Scholars Journal of Applied Medical Sciences (SJAMS) **ISSN 2320-6691 (Online)**
Sch. J. App. Med. Sci., 2017; 5(9B):3598-3604 **ISSN 2347-954X (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublisher.com

High sensitive C- reactive protein in acute ischemic stroke and its short term Prognostic significance: A study from rural hospital.

Madhura Talkad Lakshmikumar[1], Shruthi Bettegowda*[2], Addepalli Yamini[3]
[1]Professor, Department of Medicine, Adichunchanagiri Institute of Medical Sciences, Balagangadharanatha Nagar, Nagamangala, Mandya -571448, India.
[2]Associate Professor, Department of Medicine, Adichunchanagiri Institute of Medical Sciences, Balagangadharanatha Nagar, Nagamangala, Mandya -571448, India.
[3]3rd Year Resident Department of Medicine, Adichunchanagiri Institute of Medical Sciences, Balagangadharanatha Nagar, Nagamangala, Mandya- 571448, India.

***Corresponding author**
Shruthi Bettegowda

Article History
Received: 08.09.2017
Accepted: 16.09.2017
Published: 30.09.2017

DOI:
10.21276/sjams.2017.5.9.25

Abstract: Stroke is the third leading cause of death in developed countries. Ischemic brain Injury is characterized by acute local inflammation and changes in levels of inflammatory cytokines, notably C reactive protein. High sensitivity C reactive protein can predict recurrent cardiovascular disease, stroke and death in different settings. There is lack of studies on high sensitive C reactive protein in acute ischemic stroke patients from rural area in our nation. The objective of the study was to measure high sensitivity C reactive protein levels in acute ischemic stroke and to assess short term prognosis in terms of mortality and morbidity with reference to high sensitivity C reactive protein levels during one week of hospital stay. It was a longitudinal study involving 50 patients admitted with acute ischemic stroke in medicine department. Routine investigations, high sensitivity C reactive protein levels and computed tomography scan of brain were done in all these patients. High levels of high sensitivity C reactive protein at admission showed high mortality and morbidity during one week of hospital stay. High levels of high sensitivity C reactive protein correlated with poor functional outcome using Barthel index. Thus quantitative estimation of high sensitivity C is reactive protein a simple test and helps in predicting prognosis.
Keywords: Acute ischemic stroke, Barthel Index, Cerebrovascular disease, Dyslipidemia, Hypertension, High sensitivity C-reactive protein

INTRODUCTION

Stroke is the third leading cause of death in developed countries. It ranked as the sixth leading cause of Disability Adjusted Life in 1990 and is projected to rank fourth by the year 2020 [1]. According to the World Health Organization, 15 million people suffer from stroke each year. About 87% of all strokes are due to ischemia. Acute ischemic stroke develops as a result of a sudden interruption in the focal cerebral blood flow [2]. Recent research has shown that an inflammatory reaction is triggered within hours in the brain tissue injured by an ischemic stroke and continues in the days following the appearance of symptoms and that this reaction contributes to neuronal damage. Ischemic brain injury is characterized by acute local inflammation and changes in levels of inflammatory cytokines, notably C reactive protein [3]. High Sensitivity C-reactive protein(hs CRP) is an acute- phase reactant produced by the liver under the control of interleukin-6, almost certainly the primary circulating physiological mediator, because most other cytokines rarely reach effective concentrations in plasma. The hs-CRP assay has been shown to be able to detect concentrations below 0.2 mg /l. hs- CRP can predict recurrent cardiovascular disease, stroke and death in different settings [3]. Recovery from neuronal shock takes time. It depends mainly on extent of neuronal damage due to hemorrhage or ischemia. The extent of neurological deficit can be assessed clinically and the same can be graded on the basis of motor deficit, as suggested by Medical Research Council grading (MRC). Another commonly used method of assessment is to assess the functional disability of the individual to do the daily activities of living, called Barthel Index [4]. Although infarct size and stroke severity are major determinants of short term prognosis after ischemic stroke, hs-CRP predicts prognosis, in particular mortality or new vascular events during the first year independent of infarct size and stroke severity [3].

