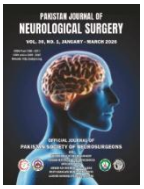

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Original Research

Frequency of Raised Serum C-Reactive Protein (CRP) Levels Among Stroke Patients at A Tertiary Care Hospital

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ABSTRACT

Objective: To determine the frequency of raised serum C-reactive protein levels among stroke patients at a tertiary care hospital.

Materials and Methods: This was a descriptive cross-sectional study designed to estimate the frequency of raised serum C-reactive protein (CRP) levels among stroke patients. The study was not intended to establish causal relationships. A descriptive cross-sectional case series study was conducted at the Department of Neurology, Nishtar Medical University Hospital, Multan, from 26-10-2018 to 26-04-19. A total of 85 stroke patients were enrolled. Once registered in the study, a 3 ml venous blood sample was drawn in a sterilized syringe under aseptic conditions and sent to the Central Laboratory of the hospital for serum CRP levels. Data was entered and analyzed by the computer program SPSS version 26.

Results: Out of 85 patients, 54 (63.5%) were male, and 55 (62.4%) were above 55 years. Serum CRP levels were raised in 46 (54.1) patients. CRP has a significant association with age >55 years (p=0.007), rural residence (p=0.048), hypertension (p=0.001), and diabetes (p=0.001. Whereas other variables showed no statistically significant correlation.

Conclusion: A very high frequency of raised serum C-reactive protein (CRP) was observed among stroke patients in our study. Raised CRP was significantly associated with hypertension, diabetes, age, and residential status. All clinicians who care for this type of patient should regularly monitor serum C-reactive protein levels, since this monitoring contributes to a better clinical evolution, favoring the prognosis and functional stability of the patient.

Keywords: Stroke, C-reactive Protein, Raised, Frequency.

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INTRODUCTION

Stroke is the second leading cause of death globally and is associated with up to 5.54 million deaths every year, two-thirds of which occur in resource-poor countries (RPC).[1] Stroke is a global health problem, which is the leading cause of adult disability and the second leading cause of mortality worldwide.[2] According to World Health Organization (WHO) estimates for the year 2020, stroke will remain the 2nd leading cause of death, along with ischemic heart disease, both in developing and developed countries.[3] It has two main subtypes, ischemic and hemorrhagic.[1] For optimal management, a distinction must be made between the subtypes since the therapy is different.[4] Ischemic stroke requires initiation of thrombolytic and antiplatelet therapy, while in the case of hemorrhagic stroke, hemostatic therapy may be administered hemostatic therapy. Ideally, either thrombolytic or hemostatic therapy should be given soon after the onset of stroke to improve outcome.[5] In addition, stroke patients in underdeveloped countries are 10 years younger than their Western counterparts, and hence, the burden of sustained disability in survivors is greater.[6] Ischemic Stroke accounts for 60- 90% percent of all stroke cases, and it occurs as a result of an obstruction within a blood vessel supplying blood to the brain.[7] The risk factors for stroke are classified as non-modifiable (age, family history, prior stroke, gender, and ethnicity) and modifiable risk factors (hypertension, diabetes mellitus, coronary artery disease, arterial fibrillation, dyslipidemia, smoking, obesity, alcohol abuse, and physical inactivity.[8]

Accumulating evidence suggests that inflammation plays an important role in the development of cardiovascular and cerebrovascular diseases.[9] Inflammatory processes and infection can promote the development of atherosclerosis and thrombosis by increasing serum levels of CRP, leukocytes, coagulation factors, fibrinogen, and cytokines, as well as by altering metabolism and endothelial cells and macrophages' function. Various inflammatory markers, like proinflammatory cytokines, CRP, have been associated with cerebrovascular events. Elevated concentrations of CRP are predictive of cardiovascular disease in men and women.[10] A study conducted by Shaikh et al, has documented 67 % raised levels of serum CRP among stroke patients.[6]

As evident from the above statistics, high levels of raised serum CRP have been reported due to genetic differences and variation in geographic distribution. The need to evaluate the current magnitude of the problem in our local population. Moreover, serum CRP levels are not routinely monitored in our daily routine practices; if values are found to be deranged to such levels, then routine monitoring of the CRP levels will be adopted to avoid further complications. The results of this proposed study will generate a useful baseline database of our local population. Thus, the current study aims to determine the frequency of raised serum C-reactive protein levels among stroke patients at a tertiary care hospital.

MATERIAL AND METHODS

Study Design and Study Setting

This was a descriptive cross-sectional study designed to estimate the frequency of raised serum C-reactive protein (CRP) levels among stroke patients. The study was not intended to establish causal relationships.

