



A Study of High Sensitivity C - reactive Protein in Cerebrovascular Accident

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Authors' contributions

This work was carried out in collaboration between all authors. Author NS designed the study protocol and analysis with the help of author MR. Manuscript wrote by author MR. Author CJ guide authors NS and MR in every stage of research. All authors read and approved the final manuscript.

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ABSTRACT

Background: Inflammation plays an important role in the pathogenesis of stroke. C-reactive protein (CRP) is the most reliable marker of inflammation. Cerebrovascular accident is the second most common cause of death in the world causing about 5 million deaths in a year. High sensitivity CRP (hsCRP) refers to lower detection limits of assay procedure being used (1 mg/L). High levels of hsCRP in stroke indicates poor prognosis.

Objectives: The objectives of the study are to observe the levels of hsCRP in cerebrovascular accident, the role of hsCRP in differentiating ischemic and hemorrhagic stroke, the relation between the levels of hsCRP and the size of the lesion and the outcome of patients with stroke in relation to hsCRP.

Methodology: Fifty patients with first episode of stroke as evidenced by CT scan, presenting to the Department of General Medicine, SVRRGG Hospital, Tirupati from August 2013 to August 2014 are studied and the levels of hsCRP are measured and analyzed.

Results: In the study, majority of the patients (58%) are in the age group of 56-70 years with a

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male preponderance. Hypertension (62%) is the commonest risk factor observed followed by smoking (40%) and diabetes (36%). Most of the study population (96%) has raised hsCRP levels. Mean hsCRP (in mg/L) is high in patients with large (>3 cm) infarcts (53.51±18.13) compared to those with small (<3 cm) infarcts (8.71±6.27). In hemorrhagic stroke, mean hsCRP is high in patients with large (32.11±28.11) bleeds than those with small bleeds (12.90±11.14). In both ischemic and hemorrhagic stroke non survivors have hsCRP levels higher than survivors and the levels correlate with GCS score.

Conclusion: hsCRP is raised in both ischemic and hemorrhagic stroke. The rise in hsCRP is less in small lesions compared to that of large lesions and the levels are high in diseased than in survivor group.

Keywords: High sensitivity C-reactive protein; hemorrhagic stroke; ischemic stroke; prognosis.

1. INTRODUCTION

Cerebrovascular accident (Stroke) is defined as rapidly developing signs of focal or global disturbance of cerebral function lasting more than 24 hours or leading to death with no apparent cause other than vascular origin [1]. After coronary heart disease, stroke is the second most common cause of death in the world causing about 5 million deaths in a year [2].

Incidence of first ever stroke varies from 13 per 1,00,000 population per year to 27 per 1,00,000 population per year [3] and prevalence of stroke is around 84 per 1,00,000 population [3]. Stroke mortality in India is estimated to be about 73 per 1,00,000 population [3]. Investigations for stroke include erythrocyte sedimentation rate, high sensitive C- reactive protein, electrocardiogram, lipid profile, CT scan etc. Inflammation plays an important role in the pathogenesis of stroke.

C-reactive protein is the most reliable marker of inflammation. CRP is synthesized in the liver [4] and it activates the classical complement pathway as a response to inflammation. CRP levels in serum can rise dramatically after myocardial infarction, trauma, infection, stroke, inflammation, surgery and neoplasia [5]. The increase starts within 6 hours of start of inflammation and the level may be several times compared to normal [6].

There is growing evidence of prognostic importance of C-reactive protein in stroke. High sensitivity C-reactive protein is not different from conventional CRP. High sensitivity CRP simply refers to lower detection limits of assay procedure being used (1 mg/L) [7]. Many studies showed increased hsCRP levels in acute ischemic stroke [8,9,10]. Increased levels of hsCRP correlate with large bleed and infarct, severe neurological deficit and worse outcome

[11,12]. There are no studies available on the role of hsCRP in differentiating Ischemic and Hemorrhagic stroke. Studies on hsCRP levels in stroke in India are very few. Therefore this study is undertaken to assess the relationship between hsCRP levels and stroke.

