

FREQUENCY OF RAISED C-REACTIVE PROTEIN IN ACUTE ISCHEMIC STROKE

Adnan Khan¹, Zafar Ali¹

ABSTRACT

Objective: To find out the frequency of raised C-reactive protein (CRP) levels in patients with first-ever acute ischemic stroke.

Methodology: This hospital based descriptive (case series) study was carried out in Neurology Unit, Lady Reading Hospital, Peshawar, Pakistan from March 2011 to December 2011. A total of 100 patients with first-ever acute ischemic stroke, aged 18 years and above and of either gender, were included by convenient sampling technique. National Institute of Health stroke scale (NIHSS) was measured at the time of admission to assess stroke severity. Within 24 hours of admission high-sensitivity (hs)-CRP levels were measured. Data were analyzed using SPSS version 15.0.

Results: Out of 100 patients, 58(58%) were females and 42 (42%) were males. Mean age was 64.7 ± 14 years. Sixty seven patients (27 males & 40 females) had raised hs-CRP levels. Out of 67 patients with raised hs-CRP, 25 (37.31%) patients had a severe (NIHSS 15-24) and 19 (28.36%) patients had a very severe stroke (NIHSS >25). Thirty one (46.27%) patients had hs-CRP level of >3.0 mg/L having a high risk of ischemic stroke while 22/67 (32.8%) with hs-CRP level of 1.0-3.0 mg/L had an average risk of ischemic stroke. Fourteen (20.89%) patients had hs-CRP level of <1.0 mg/L and had low risk of ischemic stroke. Mean serum level of hs-CRP in ischemic stroke patients was 23 ± 11.24 mg/L.

Conclusion: hs-CRP is elevated in a significant number of patients with acute ischemic stroke. An elevated CRP was associated with increased stroke severity.

Key Words: Stroke, Acute Ischemic Stroke, C-reactive Protein, High-sensitivity C-reactive Protein, Inflammatory Markers, National Institute of Health Stroke Scale.

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INTRODUCTION

Acute stroke is the leading cause of death worldwide and one of the main causes of long-term disability. According to the World Health Organization, 15 million people suffer from stroke each year^{1,2}. About 87% of all strokes are due to ischemia³.

There is an increasing evidence that inflammatory processes are involved in cerebral ischemia^{4,5}. 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 C-reactive protein. Many patients with elevated CRP levels within 72 hours of stroke have an increased risk of death^{6,7}.

CRP is an acute phase protein and serves as biomarker for systemic inflammation. However, vascular inflammation is more related to high-sensitivity CRP (hs-CRP)⁸. Consequently, hsCRP levels have attracted clinical attention as a predictive marker of atherosclerosis.

Induction of CRP is rapid and its half-life (19 hours) is long enough. There does not appear to be any diurnal variation⁹. It is an easily-measured and readily available inflammatory marker. These properties make plasma CRP very useful for the diagnostic workup of inflammatory diseases. 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^{10,11}. Stroke risk prediction is based only on conventional risk factors which is still not completely reliable, therefore a continued search for predictive markers is of interest. Early identification of those at increased risk of stroke may help in contribution to therapeutic decision making and health improvement.

1 Department of Neurology, Post Graduate Medical Institute, Lady Reading Hospital Peshawar, Pakistan.

Address for Correspondence:

Dr. Adnan Khan

MRCP (UK),

Department of Neurology, Government Lady Reading Hospital, Peshawar, Pakistan

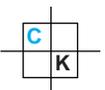
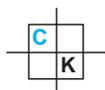
Cell #: +92-308-8881961.

Email: dradnankhan1961@yahoo.com

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The purpose of this study was to determine the frequency of raised C-reactive protein levels in patients with first-ever acute ischemic stroke in our set up.

METHODOLOGY

This was a hospital based descriptive (case series) study. The study was carried out in neurology unit Post graduate Medical Institute, Lady Reading Hospital, Peshawar, Khyber Pukhtoonkhwa, from March 2011 to December 2011. Patients were admitted through out-patient (OPD) and emergency departments.