A descriptive, Cross-sectional study at the Department of Neurology, Nishtar Medical University/Hospital, Multan, after approval of synopsis from the College of Physicians and Surgeons Pakistan (CPSP/REU/NEU-2017-099-432) and taking IRB approval from Nishtar Medical University (Ref no: 22110) from 26-10-2018 to 26-04-19. Sample size of 85 cases, calculated by using the following formula: $n= z^2pq/d^2$ (Where z = 1.96, p = 67% (frequency of raised CRP levels), q = 100-p, d = 10% at 95% confidence level)[11] and were enrolled in the study using non-probability,

consecutive sampling. A form was designed to systematically record study findings. Informed consent was obtained from each patient after a detailed explanation of the research objectives. The confidentiality of the data provided was guaranteed, and the patient was assured that participation did not pose any risk to their health. Once registered in the study, a 3 ml venous blood sample was drawn in a sterilized syringe under aseptic conditions and sent to the Central Laboratory of the hospital for serum CRP levels. All the relevant information, such as raised CRP levels (Yes/No), age groups, gender, history of hypertension, diabetes, educational level, residential status, family history of stroke, and smoking, was noted on the proforma specifically designed for the study by the researcher.

Inclusion & Exclusion Criteria

Patients aged 40-70 years, both genders, and with stroke. Patients with a history of recurrent cerebrovascular events, metabolic disorders, coronary artery disease, heart failure, a previous diagnosis of brain tumors (based on medical history), and those who did not provide consent to participate were excluded from the study.

Statistical Analysis

Data were entered and analyzed using SPSS version 26 software. Descriptive statistics were used to calculate the mean and standard deviation of patient age and C-reactive protein (CRP) levels. Frequencies and percentages were calculated for categorical variables, such as elevated CRP levels (Yes/No), age groups, gender, history of hypertension, diabetes, educational level, place of residence, family history of stroke, and smoking. Confounding factors such as age, gender, hypertension, educational level, place of residence, family history of cerebrovascular disease, diabetes, obesity, and smoking were controlled for through stratification. The chi-square test was then applied to evaluate their effect on the results. A p-value of 0.05 or less was considered statistically significant.

RESULTS

Distribution of Demographic Variables

Out of the total 85 stroke patients, a majority were male (54 patients, 63.5%), while females comprised 31 (36.5%). In terms of age, 53 patients (62.4%) were older than 55 years, whereas 32 (37.6%) were aged 55 or below. Regarding residential status, 48 patients (56.5%) belonged to urban areas, and 37 (43.5%) were from rural backgrounds. The socioeconomic distribution showed that 53 participants (62.4%) were from a middle-income background, while 32 (37.6%) fell into the poor category.

When looking at comorbid conditions, 28 patients (32.9%) were diabetic, and 57 (67.1%) were not. Hypertension was present in 50 patients (58.8%), while 35 (41.2%) did not have hypertension. Obesity was identified in 19 patients (22.4%), whereas 66 (77.6%) were not obese. A positive family history of stroke was seen in only 6 patients (7.1%), with the vast majority, 79 (92.9%), reporting no such history. Smoking was reported by 24 patients (28.2%), and 61 (71.8%) were non-smokers. Literacy levels were notably low, with 66 participants (77.6%) being illiterate, and only 19 (22.4%) being literate. In terms of stroke type, ischemic stroke was more common (50 patients, 58.8%), compared to hemorrhagic stroke (35 patients, 41.2%). Importantly, raised serum CRP levels were observed in 46 patients (54.1%), indicating a potential association with inflammatory processes in stroke, while 39 patients (45.9%) had normal CRP levels, as shown in **Table 1:** Distribution of various demographic & clinical variables among the study participants.

Raised serum C-Reactive Protein levels in relation to demographic and clinical variables:

Table 2 illustrates the stratification of patients

Gender Distribution

Table 1: *Gender distribution.*

Variables	Frequency	Percentage
Gender		
Male	54	**63.5**
Female	**31**	**36.5**

Age Distribution

Variables	Frequency	Percentage
Age groups		
Up to 55 Years	32	37.6
More than 55 Years	53	62.4

Residential Status

Variables	Frequency	Percentage
Residential status		
Rural	37	43.5
Urban	48	56.5

Socioeconomic Status

Variables	Frequency	Percentage
Socioeconomic status		
Poor	32	37.6
Middle Income	53	62.4

