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To the correlation of hsCRP and ESR with severity of Acute Ischemic Stroke: A case control study

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Abstract

Background: *C-reactive protein (CRP) and ESR are acute-phase reactants, are indicators of underlying systemic inflammation and novel plasma markers for atherothrombotic disease. Hence we planned to study these variables (hsCRP and ESR) using a precise methodology in stroke patients and compare them with data from age- and sex-matched control subjects.*

Material & Methods: *The study was a case control study carried out at Mahatma Gandhi Medical College and Hospital, Jaipur (Rajasthan), which is a tertiary care referral centre. Sixty Patients of acute ischemic stroke admitted to the medical and neurology wards within 24 hrs of the onset of symptoms were taken as cases. Thirty age and sex matched controls were also recruited for study. Severity of ischemic stroke was accessed using modified Rankin Scale (mRS) score and accordingly the cases were categorized into two groups: Group 1 (less severe stroke group) including patients with mRS score 0-2, and Group 2 (more severe stroke group) including patients with mRS score 3-6. Blood samples were taken and sent for routine investigations including lipid profile and ESR by westergren method (Normal ESR: Male ≤15, Female ≤20).*

Results: *In the present study ESR level in cases and controls were elevated in 90% of cases as compared to 40% in controls, which was significant statistically with a p value of <0.01. The ESR also had a statistically significant correlation with Stroke clinical severity (mRS Score) (r = 0.4645, p = <0.05). The hsCRP also found to have a statistically significant correlation with Stroke clinical severity (mRS Score) (r = 0.5568, p = <0.05).*

Conclusion: *We concluded that Positive correlation was observed ESR and hsCRP with stroke severity. Sample size was smaller than some of the western studies.*

Keywords: *ESR, hsCRP, Acute Ischemic Stroke, mRS score.*

Introduction

A Stroke is rapidly developing clinical symptoms and /or signs of focal and at times global loss of brain function, with symptoms lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin.

They cause ~200,000 deaths each year in the United States and are a major cause of disability. The incidence of cerebrovascular diseases increases with age and the number of strokes is projected to increase as the elderly population grows, with a doubling in stroke deaths in the United States by 2030. Most cerebrovascular diseases are manifest by the abrupt onset of a focal neurologic deficit, as if the patient was "struck by the hand of God."[1]

Globally, approximately 15 million new acute stroke events occur every year. Two thirds of these individuals live in low-and middle income countries such as India.[2] About 80per cent of all first ever-in-life time strokes are ischemic, 10 per cent are due to primary intracerebral haemorrhage, and in remainder there is uncertenity.[3]

For Indian, community survey have shown a crude prevalence rate of 'hemiplegia' in the range of 200 per 100,000 persons, nearly 1.5% of all urban 1 hospital admissions ,4.5% of all medical admission and around 20% of neurological cases.[4]

Ischemic stroke is thought to occur as a result of thrombotic occlusion of a stenosed atherosclerotic blood vessel supplying the brain parenchyma. Initially platelets adhere to the damaged endothelium, resulting in recruitment of further platelets, followed by aggregation, formation of a platelet plug and finally thrombotic occlusion.[5]

An increasing body of evidence has linked inflammation with the pathogenesis of atherothrombotic stroke. Infections and inflammation may promote atherosclerosis and thrombosis by elevating serum levels of fibrinogen, leukocytes, clotting factors, and cytokines and by altering the metabolism and functions of endothelial cells and monocyte macrophages. C-reactive protein (CRP) and ESR are acute-phase reactants, are indicators of underlying systemic inflammation and novel plasma markers for atherothrombotic disease. [6,7]

The recent use of highly sensitive CRP assays, with international reference standards set by the World Health Organization (WHO), has enhanced the usefulness of CRP as a reliable predictor of cardiovascular events. A strong and consistent association between clinical manifestations of atherothrombotic disease and baseline CRP levels has been described in epidemiological studies of patients with acute myocardial ischemia or myocardial infarction, stable and unstable angina pectoris, and myocardial infarction or recurrent ischemia among those hospitalized with angina pectoris.[8]

Hence we planned to study these variables (hsCRP and ESR) using a precise methodology in stroke patients and compare them with data from age- and sex-matched control subjects.

