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Evaluation of Serum C Reactive Protein as A Prognostic Marker in Acute Ischemic Stroke: A Cross-sectional Study

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ABSTRACT
This cross-sectional study aimed to analyze risk factors and demographic characteristics to determine the association between C-reactive protein (CRP) levels and the outcomes of patients with acute ischemic stroke. The study was conducted at Tikrit Teaching Hospital between November 2023 and January 2024 and involved 51 stroke patients. CRP levels were measured upon admission, and stroke severity was assessed using the NIH Stroke Scale (NIHSS). Data on demographics, medical history, and lifestyle factors were collected using a structured questionnaire, and statistical analyses were performed with chi-square tests ($p<0.05$). The average patient age was 46 ± 15 years, with a nearly even gender distribution (54.9% male). Smoking, hypertension, and diabetes mellitus were prevalent at 62.7%, 54.9%, and 64.7%, respectively. CRP levels varied widely, with 43.1% of patients showing levels above 10 mg. A notable difference in CRP levels was found between genders ($p<0.01$), with females showing a higher likelihood of elevated levels. CRP was also significantly linked to smoking and diabetes ($p<0.01$ and $p<0.05$, respectively), but no significant associations were identified with stroke severity, hypertension, cerebrovascular accidents, or coronary artery disease. These findings suggest that while CRP is associated with certain demographic and risk factors in ischemic stroke patients, its role in predicting stroke severity is limited. Further research is required to fully elucidate its prognostic value.

Keywords: *Prognostic marker, Acute ischemic stroke, C-reactive protein*

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INTRODUCTION

Stroke is the second most common cause of disability worldwide and is a significant global health concern [18,29]. It is estimated that approximately 80–87% of stroke cases are ischemic [3]. Research over the past few decades has highlighted the crucial role those inflammatory responses play in the development of ischemic stroke [11,17]. Inflammation can worsen secondary brain injury during the acute phase of ischemic stroke by activating glial cells, increasing the expression of pro-inflammatory cytokines, and disrupting the blood-brain barrier [33]. This indicates that targeting inflammation could help reduce the risk of future strokes [24]. The liver is the primary organ producing plasma C reactive protein (CRP), a sensitive marker of inflammation [31]. Previous studies have demonstrated a connection between CRP-based inflammatory markers and several inflammatory diseases, such as hepatitis [7] and subacute thyroiditis [2], as well as diabetic nephropathy [4].

It is important to investigate CRP levels in stroke survivors because inflammation and stroke are related. Despite a great deal of study, there is still disagreement over the relationship between CRP and stroke patients' clinical results. There may be a connection between CRP and functional outcomes following a stroke, according to certain research [10,16,22,28]. However, other research has not found a substantial correlation between CRP and outcomes following a stroke [31,14,26]. Moreover, very few studies have explored the variables that may affect CRP levels in people who have experienced an acute ischemic stroke. In this study, we explored the relationship between plasma CRP levels and the functional outcomes of patients with acute ischemic stroke. Additionally, we examined various factors that could influence CRP levels.

MATERIALS AND METHODS

Study Participants

This cross-sectional study was conducted at Tikrit Teaching Hospital, involving 51 patients aged 18 to 70 years diagnosed with acute ischemic stroke between November 5, 2023, and January 2, 2024. Patients with conditions such as chronic kidney disease (CKD), intracerebral hemorrhage (ICH), chronic liver disease (CLD), systemic infections, burn injuries, and rheumatoid arthritis (RA) were excluded. The study aimed to evaluate the association between C-reactive protein (CRP) levels and stroke prognosis, with data collected through patient information and laboratory results in a clinical setting.

Questionnaire

Data collection in this study was conducted using a structured questionnaire, the National Institutes of Health Stroke Scale (NIHSS), and laboratory analysis of C-reactive protein (CRP) levels. The structured questionnaire gathered essential demographic information, medical history, lifestyle factors such as smoking status, and details of the current stroke event [15]. This tool provided the foundation for understanding the patients' backgrounds and any contributing risk factors to stroke severity and outcomes.

The NIHSS was employed to assess the neurological severity of each stroke. This scale evaluates 11 domains, including consciousness, motor function, language, and sensory perception, with scores ranging from 0 to 42, where higher scores indicate more severe stroke symptoms. Scores between 0 and 4 suggest a minor stroke, while scores above 20 represent a severe stroke. Early NIHSS scores are highly predictive of long-term functional outcomes and reliable for clinical and research applications [5,6]. Additionally, CRP levels were measured through blood samples upon admission to assess inflammatory response. Normal CRP levels are typically below 0.3 mg/dL, while elevated levels, particularly those above 10 mg/dL, indicate significant inflammation, which can correlate with stroke severity and prognosis [15,27,30].

