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Original article

Study of evaluation of predictive value of hs CRP in first ischemic stroke

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Abstract:

Introduction: Acute ischemic stroke result of sudden impairement of the supply of blood to part of brain, and demonstrated commonly by focal neurological deficits.[1]Acute Ischemic stroke constitute 85 to 87 percent of all the cases.

Materials and methods: This was a Prospective Observational Study conducted at Dr. D.Y. Patil Medical College and hospital and Research Centre, Pimpri Pune.Subject diagnosed first time with stroke in the medicine OPD or Ward of a tertiary care hospital in the city of Pune were included in this study. Blood samples drawn in 24 to 72 hrs following stroke. Fibrinogen levels, hs-CRP levels, white blood cell counts, lipid profile and Erythrocyte Sedimentation Rate was calculated. Patients reviewed after four weeks following the time of the onset of stroke and compared using Glasgow Outcome Scale.

Results : There was significantly high value for CRP among poor outcome group ($P<0.05$) but there was no much difference for mean value of age and Random Blood Sugar (RBS) for good and poor outcome groups ($P>0.05$). Among various risk factors found in study subjects only hypertension found significantly high level of Hs-CRP ($p<0.05$).

Conclusion: Cerebral ischemia could provoke an acute response monitored by significant increase in levels of hs-CRP in AIS patients especially during early days of stroke. Study demonstrated that elevated levels of hs-CRP was prevalent in ischemic strokes.

Keywords: Cerebral ischemia, hs-CRP

Introduction:

Acute ischemic stroke result of sudden impairement of the supply of blood to part of brain, and demonstrated commonly by focal neurological deficits.[1]Acute Ischemic stroke constitute 85 to 87 percent of all the cases.[2] Stroke is growing as leading cause of early death and disability in developing countries likely because of demographic changes and increased by the rise in prevalence of the key adaptable risk factors. Thus, developing countries are exposed to burden of both non-communicable and communicable diseases. The poor people are at increased risk of stroke, because of risk factors and not able to afford for care. Most of stroke affected people lives with disabilities, and the costs of rehabilitation and long time care are undertaken by family members, which destitute their families.[2,3]

The process of stroke can be divided as embolic, lipohyalinic occlusion of the small arteries, or thrombosis over atherostenotic plaques. Strokes costs over $ 70 billion yearly and have a disastrous effect on the quality of life on significant number of individuals and caregivers.[4]

CRP is acute phase protein described as the very sensitive marker of inflammation and tissue destruction[5] and helps in binding of complement to foreign and destructed cells and which affects humoral response to disease. It is believed to play an important role in innate immunity, and hence measuring and charting of the CRP values can be helpful in determining disease processes or the

effectiveness of treatment.[6] In acute ischemic stroke, CRP levels are correlated with infarct size and neurological deficits and has likely establishing the prognostic value for poor outcomes.[7] The newer study focused on High sensitivity C–Reactive protein levels in relation to the ultimate functional outcome in ischemic stroke cases and to correlate the hs-CRP levels with various risk factors.

Materials and methods:

This was a Prospective Observational Study conducted at Dr. D.Y. Patil Medical College and hospital and Research Centre, Pimpri Pune.Subject diagnosed first time with stroke in the medicine OPD or Ward of a tertiary care hospital in the city of Pune were included in this study. The sample size was estimated based on MRD data for last year admission rate for acute ischemic stroke in hospital. On an average 20-25 cases of first ischemic stroke were admitted.

For 2 years study duration considering same rate of admission total 50 subjects were included in study.Participants were selected using Purposive sampling technique.

Inclusion Criterias:

Patients who were presented in the 48 hours of the onset of the stroke for first time and who gave informed consent for participation in the study were included.

Exclusion Criterias:

1. Subarachnoid haemorrhage, subdural haemorrhage and intracerebral haemorrhage were excluded with the help of the CT scan.
2. Patients having repeated history of stroke
3. Patients having evidence of active infections and neoplastic conditions at the time of study were excluded.
4. Patients having rheumatic heart diseases and collagen vascular diseases
5. Patients having prior history of thee transient ischemic attacks or reversible ischemic neurological deficits

Ethical and institutional scientific committee approval was taken before the start of study. Written and informed consent was taken from all patients. All Patients were informed about purpose, procedure, risk and benefits of involvement in study in their own language of understanding.

Total number of 50 individuals who presented with acute ischemic stroke enrolled for study. Detailed history and clinical examination findings were recorded on case sheet (Proforma)

Blood samples drawn in 24 to 72 hrs following stroke. Fibrinogen levels, hs-CRP levels, white blood cell counts, lipid profile and Erythrocyte Sedimentation Rate was calculated.

