

ORIGINAL RESEARCH

Correlation Of C Reactive Protein And Carotid Intimal Thickness In Patients With Ischemic Stroke**Sumedha Boudh¹, Ranvir Singh Yadav², Rajaram Barde², Sudha alawe^{3*}**

¹PG Resident, Department Of Medicine Gandhi Medical College Bhopal(MP) ²Associate Professor Department Of Medicine Gandhi Medical College Bhopal(MP) ³Assistant Professor Department Of Medicine Gandhi Medical College Bhopal(MP)

Corresponding author**Dr Sudha Alawe**

Assistant Professor Department Of Medicine Gandhi Medical College Bhopal(MP)

Email: sudhabarde80@gmail.com**Abstract**

Background- Stroke is the third leading cause of mortality worldwide. Carotid intima-media thickness (CIMT) and C reactive protein are markers of atherosclerosis and also a predictor for ischemic stroke. We determined the frequency of CIMT in patients with ischemic stroke along with CRP levels and their correlation in patients with ischemic stroke. The study was conducted to determine levels of C-reactive protein and carotid intima media thickness in patients with ischemic stroke.

Materials And Methods- 100 patients with ischemic stroke diagnosed by computer tomography (CT) scan/ MRI brain were studied. Patients with risk factors (hypertension, diabetes, smoking, dyslipidaemia, o/c cva /cad) as well as without risk factors were included. Patients <13 years age, known autoimmune disorders or any active inflammatory condition were excluded in the study. Subjects underwent bilateral carotid artery doppler to determine the CIMT and presence of plaques and CRP levels along with routine lab investigations. CIMT >0.8 mm and CRP >6 mg was considered significant.

Results- The mean age in the study group was 59 years and 61% were males. The average CIMT was 0.833 ± 0.240 mm ($p < 0.003$) and CRP levels were 7.877 ± 3.761 mg ($p < 0.001$). The levels of C- reactive protein and CIMT in patients with ischemic stroke were correlated and found to be statistically significant ($p < 0.001$), suggesting that they are independently associated with incidence of stroke and may be a risk factor in the development of stroke.

Conclusion- CIMT along with CRP levels can be monitored as a marker for atherosclerosis and can aid in preventing ischemic stroke in high risk individual

Keywords: Hyperlipidemia, Ischemic Stroke, Atherosclerosis.

INTRODUCTION

Stroke is the third most common cause of death in industrialized countries (9% of all deaths) and one of the biggest causes of disability worldwide. ¹ Ischemic stroke is the most frequent type of stroke, comprising 87% of all types of stroke. ² In most of the ischemic strokes the underlying pathophysiology is atherosclerosis. The risk factors for stroke are modifiable and non-modifiable. The modifiable risk factors are mostly related to the atherosclerotic burden and include diabetes, hypertension, smoking, and hyperlipidaemia. ^[3,4]

The carotid intima-media thickness (CIMT) has emerged as a reliable independent marker of cardiovascular disease. Since the carotid artery is supplying the cerebrovascular artery system, the risk for developing ischemic cerebrovascular diseases as transient ischemic attack and cerebral infarction can be predicted by evaluating the extent of arteriosclerosis of the carotid artery.^[4]

C-reactive protein (CRP) has been demonstrated to be an important contributory factor for CVD.⁵

The association of CRP with stroke is more credible in the presence of a higher carotid IMT.⁶

MATERIALS AND METHODS

This cross sectional study was performed over a period of 1 year among 100 patients in the department of medicine of a tertiary level medical college in central India.

Objective

To determine levels of c reactive protein and bilateral carotid intima media thickness in patients with ischemic stroke and correlation in between them.

Inclusion criteria

Stroke patients of age >13 years presenting to the hospital within 72 hours of onset of symptoms.

Exclusion criteria

Age <13 years

Patients with known autoimmune disease/inflammatory condition

Data collection - After obtaining informed consent and explaining the purpose of study to the participants, data collection was done. CT head/ MRI brain was performed to rule out ischemic stroke. Other relevant investigations including routine, CRP, etc. were performed. Carotid intimal thickness was measured by B/L carotid artery doppler in the department of radiology after patient stabilization. CIMT >0.8 mm and CRP >6 mg was considered significant.