After obtaining an informed consent, a total of 100 patients with first-ever acute ischemic stroke, aged 18 years and above and of either gender, were included by consecutive sampling technique.

Patients presenting with Transient ischemic attacks (TIA), hemorrhagic stroke, recurrent stroke and those who were admitted more than 24 hours after the onset of symptoms were excluded from the study.

Acute ischemic stroke was diagnosed clinically and radiologically as follow:

A focal neurological deficit (hemiparesis, dysphasia, cranial nerve palsies or hemianopia) of sudden onset that persist beyond 24 hours and documented by a brain CT scan indicating the presence of infarction.

Patients were assessed through a detailed history (from the patient or from relatives) including personnel particulars, presenting complaints, past history of stroke, smoking, alcohol consumption, hypertension, statin use and diabetes mellitus.

National Institute for Health stroke scale (NIHSS) was measured at the time of admission to assess stroke severity¹². The NIHSS ranges from 0-42 with higher values representing more severe infarcts (Table I).

Venous blood was sampled from all patients and sent for fasting lipid profile, random blood sugar and hs-CRP levels within 24 hours of admission. hs-CRP was estimated using particle enhanced turbidimetric assay in Auto-analyser (ROCHE COBAS INTERGRA 400 PLUS/immuno-nephelometry, Dade Behring, Marburg, Germany)¹³. To look for cerebral infarcts and rule out haemorrhage, CT scan of brain was done. All the informations were recorded on a standard proforma.

Computer soft ware SPSS (windows version 15.0) was used for data entry, storage, processing and analysis. Mean + standard deviation (SD) was calculated for quantitative variables like age, NIHSS score and raised CRP levels. Data were presented in the form of tables.

RESULTS

Out of 100 patients included in the study, 58(58%) were females and 42 (42%) were males, with an overall female to male ratio of 1.38: 1.

ASSESSMENT OF STROKE SEVERITY BY NATIONAL INSTITUTE OF HEALTH STROKE SCALE (NIHSS)

NIHSS Score	Neurological Impairment
>25	Very severe neurological impairment
15-24	Severe Impairment
5-14	Moderately Severe impairment
<5	Mild impairment

Table I

AGE DISTRIBUTION

Age Group (in years)	No. of patients (n=100)
18-40	12 (12%)
41-60	57 (57%)
61 and above	31 (31%)

Table II

GENDER-WISE DISTRIBUTION OF RAISED HS-CRP LEVELS

Gender	Frequency (n=100)	Raised hs-CRP* (n=67)	P value
Male	42 (42%)	27 (64.28%)	0.615
Female	58 (58%)	40 (68.96%)	
Total	100	67	

*hs-CRP-High-Sensitivity C-Reactive Protein

Table III

NIHSS SCORE AND RAISED HS-CRP LEVELS

NIHSS* Score	Number of patients (n=100)	Raised hs-CRP** (n=67)	P value
<5	17 (17%)	07 (10.45%)	0.01
5-14	27 (27%)	16 (23.88%)	
15-24	34 (34%)	25(37.31%)	
>25	22 (22%)	19(28.36%)	
Total	100 (100%)	67 (100%)	

*NIHSS- National Institute for Health stroke scale

**hs-CRP-High-sensitivity C-reactive Protein

Table IV

HIGH-SENSITIVITY C-REACTIVE PROTEIN LEVELS AND RISK STRATIFICATION OF ACUTE ISCHEMIC STROKE PATIENTS

Risk with hs-CRP* level	Frequency (n=67)	%age
Low risk (hs-CRP <1.0 mg/L)	14	20.89%
Average risk (hs-CRP 1.0 to 3.0 mg/L)	22	32.84%
High risk (hs-CRP >3.0 mg/L)	31	46.27%

*hs-CRP-HIGH-SENSITIVITY C-REACTIVE PROTEIN

Table V

Age of the patients ranged from 18-82 years with the mean age of 64.7 + 14 years. Age distribution (of different age groups) is shown in Table II.