Patients reviewed after four weeks following the time of the onset of stroke and compared using Glasgow Outcome Scale.

A. **hs-CRP:**

Levels of hsCRP estimated by VITROS 5.1 and VITROS 5600 integrated system for quantitative measurement of CRP in the human serum or plasma. As per the data from VITROS 5600 system manual and current literatures, the cardiac risk was estimated as low risk with hsCRP level of less than 1.00 mg/L, medium risk if levels are between 1.00 to 3.00 mg/L, high risk when levels are more than 3.00 mg/L.[12] In our study we have considered hsCRP level of more than or equal to 3.00 mg/L as for the high risks and less than or equal to 3.00 mg/L as for the low risks.[12]

B. **GLASGOW OUTCOME SCALE:**

GOS utilized for the assessment of the functional outcomes and residual neurological deficits. The GOS has commonly being used in trials involving strokes. It is a well validated scale having good interobserver agreement.

Observation and results:

Age wise distribution of study subjects shows, maximum (42%) study subjects were in age group of 51-60yrs followed by 61-70yrs (30%). Gender-wise distribution of study subjects shows M:F was 1.5:1 (Male : Female ratio)

Most common (62%) risk factor was diabetes followed by hypertension (32%), alcohol (22%), obesity and smoking (20% each).

Table 1: 28days follow up outcome [Glasgow Outcome Scale (GOS)] among study subjects

Outcome (Functional status)	Frequency	Percent
Poor	31	62.0
Good	19	38.0
Total	50	100.0

Table shows on 28days follow up using Glasgow outcome scale 62% had found poor functional status.

Table 2 : Age wise hs-CRP finding among study subjects

Age group	hs CRP		Total
	Normal	High	
≤50yrs	1(16.7%)	5(83.3%)	6
51-60yrs	6(28.6%)	15 (71.4%)	21
61-70yrs	6(40.0%)	9(60.0%)	15
>70yrs	2(25.0%)	6(75.0%)	8
Total	15	35	50

Table shows age-wise hs-CRP findings among study subjects. There was no difference in hs-CRP findings with increase in age group.

Table 3: Gender wise hs-CRP finding among study subjects

Gender	hs CRP		Total
	Normal	High	
Female	6(30.0%)	14(70.0%)	20
Male	9(30.0%)	21(70.0%)	30
Total	15	35	50

Table shows gender-wise hs-CRP findings among study subjects. There was no difference in hs-CRP findings among male and female.

Table 4: Relation of 28days follow up outcome [Glasgow Outcome Scale (GOS)] with hs-CRP among study subjects

Outcome (Functional status)	hs CRP		Total	P value
	Normal	High		
Good	15(78.9%)	4(21.1%)	19	**0.0001**
Poor	0	31(100.0%)	31	
Total	15	35	50	

Table shows relation of 28days follow up outcome [Glasgow Outcome Scale (GOS)] in terms of functional status with hs-CRP level among study subjects. There was significant difference in outcome among high and normal level of hs-CRP ($p<0.05$).

Table 5 : Relation of 28days follow up outcome [Glasgow Outcome Scale (GOS)] with ESR among study subjects

Outcome	ESR		Total	P value
	Normal	High		
Good	13(68.4%)	6(31.6%)	19	**0.0001**
Poor	3(9.7%)	28(91.3%)	31	
Total	15	35	50	

Table shows relation of 28days follow up outcome [Glasgow Outcome Scale (GOS)] in terms of functional status with ESR level among study subjects. There was significant difference in outcome among high and normal level of ESR ($p<0.05$).

Table 6: Mean value of age, RSB and hs-CRP among 28days follow up outcome [Glasgow Outcome Scale (GOS)] group.

Variables	Outcome	Mean ± Std Deviation	Std. Error Mean	P value
Age	Good (n=19)	60.32±8.02	1.840	0.721
	Poor (n=31)	61.29±10.02	1.800	
RBS	Good (n=19)	178.95±56.3	12.916	0.252
	Poor (n=31)	160.61±52.94	9.509	
hs CRP	Good (n=19)	9.37±1.09	0.25	**0.0001**
	Poor (n=31)	14.05±1.65	0.29	

Table shows mean hs-CRP among poor outcome group was 14.05±1.65 and 9.37±1.09 among good outcome group. There was significantly high value for CRP among poor outcome group ($P<0.05$) but there was no much difference for mean value of age and Random Blood Sugar (RBS) for good and poor outcome groups ($P>0.05$).