Statistical analysis Data was entered into MS excel 2007, analysis was done with the help of Epi info Version 7.2.2.2. Frequency and percentages were calculated. Quantitative variables were expressed as the mean and standard deviation. Categorical data was expressed as percentage. Microsoft office was used to prepare the graphs. Relevant statistical tests (Chi Square, Pearson's correlation) were applied wherever applicable, wherever needed Yates correction was also done. P<0.05 was taken as statically significant

RESULT

A total of 100 study participants were enrolled. Mean age of study participants was found to be 59.54 ± 10.23 years. Among patients 63% were hypertensive, 49% were diabetic, 57% were smokers and 63% were dyslipidaemic.

The mean carotid intimal thickness levels and C-reactive protein levels were 0.833 ± 0.24 mm and 7.877 ± 3.76 mg/dl respectively. 50 out of 100 patients reported carotid intima medial thickness to be more than 0.8 mm. Highly significant association between carotid intima thickness with the patient outcome ($p < 0.003$), whereas 65% reported CRP >6 mg/dl ($p < 0.001$). Carotid medial thickness was significantly correlated with C- reactive protein ($p < 0.001$). Mean values of Hemoglobin, TLC, Platelet count, Serum urea, Serum creatinine, Bilirubin levels, Serum Cholesterol, Serum triglycerides and RBS have been displayed in table 1. Table 2 depicts association between various parameters with the patient outcome.

Table-1: Patient characteristics parameters in patients with ischemic stroke

S. No.	Variables	Range	Minimum	Maximum	Mean	SD
1	Age (in years)	55	34	89	59.54	10.231
2	CIMT (in mm)	0.9	0.5	1.4	0.833	0.2404
3	CRP (in mg)	25.9	2.1	28	7.877	3.7611
4	Hb (in gm/dl)	6	9	15	12.314	1.3927
5	TLC (cells/ cumm)	7000	2600	9600	6028	1643.8
6	Platelets (in lakhs/ μ l)	2.4	0.8	3.2	2.039	0.5773
7	S. urea (in mg/dl)	49	16	65	30.77	8.258
8	S. creatinine (in mg/dl)	2.2	0.2	2.4	1.042	0.3499
9	T. Bilirubin (in mg/dl)	1	0.5	1.5	1.014	0.1918
10	Sr. cholesterol (in mg/dl)	102	156	258	195.58	21.85
11	Sr. triglycerides (in mg/dl)	64	132	196	158	17.125
12	Random blood sugar (in mg/dl)	160	96	256	137.9	30.884

DISCUSSION

This study was conducted to find out correlation in between CRP levels and carotid intimal thickness in patients with ischemic stroke. Other routine lab parameters were also correlated. We have demonstrated that elevated CRP levels and high CIMT values are strongly associated with ischemic stroke. Other risk factors of atherosclerosis were also correlated. The mean carotid intimal thickness level was found to be 0.833 ± 0.24 mm. 50 out of 100 patients reported carotid intima medial thickness to be more than 0.8 mm. Highly significant association between carotid intima thickness with the patient outcome ($p < 0.003$). A study by Satoko Oet al in 2019⁴ and Virendra Atamet al (2018)¹¹ found that the mean intimal thickness was 0.76 ± 0.13 mm and 0.708 ± 0.128 mm respectively. In a study by Shovan Kumar Daset al (2014)¹⁸, higher CIMT measurement was found among patients of acute ischemic stroke than healthy controls (0.849 ± 0.196 vs 0.602 ± 0.092 ; $p < 0.001$). The mean C-reactive protein levels was 7.877 ± 3.76 mg/dl. p -value < 0.001 depicts that presence of CRP levels of > 6 mg/dl was significantly associated with the patient outcome. Similarity was observed by Maria Totanet al in 2019¹ where correlations were also made between the CRP values and the risk of death. The highest death rate was seen in patients who had the highest levels of CRP (above 50 mg / L) with $p = 0.04$. As per study by Shahir Mazaheriet al¹⁹ the average level of CRP on the first day of admission was 20.03 mg/L. Of 155 stroke patients, 68 (43.8%) had CRP ≥ 7 mg/L. Our study found that 63% of patients were hypertensive. Similar observations were obtained by Satoko Oet al in 2019⁴, Ali

