OPEN ACCESS

Saudi Journal of Medical and Pharmaceutical Sciences
Abbreviated Key Title: Saudi J Med Pharm Sci
ISSN 2413-4929 (Print) | ISSN 2413-4910 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

Original Research Article

HsCRP (High-Sensitivity C - reactive protein) and its Association with Short Term Prognosis Following Ischaemic Stroke

Mohammed Momenuzzaman Khan[1*], Farhana Younus[2], Mohammad Ibrahim Hossain[3], Ayesha Tabassum Swarna[4], Nelson Taposh Mondal[5], Sajal Kumar Shil[6]

[1]Associate Professor, Department of Neurology, Enam Medical College, Savar, Dhaka, Bangladesh
[2]Consultant, Department of Ophthalmology, Bangladesh EYE Hospital, Dhaka, Bangladesh
[3]Assistant Professor, Department of Physical Medicine and Rehabilitation, Enam Medical College, Savar, Dhaka, Bangladesh
[4]Medical Officer, BRAC, Bangladesh
[5]Associate Professor, Department of Medicine, Enam Medical College, Savar, Dhaka, Bangladesh
[6]Assistant Professor, Department of Neuro-Medicine, Kumudini Women's Medical College, Tangail, Bangladesh

DOI: 10.36348/sjmps.2022.v08i04.001 | **Received:** 26.02.2022 | **Accepted:** 29.03.2022 | **Published:** 06.04.2022

***Corresponding author:** Mohammed Momenuzzaman Khan
Associate Professor, Department of Neurology, Enam Medical College, Savar, Dhaka, Bangladesh

Abstract

Introduction: Stroke is a major cerebrovascular disease is one of the most common Neurological diseases. It is the second leading cause of death worldwide. Cerebrovascular disease threatening human health and life with high morbidity, disability and mortality. Major risk factors of ischaemic strokes are hypertension, diabetes, and dyslipidaemia. High sensitivity C-reactive protein (HsCRP) is an inflammatory marker which appears to be a strong predictor of risk factor and prognostic marker of Ischaemic stroke. ***Objective:*** To find the acute course of HsCRP and its association with short term prognosis following Ischaemic stroke. ***Methods*:** A Cross sectional observational study at Dept. of Neurology, Enam Medical College Hospital, Savar, Dhaka, Bangladesh From March 2020 to April 2021. Total number of subjects in this study were 101 with power 80% (persons aged 30 years & above; both male and female). Both sexes and their plasma high sensitivity C-reactive protein (HsCRP) level was measured within 48 hours of admission and on the 5th day after admission. ***Results:*** The study showed that the level of HsCRP did not change significantly when measured within 48 hours of onset of Ischaemic stroke and on 5th day after stroke ($p=0.335$) - the prognosis and severity remained same when followed for 5 days. It, also, showed that the level of CRP ≥ 3 within 48 hours of admission is associated with increased severity and mortality of stroke ($Z=14.4$; $p<0.0001$). ***Conclusion:*** HsCRP level provides rapid and reliable information regarding severity & prognosis in patients with Ischaemic stroke. The level of HsCRP does not change significantly when measured within 48 hours of onset of Ischaemic stroke and on 5th day after stroke. Also, the level of CRP on 5th day was same as within 48 hours of stroke - the prognosis and severity remained same. If confirmed by larger, longitudinal studies this association may be used as a tool to assess the severity and prognosis in a patient with Ischaemic strokes.

Keywords: HsCRP, Ischaemic Stroke, Short Term Prognosis.

Copyright © 2022 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution **4.0 International License (CC BY-NC 4.0)** which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

INTRODUCTION

Stroke is a major cerebrovascular disease is one of the most common Neurological diseases. It is the second leading cause of death worldwide. Cerebrovascular disease threatening human health and life with high morbidity, disability and mortality [1]. The World Health Organisation (WHO) defines stroke as: 'Rapidly developing clinical signs of focal or global disturbances of cerebral function with symptoms lasting for 24hours or longer with no apparent cause other than of vascular origin". Stroke or Cerebrovascular accident is the second most leading cause of death worldwide [2]. Ischaemic stroke comprises 85 percent of all strokes; rest are due to Haemorrhagic stroke (15 percent). Hypertension, Diabetes, Dyslipidaemia, and Smoking are major risk factors of Ischaemic stroke. Various biomarkers have been studied as risk-factors and prognostic-markers for acute ischaemic Strokes. Creative protein (HsCRP) appears to be a strong predictor of Cardio vascular and cerebrovascular risk factors [3]. CRP is an acute phase reactant that is

exclusively synthesized in the liver in response to inflammation. Studies have shown the role of CRP as a predictor of outcome, severity, and mortality in Stroke patients [4-7]. In a study it has been found that high plasma CRP is associated with increased risk of stroke [8]. The Framingham study has shown that HsCRP is also used to predict future risk of stroke. Various prospective studies have found initial CRP levels to be higher in persons who develop stroke, ischemic heart disease, and peripheral artery disease.

