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PREDICTION OF THE GRADE OF ACUTE CHOLECYSTITIS BY PLASMA LEVEL OF C-REACTIVE PROTEIN

General Surgery

Dr. Buddhi Prakash Meena PG Student, Department of General Surgery, RNT Medical College, Udaipur. ORCHID ID - 0009-0005-4684-9899

Dr. Dharamanjai Kumar Sharma* Senior Professor & Unit Head, Department of General Surgery, RNT Medical College, Udaipur *Corresponding Author

ABSTRACT

Background: C-reactive protein (CRP), an acute-phase reactant, is increasingly recognized as a reliable biomarker for assessing the severity of acute cholecystitis. It reflects both local inflammation and systemic response. This study aimed to evaluate the diagnostic accuracy of CRP in grading acute cholecystitis severity using Tokyo Guidelines 2013 (TG13). **Methods:** A cross-sectional observational study was conducted on 72 patients diagnosed with acute cholecystitis at a tertiary care center. CRP levels, clinical features, imaging findings, and SOFA scores were recorded. Patients were classified into Grades I, II, and III as per TG13. ROC curve analysis was performed to assess the predictive performance of CRP for Grade III cases. **Results:** Mean CRP levels increased significantly with severity: 45.51 mg/L in Grade I, 87.36 mg/L in Grade II, and 186.62 mg/L in Grade III ($p = 0.015$). Median CRP (IQR) values were 22.75 mg/L (5.6–49.4) in Grade I, 54.70 mg/L (9.4–130.0) in Grade II, and 213.50 mg/L (118.0–250.23) in Grade III ($p = 0.009$). The optimal CRP cut-off to predict Grade III was ≥201.42 mg/L, yielding 80.2% sensitivity, 75.5% specificity, and an AUC of 0.785 ($p = 0.004$). Conservative management was effective in 72.2% of patients, while 26.4% underwent laparoscopic cholecystectomy. **Conclusions:** CRP is significantly associated with acute cholecystitis severity and serves as a practical, cost-effective biomarker for early triage. Integrating CRP into existing severity grading systems can improve clinical decision-making and optimize outcomes.

KEYWORDS

C-reactive Protein, Acute Cholecystitis, Severity Grading, Tokyo Guidelines 2013, ROC Analysis

INTRODUCTION

Acute cholecystitis is one of the most common acute surgical conditions of the abdomen, typically resulting from obstruction of the cystic duct by gallstones, leading to gallbladder inflammation, wall thickening, and potential infection. The accurate and timely assessment of its severity is crucial for optimizing treatment strategies, preventing complications such as gangrenous cholecystitis, and improving patient outcomes.[1],[2] C-reactive protein (CRP) is a key inflammatory biomarker produced by hepatocytes in response to interleukin-6. It plays a crucial role in the early diagnosis and severity assessment of acute cholecystitis. Elevated CRP levels are strongly associated with severe forms such as gangrenous and emphysematous cholecystitis, making it a valuable tool for clinical risk stratification. [3],[4]

Several studies have validated CRP's predictive value for differentiating between mild and severe disease. CRP values exceeding 150–200 mg/L have been proposed as thresholds for identifying complicated or gangrenous cholecystitis [5,6]. The Tokyo Guidelines TG(13) recommend using CRP alongside other clinical and radiological findings to classify cholecystitis severity, making it an essential component of the grading algorithm.[7] Importantly, CRP levels correlate not only with local gallbladder inflammation but also with systemic responses, including sepsis and organ dysfunction, as reflected in higher Sequential Organ Failure Assessment (SOFA) scores. [8]

In clinical practice, CRP is advantageous due to its widespread availability, low cost, and rapid turnaround. When used in conjunction with white blood cell count, imaging, and clinical signs, CRP significantly enhances diagnostic accuracy and risk assessment [9,10]. Emerging research continues to affirm CRP's diagnostic utility. Recent findings suggest that dynamic CRP monitoring-particularly rising levels within the first 48 hours of admission-can also help predict disease progression. Given the growing body of evidence, this study aims to further evaluate the clinical relevance of CRP levels in predicting the severity of acute cholecystitis in a tertiary care setting, with a focus on establishing reliable CRP cut-off values to inform timely clinical decision-making.