Raised hs-CRP was found in 27 (64.28%) of male patients and 40 (68.96%) of female patients. Gender-wise distribution of raised hs-CRP levels is shown in Table III.

Base line NIHSS score of study patients is shown in Table IV. Out of 67 patients with raised hs-CRP, 25 (37.31%) patients had a severe (NIHSS 15-24) and 19 (28.36%) patients had a very severe stroke (NIHSS >25).

Table V is showing details of hs-CRP level and risk stratification of ischemic stroke. Thirty one (46.27%) patients had hs-CRP level of >3.0 mg/L having a high risk of ischemic stroke while 22/67 (32.8%) with hs-CRP level of 1.0-3.0 mg/L had an average risk of ischemic stroke. Mean serum level of hs- CRP in ischemic stroke patients was 23±11.24 mg/L.

DISCUSSION

The use of biomarkers as predictors of stroke lesion evolution and prognosis is becoming increasingly important. They may be of useful help in the search for an optimal management of stroke patients¹⁴.

Inflammatory processes play an important role in the development of atherosclerosis and instability of atheroma and increases the risk of ischemic stroke^{15,16}. Cerebral ischemia triggers an inflammatory response characterized by activation and release of acute phase proteins such as C-reactive protein (CRP) and cytokines. The inflammatory processes may start within 2 h after stroke onset and sustain for days, and may contribute to ischemic brain damage even in that early stage¹⁷.

This suggests that CRP not only reflects the amount of tissue damage, but may also indicate a state of enhanced risk due to increased inflammation or cytokine excess. The recent JUPITER trial shows that the use of rosuvastatin in patients with high CRP has a significant impact both in reducing the CRP level and in lowering future vascular events¹⁸.

Raised hs-CRP was found in 67 (67%) of our study patients. Elevated serum levels of C-reactive protein (CRP) are found in up to three quarters of patients with ischemic stroke^{19,20}.

In our study ischemic stroke patients with high CRP at admission was associated with more severe stroke. Sixty-six percent of the patients with raised hs-CRP had a severe or very severe stroke (NIHSS 15-24 Or >25) in our study. An elevated CRP was associated with increased stroke severity (NIHSS) ($p = 0.015$)²¹. The association between high CRP and a high stroke severity remains unexplained. Elevated CRP may be a direct response to the extent of cerebral tissue injury^{22,23}.

In the present study 31 (46.27%) patients had hs-CRP level greater than 3.0 mg/L (Table V) and are there-

fore high risk for future stroke. Corso G et al showed that CRP levels > 9 mg/L, predict a higher risk of further ischemic events and mortality²⁴.

In a study by Makita S et al, elevation of serum hs-CRP levels was an independent risk factor for future ischemic stroke in men but not in women, whereas there was no association between serum hs-CRP levels and the risk of future hemorrhagic stroke in either sex⁷.

In women, conflicting effects of sex hormone have been described. Endogenous estrogen is said to protect the development of atherosclerosis as well as induction of hs-CRP levels²⁵ and might weaken the association of hs-CRP elevation with ischemic stroke. Moreover, atherosclerotic process is considered to be more severe in men than in women²⁵.

The prognostic significance of early CRP after stroke has significant clinical implications. Previous stroke studies have shown an association between high CRP and poor outcome²⁶⁻²⁹.

CONCLUSION

This study shows that hs-CRP is elevated in a significant number of patients with acute ischemic stroke. An elevated CRP was associated with increased stroke severity.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

AK: Conception and design, Analysis and interpretation of data, Critical revision, Final Approval of the manuscript

ZA: Data collection, Drafting the manuscript

CONFLICT OF INTEREST

Authors declare no conflict of interest

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