Diabetes

Variables	Frequency	Percentage
Diabetes		
Yes	28	32.9
No	57	67.1

Hypertension

Variables	Frequency	Percentage
Hypertension		
Yes	50	58.8
No	35	41.2

Obesity

Variables	Frequency	Percentage
Obesity		
Yes	19	22.4
No	66	77.6

Family History

Variables	Frequency	Percentage
Family History		
Yes	06	7.1
No	79	92.9

Smoking

Variables	Frequency	Percentage
Smoking		
Yes	24	28.2
No	61	71.8

Literacy

Variables	Frequency	Percentage
Literacy		
Illiterate	66	77.6
Literate	19	22.4

Type of Stroke

Variables	Frequency	Percentage
Type of stroke		
Ischemic stroke	**50**	58.8
Hemorrhagic stroke	35	41.2

Raised CRP

Variables	Frequency	Percentage
Raised CRP		
Yes	**46**	54.1
No	39	45.9

with raised serum C-Reactive Protein (CRP) levels in relation to various demographic and clinical variables. Out of the total 85 patients, 46 had raised CRP, while 39 did not. Several variables showed statistically significant associations with raised CRP levels. Although more females (21 out of 31) had raised CRP compared to males (25 out of 54), the association between gender and CRP levels was not statistically significant ($p = 0.072$).

Age demonstrated a significant association with CRP levels ($p = 0.007$). Among patients older than 55 years, a substantial number (35 out of 53) had elevated CRP, whereas only 11 out of 32

Table 2: *Stratification of patients with raised serum C-Reactive Protein (CRP) levels in relation to various demographic and clinical variables.*

Variables	Raised serum CRP Yes (n=46)	No (n=39)	P-Value
Gender			
Male (n=54)	25	29	0.072
Female (n=31)	21	10	
Age			
Up to 55 Years (n=32)	11	21	0.007
More than 55 Years (n=53)	35	18	
Residential status			
Rural (n=37)	25	12	0.048
Urban (n=48)	21	27	
Diabetes			
Yes (n=28)	25	03	0.001
No (n=57)	21	36	
Hypertension			
Yes (n=50)	36	14	0.001
No (n=35)	10	25	
Obesity			
Yes (n=19)	13	06	0.196
No (n=66)	33	33	
Family History			
Yes (n=06)	05	01	0.212
No (n=79)	41	38	
Smoking			
Yes (n=24)	14	10	0.809
No (n=61)	32	29	
Literacy			
Illiterate (n=66)	35	31	0.797
Literate (n=19)	11	08	
Type of stroke			
Ischemic stroke (n=50)	31	19	0.121
Hemorrhagic stroke (n=35)	15	20	

younger patients showed raised levels. Residential status was also significantly associated (p = 0.048). Rural residents (25 out of 37) showed a higher frequency of elevated CRP compared to urban residents (21 out of 48). Diabetes showed a strong correlation with raised CRP levels (p = 0.001). Among diabetic patients, 25 out of 28 had raised CRP, in contrast to only 21 out of 57 non-diabetic individuals. Similarly, hypertension was significantly associated (p = 0.001), with 36 out of 50 hypertensive patients showing raised CRP compared to only 10 out of 35 non- hypertensives. Other factors like obesity (p = 0.196), family history of stroke (p = 0.212), smoking (p = 0.809), and literacy status (p = 0.797) showed no significant association with elevated CRP levels. Regarding stroke type, a higher number of ischemic stroke patients (31 out of 50) had raised CRP compared to hemorrhagic stroke patients (15 out of 35), though this difference was not statistically significant (p = 0.121).

DISCUSSION

Stroke is one of the leading causes of mortality and morbidity of vascular diseases, and its incidence remains at a high level around the world.[11] It is a rapidly developing phenomenon of symptoms and signs of focal and at times global loss of cerebral function with no apparent cause other than that of vascular origin.[4] In this study, which included 85 patients diagnosed with cerebrovascular accident (CVA), 54.1% (46 patients) had elevated C-reactive protein (CRP) levels. A statistically significant association was found between elevated CRP and age over 55 years (76.1%, p=0.007), rural residence (67.6%, p=0.048), the presence of diabetes mellitus (89.3%, p=0.001), and high blood pressure (72%, p=0.001). These variables appear to be related to a heightened inflammatory response in patients with a cerebrovascular event. No significant associations were found with other factors such as obesity, smoking, literacy, family history of stroke, or type of event (ischemic vs. hemorrhagic).

Inflammation plays a central role in the pathophysiology of stroke, and C-reactive protein is a well-established marker of systemic inflammatory response. Previous studies have demonstrated that elevated CRP levels are associated with increased stroke severity, poor Functional outcomes, and higher mortality. Our findings are consistent with the national and International literature, which shows higher CRP levels in patients with advanced age, hypertension, and diabetes, all of which are recognized chronic inflammatory states.

