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Research Article

Association between raised high sensitivity troponin T with poor outcome after acute ischemic stroke

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ABSTRACT

Introduction: Elevated levels of high sensitivity cardiac troponin T occur in a substantial proportion of patients with acute ischemic stroke and can predict poor outcome and mortality after stroke. Whether elevated hs-cTnT levels can also predict hemorrhagic transformation or prognosis in ischemic stroke patients remains unclear.
Objective: To assess the association between raised high sensitivity troponin T with poor outcome after acute ischemic stroke.
Material & Methods: Study Design: Cohort study. **Settings:** Department of Medicine, Mayo Hospital, Lahore. **Duration:** from January 2017 to June 2017. **Procedure:** Total 100 patients were enrolled. Blood sample was obtained and was sent laboratory for analysis of serum hs-cTnT level. All patients were followed in the hospital and duration of hospital stay was noted. If patient died within 15 days of admission, then poor outcome was labeled.
Results: Among 26(26%) patients poor outcome was observed. Patients whose Hs-TnT level was raised among them 18(36%) patients outcome was poor and those patients who had normal Hs-TnT level among them only 8(16%) patients outcome was poor. Relative risk of 1.601 showed that patients with raised value of Hs-TnT had 2.25 times more chances of poor outcome as compared to those patients with normal Hs-TnT level. This same trend was seen in all age groups as well as for both genders [and even for those patients who had family history of MI.
Conclusion: Raised Hs-TnT level is associated with poor outcome in patients presenting with acute ischemic stroke.

Key Words: High sensitivity troponin T, Poor outcome, Acute ischemic stroke

INTRODUCTION

Stroke is the third most common cause of death and it is easily the leading cause of disability in developed as well as in developing countries.[1] The incidence of stroke is declining in the Western population but the burden of the disease in South Asian countries (India, Pakistan, Bangladesh, and Sri Lanka) has inclined and it is still expected to rise further in the near future.[2]In Pakistan, few limited studies conducted have shown that approximate annual incidence of stroke in Pakistan is 250/100,000, which means 350,000 new cases every year. The Stroke-specific fatality has been reported between 7% and 20% in various studies from Pakistan.[3, 4] Up to 63% of all stroke patients develop complications and up to 89% are dependent for activities of daily living.[4]

Many factors have been investigated regarding the prognosis of stroke. Recently, there has been an interest in investigating cardiac troponin T in ischemic stroke. Serum level of creatine-kinase myocardial fraction (CK-MB), lactate dehydrogenase (LDH), and cardiac troponin T (cTnT) are elevated in myocardial damage. cTnT is a highly sensitive and specific marker of myocardial injury as compared to CK-MB and it

is used in the diagnosis of acute myocardial infarction.[5]Increase in cTnT levels have been reported after myocardial damage, but increased cTnT has also been reported to occur in 5-34% of patients with acute ischemic stroke.[6] In several studies, the elevation of cTnT was studied and it was found associated with stroke severity on hospital admission, insular cortex lesions, short- and long-term clinical outcome and increased risk of mortality, indicating prognostic significance of increased cTnT in acute ischemic stroke.[7-10]

Recently, a new generation of highly sensitive troponin assays has been developed and it allows for the detection of concentrations 5 to 10 times lower than those measureable with conventional assays.[11] In a study, it was found that with raised Hs-TnT, 27.7% patients while 6.5% with low Hs-TnT had mortality (P<0.01). The mean hospital stay of raised Hs-TnT patients was 12 days while mean hospital stay of low Hs-TnT patients was 7 days (P<0.001).[12]

So, this new high sensitivity cardiac troponin T (hs-cTnT) elevation may be more valuable .than the conventional assays and it may help to better predict the association between hs-cTnTelevation on in-hospital mortality after acute ischemic stroke. Therefore, a study has been planned to be conducted in which hs-cTnT elevation will be studied in ischemic stroke patients and association of hs-cTnT elevation will be measured. Moreover, no local study has been found in this regard which can help us in implementing the screening of Hs-TnT in ischemic stroke patients so that they can be prevented from mortality by altering medication and treatment.