Material & Methods

The study was a case control study carried out at Mahatma Gandhi Medical College and Hospital, Jaipur (Rajasthan), which is a tertiary care referral centre. Sixty Patients of acute ischemic stroke admitted to the medical and neurology wards within 24 hrs of the onset of symptoms were taken as cases. Thirty age and sex matched controls were also recruited for study. The study protocol was approved by the institutional research review board and ethics committee.

Selection Criteria for Cases and Controls

Cases

Definition of stroke: Focal neurological deficit lasting more than 24 hrs with no evidence of non-vascular cause.

Inclusion Criteria

All patients of first ischemic stroke presenting within 24 hrs of symptom onset in S.M.S. hospital, Jaipur.

Exclusion Criteria

1. Patients presenting 24hrs after the onset of neurological symptoms.
2. Haemorrhagic stroke.
3. History of stroke in the past.
4. History of stable or unstable angina, myocardial infarction.
5. Recent [<3 months] major trauma, surgery, burns.

6. Known or suspected neoplastic disorders.
7. Acute infectious disease or known case of diseases that cause inflammation such as arteritis, arthritis, ankylosing spondylitis, osteomyelitis, inflammatory bowel disease.
8. Known case of Immunological disorders.
9. Known case of disorders of platelet.
10. Medications that can reduce the platelet count: hydroxyurea, antineoplastic agents, and inhibitors of the platelet integrin $\alpha_{IIb}\beta_3$.
11. Patients on steroids or other immunomodulatory drugs.
12. Peripheral smear showing platelet aggregates.
13. Patients unable to communicate because of severe stroke, aphasia or dementia without a valid surrogate respondent.

Controls

Controls will be primarily hospital based which may be relative of patient or unrelated visitors

Inclusion Criteria

Age and sex matched healthy individuals.

Exclusion Criteria

1. Present or past history of stroke.
2. History of stable or unstable angina, myocardial infarction.
3. Recent (<3 months) major trauma, surgery, burns.
4. Known or suspected neoplastic disorders.
5. Acute infectious disease or known case of diseases that cause inflammation such as arteritis, arthritis, ankylosing spondylitis, osteomyelitis, inflammatory bowel disease.
6. Known case of Immunological disorders.
7. Known case of disorders of platelet.
8. Medications that can reduce the platelet count: hydroxyurea, antineoplastic agents, and inhibitors of the platelet integrin $\alpha_{IIb}\beta_3$.
9. Patients on steroids or other immunomodulatory drugs.
10. Peripheral smear showing platelet aggregates.

Method of Collection of Data

In this study patients presenting with first ischemic stroke in wards of general medicine/ neurology at MGUHS, Jaipur within 24 hrs of symptom onset and satisfying the inclusion and exclusion criteria were taken as cases. Severity of ischemic stroke was accessed using modified Rankin Scale (mRS) score and accordingly the cases were categorized into two groups: Group 1 (less severe stroke group) including patients with mRS score 0-2, and Group 2 (more severe stroke group) including patients with mRS score 3-6. Cases were recruited till at least 30 subjects in each study group were enrolled. Detailed history was taken including risk factors, then patients examined and imaging studies done to classify stroke. Blood samples were taken and sent for routine investigations including lipid profile and ESR by westergren method (Normal ESR: Male ≤15, Female ≤20).

Results

In the present study ESR level in cases and controls were elevated in 90% of cases as compared to 40% in controls, which was significant statistically with a p value of <0.01. So elevated ESR levels were significantly associated with stroke patients. The difference of mean The difference was statistically significant with a P value of <0.01 (table 1).

