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Study Of High Sensitivity C-Reactive Protein In Acute Ischemic Stroke

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ABSTRACT *Stroke is a significant health burden for individuals and society. Elevated stroke risk has been linked to high levels of C - reactive protein. We studied hs-CRP levels in 60 patients with acute ischemic stroke and correlated it with severity of stroke. We conclude that hs-CRP levels are significantly higher in patients with acute ischemic stroke as compared to controls. Hs-CRP levels increase with age, severity of stroke as per NIHSS score and worsening GCS score.*

KEYWORDS : Stroke, hs-CRP, NIHSS score

Introduction

Stroke is a significant health burden for individuals and society. It is the third leading cause of mortality in the western world and also a major cause of disability Thus, early identification of those at increased risk of stroke represents a major contribution to health improvement so that interventions can be targeted to those most likely to benefit. Because stroke risk prediction is based only on conventional risk factors, a continued search for predictive marker is of interest. [1]

Infections and inflammation play a vital role in the pathophysiology of atherosclerosis. [2] Ischemic brain injury is characterized by acute local inflammation and changes in levels of inflammatory cytokines, notably C- reactive protein (CRP). Elevated stroke risk has been linked to high levels of CRP. However, vascular inflammation is more related to high-sensitivity CRP (hs-CRP).

Consequently, hs-CRP levels have attracted clinical attention as a predictive marker of atherosclerosis. It has a long half-life, is easily measured and readily available inflammatory marker. Elevated hs-CRP levels may help to stratify post-stroke patients into relatively low risk (hs-CRP concentration <1.0 mg/L), average risk (1.0 to 3.0 mg/L), and high risk (>3.0 mg/L) for future stroke. [3]

Similarly, several studies have shown that C - reactive protein is associated with stroke severity and outcome. [4] Moreover, hs-CRP was the only inflammatory marker that independently predicted the risk of stroke. [5] Early identification of those at increased risk of stroke may help to contribute in therapeutic decision making and health improvement. Hence we undertook this with the aim to study the high-sensitivity C-reactive protein levels in patients with acute ischemic stroke and find the correlation of high-sensitivity C-reactive protein with its severity.

Methods

We conducted a cross sectional observational study on 60 patients, from October 2013 to November 2015. Patients presenting within first 72 hours with first ever-acute ischemic stroke were included. Patients with acute coronary syndrome, infectious pathology, arthritis or cancer or prior inflammatory pathology, patients on NSAIDS, statins and hormone replacement therapy were excluded. After obtaining written informed consent, a detailed history regarding stroke and its risk factors was taken. Detailed general and neurological examination was done. Biochemical investigations and brain imaging study either in the form of CT- head or MRI brain was done. Venous sample for hs-CRP was collected within 72 hours of onset of stroke. The sample was studied by immuno-turbidimetry method.

NIHSS score and GCS were calculated at the time of admission to assess the severity of stroke. Accordingly, stroke was classified as 0 =No stroke, 1-4 = mild Stroke, 5-15=Moderate Stroke, 16-20 =Moderate to severe Stroke, 21-42=Severe Stroke. Patients were followed up for 7 days or until discharge whichever was longer. The level of hs-CRP was correlated with severity of stroke and the presence of other risk factors.

Results

Majority cases i.e. 33 (53%) were in the age group 61 to 70. It was evident that the mean level of hs-CRP was higher with as the age advanced. (Mean hs-CRP = 4.9 mg/l, in patients ≤50 yrs as compared to 8.4 in patients ≥70 years). The mean hs-CRP value in cases was 7.91±3.0 mg/L, while that in controls was 2.19±mg/L. This difference was statistically significant ($p<0.05$).

The value of hs-CRP was used to stratify stroke patients into risk groups for future cardiovascular events as: Low Risk: < 1mg/L, Average Risk: 1-3 mg/L, High Risk: >3 mg/L. [3]

There were no cases in low risk category. While 5 (8.3%) cases had average risk, a majority of patients i.e. 55 (91.7%) patients had high risk for future cardiovascular events.

It was observed that 51% patients had GCS score of 13-15 (mean hs-CRP 6.11±2.51), 25% patients had GCS score 9-12(mean hs-CRP 8.43±3.43) and 22% of patients had GCS score 3(mean hs-CRP 10.36±2.41). Higher hs-CRP values were associated with low GCS score. Table 1shows correlation of hs-CRP with NIHSS score. It was seen that the levels of hs-CRP was highest among patients with severe stroke (NIHSS score 21-42), while patients with lower hs-CRP

levels had mild stroke (NIHSS score 1-4).
The association of cardiovascular risk factors with hs-CRP levels was studied, and it was found that there was a statistically significant association of hs-CRP with hypertension (p-value = 0.028) as depicted in table 2.

