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Evaluation of Elevated C-Reactive Protein Levels to Predict Unfavourable Outcomes in Patients with Traumatic Brain Injury

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ABSTRACT

Background: Over 80% of all traumatic brain injuries are classified as mild traumatic brain injury, which is one of the most common conditions worldwide. The current study was conducted to test whether measuring CRP levels can be used to prognosticate TBI patients and aid in constructing more effective treatment protocols.

Methods: All patients satisfying the inclusion criteria, were subjected to detailed history taking and physical examination. Glasgow Coma score was assessed at the time of presentation. Routine investigations including CRP were sent at the time of presentation. CRP levels were assessed at 1 week of follow-up and again at 1 month. Cognition was assessed at the time of presentation via MMSE and GHQ-28 and reassessed with the same at 1 week and 1 month.

Results: After a complete analysis of the results, it was found that there is a strong positive correlation between CRP, GHQ-28, and MMSE scoring at the time of presentation (p=0.0001), and a moderate positive correlation between CRP, GHQ-28, and MMSE scoring at 1 week and 1 month post mild traumatic brain injury.

Conclusion: After analysis, comparison, and interpretation of the results obtained, this pilot study supports the hypothesis that elevated CRP levels are associated with unfavourable outcomes in patients with mTBI. The significant correlations between CRP levels and both psychological and cognitive outcomes suggest that CRP could serve as a valuable biomarker for identifying patients at higher risk of long-term disability.

Key-words: Traumatic brain injury, C-reactive protein, General Health Questionnaire- 28, Mini-Mental Status Examination, Post Concussional Syndrome

INTRODUCTION

Over 80% of all traumatic brain injuries are classified as mild (mTBI), which is one of the most common conditions worldwide. Axonal injury as demonstrated by diffusion tensor imaging in mild TBI, may be the trigger to induce chronic traumatic encephalopathy. Therefore, although almost all mTBI patients could return to normalcy, a small proportion may experience postconcussional complaints beyond the first week after the injury, sometimes for months or even years. Cognitive impairment and postconcussion syndrome (PCS) may persist indefinitely and are associated with high functional disability and increased healthcare utilization rates.[1]

Depending on the intensity of the trauma, all trauma patients have different levels of metabolic and endocrinological changes. These alterations are the body's way of protecting itself from harm and preserving equilibrium. It has long been recognized that trauma causes tissue damage, which causes the liver to release acute phase reactants (APR) into the blood. [2] An acute-phase protein called CRP rises sharply in the blood in reaction to burns, ischaemia, trauma, infection, and other inflammatory diseases. Most labs are equipped to measure CRP levels, and the cost of the test is not excessive.[3]

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Although psychological impairments are important sources of disability, physical and cognitive impairments are usually the focus of traumatic brain injury (TBI). Among those with TBI, major depressive disorder (MDD) can be the most prevalent and incapacitating mental illness. It is believed that MDD following TBI is linked to worse cognitive functioning, anger and anxiety, increased functional handicap, worse recovery, and increased suicide attempt rates.[4]

The idea that raised CRP levels are linked to a higher risk of long-term negative outcomes in patients with mTBI can be investigated using plasma high-sensitivity CRP levels, which are an efficient biomarker of systemic inflammation [5]. While some research has attempted to determine the risk factors for adverse outcomes following mTBI, no study has examined the relationship between systemic inflammation and adverse outcomes. Previous studies focused primarily on dyselectrolytemia and variations in blood glucose levels to prognosticate outcomes in patients with TBI.[6] The current study was conducted to test whether measuring CRP levels can be used to prognosticate TBI patients and aid in constructing more effective treatment protocols.

MATERIALS AND METHODS

Place of the study- This prospective observational study was conducted between February 2023 to March 2024 with patients presenting with mild traumatic brain injury to the Department of General Surgery, Mandya Institute of Medical Sciences, Mandya.

Study Population- All patients of mild traumatic brain injury who present to casualty and OPD in the Department of General Surgery at Mandya Institute of Medical Sciences, Mandya.

Inclusion Criteria- Patients of age 18 years to 60 years of age, with a Glasgow Coma Score ranging from 13-15 points, loss of consciousness less than 30 mins, post-traumatic amnesia less than 24 hours, with a normal CT brain, who were able to complete the questionnaires without misunderstanding, and who gave their written informed consent were included in the study.

Exclusion Criteria- Patients with previous head trauma, head injuries, neurological disorders, and chronic inflammatory pathologies like tuberculosis were excluded. All patients satisfying the inclusion criteria were subjected to detailed history taking and physical examination.