In the cases among two severity groups level of hsCRP were 8.18±6.27 mg/L in group1 compared to 13.92 ± 7.11 mg/L in group2. Thus the level was significantly higher in severe stroke group with a P value of <0.002. hsCRP level of >3 mg/L indicates high risk for ischemic stroke. Among cases 29 patients of group 2 had hsCRP level of >3 mg/L compared to 20 patients in group 1. Higher hsCRP lavel (>3 mg/L) was associated with more severe stroke (group 2) patients and the association was also statistically significant (p value 0.008) (graph 1).

The ESR also had a statistically significant correlation with Stroke clinical severity (mRS Score) (r = 0.4645, p = <0.05) (graph 2).

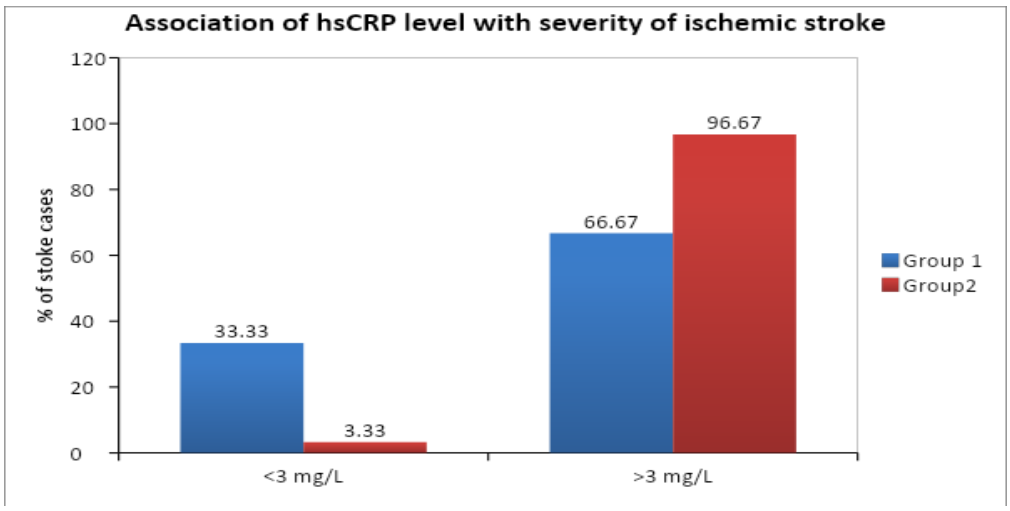
The hsCRP also found to have a statistically significant correlation with Stroke clinical severity (mRS Score) (r = 0.5568, p = <0.05) (graph 3).

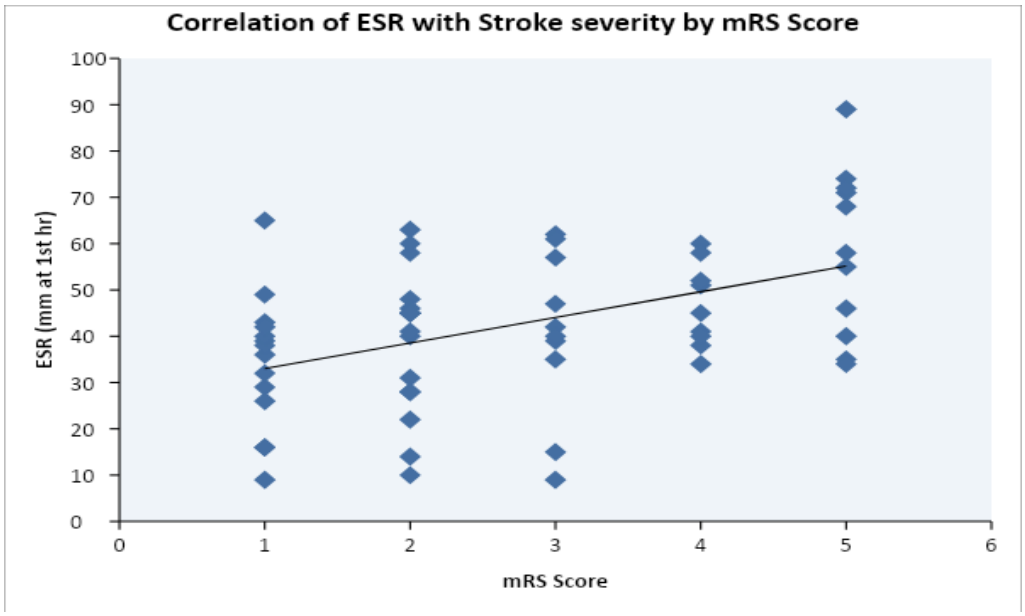
Table 1: ESR levels among study subjects

