ISSN 0973-2063 (online) 0973-8894 (print)

Bioinformation 20(10): 1413-1417 (2024)

BIOINFORMATION
Discovery at the interface of physical and biological sciences

BIOMEDICAL INFORMATICS

www.bioinformation.net

Volume 20(10)

Research Article

Received October 1, 2024; Revised October 31, 2024; Accepted October 31, 2024, Published October 31, 2024

DOI: 10.6026/9732063002001413

BIOINFORMATION 2022 Impact Factor (2023 release) is 1.9.

Declaration on Publication Ethics:
The author's state that they adhere with COPE guidelines on publishing ethics as described elsewhere at https://publicationethics.org/. The authors also undertake that they are not associated with any other third party (governmental or non-governmental agencies) linking with any form of unethical issues connecting to this publication. The authors also declare that they are not withholding any information that is misleading to the publisher in regard to this article.

Declaration on official E-mail:
The corresponding author declares that lifetime official e-mail from their institution is not available for all authors

Comments from readers:
Articles published in BIOINFORMATION are open for relevant post publication comments and criticisms, which will be published immediately linking to the original article without open access charges. Comments should be concise, coherent and critical in less than 1000 words.

Disclaimer:
The views and opinions expressed are those of the author(s) and do not reflect the views or opinions of Bioinformation and (or) its publisher Biomedical Informatics. Biomedical Informatics remains neutral and allows authors to specify their address and affiliation details including territory where required. Bioinformation provides a platform for scholarly communication of data and information to create knowledge in the Biological/Biomedical domain.

Edited by Neelam Goyal & Shruti Dabi
E-mail: dr.neelamgoyal15@gmail.com & shrutidabi59@gmail.com; Phone +91 98188 24219
Citation: Billa *et al.* Bioinformation 20(10): 1413-1417 (2024)

C-reactive protien levels among Indian patients with acute ischemic stroke

Nityanand Billa*, Anjali More & Vasant Deokar

Krishna Institute of Medical Sciences, Karad, Maharashtra, India; *Corresponding author

Affiliation URL:
https://kvv.edu.in/

Author contacts:
Nityanand Billa - E - mail: nitya9797@gmail.com
Anjali More - E - mail: moreanjali967@gmail.com
Vasant Deokar - E - mail: vasantvd967@gamil.com

ISSN 0973-2063 (online) 0973-8894 (print)
Bioinformation 20(10): 1413-1417 (2024)

Abstract:
Studies have shown that stroke (ST), a grave neurological condition (NL-CD), delineates a clinical syndrome characterized by the abrupt onset of focal or global cerebral function disturbances (G-CB-FN-DTB), persisting for more than 24 hours or resulting in death, primarily attributed to a vascular origin. Therefore, it is interest to elucidate the relationship between plasma CRP levels and acute ischemic stroke (A-IS-ST), analyzing their dynamic interplay concerning ST incidence (ICD), severity (SV) and outcomes (OT). 50 patients were involved to assess C-reactive protien (CRP) level for ST estimated myocardial infarction (STEMI). We found that, significant difference in below and above levels of CRP level in STEMI patients. Thus, incorporating CRP level assessments into routine diagnostic test is important for the evaluation of ST.

Keywords: Neurological condition, stroke (ST) incidence**,** severity, outcomes**,** acute ischemic stroke & cerebral function disturbances.

Background:
A study have shown that, cerebral B/V, accounts for the majority, ranging between 60–80% of stroke cases, whereas hemorrhagic stroke(HMH-ST) stems from vascular rupture(VS-R), leading to intracranial bleeding (IC-B) **[1].** In addition to this, classification of HMH-ST according to studies, includes IC-HMH & subarachnoid (SACH)-HMH, each presenting unique challenges in management & prognosis **[1, 2].** Globally, ST is the second leading cause of death mortality (MT) and the third leading cause of long-term disability, inflicting a significant socioeconomic burden (SE-B) **[3]**. According to current estimates, roughly 68% of all ST worldwide is IS, with HMH accounting for the remaining 32% **[4]**. In the United States, data indicates a significant prevalence of IS-ST, which represents 87% of cases. HMH-ST follows at 10%, while SACH-HMH accounts for a minority proportion of approximately 3% **[3]**. Remarkably, a study has shown that gender disparities in the prevalence of sexually transmitted infections (STIs) and incidence of disease (ICD) are evident, with women exhibiting significantly higher age-adjusted rates compared to men. This finding indicates a noteworthy public health concern **[5]**. Acute coronary syndrome (ACS) is highly prevalent in the Indian demographic, ranking among the highest worldwide **[6]**. Even with the reestablishment of blood circulation, neurons within the penumbra face significant threats to their viability, particularly from excitotoxicity and inflammation **[7]**. Studies have also shown that neuronal depolarization (NR-DP) or cell death causes the neurotransmitter glutamate (NT-GT) to be released without control. This leads to excitotoxicity, which is a major cause of neuronal damage in IS-ST **[8]**. Once this disturbance occurs, it triggers the activation of the apoptotic cascade, mitochondrial malfunction, the production of reactive oxygen (RO) and nitrogen species, and the activation of (adenosine diphosphate-ribose) polymerase **[3]**. An acute-phase reactant called CRP can rise dramatically, up to 1,000fold, at sites of infection or inflammation **[4]**. Therefore, it is of interest to investigate the role of CRP as a biomarker for risk assessment, prognosis & treatment response for AIS cases.

