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Correlation of C-reactive protein with stroke severity in patients with acute ischemic cerebrovascular stroke.

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ABSTRACT… Objective: To determine the correlation of mean serum C - reactive protein with frequency of stroke severity in patients with acute ischemic cerebrovascular stroke. **Study Design:** Descriptive Cross Sectional study. **Setting:** Department of Medicine, Allied Hospital Punjab Medical College Faisalabad. **Period:** March 2016 to September 2016 **Material & Methods:** Patients fulfilling the selection criteria were enrolled in the study. Besides routine laboratory tests, plasma CRP levels on admission were measured in all patients through hospital pathology laboratory. CRP levels were correlated with the results of NIHSS (National institute of health stroke scale) score based assessment of ischemic stroke severity at admission. **Results:** In our study, out of 50 cases of acute stroke, 62%(n=31) were male and 38%(n=19) were females, mean±sd for age was calculated as 46.82+8.65 years, mean CRP levels was calculated as 8.04+2.15mg/dL, mean NIHSS levels were calculated as 10.08+3. Correlation of mean serum C-reactive protein with frequency of stroke severity in patients with acute ischemic cerebrovascular stroke was calculated where r value was 0.9183 showing a strong positive correlation, which means that high CRP goes with high NIHSS (and vice versa). **Conclusion:** We concluded that CRP levels are positively correlated with the frequency of stroke severity in patients with acute ischemic cerebrovascular stroke.

Key words: C -reactive Protein, Ischemic CVA, NIHSS, Stroke Severity.

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INTRODUCTION

Cerebrovascular stroke (CVS) is a leading cause of death and disability worldwide.[1] The developing world accounts for 85.5% of mortality due to all stroke deaths worldwide.[2] Patients who suffer from stroke in countries such as Pakistan are almost a decade younger than their western counterparts and thus, the disability in stroke survivors and resulting economic losses may be greater.[3] Given the high prevalence of modifiable risk factors like hypertension, diabetes mellitus, obesity and tobacco use, the burden of stroke in Pakistan is likely to be substantial.[4]

Although CVS is one of the leading causes of death and disability, indicators predicting prognosis in stroke patients are not clearly defined.[5] Inflammatory response triggered during acute stroke leads to increased levels of serum C-Reactive Proteins (CRP). Increases in CRP may reflect a systemic inflammatory response following stroke, the extent of tissue injury, or concurrent infections.[6] Rise in CRP during acute inflammation and relationship between inflammation and atherosclerosis makes CRP a potential prognostic marker after vascular events and a potential predictor of future vascular events. High levels of CRP may be associated with increased stroke severity and poor outcome because they reflect either an inflammatory reaction or tissue damage. Elevated serum levels of CRP are found in up to three quarters of patients with ischemic stroke. In animal models of focal cerebral ischemia, CRP increases secondary brain damage through activation of the complement system.[7] Less evidence is available for hemorrhagic stroke. Plasma CRP was seen to increase shortly after admission and was related to hematoma volume at later time points in hemorrhagic stroke. This was attributed to inflammatory response to the

hematoma.[8]

Several studies have assessed the value of CRP in the very early phases of ischemic stroke. The study by M A Shoaeb et al has shown that the serum CRP level on admission can be used to predict severity in ischemic stroke. They found that serum CRP level on admission was predictive of stroke severity (positively correlated with NIHSS ($r = 0.54$, $P = 0.006$)).[9]

No local data is available regarding the significance of CRP in acute ischemic cerebrovascular stroke. Serum CRP levels are easily measured, inexpensive and readily available in our setup and are predictive of stroke severity in the early phases of ischemic stroke. Keeping above facts in mind, I have planned this study to evaluate the correlation of C - reactive protein with stroke severity in patients with acute ischemic cerebrovascular stroke.

MATERIAL & METHODS

This study was conducted in department of Medicine, Allied Hospital Punjab Medical College Faisalabad**.** Total duration of this study was 6 months from March 2016 to September 2016. Patients were selected by using non-probability consecutive sampling. Study design was descriptive Cross sectional. Using WHO sample size calculator 50 patients were selected.

- $r = 0.54$[9]
- Type I error= 5%
- Type II error= 10%
- Confidence level = 95%
- Sample size = 50

Inclusion Criteria

Age between 18 and 70 years.
Gender, both male and female.
Patients admitted in hospital with first ever acute ischemic stroke within the first 24 hour of onset of stroke.