Moghtaderiet al(2014) ¹² and AvishekSahaet al (2011) ¹⁷ with incidence of hypertension in 55%, 55% and 82% respectively. Maria Totanet al in 2019 ¹ indicated hypertension as an important risk factor for stroke.49% patients were diabetic, Similarity was found with the study by Mahmoud Eet al (2019) ¹⁰ where glycated hemoglobin (HbA1c) showed an increased mean value. ZhiyouCaiet al (2018) ¹⁶, found that the percentages of diabetes were raised among stroke patients.History of smoking was found to be 57% (p=0.481). Similar results were observed in studies by Satoko Oet al (2019) ⁴ andAvishekSahaet al (2011) ¹⁷ with 66% and 61.3% smokers among participants. In this study higher levels of CRP and CIMT were also strongly correlated with hypertension, diabetes, h/o smoking and dyslipidaemia as well.

Table 2: Association between various factors with Patient Outcome

Sl. No.	Variable	Outcome (n = 100)			χ^2 (p- value)
		Positive	Negative	Total	
1	Gender (Male)	52	9	61	0.559 (0.455)
2	HTN (Yes)	52	11	63	0.26 (0.873)
3	Diabetes (Yes)	44	5	49	3.145 (0.076)
4	Smoking (Yes)	46	11	57	0.496 (0.481)
5	CIMT (>0.8mm)	36	14	50	8.575 (0.003)*
6	CRP (>6 mg/dl)	48	17	65	11.029 (0.001)*
7	Hb. Levels (Low Hb)	49	7	56	1.827 (0.177)
8	TLC (<4000 cells/cc)	8	1	9	0.243 (0.622)
9	Platelets (<1.5 lakhs/cc)	16	3	19	0.024 (0.876)
10	Sr. Urea (\leq 500 mg/dl)	81	17	98	0.418 (0.518)
11	Sr. Creatinine (\leq 1.4 mg/dl)	79	17	96	0.853 (0.356)
12	Bilirubin (>1.1 mg/dl)	14	7	21	5.026 (0.025)*
13	Cholesterol (>200 mg/dl)	23	6	29	0.394 (0.530)
14	Sr. triglyceride (>150 mg/dl)	52	11	63	0.026 (0.873)
15	RBS (>126mg/dl)	53	8	61	1.673 (0.196)

CONCLUSION

It is concluded that among various clinical and laboratory parameters studied in relation to ischaemic stroke outcome, C- reactive protein and carotid medial thickness holds a significant value as a marker to predict ischaemic stroke in comparison to other parameters. Elevated levels of CRP and CIMT were found to be independently correlated with the disease state. This study also underlines the importance of assessing multiple conventional risk factors in the causation of stroke episode. Addition of CRP and/or carotid thickness to conventional risk factors resulted in a modest increase in the ability to predict the event. Episodes leading to morbidity and mortality can be lowered by routine monitoring of identified risk factors among high-risk individuals and wider acceptance of expected line of treatment in tertiary centre with provision of emergency intensive care unit.

Limitation As this was a cross-sectional study, a prospective longitudinal study is needed to confirm the relationship between various risk factors.