Materials & Methods:
The current single-center, hospital-based, prospective, observational analytical study was conducted over a period of 18 months from November 2022 to April 2024 with sample size of 50 patients (P). CRP levels were measured & recorded at the time of admission and detailed clinical evaluations & necessary investigations were performed to assess the neurological status (NL-S) and confirm the diagnosis of A-IS-ST.

Inclusion criteria:
[1] ST-P
[2] Developing clinical signs of focal or global (coma) NL deficit which lasted for more than 24 hours or leading to death, with no other apparent cause than vascular origin.
[3] Patients that presented within 48 hours of onset of ST.

Exclusion criteria:
Patients with SACH-HMH, extradural(ED) HMH, subdural (SD) HMH, and intracerebral (IC) HMH based on CT scan results of the brain.

Statistical analysis:
Data was analyzed using SPSS version 25.0. Independent t- tests & ANOVA were employed to compare mean CRP levels between two or more groups, respectively. Pearson correlation coefficients assessed the relationship between CRP levels and NIHSS scores.

Table 1: DMG distribution

Age (Mean ± SD)	**69.1 ± 11.58**	
Gender	**Total**	**Percentage**
Female	24	48.00%
Male	26	52.00%
Total	50	100.00%

Table 2: According to CRP level

CRP level (N=50)	**CRP<7**		**CRP>7**	
	No. of cases	**Percentage**	**No. of cases**	**Percentage**
No of cases	6	12.00%	44	88.00%

Table 3: Age wise distribution

Age	**CRP<7**	**CRP≥7**	**t-test**	**p-value**
(Mean ± SD)	70.17 ± 15.70	68.95 ± 11.13	-0.24	0.81

Table 4: Gender wise distribution

Gender	**CRP<7**	**CRP≥7**	**Chi square**	**p-value**
	No of cases (%)	**No of cases (%)**		
Female	2(33.33%)	22(50.00%)	0.57	0.44
Male	4(66.67%)	22(50.00%)		
Total	6(100.00%)	44(100.00%)		

Table 5: Distribution of weight

Weight	**CRP<7**	**CRP≥7**	**t-test**	**P- value**
(Mean ± SD)	69.17 ± 11.10	71.79 ± 15.34	0.40	0.68

Results:

Table 1 shows that, the average age was seen up to 69.1 years & standard deviation with 11.58 years. Whereas, male dominancy was seen with 26 in number (52%) followed by female with 24 in number (48%) respectively. **Table 2** shows that, 12% CRP levels below 7 mg/L, while 88% had levels exceeding 7 mg/L. **Table 3** shows that, no significant difference in age between participants with CRP levels below 7 mg/L (mean age 70.17 years, SD 15.70) & those with CRP levels of 7 mg/L or higher (mean age 68.95 years, SD 11.13), as the p-value was 0.81. **Table 4** shows that, among females, 33.33% had CRP levels below 7 mg/L & 50.00% had levels of 7 mg/L or higher. Among males, 66.67% had CRP levels below 7 mg/L & 50.00% had levels of 7 mg/L or higher. Therefore, found non-significant difference as the p value was 0.44. **Table 5** shows that, CRP levels below 7 mg/L had a mean weight of 69.17 kg (SD = 11.10), while those with CRP levels of 7 mg/L or higher had a mean weight of 71.79 kg (SD = 15.34). Therefore, found non- significant difference as the p value was 0.68. **Table 6** shows that, CRP levels below 7 mg/L had lower NIHSS scores initially (15.33 ±10.27) & after 5 days (13.83 ±8.97) compared to those with CRP levels of 7 mg/L or higher, who had higher scores both initially (25.45 ±10.01) and after 5 days (25.45 ±10.07). Therefore, found statistically significant difference as the p value was 0.02 and 0.01 respectively. **Table 7** shows that HCST 100.0% had CRP levels below 7 mg/L, while 68.18% of them had levels of 7 mg/L or higher.