Exclusion Criteria

Patients with recent history of traumatic brain injury, acute hemorrhagic stroke, acute coronary syndrome, past cerebrovascular events, autoimmune disease, hepatic failure, chronic renal failure or any other disease leading to central nervous system dysfunction other than ischemic stroke.

Patients with common causes of raised CRP (burns, trauma, infections, inflammation, active inflammatory arthritis and certain cancers).

After taking approval from hospital ethical review committee (R. No. 572/2015), patients fulfilling the selection criteria were enrolled in the study and informed consent was taken from patients/ caregivers. Detailed history was recorded in each case. Detailed physical examination with special emphasis on hemodynamics and neurological evaluation was conducted in all patients. Besides routine laboratory tests, plasma CRP levels on admission were measured in all patients through hospital pathology laboratory. CRP levels were correlated with the results of NIHSS score based assessment of ischemic stroke severity at admission. Collected data was recorded in a structured Performa by me.

Data was analyzed using computer software SPSS Version 21. Mean (±) SD was calculated for all quantitative variables like age, duration of stroke, CRP levels and NIHSS score. Frequency and percentages were calculated for all qualitative variables like gender and severity of stroke. Spearman correlation coefficient (r) was used to correlate CRP levels with severity of stroke. Effect modifiers like age, gender and duration of stroke was controlled by stratification. Post stratification Spearman correlation coefficient (r) was applied. P-value ≤ 0.05 was considered significant.

RESULTS

The age distribution of the patients was done, it shows that 56% (n=28) were between 18-50 years of age while 44% (n=22) were between 51-70 years of age, mean+sd was calculated as 46.82+8.65 years.

Patients were distributed according to gender, it shows that 62% (n=31) were male and 38% (n=19) were females. (Table-I). Mean duration of stroke was calculated as 8.76+3.10 hours. (Table-I). Mean CRP levels was calculated as

8.04+2.15mg/dl. (Table-II) Mean NIHSS levels were calculated as 10.08+3. (Table-II) Frequency of stroke severity was recorded in 20% (n=10) while 80% (n=40) were not severe.

Correlation of mean serum C-reactive protein with frequency of stroke severity in patients with acute ischemic cerebrovascular stroke was calculated where r value was 0.9183 showing a strong positive correlation, which means that high CRP goes with high NIHSS (and vice versa).

The results of our study are in agreement with several previous studies who assessed the value of CRP in the very early phases of ischemic stroke. A study by M A Shoaeb et al has shown that the serum CRP level on admission can be used to predict severity in ischemic stroke. They found that serum CRP level on admission was predictive of stroke severity (positively correlated with NIHSS (r = 0.54, P = 0.006)).[9]

		No. of Patients
Gender	Male	31 (62%)
	Female	19 (38%)
Age	18-50	28
	51-70	22
Severity	Yes	10
	NO	40

Table-I.

			NIHSS	C-Reactive Protein
Age	18-50	Mean±SD	10.04±3.74	7.96±2.13
	51-70	Mean±SD	10.14±3.62	7.14±2.21
Gender	Male	Mean±SD	10.06±3.67	8.13±2.31
	Female	Mean±SD	10.11±3.71	7.89±1.91
Hours	<=6hrs	Mean±SD	9.75±3.69	7.66±2.05
	>6hrs	Mean±SD	10.18±3.68	8.16±2.19

Table-II.

The value of R is 0.947. This is a strong positive correlation, which means that high CRP goes with high NIHSS (and vice versa).

Elevated level of CRP had a higher value in 130 stroke patients (61.9%) compared to 10 controls (6.6%), p <0.001. An elevated level of CRP was more prevalent in the stroke subtypes of cardioembolic stroke (83.3%) and large artery atherosclerosis (72%). An elevated level of CRP was significantly associated with hypercholesterolemia (P = 0.001), age (P = 0.01) and mortality (0.04). After regression analysis, it was observed that an elevated level of CRP is independently associated with acute ischemic stroke (score 4.5; 95% CI: 2.5-12.2); particularly the stroke due to cardioembolic reasons (odds ratio 3.4, 95% CI: 1.9-10.5) and atherosclerosis of the large arteries (odds ratio 2.1, 95% CI %: 1.5-3.8) They found that an elevated level of CRP is an independent predictor of acute ischemic stroke. The association has been found in all types of ischemic stroke.