2. MATERIALS AND METHODS

This study is done in the Department of General Medicine, SVRRGG Hospital, Tirupati, Andhra Pradesh, India between 1st August 2013 to 31st August 2014.

2.1 Study Design

Hospital based prospective study.

2.2 Sample Size

Fifty stroke patients are enrolled in the present study that met the inclusion and exclusion criteria.

2.2.1 Inclusion criteria

1. Patients with first episode of stroke documented with CT scan within 48 hours of onset of symptoms of focal neurological deficit.
2. Age >15 years
3. Patients with risk factors like diabetes mellitus, hypertension and dyslipidemia are also included in study.

2.2.2 Exclusion criteria

1. Patients with recurrent stroke.
2. Patients with subdural haematomas, extradural hematomas, intracranial tumours or other space occupying lesions.
3. Patients with meningitis, brain abscess and other intracranial infections.

4. Patients with head injury, neoplasia and postoperative patients.
5. Patients suffering from rheumatoid arthritis, ankylosing spondylitis, chronic infection and inflammatory conditions and coronary artery disease.

Ethical clearance is obtained from Institutional ethics committee, S. V. Medical College, Tirupati prior to the study. After taking the written and informed consent from the patient / relative of selected patients, the blood samples are collected between 48 – 72 hours of onset of stroke. Samples are centrifuged and the serum obtained is tested by using hsCRP immunoturbid kit with the help of analyzer. In the analyzer after programming the test, standardization is done.

Data is expressed as mean ± standard deviation. Comparison of the data is done using chi-square test and a p value of less than or equal to 0.05 is considered as statistically significant.

3. RESULTS

Fifty patients with first episode of cerebrovascular disease who are admitted during the study period are included in the study group. Ischemic stroke and hemorrhagic stroke patients constituted 50% each. 58% of the study population are between 56-70 years with mean age of 56.7±8.8. 70% are males and 30% are females.

Most common risk factor in the study is hypertension, observed in 62% of the patients followed by smoking which is present in 40% of the patients. 36% of patients have Diabetes.

In the study most common presenting symptoms are hemiplegia present in 94% of the patients and speech disturbance in the form of dysarthria or aphasia that is present in 52% of the patients. Altered sensorium in the form of unconsciousness is present in 40% patients and features of raised intracranial tension like headache, vomiting and convulsions are present in 34% of patients.

hsCRP < 1 mg/L is considered as normal. hsCRP levels are raised in majority of the patients (96%) in study group. Only 4% of patients have hsCRP < 1 mg/L and their presentation is lacunar infarct. 30% of the patients have hsCRP levels higher than 30 mg/L. Among them ischemic stroke patients constitute 53% and hemorrhagic stroke

patients constitute 47%. Highest hsCRP level observed in the study is 77 mg/L with massive ischemic stroke.

Mean hsCRP in ischemic stroke is 24.84 and in hemorrhagic stroke is 22.89 and the difference is not statistically significant.

In ischemic stroke, mean hsCRP is high in patients with large (>3 cm) infarcts (53.51±18.13) compared to those with small (<3 cm) infarcts (8.71±6.27) and is statistically significant. In hemorrhagic stroke, mean hsCRP is high in patients with large (32.11±28.11) bleeds compared to those with small bleeds (12.90±11.14) and it is statistically significant.

In the study, 76% of the patients with ischemic stroke survived and 24% expired. In hemorrhagic stroke 68% of the patients survived and 32% expired.

hsCRP levels are higher in non survivor group in both types of stroke i.e. ischemic stroke (58.9±23.2) and hemorrhagic stroke (45.76±27.7) compared to survivor group in both types of stroke i.e. ischemic (14.0±12.7) and hemorrhagic stroke (12.13±10.0) and is statistically significant.

Mean GCS at the time of admission is better in patients who survived from the stroke when compared with non survivors and they have lower levels of hsCRP. In non survivors mean GCS is low and hsCRP levels are higher.

Table 1. Risk factors

S. no.	Risk factors	No. of patients	Percentage of patients
1	Hypertension	31	62%
2	Diabetes	18	36%
3	Smoking	20	40%

Table 2. Clinical features of the patients

S. no.	Clinical features	No. of patients	Percentage (n=50)
1	Hemiplegia	47	94%
2	Dysarthria/ Aphasia	26	52%
3	Altered sensorium		
	A. Drowsy	14	28%
	B. Unconscious	20	40%
4	Signs of raised intracranial tension	17	34%

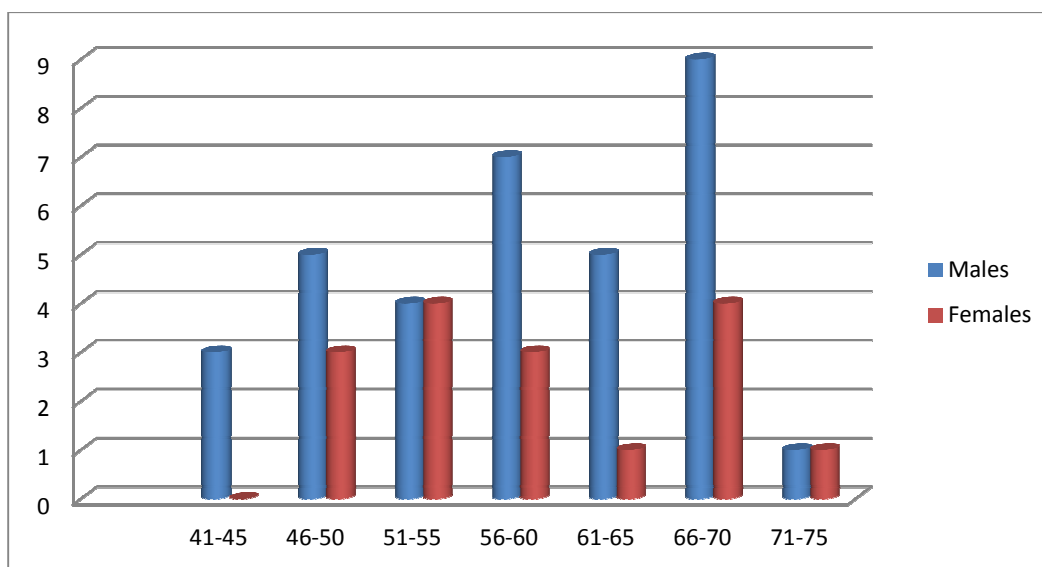


Fig. 1. Age and sex distribution

Table 3. Levels of hsCRP in stroke

S. no.	hsCRP (mg/L)	Number of patients	Percentage of patients
1	<1	2	4%
2	1-3	3	6%
3	3-10	17	34%
4	11-20	9	18%
5	21-30	4	8%
6	>30	15	30%

Table 4. Mean hsCRP levels and type of stroke

S. no.	Type of stroke	Mean hsCRP (mg/L)
1	Ischemic (n=25)	24.84
2	Hemorrhagic (n=25)	22.89

4. DISCUSSION

Aging is a non-modifiable risk factor for stroke and stroke is commonly seen in individuals aged

> 55 years. For each successive 10 years after age of 55, the stroke rate more than doubles in both men and women [13]. In the study majority of the patients are in the age group of 56- 70 years with mean age of 56.7±8.8. Similar results were noted by Nambi et al. [14] and Pinky Talreja Mishra et al. [11] with the mean age of 59.7 years and 58.3 years respectively. In this study mean age is 57±9.1 in males and 56±8.2 in females. The mean age in our study correlates with the study by Wakugawa et al. [15] where mean age was 58.1±11.4 for males and 59.4±11.9 for females. In this study commonest risk factor is hypertension (62%) which correlated with the study results of Pinky Talreja Mishra et al. [11] (73%) and Nambi et al. [14] (58%). Next common risk factors in this study are smoking and diabetes.