Statistical analysis

The data collected through the questionnaires and laboratory results were analyzed using Excel 2020 and SPSS 27. The chi-square test was used to evaluate the association between categorical variables, with a p-value of less than 0.05 considered statistically significant.

RESULTS

Characteristics and Clinical Presentations of Patients

A total of 51 patients were enrolled during the study period to examine the relationship between C-reactive protein (CRP) levels and prognosis in acute ischemic stroke patients. The participants had a mean age of 46 ± 15 years, with a fairly even gender distribution—54.9% (n=28) were male and 45.1% (n=23) were female. A high proportion of participants were smokers (62.7%, n=32). Additionally, hypertension and diabetes mellitus were common comorbidities, present in 54.9% (n=28) and 64.7% (n=33) of the cohort, respectively. There was a notable prevalence of cerebrovascular accidents (39.2%, n=20) and coronary artery disease (64.7%, n=33) among the participants (Table 1).

CRP levels varied widely among patients, with 31.4% (n=16) having levels below 3mg, 25.5% (n=13) with levels between 3-9.9mg, and 43.1% (n=22) with levels above 10mg. The timing of the blood test post-stroke onset showed that a significant number of tests were conducted within the first 12 hours. Stroke severity was categorized as mild in 11.8% (n=6) of cases, moderate in 49% (n=25), and severe in 39.2% (n=20) (Table 1).

CRP levels across various variables and their corresponding significance

The analysis of CRP levels across various health conditions and demographics reveals some notable findings. A significant difference in CRP levels was observed between males and females, with females generally having higher levels (P-value <0.01). Additionally, patients with diabetes mellitus also exhibited significantly different CRP levels compared to those without diabetes (P-value <0.05). However, CRP levels did not show significant differences when comparing stroke severity, smoking status, hypertension, cerebrovascular accidents, or coronary artery disease, as all these comparisons yielded P-values greater than 0.05, indicating no statistical

significance.

Table 1 Demographic and Clinical Characteristics of the Study Population (Total = 51)

Characteristics	Count (n)	%
Age (Mean ± SD)	46 ± 15	-
Gender		
Male	28	54.9%
Female	23	45.1%
Smoking		
No	19	37.3%
Yes	32	62.7%
Hypertension		
No	23	45.1%
Yes	28	54.9%
Diabetes Mellitus		
No	18	35.3%
Yes	33	64.7%
Cerebrovascular Accidents		
No	31	60.8%
Yes	20	39.2%
Coronary Artery Disease		
No	18	35.3%
Yes	33	64.7%
CRP levels		
<3mg	16	31.4%
3-9.9mg	13	25.5%
>10mg	22	43.1%
The interval between the onset of symptoms and the blood test		
<3 hours	15	29.4%
3-6 hours	8	15.7%
6-12 hours	17	33.3%
12-24 hours	4	7.8%
>24 hours	7	13.7%
Stroke Severity		
Mild	6	11.8%
Moderate	25	49.0%
Severe	20	39.2%

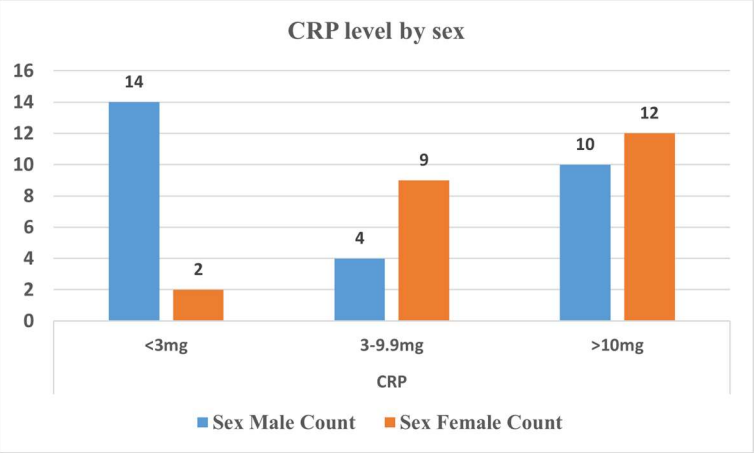

Fig. 1 This figure illustrates the distribution of CRP levels by sex with a higher percentage of females (52.2%) having CRP levels above 10mg compared to males (35.7%). Conversely, 50.0% of males had CRP levels below 3mg, compared to only 8.7% of females

