STUDY OF ACUTE PHASE REACTANTS (ESR, CRP, SERUM FERRITIN) AND THEIR RELATIONSHIP TO THE SEVERITY AND OUTCOME OF ACUTE STROKE

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ABSTRACT

Stroke is one of the most common cause of mortality and long term severe disability. The measurement of inflammatory markers has been proposed as a method to improve the prediction of risk and outcome in patients with vascular disease. The objective of the study is to estimate the levels of acute phase reactants (ESR, CRP, Serum FERRITIN) in acute ischemic stroke patients. 104 acute ischemic stroke patients were selected based on CT/MRI findings. National Institute of Health Stroke Scale (NIHSS) is used to assess the severity caused by stroke and Modified Rankin Scale (MRS) used to assess the outcome of the patients. The mean age of study population is 58.58 ± 10.11 years. Old age, presence of co-morbidities (DM/HTN), elevated
ESR, C-Reactive Protein, Serum FERRITIN were found to be better predictors of stroke severity and outcome. All the three parameters namely, ESR, CRP and Serum FERRITIN individually had a significant correlation with the prediction of severity and outcome in subjects with acute ischemic stroke.

**KEY WORDS:** ESR, CRP, Serum FERRITIN


**INTRODUCTION**

Stroke is one of the most common cause of mortality and long term severe disability. The measurement of inflammatory markers has been proposed as a method to improve the prediction of risk and outcome in patients with vascular disease. Several studies have also established the association between acute phase reactants and stroke severity and outcome. And the studies established that the elevated ESR, C-Reactive protein and Serum FERRITIN are independent predictors of severity and outcome of stroke.

WHO definition for stroke as —the rapidly developing clinical symptoms and/or signs of local [at times global] disturbance of cerebral functions, in which signs and symptoms will last for > 24 hours or leading to death with no apparent cause other than that of vascular origin ¹.

TIA is a clinical syndrome characterised by an acute focal cerebral or mono-ocular function loss with symptoms last < 24 hours and which thought to be due to insufficient cerebral or ocular blood supply as a consequence of arterial thrombosis or embolism associated with arterial, cardiac or hematological disease ².

- risk factor for atherothrombotic stroke and MI
- depends on blood vessels involved
several minutes to hours (usually <10min) up to 24hrs.

The study assesses the severity and outcome of stroke in relation with ESR, C-Reactive protein and Serum FERRITIN levels.

**MATERIAL AND METHODS**

The study is a prospective observational study and was conducted only after getting clearance from Institutional Human Ethics committee. Results will be analyzed with the help of appropriate statistical methods.

**SAMPLING FRAME** All the Patients admitted with Acute ischemic stroke in Chettinad Hospital and Research Institute, Kelambakkam, TN, India.

**SAMPLE SIZE** - Census method Patients admitted with acute ischemic stroke in Chettinad hospital and research institute during study period. Based on the inclusion and exclusion criteria total patients selected for this study were 104.

104 stroke patients were selected based on CT/MRI findings. National Institute Health Stroke Scale (NIHSS) is used to assess the severity caused by stroke (Minor- 1-4, Moderate- 5-15, Severe- 15-20, Very severe- 21-42). Modified Rankin Scale (MRS) used to assess the outcome of the patients (0 – 6).

National Institute of Health Stroke Scale (NIHSS) is used to quantify the impairment caused by stroke at the time of admission. This score consist of 11 components:

- Level of consciousness
- Horizontal eye movement
- Visual field test
- Facial palsy
- Motor arm (left and right)
• Motor leg (left and right)
• Limb ataxia
• Sensory
• Language
• Dysarthria (speech)
• Inattention

For each component score of zero indicates normal function, where the higher score indicates level of impairment (severity). Minimum score is zero. A maximum score of 42 represents the most severe and devastating stroke.

STATISTICAL ANALYSIS

Data entry was done in MS Excel spread sheet. Data analysis and validation was carried out by SPSS software version 22. Comparison of categorical variables was done by using chi square test based on the number of observations. Values of P < 0.05 were taken as Significant P value.

