International Journal of Scientific Research in Dental and Medical Sciences

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Study of Serum C-reactive Protein as Prognostic Factor in Patients with Cerebrovascular Accidents

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ARTICLE INFO

Article history:
Received 19 January 2023
Received in revised form 02 March 2023
Accepted 09 March 2023
Available online 11 March 2023

Keywords:
C-Reactive Protein
Hemorrhagic Stroke
Inflammation
Ischemic Stroke
Prognosis

ABSTRACT

Background and aim: Cerebrovascular accident may trigger the inflammatory response, increasing serum c-reactive protein (CRP) level. High CRP levels may be related to poor outcomes. We aimed to study the relationship between serum CRP levels in patients with cerebrovascular accidents and its outcome.

Material and methods: A total of 154 subjects of CVA were screened for the diagnostic and prognostic significance of serum CRP using Barthel index scoring and the National Institute of Health Stroke Scale on admission and the seventh day of admission.

Results: There was a significant rise in CRP levels in patients with stroke at the time of admission ($p<0.001$). More than 73% of total cases showed increased CRP levels at the time of admission. The National Institute of Health Stroke Scale (NIHSS) and Barthel index are good tools to assess the functional outcome of patients following a stroke with the rise in CRP levels.

Conclusions: Our study showed the short-term prognostic value of Serum c-reactive protein. The study showed that CRP concentration is an independent predictor of severity after cerebrovascular accidents. Thus, developing new neuroprotective therapies, if targeted to modulate cytokine-induced inflammation, could be a promising way to prevent early deterioration in acute stroke.

1. Introduction

Ischemic and hemorrhagic strokes are common and devastating disorders of the cerebrovascular system. Strokes are the second leading cause of death worldwide, with 6.2 million deaths in 2015.[1-2] Acute stroke may cause an inflammatory response that increases CRP levels.[3] Because of the link between inflammation and atherosclerosis, CRP is a potential prognostic marker following vascular events as well as a potential predictor of future vascular events. High CRP levels may be linked to poor outcomes because they reflect an inflammatory response or tissue damage.[4] It is considered a sensitive predictor of new and recurring ischemic events.[5-7] There is limited data on CRP as a prognostic factor in cerebrovascular accidents.[8] CRP levels are elevated in approximately three-quarters of ischemic stroke patients.[9] CRP has increased secondary brain damage in animal models of focal cerebral ischemia by activating the complement system.[10] Recent studies conducted to establish the relationship between the rise in CRP levels and hemorrhagic stroke have not been conclusive. Several studies have examined the role of CRP in the early stages of stroke as a prognostic factor of functional outcomes. Most studies focus solely on the relationship between CRP and mortality with varying results instead of functional outcomes. The findings were inconclusive; some found a positive association, while others did not.[11-12] We aim to determine serum CRP level as an early prognostic factor of functional outcome after stroke as it is an easily measured and readily available inflammatory marker to understand its role in cerebrovascular stroke better. This study aimed to determine the prognostic value of C-reactive protein measured in Cerebrovascular Accident and evaluate C - reactive protein as a Prognostic tool in Cerebro-vascular Accidents using the Barthel Index scoring and the National Institute of Health Stroke Scale. Also, this study was conducted to assess the etiology and clinical features as well as to estimate CRP as prognostic markers in patients suffering from cerebrovascular events.

2. Material and methods

The Institutional Ethics Committee S.S Medical College, Rewa (M.P.) approved the study protocol, and ethical code S.No./IEC/MC/2020472 was obtained for the study. The study was conducted on 154 patients (age>18 years) under the department of General Medicine, Sanjay Gandhi Memorial Hospital, Rewa (M.P) India, from July 2021 to June 2022, with the cerebrovascular accident, who fulfilled the inclusion criteria over 12 months from July 2021 to June 2022, was included in the analysis.

Study design

Prospective and observational study.

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https://doi.org/10.30485/IJSRDMS.2023.382195.1431

Sample size

154

Inclusion and exclusion criteria

Inclusion criteria

All symptomatic patients (age>18) with CVA who were admitted to the medicine department, Sanjay Gandhi Memorial Hospital, Rewa (M.P.), were included in the study. Patients with stroke (ischemic and hemorrhagic) documented with a CT scan within 48 hours of the onset of symptoms of the focal neurological deficit with risk factors like diabetes mellitus, hypertension, and dyslipidemia are also included in this study.

Exclusion criteria

Patients with subdural hematomas, extradural hematomas, intracranial tumors, other space-occupying lesions, meningitis, brain abscess, other intracranial infections, head injury, and neoplasia. Postoperative patients, rheumatological diseases like rheumatoid arthritis, Ankylosing spondylitis, acute or chronic infection, or any other inflammatory conditions, coronary artery disease, pregnant and lactating mothers, and Patients who refused to give consent.

Data collection

Patients included in the study were subjected to full history taking with special emphasis on smoking, hypertension, and patients on anti-diabetic medication for diabetes mellitus and dyslipidemia. The neurological evaluation included an assessment of stroke severity by the National Institute of Health Stroke Scale (NIHSS), and stroke was categorized as follows:

Mild (NIHSS 0–4)
Moderate (NIHSS 5–20)
Severe (NIHSS >20) (15).

