical Analyses: Statistical analysis was done using SPSS version 20. Results were expressed as mean ± standard deviation and percentage. Univariate analysis was performed using Independent T test for continuous variables and Chi Square test for categorical variables. Spearman's correlation coefficient (r) was used to show correlation between variables.

Results: Mean age of the patients was 64.69 ± 8.735 years. Out of 102 patients, 60 (59%) were males and 42 (41%) were females. Out of 102 patients, 40 (39%) were smokers. 22 (21.5%) out of 102 patients of acute ischemic stroke were alcoholic, and all were males.

In our study, 58 (57%) patients were known cases of hypertension. The mean ± SD of systolic BP was 137.71 ± 17.85mm Hg in patients with good outcome. For diastolic BP, mean ± SD was 90.10 ± 13.73mmHg in patients with good outcome and 106.60 ± 20.30 mmHg in patients with poor outcome. Out of 102 patients, 26 (25%) patients were found to be known cases of diabetes

mellitus. Out of 102 patients, 20 patients were known cases of coronary artery disease. 18 out of 102 patients presented with atrial fibrillation.

TOAST Classification: When patients were classified according to TOAST subtype, maximum numbers of patients were found to be of large vessel disease stroke (n=28). There were 24 patients each in the small vessel disease and undetermined etiology group. 22 patients suffered from cardio embolic stroke and 4 patients were classified as having other subtype of stroke. Table 1

Table 1 : Distribution According To TOAST Classification In Study Group

TOAST SUBTYPE	N = 102
LVD	28 (27%)
SVD	24 (23%)
CE	22 (22%)
OTHER	(4%)
UE	24(24%)

OCSP Classification: When patients were classified according to OCSP classification, maximum number of patients were found to be having PACS subtype of stroke (n=38). There were 22 patients each of TACS and POCS subtype and 20 patients of LACS subtype. Table 2

Table 2: Distribution According To OCSP Classification In Study Group.

OCSP	N = 102
LACS	20 (20%)
TACS	22 (21%)
PACS	38 (37%)
POCS	22 (22%)

Mean cortisol was 450.84 ± 190.35 nmol/L. The (mean ± SD) of serum cortisol was 258.10 ± 77.91 ng/ml in patients with good outcome and 585.77 ± 113.34ng/ml in patients with poor outcome. The difference between the 2 groups was statistically significant (p<0.05). There was also a positive correlation between serum cortisol and functional outcome according to m RS (r= 0.812).

Mean serum albumin was 2.83 ± 0.76 gm/dl. The (mean ± SD) of serum albumin was 3.47 ± 0.64mg/dl in patients with good outcome and it was comparatively lower in patients with poor outcome (2.38 ± 0.45mg/dl) and this difference was statistically significant (p <0.01). There was also a negative correlation between serum albumin and functional outcome according to m RS (r=-0.659).

Modified Rankin Scale (M RS): Out of 102 patients, 60 patients had poor outcome (m RS >2) and 42 patients had good outcome (m RS ≤ 2). Table 3

Table 3 : Distribution Of Poor And Good Outcome In Study Group.

m RS	N = 102
≤ 2	42 (41%)
>2	60 (59%)

Correlation of variables with outcome: For the purpose of correlation of various variables with outcome, patients were divided into 2 groups
Good Outcome : m RS ≤ 2
Poor Outcome : m RS > 2

Serum Cortisol: The (mean ± SD) of serum cortisol was 258.10 ± 77.91 nmol/l in patients with good outcome and 585.77 ± 113.34nmol/l in patients with poor outcome. The difference between the 2 groups was statistically significant (p<0.05). There was a positive correlation between serum cortisol and functional outcome according to m RS. As serum cortisol increased, m RS grade also increased with a correlation coefficient of 0.812 and the result was statistically significant(p <0.01)

Table 4: Difference In Mean Cortisol In The 2 Outcome Groups

	Serum Cortisol (mean ± SD)	p value
m RS ≤ 2	258.10 ± 77.91	< 0.05
m RS > 2	585.77 ± 113.34	

Figure 1: Box Plot Showing Correlation Between Serum Cortisol And Functional Outcome According To M RS.

