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Original Article

C-Reactive Protein levels in Acute Stroke: Ischemic vs Hemorrhagic in a Tertiary Care Hospital

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ABSTRACT

There is growing evidence of the prognostic importance of C-reactive protein (CRP) in ischemic stroke. However, the independent value of CRP in ischemic vs hemorrhagic stroke has not been established. **Objective:** To assess the diagnostic value of CRP as biomarker in ischemic stroke in comparison to hemorrhagic stroke **Methods:** This prospective study was conducted from March 2020 to March 2022 in the Department of Medicine, Ayub Medical College. Sample size of 71 was calculated including patients of both genders having age 22-105 years admitted with first-ever acute stroke within the first 24 hours of onset. Data was analyzed using SPSS latest version. Quantitative variables are shown as frequency and percentages. Paired T Test was applied to see the association of CRP levels with effect on CT- Scan of Brain. *p value* less than 0.05 was considered significant **Results:** 69% of the participants were women, far outnumbering the men. 45 patients found to have ischemic stroke (63.38%) whereas 26 (36.62%) reported having Hemorrhagic stroke. *Paired t test* applied to see the association of CRP Levels with CT Scan Brain was found significant having *p value 0.002* **Conclusions:** CRP levels are important in the diagnosis of stroke based on data. CRP levels must be compared to those of other stroke biomarkers in order to make this determination. The serum CRP level within 24 hours can be used to predict severity in ischemic but not hemorrhagic stroke.

INTRODUCTION

C-Reactive Protein (CRP) levels may rise after an acute ischemic stroke because of an inflammatory response. CRP levels that are too high may indicate an inflammatory reaction or tissue damage, both of which can lead to a poor outcome [1]. An intracerebral hemorrhage-induced brain injury is thought to be the result of mechanical damage followed by ischemic, cytotoxic, and inflammatory changes in the tissue beneath and around it. Inflammatory biomarkers and growth factors secreted during intracerebral hemorrhage have piqued researchers' interest in recent years [2]. Blood CRP levels rise during the acute phase of ischemic stroke as a result of ischemic brain damage. In patients with acute ischemic stroke, plasma CRP levels are elevated because of the underlying vascular lesions and the inflammation caused by brain infarction. CRP administration in an adult rat model of middle cerebral artery occlusion led to significantly larger infarcts than control subjects. In addition, a specific small-molecule inhibitor of CRP was administered to rats undergoing acute myocardial infarction to prevent the increase in infarct size and cardiac dysfunction induced by injection of human CRP [3]. After adjusting for confounding

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variables, some studies found that CRP was associated with post-stroke functional outcomes, while others found that the association disappeared. As a result, the relationship between CRP levels in the blood and clinical outcomes in patients with acute ischemic stroke remains inconclusive [4]. Haemorrhagic Stroke has a worse prognosis in terms of long-term disability and mortality. Many studies have been done to find suitable markers for stroke diagnosis, but none of them are universally accepted. A population-specific biomarker for stroke could be identified based on these findings [5]. Our aim was to assess the diagnostic value of CRP as biomarker in ischemic stroke in comparison to hemorrhagic stroke.

METHODS

This prospective study was conducted from March 2020 to March 2022 in the Department of Medicine, Ayub Medical College. Sample size of 71 was calculated using WHO calculator keeping confidence interval 95% & margin of error 5%. Non-probability consecutive sampling technique was used. Patients of both genders having age 22-105 years admitted with first-ever acute stroke within the first 24 hours of onset were included in our study. Patients admitted more than 24 hours after symptoms onset were excluded from our study. Patients with recent history of traumatic brain injury, unstable angina, Aspiration pneumonia, autoimmune disease, liver failure, acute or chronic renal and diabetic foot were also excluded from study. The study protocol was approved by the institutional review board at Ayub Teaching Hospital Abbottabad and written informed consent to participate and publish data were obtained from all participating patients or first degree relatives. A CT scan plain of brain was done on admission differentiate between ischemic and hemorrhagic stroke. Three ml of venous blood was taken through a venipuncture and sent to the laboratory. The CRP assay was done using solid phase enzyme-linked immunosorbent assay. Normal reference of CRP was less than 5 mg/L. Data was analyzed using SPSS latest version. Quantitative variables are shown as frequency and percentages. *Paired t test* was applied to see the association of CRP levels with effect on CT- Scan of Brain. *p value* less than 0.05 was considered significant

