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Original Research Article

Study of High Sensitivity C Reactive Protein in Acute Ischemic Stroke

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Abstract

Background: Stroke is one of the most devastating neurological diseases, often resulting in death or disability. It is the second most common cause of death and the leading cause of adult disability. The present study was undertaken to assess high sensitivity C Reactive Protein (hs CRP) levels in acute ischemic stroke and hence correlate the inflammatory marker as a predictor and prognostic factor in atherothrombotic disease.

Material & Methods: 30 cases of ischemic stroke within initial 72 hours of presentation diagnosed based on history, neurological examination and neuroimaging- CT Brain and MRI Brain, and 30 controls without evidence of active infection or inflammation were enrolled in this study, their hsCRP levels were estimated and compared. Results were recorded in Microsoft Excel sheet and data was analysed by SPSS software.

Results: We found that mean hsCRP of case group was 8.69 and that of control group was 2.02 and there was a statistically significant difference between these groups. Increasing age, male sex and hypertension were found to be risk factors contributing to ischemic stroke.

Conclusion: This study demonstrated that high levels of hsCRP are prevalent in all ischemic stroke subtypes and high hsCRP levels may be a marker for starting therapy with statins for both primary and secondary prevention.

Keyword: Ischemic stroke, hsCRP

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Introduction

Stroke is one of the leading causes of death and long-term disability worldwide. According to WHO, 15 million people suffer from stroke each year. Stroke is defined as an abrupt onset of neurological deficit that persist more than 24 hours and attributable to a focal vascular cause. [1] Ischemic stroke is the most common type of stroke and accounts for about 80%–85% of cases.

Over the last few decades, inflammation has been proposed to play an important role in the pathogenesis of acute ischemic stroke (AIS), cerebral ischemia, and atherosclerosis.[2,3] Inflammatory markers such as fibrinogen, interleukins, cytokines

and hs-CRP have been reported as predictable markers for stroke severity and outcome. [4] High sensitivity C-reactive protein (hs-CRP) is a sensitive marker of inflammation and tissue injury. [5] A growing body of evidence supports the concept that local & systemic inflammation plays a role in initiation & progression of atherosclerosis & its complications. However, vascular inflammation is more related to high-sensitivity CRP (hs-CRP). The association between hs-CRP and high stroke severity remains unexplained. There is a distinct possibility that elevated hs-CRP may be a direct response to the extent of cerebral tissue injury.[6] The role of CRP as a marker during and after ischemic stroke is less extensively studied in comparison to coronary artery disease. The Rotterdam study shows that although high CRP is associated with the risk for future stroke, it is not useful for individual stroke prediction. [7] On the other hand the Framingham study shows that high CRP is associated with a greater risk for ischemic stroke or TIA. [8] Currently neuroimaging modalities such as non-contrast CT scan and diffusion weighted MRI are the standard clinical tools for diagnosis of stroke. Biomarkers can assist with patient care by helping to confirm the diagnosis and predicting prognosis. Hs-CRP is emerging as a prognostic marker in stroke. The prognostic importance of hs-CRP may be partly related to the extent of necrosis in the brain parenchyma and partly to unknown determinants of intensity of acute phase reactants. The prognostic value of hs-CRP with respect to neurologic deficits and death as outcomes of stroke helps clinicians to offer realistic expectations to families of stroke victims. Infectious and inflammatory diseases are more common in India compared to western countries; a very limited number of studies are available from India on the association of hs-CRP with ischemic stroke and its sub-types.

This study is carried out to assess the level of high sensitivity C - reactive protein in acute ischemic cerebrovascular accident (stroke) and determine the outcomes with regards to survival.

Material and Methods

This hospital based observational study was done in department of medicine, SMS Medical College, Jaipur from July 2020 to July 2021 after obtaining permission from Institutional Ethic Committee.

30 cases diagnosed with acute ischemic stroke within 72 hours of presentation by history, neurological examination and neuroimaging- CT brain or MRI brain and 30 controls without ischemic stroke and without any evidence of active infection and inflammation were enrolled in this study.