Hence the present study is taken up to find the correlation of hs CRP level with stroke patient's prognosis. Mortality and morbidity of stroke is evaluated on the basis of barthel index, at the onset of stroke and at the end of first week with reference to hs-CRP levels.

MATERIAL AND METHODS

This is a prospective hospital based study. 50 patients admitted with acute ischemic stroke in medicine department were included in this study. Study protocol included detailed clinical history, clinical examination and investigations. A detailed clinical work up incorporating details of age, presenting complaints, diet, smoking, alcohol consumption, physical activity, reproductive history, socioeconomic status, body mass index and pedigree chart was made. Risk factors for ischemic stroke like hypertension, diabetes, dyslipidaemia; family history of stroke was evaluated. After taking consent, patients were subjected for computed tomography (CT) scan head and other relevant investigations pertaining to their clinical status. The first evaluation was conducted within 6 hours of admission. Neurological deficits such as aphasia, cranial nerve palsies, limb weakness, sensory impairment, cerebellar dysfunction, conjugate gaze deviation and hemianopia were elicited by a standard comprehensive bedside neurological examination. Measurement of hs-CRP was done by immune turbidometry assay. Functional score was assessed using Barthes index. Hs-CRP was measured within 6 hours of admission. Follow-up was done at one week of hospital stay to assess the mortality and morbidity. Ethics committee approval was taken for the study.

INCLUSION CRITERIA

- All patients of first episode of ischemic stroke

EXCLUSION CRITERIA

- Patients of haemorrhagic stroke.
- Patients of transient ischemic attack.
- Patients of stroke secondary to vasculitis and neoplasia.
- Patients of acute coronary syndrome
- Patients of peripheral vascular disease.

Definition of terms

Patients on oral hypoglycaemic drugs, Insulin or those having fasting blood sugar > 126 g/dl were regarded as having diabetes mellitus. Those with blood pressure > 140 / 90 mmHg taken twice or those on antihypertensive drugs were defined as hypertensive. A diagnosis of hyperlipidaemia was made if total Cholesterol is > 200 mg/dl, Triglycerides > 150 mg/dl, and LDL > 130 mg/dl. Height, waist and hip circumference were measured in centimetres by using a non-stretchable standard tape with a metal buckle at one end over the light clothing. Waist circumference was measured in the centre of the iliac crest and the coastal margin, and hip circumference was measured at the widest point on buttocks below the iliac crest. . Patients were divided in to non-obese and obese on the basis of body mass index (BMI). A BMI of 27.3 Kg/m^2 or more in subjects indicates obesity. BMI=Body weight (Kg) / $Height^2$ (meters) .Current smokers were defined as those who smoked any form of tobacco in the previous 6 months while former smoker were those who had quit more than 6 months earlier.

STATISTICAL ANALYSIS

Data are presented as means for continuous data and as n (%) for frequency data. A P value of < 0.05 was considered to indicate statistical significance.

RESULTS

Age distribution

In our study maximum incidence of acute ischemic stroke occurred in fifth decade (Table 1).

Table -1: Age distribution

Age in years	Number of patients	Percentage
<41	7	14%
41-50	7	14%
51-60	13	26%
61-70	11	22%
71-80	10	20%
>80	2	4%
Total	50	100%
Mean ±SD	60.36 ±14.21	

Sex distribution

The incidence of stroke is predominantly in males when compared to females. 64% of the patients were male in the present study (Table 2).

Table-2: Sex distribution

Sex	Number of patients	Percentage
Male	32	64%
Female	18	36%
Total	50	100%

Clinical features

Among the 50 patients, Left hemiplegia was observed more than right side. Left sided weakness was observed in 29 (58%), right sided weakness was observed in 20 subjects (40%) and in 1 (2%) weakness of all the limbs. Also 15(30%) patients had UMN facial palsy, aphasia was observed in 7(14%), cerebellar involvement and sensory impairment was observed in 2(4%) and gaze deviation and homonymous hemianopia was observed in 1(2%) (Table 3).