RESULTS

A total of 71 individuals were in harmony with the inclusion criteria. The demographics section included the names, age, gender and medical record number. Names were just taken for the marking of data; it neither adds nor decreases the weight of this research. The ages ranged from 22-105 years, but the mean age was 62 years. More than were females (69%) overshadowing males. The medical record number was taken to ease the process of data keeping a track and follow up the patients and doesn't have any other significance, as shown in Table 1.

Gender	Frequency
Male	22 (31.0)
Female	49 (69.0)
Age	
22-50	20 (28.17)
51-105	51 (71.83)

Table 1: Patient Demographics

Upon arrival in an emergency, the customary vitals blood pressure and blood sugar levels were taken and noted. A major portion of ⅔ lied in the category of less than 140/90 mmHg (40.8%), meanwhile, the mean systolic pressure was found to be around 150 and diastolic was 98 mmHg approximately. Tests for random blood glucose highlighted that half of the numbers had normal levels of glucose i.e. <160mg/dl. In addition, more than of the study population were known diabetics, as shown in Table 2.

Characteristics	Frequency (%)
Blood Pressure on Arrival	
Less than 140/90mmHg	29 (40.8)
140/90 to 159/99	14 (19.7)
160/100 to 179/109	12 (16.9)
Equal to or more than 180/110	16 (22.5)
Blood Glucose Levels	
Less than 200 mg/dl	Less than 200 mg/dl
More than 200 mg/dl	More than 200 mg/dl

Table 2: Frequency of Blood Pressure & Glucose Levels

The CT scan conducted on patients revealed that almost suffered from hemorrhagic stroke and the rest endured ischemic stroke. Furthermore, the basis and defining factor of this research is the CRP levels, CRP levels were measured within 24 hours of admission, results depicted a balance distribution, almost half of the patients had CRP levels less than 5mg/dl and the other half had levels more than 5mg/dl. Paired t test was applied to see the association of CRP Levels with CT Scan Brain and was found significant having p value 0.002, as shown in Table 3. A total of 45 patients were found to have ischemic stroke (63.38%) whereas 26 (36.62%) reported having Hemorrhagic stroke, shown in Figure 1.

C-Reactive protein levels	CT scan (brain)	Hemorrhagic Ischemic	Total	P-value
Less than 5 mg/d	20	18	38	0.002
IMore than 5 mg/dl	6	27	33	

Table 3: C-Reactive protein levels & CT scan (brain) Association

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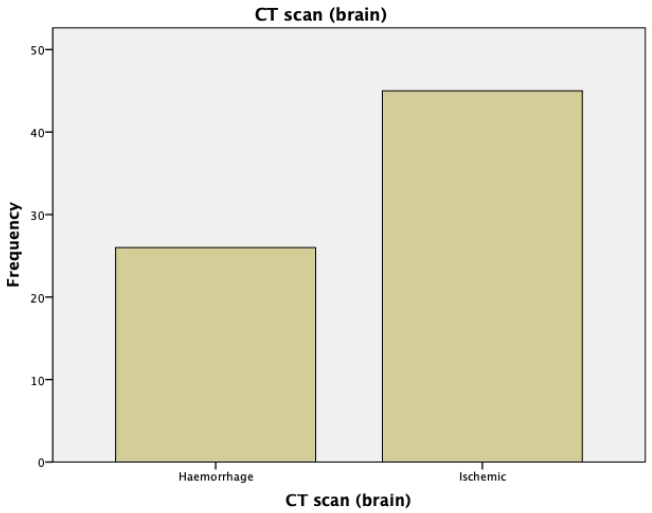