Individual with Transient ischemic attack, Recurrent stroke, Intracerebral and sub arachnoid haemorrhage, Lack of baseline data and admission after 72 hours of onset of stroke, Patients with clinical signs and symptoms of active infection and patients with prior history of inflammatory diseases were excluded. All Ischemic stroke patients and control underwent for CBC, Blood Sugar Fasting and Post Prandial, Lipid Profile, Homocystine Level, Collagen disease profile and test for Prothrombotic states. Echocardiography, neck vessel doppler and cerebral angiographies were done in cases to assess the stroke subtype.

Estimation of hs-CRP was done by VITROS 5.1 chemistry system and VITROS 5600integrated system. We have taken Hs-CRP Level <3 mg/L as negative for inflammation and Level>3 mg/L as positive for inflammation. The data was compiled on M.S. Exceland analysed by SPSS software. Chi square test, student's t test and Karl Pearson correlation coefficient were used to assess the statistical significance.

Results

Table 1: Distribution of patients according to hsCRP.

Parameter	Case Group		Control Group		P-Value
	Mean	SD	Mean	SD	
hsCRP	8.69	9.88	2.02	1.4	**0.0005**

Mean hsCRP of case group was 8.69 and that of control group was 2.02. The p value was 0.0005. There was a significant difference in these groups as p-value was <0.05.

Table 2: Distribution of patients according to Age (in years)

Age Distribution	Case Group		Control Group	
	No. of Patients	Percentage	No. of Patients	Percentage
15-40	4	13.33	12	40
41-65	13	43.33	9	30
66-90	13	43.33	9	30
Total	30	100	30	100
Mean±SD	61.06±16.39		48.43±18.08	
P-Value	**0.006**			

Mean age of case group was 61.06 years and of control group was 48.43 years. The p value was 0.006. There was a significant difference in these groups as p-value was <0.05.

Table 3: Distribution of patients according to Gender

Gender Distribution	Case Group		Control Group		P-Value
	No. of Patients	Percentage	No. of Patients	Percentage	
Female	7	23.33	17	56.66667	**0.009**
Male	23	76.66	13	43.33333	**0.009**
Total	30	100	30	100	

In the above table, we found that 76.6% males were present in case group and 43.3% males were present in control group. The p value was 0.009. There was a significant difference in these groups as p-value was <0.05.

Table 4: Distribution of cases according to Diagnosis Subtype.

Diagnosis Subtype	hs-CRP ≤3.0 mg/L		hs-CRP >3.0 mg/L		p-Value
	No. of Patients	Percentage	No. of Patients	Percentage	
Cardio Embolic	5	33.33	3	20	0.41
Large Artery Atherosclerosis	8	53.33	9	60	0.71
Unknown	2	13.33	3	20	0.62
Total	15	100	15	100	

Majority (53.3%) patients were of large artery atherosclerosis followed by 33.3% patients of cardio embolic stroke in hs-CRP<3mg/dL group. In hs-CRP >3.0 mg/L group, majority (60%) of patients had large artery atherosclerosis followed by 20% cardio embolic subtype.

Table 5: Distribution of patients according to initial 72h Mortality.

Mortality	Case Group	
	No. of Patients	Percentage
Death	3	10
Survived	27	90
Total	30	100

In above table, we found that 10% patients died in case group and 90% survived the initial 72 hours.

Table 6 : Correlation of Mortality with hsCRP.

Mortality	hsCRP ≤3.0 mg/L		hsCRP >3.0 mg/L		P-Value
	No. of Patients	Percentage	No. of Patients	Percentage	
Death	1	6.66	2	13.33	0.54
Survived	14	93.33	13	86.66	0.54
Total	15	100	15	100	

We found that 6.66% patients died in group A and 13.3% in group B. The p value was 0.54. There was no significant difference as p value was >0.05.

