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ISSN: 2663-9491 e-ISSN: 2789-6897

ORIGINAL ARTICLE

Estimating Acute Cholecystitis Severity Using C-Reactive Protein and ESR Levels

DOI: dx.doi.org

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Received: 07 Aug 2025
Accepted: 12 Aug 2025
Published: 27 Aug 2025

Published by:
Gopalganj Medical College, Gopalganj, Bangladesh

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ABSTRACT

Background: *Acute cholecystitis (AC) is a common inflammatory condition of the gallbladder, and timely severity assessment is crucial for appropriate management. While the Tokyo Guidelines (TG18) provide a framework for diagnosis and grading, they lack specific biomarker thresholds for severity estimation. This study explores the role of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) as potential predictors of disease severity.* ***Aim of the study:*** *To evaluate the association of CRP and ESR levels with the severity of acute cholecystitis and propose potential cut-off values for clinical application.* ***Methods & Materials:*** *A descriptive cross-sectional study was conducted on 130 patients diagnosed with acute cholecystitis between June 2023 and June 2025. Patients were classified into mild, moderate, or severe categories based on clinical, laboratory, and imaging findings. CRP and ESR levels were analyzed in relation to disease severity.* ***Result:*** *CRP and ESR levels were significantly associated with disease severity ($p<0.001$). All mild cases had CRP <1 mg/L, while all severe cases had CRP >6 mg/L. Mean CRP values were 0.646±0.231 mg/L (mild), 5.30±1.76 mg/L (moderate), and 13.78±4.48 mg/L (severe). ESR followed a similar trend: 14.76±3.54 mm/hr (mild), 36.78±2.35 mm/hr (moderate), and 47.45±2.97 mm/hr (severe). Ultrasound findings such as gallbladder wall thickening, common bile duct dilation, and bile spillage were also significantly associated with severity.* ***Conclusion:*** *CRP and ESR levels correlate strongly with the severity of acute cholecystitis and may serve as practical biomarkers for early risk stratification. These findings support their integration into routine diagnostic and prognostic evaluation, particularly in resource-limited settings.*

Keywords: *Acute cholecystitis, C-reactive protein, Erythrocyte sedimentation rate,*

(The Insight 2025; 8(1): 31-35)

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INTRODUCTION

Acute cholecystitis (AC) is one of the most common complications of gallstone disease and a leading cause of emergency hospital admissions for abdominal pain requiring surgical intervention[1]. Globally, gallstone disease affects approximately 10–20% of the adult population, with acute cholecystitis developing in up to 20% of symptomatic patients[2]. In Bangladesh, gallbladder disease has shown a rising trend, with hospital-based studies reporting a prevalence of 6–8% among adults, and acute cholecystitis accounting for a significant portion of gallstone-related admissions, especially among women aged 30–60 years[3]. Despite advances in diagnostic modalities and surgical techniques, early and accurate severity assessment of acute cholecystitis remains a key challenge for optimizing treatment decisions and improving patient outcomes[4]. The diagnosis and grading of acute cholecystitis were largely subjective and varied across institutions. The Tokyo Guidelines (TG), first proposed in 2007 and subsequently updated in 2013 and 2018, established internationally recognized diagnostic and severity grading criteria for acute cholecystitis to unify clinical practice and improve patient care[5]. These guidelines integrate clinical, laboratory, and radiological findings to improve diagnostic accuracy and guide therapeutic strategies[6]. According to the Tokyo Guidelines 2018 (TG18), the diagnosis of acute cholecystitis is based on a combination of local signs of inflammation e.g., Murphy's sign, right upper quadrant tenderness, systemic signs of inflammation e.g., fever, elevated white blood cell count, or elevated C-reactive protein [CRP], and imaging findings characteristic of

ISSN: 2663-9491 e-ISSN: 2789-6897

gallbladder inflammation[7]. Following diagnosis, the clinical severity is stratified into three grades: mild, moderate, and severe, based on clinical, laboratory, and organ dysfunction parameters[8]. While CRP is listed in the TG18 as part of the diagnostic workup, it is not formally included in the severity grading criteria. However, emerging evidence suggests that CRP, as a sensitive and dynamic acute-phase reactant, correlates well with the severity of inflammation in acute cholecystitis and can serve as a useful prognostic indicator[9]. Numerous studies have demonstrated that higher CRP levels are associated with complicated or severe cases, such as gangrenous cholecystitis, empyema, or perforation[10]. Despite this, the guidelines do not propose specific CRP cut-off values for grading severity, leaving clinicians without a standardized threshold to differentiate mild from moderate or severe disease[11]. Similarly, erythrocyte sedimentation rate (ESR), although less frequently used in acute settings due to its slower kinetics, may complement CRP in identifying prolonged or subacute inflammation[12]. Given the wide availability, low cost, and clinical utility of CRP and ESR, establishing their predictive value for assessing the severity of acute cholecystitis may enhance early risk stratification, particularly in low-resource settings[13]. This study aims to evaluate the role of CRP and ESR in estimating disease severity among patients with acute cholecystitis, with the goal of determining potential cut-off values that can support clinical decision-making alongside the Tokyo Guidelines criteria.