Table-3: Clinical features

Neurological deficits	Number of patients	Percentage
Left sided weakness	29	58%
Right sided weakness	20	40%
Bilateral weakness	1	2%
UMN facial palsy	15	30%
Aphasia	7	14%
Cerebellar involvement	2	4%
Sensory impairment	2	4%
Gaze deviation	1	2%
Homonymous hemianopia	1	2%

Time of hospitalization

In the present study it was observed that more patients 39(78%) were brought to the hospital within 24 hrs to seek medical intervention.11 (22%) patients were brought within 24 – 48 hrs (Table 4).

Table-4: Time of hospitalization

Time of hospitalization	Number of patients	Percentage
0-24 hrs	39	78%
24 -48 hrs	11	22%
Total	50	100%

Risk factors

In this study, 37(74%) patients had history of hypertension, 27(54%) patients had history of smoking, 26(52%) had history of diabetes mellitus, 10(20%) had history of old Ischemic heart disease (Table 5).

Table-5: Risk factors

Risk factors	Number of patients	Percentage
Hypertension	37	74%
Smoking	27	54%
Diabetes mellitus	26	52%
Previous Ischemic heart disease	10	20%

Lipid profile

Increase in the level of low density lipoprotein (LDL) was the commonest lipid abnormality noted seen in 66%of cases. Total cholesterol was increased in 18 cases, triglycerides was increased in 10 cases, high density lipoprotein (HDL) decreased in 4 cases (Table 6).

Table-6: Lipid profile

Lipid profile	Number of patients	Percentage
Total cholesterol (>200 mg/dl)	18	36%
Triglycerides (>150 mg/dl)	10	20%
HDL (<40 mg/dl)	4	8%
LDL (>130 mg/dl)	33	66%

Hs-CRP levels

In this study,hs-CRP level <1(low risk) was seen in 2 patients,hs-CRP between 1-3(moderate risk)was seen in 20 patients of acute stroke, hs- CRP level between 3.1-10(high risk) was seen in 18 patients,10 patients showed hs-CRP levels >10(very high-risk). The mean hs-CRP levels in this study are 6.02±4.94 (Table 7).

Table-7: hs-CRP levels

hs-CRP levels(mg/l)	Number of patients	Percentage
<1	2	4%
1 -3.0	20	40%
3.1-10.0	18	36%
>10.0	10	20%
Total	50	100%
Mean ±SD	6.02±4.94	

Barthel Index

In this study, 12 patients had mild disability (Barthel Index >60), 29 patients had moderate (Barthel Index 41-60) and 9 patients had severe disability(Barthel Index <40) at admission. After 1 week, 24 patients had mild, 17 patients had moderate, 7 patients had severe disability and 2 patients died during 1 week (Table 8).

Table-8: Barthel Index

Barthel Index	At admission	At 1 week
Mild (>60)	12	24
Moderate (41-60)	29	17
Severe (<40)	9	7
Died	0	2
Mean barthel index	45.33±14.93	58.05±15.41

Sex wise distribution of hs-CRP level in ischemic stroke

In this study, out of 18 females with acute ischemic stroke, 1patient had low risk(<1) 09 patients had hs-CRP level between 1-3(moderate risk),5 patients hadlevels between 3.1-10(high risk),3 patients had levels >10(very high risk).In this study, out of 32 males with acute ischemic stroke,1 patient had lowrisk(<1), 11 patients had hs-CRP level between1-3(moderate risk),13 patients had levels between 3.1-10(high risk),7 patients had levels >10(very high risk)(Table 9).

Table -9: Sex wise distribution of hs-CRP level in ischemic stroke

Sex	hs-CRP levels(mg/l)				Total
	<1	1-3	3.1-10	>10	
Male	1	11	13	7	32
Female	1	9	5	3	18
Total	2	20	18	10	50
P value	0.66				

Age wise distribution of hs-CRP level in ischemic stroke

In this study, high hs-CRP levels were seen in the age group between 71-80 years and greater than 80 years age group (Table 10).