Discussion

Cerebrovascular disease is the second most common cause of death worldwide. Male gender and older age are non-modifiable risk factors, whereas, smoking, hypertension, diabetes and dyslipidaemia are well-known modifiable risk factors for ischemic stroke. CRP, one of the acute phase reactants, is an indicator of underlying systemic inflammation and a novel plasma marker of atherothrombotic disease. [9,10,11] It is likely that CRP has many pathophysiological roles in the inflammatory process, including binding of phosphocholine and recognition of foreign pathogens and phospholipid constituents of damaged cells. [12]

We found that mean hsCRP of case group was 8.69 and that of control group was 2.02. The p value was 0.0005. There was a significant difference in these groups as p-value was <0.05. Our finding were in concordance with study by Chaudhari J R et al [13] found that mean hs-CRP in stroke patients was 3.8 and for control subjects it was 1.8. There was significant difference between these groups as p value was <0.001. Bhaisare S D et al [14] also found that average hs-CRP level was 45.12±38.07 mg/L and mean hs-CRP level in ischemic stroke patients was 31.68±31.79 mg/L. We observed that majority (43.3%) of patients in case group was present in 41-65 years and 66-90 years age group and 40% patients in control group was in 15-40 years age group. Mean age of case group was 61.06 years and for control group it was 48.43 years. The p value was 0.006. There was significant difference in these groups as p-value was <0.05.Age is generally considered as a non-modifiable risk factor for stroke. Similar results were obtained in studies conducted by Pinky Talreja Mishra et al [15], Sujit Kumar et al. [16] High hs-CRP level was significantly associated with older age. It may be a significant predictor of future risk of ischemic cerebrovascular accident in the elderly. Large prospective studies in apparently healthy subjects have confirmed the prognostic relevance of CRP in the elderly. [17,18]

We found that 76.6% males were present in case group and 43.3% males were present in control group. The p value was 0.009. There was significant difference in these groups as p-value was <0.05. Our results were also similar to Bhaisare S Det al[14]who observed male preponderance with

70.66% cases being male and 29.33% cases being female. Male to female ratio in their study was 2.4:1. Male sex is also considered as a fixed risk factor for stroke.

We found that majority (53.3%) of patients were of large artery atherosclerosis followed by 33.3% patients of cardio embolic stroke in CRP ≤3.0 mg/L group. In CRP >3.0 mg/L group majority (60%) of patients were of large artery atherosclerosis followed by 20% of cardioembolic stroke. These findings were similar to reports by Huang et al. (63.9% in large artery atherosclerosis) and Rajeshwar et al [19] who observed high CRP in both intracranial (48.7%) and extra cranial large artery atherosclerosis (54.9%). [20]

We found that 10% patients died in case group and 90% survived. We found that 6.66% patients died in group A and 13.3% died in group B. The p value was 0.54.There was no significant difference as p value was >0.05. However, Bhaisare S D et al[14] [B] found that the hs-CRPlevels were related to outcomes in terms of death. The mean hs-CRP level in survivors was 21.83 ±23.17 mg/L and in non survivors was82.07 ±25.83 mg/L. The difference between mean hs-CRP levels in survivors and non survivors was significant. Thus higher hs-CRP levels are associated with more mortality.

Conclusion

This study demonstrated that high levels of hs-CRP are prevalent in all ischemic stroke subtypes and are independently associated with large artery atherosclerosis and cardioembolic stroke. High hs-CRP levels were associated with an increase in risk of developing cardioembolic stroke as well as large artery atherosclerosis. Hence, in these subtypes high hs-CRP may be a marker to initiate primary preventive strategies. Thus, high hs-CRP levels may be a marker for starting therapy with statins for both primary and secondary prevention. Future large scale studies are required to explore these findings.