MATERIAL AND METHODS

A Cross sectional observational study at Dept. of Neurology, Enam Medical College Hospital, Savar, Dhaka, Bangladesh From March 2020 to April 2021. Total number of subjects in this study were 101 with power 80% (persons aged 30 years & above; both male and female). Both sexes and their plasma high sensitivity C-reactive protein (HsCRP) level were measured within 48 hours of admission and on the 5th day after admission.

Inclusion criteria

1. Patients with first ever Ischaemic stroke.
2. Age more than 30 years.
3. Patients attending Emergency Department of neurology at EMCH, within 48 hours of onset of neurological symptoms.

Exclusion criteria

1. Patients with hg, subarachnoid hg, or extradural hg.
2. Patients attended with neuropathic symptoms secondary to intracranial tumor, infection, head injury, subdural hematoma.
3. Patients attending with features of old stroke.
4. Patients attending after 48 hours of stroke.
5. Conditions associated with high CRP elevation: fever, information, peripheral vascular disease, acute myocardial infarction.
6. Patients attending with features of TIA transient cerebral ischemia.

RESULTS

Table-1: Age Distribution (N=101)

Age Group (in years)	Number	%
30-45	13	12.87%
46-55	21	20.79%
56-65	35	34.65%
66-75	21	20.79%
≥80	11	10.89%
Total	101	100.00%

Table 1 show that the mean age (mean±s.d.)Of the patients were 62.06±11.18 years with range of 30-85 years. The median age was 65 years. Test proportion showed that the proportion of the age group 56- 65 years (34.65%) was significantly higher than other age groups (Z=2.06; p<0.05).

Table 2: Gender Distribution (N=101)

Gender	Number	%
Male	65	64.35%
Female	36	35.64%
Total	101	100.0%

Table 2 show that Gender distribution of test proportion showed that proportion of males (64.35%) was significantly higher than females (35.64%) (Z=3.96; p<0.001).

Table-3: High sensitivity CRP within 48hours (N=101)

HsCRP within 48 hours	Number	%
≥3	27	26.73%
< 3	74	73.26%
Total	101	100.0%

Table 3 show that High sensitivity CRP within 48hrs.The mean HsCRP within 48hours (mean±s.d.) of the patients was 2.69±2.66 with range 0.6 - 12.6 and median 1.55. 27%of the patients had higher HsCRP (≥3) which was not statistically significant (p>0.05).

Table-4: Highly sensitive CRP on 5th Day (N=101)

HsCRP on 5th Day	Number	%
≥3	26	25.74%
< 3	75	74.25%
Total	101	100.0%

Table 4 shows that High sensitivity CRP on5th day: The mean HsCRP on 5th day (mean±s.d.) was 2.65±2.70 with range of 0.6-12.3 and median was 1.60. 25.74% of the patients had higher HsCRP (≥3) which was not statistically significant (p>0.05).

Table-5: Outcome and level of HsCRP within 48 hours (N=101)

Outcome	HsCRP≥ 3 (n= 27)	HsCRP< 3 (n = 74)	Total
Dead	7	0	7
Row %	100.0%	0.0%	100.0%
Col %	25.9%	0.0%	6.9%
Alive	21	74	95
Row %	22.3%	77.7%	100.0%
Col %	77.7%	100.0%	94.0%
Total	27	74	100
Row %	26.7%	73.3%	100.0%
Col %	100.0%	100.0%	100.0%

Table-5 show that outcome and level of HsCRP within 48 hours: Test of proportion showed that proportion of deaths were significantly higher for HsCRP≥ 3 as compared to HsCRP< 3 (Z = 14.14; p<0.0001).

