Potentiality of liver biomarkers in predicting outcome of Stroke patients

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Abstract

Background: Minor changes of liver biomarkers are usually found during the acute phase of stroke, but importance and outcomes are not clearly understood. Liver enzymes aspartate aminotransferase (AST), alanine aminotransferase (ALT), and Alanine phosphatase (ALP) are known to be associated with Cardiovascular risk factor. However, the association between liver enzymes in predicting the outcome in stroke patients is poorly understood. **Objective:** We assessed the relation of liver enzymes with 28 days mortality among patients hospitalized with Ischemic Stroke. **Materials and Methods:** Study was retrospective. 74 patients admitted to ICU were recruited with a diagnosis of stroke. The data were analyzed in the terms of demographic details, plasma glucose, Aspartate transaminase(AST), Alanine transaminase(ALT) and Alkaline Phosphatase (ALP). **Results:** 74 patients were analyzed. In our study 40(54.1%) patients had high AST levels, 24 (32.4%) patients had high ALT levels and 38 (51.4%) patients had high ALP levels. Among 40 (54.10%) non survivor patients, 18 (45%) patients had high AST levels, 8 (20%) patients had high ALT levels and 22 (55%) patients had high ALP levels with p value of > 0.05. The high values of AST and ALT were statistically significant. ALT values were not statistically significant. 28 days mortality was high in patients with AST and ALP levels higher than the normal, there was no association between high ALT levels and mortality. **Conclusion:** In conclusion, we found an independent positive association between serum aminotransferase level and the 28 days mortality. A good number of stroke patients had high AST and ALP at onset of stroke. ALT values were not significant. Increased rate of mortality up to 28 days was found in such patients. Targeted interventions may improve outcomes and require further assessment.
Key Words: Stroke, Plasma glucose, Aspartate transaminase, Alanine transaminase and Alkaline Phosphatase.

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INTRODUCTION

Elevated serum enzyme levels has been shown in patients with nervous system injury , specifically in patients with traumatic brain injury[1]. Many observational studies having reported an inverse relation of liver biomarkers on post-stroke mortality outcome[2], the relationship between the two is not well comprehended. Stroke is an important cause for mortality and long-term disability. Some patient studies reported a positive association between hemorrhagic stroke and a history of liver dysfunction, which was defined by elevated liver enzymes[3]. However, there are no data on the association between aminotransferase levels and the incidence of stroke. Studies carried to decipher the relation between liver enzymes and mortality in patients of stroke showed controversial outcomes[4]. Important challenge, is the identification of a cost-effective diagnostic and prognostic biomarker for stroke. Alkaline phosphatase (AP) enzyme has been evaluated as a potential biomarker in stroke[5]. The aim of this study was to assessed the relation of liver

enzymes with 28 days mortality among patients hospitalized with Ischemic Stroke.

MATERIALS AND METHODS

This was a retrospective study, conducted from January 2019 to December 2019 in the department of biochemistry and Critical Care Medicine , Yenepoya medical college hospital ,Mangaluru. 74 diabetic patients of ischemic stroke admitted in MICU were enrolled in this study. Clearance from institutional ethical committee was obtained and data was collected from all diabetic patients admitted to MICU . Demographic details, plasma glucose, Aspartate transaminase (AST), Alanine transaminase (ALT) and Alkaline Phosphatase (ALP) , Age, sex, duration of ICU stay, duration of DM, other co-morbidities, medication history was recorded for all patients. 28 days mortality was taken into consideration.

STATISTICAL ANALYSIS

The descriptive analytical statistics were evaluated statistically with IBM SPSS Statistics for Windows, Version 23.0 . Data collected was entered in Microsoft Excel and reported as frequency and proportions. Test of significance (Chi square tests) was applied to categorical variables using SPSS version 23 . Unpaired T test was used to test the significant difference between liver enzyme levels with mortality. P value less than 0.05 was considered as statistically significant.

RESULTS

74 diabetic patient's, medical records were analyzed retrospectively to assessed the relation of liver enzymes with with 28 days mortality among patients hospitalized with Ischemic Stroke. Among 74 analyzed patients, 42 (56.70%) were men and 32 (43.30%) were females. The mean age of our study population was 51-60 years. The clinical data, characteristics and enzyme levels of study population with stroke among survivors and non survivors along with percentage are shown in table 1. In our study 40(54.1%) patients had high AST levels, 24 (32.4%) patients had high ALT levels and 38 (51.4%) patients had high ALP levels as shown in Table 1. Our study showed that non-survivors had higher blood sugar values compared to those of survivors thus showing a significant relationship between blood sugar value and mortality rate.