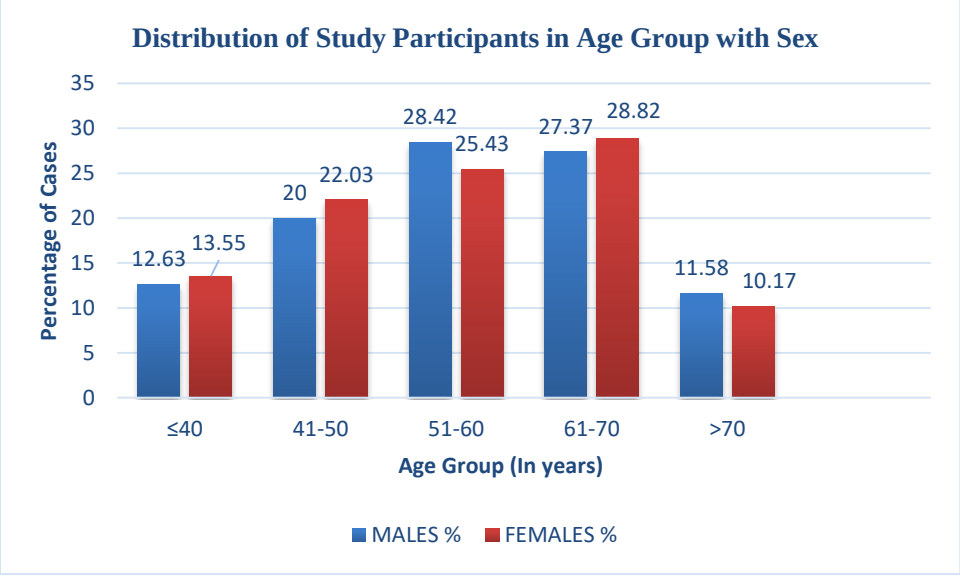
A similar assessment was done by using the Barthel index, and the cases were categorized as follows:

Dependent (0-19)
Very Dependent (20-39)
Partially Dependent (40-59)
Need Minimal Help (60-79)
Independent (80-100)

All the patients had a CT scan on admission to differentiate between ischemic and hemorrhagic strokes. Routine laboratory tests and CRP-level assays were conducted on blood samples upon admission. The lab was blinded to the samples. The severity of the patients was evaluated clinically on the bases of NIHSS and Barthel Index on day 1, and the 7th-day blood sample was sent again for CRP assay. The progression of severity was assessed based on NIHSS and Barthel Index.[13]

3. Results

In our present study, the maximum number of cases were seen in the age group of 61-70, constituting around 27.37%, and among them, males were predominantly affected, constituting around 62%. The mean age (SD) of the study participants is 55.60±12.01 years. Among females, stroke incidence is higher in age groups >50 years, maximum between 61-70 years. (Fig. 1)



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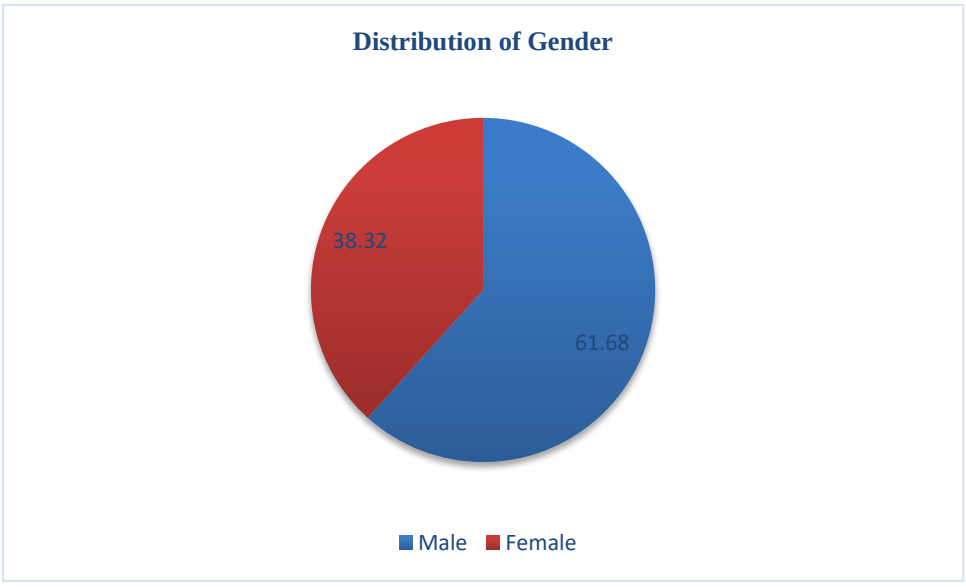