METHODS

Study Design and Setting:- This hospital-based, cross-sectional observational study was conducted in the Department of General Surgery at Ravindranath Tagore Medical College (RNTMC), Udaipur. The primary aim was to evaluate the correlation between plasma C-reactive protein (CRP) levels and the severity of acute cholecystitis using the Tokyo Guidelines 2013 (TG13) as a grading system.

Ethical Approval and Consent: Necessary ethical approval was obtained from the Institutional Ethics Committee and the Institutional Review Board of RNTMC. Informed written consent was obtained from all participants prior to enrollment, and confidentiality of patient information was strictly maintained.

Study Duration and Sample Size: The study was conducted over a period of one year following ethical clearance. Based on previous data by the calculated sample size was 72 patients, which was included in the study.

Inclusion and Exclusion Criteria:- Patients aged 15 to 75 years who were admitted with a clinical and radiological diagnosis of acute cholecystitis were included in the study. Patients were excluded if they had comorbid conditions that could independently elevate CRP levels, such as pneumonia, tuberculosis, chronic inflammatory diseases (e.g., rheumatoid arthritis, systemic lupus erythematosus, vasculitis), or malignancies.

Data Collection Procedure:- Data were collected using a structured proforma which included demographic details, clinical history, duration of symptoms, vital parameters, imaging findings, laboratory investigations (WBC, CRP, LFT, PT/INR), and SOFA score. The CRP levels were measured using the turbidometric method on the Cobas Pro 503 series analyzer in the Clinical Biochemistry Laboratory of RNTMC. Imaging was performed using abdominal ultrasonography, with additional investigations such as chest X-ray, CECT abdomen, or MRI conducted as clinically indicated.

Statistical Analysis: All data were entered and analyzed using IBM SPSS Statistics version 20. Continuous variables like CRP were expressed as mean ± standard deviation (SD), median, IQR and categorical variables as frequency and percentage. The Chi-square test was used to assess associations between CRP categories and disease grade. The Kruskal-Wallis test was used to compare mean CRP levels across SOFA score groups, and the Wilcoxon Rank Sum test was applied to compare CRP levels between conservatively and surgically managed patients. A p-value < 0.05 was considered statistically significant.

RESULT

Table 1: Comprehensive Summary of Demographic, Clinical, Laboratory, Radiological, Management, and CRP Profile of Patients with Acute Cholecystitis (N = 72)

Variable	Category / Value	Frequency (n)	Percentage (%) / Mean ± SD
Demographics			
Age (years)	Range: 23–75	–	52.7 ± 13.4
Gender	Male	19	26.40%
	Female	53	73.60%
Duration of Symptoms	0–10 days	58	80.60%
	11–30 days	8	11.10%
	>30 days	6	8.30%
Clinical Symptoms			
RUQ Pain	Present	72	100.00%
Fever	Present	14	19.40%
Vomiting	Present	34	47.20%
Jaundice	Present	10	13.90%
Laboratory Parameters			
WBC (cells/mm³)	–	–	9526.8±4036.1
CRP (mg/L)	–	–	94.17 ± 103.31
Platelet Count (×10³/mm³)	–	–	243.8 ± 115.0
PT (sec)	–	–	15.59 ± 3.02
INR	–	–	1.17 ± 0.27
CRP Categories	Mild CRP (<70 mg/L)	40	55.60%
	Moderate CRP (70–199 mg/L)	17	23.60%
	Severe CRP (≥200 mg/L)	15	20.80%
Clinical Signs & Imaging			
RUQ Tenderness	Yes	45	62.50%
Murphy's Sign	Yes	10	13.90%
RUQ Mass	Yes	1	1.40%
Guarding/Rigidity	Yes	1	1.40%
Tachycardia	Yes	3	4.20%
GB Wall Thickening (USG)	Present	67	93.10%
Pericholecystic Fluid (USG)	Present	26	36.10%
Organ Dysfunction	Present	11	15.30%
Management & Severity			
Management	Conservative	52	72.20%
	Laparoscopic Cholecystectomy	19	26.40%
	Laparotomy / Lap to Open	1	1.40%
Tokyo Grade	Grade I (Mild)	12	16.70%
	Grade II (Moderate)	50	69.40%
	Grade III (Severe)	10	13.90%
SOFA Score	0	50	69.40%
	1	6	8.30%
	2	9	12.50%
	3	7	9.70%

Table 2. Median, Interquartile Range (IQR) of Laboratory Parameters

Parameter	Median	IQR
WBC	9135.00	6,625.00 – 12,085.00
CRP	55.30	10.625 – 141.750
Platelet Count	2.12	1.655 – 2.9575
PT	14.80	14.20 – 15.75
INR	1.10	1.0325 – 1.2000