DISCUSSION

The study showed that males are predominantly affected. The age range was 30-85 years with a mean of 62.06 years. According to data obtained from Framingham study, incidents of stroke increase steeply with age becoming double in each successive decade from 55years onwards. In this study, the risk of HsCRP ≥3 was 11.21 times more among the patients having ≥ 55years of ages compared to patients having ≥55 years of ages compared to patients having <55years of age. Stroke is an abrupt onset neurologic deficit due to focal vascular cause. It is a major concern for the community regarding disability, social and mental burden. All patients were selected strictly and carefully as per protocol (after satisfying inclusion and exclusion criteria) to avoid any confounding factor of increasing inflammatory markers (HsCRP). Ischaemic stroke is caused mainly by atherosclerotic narrowing or occlusion of cerebral circulation. The prevalence of Ischaemic stroke has been increasing over the last decade. This may be attributed to increase in life expectancy and aging of population [9, 10]. Nevertheless, Ischaemic stroke is much less studied in terms of its prognosis. This study was conducted to elucidate relationship between high sensitivity C-reactive protein (HsCRP) and Ischaemic stroke. Studies have shown that atherosclerosis is an inflammatory condition [11]. HsCRP is an indicator of inflammatory response to atherosclerosis. Indians have higher prevalence of hypertension and diabetes which puts more risk of atherosclerosis. The elevation of CRP following Ischaemic stroke suggests its role in inflammation. Some studies have shown the role of CRP as the predictor of outcome, severity and mortality in stroke patients. In a study it has been found that high plasma CRP concentrations are associated with increased risk of stroke [8, 12] and its recurrence [13]. The Framingham study has shown that HsCRP is also used to predict future risk of stroke [14]. In this study we found that levels of acute phase proteins are stable after stroke for at least five days. There is no significant time trend in this period of time. Chi-square ($\chi 2$) test showed that there was significant association between HsCRP within 48 hours and on 5th day after acute stroke (p=0.000001). To examine the effect of HsCRP level, we divided the patients into two groups: low HsCRP group (HsCRP<3mg/L) and high HsCRP group (≥3mg/L). The risk of HsCRP≥3 on 5th day was 134.16times more among patients with HsCRP≥3 within 48 hours and the risk was significant. This means patients with high HsCRP on 48hrs of onset of stroke remained high on 5th day when followed. As per Wilcoxon Signed Rank Test, there was no significant difference between level of HsCRP within48hours and on 5th day (p=0.335). This means level of HsCRP remained stable over short-term course followed for 5 days. This result is supported by a study by Mitchell SV Elkind *et al*. [16]. There is a crude association between high CRP and short-term outcome which is likely secondary to stroke severity as seen by NIHSS and marker of inflammation HsCRP. Mechanism of CRP elevation is not completely defined in patients with Ischaemic stroke. Possible theory includes hyper fusion and congestion in the nervous tissue influence secretion of IL_6 thereby promoting CRP production by the liver tissue. It has been found that high CRP value within 48 hours of admission, the severity of neurological

impairment was also high. As per Pearson correlation co-efficient in this study, significant correlation was observed between HsCRP within 48hours (r=0.616; p=0.0001,) NIHSS on 5th day (r=0.566; p=0.0001) and NIHSS on 90th day (r=0.616; p=0.0001). So, the patients having higher CRP within 48 hours were significantly correlated with severity of stroke over time followed till 90 days. Also, deaths were significantly higher in HsCRP more than 3 times within 48 hours (Z=14.4; p<0.0001). The association of HsCRP and Ischaemic stroke in this study may be attributed to high prevalence of patients with hypertension and diabetes. Previously many studies have demonstrated association between CRP and hypertension and also with diabetes [16]. In our study 44% of patients had hypertension, 47% had diabetes, 23% had heart disease. Systolic blood pressure if maintained<130 is favourable to reduce the risk of stroke [17]. The mean CBG (mean ±s.d) of the patients was 160.94mg% with a range of 66.422mg% and the median was 120mg%. 43% patients had CBG >200. In previous studies it was found that high blood glucose within 24hours is associated with poor outcome [18]. In our study, we found that patients who died due to Ischaemic stroke had significantly higher blood glucose at the time of admission (212.83±137.86) than who survived (157.37±183.85).

CONCLUSION

HsCRP level provides rapid and reliable information regarding severity & prognosis in patients with Ischaemic stroke. The level of HsCRP does not change significantly when measured within 48 hours of onset of Ischaemic stroke and on 5th day after stroke. Levels are not influenced by the site of infarction as seen by CT scan of brain. Level of CRP ≥ 3 within 48 hours of admission is associated with increased severity and mortality of stroke. Also, the level of CRP on 5th day was same as within 48 hours of stroke - the prognosis and severity remained same. If confirmed by larger, longitudinal studies this association may be used as a tool to assess the severity and prognosis in a patient with Ischaemic strokes.