Sampling Method- Consecutive enrolment. The Glasgow Coma Score (GCS) was recorded at the presentation, along with routine investigations, including C-reactive protein (CRP) levels. CRP levels were reassessed at 1-week and 1-month follow-ups. Cognitive function was evaluated using the Mini-Mental Status Examination (MMSE) and General Health Questionnaire-28 (GHQ-28) at the presentation, and the same assessments were repeated at both 1-week and 1-month follow-ups.

Statistical Analysis- Data was analyzed for descriptive and inferential statistics. For descriptive statistics, we calculated mean, standard deviation, range, and proportion. For inferential statistics, the continuous variable is converted to categorical variables. Percentages were calculated data were compared and conclusions were drawn.

RESULTS

Participants ranged in age from 18 to 60, with a mean age of 40.83±12.18 years. Many participants (28%) were between the ages of 51 and 60, followed by those between the ages of 31 and 40 (27%), 18 and 30 (24%), and 41 and 50% (21%) (Table 1).

Table 1: Distribution of study participants according to age

Age Group	Frequency	Percentage
18-30	24	24%
31-40	27	27%
41-50	21	21%
51-60	28	28%
Total	100	100%

CRP levels were lowest at arrival (median=0.90 mg/dL) and progressively increased at 1-week post-injury (median=1.21 mg/dL) and 1-month post-injury (median=1.50 mg/dL). The increase was statistically significant across the 3 time points (p=0.0001) (Table 2).

GHQ-28 scores were significantly higher over time, with the lowest median score at arrival (36), increasing to 40 at 1-week post-injury, and 44 at 1-month post-injury. This upward trend was statistically significant (p=0.0001) (Table 3).

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Table 2: Comparison of CRP at different time points

	Time	Mean	SD	Percentiles			Test statistic	p-value
				25th	50th	75th		
CRP	Arrival	0.86	0.45	0.67	0.90	1.3	78.07	0.0001*
	1-week post-injury	1.10	0.44	0.9	1.21	1.5		
	1-month post-surgery	1.40	0.34	1.2	1.50	1.7		

Table 3: Comparison of GHQ-28 at different time points

	Time	Mean	SD	Percentiles			Test statistic	p-value
				25th	50th	75th		
GHQ-28	Arrival	34.37	2.66	32	36	36	218.78	0.0001*
	1-week post-injury	38.18	2.23	36	40	40		
	1-month post-surgery	43.7	2.72	42	44	45		

MMSE scores demonstrated a significant decline over time. The median score was 26 at arrival, which decreased to 24 at 1-week post-injury and further dropped to 21 at 1-month post-injury (p=0.0001) (Table 4).

Table 4: Comparison of MMSE score at different time points

	Time	Mean	SD	Percentiles			Test statistic	p-value
				25th	50th	75th		
MMSE score	Arrival	25.87	1.38	26	26	26	233.1	0.0001*
	1-week post-injury	24	1.45	24	24	24		
	1-month post-surgery	20.59	1.82	20	21	21		

There was a strong positive correlation between CRP and GHQ-28 scores at arrival (r=0.81, p=0.0001). However, no significant correlation was found between CRP and MMSE or GHQ-28 and MMSE scores at this time point (Table 5).

Table 5: Correlation between CRP, GHQ 28 and MMSE score on arrival

		CRP on arrival (mg/dl)	GHQ-28 Score on arrival	MMSE score on arrival
CRP on arrival (mg/dl)	Spearman's rho	—	—	—
	p-value	—	—	—
GHQ-28 Score on arrival	Spearman's rho	0.81	—	—
	p-value	0.0001*	—	—
MMSE score on arrival	Spearman's rho	0.18	-0.018	—
	p-value	0.06	0.86	—

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A moderate positive correlation was found between CRP and GHQ-28 scores at 1-week post-injury (r=0.65, p=0.0001). No significant correlation was observed between CRP and MMSE or between GHQ-28 and MMSE scores (Table 6).

Table 6: Correlation between CRP, GHQ 28, and MMSE score 1-week post-injury

		CRP 1-week post-injury	GHQ-28 score 1-week post-injury	MMSE Score 1-week post-injury
CRP 1-week post-injury	Spearman's rho	—	—	—
	p-value	—	—	—
GHQ-28 score 1-week post-injury	Spearman's rho	0.65	—	—
	p-value	0 .0001*	—	—
MMSE Score 1-week post-injury	Spearman's rho	0.10	-0.03	—
	p-value	0.31	0.74	—

At 1-month post-injury, a moderate positive correlation was noted between CRP and GHQ-28 scores (r=0.48, p=0.0001). A significant negative correlation was also observed between CRP and MMSE scores (r=-0.35, p=0.0001) and between GHQ-28 and MMSE scores (r=-0.28, p=0.004) (Table 7).