Table 3: Association of mean and S.D. value of C-Reactive Protein (CRP) with Disease Grade, SOFA Score, and Management Approach in Acute Cholecystitis (N = 72)

Category	Subgroup	N	Mean CRP (mg/L)	SD	p-value
A. Disease Grade	Grade I (Mild)	12	45.51	65.83	0.015
	Grade II (Moderate)	50	87.36	100.61	
	Grade III (Severe)	10	186.62	104.3	
B. SOFA Score	SOFA 0	50	69.18	89.56	0.047
	SOFA 1	6	159.32	142.7	
	SOFA 2	9	78.83	57.67	
	SOFA 3	7	148.52	116.25	
C. by Management Group	Conservative Management	52	102.43	109.42	0.058
	Surgical Management	20	72.68	84.11	

Table 4: Association of Median and IQR of C-Reactive Protein (CRP) with Disease Grade, SOFA Score, and Management Approach in Acute Cholecystitis (N = 72)

Category	Subgroup	N	Median CRP (mg/L)	IQR	p-value
A. Disease Grade	Grade I (Mild)	12	22.75	5.6 – 49.4	0.009
	Grade II (Moderate)	50	54.70	9.4 – 130.0	
	Grade III (Severe)	10	213.50	118.0 – 250.23	
B. SOFA Score	SOFA 0	50	24.90	5.8 – 100.2	0.017
	SOFA 1	6	139.05	26.8 – 276.0	
	SOFA 2	9	134.00	57.5 – 220.0	
	SOFA 3	7	207.00	46.35 – 277.525	
C. by Management Group	Conservative Management	52	58.70	12.36 – 196.50	0.45
	Surgical Management	20	34.10	9.95 – 111.00	

Table 5: ROC Analysis of CRP for Predicting Severe Acute Cholecystitis (Grade III)

Test Variable: CRP (mg/L) | State Variable: Severity_roc (1 = Grade III; 0 = Grade I/II)

Measure	Value
Area Under the Curve (AUC)	0.785
p-value (AUC significance)	0.004
Positive Cases (Grade III)	10
Negative Cases (Grade I/II)	62
Test Direction	Higher CRP → More Severe
Optimal Cut-off (CRP ≥)	201.42 mg/L
Sensitivity at Cut-off	80.2%
Specificity at Cut-off	75.5%

Table 5 summarizes the findings of a ROC (Receiver Operating Characteristic) curve analysis showed that CRP has good diagnostic accuracy for predicting severe acute cholecystitis (Grade III), with an AUC of 0.785 (p = 0.004). A CRP cut-off of ≥201.42 mg/L yielded 80.2% sensitivity and 75.5% specificity, confirming its clinical utility as a reliable non-invasive marker for identifying severe cases.

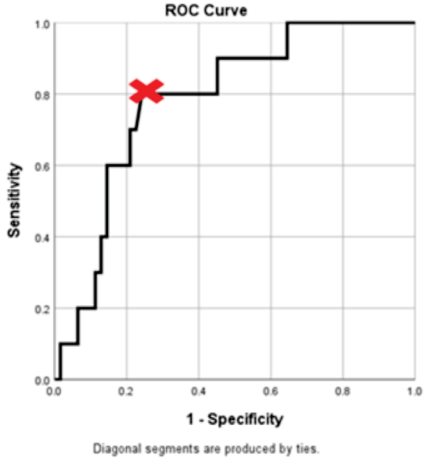

Figure 1: ROC Curve Showing Diagnostic Accuracy of CRP Levels for Predicting Severe Acute Cholecystitis (Grade III)

DISCUSSION

This cross-sectional study conducted among 72 patients at Ravindranath Tagore Medical College, Udaipur, examined the role of C-reactive protein (CRP) as a predictive biomarker for severity grading in acute cholecystitis (AC), based on the Tokyo Guidelines 2013.(TG13)[11] In the present study, median CRP levels increased significantly with disease severity: 22.75 mg/L (IQR 5.6–49.4) in Grade I, 54.70 mg/L (IQR 9.4–130.0) in Grade II, and 213.50 mg/L (IQR 118.0–250.23) in Grade III ($p = 0.009$), indicating a strong association between higher CRP values and advanced acute cholecystitis, consistent with findings from other cross-sectional studies.[12]

