

A Clinical and Public Health Approach: CRP Level and Severity of Stroke is there a Link?

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ABSTRACT

Introduction: Ischemic stroke is a devastating disease, affecting mostly old age people. Studies in different populations have shown that ischemic stroke can trigger an acute phase response resulting in a rise of plasma concentration of C-reactive protein.

Objective: To determine the correlation C-reactive proteins levels with severity of acute ischemic stroke

Place and Duration of Study: Department of Medicine, Hayatabad Medical Complex, Peshawar; Pakistan, from January September 2020 to February 2020.

Study Design: A Descriptive Cross Sectional Study

Methodology: This study was conducted in which n=180 stroke patients were selected through non-probability consecutive sampling technique. All the stroke patients presenting within 72 hours of acute ischemic stroke were enrolled in study. The stroke severity was assessed using NIH stroke scale. Moreover, serum CRP level was measured and data was entered in SPSS 24.0. Finally results were presented in form of tables.

Results: Out of total stroke patients; 67.22% were male, 88.89% had age more than 40 years, 78.33% were married, & 38.33% had monthly income more than Rs. 80000. 31.67% had family history of stroke, 57.78% were overweight and obese, 65% & 35% prefer high caloric and vegetable foods respectively. Moreover, 81.11% presented within 24 hours, 83.89% had NIHSS score of more than 5, and 79.44% had high CRP levels.

Conclusion: It was concluded that CRP showed significant values among most of the patients with acute stroke, and was associated with increased stroke severity. The stroke showed strong association with NIHSS score, type of food preference, obesity/overweight, family history of stroke and physical in-activity.

Key Words: Acute ischemic stroke, C reactive Protein, Serum level

INTRODUCTION

Globally, cardio-vascular diseases are the second leading cause of death, and resulting in more than 7.5 million deaths annually¹. Incidence of stroke is more, and 20% of these patients die within the first year after stroke, and the current prevalence is increasing day by day². Moreover, stroke is the third leading cause of death and the leading cause of disability worldwide³. Although stroke often is considered a disease of elderly persons, one third of strokes occur in persons younger than 65 years⁴.

According to World Health Organization (WHO) estimates, there are globally 12.7 million new cases of stroke annually⁵. Acute ischemic stroke has been associated with acute cardiac dysfunction and arrhythmia^{6, 7}. Because of the ageing population, the burden will increase greatly during the next 20 years, especially in developing countries⁸.

Many international studies revealed that both elevated and low blood pressure is associated with poor outcomes in patients with acute stroke^{9, 10}. A community based study conducted, revealed 11% stroke prevalence in Pakistan¹¹. It is a complex condition influenced by inflammatory process, & genetic factors. Moreover, certain risk factors i.e. factor V Leiden, leukocyte count, serum calcium; IL-6, IL-18, fibrinogen, platelet aggregation, homocystiene, metabolic syndrome, and high sensitivity C reactive protein are increasingly associated with risk and severity of stroke¹². Furthermore, the inflammation plays a critical role and C-reactive protein (CRP), a plasma protein synthesized by the liver, is a sensitive and dynamic systemic marker of inflammation^{13, 14}.

Myocardial infarction is associated with a 2-3% incidence of embolic stroke, of which 85% occur in the first month after MI¹⁵. In an international study published by Beck et al, 2018; found significant association between serums CRP level of stroke patients with stroke

severity. Another study demonstrated that higher selective CRP levels were associated with larger infarct among patients with acute ischemic stroke; and found that baseline CRP values were normal in 72.3% patients but were elevated in 27.7% patients with stroke¹⁶.

The NIHSS is a 42-point scale with minor strokes usually being considered to have a score less than 5¹⁷. Moreover, transient ischemic attacks developed due to stroke. Data suggested that half of these patients suffer stroke within one month and 10% of patients with TIA suffer stroke within 90 days^{3,18}. Moreover, the presence of CT evidence of infarction early in presentation has also been associated with poor outcome and increased propensity for hemorrhagic transformation after thrombolytics^{19, 20, 21}. Moreover, CT Angiography also has a higher sensitivity than standard non-contrast CT for detecting subarachnoid hemorrhage^{22, 23}. Thus the recommendations for acute management of the stroke are in accordance to American Heart Association (AHA) i.e. Guidelines for the Early Management of Adults with Ischemic Stroke⁴.

Pakistan is a developing country and has high prevalence of communicable and non-communicable diseases. All the important determinants of non-communicable diseases are present in the community. Therefore this study was conducted to determine serum C-reactive protein levels and to correlate with the severity of acute ischemic stroke among the patients visiting medical department Hayatabad medical complex Peshawar Pakistan. Moreover, the stroke patients with stroke can be properly and effectively managed.

METHODOLOGY

After approval from hospital ethical and research committee, a descriptive cross sectional study was conducted at the Department of Medicine, Hayatabad Medical Complex, Peshawar; Pakistan; from January September 2020 to February 2020. The total sample size was n=180 using 0.239 correlation coefficient, 90 % power of test and 5% significance level. The sampling technique was non-probability consecutive sampling. All the patients presenting within 72 hours of first acute ischemic stroke & confirmed on CT Scan brain were included while patients age less than 15 years and with end stage co-morbidities and not permanent resident of district Peshawar Pakistan were excluded from the study.