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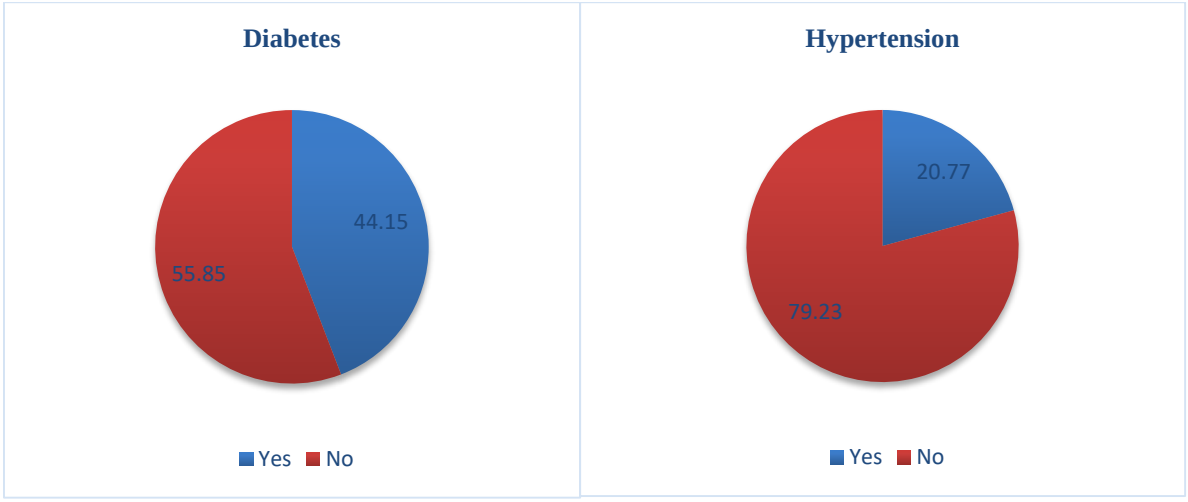
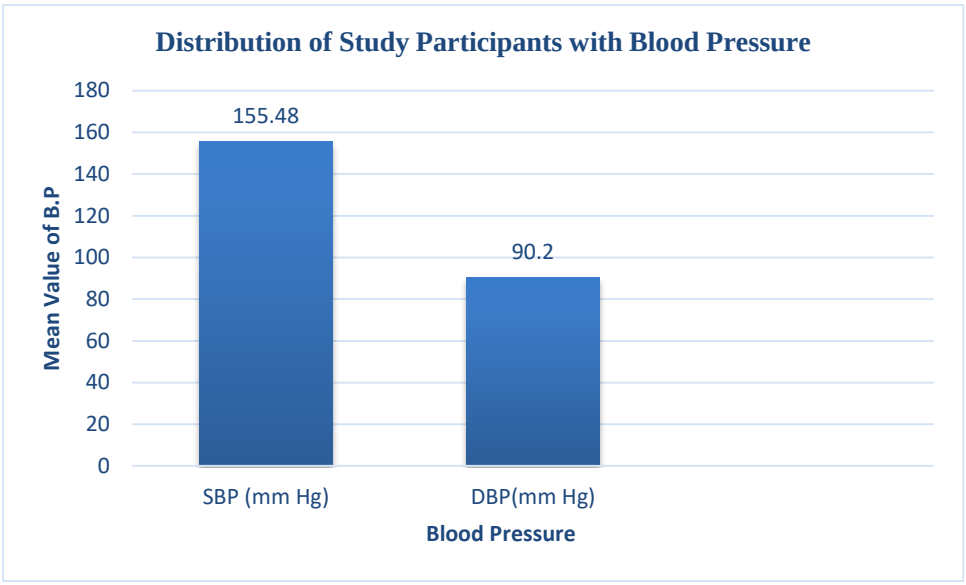
Fig. 1. Distribution of study participants in (a) Age group with sex, (b) Gender wise.



(a) **(b)**

Fig. 2. Distribution of study participants with etiology-wise (a) Diabetes, (b) Hypertensive.

According to etiology and complication, diabetic cases predominated about 44.15% (n=68), followed by those with smoking at about 41.55% (n=64). Patients with alcohol-consuming constituted 40.91% (n=63). Patients with tobacco chewing constituted 34.41% (n=53), followed by patients with hypertension was about 20.77% (n=32). (Fig. 2). In our study group, the average systolic and diastolic blood pressure of participants were 155.48 ± 23.42 and 90.2 ± 11.91, respectively. The mean total cholesterol in the cases (186.91± 36.15) was elevated so, as in Triglyceride (TG) levels and Low-Density Lipoprotein (LDL) in the study group. The mean High-Density Lipoprotein (HDL) is low in the cases. (Fig. 3).



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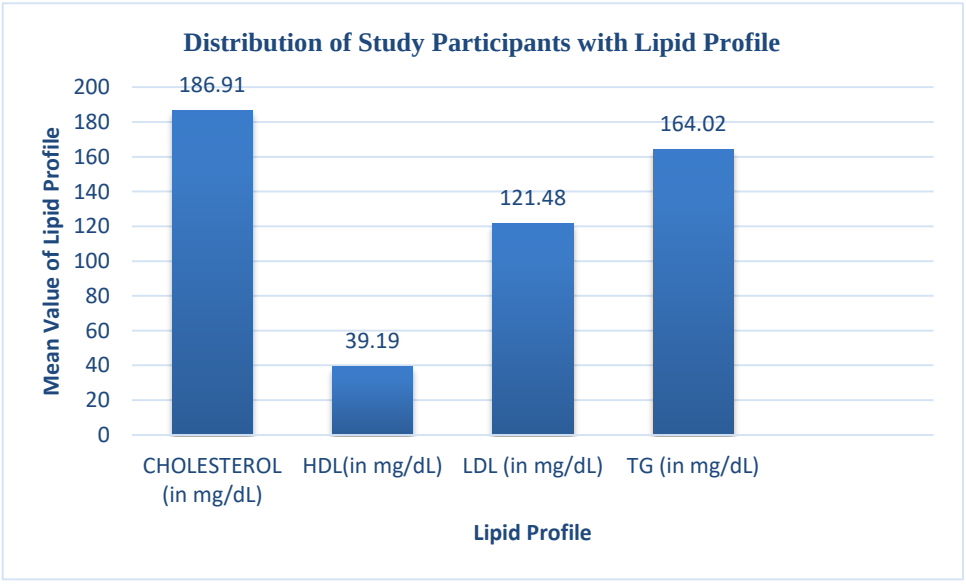