RESULTS

Total of 104 patients with acute ischemic stroke were included in the study with the mean age of the population is 58.58 ± 10.11 years (77 males and 27 females). NIHSS is used to quantify the severity of stroke. Mild- 1-4 Moderate- 5-15 Severe- >15. MRS is used to assess the outcome of stroke Good outcome- 1-2 Poor outcome- 3-6. Among 104 study subjects, 15 had minor stroke, 56 had moderate stroke and 33 had severe stroke as measured by NIHSS. Among the 104 study population 61 had good outcome and 43 had poor outcome as measured by modified Rankin Scale. Risk factor distribution among the study population was, 74 of them had either DM or HTN, 59 of them were diabetic, and 45 of them had systemic hypertension. Positive correlation between age and severity of stroke is observed and it is statistically significant with a p value
of <0.001. Positive correlation between age and outcome of stroke is observed and it is statistically significant with a p value of <0.001. Male gender was found to be a better predictor of severe stroke with a p value of 0.339 which is statistically not significant. Male gender was found to be a better predictor of poor outcome of stroke with a p value of 0.704 which is statistically not significant. Overall co-morbidities are established as predictor of severe stroke with a statistically significant p value of < 0.001 which is statistically significant. Overall co-morbidities are established as predictor of poor outcome of stroke with a statistically significant p value of < 0.001 which is statistically significant. Existence of diabetes or hypertension was found to be a better predictor of severe stroke and poor outcome with a p value of < 0.001 which is statistically significant. Elevated ESR level when associated with other co-morbidities is a predictor of severe stroke and poor outcome with a p value of < 0.001 which is statistically significant. Elevated CRP level when associated with other co-morbidities was found to be a predictor of severe stroke and poor outcome with a p value of < 0.001 which is statistically significant. Elevated serum FERRITIN level when associated with other co-morbidities was found to be a predictor of severe stroke and poor outcome with a p value of < 0.001 which is statistically significant. Serum FERRITIN is a better predictor of stroke severity and outcome than ESR and C-Reactive protein. Combination of variables also significant in predicting the severity and outcome of stroke.

DISCUSSION

This study involved a total of 104 subjects of which 77 were males and 27 were females. The mean age of the study population was 58.58 ± 10.11 years. 59 patients had diabetes, 45 had
hypertension, 74 had overall comorbidities (DM/HTN), 30 had diabetes and hypertension, and 30 had no co-morbidities.

DEMOGRAPHICS

Present study showed a positive correlation between age and severity of stroke with a p value of < 0.001 which is statistically significant. It also showed showed a positive correlation between age and outcome of stroke with a p value of < 0.001 which is statistically significant. Where as in other earlier study by O. Bill et al which showed there is no significant relation between the age and severity of stroke. In the study male gender was found to be a better predictor of severe stroke when compared with female gender with a p value of 0.242 which is statistically not significant. This is in contrary to previous studies like The Framingham study and O. Bill et al study where female gender is established as a predictor of severe stroke. And even for outcome also male gender was found to be a better predictor when compared with a female gender with a p value of 0.704 which is statistically not significant. In the study equal proportion of males and females were not taken as our main aim is to assess ESR, CRP and Serum FERRITIN as predictors of stroke severity and outcome. Out of 77 males 24 had severe stroke and out of 27 females 09 had severe stroke, out of 77 males 31 were in poor outcome and out of 27 females 12 were in poor outcome.

RISK FACTORS

In the current study overall co-morbidities (DM/HTN) was established as predictor of severe stroke with a p value of < 0.001 which is statistically significant, and also associated with Poor outcome with a p value of < 0.001 which also statistically significant. Out of 74 patients with co-morbidities 32 (43.24%) had severe stroke whereas out of 30 patients without any co-morbidity, 01 (3.3%) of them had severe stroke.
The most frequent co-morbidity was diabetes. In our study diabetes individually was established as predictor of severe stroke with a p value of < 0.001 which is statistically significant, and also associated with Poor outcome with a p value of < 0.001 which also statistically significant. Out of 59 diabetics 28 (47.45%) had severe stroke, and 35 (59%) had poor outcome.

In the study hypertension was established as predictor of severe stroke with a p value of < 0.001 which is statistically significant, and also associated with Poor outcome with a p value of < 0.001 which also statistically significant. Out of 45 hypertensives 23 (51.11%) had severe stroke and 28 (62.22%) had poor outcome. Study by Willmot et al showed that high blood pressure associated with poor outcome of stroke.

**ESR**

This study showed that elevated ESR level associated with co-morbidities is a predictor of severe stroke with a p value of < 0.001 which is statistically significant. The mean value of ESR in patients with severe stroke is 46.27 ± 20.69 (mm/hr). As the ESR level increased the severity of stroke also increased. This is similar to Study by Kisialiou et al which showed that there is increased ESR at admission in acute stroke patients, and its monitoring at the time of admission serve as a marker for severity after AIS.