Discussion
Stroke is the third leading cause of mortality in the western world and also a major cause of disability. To analyse the role of hs-CRP in stroke, the present study was undertaken.

In our study, the mean age of stroke cases was 66 years. Similarly, Jaydip et al[2] in their study found that the mean age was 62 years for stroke cases. Moreover, Elkind et al [6] in Merritt's Neurology have mentioned that the strongest determinant of stroke is age. This was in accordance to our study in which we found that the levels of hs-CRP increased as age increased.

We found that hs-CRP had significant association with NIHSS score with p value <0.05 depicting that more the NIHSS score, more is the rise in hs-CRP level.

Adnan et al [3] conducted a study in 2010 and found that out of 67 patients with raised hs-CRP, 25 (37.31%) patients had severe (NIHSS 15-24) and 19 (28.36%) patients had very severe stroke (NIHSS >25). In acute ischemic stroke, higher hs-CRP concentration correlates with more severe neurological deficit, i.e. with higher NIHSS score. This finding was similar to our observation as well as to a study conducted by Guo et al[7] in 2003 in which they observed that higher concentrations of hs-CRP on admission correlated with higher leucocyte count and blood glucose level, larger infarct, severe neurological deficit and had more NIHSS score and worse outcome.
In our study we found that the level of hs-CRP was inversely related to GCS score. Khalil et al [68] found that patients with GCS less than 8 and APACHE II more than 14 increased the relative risk of mortality and morbidity by 2.16 and 2.20 fold respectively than those with GCS more than 8 and APACHE II less than 14.

Khalil et al [8] at Zagazig found that smoking, and presence of diabetes, hypertension and dyslipidemia increased the relative risk of mortality and morbidity in patients with ischemic stroke by 1.2, 1.37, 1.26 and 1.27 fold respectively. Jimenez et al [9] conducted a study in US in 2015 and concluded that elevated hs-CRP levels were associated with a greater risk of total stroke, even after adjustment for potential confounders and cardiovascular risk factors. Risk of total stroke was significantly higher among hypertensive men with elevated hs-CRP compared to normotensive men with low hs-CRP, which showed similar findings like our study. High hs-CRP concentrations (1 mg/L) were associated with higher prevalence of traditional stroke risk factors, including hypertension (both systolic and diastolic), diabetes, dyslipidemia, high BMI, and elevated concentrations of fasting glucose, total cholesterol (TC), triglycerides (TG) and low-density lipoprotein (LDL).

Conclusions
We conclude that hs-CRP levels are significantly higher in patients with acute ischemic stroke as compared to controls, most of them in a range that predicts a high risk for future cardiovascular events. Hs-CRP levels increase with age, severity of stroke as per NIHSS score and worsening GCS score. Among the traditional risk factors associated with stroke, namely hypertension, diabetes mellitus, smoking, and dyslipidemia, only hypertension was found to have a significant co-relation with the levels of hs-CRP among cases and controls. There is ample evidence that inflammatory markers predict prognosis after first coronary event. However, the role of elevated after first ischemic stroke is less clear. The determination of plasma hs-CRP level, as a marker of inflammation, will help in predicting severity and prognosis in ischemic stroke.

Limitations
Cases were observed only up to 7 days or until discharge, whichever was longer. Therefore, the subjects could not be followed up to study whether increased hs-CRP was predictive of future risk of cardiovascular events.

TABLES Table1: Correlation of hs-CRP with NIHSS score.

NIHSS score	Cases n=60(%)	Mean hs-CRP levels (mg/L)
1-4	6(10)	2.67 ± 0.73
5-15	16(25)	5.81 ± 1.34
16-20	19(40)	7.96 ± 0.96
21-42	18(25)	11.46 ± 1.76

Table 2: Distribution of cases as per hs-CRP levels with cardiovascular risk factors

Cardiovascular Risk factor	Frequency (%)		Mean hs-CRP levels		
	Case n=60(%)	Controls n=60(%)	Cases	Controls	
Hypertension	38(63%)	15(25%)	9.67	3.09	0.028
Diabetes Mellitus	28(47%)	15(25%)	10.37	3.09	0.192
Smoking	16(27%)	8(13.3%)	11.33	3.25	0.672
Dyslipidemia	13(22%)	9(15%)	11.36	3.02	0.857

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