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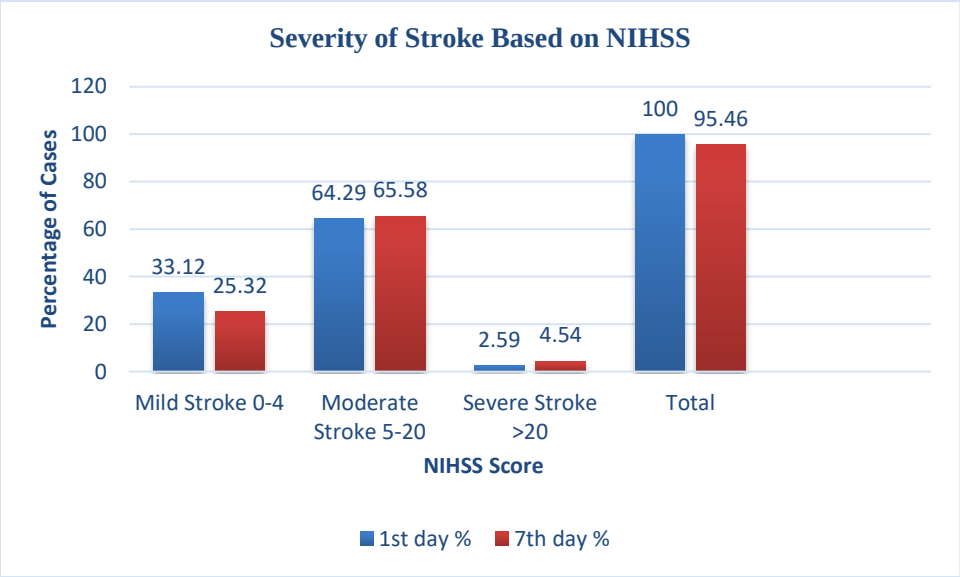
Fig. 3. Distribution of study participants with (a) Blood pressure, (b) lipid profile.

In the present study, 113 out of 154 cases (73.3%) had high serum CRP levels (>5mg/dl) at admission. It is observed that most cases deteriorated by day seven and had higher baseline CRP values than at admission. Moderate and severe cases increased from 64.29% to 65.58% and 2.5% to 4.54% (Fig. 4). Similarly, the mean value of CRP in 'moderate' cases was 40.39; in 'severe' cases, it was 202.5, significantly higher than the former group on day 1. On day 7, we see a similar trend of increase in the mean CRP value from 40.98 to 157.2 when we move from the moderate to severe category. (Fig. 5). This signifies the short-term prognostic value of CRP. On categorizing these cases using NIHSS score with CRP, in our present study, on day 1, 51 out of 154 mild stroke cases were reported with the mean value of NIHSS and CRP was 3.39 ± 0.63 and 26.0 ± 18.55 respectively. Moderate stroke cases were 99 out of 154 with a mean value of NIHSS, and CRP was 7.52 ± 3.66 and 40.39 ± 49.05, respectively, and severe stroke cases were 04 out of 154 with a mean value of NIHSS, and CRP was 23.5 ± 1.91 and 202.5 ± 62.21 respectively.



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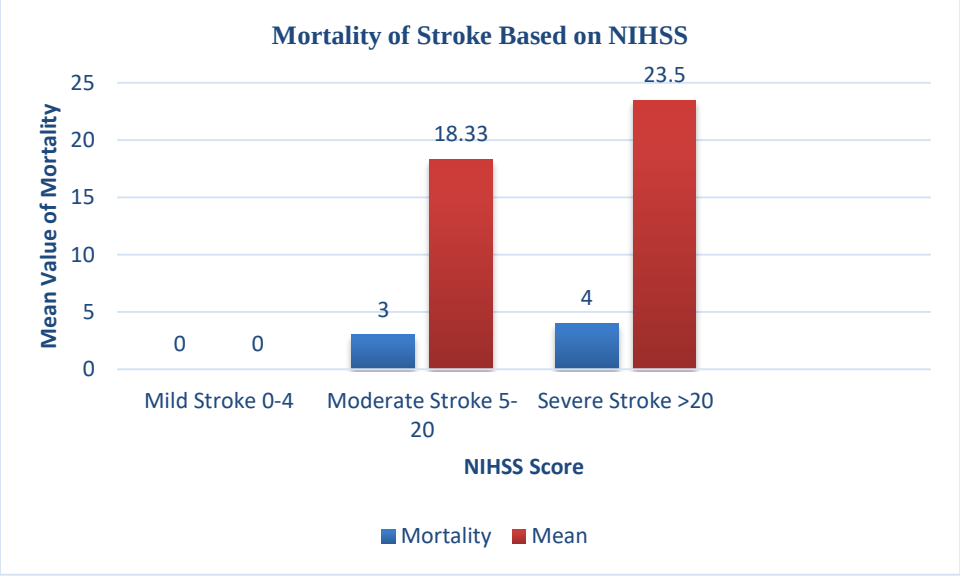