REFERENCES

1. Heiss, W. D., Thiel, A., Grond, M., & Graf, R. (1999). Which targets are relevant for therapy of acute ischemic stroke?. *Stroke*, *30*(7), 1486-1489.
2. Di Napoli, M., Papa, F., & Bocola, V. (2001). C-reactive protein in ischemic stroke: an independent prognostic factor. *Stroke*, *32*(4), 917-924.
3. Di Napoli, M., Di Gianfilippo, G., Sollecito, A., & Bocola, V. (2000). C-reactive protein and outcome after first-ever ischemic stroke. *Stroke*, *31*(1), 231-239.
4. Idicula, T. T., Brogger, J., Naess, H., Waje-Andreassen, U., & Thomassen, L. (2009). Admission C–reactive protein after acute ischemic stroke is associated with stroke severity and mortality: The'Bergen stroke study'. *BMC neurology*, *9*(1), 1-9.
5. Huang, Y., Jing, J., Zhao, X. Q., Wang, C. X., Wang, Y. L., Liu, G. F., ... & Gu, W. K. (2012). High-sensitivity C-reactive protein is a strong risk factor for death after acute ischemic stroke among Chinese. *CNS neuroscience & therapeutics*, *18*(3), 261-266.
6. M.S.V. Elkind, MD, MS, J.M. Luna, M.P.H., Moon, Y.P., & MS. (2009): High-sensitivity Creacitve protein (hs CRP) predicts stroke, vascular events, and mortality in prospective cohort study. *Neurology*, *73*(16) 1300-1307.
7. Rordorf, G., Koroshetz, W., Efird, J. T., & Cramer, S. C. (2000). Predictors of mortality in stroke patients admitted to an intensive care unit. *Critical care medicine*, *28*(5), 1301-1305.
8. Makita, S., Nakamura, M., Satoh, K., Tanaka, F., Onoda, T., Kawamura, K., ... & Ogawa, A. (2009). Serum C-reactive protein levels can be used to predict future ischemic stroke and mortality in Japanese men from the general population. *Atherosclerosis*, *204*(1), 234-238.
9. Das, S. K., & Banerjee, T. K. (2008). Stroke: indian scenario. *Circulation*, *118*(25), 2719-2724.
10. Das, S. K., Banerjee, T. K., Biswas, A., Roy, T., Raut, D. K., Mukherjee, C. S., ... & Roy, J. (2007). A prospective community-based study of stroke in Kolkata, India. *Stroke*, *38*(3), 906-910.
11. Ross, R. (1999). Atherosclerosis—an inflammatory disease. *New England journal of medicine*, *340*(2), 115-126.
12. Van Exel, E., Gussekloo, J., De Craen, A. J. M., Bootsma-Van Der Wiel, A., Frolich, M., & Westendorp, R. G. J. (2002). Inflammation and stroke: the Leiden 85-plus study. *Stroke*, *33*(4), 1135-1138.
13. Whiteley, W., Jackson, C., Lewis, S., Lowe, G., Rumley, A., Sandercock, P., ... & Sudlow, C. (2011). Association of circulating inflammatory markers with recurrent vascular events after stroke: a prospective cohort study. *Stroke*, *42*(1), 10-16.
14. Rost, N. S., Wolf, P. A., Kase, C. S., Kelly-Hayes, M., Silbershatz, H., Massaro, J. M., ... & Wilson, P. W. (2001). Plasma concentration of C-reactive protein and risk of ischemic stroke and transient ischemic attack: the Framingham study. *Stroke*, *32*(11), 2575-2579.
15. Elkind, M. S., Coates, K., Tai, W., Paik, M. C., Boden-Albala, B., & Sacco, R. L. (2006). Levels of acute phase proteins remain stable after ischemic stroke. *BMC neurology*, *6*(1), 1-6.
16. Shantha, G. P. S., Kumar, A. A., Bhaskar, E., Sivagnanam, K., Srinivasan, D., Sundaresan, M., ... & Abraham, G. (2010). Hypertensive retinal changes, a screening tool to predict microalbuminuria in hypertensive patients: a cross-

sectional study. *Nephrology Dialysis Transplantation*, *25*(6), 1839-1845.

17. Rodriguez, B. L., Lau, N., Burchfiel, C. M., Abbott, R. D., Sharp, D. S., Yano, K., & Curb, J. D. (1999). Glucose intolerance and 23-year risk of coronary heart disease and total mortality: the Honolulu Heart Program. *Diabetes care*, *22*(8), 1262-1265.
18. Mogensen, U. B., Olsen, T. S., Andersen, K. K., & Gerds, T. A. (2013). Cause-specific mortality after stroke: relation to age, sex, stroke severity, and risk factors in a 10-year follow-up study. *Journal of stroke and cerebrovascular diseases*, *22*(7), e59-e65.

© 2022 |Published by Scholars Middle East Publishers, Dubai, United Arab Emirates