Figure 1: Frequency of Ischemic & Hemorrhagic Stroke

DISCUSSION

As prevalence of stroke in South Asia countries is high, it is important to determine the easy diagnostic tools. Based on blockage or rupture strokes are categorized as being hemorrhagic or ischemic. This research is designed to signify and emphasize on the decisive and diagnostic distinction of CRP levels in patients with a stroke. Multiple associations were made to endorse the findings, patients with age 50 or above were at higher risk of getting a stroke, study by Mehta et al., strengthened by providing strongly abiding evidence with a p=0.001[6]. Similar evidence was extracted in case of age and blood pressure that with an increasing age blood pressure abnormalities were more eminent. The fact that the older patients suffered more from strokes may be because there were more known diabetics in the same age groups. Debrah et Al highlighted the age-related association of type 2 diabetes mellitus [7]. On the other hand, Nicolas et al., reported the correlation among elderly age and the development of hypertension [8]. Gender based approach was taken and percentages were compared to signify and eliminate the bias of females being greater in numbers. Gender differences were not remarkable in terms of ischemic or hemorrhagic stroke, this depicts no gender predisposition. Though more females were found to be hypertensive on arrival than males but it may be physiological. This was an ambiguous finding as usually males are prone to hypertension, females tend to show high blood pressure symptoms after menu pause [9]. Coming onto the core or bedrock of our study chi-square test revealed significant results, patients with hemorrhagic stroke had a value of <5mg/dl and with ischemic stroke had a value of >5mg/dl with a p value of 0.300 and Fisher test showing a value of 0.005. Napoli et al., braced and aided the discoveries of our study, moreover, a meta-analysis by Zhou et al., affirmed that the higher CRP levels were found in patients with ischemic heart stroke [10,11]. Contrary to this, Erdal et al., portrayed a different dimension in which hemorrhagic group of both males and females showed higher CRP levels, with values of ≥0.74 mg/dL [12]. Kristine et al., researched the usefulness of CRP levels in diagnosis and prognosis of cancer patients and the higher CRP values are found to be related to poor prognosis. Studies identified the association of CRP levels with smoking and intake of anti-inflammatory compounds like coffee etc., [13,14]. Neither Blood pressure on admission had an impact on CRP values nor the diabetes was able to grasp the attention. In Texas, a secondary study found that patients admitted to inpatient rehabilitation centres and skilled nursing facilities for post-acute rehabilitation had distinct demographic and clinical characteristics. When it comes to patient and facility characteristics, a closer assessment of ischemic and hemorrhagic stroke discharges implies a need for more comprehensive comparisons of inpatient rehabilitation centres vs skilled nursing facilities [15]. According to systematic review published in 2021, persons with AIS treated with IVT who had elevated levels of plasma CRP had a bad 3-month prognosis. Risk categorization of AIS patients as candidates for IVT or other alternative therapies, such as mechanical thrombectomy, may be aided by CRP levels [16]. HsCRP levels were found to be high in both ischemic and hemorrhagic strokes, suggesting an inflammatory response in acute stroke. The greater the hsCRP levels, the worse the prognosis and neurological damage, according to a study conducted in 2022 India [17]. High CRP levels were found to be independently related with poor clinical outcomes and greater in-hospital mortality in patients with ICH, according to research from the Chinese Stroke Center Alliance (CSCA) [18]. Whereas a prospective population-based study in Sweden shows CRP has been found to be a major risk factor for first-time ischemic stroke, particularly in patients with small-vessel disease. A polymorphism in CRP 1444C>T did not have a significant connection with any type of stroke [19]. Serum CRP levels, according to researchers at the University of Ulsan College of Medicine, have little discernible utility in diagnosing acute stroke in patients with dizziness but no obvious neurological abnormalities [20]. Factors such as obesity or cholesterol levels, genetic makeup, ethnicity and socioeconomic conditions were not accounted. Relying on the available literature and knowledge CRP levels may be to be a breakthrough and effective method serving in diagnostic and prognostic domains.

CONCLUSION

The role of CRP in the early diagnosis of type of stroke in ER

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is crucial in this context and will be helpful in setting where facilities of early CT scan or MRI brain is not available. Moreover, our research will lay the foundation for future research projects in our area and future studies are warranted to find if CRP can serve as a prognostic factor in stroke or not.

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