The diagnosis of acute ischemic stroke was based on symptoms of focal neurologic deficit and CT brain evidence of infarct. The purpose and benefits of study was explained to the patients and a written informed consent was obtained. Moreover, all the patients were subjected to detailed history and examination. Stroke severity was assessed using NIH stroke scale. From all patients 5 cc of blood was taken under strict aseptic technique and was sent to hospital laboratory on the same day. Serum CRP level was measured under the supervision of a pathologist. Finally data was entered in SPSS 24.0 Mean $\pm$ SD was calculated for continuous variable like age, NIH stroke scale score and serum CRP and categorical variable like gender was expressed as frequencies and percentages. Pearson's correlation coefficient was calculated to investigate the bivariate relationship between serum CRP and stroke severity on NIH scale. Serum CRP Levels and NIH stroke scale score was stratified among the age and sex to see the effect modification. Results were presented as tables and graphs.

RESULTS**Table No. 1. Demographics of Acute Stroke Patients (n=180) Visiting Medical Unit of Hayatabad Medical Complex, Peshawar Pakistan**

Demographics	Frequency	Percentage
Gender Distribution		
Male	121	67.22
Female	59	32.78
Age Distribution		
18-40 years	20	11.11
41-60 years	101	56.11
61 and above	59	32.78
Marital status		
Married	141	78.33
Unmarried	39	21.67
Occupation		
Govt	31	17.22
Private	55	30.56
Labors	29	16.11
others	65	36.11
Monthly Income		
< 25000	33	18.33
25000 - 50000	41	22.78
50000- 80000	37	20.56
> 80000	69	38.33

Table No. 2. Determinants of Acute Stroke Patients (n=180) Visiting Medical Unit of Hayatabad Medical Complex, Peshawar Pakistan

Determinants	Frequency	Percentage
Family History of Stroke		
Yes	57	31.67
No	123	68.33
BMI		
Underweight	27	15.00
Normal	49	27.22
Overweight	64	35.56
Obese	40	22.22
Prefer High Caloric Food		
Yes	117	65.00

No	63	35.00
Prefer Fruits		
Yes	59	32.78
No	121	67.22
Prefer Vegetables		
Yes	63	35.00
No	117	65.00
Tobacco Smoking		
Yes	69	38.33
No	111	61.67
Physically Active		
Yes	72	40.00
No	108	60.00

Table No. 3. Frequency of Determinants (Time of Presentation (Hours, of Acute NIHSS* Score, Risk with CRP ** Level) of Stroke Patients (n=180) Visiting Medical Unit of Hayatabad Medical Complex, Peshawar Pakistan

Determinants	Frequency	Percentage
Time of Presentation (Hours)		
0 - 12	97	53.89
13 - 24	49	27.22
25 - 36	21	11.67
36 - 48	7	3.89
49 - 60	5	2.78
60 - 72	1	0.56
NIHSS * Score		
< 5	29	16.11
5 five 2 14	48	26.67
15-24	63	35.00
>25	40	22.22
Risk with CRP ** Level		
Low Risk (CRP < 1.0 mg/L)	37	20.56
Average Risk (CRP 1.0 – 3.0 mg/L)	59	32.78
High Risk (CRP > 3.0 mg/L)	84	46.67

NIHSS * National Institute of Health Stroke Scale
CRP ** C Reactive Protein

DISCUSSION

Stroke ranked as a third most common cause of death and most common cause of permanent disability in adults²⁴. At the same time stroke is a potentially preventable disease because most of the causes of stroke are modifiable²⁵. Timely recognition and treatment of the modifiable risk factors is imperative to reduce stroke related morbidity and mortality. Control of these modifiable risk factors is also important for prevention of recurrence of stroke^{24,25}.

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 patients²⁶. Inflammatory processes play an important role in the development of atherosclerosis and instability of atheroma and increases the risk of ischemic stroke^{27,28}. 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 stage¹⁶. 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. In our study ischemic stroke patients with high CRP at admission was associated with more severe stroke. Elevated CRP may be a direct response to the extent of cerebral tissue injury and is a strongly related with blood pressure level^{15,29}. The 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^{11,30}.

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)¹⁶. The association between high CRP and a high stroke severity remains unexplained. In the present study 31 (46.27%) patients had hs- CRP level greater than 3.0 mg/L (Table V) and are therefore 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 mortality^{2,31}.

In a study conducted by Hurford et al., in 2018, published in Neurology Journal found that prognosis of stroke depends on inflammatory indicators and the elevation of serum hs-CRP levels was an independent risk factor for future ischemic stroke and thus strong association was found between serum CRP levels and the risk of stroke²⁵.

The atherosclerotic process is considered to be more severe in men than in women^{3,4}. The prognostic significance of early CRP after stroke has significant clinical implications. Many international research studies, found strong association of stroke with BMI, obesity, high CRP and thus affects the outcome of stroke^{16,32}.

CONCLUSION

From our results it was concluded that hs-C reactive protein showed elevated significant values among most of the patients with acute stroke as compared to normal or reduce CRP

level. Moreover, the elevated CRP was associated with increased stroke severity. The stroke showed strong association with food preference, body mass index, tobacco smoking, family history of smoking and physical activity. Thus comprehensive and standard protocols are needed for the prevention, control and management of stroke to avoid the burden of morbidity and mortality in the communities.

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