Table 7: Correlation between CRP, GHQ 28 and MMSE score on 1-month post-injury

		CRP 1-month post-injury	GHQ-28 score 1-month post-injury	MMSE Score 1-month post-injury
CRP 1-month post-injury	Spearman's rho	—	—	—
	p-value	—	—	—
GHQ-28 score 1-month post-injury	Spearman's rho	0.48	—	—
	p-value	0.0001*	—	—
MMSE Score 1-month post-injury	Spearman's rho	-0.35	-0.28	—
	p-value	0.0001*	0.004*	—

CRP levels at all time points (arrival, 1 week, and 1 month) showed a moderate negative correlation with GCS scores (ranging from -0.51 to -0.66, p=0.0001), suggesting that higher CRP levels are associated with lower GCS scores (Table 8).

Table 8: Correlation between CRP and GCS

		GCS
CRP on arrival (mg/dl)	Spearman's rho	-0.66
	p-value	0 .0001*
CRP 1-week post-injury	Spearman's rho	-0.58
	p-value	0 .0001*
CRP 1-month post-injury	Spearman's rho	-0.51
	p-value	0 .0001*

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DISCUSSION

There has been a rapid acceleration in the research of TBI biomarkers in the past decade mainly owing to the heterogeneous nature of TBI pathologies and management posing challenges to TBI evaluation, management, as well as prognosis (Ghaith *et al.*) [7]. The present prospective observational study was conducted in patients admitted with mild traumatic brain injury in a tertiary care hospital for one year to know the role of CRP levels in persistent post concessional syndrome and to determine its correlation with persistent psychological problems as well as persistent cognitive impairment.

In our study, 49% of the study participants who came with head injury were due to RTA followed by 28% due to fall and 23% due to assault. Similar findings were seen in Xu et al with the majority of the injuries being due to RTA (58.5%) followed by 26.1% being due to falls and only 6.8% being assaulted. Su et al study had more cases due to fall (44.5%) than RTA (41.8%) and 10.7% were assault cases. All the studies showed that RTA was the main cause of head injury followed by slip and fall except for Pattnaik et al where the assault was a more common cause than slip and fall.[8]

Our study had a total of 48% of study participants who consumed alcohol. Among the 47 who lost, consciousness the mean time was 9.21±5.50 mins. 37% had post-traumatic amnesia. Su et al study showed that 61.5% consumed alcohol, 55.8% had post-traumatic amnesia and 55.8% had a loss of consciousness. The present study shows a strong positive correlation between CRP levels at admission and GHQ 28 and that during follow up CRP levels showed a significant increasing trend during one-week post-injury as well as 1-month post-surgery.

Gender-wise analysis was done by Naghibi *et al.* study and found that in the male group, CRP level did not have a significant correlation with ICU stay (r=0.97, p=0.59) or mechanical ventilation (r=0.147, p=0.416) duration and GCS at discharge (r=0.28, p=0.10) while the female group showed a positive correlation of CRP level with ICU stay duration (r=0.554, p=0.001) as well as the duration of mechanical ventilation (r=0.48, p=0.005); but not with GCS at discharge (r=0.23, p=0.20).[9]

Another study by Naghibi *et al.* categorized the mTBI patients into tertiles based on their CRP levels (Tertile 1 with CRP<0.49 mg/L, Tertile 2 with CRP level 0.49–1.07 mg/L and Tertile 3 with CRP>1.07 mg/L) and on follow up (1, 2 and 3 months) found that CRP levels increased over time. This increase was significantly higher in tertile 3 compared to tertile 1 and tertile 2 ($p<0.05$). It was also seen that elevated CRP levels independently predicted persistent psychological problems, PCS, and cognitive impairment in patients. The study concluded that baseline CRP levels had clinically relevant prognostic value in patients with mTBI indicating a risk of persistent unfavourable outcomes.[9]

In mTBI subjects, an increase in hs-CRP with Injury Severity Score (ISS) was seen at all time points which reached a significant association on days 1, 3, and 5. Two-week hsCRP as a predictor of injury severity was found to be higher, especially in patients with milder TBI (AUC=0.779 for GCS 3–12 and 0.928 for 13–15).[10]

In conducting a comprehensive literature search, Eghzawi *et al.* [11] identified CRP as one of the mortality predictor biomarkers in mild-moderate TBI adult patients in one of the (Gabbe *et al.*) [12] with a positive correlation between CRP levels and the mortality rates, which reflects the response to injury by the systemic inflammation. Rodney *et al.* study also found that higher CRP levels within the initial 48 h post-injury were found to be associated with unfavorable outcomes as well as higher mortality rates in patients with mild TBI [13]

Another study by Malik *et al.* in chronic mTBI also found elevated CRP levels in comparison to the controls which was statistically significant. In the chronic mTBI population, Malik et al found that poor psychological outcomes which may involve PTSD and/or depression were most associated with cytokines, IL-6, TNF, IL-10, and CRP. [14] Another study by Ghai *et al.* in chronic mTBI also found elevated CRP levels in comparison to the controls which was statistically significant.[15]