Receiver operating characteristic (ROC) curve analysis identified a CRP cut-off of 201.42 mg/L for predicting severe (Grade III) cholecystitis, yielding an area under the curve (AUC) of 0.785 ($p = 0.004$), sensitivity of 80.2%, and specificity of 75.5%. These values demonstrate the reliability of CRP as a diagnostic tool, comparable to previous studies.[13] CRP also demonstrated greater diagnostic precision than white blood cell (WBC) count, a trend that has been noted in other research as well.[14,15]

The average age in the present cohort was 52.7 ± 13.4 years, aligning with studies that reported peak prevalence of AC in the 40–70-year age group.[12,16] A female predominance (73.6%) was noted, consistent with other literature, although previous studies have reported no significant gender-based variation in CRP levels or disease severity.[14,17] Right upper quadrant (RUQ) pain was present in all patients (100%), affirming its status as a hallmark symptom of acute cholecystitis.[18] However, Murphy's sign was elicited in only 13.9% of cases, which is similar to earlier findings suggesting reduced sensitivity of this sign, particularly in elderly or critically ill patients.[19] RUQ tenderness was noted in 62.5% of cases, which aligns with earlier studies.[18,19]

Mild leukocytosis was observed, with a median WBC count of 9,135 cells/mm³, with an interquartile range (IQR) of 6,625–12,085 cells/mm³; however, CRP proved to be a more reliable indicator of disease severity than WBC. This has also been highlighted in multiple studies that suggest CRP's superior utility in this context.[14,15] Grade II cholecystitis was the most frequent presentation, occurring in 69.4% of patients. This pattern is consistent with recent evidence suggesting that moderate cases of AC are most common and often respond well to conservative therapy [20]. In the current study, 72.2% of patients were managed conservatively, consistent with TG13 recommendations [11] and prior reports that advocate for non-operative management to reduce surgical risks and complications[21]. Laparoscopic cholecystectomy was carried out in 26.4% of patients, reaffirming its role as the standard surgical approach worldwide for managing cholecystitis [22,23]. SOFA scores indicated no organ dysfunction (score 0) in 69.4% of cases, suggesting clinical stability in the majority of patients. This supports the utility of SOFA scoring in evaluating systemic involvement in acute cholecystitis [17,24]. Median CRP values rose with increasing SOFA score: 24.90 mg/L (IQR 5.8–100.2) for SOFA 0, 139.05 mg/L (IQR 26.8–276.0) for SOFA 1, 134.00 mg/L (IQR 57.5–220.0) for SOFA 2, and 207.00 mg/L (IQR 46.35–277.525) for SOFA 3 ($p = 0.017$), reflecting the link between systemic organ dysfunction and elevated CRP.

Interestingly, CRP levels were higher among conservatively treated patients (median 58.70 mg/L, IQR 12.36–196.50) compared to surgically managed patients (34.10 mg/L, IQR 9.95–111.00), although this difference was not statistically significant ($p = 0.45$). This inverse trend may be attributed to variability in surgical decision-making or timing of CRP assessment. Similar observations have been reported in earlier studies [12,25]. The CRP cut-off of 201.42 mg/L for predicting Grade III cholecystitis aligns closely with other reports, though some studies have proposed much lower thresholds (e.g., 40 mg/L), possibly due to differences in study populations or classification systems [12,26]. Additional support for CRP's prognostic value has been provided in recent findings demonstrating its usefulness in triaging patients and anticipating complications [27]. Nonetheless, the present study has several limitations. The relatively small sample size ($n = 72$), particularly the limited number of Grade III cases ($n = 10$), restricts the generalizability of the findings. Being a single-center study, there is a risk of selection bias. Furthermore, CRP levels were measured only once, limiting the ability to evaluate temporal changes. Despite excluding patients with known inflammatory comorbidities, some residual confounding factors cannot be ruled out. Future research should involve larger, multicenter cohorts and incorporate serial CRP measurements to better understand the biomarker's kinetics and prognostic implications.

CONCLUSION

CRP levels showed a significant association with acute cholecystitis severity per Tokyo Guidelines 2013. Higher CRP values correlated with advanced disease grades and organ dysfunction, with good predictive accuracy for severe cases (cut-off ≥201.42 mg/L). CRP outperformed WBC count in severity assessment and remains a practical tool for early risk stratification. Further multicenter studies are needed to confirm these findings.

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