Table 7: Relation of risk factors with hs-CRP

Risk factors	hs-CRP		P value
	Normal	High	
Obesity	4(40.0%)	6(60.0%)	0.341
Smoking	5(50.0%)	5(50.0%)	0.125
Alcohol	6(54.5%)	5(45.5%)	0.054
Diabetes	6(37.5%)	10(62.5%)	0.318
Hypertension	2(6.5%)	29(93.5%)	**0.001**
LDL	4(26.3%)	11(73.7%)	0.507

Table shows relation of risk factors with hs-CRP level. Among various risk factors found in study subjects only hypertension found significantly high level of Hs-CRP ($p<0.05$).

Table 8: Relation of risk factors with 28days follow up outcome [Glasgow Outcome Scale (GOS)]

Risk factors	Outcome		P value
	Good	Poor	
Obesity	4(40.0%)	6(60.0%)	0.884
Smoking	5(50.0%)	5(50.0%)	0.382
Alcohol	7(63.6%)	4(36.4%)	0.078
Diabetes	7(43.8%)	9(56.2%)	0.566
Hypertension	6(19.4%)	25(80.6%)	**0.0001**
LDL	5(33.3%)	10(66.7%)	0.454

Table shows relation of risk factors with 28days follow up outcome. Among various risk factors

found in study subjects only hypertension found significantly poor outcome ($p<0.05$).

Discussion :

Stroke is a clinical syndrome with rapidly developing loss of brain functions due to impairment in the blood supply to the brain because of blocked or burst blood vessel. This can occur due to ischemia caused by thrombosis or embolism or due to haemorrhage.[8] Recent studies have found 7 percent of the medical and 45 percent of neurological admissions were because of stroke with a mortality rate of 9 percent at discharge and 20 percent at 28 days.[9]

Inflammatory theory in atherosclerosis suggests CRP is pro-inflammatory, pro-thrombotic and pro-atherosclerotic. It involves directly with endothelial cells and stimulates the production of cytokines like Interleukin-6, Interleukin-1b, Tumour Necrosis Factor, ET-1 and up-regulation of adhesion molecules expressions namely ICAM and VCAM. It increases the production of monocyte chemoattractant protein and monocytes recruitment as well as activates complements, promotes Low Density Lippoproteins uptake by macrophages and plaque formation which subsequently results in atherosclerosis and ultimately stroke.[10]

Many studies have shown that stroke is having inflammatory pathology and the markers of inflammation have been proposed as new risk factors for stroke like elevated white blood cell count, endothelial nitric oxide synthase, intercellular adhesion molecule, lipoprotein associated PhospholipaseA2, Homocysteine, lipoprotein (a), small dense LDL, Tumour Necrosis Factor, Interleukin, D-dimer and serum Amyloid-A etc.[10] C-reactive protein and dyslipidaemia are some additional markers to this growing list.

CRP has been the most widely studied marker of inflammation. CRP which is the acute phase reactant synthesized in Liver, vascular smooth muscle cells and adipocytes. Synthesis and secretion of CRP tends to increase within hours of an acute injury or onset of inflammation.[11]

Present study was carried out to find association of acute ischemic stroke outcome with hs-CRP among study subjects admitted in a tertiary care centre during study period.

This was a prospective observational study involving 50 cases of first attack of acute ischemic stroke and admitted to medicine ward within 24hrs of attack and assessed for the functional outcome using Glasgow Outcome Scale (GOS) at end of 28dyas(4weeks) after discharge from wards.

The age distribution of the patients in this study was between 35-79 years with mean age of 60.92±9.24yrs. The risk of stroke increased with increasing age as maximum (88%) incidence was found in age >50years in the present study. These findings were in corroboration with studies by Mishra Talreja P, et al [72]and Chowdhury N et al.[10]

In our research, proportion of men and women with elevated levels of hsCRP was higher (70%) compared to low levels of the hsCRP (30%). Devaraj et al.[110] and Wakugawa et al.[11] noticed that high hsCRP level was non dependent risk factors for anticipated ischemic stroke only in men but not in women. Endogenous estrogen is believed to protect the formation of atherosclerosis, and also has anti-inflammatory effect in women.[12.13] However, Muir et al. not found any type of relation between gender and elevated C-Reactive Protein (>10mg/L) levels in acute ischemic stroke individuals.[114] studies have shown a five times increase in the risk of any vascular incident in women having highest CRP levels.[15,16] Hence, increased CRP level may be responsible for damage to men as well as women. Our study findings has no significant difference in increased levels of hs-CRP among male and female ($p>0.05$)