The findings of this study are consistent with existing scientific literature linking elevated CRP levels with a worse prognosis and greater stroke severity.[12] CRP is an acute-phase protein that is elevated in response to systemic inflammatory processes, and its elevation has been widely recognized as a marker of cardiovascular risk.[13] A study by Lin et al, demonstrated that elevated CRP levels were associated with an increased risk of ischemic stroke, even in individuals with no prior history of cardiovascular disease.[14] Similarly, another study by Wang et al, showed that CRP levels in patients with ischemic stroke were directly related to infarct size and clinical outcome, suggesting that it may be a useful biomarker not only for diagnosis but also for prognosis.[15]

The significant association between advanced age and elevated CRP levels has also been documented in previous studies.[16] Aging is associated with a progressive increase in the baseline inflammatory state, a phenomenon known as "inflammation," which may explain the greater susceptibility of older patients to inflammatory processes such as those that occur in stroke.[17] Moreover, the high frequency of elevated CRP in diabetic and hypertensive patients observed in this study is consistent with previous research that has identified these conditions as chronic inflammatory states. For example, studies such as those by Jiang et al, have shown that patients with type 2 diabetes and high blood pressure consistently have higher CRP levels, which could contribute to the progression of vascular damage and increase the risk of stroke.[18] The relationship between rural residence and elevated CRP, although less reported in the literature, could be related to poorer access to health services, late diagnosis of chronic diseases, and suboptimal control of cardiovascular risk factors in rural areas. This reinforces the need to implement prevention and timely management strategies in these communities to reduce the burden of cerebrovascular disease.[19-20]

On the other hand, variables such as obesity, smoking, and stroke type did not show a statistically significant association in this study. Although several studies have shown that smoking and obesity can elevate CRP levels.[21-23,] It is possible that in this particular cohort, the sample size or distribution of these factors was not sufficient to demonstrate a clear relationship. However, although some studies have reported higher CRP levels in ischemic stroke compared to hemorrhagic stroke, the results are not always consistent, and larger studies are needed to clarify this point.[24]

Although stroke subtype (ischemic vs hemorrhagic) was identified, imaging severity, infarct volume, and functional outcomes were not assessed. Therefore, a correlation between CRP levels and radiological severity or clinical outcomes could not be established in the present study.

LIMITATION

This study has some limitations. Its cross-sectional design limits causal inference. The sample size was relatively small, which may have reduced statistical power. Serum CRP was measured only once at admission, despite being a dynamic inflammatory marker that may vary during the acute and recovery phases of stroke. Serial CRP measurements were not performed. Additionally, imaging severity, lesion size, and functional outcomes were not analyzed. These limitations should be considered when interpreting the results.

CONCLUSION

The study found that a high frequency of raised serum C-reactive protein (CRP) was observed among stroke patients. Raised CRP was significantly associated with age, residential status, diabetes, and hypertension. All the clinicians treating such patients should always monitor serum C-reactive protein at regular basis for better clinical outcomes, which will improve prognosis

and functional stability of these patients.

While causality cannot be inferred, the findings support the role of inflammation in acute stroke and highlight CRP as a potentially useful adjunctive inflammatory marker in clinical evaluation.

RECOMMENDATIONS

Future studies should adopt longitudinal designs with larger sample sizes, incorporate serial CRP measurements, and correlate inflammatory markers with CT/MRI-based imaging severity and functional outcomes.

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Additional Information

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Ethical Review Board Approval: Approval was obtained from the Registration & Research Cell of the College of Physicians and Surgeons, Pakistan (Ref no: CPSP/REU/NEU-2017-099-432) and an ethical approval letter from Nishtar Medical University**,** Multan (Ref no: 22110).

Human Subjects: Consent was obtained from all patients/participants in this study.

Conflicts of Interest: In compliance with the ICMJE uniform disclosure, all authors declare the following:

Financial Relationships: All authors have declared that they have no financial relationship at present or within the previous three years with any organizations that might have an interest in the submitted work.

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AUTHOR CONTRIBUTION

Sr.#	Author's Full Name	Intellectual Contribution to Paper in Terms of:
1	Umair Zafar	1. Study design and methodology, Paper writing, Data collection, and calculations
2	Sohaib Hassan	2. Data collection and calculations, Literature review and referencing, Editing and quality insurer
3	Madeeha Qamar	3. Paper writing, Analysis of data and interpretation of results
4	Fatima Nazir Siddqui	4. Statistical analysis, paper writing
5	Hareem Tariq	5. Collection of data
6	Ashraf Mahmood	6. Editing and Reference