In contrast, none of the participants without hypercholesterolemia had CRP levels below 7 mg/L, and 31.82% had levels of 7 mg/L or higher. Therefore, found non-significant difference as the p value was 0.10. **Table 8** shows that, none of the participants with a history of MI had CRP levels below 7 mg/L, and 34.09% had levels of 7 mg/L or higher. Therefore, found non-significant difference as the p value was 0.09. **Table 9** shows that, significant difference in S-BP between participants with CRP levels below 7 mg/L (mean 146.67 mmHg) and those with levels of 7 mg/L or higher (mean 160.22 mmHg). Therefore, found significant difference as the p value was 0.007. However, there was no significant difference found for D-BP as the p value was 0.54 respectively. **Table 10** shows that, 0 patients had CRP levels (<7) while 10 patients found CRP < 7 group. Therefore, found non-significant difference as the p value was 0.19. **Table 11** shows that, only 1 patient (16.67%) had CRP levels below 7, while a substantial (79.55%) 35 patients had CRP levels of 7 or higher. Therefore, found highly significant difference as the p value was 0.001 respectively. **Table 12** shows that, only 1 patient (16.67%) showed CRP levels below 7, while 36 patients (81.82%) had CRP levels of 7 or higher. Therefore, found highly statistically significant difference as the p value was 0.0007. **Table 13** shows that, 2 patients (33.33%) had CRP levels below 7, while 36 patients (81.82%) had CRP levels of 7 or higher.

Therefore, found significant difference as the p value was 0.009. **Table 14** shows that, among individuals with ST, 12.00% had CRP levels below 7, while a significant majority of 88.00% had CRP levels of 7 or higher. In contrast, among those without ST, 68.00% had CRP levels below 7, with 32.00% having CRP levels of 7 or higher. Therefore, found highly significant association as the p value was <0.0001 respectively.

Discussion:

Our study investigates the levels of CRP in patients with A-IS cerebrovascular accident (CBV-AC) & their association with various DMG, clinical & treatment-related factors (TRF). The average age of the study participants was 69.1 years with a standard deviation of 11.58 years. The gender distribution was balanced, with 48% females and 52% males. This DMG data aligns with the typical age range for ST patients, indicating that the sample is representative of the broader population affected by A-IS-ST. This finding highlights the role of inflammation, as indicated by elevated CRP levels, in A-IS-ST. Men had greater average serum CRP levels than women did, according to Almeida *et al.* **[9].** The distribution of these CRP serum levels did vary by age and sex, however. The C-reactive protein serum levels and were found to be much lower in men aged 75, whereas in women it was reverse. In the study by Lakoski *et al.* women had substantially higher median CRP levels compared with men (2.56 vs 1.43 mg/L, P < .0001) **[10].** According to Khera *et al.* women had higher CRP levels than men (median, 3.3 vs. 1.8 mg/l; p < 0.001) **[11]**. In Straatman *et al.* showed no effect was observed for gender, age, and BMI on postoperative CRP levels. The mean weight of patients with CRP levels less than 7 mg/L was 69.17 kg, compared to 71.79 kg in those with higher CRP levels. The p-value of 0.68 suggests no significant difference in weight between the two groups, implying that the weight of the patient does not significantly affect CRP levels in acute ischemic stroke patients **[12].** In our study, analysis of clinical parameters revealed significant associations between elevated CRP levels and higher NIHSS scores both on admission and after 5 days, reflecting more severe strokes among patients with higher CRP levels. This finding underscores the potential of CRP as a prognostic marker for stroke severity and functional outcome. Elevated levels of CRP might be a reflection of the extent of brain injury. Patients with CRP levels 7 mg/L had better NIHSS scores on admission; according to a study by Hertog *et al.* **[13]** Patients with higher CRP levels have larger infarctions, according to older studies. In addition to indicating the degree of tissue damage, CRP may also point to a condition of higher risk brought on by higher inflammation or an excess of cytokines **[14, 15]**. Recent experimental studies revealed that CRP itself may cause additional damage to the brain after localized cerebral ischemia, potentially via a complement-mediated aggravation of tissue injury **[16].** The difference was not statistically significant, despite the fact that a larger proportion of HCST patients had increased CRP levels.