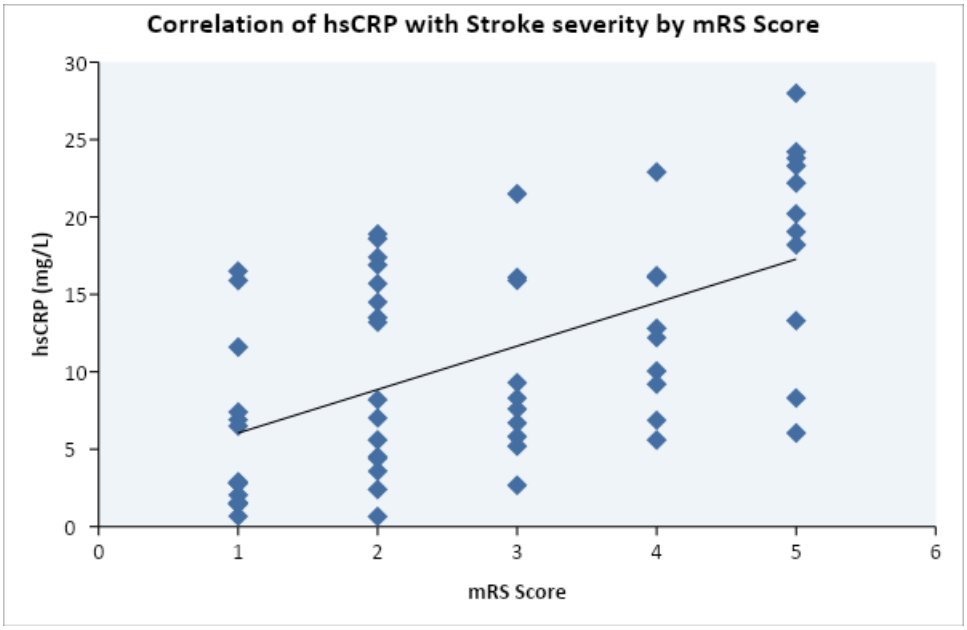
ESR (mm at 1st hr)	Cases		Controls		P Value
	No	%	No	%	
Elevated Male >15; Female >20	54	90	12	40	<0.01S
Normal Male ≤15; Female ≤20	6	10	18	60	
Total	60	100	30	100	
Mean±SD	42.87 ± 17.15		19.4 ± 11.17		< 0.01 S

Table 2: Level of hsCRP in stroke cases according to severity groups

	Group 1 (n=30)	Group 2 (n=30)	P value
hsCRP (mg/L)	8.18 ± 6.27 (0.65 – 18.9)	13.92 ± 7.11 (2.67 – 28)	< 0.002 S







Discussion

In the present study we compared the ESR in stroke cases and controls. ESR level was significantly raised in patients of acute ischemic stroke. ESR level in cases was 42.87 ± 17.15 mm at 1st hr when compared to 19.4 ± 11.17 mm at 1st hr in controls (p value <0.01). In a similar study Krishna Murthy H. A. et al[9] also reported that mean ESR value was significantly raised in stroke cases, values being 32.33 ± 11.8 and 19.80 ± 6 .80 in cases and controls respectively (p value <0.001). Another study was done by Agarwal MP at al[10] who also observed higher mean ESR value among stroke cases compared to controls, values being 33.92 ± 5.73 and 14.08 ± 3.73 respectively (p value <0.001).