MATERIAL AND METHODS

Study Design: Cohort study

Setting: Medical Outdoor and Indoor departments of Mayo Hospital, Lahore

Inclusion Criteria: Patients having age 40-65 years of either gender diagnosed with acute ischemic stroke (hypo-dense area in CT scan brain within 24hrs of onset of weakness of one or more parts of body) presented within 24 hours of onset of symptoms, confirmed with CT scan.

Group I: patients of AIS with raised Hs-TnT

Group II: patients of AIS without raised Hs-TnT

Exclusion Criteria

1. Patient who present with central chest at presentation.
2. Patients who had weakness but weakness improves within 24 hrs of onset (transient ischemic attack).
3. Patients with history of previous stroke in the past.
4. Patients who has had MI in past one month.
5. Patients with diagnosed malignancy in previous medical records.
6. Patients with diagnosed chronic renal disease (creatinine>1.2mg/dl).
7. Pregnant patients.

Data Collection Procedure: Total 100 patients (50 patients with raised Hs-TnT and 50 without raised Hs-TnT) fulfilling selection criteria were enrolled in the study through emergency of Department of Medicine, Mayo Hospital, Lahore. A written consent was taken. Demographic information (name, age, gender) was noted. Then blood sample was obtained and was sent laboratory for analysis by taking 3 cc venous blood sample in a disposable syringe within 24hrs of on-set of symptoms and raised serum hs-cTnT level was recorded. All patients were followed in the hospital and duration of hospital stay was noted. If patient died within 15 days of admission, then poor outcome was labeled (as per operational definition). Follow-up was maintained through telephone and OPD visits. All the data was collected by the researcher himself on a prescribed Proforma.

Statistical Analysis: All data was entered and analyzed using computerized software i.e. SPSS version 20. Mean and standard deviation was calculated for numerical variables like age. Frequency and percentage was done for nominal variable like gender and poor outcome. Relative risk was calculated to measure association between raised Hs-TnT(value≥14ng/L) and poor outcome (death during 15 days of attack). RR>1 was considered as risk of association. Data was stratified for age, gender and family history of MI. Post-stratification, adjusted RR was

calculated. P-value ≤0.05 was considered as significant.

RESULTS

Mean age of patients was 51.59±±7.22 years. There were 53(53%) male and 47(47%) female included in the study.There were 15(15%) patients who had family history for MI.***(Table-1)***Patients who had raised Hs-TnT among them chances of poor outcome was significantly 1.601 times higher as compared to those patients who had normal Hs-TnTi.e. RR: 1.601 & p-value=0.023 ***(Table-2)***

Table-1: Baseline characteristics

n	100
Age (years)	51.59±7.22
Male	53 (53%)
Female	47 (47%)
Family History of MI	15 (15%)

Table-2: Association between raised hs-TnT with poor outcome after acute ischemic stroke

Poor Outcome	**Raised Hs-TnT**	**Normal Hs-TnT**	**Total**
Yes	18(36%)	8(16%)	**26**
No	32(64%)	42(84%)	**74**
Total	**50**	**50**	**100**

Relative Risk= 1.601, **95% CI=** 1.079-4.691, **p-value=** 0.023

DISCUSSION

Several lines of evidence point to elevated levels of cTnT as a prognostic indicator in stroke patients. Elevated cTnT levels occur in 5–36% of patients with acute ischemic stroke, and they are associated with greater stroke severity on admission and higher risk of insular lobe damage, poor clinical outcome and mortality.[10, 13-15]

hs-TnT assays, for which the measurements are termed hs-cTnT, have greatly expanded the potential use of cTnT levels as markers in myocardial infarction, even other cardiac diseases such as structural heart disease and atrial fibrillation end-stage renal disease pulmonary embolism, and other conditions.[16-18] The literature has established hs-cTnT levels as a specific and sensitive biochemical marker of myocardial damage, and potentially of other types of tissue damage, such as stroke. Interestingly, increased cTnT was also reported to occur in 5-34% of patients with acute ischemic stroke.[6]

In several studies, the elevation of cTnT was associated with stroke severity on hospital admission, insular cortex lesions, short- and long-term clinical outcome and increased risk of mortality,[8, 10, 19] indicating prognostic significance of increased cTnT in acute ischemic stroke.

