Original Research Article

Study Of C – Reactive Protein With Carotid Intimal Thickness In Ischemic Stroke And Relation With Patient Outcome

Gurrala Kartheek Krishna[1], V Sravani[2], Songa Krishna Mohana Rao[3], Geddada Sunitha[4]

[1]Postgraduate, Department of General Medicine, Alluri Sitarama Raju Academy of Medical Sciences, Eluru, West Godavari District, Andhra Pradesh, India
[2]Assistant Professor, Department of General medicine, Alluri Sitarama Raju Academy of Medical Sciences, Eluru, West Godavari District, Andhra Pradesh, India
[3]Associate Professor, Department of General medicine, Alluri Sitarama Raju Academy of Medical Sciences, Eluru, West Godavari District, Andhra Pradesh, India
[4]House Surgeon, Department of General Medicine, Alluri Sitarama Raju Academy of Medical Sciences, Eluru, West Godavari District, Andhra Pradesh, India

Received: 19-11-2021 / Revised: 2-12-2021 / Accepted: 11-01-2022

Abstract

Background: 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. The carotid intima-medial thickness (IMT) has surfaced as a dependable independent marker of cardiovascular complaint. C- reactive protein(CRP) has been demonstrated to be an important contributory factor for Cardiovascular disease. The association of CRP with stroke is more credible in the presence of a higher carotid IMT.**Objective**s: To correlate between the levels of c reactive protein and bilateral carotid intima-medial thickness in patients with Acute ischemic stroke.**Material & Methods**: This is a prospective cross sectional study performed over a period of 1 year in 100 patients who presented to the department of general medicine at Alluri Sitarama Raju Academy of Medical Sciences, Eluru.**Results**: A total of 100 study participants were enrolled. 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 ($p<0.001$).
Conclusions: Addition of CRP and carotid intima-medial thickness to conventional risk factors resulted in a modest increase in the ability to predict cerebrovascular accident. 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.
Keywords: CRP,Stroke

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 utmost of the ischemic strokes the underpinning pathophysiology is atherosclerosis. The threat factors for stroke are adjustable and non-modifiable. The adjustable threat factors are substantially related to the atherosclerotic burden and include diabetes, hypertension, smoking, and hyperlipidaemia [3,4] .The carotid intima-medial thickness(IMT) has surfaced as a dependable independent marker of cardiovascular complaint. Since the carotid artery is supplying the cerebrovascular arterial system, the threat for developing ischemic cerebrovascular conditions as transient ischemic attack and cerebral infarction can be prognosticated by assessing the extent of arteriosclerosis of the carotid artery [5]. C- reactive protein (CRP) has been demonstrated to be an important contributory factor for Cardiovascular disease. The association of CRP with stroke is more credible in the presence of a higher carotid IMT [6] .Recent infections may be a potential risk factor for ischemic stroke, according to several case-control studies with patients who had ischemic strokes. There is growing evidence, in particular, that inflammatory processes contribute to cerebral ischemia. Acute localised inflammation and alterations in the levels of inflammatory cytokines in body fluids of human patients are characteristics of ischemic brain injury secondary to an arterial occlusion. Additionally, it has been shown in a number of prospective studies that people who are at risk of having their first myocardial infarction (MI) or stroke in the future have elevated levels of inflammation markers, particularly C-reactive protein (CRP). If thrombolytic drugs have been administered, elevated CRP is a more accurate predictor of outcome than peak creatine kinase and also predicts mortality in MI patients[9].

Material & Methods

This is a prospective cross sectional study performed over a period of 1 year from September 2020 to September 2021 in 100 patients who presented to the department of general medicine at Alluri Sitaramaraju Academy of Medical Sciences, Eluru.

Inclusion criteria

Stroke patients of age >18 years presenting to the hospital within 72 hours of onset of symptoms.

Exclusion criteria

Age <18 years Patients with known autoimmune disease/inflammatory conditions.

*Correspondence
Dr. Songa Krishna Mohana Rao
Associate Professor, Department of General medicine, Alluri Sitarama Raju Academy of Medical Sciences, Eluru, West Godavari District, Andhra Pradesh, India
E-mail: kartheek038@gmail.com

Data collection

After taking informed consent and explaining the purpose of study to the patients, data collection was done. CT head/MRI Brain was performed to confirm ischaemic stroke. Other investigations including complete blood count and renal function tests were done.C-reactive protein(CRP) levels were obtained and carotid-intima medial thickness was measured with carotid arterial Doppler in the department of radio-diagnosis after patient stabilization. Carotid IMT>0.8mm and CRP>6mg/L was considered significant.

Statistics

The results of the study were tabulated and evaluated descriptively by Microsoft Excel. Descriptive statistical analysis was carried out to explore the distribution of several categorical and quantitative variables. Categorical variables were summarized with n(%), while quantitative variables were summarized by mean ± S.D. All results were presented in tabular form and are also shown graphically using bar diagram or pie diagrams appropriately.

Results

A total of 100 study participants were enrolled. Mean age of study participants was found to be 59.54 ± 10.23 years(table 1). Among patients 63% were hypertensive(table 2)(fig 1), 49% were diabetic(table 3)(Fig 2), 57% were smokers(table 4) and 63% were dyslipidaemic.