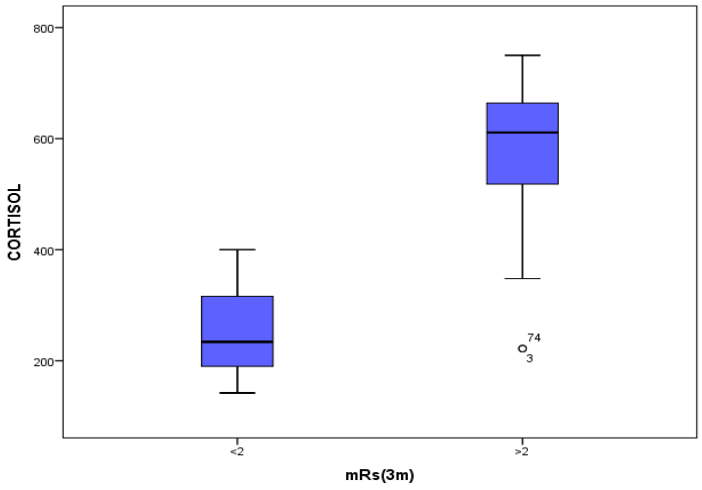
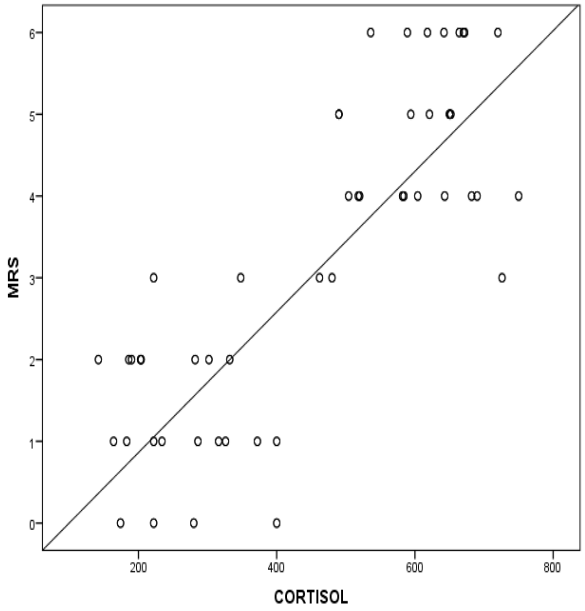


Figure 2: Scatter Plot Showing Correlation Between Serum Cortisol And Functional Outcome According To M RS.



Serum Albumin: The (mean ± SD) of serum albumin was 3.47 ± 0.64mg/dl in patients with good outcome and it was comparatively lower in patients with poor outcome (2.38 ± 0.45mg/dl) and this difference was statistically significant (p <0.01).

CCA-IMT: Mean CCA-IMT was 0.858 ± 0.150. Minimum CCA-IMT was 0.60 mm and maximum CCA-IMT was 1.20 mm. The mean ± SD of CCA-IMT was 0.84 ±0.17 mm in patients with good outcome and 0.87 ± 0.13 mm in patients with poor outcome. The difference between the two groups was not statistically significant (p>0.05).There was no correlation between CCA-IMT and functional outcome (r=0.091) and neither was the result statistically significant.

Figure 3 : Box Plot Showing No Correlation Between CCA-IMT And Functional Outcome According To M RS.

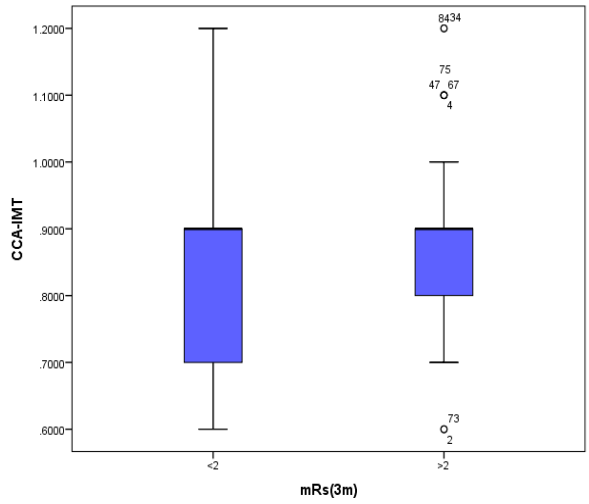
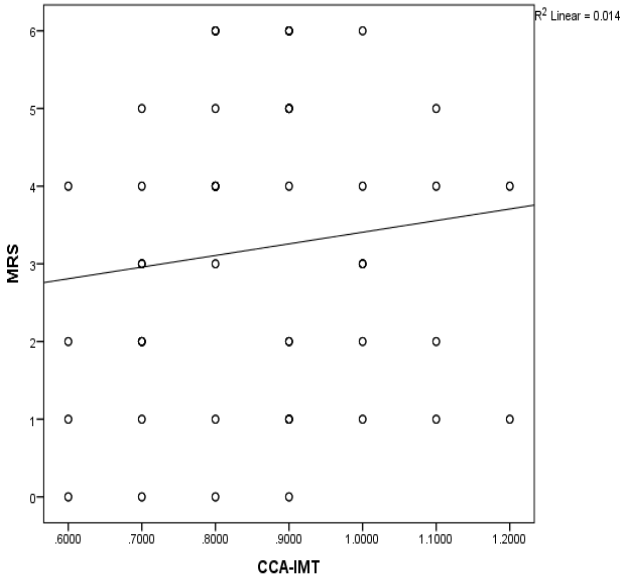


Figure 4: Scatter Plot Showing No Correlation Between CCA-IMT And Functional Outcome According To M RS.