This study showed that elevated ESR level associated with a predictor of poor outcome of stroke with a p value of < 0.001 which is statistically significant. The mean value of ESR in patients with poor outcome of stroke is 43.16 ± 19.5 (mm/hr). As the admission ESR level increased the outcome of stroke is poor .This is similar to Study by Chamorro et al. (1995) which suggested that increasing in-admission ESR is independently accompanied by a worse prognosis in acute stroke patients.
CRP

The study elevated CRP level found to be a predictor of severe stroke with a p value of < 0.001 which is statistically significant. The mean value of CRP in patients with severe stroke is 52.79 ± 34.56 (mg/l). As the CRP level increased the severity of stroke also increased. This is similar to Study by Kouchaki Ebrahim et al. which showed that there is high CRP level at admission is associated with severity in acute ischemic stroke patients.

This study showed that high CRP level associated with a predictor of poor outcome of stroke with a p value of < 0.001 which is statistically significant. The mean value of CRP in patients with poor outcome of stroke is 48.37 ± 32.39 (mg/l). As the admission CRP level is high the outcome of stroke is poor. This is similar to Study by Weinbeck et al. in which patients who presented with ischemic stroke, C-Reactive Protein levels taken at 12 and 24 hours can be used independently as predictors of unfavourable outcomes.

SERUM FERRITIN

Present study showed that elevated serum Ferritin level associated with co-morbidities is a predictor of severe stroke with a p value of <0.001 which is statistically significant. The mean value of serum Ferritin in patients with severe stroke is 359.91 ± 68.29 (ng/ml). And the elevated serum Ferritin level associated with poor prognosis with a p value of <0.001 which is statistically significant. As the serum Ferritin level increased the severity of stroke also increased and prognosis also poor. The mean value of serum Ferritin in patients with poor outcome of stroke is 331.95 ± 88.52 (ng/ml). This is similar to Study by Koul, et al. which showed that high values of serum Ferritin were associated with high NIHSS, which indicated the severity of the stroke, also it had a positive correlation with the MRS which indicates poor outcome in high MRS patients of acute stroke. Similar studies by Davalos et al, 2000; Erdemoglu AK et al.
showed that elevated serum Ferritin on admission of acute stroke patients (within 24 to 48 h after stroke onset) was reported to predict a bad prognosis.

**COMPARISON OF ESR, CRP AND SERUM FERRITIN**

Many previous trials have established ESR, C-Reactive protein and Serum Ferritin as independent predictors of severe stroke and poor outcome, but none of them compared their predictive value. Here in our study we compared predictive value of these three variables in assessing the severity of stroke and short term outcome. We found that Serum Ferritin is a better predictor of severe stroke and outcome than ESR and C-Reactive protein. Comparison of ROC curves of all three parameters in our study showed that Serum Ferritin has a area under the curve of 0.967 for severity of stroke and 0.947 for outcome of stroke, whereas ESR has a area under the curve of 0.850 for severity of stroke and 0.841 for outcome of stroke, and C-reactive protein has a area under the curve of 0.870 for severity of stroke and 0.881 for outcome of stroke. So from our study the order of predictive value would be increase in Serum Ferritin > C-Reactive protein > Erythrocyte Sedimentation Rate for both severity and outcome.

The study tried to assess the combination of variables in predicting the severity and outcome of stroke. The combinations are significant in predicting the severity and outcome of stroke. But the combination of variables with ESR is more sensitive and the combination of variables with Serum Ferritin is more specific. Thus there was a more need for sample size and further studies to establish the better combination to predict the severity and outcome of stroke.
CONCLUSION

- All the three parameters namely, ESR, CRP and Serum FERRITIN individually had a significant correlation with the prediction of severity and outcome in subjects with acute stroke.

- When we come across acute ischemic stroke patients we can use. ESR, C-Reactive protein and Serum FERRITIN as predictors of stroke severity and outcome, with Serum FERRITIN being a better predictor.

- As reliable early prediction of severe stroke helps in improving the patient’s functional outcome and long term disability, this area requires further research.

REFERENCES


biomarkers role in acute ischemic stroke patients: higher is worse or better? Immun Ageing 9:2 2