The mean carotid intimal thickness levels and C-reactive protein levels were 0.833 ± 0.24 mm(table 5)(fig 3) and 7.877 ± 3.76 mg/dl(table 6)(fig 4) 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).

Table 1: Distribution of study participants on the basis of their age

Sl. No	Age in Years	Frequency	Percentage %
1	≤50	20	20
2	51-60	37	37
3	61-70	34	34
4	71-80	7	7
5	> 80	2	2
	Total	100	100

Table 2: Distribution of study participants on the basis of presence of hypertension

Sl. No.	History of HTN	Frequency	Percentage %
1	Present	63	63
2	Absent	37	37
	Total	100	100

Table 3: Distribution of study participants on the basis of history of Diabetes

Sl. No.	History of Smoking	Frequency	Percentage
1	Present	49	49.0
2	Absent	51	51.0
	Total	100	100.0

Table 4: Distribution of study participants on the basis of history of smoking

Sl. No.	History of Smoking	Frequency	Percentage
1	Present	57	57.0
2	Absent	43	43.0
	Total	100	100.0

Table 5: Distribution of study participants on the basis of Carotid intima-medial thickness

Sl. No.	Carotid intima medial thickness (in mm)	Frequency	Percentage
1	≤ 0.8	50	50%
2	>0.8 – 1.0	32	32%
3	>1.0 – 1.2	13	13%
4	>1.2 – 1.4	5	5%
		100	100%

Table 6: Distribution of study participants on the basis of Levels of C Reactive Protein

Sl. No.	Levels of C Reactive Protein (in mg/dl)	Frequency	Percentage
1	< 3	3	3%
2	3-6	32	32%
3	>6 – 10	49	49%
4	>10	16	16%
	Total	100	100%

Discussion

This study was conducted to find out correlation between CRP levels and carotid intima-medial thickness in patients with ischemic stroke. Other routine lab parameters were also correlated.We have demonstrated that elevated CRP levels and high Carotid IMT values are strongly associated with ischemic stroke. Other risk factors of atherosclerosis (hypertension, diabetes, smoking, dyslipidemia) were also correlated. The mean carotid intima-medial 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 is seen between carotid intima-medial thickness and the patient outcome (p<0.003).

A study by Satoko Oet al in 2019 [4] and Virendra Atamet al (2018) [7] found that the mean intimal thickness was 0.76±0.13mm and 0.708±0.128 mm respectively. In a study by Shovan Kumar Daset al (2014) [8], 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 level 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 Totan et al in 2019 [1] where correlations were also made between the CRP values and the risk of death.In this study higher levels of CRP and CIMT were also strongly correlated with hypertension, diabetes, history of smoking and dyslipidaemia as well.

CRP and prognosis may be related, but the pathophysiological basis for this association is unclear. The crucial part that tissue factor expression plays in coagulation may be affected by increased CRP levels[9].

Increased IMT was linked to an increased risk of stroke in a case-control study. In a different study, an association between elevated IMT and the risk of incident stroke was found; the relative risk rose linearly with elevated IMT and was on par with the relative risk for myocardial infarction in terms of magnitude. Touboul et al. came to the conclusion that an elevated IMT may aid in the identification of patients who are at high risk for brain infarction after observing that an elevated CCA-IMT was linked to brain infarctions both generally and in the major subtypes. The potential value of CCA-IMT and plaque score has been shown in several studies, but not for other stroke subtypes, such as cardioembolic infarction, cerebral haemorrhage, or other or unclassified stroke. These studies only assessed the risk of atherothrombotic infarction and lacunar infarction. They showed that cerebral haemorrhage, other or unclassified stroke, and cardioembolic infarction do not significantly involve atherosclerosis[10,11].

Conclusion

It is concluded that among various clinical and laboratory parameters studied in relation to ischaemic stroke outcome, C- reactive protein and carotid intima-medial thickness holds a significant value as a marker to predict ischaemic stroke in comparison to other parameters.Elevated levels of CRP and Carotid IMT 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 carotid intima-medial 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.

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. Singh AS, Atam V, Jain N, Yathish BE, Patil MR, Das L. Association of carotid plaque echogenicity with recurrence of ischemic stroke. North American journal of medical sciences. 2013;5(6):371.
8. 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 atherosclerosis and/or stroke. Asian Journal of Medical Sciences. 2015;6(1):22-7.
9. Di Napoli M, Papa F, Bocola V. C-reactive protein in ischemic stroke: an independent prognostic factor. Stroke. 2001;32(4):917-24.
10. Van Der Meer IM, Bots ML, Hofman A, Iglesias del Sol A, van der Kuip DA, Witteman JC. Predictive value of noninvasive measures of atherosclerosis for incident myocardial infarction: the Rotterdam Study. Circulation. 2004;109(9):1089-94.
11. Lee EJ, Kim HJ, Bae JM, Kim JC, Han HJ, Park CS, Park NH, Kim MS, Ryu JA. Relevance of common carotid intima-media thickness and carotid plaque as risk factors for ischemic stroke in patients with type 2 diabetes mellitus. American journal of neuroradiology. 2007;28(5):916-9.

Conflict of Interest: Nil Source of support: Nil