DISCUSSION

Stroke is a vascular event having certain modifiable and non-modifiable risk factors. High sensitivity CRP is a biochemical marker of inflammation in cardiovascular and cerebrovascular events. Recent trials also proved that high level of CRP is also risk factor for ischemic stroke. This study was planned because no local data was available regarding the role of CRP in ischemic stroke.

In our study, out of 50 cases of acute stroke, 62% (n = 31) were male and 38% (n = 19) were female, the mean + sd for age was calculated to be 46.82 + 8.65 years, mean CRP levels were calculated as 8.04 + 2.15 mg / dL, mean NIHSS levels were calculated as 10.08 + 3. Correlation of mean serum C-reactive protein with the frequency of stroke severity in patients with acute ischemic stroke was calculated where the r-value was 0.9183 showing a strong positive correlation, which means that a high CRP goes hand in hand with an NIHSS high (and vice versa).

The result of our study are consistent with the studies done previously that evaluated the role of hsCRP in early stages of ischemic stroke. A study done by Shoaeb et al showed that the serum CRP level in measured on admission can be used to predict the severity of ischemic stroke. They proved that serum CRP level on admission can be used to predict stroke severity. Stroke (positively correlated with NIHSS (r = 0.54, p = 0.006)).

Jaydip Ray Chaudhur and others[10] evaluated the association of high levels of CRP (> 3 mg / L) with ischemic stroke and its subtypes in Indian patients, who noted that the mean CRP was significantly higher in stroke patients (3.8 ± 2.5) than controls (1.8 ± 1.5) (P <0.001).

Further studies reveal CRP not only predict the severity of ischemic stroke but is also an independent risk factor for cardiovascular and cerebrovascular events.

Zacho et al, in their population-based study, found an increased frequency of coronary artery disease (32%) and ischemic cerebrovascular stroke (25%) in patients with elevated CRP levels in Denmark.[11]

In the United States, Ridker and al. found that an elevated CRP level predicted the risk of myocardial infarction and stroke in healthy men.[12]

Among the Japanese, Arima et al. found a positive correlation between elevated CRP and a future risk of coronary artery disease.[13]

Additionally CRP has been implicated with poor prognosis in cardiovascular and cerebrovascular disease.

Different studies on labortary biomarkers including atrial and cerebral natriuretic peptides, CRP and homocystiene, it was found CRP has been implicated with increased risk of congestive cardiac failure.[14] So there are increasing number of studies which estimate that CRP is not only a prognostic factor but a risk factor as well for ischemic cardiovascular and cerebrovascular events.[15-16]

There are other risk factors as well apart from elevated CRP. A large case-control study found that a family history of vascular disease was a risk factor for large-vessel and small-vessel stroke. These findings suggest that studies of genetics might possibly be more successful in they were focused on specific stroke subtypes.[17]

Another trial of carotid artery intimal media thickness (IMT) found that after controlling for conventional risk factors, IMT is strongly associated with parental history of stroke.[18] This association was stronger for internal carotid IMT as compared with common carotid IMT.

Two recent reviews have re-examined the issue of hypercoagulability and the risk of ischemic strokes.[19] The genetic study of intracranial aneurysms and subarachnoid hemorrhage (SAH) is another reason for stroke. A case-control study from Japan found that having a family history of SAH increased the risk of SAH with an odds ratio (OR) of 4.0. The risk was higher with a maternal history of SAH (OR 5.4) compared with a paternal history (OR 3.2).[20]

A large literature review found that patients with adult polycystic kidney disease and SAH were more likely to have aneurysms at the middle cerebral artery (38%), more likely to bleed at an early age (41 years), and relatively more likely to be male (48%) compared with those with sporadic SAH.[21]

Serum CRP levels are easily measured and readily available in our hospital laboratories. CRP is not only prognostic factor but also risk factor for cerebrovascular and cardiovascular events also predict the severity of ischemic stroke during early stages of admission.

CONCLUSION

We concluded that CRP levels are positively correlated with the frequency of stroke severity in patients with acute ischemic cerebrovascular stroke.

REFERENCES

1. World Health Organization. **Global status report on non-communicable diseases 2010.** Geneva: World Health Organization 2011.