We noticed that high serum hsCRP levels was significantly associated with older age group in our patients; identical to other studies. Rost et al. noticed increased levels of

CRP as a significant predictor of future risks of ischemic strokes in the elder individuals.[17] Large prospective studies in healthy subjects have proven prognostic importance of CRP in the elder individuals.[18,19]

It was demonstrated that stroke activates an acute phase responses. Elevated values in of CRP and fibrinogen is noticed in nearly 25 percent of individuals with ischaemic cerebro-vascular accidents.[120]In our study we confirmed 70% had elevated levels of hs-CRP (>3mm) at the admission time.

Conclusion:

Cerebral ischemia could provoke an acute response monitored by significant increase in levels of hs-CRP in AIS patients especially during early days of stroke. Study demonstrated that elevated levels of hs-CRP was prevalent in ischemic strokes.

References:

1. Go AS, Mozaffarian D, Roger VL, et al.; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics — 2014 update: a report from the American Heart Association. Circulation 2014;129:e28-e292.
2. Bonita R, Beaglehole R. Stroke prevention in poor countries: time for action. Stroke. 2007;38(11):2871-2.
3. Pandian JD, Srikanth V, Read SJ, Thrift AG. Poverty and stroke in India: a time to act. Stroke. 2007;38(11):3063-9.
4. Lloyd-Jones D, Adams RJ, Brown TM, et al., for the American Heart Association Stroke Council. Heart disease and stroke statistics—2010 update: a report from the American Heart Association. Circulation 2010;121:e46–215.
5. Du Clos, T.W., 2000. Function of C reactive protein. Ann Med., 32: 274-278.
6. Verma S, Chao-Hung Wang, Shu-Hong Li, Aaron S. Dumont, Paul W.M. Fedak, Mitesh V. Badiwala, Bikramjit Dhillon, Richard D. Weisel, Ren- Ke Li, Donald A.G. Mickle, Duncan J. Stewart, 2002. Circulation., 106: 913-919
7. Rajeshwar K, Kaul S, Al-Hazzani A, Babu MS, Balakrishna N, Sharma V, Jyothy A, Munshi A. Creactive protein and nitric oxide levels in ischemic stroke and its subtypes: correlation with clinical outcome. Inflammation 2012; 35(3): 978-984.
8. Shaylika Chauhan, Shailesh Jayade , Arundhati Kanbur , Cross sectional study to assess the prevalance, presenting features and factors affecting outcome of stroke , Indian Journal of Basic and Applied Medical Research; June 2017: Vol.-6, Issue- 3, P. 321-342
9. Gallego J, Martinez EV, Muiioz R. Patients at high risk for ischemic stroke.
10. Taylor FC, K SK. Stroke in India, Factsheet. 2012; 2(updated):1–25
11. Wade S. Smith, Joey D. English, S. Claiborne Johnston. In: Fausi AS, Braunwald Kasper D, Hauser S, Longo D, Jameson J et al, editors. Har-risson's Principle of Internal Medicine. 17th ed. New York. McGraw Hill companies; 2008. p. 2512-34
12. Mendelsohn ME, Karas RH. The protective effects of estrogen on the Cardiovascular system. N Engl J Med 1999; 340(23): 1801-11.
13. Pfeilschifter J, Koditz R, Pfohl M, Schatz H. Changes in proinflammatory cytokine activity after menopause. Endocr Rev 2002; 23(1): 90-119.
14. Muir KW, Weir CJ, Alwan W, Squire IB, Lees KR. C-reactive protein and outcome after ischemic stroke. Stroke 1999; 30(5): 981-5.
15. Ridker PM, Buring JE, Shih J, Matias M, Hennekens CH. Prospective study of Creactive protein and the risk of future cardiovascular events among apparently healthy women. Circulation 1998; 98(8): 731-3.
16. Arima H, Kubo M, Yonemoto K, Doi Y, Ninomiya T, Tanizaki Y, et al. , Highsensitivity C-reactive protein and coronary heart disease in a general population of Japanese: the Hisayama study. Arterioscler Thromb Vasc Biol 2008; 28(7): 1385-91.
17. 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(11): 2575-9.
18. 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
19. Gussekloo J, Schaap MC, Frolich M, Blauw GJ, Westendorp RG. C-reactive protein, Is a strong but nonspecific risk factor of fatal stroke in elderly persons. Arterioscler Thromb Vasc Biol 2000; 20(4): 1047-51.

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