CONCLUSIONS

After thorough analysis, comparison, and interpretation of the results, this pilot study supports the hypothesis that elevated CRP levels are associated with unfavourable outcomes in patients with mTBI. The significant correlations observed between CRP levels and both psychological and cognitive outcomes suggest that CRP could serve as a valuable biomarker for identifying patients at higher risk of long-term disability. Future large-scale studies are warranted to validate the utility of CRP as a reliable prognostic biomarker in mTBI. Further research should focus on integrating CRP levels with

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other inflammatory markers and neuroimaging techniques to develop a comprehensive predictive model for the early identification of patients at risk of long-term cognitive and psychological impairments.

CONTRIBUTION OF AUTHORS

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REFERENCES

[1] Su S, Xu W, Li M, Zhang L, Wu Y, et al. Elevated C-reactive protein levels may be a predictor of persistent unfavourable symptoms in patients with mild traumatic brain injury: A preliminary study. Brain Behav Immun., 2014; 38: 111-17.

[2] Sogut O, Guloglu C, Orak M, Sayhan MB, Gokdemir MT, et al. Trauma scores and neuron-specific enolase, cytokine and C-reactive protein levels as predictors of mortality in patients with blunt head trauma. J Int Med Res., 2010; 38(5): 1708-20.

[3] Lee DG, Lee KS, Shim JJ, Yoon SM, Bae HG. Prognostic value of the C-reactive protein levels in head injury. J Korean Neurotraumatol Soc., 2005; 1(1): 57-60.

[4] Bombardier CH, Fann JR, Temkin NR, Esselman PC, Barber J, et al. Rates of major depressive disorder and clinical outcomes following traumatic brain injury. JAMA, 2010; 303(19): 1938-45.

[5] Dewan MC, Rattani A, Gupta S, Baticulon RE, Hung YC, Punchak M, et al. Estimating the global incidence of traumatic brain injury. J Neurosurg., 2018; 130(4): 1080-95. doi: 10.3171/2017.10.JNS17352.

[6] Sharma R, Rosenberg A, Bennett ER, Laskowitz DT, Acheson SK. A blood-based biomarker panel to risk-stratify mild traumatic brain injury. PLoS One, 2017; 12(3): e0171739.

[7] Ghaith HS, Nawar AA, Gabra MD, Abdelrahman ME, Nafady MH, et al. A literature review of traumatic brain injury biomarkers. Mol Neurobiol., 2022; 59(7): 4141-58. doi: 10.1007/s12035-022-02762-9. doi: 10.1007/s12035-022-02762-9.

[8] Pattnaik S, Panda BB, Swain SC. Spectrum of ocular findings in closed head injuries, correlation with severity of neurological involvement, and treatment outcome: A hospital-based cross-sectional study. Cureus, 2021; 13(7): e16515.

[9] Naghibi T, Mohajeri M, Dobakhti F. Inflammation and outcome in traumatic brain injury: Does gender affect survival and prognosis? J Clin Diagn Res., 2017; 11(2): PC06-PC09.

[10] Xu LB, Yue JK, Korley F, Puccio AM, Yuh EL, et al. High-sensitivity C-reactive protein is a prognostic biomarker of six-month disability after traumatic brain injury: Results from the TRACK-TBI study. J Neurotrauma, 2021; 38(7): 918-27.

[11] Eghzawi A, Alsabbah A, Gharaibeh S, Alwan I, Gharaibeh A, et al. Mortality predictors for adult patients with mild-to-moderate traumatic brain injury: A literature review. Neurol Int., 2024; 16(2): 406-18. doi: 10.3390/neurolint16020030.

[12] Gabbe BJ, Simpson PM, Lyons RA, Ameratunga S, Harrison JE, et al. Association between the number of injuries sustained and 12-month disability outcomes: Evidence from the injury-VIBES study. PLoS One, 2014; 9(12): e113467.

[13] Rodney T, Osier N, Gill J. Pro- and anti-inflammatory biomarkers and traumatic brain injury outcomes: A review. Cytokine, 2018; 110: 248-56.

[14] Malik S, Alnaji O, Malik M, Gambale T, Rathbone MP. Correlation between mild traumatic brain injury-induced inflammatory cytokines and emotional symptom traits: A systematic review. Brain Sci., 2022; 12(1): 102. doi: 10.3390/brainsci12010102.

[15] Ghai V, Fallen S, Baxter D, Scherler K, Kim TK, et al. Alterations in plasma microRNA and protein levels in war veterans with chronic mild traumatic brain injury. J Neurotrauma, 2020; 37(12): 1418-30. doi: 10.1089/neu.2019.6826.