So our study supported the previous studies and we also found a significant association of raised ESR level with acute ischemic stroke. The significant association of raised ESR level with ischemic stroke can be explained as there are evidences which has linked inflammation with the pathogenesis of atherothrombotic stroke.[6,7] It is thought that Infections and inflammation may promote atherosclerosis and thrombosis. ESR is an acute-phase reactant, an indicator of underlying systemic inflammation.[6,7]

In the present study we compared the level of hs-crp with severity of acute ischemic stroke. We found that hs-crp level was higher in severe stroke group. Value of hs-crp was 13.92 ± 7.11 mg/L in more severe stroke group (mRS score ≥3) compared to 8.18 ± 6.27 mg/L in less severe stroke group (mRS score <3). High hs-CRP level in severe stroke cases was found statistically significant. (p value <0.002).

Adnan Khan et al[11] recruited 100 patients of acute ischemic stroke. 67 patients had raised hs-CRP levels. Mean serum level of hs- CRP in ischemic stroke patients was 23 ±11.24 mg/L. Higher hs-CRP at the time of admission was associated with a more severe stroke. Sixty-six percent of the patients with raised hs-CRP had a severe or very severe stroke (NIHSS 15-24 0r >25). An elevated CRP was associated with increased stroke severity (NIHSS) (p = 0.015)

Yun Luo et al[12] studied 316 patients of acute ischemic stroke. CRP was elevated in 21% of the acute ischemic stroke compared to 4% in the control group (p = 0.000). Within the acute ischemic stroke group, patients with CRP levels ≥7mg/L had a significantly increased risk of severe stroke (OR 3.33, 95% CI 1.84-6.00, p =0.00). Acute ischemic stroke patients with NIHSS levels ≥8 more often had a elevated CRP than patients with lower NIHSS levels (39% versus 16%; p =0.000).

M.A. Shoaeb et al[13] recruited 50 patients with a first-ever acute stroke. Stroke severity was accessed by the National Institute of Health Stroke

Scale (NIHSS) on admission. Serum CRP level was 14.4 ± 6 mg/L in patients with severe ischemic stroke compared to 7.7 ± 4.5 mg/L in patients with mild and moderate presentation (P value 0.01).

Hasan Kara et al[14], recruited 102 patients of acute ischemic stroke and 98 controls. They found that mean hs-CRP level were higher in patients who had greater stroke severity (lower Canadian neurological scale score) and were higher in patients who had larger volume strokes. Thirteen patients who had severe stroke (Canadian neurological scale 0-2) had hs-crp level 12 ± 7 mg/dL, twenty patients with moderate stroke (Canadian neurological scale 2.5-8) had hs-crp level 8 ± 6 and sixty nine patients with mild stroke (Canadian neurological scale 8.5-10) had hs-crp level 5 - 6 mg/dL. (p value <0.001).

An increasing body of evidence has linked inflammation with the pathogenesis of atherothrombotic stroke. Infections and inflammation may promote atherosclerosis and thrombosis by elevating serum levels of fibrinogen, leukocytes, clotting factors, and cytokines and by altering the metabolism and functions of endothelial cells and monocyte macrophages. C-reactive protein (CRP) being an acute-phase reactant, is an indicator of underlying systemic inflammation and thus may be a plasma markers for atherothrombotic disease.[6,7]

M.A. Shoaeb et al[13] studied 50 patients and found that serum CRP level on admission was predictive of stroke severity (positively correlated with NIHSS (r = 0.54, P = 0.006). Rasha H. Soliman et al[15] studied 41 patients of acute ischemic stroke and reported that serumhs-CRP level was positively correlated with stroke severity detrmined by mRS score (r = 0.441, p = 0.004). Chun Song Youn et al[16] recruited 96 patients with acute ischemic stroke. The relationship between hs-CRP levels and DWI infarct volume quartiles was examined. There was a significant correlation between hs-CRP and DWI volumes (r = 0.239, P = .010).