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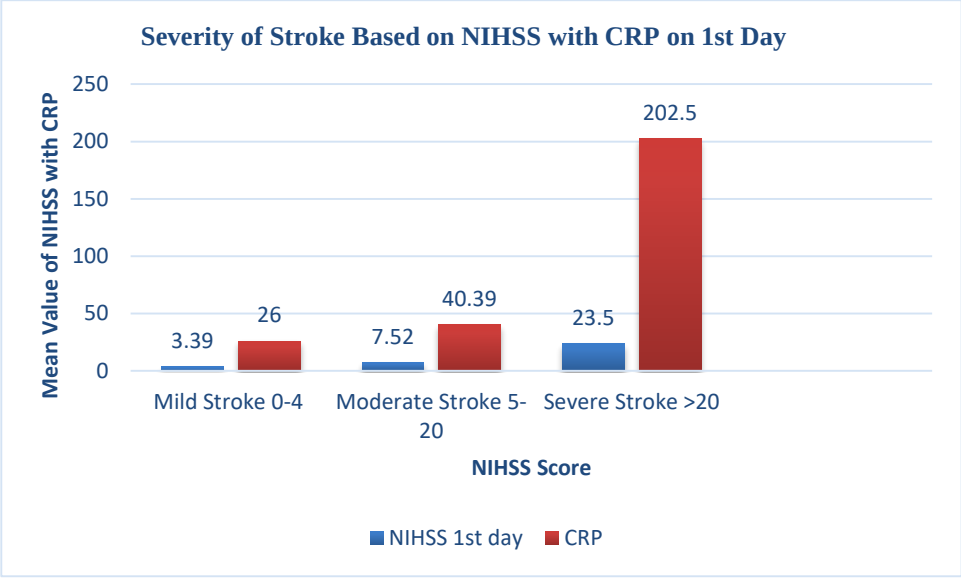
Fig. 4. (a) Severity of stroke based on NIHSS, (b) Mortality of stroke based on NIHSS.



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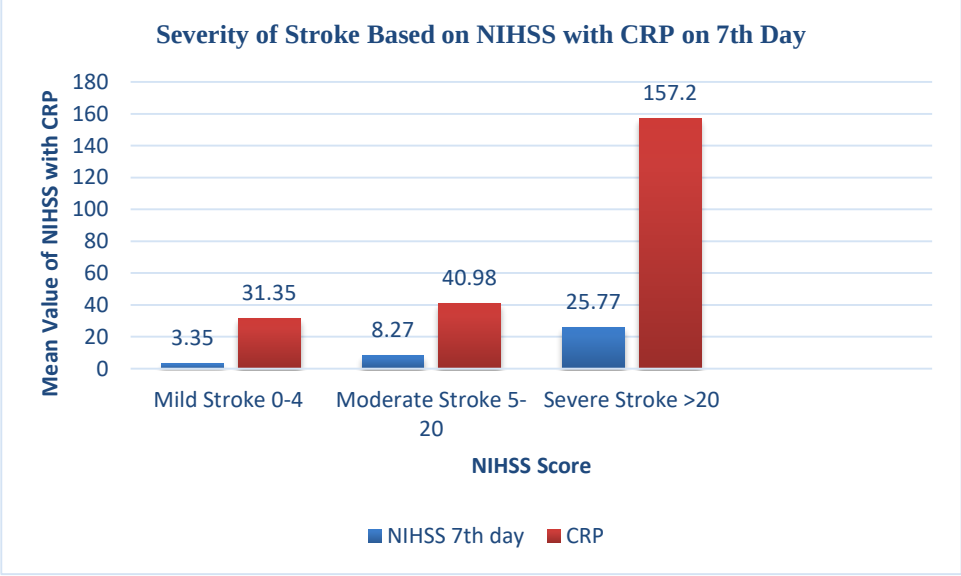

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Fig. 5. (a) Severity of stroke based on NIHSS with CRP on 1st Day, (b) Severity of stroke based on NIHSS with CRP on the seventh day.

On day seven, the outcome was assessed. There was a strong positive correlation between disease severity assessed by NIHSS with the CRP levels, as 39/147 cases of mild stroke were reported, with the mean value of NIHSS being 3.35 ± 0.67 and CRP 31.35 ± 22.94. A total of 99/147 cases of moderate stroke were reported, with a mean value of NIHSS was 8.27 ± 4.14, and CRP was 40.98 ± 36.58, and a total of 9/147 cases of severe stroke were reported, with a mean value of NIHSS of 25.77 ± 2.63 and CRP was 157.2 ± 69.29. Among them, a total of 7 patients died before the seventh day. (Fig. 5) So it was found that there is an increasing trend of CRP with the severity.