References

1. Yip HK, Tsai TH, Lin HS, et al. Effect of erythropoietin on level of circulating endothelial progenitor cells and outcome in patients after acute ischemic stroke. Crit Care 2011;15(1): R40.
2. Seo, W.K.; Yu, S.W.; Kim, J.H.; Park, K.W.; Koh, S.B. The impact of hyperthermia and infection on acute ischemic stroke patients inthe intensive care unit. Neurocrit. Care 2008, 9, 183 –188.
3. Nakase, T.; Yamazaki, T.; Ogura, N.; Suzuki, A.; Nagata, K. Theimpact of inflammation on the pathogenesis and prognosis of ischemic stroke. J. Neurol. Sci. 2008, 271, 104–109.
4. Vibo R, Korv J, Roose M, et al. Acute phase proteins and oxidized low-density lipoprotein in association with ischemic stroke subtype, severity and outcome. Free Radic Res 2007;41(3): 282-7.
5. Pfutzner A, Forst T. High-sensitivity Creactive protein as cardiovascular risk marker in patients with diabetes mellitus. Diabetes Technol Ther 2006; 8(1): 28-36.
6. Den Hertog HM, Van Rossum JA, Van der Worp HB, Van Gemert HMA, De Jonge R, Koudstaal PJ, et al. C-reactive protein in thevery early phase of acute ischemic stroke: association with pooroutcome and death. J Neurol. 2009;256(12):2003-8
7. Bos MJ, Schipper CM, Koudstaal PJ, Witteman JC, Hofman A, Breteler MM: High serum C-reactive protein level is not an independent predictor for stroke: the Rotterdam Study. Circulation2006, 114:1591-1598.
8. Rost NS, Wolf PA, Kase CS, Kelly-Hayes M, Silbershatz H, Massaro JM, et al.: Plasma concentration of C-reactive protein and risk of ischemic stroke and transient ischemic attack: the Framingham study. Stroke 2001, 32:2575-2579.
9. Danesh J, Collins R, Appleby P, Peto R. Association of fibrinogen, C-

reactive protein, albumin, or leukocyte count with coronary heart disease: Meta-analyses of prospective studies. JAMA1998; 279:1477-82.
10. Wilson PW. Metabolic risk factors for coronary heart disease: Current and future prospects. Curr Opin Cardiol 1999; 14:176-85.
11. Ridker PM. Evaluating novel cardiovascular risk factors: Can webetter predict heart attacks? Ann Intern Med 1999; 130:933-7.
12. Gabay C, Kushner I. Acute-phase proteins and other systemic responses to inflammation. N Engl J Med 1999; 340:448-54.
13. Chaudhuri J R, Mridula K R, Umamahesh M, Swathi A, Balaraju B, Bandaru V C S. High sensitivity C-reactive protein levels in Acute Ischemic Stroke and subtypes: A study from a tertiary care center. Iranian Journal of Neurology (2013); 12(3): 92 -97.
14. Bhaisare S D, Jog A S, Rao A K, Kolapkar H U. High Sensitivity C-Reactive Protein Level in Acute Cerebrovascular Accident (Stroke) at a Tertiary Care Centre. J. Evolution Med. Dent. Sci (2020); 9(10): :764-767.
15. Mishra PT, Chandra R, Saxena SK, et al. High Sensitivity C -reactive protein (hs-CRP) level in cerebrovascular accident (Stroke). JIACM 2010;11 (3) :204-7.
16. Kumar S, Kumar AG. Evaluation of the role of plasma high sensitivity C -reactive protein levels as a prognostic and diagnostic marker in acute ischemic stroke. Int J Sci Study 2016;4(2):148-53.
17. Tracy RP, Lemaitre RN, Psaty BM, Ives DG, Evans RW, Cushman M, et al. Relationship of C-reactive protein to risk of cardiovascular disease in the elderly. Results from the Cardiovascular Health Study and the Rural Health Promotion Project. Arterioscler Thromb Vasc Biol 1997; 17(6): 1121-7.
18. Gussekloo J, Schaap MC, Frolich M, Blauw GJ, Westendorp RG. C-reactive protein is a strong but nonspecific risk factor of fatalstroke in elderly persons. Arterioscler Thromb Vasc Biol 2000; 20(4): 1047-51.
19. Rajeshwar K, Kaul S, Al-Hazzani A, Babu MS, Balakrishna N, Sharma V, et al. Creactive protein and nitric oxide levels in ischemic stroke and its subtypes: correlation with clinical outcome. Inflammation 2012; 35(3): 97 8-84.
20. Khan, A., Tidman D. M. M., Shakir, D. S., & Darmal D. I. Breast Cancer in Afghanistan: Issues, Barriers, and Incidence. Journal of Medical Research and Health Sciences, 2022;5(8), 2125–2134.