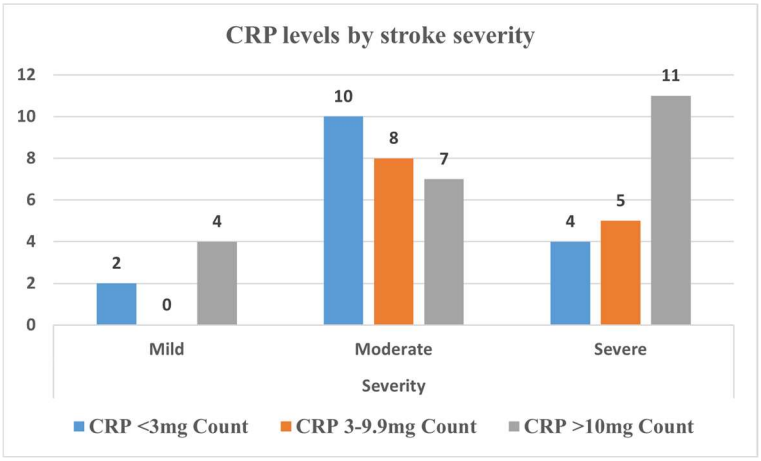

Fig. 2 This figure shows the distribution of CRP levels by stroke severity. A higher percentage of patients with severe stroke (50.0%) had CRP levels above 10 mg, compared to those with moderate stroke (31.8%) and mild stroke (18.2%). Conversely, 62.5% of patients with moderate stroke had CRP levels below 3 mg, while only 12.5% of those with mild stroke and 25.0% with severe stroke had similarly low CRP levels.

Table 2 CRP levels across various variables and their corresponding significance:

Variable	CRP Levels Comparison	P-value	Significance
Sex	Males vs Females	<0.01	Significant
Stroke Severity	<3 mg, 3-9.9 mg, >10 mg	>0.05	Not Significant
Smoking	Smokers vs Non-Smokers	>0.05	Not Significant
Hypertension	Yes, vs No	>0.05	Not Significant
Diabetes Mellitus	Yes, vs No	<0.05	Significant
Cerebrovascular Accidents	Yes, vs No	>0.05	Not Significant
Coronary Artery Disease	Yes, vs No	>0.05	Not Significant