Discussion: The TOAST (Trial of Org 10 172 in Acute Stroke Treatment) classification was based on clinical findings detected by history and examination, the results of brain imaging, and the findings of ancillary testing including vascular and cardiac imaging. In our study, amongst patients with LVD, majority had poor outcome (n=24, 85%) and 4 had good outcome. Similarly, greater number of patients of cardio embolic stroke had poor outcome (n=16, 72%). Amongst patients of SVD, greater number (n=18, 75%) had good outcome and 6 had poor outcome. There were 4 patients of other subtype and all had good outcome. 10 (41%) patients of undetermined etiology subtype had good outcome and 14 (59%) patients had poor outcome. The difference between the 2 outcome groups with respect to TOAST classification was statistically significant (p<0.05). Also, on application of regression analysis, LVD was found to be an independent predictor of poor outcome and SVD was found to be an independent predictor of good outcome.

Shuolin wu[5] (2017) conducted a study on 2907 patients and found that subtype of stroke according to TOAST classification significantly affected long term functional outcomes. It was reported that 67% patients of cardio embolic stroke had poor outcomes, 59% patients of LVD had poor outcomes, and 65% patients of SVD had good outcomes. Omori et al[6] (2013) conducted a study on 2052 patients and found that statistically significant difference was found in m RS grades according to causal subtypes.

Poor outcomes were seen the most in CE stroke (41%), and LVD (36.7%) and least in SVD stroke (20%).

The Oxfordshire Community Stroke Project (OCSP) classification uses the clinical pattern at the time of maximum deficit from first cerebrovascular event to classify the patient into 4 subtypes. In our study, greater number of patients with LACS (n=16.80%) had good outcome and only 4 had poor outcome. All patients of TACS had poor outcome. 16(43%) patients of PACS had good outcome and 22(57%) had poor outcome. 10(46%) patients of POCS had good outcome and 12(54%) had poor outcome.

The difference between the 2 outcome groups with respect to OCSP classification was statistically significant ($p<0.05$). On regression analysis, LACS was found to be an independent predictor of good outcome. Zi and Shuai et al[7] (2013) conducted a study on 226 subjects and found that subtypes of stroke had significant correlation with outcome. 77% of patients with TACS had poor outcome and 74% patients of POCS had good outcome. A study of 147 patients by Osmani, Durrani, & Ara, 2010[8] showed that 80.5% of patients TACS had expired by the end of 3 months, 16% were dependent and 3% were independent. 70% of patients of LACS were independent by the end of 3 months and 20% had dependent outcome and 10% had died.

On regression analysis, serum cortisol was found to be an independent predictor of poor functional outcome. Zi and shuai et al[7] (2013) conducted a study on 226 patients and found that the mean cortisol was 441 nmol/L in patients with good outcome and 643 nmol/L in patients with poor outcome and the difference was statistically significant. Christensen et al[9] (2004) studies 172 patients and found mean serum cortisol in deteriorating patients was 649 nmol/l (95% CI 511–826 nmol/l) and in not deteriorating patients, mean s-cortisol was 525 nmol/l (95% CI 483–571 nmol/l) , which was significantly lower.

These results agree with the results obtained by most authors, who have shown that hypercortisolemia is related to a greater neurological deficit. Neidert et al[2] (2011) studied 281 patients and reported that cortisol was an independent prognostic marker of poor functional outcome and death within 90 days and at 1 year. Hence, the main finding in our study is that cortisol is an independent prognostic marker of functional outcome and death in patients with ischaemic stroke. A systematic review of 48 studies conducted by Barugh et al[10] (2014) found that elevated cortisol levels were associated with higher dependency, length of hospital stay, depression, delirium, and mortality.

In our study, the (mean ± SD) of serum albumin was 3.47 ± 0.64mg/dl in patients with good outcome and it was comparatively lower in patients with poor outcome (2.38 ± 0.45mg/dl) and this difference was statistically significant ($p <0.01$). Idicula et al[11] (2009) conducted a study on 444 patients and showed that high albumin levels were an independent predictor of good functional outcome and lower mortality.

Dziedzic et al[3] (2004) recruited 818 subjects in whom the mean albumin levels were 3.41 g/dl in patients with poor outcome and 3.68 g/dl in patients with good outcome ($p<0.01$). Abu bakar et al (2013) reported mean serum albumin levels of 2.08 g/dl in patients with poor outcome and 3.03 g/dl in patients with good outcome. Similar findings were recorded by Sandeep et al[12] (2017) along with a negative correlation between serum albumin and m RS. A study conducted by Zhang et al[13] (2016) concluded that lower serum albumin levels increased the risk of recurrence in patients with acute ischemic stroke. Chakraborty et al[14] (2013) also reached the same results. Moderate to high dose albumin therapy has been shown to be neuroprotective in animal models with focal as well as global cerebral ischemia.

Conclusion: Serum albumin, serum cortisol are prognostic indicators of functional outcome in patients of ischemic stroke. Serum cortisol level was found to have a significant positive correlation with worsening functional outcome. Serum albumin was found to have a neuroprotective effect. CCA-IMT, which is an established risk factor for atherosclerosis and cerebrovascular disease, was not found to be related to post stroke functional outcome in our study.

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