Table-10: Age wise distribution of hs-CRP level in ischemic stroke

Age in years	hs-CRP levels(mg/l)				Number
	<1	1-3	3.1-10	>10	
<41	1	1	3	2	7
41-50	1	3	1	2	7
51 -60	0	9	3	1	13
61-70	0	4	7	0	11
71-80	0	3	3	4	10
>80	0	0	1	1	2
Total	2	20	18	10	50

Association of hs-CRP with Barthel Index at one week

In this study, out of 24 patients with mild disability 2 patients had hs-CRP levels <1, 19 patients had 1-3, 3 patients had 3.1-10 mg/l. In this study, out of 17 patients with moderate disability 13 patients had 3.1-10, 4 patients had >10 mg/l. In this study, out of 7 patients with severe disability 3 patients had 3.1-10, 4 patients had >10mg/l. 2 patients died during the study. P value of this assosciation is <0.00001, which is statistically significant (Table 11).

Table-11: Association of hs-CRP with Barthel Index at one week

hs-CRP levels(mg/l)	Barthel Index				Total
	Mild	Moderate	Severe	died	
<1.0	2	0	0	0	2
1 -3.0	19	0	0	0	19
3.1-10.0	3	13	3	0	19
>10.0	0	4	4	2	10
Total	24	17	7	2	50
P value	<0.00001				

Correlation of hs-CRP with h/o hypertension

In this study, hypertensives showed high hs-CRP levels compared to normotensives.9 hypertensive patients showed hs-CRP levels >10mg/l, 1 normotensive patient showed hs-CRP level>10 mg/l, but not statistically significant(p value-0.24)(Table 12).

Table -12: correlation of hs-CRP with h/o hypertension

hs-CRP levels(mg/l)	Hypertensives	Normotensives
<1	2	0
1 -3.0	12	8
3.1 -10.0	14	4
> 10	9	1
Total	37	13
P value	0.24	

Correlation of hs-CRP with altered lipid profile

In this study, 13 out of 18 hypercholesteraemic patients showed high hs-CRP levels(>3mg/l),7 out of 10 hypertriglyceridemia patients, all the 4 patients with low HDL,23 out of 34 patients with high LDL showed high hs-CRP levels(>3 mg/l)(Table 13).

Table -13: correlation of hs-CRP with altered lipid profile

Lipids	Hs-CRP levels(mg/l)				Total
	1	1-3	3.1-10	>10	
Total cholesterol(>200mg/dl)	0	5	4	9	18
Triglycerides (>150mg/dl)	0	3	5	2	10
LDL(>130 mg/dl)	0	10	12	11	33
HDL(<40 mg/dl)	0	0	2	2	4

DISCUSSION

Acute ischemic stroke develops as a result of a sudden interruption in the focal cerebral blood flow [2]. Ischemic brain injury is characterized by acute local inflammation and changes in levels of inflammatory cytokines, notably C reactive protein. Although infarct

size and stroke severity are major determinants of short-term prognosis after ischemic stroke, hs-CRP predicts prognosis, in particular mortality or new vascular events during the first year independent of infarct size and stroke severity. Higher hs- CRP levels also are associated with lower survival rate of these people [3].

The mean age of the patients in our study was 60.36±14.21 years. These findings were in corroboration with a study by Panicker *et al*. [5]. Many studies showed elderly patients are more prone for stroke than younger patients [6-10]. In this study population, 32 were males and 18 were females. This study is comparable with Winbeck et al study [9]. The most common presentation in our study was left sided weakness, comparable with Panicker et al study [5]. In our study pateints with advanced age, males, altered lipid profile showed high hs-CRP levels. In this study, mean hs-CRP levels were 6.02±4.94. This value was comparable with value found in Rost et al study [7]. In this study, 26 patients had poor functional outcome with moderate and severe disability with mean barthel index of 43.2±8.2 and these patients had mean hs-CRP levels 9.43±4.65 which is statistically significant which is slightly less compared to study conducted by Shoaeb MA *et al*.[11]. In this study, mortality in these patients was 4%.It is comparable with study conducted by Chaudhuri JR *et al*. [10].

In a study conducted by Shoaeb MA *et al* concluded high hs-CRP levels correlated with poor outcome [11]. In a study conducted by Yanfang Liu, Jing Wang et al showed that higher hs-CRP concentration was more prone to be a risk factor for all stroke [12]. In a study conducted by Chaudhuri JR, Mridula K.R *et al*. showed high hsCRP level is strongly associated with and an independent predictor of acute ischemic stroke. The association was found in all ischemic stroke subtypes [10]. Appandraj S *et al.* reported in their study that the hs -CRP level is increased in all patients after acute ischemic stroke. The hs- CRP level strongly correlates with short term outcome in patients of ischemic stroke [13]. Mishra PT *et al.* study concluded that hs-CRP level is increased in cases of stroke – ischaemic as well as haemorrhagic, suggesting an inflammatory response in acute stroke. Furthermore, the increased levels correlated with larger infarct and bleed, severe neurological deficit and worse outcome [14].