REFERENCES

1. Totan M, Antonescu E, Catana MG, Mitariu MM, Duica L, Filip CR et al. C-Reactive Protein-A Predictable Biomarker in Ischemic Stroke. *Rev. Chim.* 2019;70 (6).
2. Hashimoto H, Kitagawa K, Hougaku H, Shimizu Y, Sakaguchi M, Nagai Y et al. C-reactive protein is an independent predictor of the rate of increase in early carotid atherosclerosis. *Circulation.* 2001;104(1):63-7.
3. Hakimelahi R, Vachha BA, Copen WA, Papini GDE, He J, Higazi MM et al. Time and diffusion lesion size in major anterior circulation ischemic strokes. *Stroke.* 2014; 45:2936–2941.
4. Ojima S, Kubozono T, Kawasoe S, Kawabata T, Miyata M, Miyahara H et al. Association of risk factors for atherosclerosis, including high-sensitivity C-reactive protein, with carotid intima-media thickness, plaque score, and pulse wave velocity in a male population. *Hypertension Research.* 2020; 43(5):422-30.
5. Haverkate F, Thompson SG, Pyke SD, Gallimore JR, Pepys MB; European Concerted Action on Thrombosis and Disabilities Angina Pectoris Study Group. Production of C-reactive protein and risk of coronary events in stable and unstable angina. *Lancet.* 1997;349: 462–6.
6. Cao JJ, Thach C, Manolio TA, Psaty BM, Kuller LH, Chaves PH et al. C-reactive protein, carotid intima-media thickness, and incidence of ischemic stroke in the elderly: the Cardiovascular Health Study. *Circulation.* 2005;108: 166–70.
7. Makita S, Nakamura M, Hiramori K. The association of C-reactive protein levels with carotid intima-media complex thickness and plaque formation in the general population. *Stroke.* 2005;36(10):2138-42.
8. Yu B, Yang P, Xu X, Shao L. C-reactive protein for predicting all-cause mortality in patients with acute ischemic stroke: a meta-analysis. *Bioscience reports.* 2019;39(2):BSR20181135.
9. Hou D, Liu J, Feng R, Gao Y, Wang Y, Wu J. The role of high-sensitivity C-reactive protein levels in functional outcomes in patients with large-artery atherosclerosis and small-artery occlusion. *Neurological research.* 2017;39(11):981-7.
10. Elbelkimy M, ELkhayat N, ElSadek A, Mansour A, Aboutaleb M. Predictive value of C-reactive protein and carotid intimal medial thickness in acute ischemic stroke. *The Egyptian Journal of Neurology, Psychiatry and Neurosurgery.* 2019;55(1):1-6.

11. Atam V, Gupta A, Koonwar S, Kumar M, Atam I. Correlation of High Sensitivity C-Reactive Protein and Carotid Intimal Medial Thickness in Patients with Ischemic Stroke. *Int J Cur Res Rev*. 2018; 10 (4): 25-8.
12. Moghtaderi A, Sanei-Sistani S, Abdollahi G, Dahmardeh H. Comparison of intima-media thickness of common and internal carotid arteries of patients with ischemic stroke and intracerebral hemorrhage. *Iranian journal of neurology*. 2014;13(4):226.
13. Sahoo R, Krishna MV, Subrahmaniyan DK, Dutta TK, Elangovan S. Common carotid intima-media thickness in acute ischemic stroke: A case control study. *Neurology India*. 2009;57(5):627.
14. Mathiesen EB, Johnsen SH, Wilsgaard T, Bønaa KH, Løchen ML, Njølstad I. Carotid plaque area and intima-media thickness in prediction of first-ever ischemic stroke: a 10-year follow-up of 6584 men and women: the Tromsø Study. *stroke*. 2011;42(4):972-8.
15. Liu Y, Wang J, Zhang L, Wang C, Wu J, Zhou Y et al. Relationship between C-reactive protein and stroke: a large prospective community based study. *PloS one*. 2014;9(9):e107017.
16. Cai Z, He W, Zhuang FJ, Chen Y. The role of high high-sensitivity C-reactive protein levels at admission on poor prognosis after acute ischemic stroke. *International Journal of Neuroscience*. 2019;129(5):423-9.
17. Saha A, Sinha PK, Paul R, Bandyopadhyay R, Biswas K, Banerjee AK. Study of carotid intima media thickness and its correlation with novel risk factors in ischemic stroke. *Neurology asia*. 2011;16(1).
18. Das SK, Sarkar A, Pramanik S, Bandyopadhyay M, Mondal K, Singh SK. Carotid artery intima-media thickness in patients with acute ischemic stroke and its correlation with risk factors for 19]atherosclerosis and/or stroke. *Asian Journal of Medical Sciences*. 2015;6(1):22-7.
19. Mazaheri S, Reisi E, Poorolajal J, Ghiasian M. C-reactive protein levels and clinical outcomes in stroke patients: A prospective cohort study. *Archives of Iranian medicine*. 2018;21(1):8-12.
20. : a cross-sectional study. *International breastfeeding journal*. 2016Dec;11(1):1-7.