In this study patients were classified on the basis of Hs-Tnt level. There were 50 patients whose Hs-TnT level was raised and 50 patients with normal Hs-TnT level. Among 26(26%) patients poor outcome was observed. Patients whose Hs-TnT level was raised among them 18(36%) patients outcome was poor and those patients who had normal Hs-TnT level among them only 8(16%) patients outcome was poor. Relative risk value of 1.601 showed that patients with raised value of Hs-TnT had 2.25 times more chances of poor outcome as compared to those patients with normal Hs-TnT level. This same trend was seen in all age groups [40-50 years (Poor Outcome): RR=1.45, & 51-60 years (Poor Outcome):RR=1.86 &>60 years (Poor outcome): RR=1.37] patients as well as for male and female patients [Male (Poor Outcome): RR=1.74 & Female (Poor Outcome):RR=1.43]. and even for those patients who had family history of MI [Family History for MI (Poor outcome): (Yes): RR=2.75 & No=1.43].

Recently in 2016 Junfeng Liu in his study examined possible relationships of hs-cTnT levels with risk of hypertension and with overall prognosis of acute ischemic stroke patients with RHD in China. As per his findings patients with

elevated hs-cTnT levels were at significantly higher risk of hypertension, 3-month mortality and 3-month disability/mortality (all P-value<0.029). After controlling for age, sex, hypertension, renal impairment and National Institutes of Health Stroke Scale score on admission, the risk of hypertension and 3-month mortality was, respectively, 4.0- and 5.5-fold higher in patients with elevated hs-cTnT levels than in patients with normal hs-cTnT levels.[20]

In a study, it was found that with raised Hs-TnT, 27.7% patients while 6.5% with low Hs-TnT had mortality (P<0.01). The mean hospital stay of raised Hs-TnTpatients was 12 days while mean hospital stay of low Hs-TnT patients was 7 days (P<0.001).[12]Raoul Stahrenberg in his study reported that Hs-TnT predicts vascular events and all cause mortality in patients with acute cerebral ischaemia and improves prediction beyond established clinical scores.[21]Results of this study are in line with the results of above mentioned studies showing that with raised Hs-TnT level patients chance for poor prognosis, mortality and other morbid conditions is higher. However none of the studies have calculated relative risk for poor outcome in relation to raised Hs-TnT level.

Two candidate mechanisms are regarded to be relevant for troponin elevation in acute ischemic stroke when renal insufficiency is excluded. First, coincident acute coronary syndrome may lead to focal ischemic myocardial necrosis by means of thrombotic occlusion of a coronary vessel. Second, stroke-induced autonomic imbalance with subsequent surge of catecholamines could induce global damage and dysfunction of myocardial tissue and the release of cTnT. However, the underlying cause of cTnT elevation in the individual stroke patient remains questionable, leading to a diagnostic and therapeutic dilemma for the attending physician. In order to rule out coincident acute coronary syndrome reliably coronary status has to be clarified. However, estimated risks of cerebral bleeding complications limit the diagnostic work-up using coronary angiogram in patients with acute stroke.[11]

Levels of the cTnT are frequently elevated in patients with acute ischemic stroke and elevated cTnT predicts poor outcome and mortality. The pathomechanism of troponin release may relate to co-morbid coronary artery disease and myocardial ischemia or, alternatively, to neurogenic cardiac damage due to autonomic activation after acute ischemic stroke. Therefore, there is uncertainty about how acute ischemic stroke patients with increased cTnT levels should be managed regarding diagnostic and therapeutic workup.

Although clinical risk prediction scores have been repeatedly validated and are therefore established prognostic tools for patient management in cerebral ischaemia, their predictive value is only moderate.[22] Commercially available biomarkers like hs-TnT are highly standardized and reproducible surrogates for biological processes that are extremely objective and easy to interpret when physicians are provided with clear rules on their use. Due to their high degree of standardisation, they allow for comparisons across different settings.

CONCLUSION

Results of this study demonstrated that raised Hs-TnT level is associated with poor outcome in patients presenting with acute ischemic stroke. Using Hs-TnT as a routine marker in stroke patients lead to better risk prediction as well as improvement in risk-tailored secondary preventive measures and ultimately in outcomes for these patients.

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