Conclusion

We concluded that Positive correlation was observed ESR and hsCRP with stroke severity. Sample size was smaller than some of the western studies.

References

1. Fauci, Braunwald, Kasper, Hauser, Longo Jameson. “Harrisons Principal and practices of Medicine, Chapter 364 ,17 Edition vol.II 2513-23.
2. Jeyaraj D Pandian, Velandai Srikanth “Poverty and stroke in India”, Stroke 2007. 38;3063-306.
3. J .Van Ginn “Brain’s disease of nervous system, stroke, Transient ischemic attacks and intracranial venous thrombosis, Charles Warlow” 2002 ,11 edi,776-801.
4. Siddharth.N. Shah “API text book of medicine” Chapter 13,8th Edition, vol II, Ischemic cerebrovascular disease, P. MDalal.
5. Greisenegger S, Endler G, Hsieh K, Tentschert S, Mannhalter C, Lalouschek W. Is elevated mean platelet volume associated with a worse outcome in patients with acute ischemic cerebrovascular events?, Stroke 2004;35:1688–91.
6. Di Napoli M, Papa F, Bocola V. “Prognostic Influence of increased CRP and fibrinogen levels in ischemic stroke”. Stroke 2001;32:133-138.
7. Guo Y, Jiang X, Zhou Z, Chen S, Zhao H, Li F ‘’Relationship between levels of serum c- reactive protein, leucocyte count and carotid plaque in patients with ischemic stroke’’ J Huazhong Univ Sci Technolog Med Sci . 2003;23[3];263-5.
8. Natalia S .Roast, Philip A Wolf, Carlos S, Kase et al ’’Plasma concentration of C-Reactive Protein and risk of ischemic stroke and trancient ischemic attack’’. The Framingham Study. Stroke Nov 2001;32;2575-2579.
9. Krishna Murthy H.A., Renuka Prasad Y.S.

"STUDY OF PROGNOSTIC SIGNIFICANCE OF SERUM C-REACTIVE PROTIEN AND ESR IN ACUTE ISCHEMIC STROKE" IJCRR. 2013; 5(2): 127-134.

10. Agarwal MP, Singh NR, Kaur IR. "C-Reactive Protein in acute cerebral infarction". JAPI. Vol51;Dec 2003.
11. Adnan Khan, Zafar Ali. Frequency of raised C- reactive protein in acute ischemic stroke. KMUJ 2012; Vol. 4, No. 2: 45-48.
12. Yun Luo, Zhongyuan Wang, Jingwei Li, Yun Xu. Serum CRP concentrations and Severityof Ischemic Stroke Subtypes. Can. J. Neurol. Sci. 2012; 39: 69-73
13. M.A. Shoaeb, M.A. Shehata, K.M. Taema, M.A. Hammouda. CRP in cerebrovascular stroke: Prognostic implications. The Egyptian Journal of Critical Care Medicine (2014) 2, 43–52.
14. Hasan Kara, Murat Akinci, Selim Degirmenci, Aysegul Bayir, Ahmet Ak, Alaaddin Nayman, Ali Unlu, Fikret Akyurek, Mesut Sivri. High-sensitivity C-reactive protein, lipoprotein-related phospholipase A2, and acute ischemic stroke. Neuropsychiatric Disease and Treatment 2014:10 1451–1457.
15. Rasha H. Soliman, Noha A. Abdel-Monem, Azza A. Helmy, SanaaAbd El-Shafy. High Sensitivity C-Reactive Protein and its Gene Polymorphism in Acute Ischemic Stroke; Egypt J Neurol Psychiat Neurosurg. Jan 2010, Vol 47, Issue 1, 373-79.
16. Chun Song Youn, Seung Pill Choi, Soo Hyun Kim, Sang Hoon Oh, Won Jung Jeong, Han Joon Kim, Kyu Nam Park. Serum highly selective C-reactive protein concentration is associated with the volume of ischemic tissue in acute ischemic stroke; The American Journal of Emergency Medicine. January 2012Volume 30, Issue 1, Pages 124–128.