The severity of stroke based on the Barthel index

On categorizing these cases using the Barthel index, the majority of cases on the first [77 patients (50%)] and seventh day [68 patients (44.15%)] were fallen into the "independent" category. A total of 54 (35.06%) patients on the first day and 52 (33.76%) patients on day seventh were categorized as patients "who need minimal help ."Partially dependent patients are 13(5.19%) on the 1st and seventh day and 16 (10.38%). Very dependent patients are 8 (5.1%) on the 1st and seventh days and 09(5.84%). Patients dependent on day 1 are 2 (1.29%) and 02 (1.29%) on the seventh day. Seven patients died before seven days and were from dependent or very dependent categories, assessed on day one according to the Barthel index. (Fig. 6)

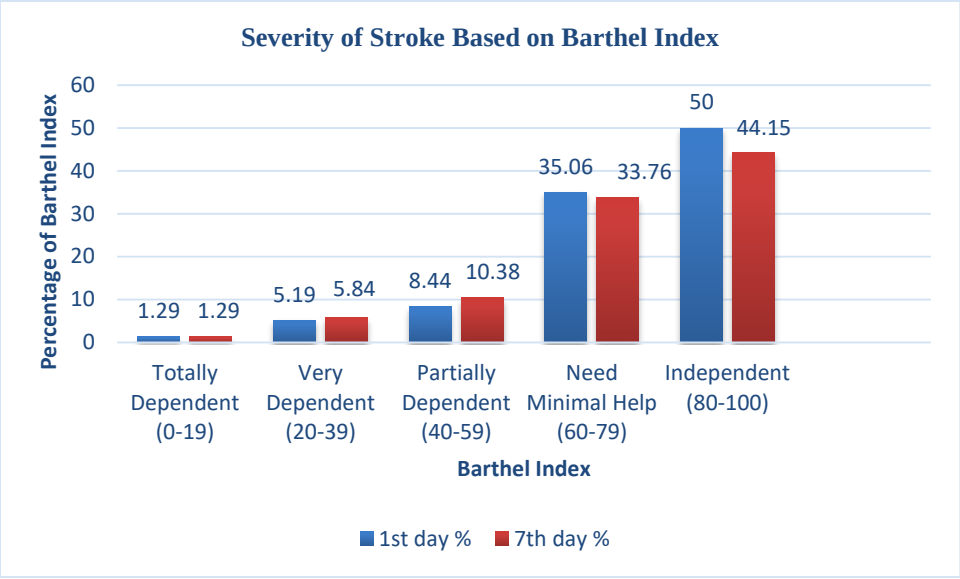
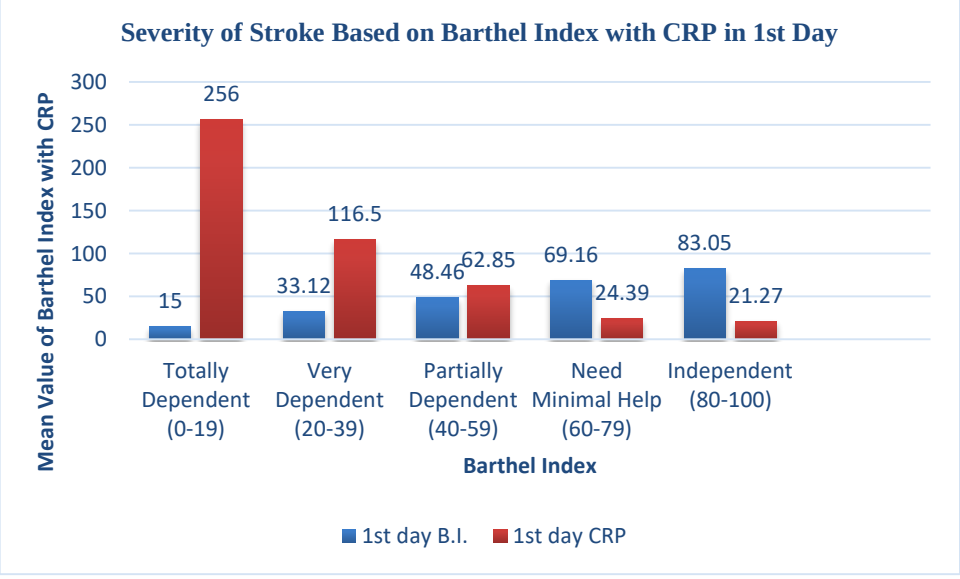


Fig. 6. Severity of stroke based on Barthel index with CRP.

On classifying these cases using Barthel Index with CRP, on Day one, 02 out of 154 cases were dependent, with the mean value of the Barthel Index with CRP being 15 ± 0 and 256 ± 0, respectively. 08 out of 154 cases were very dependent with a mean value of the Barthel Index with CRP was 33.12 ± 3.72 and 116.5 ± 49.9 respectively. 13 out of 154 cases were partially dependent with the mean value of Barthel Index with CRP was 48.46 ± 5.91 and 62.85 ± 69.89 respectively. 54 out of 154 cases need minimal help. The mean value of the Barthel Index with CRP was 69.16 ± 5.88 and 24.39 ± 21.95, respectively. 77 out of 154 normal cases were independent on day one according to the Barthel index with CRP, with the mean value of the Barthel Index being 83.05±3.90 and 21.278 ± 20.82, respectively. (Fig. 7)