Table 1: Characteristics and enzyme levels of study population with stroke among survivors and non survivors

|	N	%
Male	42	56.8
Female	32	43.30
AST		
Normal	34	45.5
High	40	54.1
ALT		
Normal	50	67.6
High	24	32.4
ALP		
Normal	36	48.6
High	38	51.4
Mortality		
Survival	34	45.9
Non Survival	40	54.1

Out of 74 analyzed patients, a total of 40 (54.10%) patients expired during 28 days period of time following stroke(Table 2). Among 40 (54.10%) non survivor patients, 18 (45%) patients had high AST levels , 8 (20%) patients had high ALT levels and 22 (55%) patients had high ALP levels with p value of < 0.05, shown in Table 2. The high values of AST and ALT were statistically significant. ALT values were not statistically significant. The association between enzymes levels and 28 days mortality is graphically represented in Fig 1.

28 days mortality was high in patients with AST and ALP levels higher than the normal, but there was no association between high ALT levels and mortality.

Table 2: Comparison of liver biomarkers in Non Survivor patients

Variable	n(%)	P value
AST		
Normal	22(55 %)	0.05
High	18(45 %)	54.1
ALT		
Normal	32(80%)	0.05
High	8(20%)	
ALP		
Normal	18(45%)	0.05
High	22(55 %)	

*P < 0.05 is considered as statistically significant
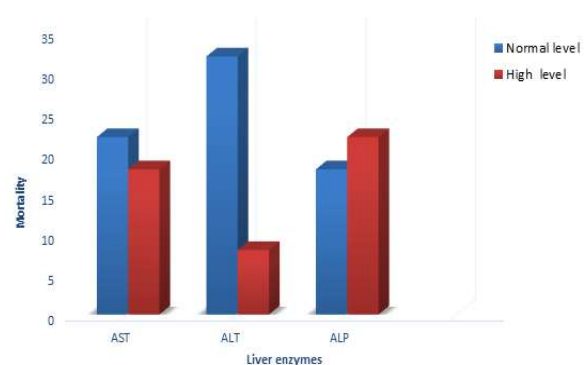
Figure 1: Association of liver biomarkers in Non Survivor

DISSCUSION

We investigated the relation of liver enzymes with 28 days mortality among patients hospitalized with Ischemic Stroke. 28 days mortality was high in patients with AST and ALP levels higher than the normal, but there was no association between high ALT levels and mortality.

Previous studies have reported positive associations between serum aminotransferase levels and various conventional Stroke risk factors[6,7]. Some patient studies reported a positive association between hemorrhagic stroke and a history of liver dysfunction, which was defined by elevated liver enzymes[8,9]. However, there are no data on the association between aminotransferase levels and the incidence of stroke. Allison *et al.*; reported that Alkaline phosphotse isoenzymes can be a used as potential blood biomarkers for stroke[10]. Many pathological mechanisms, can explain the relation between high enzyme levels and higher risk of mortality in stroke patients. Homeostasis abnormalities may partially contribute to the adverse effects of liver enzyme dysfunction on hemorrhagic stroke. However, it is likely that nonhemostatic mechanisms may also be involved, because impairment of the hemostatic system in men with abnormal liver enzymes is too modest to cause bleeding[11]. Hyeon C *et al.*; reported that an elevated serum aminotransferase level may be an independent predictor of ICH[12]. In a previous prospective study done in Korean population, ALT was a risk factor for intracerebral hemorrhage, but not ischemic stroke[13]. A German study reported that, there was no relationship between ALT and overall risk of stroke in middle aged men and women, but noted an inverse association with ischemic stroke[14]. Our study did not show association between high ALT levels and 28 days mortality. Interestingly, a meta-analysis found that low ALT predicted stroke mortality, particularly in older people[15]. The researchers speculated that low ALT may be an indicator of poor nutrition, reduced liver cell turnover, or low skeletal muscle mass[16].

LIMITATION: Sample sizes was small, and no alcoholic history was taken.

CONCLUSION

To conclude we found an independent positive association between serum aminotransferase level and the 28 days mortality. A good number of stroke patients had high AST and ALP at onset of stroke. ALT values were not significant. Increased rate of mortality up to 28 days was found in such patients. In such patients, targeted interventions may improve outcomes. Further studies are needed to examine the effectiveness of interventions in terms of clinical and financial outcomes in patients in an acute stroke setting. Since high enzymes levels are correctable abnormalities in the stroke patients, they should be managed accordingly as a therapeutic target so as to improve the outcome in hospital admitted patients and reduce the mortality.

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