METHODS & MATERIALS

This descriptive cross-sectional study was conducted at the Department of Surgery, Khulna Medical College Hospital, Khulna, Bangladesh. The study was carried out over a period of two year, from June 2023 to June 2025. This study was designed as a diagnostic, observational cohort study aimed at evaluating the association between the severity of acute cholecystitis and levels of inflammatory markers, specifically CRP and ESR. The study was conducted in a clinical setting where all relevant laboratory and imaging assessments were performed as part of routine care. The study included total 130 patients with acute cholecystitis.

Inclusion Criteria

- Aged 18 years or older.
- Underwent serum CRP and ESR testing at the time of hospital admission.
- Diagnosed with acute cholecystitis based on clinical, laboratory, and ultrasonographic findings.

Exclusion Criteria

- Individuals with coexisting conditions known to influence inflammatory markers, such as diabetes mellitus, HIV, hepatitis, intestinal tuberculosis, or other immunocompromised states.
- Patients with histopathological findings suggestive of malignancy.
- Pregnant individuals.
- Patients with conditions that could confound CRP levels, such as acute pancreatitis or systemic infections.

Ethical Consideration

Approval was obtained from the Institutional Ethics Committee before the commencement of data collection. All participants were fully informed about the study's purpose, procedures, and any potential risks. Informed consent was obtained in written form. Confidentiality of patient information was maintained. As no experimental interventions were involved and only routine laboratory investigations were analyzed, the study posed minimal risk to participants.

Surgical Technique

Most patients underwent laparoscopic cholecystectomy under general anesthesia. The standard technique included the use of four ports (two 5 mm and two 10 mm) with visualization of Rouviere's sulcus and critical view of safety for identifying Calot's triangle. Cystic duct and artery were clipped, and the gallbladder was removed from the liver bed. In cases requiring open cholecystectomy, a right subcostal incision was made to facilitate gallbladder removal using electrocautery or harmonic scalpel. When indicated, cholangiography or common bile duct exploration was also performed.

Data collection

Medical records were reviewed to collect demographic data, including age, sex, and body mass index (BMI), as well as comorbidities. Laboratory investigations performed at initial presentation included complete blood count (hemoglobin and WBC), liver enzymes (ALT, AST), amylase, total bilirubin, CRP, and ESR levels. Radiological findings, including gallbladder wall thickness, common bile duct (CBD) diameter, number and size of gallstones, presence of impacted stones at the gallbladder neck, and bile spillage, were retrieved from ultrasound reports. The severity of acute cholecystitis was classified into mild (n=80), moderate (n=30), and severe (n=20) categories based on clinical, radiological, and surgical criteria.

Statistical Analysis

Data were entered and analyzed using SPSS version 26. Descriptive statistics were used to summarize the data. Categorical variables were presented as frequencies and percentages, while continuous variables were reported as mean ± standard deviation (SD). Associations between AC severity and categorical variables were analyzed using the Fisher's exact test or Chi-square test, as appropriate. A p-value less than 0.05 was considered statistically significant.

RESULT

The mean BMI was 25.7 ± 5.1 kg/m^2. Comorbidities were present in 24 patients (18.46%). The mean hemoglobin level was 12.5 ± 2.6 g/dL, and the average white blood cell count was $11.8 \pm 3.7 \times 10^3$/mL. Liver function parameters showed a mean total bilirubin of 1.56 ± 1.28 mg/dL, ALT of 50.6 ± 51.4 IU/L, and AST of 55.3 ± 61.7 IU/L (Table 1). Female (55.38%)

ISSN: 2663-9491 e-ISSN: 2789-6897

participants were more common than male (44.62%) participants (Figure 1). Mild cholecystitis was more common in younger age groups, particularly 31–40 years (37.5%) and 41–50 years (30%). Moderate and severe cases were more frequent in older patients, with 26.67% and 40% of moderate and severe cases, respectively, occurring in the 51–60 age group (Table 2). Table 3 shows that ultrasound findings showed significant associations with cholecystitis severity. Gallbladder wall thickening (>4 mm) was more prevalent in moderate (20%) and severe cases (30%) compared to none in mild cases (p=0.02). A dilated common bile duct (>6 mm) was observed in 26.67% of moderate and 40% of severe cases versus only 5% of mild cases (p=0.005). Multiple stones were more common in severe cholecystitis (50%) compared to mild (10%) (p=0.014). Larger stones (>1 cm) predominated in mild and moderate cases but were less frequent in severe cases (p=0.052). Impacted stones at the gallbladder neck were significantly associated with increasing severity (p=0.001), present in 50% of severe cases. Bile spillage was also strongly correlated with severity, occurring in 90% of severe and 33.33% of moderate cases but absent in all mild cases (p=0.001) (Table 3). All patients with mild cholecystitis had CRP levels below 1 mg/L. In moderate cases, 66.67% had CRP levels between 1–6 mg/L, while 33.33% had levels above 6 mg/L. All patients with severe cholecystitis had CRP levels greater than 6 mg/L. The mean CRP levels increased with severity: 0.646±0.231 mg/L in mild, 5.30±1.76 mg/L in moderate, and 13.78±4.48 mg/L in severe cases (Table 4). