

Bio-markers of Serum High Sensitive C-reactive Protein in Patients of Strokes

Anuj Kumar Dwivedi¹, Swati Sharma²

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Abstract

Background: Stroke is among the most common causes of adult-onset disability. 70–85% of first strokes are accompanied by hemiplegia. Several case control studies with ischemic stroke patients have indicated that recent infections are a possible risk factor for ischemic stroke. Stroke occurs when reduced blood supply to the brain results in cell death.

Aim: The aim of this study is to compare serum high sensitive C-reactive protein levels in stroke patients to controls.

Objective: The primary goal of this study is to examine serum high sensitive C-reactive protein levels in stroke patients and to link them to stroke related death. The secondary goal is to enhance AMI early detection, management and therapy, and prognosis.

Material & Methods: The present study was carried out in the Department of physiotherapy and Central Investigation Laboratory in collaboration with the Department of Biochemistry Medicine, Intense cardiac care units, medical intensive care units, and emergency and private hospitals. The study was approved by Institutional Ethical and Research Committee to use human subjects in the research study. Informed consent was taken from patient and control subjects. Out of 100 subjects, 50 were strokes patients and 50 were age matched healthy controls. The study was conducted from June 2023 to March 2024. The Microlab 300 analyzers (semi-auto analyzer) were used to assess High Sensitive C-reactive Protein concentrations, and the comparisons between the two groups were examined using an unpaired t-test. A $P < 0.05$ was deemed statistically significant.

Results: There was a substantial elevated in the mean serum high sensitive C-reactive protein in strokes cases were 5.86 ± 3.12 mg/dl, which were higher than controls group 2.41 ± 1.27 mg/dl. Comparison between control and serum high sensitive C-reactive protein on strokes cases was found to be more significant. Unpaired t-test showed that there was significant increase in serum high sensitive C-reactive protein level in cases as compared to controls ($p < 0.005$).

Conclusion: The analysis of serum high sensitive C-reactive protein in serum plays an important role in the diagnostic marker and management of ischemic strokes.

Keywords: Strokes; High Sensitive C-reactive Protein; Acute ischemic strokes and Mortality.

Author Affiliation: ^{1,2}Assistant Professor, Department of Physiotherapy, SCPM College of Nursing and Paramedical Sciences, Gonda 271003, Uttar Pradesh, India.

Corresponding Author: Anuj Kumar Dwivedi, Assistant Professor, Department of Physiotherapy, SCPM College of Nursing and Paramedical Sciences, Gonda 271003, Uttar Pradesh, India.

E-mail: anujdwivedi.physio9@gmail.com

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INTRODUCTION

Strokes are among the leading causes of adult disability. Hemiplegia is present in 70-85% of the first stroke cases.¹

Several case control studies with ischemic stroke patients have revealed that recent infections are a potential risk factor for ischemic stroke.²

There is emerging evidence that inflammatory processes have a role in cerebral ischemia.³ Ischemic brain damage caused by artery blockage is characterised by immediate local inflammation and increases in inflammatory cytokine levels in human bodily fluids. Elevated CRP also predicts death in MI patients and is a better predictor of prognosis than peak creatine kinase if thrombolytic medications have been used. Clinical data on CRP and prognosis following ischemic stroke are limited; many individuals with elevated CRP levels within 72 hours of stroke have an increased risk of death, particularly cardiovascular mortality.⁴

Stroke happens when the brain's blood flow is restricted, causing cell death. The World Health Organisation defines stroke as a "neurological deficit of cerebrovascular cause that persists beyond 24 hours or is interrupted by death within 24 hours" There are two types of strokes: ischemic (due to a lack of blood flow) and hemorrhagic (related to bleeding), both of which cause part of the brain to function improperly. A stroke's signs and symptoms can include loss of vision, movement or sensation, the sensation that the world is spinning, and difficulty understanding or communicating.⁵ In 2013, approximately 3.4 million people suffered hemorrhagic strokes, whereas 6.9 million experienced ischemic strokes. About 33 million people who had suffered a stroke in 2010 were still alive. Stroke was the second leading cause of mortality in 2013, following atherosclerotic CAD, accounting for 6.4 million deaths.⁶

Although High Sensitive-CRP has been shown to be predictive in persons with acute coronary syndromes, its most promising application is in primary prevention. High sensitive-CRP levels may indicate low-grade chronic systemic inflammation and contribute directly to atherosclerosis.⁷

CRP has been recognised as a key indicator of endothelial dysfunction and future CVD risk. CRP has emerged as a useful biomarker for vascular inflammation associated with atherosclerosis, and it may directly promote atherosclerotic processes.⁸

Raised Serum Hs-CRP: It will be defined as serum Hs-CRP more than 3.0 mg/L determined by laboratory. (Technician having experience of more than 20 yrs).

Hypothesis: Raised high sensitivity C-reactive protein (Hs-CRP) is associated with ischemic stroke.

METHODS

The present study was carried out in the Department of physiotherapy and Central Investigation Laboratory in collaboration with the Department of Biochemistry. The study was approved by Institutional Ethical and Research Committee to use human subjects in the research study. Informed consent was taken from patient and control subjects. The study was conducted from June 2023 to March 2024. The Strokes patients and healthy controls subject participated in the study. With the help of WHO sample size calculator, following are the calculations;

Level of significance = 5%

Power of test = 80%

Anticipated population proportion = 61.9%⁹

Anticipated population proportion = 6.6%⁹

Sample Size = n=50 patients in each group (i.e. total 100 patients).

Inclusion Criteria: Age matched normal healthy subjects without any major illness belonging to the same socio-economic status with normal High Sensitive-CRP parameters were considered as controls.¹⁰

1. Age 30 – 80 years
2. Both Genders
3. Patients with first acute ischemic stroke according to operational definition (determined by history and CT scan reported by HOD Radiology Department).
4. Controls were patients from wards admitted for other diseases matched by age and gender.

Exclusion criteria:

1. Recent surgery or trauma determined by history.
2. Any liver disease determined by abnormal alanine aminotransferase.
3. Patient with autoimmune disease ruled out with help of antinuclear antibody.
4. History fever.
5. Patients with chronic kidney disease.
6. Patients with history of previous stroke.
7. Controls with history of Cardiac disease.

Data collection procedure: Ischemic stroke presenting to outdoor, indoor and emergency department of Satish Chandra Pandey Memorial hospital, (SCPM) gonda was offered to be enrolled

in the study. After explaining the purpose of study, informed consent was taken from patients. After matching for age and gender, controls were enrolled preferably the patients with other diseases admitted in wards. CT scan of brain was performed and diagnosis confirmed. Blood samples were withdrawn from cases at the time of presentation in emergency. Serum Hs CRP levels were measured. Data was collected in a predesigned Proforma containing background information like age, sex and Hs CRP level.

Statistical analysis:

Mean and standard deviation were worked out for estimating the levels of serum high sensitive C-reactive protein (hs-CRP) in patients of stroke and age matched controls. In order to compare these parameters between patients and controls, student's t-test was applied and the results were presented in tabular and graphical presentation.

Using the student's *t*-test values, the '*p*' values (probability values) were obtained. '*p*' value less than 0.05 was considered as significant.

RESULTS

Table 1: Distribution of patients according to gender.

| Gender | Case | | Control | |
|--------|------|------|---------|------|
| | No. | % | No. | % |
| Male | 42 | 84% | 40 | 80% |
| Female | 08 | 16% | 10 | 20% |
| Total | 50 | 100% | 50 | 100% |

Table 1: Present study comprise of 50 cases and 50 controls. Among cases, 42 were male (84%), 8 were female (16%). Out of 50 controls 40 were male (80%) and 10 were female (20%).

Table 2: Age group mean value of case & control.

| | Case | Control | p value |
|-------------|------------------|-------------------|---------|
| | Mean \pm SD | Mean \pm SD | |
| Age (years) | 58.96 \pm 9.36 | 47.02 \pm 12.43 | p<0.001 |

Table 2: The mean age of cases and controls were 58.96 \pm 9.36 years and 47.02 \pm 12.43 years respectively. This is statistically significant.

Table 3: Age and sex wise distribution.

| Age in years | Cases group (n=50) | | Control group (n=50) | |
|--------------|--------------------|---------|----------------------|---------|
| | male | Female | Male | Female |
| | No. (%) | No. (%) | No. (%) | No. (%) |
| 30-40 | 04 (8%) | 1 (2%) | 7 (14%) | 1 (2%) |

| | | | | |
|------------|----------|----------|----------|------------|
| 41-60 | 13 (26%) | 7 (14%) | 13 (26%) | 4 (8%) |
| 61-70 | 12 (24%) | 4 (8%) | 11 (22%) | 6 (12%) |
| 71 & above | 7 (14%) | 2 (4%) | 06 (12%) | 2 (4%) |
| Total | 36 (72%) | 14 (28%) | 37 (74%) | 13 (23.3%) |

Table 3: The most men 13 (26%) were in the age groups 41-60 years, followed by 12 (24%) in the age groups 61-70 years, and 7 (14%) in the age groups over 71 years. The majority of the males in the 4 (8%) case group were between the ages of 30 and 40. In some cases, 7 (14%) of the females were 41-60 years old, followed by 4 (8%) females 61-70 years old. While 1 (2%) of females were between the ages of 30 and 40, and 2 (4%) were over the age of 71 years.

Table 4: Risk Factors for Stroke (n=50)

| Characteristics | Number of patients | Percentage |
|-------------------|--------------------|------------|
| Hypertension | 17 | 34 % |
| Diabetes mellitus | 12 | 24 % |
| Smoking | 8 | 16 % |
| Alcoholism | 5 | 10 % |
| Total | 42 | 84.00 % |

Table 4: In the present study, out of 50 strokes cases 42 (84%) had hypertension, diabetes mellitus, smoking and Alcoholism habit. Maximum i.e. 17 cases (34%) had hypertension followed by diabetes 12 cases (24%) smoking 8 cases (16%) Alcoholism 5 case (10%). 8 cases (16%) had no hypertension, diabetes mellitus, smoking and Alcoholism habit.

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

| Mortality Case Group | No. of Patients | Percentage |
|----------------------|-----------------|------------|
| Death | 7 | 14% |
| Survived | 43 | 86% |
| Total | 50 | 100 |

Table 5: In the present study, we found that 14% patients died in case group and 86% survived the initial 72 hours.

Table 6: Comparison of serum high sensitive C-reactive protein (hs-CRP) in case strokes and control group.

| Serum hs-CRP | Mean | SD | t-value | p-value |
|------------------|------|------|----------|---------|
| Strokes Patients | 5.86 | 3.12 | t= 10.26 | p<0.01 |
| Control | 2.41 | 1.27 | t= 4.43 | p<0.01 |

As shown in table No. 6, mean serum high sensitive C-reactive protein in strokes cases 5.86 \pm 3.12 mg/dl which was higher than controls group 2.41 \pm 1.27 mg/dl. Comparison between control and serum high sensitive C-reactive protein on strokes

cases was found to be more significant. Unpaired t-test showed that there was significant increase in serum high sensitive C-reactive protein level in cases as compared to controls.

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 and diabetes 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.¹¹⁻¹³

As shown in Table 1 Present study comprise of 50 cases and 50 controls. Among cases, 42 were male (84%), 8 were female (16%). Out of 50 controls 40 were male (80%) and 10 were female (20%). Table 2: The mean age of cases and controls were 58.96 ± 9.36 years and 47.02 ± 12.43 years respectively. This is statistically significant. Our result correlated well with finding showed by Nair SJ. (2022),¹¹ Chaudhuri JR (2013).¹⁴

As shown in Table 3: The most men 13 (26%) were in the age groups 41-60 years, followed by 12 (24%) in the age groups 61-70 years, and 7 (14%) in the age groups over 71 years. The majority of the males in the 4 (8%) case group were between the ages of 30 and 40. In some cases, 7 (14%) of the females were 41-60 years old, followed by 4 (8%) females 61-70 years old. While 1(2%) of females were between the ages of 30 and 40, and 2 (4%) were over the age of 71 years. Our result correlated well with finding showed by Nair SJ. (2022).¹¹

As shown in Table 4: We observed that the current study out of 50 strokes cases 42 (84%) had hypertension, diabetes mellitus, smoking and Alcoholism habit. Maximum i.e. 17 cases (34%) had hypertension followed by diabetes 12 cases (24%) smoking 8 cases (16%) Alcoholism 5 case (10%). 8 cases (16%) had no hypertension, diabetes mellitus, smoking and Alcoholism habit. Our result correlated well with finding showed by Anwar R. (2018),¹⁰ Nair SJ. (2022),¹¹ Chaudhuri JR (2013),¹⁴ Napoli MD (2001).⁴

Table 5: In the present study, we found that 14% patients died in case group and 86% survived, Our result correlated well with finding showed by Nair SJ. (2022),¹¹ Bhaisare S D. et al (2020).¹⁴ Who observed high CRP in both intracranial (48.7%) and extra cranial large artery atherosclerosis (54.9%).¹⁵

As shown in table 6, the mean serum high sensitive C-reactive protein in the case group was 5.86 ± 3.12 mg/dl, while in the control group it was 2.41 ± 1.27 mg/dl. The p-value was 0.05. There was a significant difference between these groups (p value < 0.05). There was a significant difference in these groups as p value was <0.05. Our result correlated well with finding showed by Nair SJ. (2022),¹¹ Chaudhuri J R et al., (2013).¹⁶ CRP, an acute-phase protein synthesised by hepatocytes, is released in the blood stream in response to inflammation and tissue damage. CRP stimulates the endothelial cells to produce various adhesion molecules, such as intracellular adhesion molecule-1, vascular cell adhesion molecule-1.¹⁷

CONCLUSION

This study found that high levels of Hs-CRP are present in all stroke subtypes and independently linked to major artery atherosclerosis and cardio-embolic stroke. The analysis of serum high sensitive C-reactive protein in serum plays an important role in the diagnostic marker and management of ischemic strokes.

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