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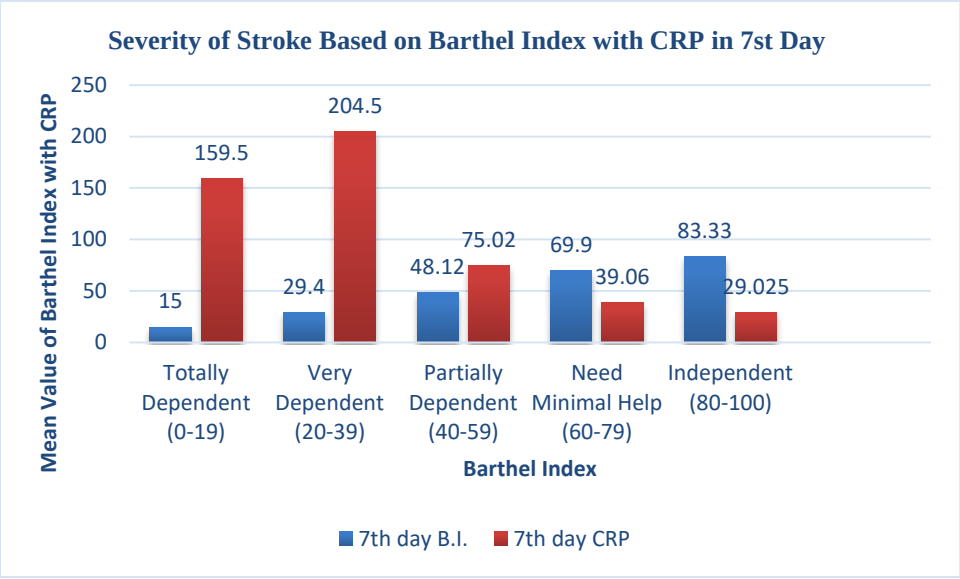

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Fig. 7. Severity of stroke based on Barthel index with CRP on (a) the first day, (b) the seventh day.

Barthel index with CRP, in the present study, on day 7, 02 out of 147 cases were dependent, with the mean value of Barthel index with CRP being 15 ± 0 and 159.5± 17.87, respectively. 09 out of 147 cases were very dependent; the mean value of the Barthel index with CRP was 29.4 ± 6.34 and 204.5 ± 10.60, respectively. 16 out of 147 cases were partially dependent, with the mean value of Barthel index with CRP being 48.12 ± 6.56 and 75.02 ± 53.55, respectively. 52 out of 147 cases need minimal help with the mean value of the Barthel index, with CRP being 69.90 ± 5.19 and 39.06 ± 27.36, respectively. 68 out of 147 cases were normal, with the mean value of Barthel index with CRP being 83.33 ± 28.40 and 29.025 ± 45.8, respectively. Seven patients who died before seven days were from dependent and very dependent categories, assessed on day one according to the Barthel index.

4. Discussions

Globally, 70% of strokes and 87% of stroke-related deaths and disability-adjusted life years occur in low- and middle-income countries. Stroke incidence has doubled in low- and middle-income countries over the past four decades.[14] There was a significantly raised level of CRP in stroke patients at the time of admission, and it reflects the role of inflammation or tissue damage in CVA. Cases were carefully selected to determine the specific role of CRP in CVA patients. In this study, a rise in CRP is taken as a prognostic tool concerning the functional outcome following stroke as per the National Institute of Health Stroke Scale (NIHSS) and the Modified Barthel index to assess the functional outcome of patients following stroke, in correlation with CRP levels. Elevated CRP level is highly sensitive in determining the severity of patients with stroke. Age-wise analysis showed that the majority of the cases were fallen into the age group of 61-70 years, with male predominance. Stroke incidence is higher in females of the age group >50 years. Gender-wise, males are more predominated to stroke than females. Similarly, Keith W Muir et al. studied the same association of C - reactive protein and outcome after stroke. Two hundred twenty-eight patients diagnosed with stroke were studied. Survival in those with CRP >10.1 mg/L was significantly worse than those with CRP ⩽10.1 mg/L (P=0.00009, log-rank test). According to etiology and complication, diabetic cases were predominant. The study also concluded that hypertension, smoking, alcohol, and tobacco, could be the common risk factors. In patients with hemorrhagic stroke, CRP levels are significantly higher than those of those with ischemic stroke, and so is the severity.[8]

Winbeck et al.,[15] investigated the impact of early serial CRP measurement in ischemic stroke on long–term outcomes. One hundred twenty-seven patients with a first ischemic stroke were examined within 12 hours of symptom onset. Serial CRP measurements were done at admission (CRP1), within 24 hours (CRP2), and within 48 hours (CRP3). MRI of the brain was performed, and infarct volume was determined. The patients were followed up for one year. The Barthel index and the modified Rankin scale were used to assess functional disability and were evaluated at admission and during follow-up. A Barthel Index score >85 was defined as favorable and functionally independent. Patients were divided according to the modified Rankin scale into the following categories: independent of day-to-day activities and with a good outcome (score 0 to 2) and dependent or dead (score 3 to 6). Thus this study concluded that CRP level measured within 12 hours after symptom onset of an acute ischemic stroke is not independently related to long-term prognosis. In contrast, a CRP increase between 12 and 24 hrs after symptom onset predicts an unfavorable outcome, and it is associated with an increased incidence of cerebrovascular or cardiovascular events.[15]

Limitations

Instead of focusing on the radiological results, the main goal of our investigation was to discover a correlation between the CRP and the clinical outcome. Another limitation is that the CRP was measured only twice in the whole study duration rather than multiple measurements, which could have provided more information about the later stages of the stroke; however, our study aimed to assess the biomarker's early predictive value. As it was a very short study duration, and patients were not followed up after seven days, we could not evaluate the long-term variation of the CRP levels with the extent of the severity. A limited number of subjects have participated. Unavailability of cause-specific data because we got the information bias from the patients

or their attendants. Our study was performed in the hospital, so we could not report asymptomatic individuals.