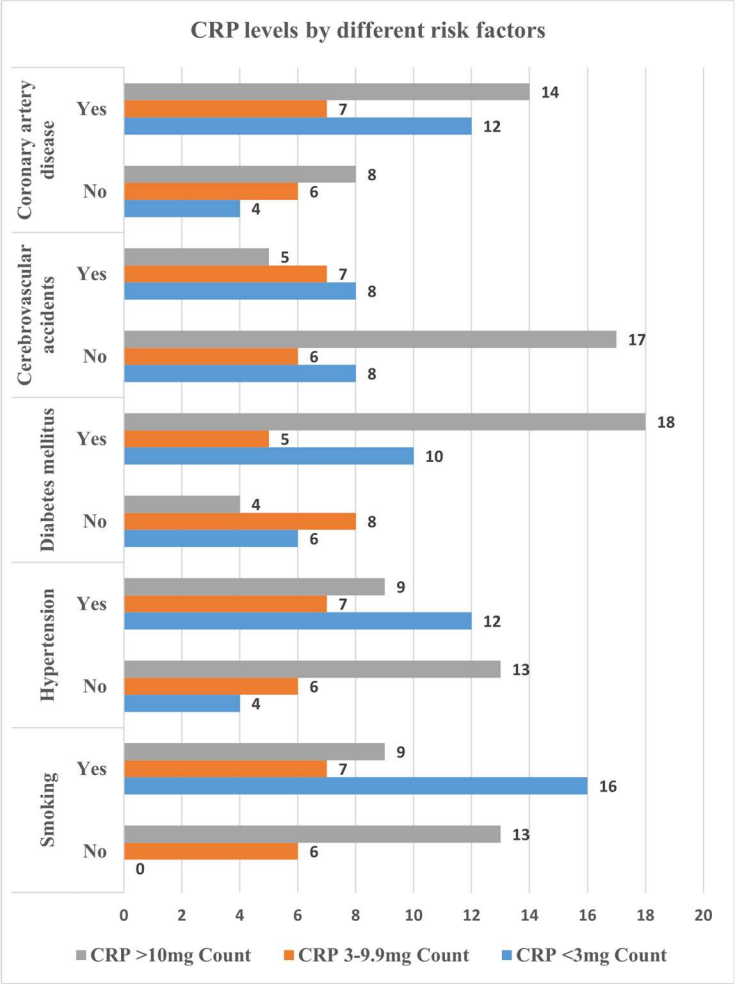

Fig.3 This figure illustrates the distribution of CRP levels across different health conditions. Among non-smokers, the majority (68.4%) had CRP levels greater than 10mg, while 50% of smokers had CRP levels below 3mg. In hypertensive patients, 42.9% had CRP levels below 3mg, compared to 17.4% of non-hypertensive patients. A higher proportion of diabetic patients (54.5%) had CRP levels greater than 10mg, while only 22.2% of non-diabetic patients showed the same. Similarly, patients without a history of cerebrovascular accidents showed higher CRP levels (>10mg in 54.8%), while 44.4% of those without coronary artery disease had CRP levels greater than 10mg, compared to 42.4% of those with the disease.

DISCUSSION

Recent research indicates that higher baseline CRP levels are independently linked to an increased risk of ischemic stroke [35]. CRP is also a significant predictor of ischemic stroke in patients with preexisting cardiovascular disease, which aligns with the findings in 39% of the current study population [25]. However, our analysis did not reveal a statistically significant connection between CRP levels and the severity of stroke. This is consistent with literature suggesting that early CRP levels post-stroke may not directly correlate with long-term outcomes. However, CRP levels measured within 12–24 hours may predict unfavorable outcomes and an increased risk of future cerebrovascular and cardiovascular events [32]. Higher CRP levels have been linked to stroke severity and poor functional and cognitive outcomes at discharge [12], as well as larger infarct volumes in acute ischemic stroke patients [34]. The difference between our findings and those of previous studies might be attributed to factors like the smaller sample size in our study.

A significant gender-based difference in CRP levels was observed in our study, with more females (52.2%) having CRP levels above 10 mg compared to males (35.7%). Conversely, 50% of males had CRP levels below 3 mg, compared to only 8.7% of females. CRP is recognized as an independent risk factor for cardiovascular disease in women, increasing the risk of vascular events by 5- to 7-fold compared to control subjects [21]. Additionally, CRP is the only independent predictor of ischemic stroke in postmenopausal women, with higher CRP levels correlating with an increased risk [13]. In women, CRP and lipid levels are more significant predictors of future ischemic stroke risk than coronary heart disease, with the ratio of total cholesterol (TC) to high-density lipoprotein cholesterol (HDL-C) being the most critical factor [9].

More than half of the cases in the current study had CRP levels measured within 12 hours of stroke onset. Early measurement of CRP is critical, as elevated CRP levels in the first 12 hours may reflect an acute inflammatory response to cerebral ischemia. Timely CRP measurements can provide valuable prognostic information and assist in managing potential adverse outcomes [8].

This study also explored the association between CRP levels and various risk factors, including smoking, hypertension, cerebrovascular accidents, diabetes mellitus, and coronary artery disease. Notably, non-smokers were more likely to have higher CRP levels, with 68.4% having CRP levels above 10 mg, while 50% of smokers had CRP levels below 3 mg. Research on the relationship between smoking and CRP levels is mixed. Some studies have reported significantly higher CRP levels in smoker diabetics, which could indicate an increased cardiovascular risk in this subgroup [20].

Diabetes mellitus also showed a significant association with elevated CRP levels, with 54.5% of diabetics having CRP levels above 10 mg. The link between diabetes and elevated CRP levels is well-documented, reflecting a higher inflammatory status and increased cardiovascular risk in diabetic patients. Additionally, diabetes is known to impair coronary collateral circulation [23,19].

Despite these findings, this study did not observe significant associations between CRP levels and hypertension, cerebrovascular accidents, or coronary artery disease. However, previous research has shown that elevated CRP levels are associated with severe coronary artery disease in ischemic heart disease patients [1].

List of abbreviation

CRP, C-reactive protein; NIHSS, National Institute of Health Stroke Scale; CKD, chronic kidney disease; ICH, intracerebral hemorrhage; CLD, chronic liver disease; RA, rheumatoid arthritis; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol.

DECLARATIONS

Ethics approval and consent to participate

The study was conducted following ethical guidelines. Approval was obtained from the relevant authority at Tikrit Teaching Hospital, and informed consent was secured from all participants.

Availability of data and materials

The datasets used and/or analyzed in the current study are available from the corresponding author upon reasonable request.

Conflict of Interest Declaration

The authors declare no conflicts of interest related to this study.

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