2. Wasay, M, khatri IA, Kaul S. **Stroke in South Asian countries.** Nat. Rev. Neurol 2014; 10:135–43.

3. Hashmi M, Khan M, Wasay M. **Growing burden of stroke in Pakistan: A review of progress and limitations.** Int JStroke 2013; 8:575-81.

4. Aquil N, Begum I, Ahmed A, Vohra EA & Soomro BA. **Risk factors in various subtypes of ischemic stroke according to TOAST criteria.** JCPSP, 2011; 21:280–83.

5. Jauch EC, Saver JL, Adams Jr HP, Bruno A, Connors JJ, Demaerschalk BM. **Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association.** Stroke 2013; 44(3):870–947.

6. **Das,** Undurti N. **Molecular basis of health and disease.** 1st ed. Netherlands: Springer, 2011.

7. Seo WK, Seok HY, Kim JH, Park MH, Yu SW, Oh K, Koh SB, Park KW. **C - reactive protein is a Predictor of Early Neurologic Deterioration in Acute Ischemic Stroke.** J Stroke Cerevascu Dis, 2012; 21(3):181-86.

8. Di Napoli M, Godoy DA, Campi V, Masotti L, Smith CJ, Parry Jones AR. **C-reactive protein in intracerebral hemorrhage: time course, tissue localization, and prognosis.** Neurology 2012; 79(7):690–9.

9. Shoaeb MA, Shehata MA, Taema KM, Hammouda MA. **CRP in cerebrovascular stroke: Prognostic implications.** Egy j crit care med, 2014; 2(1):43-52.

10. Chaudhuri JR, Mridula KR, Umamahesh M, Swathi A, Balaraju B. **High sensitivity C-reactive protein levels in Acute Ischemic Stroke and subtypes: A study from a tertiary care center.** Iran J Neurol. 2013; 12(3):92–7.

11. Zacho J, Tybjaerg-Hansen A, Jensen JS, Grande P, Sillesen H, Nordestgaard BG. **Genetically elevated C-reactive protein and ischemic vascular disease.** N Engl J Med. 2008; 359(18):1897–908.

12. Ridker PM, Cushman M, Stampfer MJ, Tracy RP, Hennekens CH. **Inflammation, aspirin, and the risk of cardiovascular disease in apparently healthy men.** N Engl J Med. 1997; 336(14):973–9.

13. Arima H, Kubo M, Yonemoto K, Doi Y, Ninomiya T, Tanizaki Y, et al. **High-sensitivity C-reactive protein and coronary heart disease in a general population of Japanese: The Hisayama study.** Arterioscler Thromb Vasc Biol. 2008; 28(7):1385–91.

14. Ahluwalia N, Blacher J, Szabo de EF, Faure P, Julia C, Hercberg S, et al. **Prognostic value of multiple emerging biomarkers in cardiovascular risk prediction in patients with stable cardiovascular disease.** Atherosclerosis. 2013; 228(2):478–84.

15. Mishra PT, Chandra R, Saxena S, Verma S, Jain R, Bhuyan A. **High Sensitivity C-reactive Protein (hsCRP) Level in Cerebrovascular Accident (Stroke) JIACM.** 2010; 11(3):204–7.

16. Rifai N, Ridker PM. **High-sensitivity C-reactive protein: A novel and promising marker of coronary heart disease.** Clin Chem. 2001;47(3):403–11

17. Dong Y, Hassan A, Zhang Z, Huber D, Dalageorgou C, Markus HS. **Yield of screening for CADASIL mutations in lacunar stroke and leukoaraiosis.** Stroke. 2003; 34:203–05.

18. Jerrard-Dunne P, Markus HS, Steckel DA, Buehler A, von Kegler S, Sitzer M. **Early carotid atherosclerosis and family history of vascular disease: Specific effects on arterial sites have implications for genetic studies.** Arterioscler Thromb Vasc Biol. 2003; 23:302–06.

19. Moster ML. **Coagulopathies and arterial stroke.** J Neuroophthalmol. 2003; 23:63–71.Review.

20. Okamoto K, Horisawa R, Kawamura T, Asai A, Ogino M, Takagi T, Ohno Y. **Family history and risk of subarachnoid hemorrhage: A case-control study in Nagoya, Japan.** Stroke. 2003;34:422–26

21. Gieteling EW, Rinkel GJ. **Characteristics of intracranial aneurysms and subarachnoid haemorrhage in patients with polycystic kidney disease.** J Neurol. 2003;250:418–23

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