5. Conclusion

Serum CRP has an important role as a prognostic tool in stroke patients. Our study observed that disability was associated with higher concentrations of CRP levels in plasma, and early neurological deterioration was also observed in cases with high levels of CRP. With the help of CRP levels, we can predict the functional outcome with risk stratification. Thus, developing new neuroprotective therapies, if targeted to modulate cytokine-induced inflammation, could be a promising way to prevent early deterioration in acute ischemic stroke.

Conflict of Interest

The authors declared that there is no conflict of interest.

Acknowledgements

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

References

[1] Goldstein LB. Introduction for focused updates in cerebrovascular disease. Stroke. 2020;51(3):708-10. https://doi.org/10.1161/STROKEAHA.119.024159.

[2] Jauch EC, Saver JL, Adams Jr HP, Bruno A, Connors JJ, Demaerschalk BM, et al. 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. https://doi.org/10.1161/STR.0b013e318284056a.

[3] McColl BW, Allan SM, Rothwell NJ. Systemic inflammation and stroke: aetiology, pathology and targets for therapy. Biochemical Society Transactions. 2007;35(5):1163-5. https://doi.org/10.1042/BST0351163.

[4] Den Hertog HM, Van Rossum JA, Van Der Worp HB, Van Gemert HM, de Jonge R, Koudstaal PJ, et al. C-reactive protein in the very early phase of acute ischemic stroke: association with poor outcome and death. Journal of neurology. 2009;256:2003-8. https://doi.org/10.1007/s00415-009-5228-x.

[5] Di Napoli M, Elkind MS, Godoy DA, Singh P, Papa F, Popa-Wagner A. Role of C-reactive protein in cerebrovascular disease: a critical review. Expert review of cardiovascular therapy. 2011;9(12):1565-84. https://doi.org/10.1586/erc.11.159.

[6] Di Napoli M, Papa F, Bocola V. C-reactive protein in ischemic stroke: an independent prognostic factor. Stroke. 2001;32(4):917-24. https://doi.org/10.1161/01.STR.32.4.917.

[7] Rost NS, Wolf PA, Kase CS, Kelly-Hayes M, Silbershatz H, Massaro JM, et al. Plasma concentration of C-reactive protein and risk of ischemic stroke and transient ischemic attack: the Framingham study. Stroke. 2001;32(11):2575-9. https://doi.org/10.1161/hs1101.098151.

[8] Muir KW, Weir CJ, Alwan W, Squire IB, Lees KR. C-reactive protein and outcome after ischemic stroke. Stroke. 1999;30(5):981-5. https://doi.org/10.1161/01.STR.30.5.981.

[9] Smith CJ, Emsley HC, Vail A, Georgiou RF, Rothwell NJ, Tyrrell PJ, et al. Variability of the systemic acute phase response after ischemic stroke. Journal of the neurological sciences. 2006;251(1-2):77-81. https://doi.org/10.1016/j.jns.2006.09.011.

[10] Gill R, Kemp JA, Sabin C, Pepys MB. Human C-reactive protein increases cerebral infarct size after middle cerebral artery occlusion in adult rats. Journal of Cerebral Blood Flow & Metabolism. 2004;24(11):1214-8. https://doi.org/10.1097/01.WCB.0000136517.61642.99.

[11] Montaner J, Fernandez-Cadenas I, Molina CA, Ribó M, Huertas R, Rosell A, et al. Poststroke C-reactive protein is a powerful prognostic tool among candidates for thrombolysis. Stroke. 2006;37(5):1205-10. https://doi.org/10.1161/01.STR.0000217744.89208.4e.

[12] Topakian R, Strasak AM, Nussbaumer K, Haring HP, Aichner FT. Prognostic value of admission C-reactive protein in stroke patients undergoing iv thrombolysis. Journal of neurology. 2008;255:1190-6. https://doi.org/10.1007/s00415-008-0866-y.

[13] Collin C, Wade DT, Davies S, Horne V. The Barthel ADL Index: a reliability study. International disability studies. 1988;10(2):61-3. https://doi.org/10.3109/09638288809164103.

[14] O'Donnell MJ, Chin SL, Rangarajan S, Xavier D, Liu L, Zhang H, Rao-Melacini P, et al. Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study. The lancet. 2016;388(10046):761-75. https://doi.org/10.1016/S0140-6736(16)30506-2.

[15] Winbeck K, Poppert H, Etgen T, Conrad B, Sander D. Prognostic relevance of early serial C-reactive protein measurements after first ischemic stroke. Stroke. 2002;33(10):2459-64. https://doi.org/10.1161/01.STR.0000029828.51413.82.

How to Cite this Article: Giri N, Patel R, Kapur KS. Study of Serum C-reactive Protein as Prognostic Factor in Patients with Cerebrovascular Accidents. International Journal of Scientific Research in Dental and Medical Sciences. 2023;5(1):7-15. https://doi.org/10.30485/IJSRDMS.2023.382195.1431.