Table 6: NIHSS type

NIHSS	CRP<7 (Mean ± SD)	CRP≥7 (Mean ± SD)	P- value
NIHSS on admission	15.33 ± 10.27	25.45 ± 10.01	0.02
NIHSS after 5 days	13.83 ± 8.97	25.45 ± 10.07	0.01

Table 7: HCST

Hypercholesterolemia (HCST)	CRP<7	CRP≥7	Chi square	P- value
	No of cases (%)	No of cases (%)		
No	0(0.00%)	14(31.82%)	2.59	0.10
YES	6(100.00%)	30(68.18%)		
Total	6(100.00%)	44(100.00%)		

Table 8: MI distribution

Myocardial infarction (MI)	CRP<7	CRP≥7	Chi square	P- value
	No of cases (%)	No of cases (%)		
NO	6(100.00%)	29(65.91%)	2.86	0.09
Yes	0(0.00%)	15(34.09%)		
Total	6(100.00)	44(100.00%)		

Table 9: Physical examination distribution

Physical examination	CRP<7	CRP≥7	t-test	P- value
Systolic blood pressure (S-BP)	146.67 ± 8.16	160.22 ± 11.51	2.78	0.007
Diastolic blood pressure (D-BP)	91.67 ± 7.52	94.09 ± 9.23	0.61	0.54

Table 10: Death distribution

Death	CRP<7	CRP≥7	Chi-square	P-value
	No of cases (%)	No of cases (%)		
NO	6(100.00%)	34(77.27%)	1.67	0.19
Yes	0(0.00%)	10(22.73%)		
Total	6(100.00%)	44(100.00%)		

Table 11: Arterial hypertension (at-hy-t)

Arterial hypertension	CRP<7		CRP≥7		Chi square	P- value
Case	No. of case	Percentage	No. of case	Percentage		
NO	5	83.33%	9	20.45%	10.14	0.001
YES	1	16.67%	35	79.55%		
Total	6	100.00%	44	100.00%		

Table 12: Diabetes mellitus distribution

Diabetes mellitus	CRP<7		CRP≥7		Chi square	P- value
Case	No. of cases	Percentage	No. of cases	Percentage		
NO	5	83.33%	8	18.18%	11.41	0.0007
YES	1	16.67%	36	81.82%		
Total	6	100.00%	44	100.00%		

Table 13: SMK/ tobacco consumption

Smoker/ Tobacco consumption	CRP<7		CRP≥7		Chi square	P- value
Case	No. of cases	Percentage	No. of cases	Percentage	6.66	0.009
NO	4	66.67%	8	18.18%		
YES	2	33.33%	36	81.82%		
Total	6	100.00%	44	100.00%		

Table 14: ST type

	CRP<7		CRP≥7			Chi-square	P-value
Type of stroke	No. of cases	Percentage	No. of cases	Percentage	Total		
Stroke	6	12.00%	44	88.00%	50	32.67	<0.0001
Non stroke	34	68.00%	16	32.00%	50		
Total	40		60		100		

In a prospective study by Pradhan *et al.* patients with type 2 DM had higher CRP levels compared to non-diabetic patients **[17].** Another nested case-control study of 550 middle-aged women followed for four years found that those in the top quartile of the CRP distribution had a nearly 16-fold higher chance of acquiring type 2 diabetes than those in the bottom quartile. Although the correction for BMI and other variables reduced the connection, it remained substantial and significant, with a relative risk of 4.2 **[18].** In our study, significant association was observed between SMK/tobacco use and elevated CRP levels (p = 0.009). This indicates that smokers and tobacco users are more likely to have higher CRP levels, suggesting that smoking contributes to inflammation in A-IS-ST **[19].** Moreover, Tonstad *et al.* found that CRP levels were significantly higher in both male and female smokers compared with non-smokers (median values of 1.0 mg/l and 11.2 mg/l for male non-smokers and smokers, respectively, and for females 2.0 mg/l and 11.6 mg/l, respectively). This highlights the substantial impact of smoking on systemic inflammation, as evidenced by elevated CRP levels **[20].** A study has also shown that, elevated levels of CRP are

associated with more severe ST, higher S-BP, and worse functional OT **[21].** It has been shown that high levels of hsCRP are present in all subtypes of ischemic stroke and that these levels are independently related to atherosclerosis of the large arteries and cardioembolic stroke. A threefold increase in the risk of acquiring a cardioembolic stroke and a twofold increase in the risk of developing atherosclerosis in the large arteries were related to high levels of high-sensitivity C-reactive protein (hsCRP) in stroke subtypes. Because of this, higher levels of hsCRP in these subtypes might be a sign that primary prevention efforts should start. Because of this, high levels of hsCRP may be a sign that it's time to start taking statins for both primary and secondary prevention. To investigate these results, further studies on a large scale are necessary in the future **[22].** It has a sensitivity of 80% and a specificity of 75%. A CRP level of 10.25 mg/L is linked to a severe ischemic stroke. Additionally, this level correlates with an unfavorable stroke outcome as measured by the modified Rankin Scale (mRS), exhibiting a specificity of 75% and an outcome prediction of 82%. The CRP level did not correlate with the severity of illness or the outcomes of stroke scores in cases of hemorrhagic stroke. It is feasible to predict the severity and early outcome of an ischemic stroke based on the serum C-reactive protein level at the time of admission; however, this predictive capability does not extend to hemorrhagic stroke **[23].** In addition to the widely acknowledged disorders, elevated C-reactive protein levels represent an independent risk factor **[24].**