Majority of the stroke patients in the study presented with motor weakness followed by speech disturbance. Similar observations are found in Kara et al. [12] study.

Table 5. Mean hsCRP level in different types of stroke in relation with size of lesion

S. no.	Type of lesion	Size	No of patients	Mean hsCRP (mg/L) ±S.D	P value
1	Ischemic (25)	Small (<3 cm)	16	8.71± 6.27	<0.05
		Large (>3 cm)	9	53.51±18.13	<0.05
2	Hemorrhagic (25)	Small (<3 cm)	13	12.90±11.1	<0.05
		Large(>3 cm)	12	32.11±28.1	<0.05
3	Total		50		

Table 6. Mean hsCRP levels in relation with GCS level and outcome in stroke

S. no.	Type of lesion	Study group	Number of patients	Mean GCS	Mean hsCRP (mg/L)±S.D	Percentage of patients
1	ISCHEMIC(25)	Survivors	19	11.5	14±12.7	76%
		Non survivors	6	4.4	58.91±23.2	24%
2	Hemorrhagic(25)	Survivors	17	13.2	12.13±10.0	68%
		Non survivors	8	5.7	45.76±27.7	32%
3	Total		50			

In the present study mean hsCRP in stroke patients is 23.8 mg/L. In Pinky Talreja Mishra et al. study [11] and in the study by S. A. Roudbary et al. [8], the mean hsCRP level are 8.02 mg/L and 10.7 mg/L respectively. Higher levels of hsCRP in the present study may be due to larger size of lesion in both types of stroke.

In ischemic stroke mean hsCRP in our study is 24.84±24.81 mg/L. In Adnan Khan et al. [9] study on hsCRP and ischemic stroke mean hsCRP is 23±11.24 mg/L. It is 18.92±11.28 mg/L in S. A. Roudbary et al. [8] study and is 23.5±28.4 mg/L in Mitchell S. V. Elkind et al. [16] study. Similar results are observed in our study.

The mean hsCRP level in hemorrhagic stroke in our study is 22.89±23.4 mg/L. In study by Pinky Talreja Mishra et al. [11] mean hsCRP is 11.27 mg/L. In our study the higher levels of mean hsCRP may be due to larger size of lesion.

In larger lesions, hsCRP levels are more compared to the smaller lesions and the levels correlate with the size of the lesion. This is supported by the study of Youn CS, et al. [17] who states that raised hsCRP levels correlate with the volume of the affected tissue in stroke. Pinky Talreja Mishra et al. [11] also concluded that increased levels of hsCRP correlate with large infarct and large bleeds and severe neurological deficits.

In our study there is correlation between the levels of hsCRP and GCS in ischemic and hemorrhagic stroke. GCS is low in patients with large infarcts and bleeds who also have high hsCRP levels. Similar results are found in the study done by Pinky Talreja Mishra et al. [11] and Khalil et al. [10].

In the present study high hsCRP levels are associated with unfavourable outcome in ischemic stroke. Similar results are observed in the studies of Pinky Talreja Mishra et al. [11] and Mitchell S. V. Elkind et al. [16]. In hemorrhagic

stroke similar association of hsCRP and outcome is found which was also observed in Pinky Talreja Mishra et al. [11] study.

5. LIMITATIONS

1. The study has small sample size.
2. The findings are based on single time measurement of hsCRP rather than serial measurements of hsCRP.
3. Follow up was not done.

6. CONCLUSION

hsCRP is raised in stroke irrespective of the type of stroke and cannot be used to differentiate the type of stroke. Levels of hsCRP correlate with the size of the lesion. High levels of hsCRP are associated with poor outcome. Therefore hsCRP level estimation can be used to predict the outcome. However as this is a small study further large studies are needed before using the test for predicting the prognosis of stroke.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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