CONCLUSION

This study shows that high hs-CRP levels at admission showed high mortality and morbidity during short term prognosis i.e. one week of hospital stay. High hs-CRP levels correlated with poor functional outcome using barthel index. High hs-CRP levels correlated well with altered lipid profile, hypertension as risk factor. Quantitative estimation of hs- CRP is a simple test and helps in predicting prognosis. As we had a small sample size, a larger study is needed to support our observations, and a larger study should also focus on whether hsCRP level needs to be included as a routine screening test in rural hospitals.

REFERENCES

1. Dhamija RK, Arora S, Gaba P, Jais M, Kaintura A, Kumar M, Bhattacharjee J. Study of genetic, metabolic and inflammatory risk factors in patients of acute ischemic stroke. Indian Journal of Clinical Biochemistry. 2008 Apr 1;23(2):136-43.
2. Zivin JA. Factors determining the therapeutic window for stroke. Neurology. 1998;50(3):599–603.
3. Calabro P, Golia E, TH Yeh E. Role of C-reactive protein in acute myocardial infarction and stroke: possible therapeutic approaches. Current pharmaceutical biotechnology. 2012 Jan 1;13(1):4-16.
4. Panicker JN, Thomas M, Pavithran K, Nair D, Sarma PS. Morbidity predictors in ischemic stroke. Neurology India. 2003 Jan 1;51(1):49.
5. Muir KW, Weir CJ, Alwan W, Squire IB, Lees KR. C-reactive protein and outcome after ischemic stroke. Stroke. 1999;30(5):981–985.
6. Rost NS, Wolf PA, Kase CS, Kelly-Hayes M, Silbershatz H, Massaro JM, D'agostino RB, Franzblau C, Wilson PW. Plasma concentration of C-reactive protein and risk of ischemic stroke and transient ischemic attack. Stroke. 2001 Nov 1;32(11):2575-9.
7. Di Napoli M, Di Gianfilippo G, Sollecito A, Bocola V. C-reactive protein and outcome after first-ever ischemic stroke. Stroke. 2000 Jan 1;31(1):231-9.
8. Winbeck K, Poppert H, Etgen T, Conrad B, Sander D. Prognostic relevance of early serial C-reactive protein measurements after first ischemic stroke. Stroke. 2002 Oct 1;33(10):2459-64.
9. Chaudhuri JR, Mridula KR, Umamahesh M, Swathi A, Balaraju B, Bandaru VC. 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.
10. Shoaeb MA, Shehata MA , Taema KM , Hammouda MA. CRP in cerebrovascular stroke:Prognostic implications. The Egyptian Journal of Critical Care Medicine. 2014; 2(1): 43–52.
11. Chatrchyan S, Khachatryan V, Sirunyan AM, Tumasyan A, Adam W, Aguilo E, Bergauer T, Dragicevic M, Erö J, Fabjan C, Friedl M. Observation of a new boson at a mass of 125 GeV with the CMS experiment at the LHC. Physics Letters B. 2012 Sep 17;716(1):30-61.

12. Liu Y, Wang J, Zhang L, Wang C, Wu J, Zhou Y, Gao X, Wang A, Wu S, Zhao X. Relationship between C-reactive protein and stroke: a large prospective community based study. PLoS One. 2014 Sep 5;9(9):e107017.
13. Appandraj S, Sivagamasundari V. A Study on High Sensitivity Crp as a Short Term Prognostic Factor in Acute Ischemic Stroke. Int. J. Pure App. Biosci. 2014;2 (4):142-146.
14. Mishra PT, Chandra R, Saxena SK, Verma S, Jain R, Bhuyan A. High sensitivity C-reactive protein (hsCRP) level in cerebrovascular accident (stroke). Age (yrs). 2010;58:52-76.