Conclusions:

Data shows statistically significant associations between elevated CRP levels and the presence of AT-HY-T, DM and SMK/tobacco use. This suggests that, although CRP is a valuable indication of inflammation and stroke severity, its levels may vary greatly depending on DEM variables, although non-significant association was seen for age & gender between 2 groups. Thus, these variations must be taken into account in clinical evaluations.

Limitations:

[1] Small sample size
[2] Single centered study could limit the generalized finding
[3] Study not conducted long term study
[4] The inclusion criteria required patients to present within 48 hours of stroke onset and give informed consent. This might exclude patients who present later or are unable to consent, potentially introducing selection bias.
[5] CRP levels were measured at specific time points.
[6] Variation in the timing of CRP measurements relative to stroke onset could affect the results, as CRP levels can fluctuate significantly post-stroke.
[7] Although the study adjusted for confounding like age, sex, and comorbidities, there might be other variables that are unmeasured could influence the results.
[8] Different treatment protocols, lifestyle factors, and genetic predispositions were not controlled for in the study.

References:

[1] Jauch EC *et al*. *Stroke*. 2013 **44**:870. [PMID: 23370205]
[2] Feigin VL *et al*. *Circ Res*. 2017 **120**:439. [PMID: 28154096]
[3] Benjamin EJ *et al*. *Circulation*. 2018 **137**:e67. [PMID: 29386200]
[4] Banerjee TK & Das SK. *Neurology Asia*. 2006 **11**:1.
[5] Joshi R *et al*. *Int J Epidemiol*. 2006 **35**:152. [PMID: 16997852]
[6] Yusuf S *et al*. *Lancet*. 2004 **364**:937. [PMID: 15364185]
[7] Hacke W *et al*. *N Engl J Med*. 2008 **359**:1317. [PMID: 18815396]
[8] Moskowitz MA *et al*. *Neuron*. 2010 **67**:181. [PMID: 20670828].
[9] Roediger MDA *et al*. *Health and Quality of Life Outcomes*. 2019 17:26. [PMID: 30728031] [DOI: 10.1186/s12955-019-1092-2].
[10] Lakoski SG *et al*. *Am Heart J*. 2006 **152**:593. [PMID: 16923436]
[11] Khera A *et al. J Am Coll Cardiol*. 2005 **46**:464. [PMID: 16053959]
[12] Straatman J *et al*. *Ann Surg*. 2017 **266**:232. [PMID: 28187044]
[13] Den Hertog HM *et al. J Neurol*. 2009 **256**:2003. [PMID: 19609738]
[14] Dirnagl U *et al*. *Trends Neurosci*. 1999 **22**:391. [PMID: 10441299]
[15] Iadecola C & Anrather J. *Nat Med*. 2011 **17**:796. [PMID: 21738161]
[16] Black S *et al*. *J Biol Chem*. 2004 **279**:48487. [PMID: 15337754]
[17] Pradhan AD *et al*. *JAMA*. 2001 **286**:327. [PMID: 11466099]
[18] Ridker PM *et al*. *N Engl J Med*. 2000 **342**:836. [PMID: 10733371]
[19] Reeves MJ *et al. Stroke*. 2009 **40**:1127. [PMID: 19211482]
[20] Tonstad S & Cowan J.L. *Int. J of clinical practice*. 2009 **63**:1634. [PMID: 19732183]
[21] Robson B *et al*. *The Engines of Hippocrates.* John Wiley & Sons; USA, 2009, P512.
[22] Chaudhuri JR *et al. Iranian journal of neurology*. 2013 **12**:92.[PMID: 24250912]
[23] Shoaeb MA *et al. Journal of Critical Care Medicine*. 2014 **2**:43.[https://doi.org/10.1016/j.ejccm.2014.03.001]
[24] Reddy YG *et al. International Journal Dental and Medical Sciences Research.* 2024 **6**:416.[DOI: 10.35629/5252-0601416420]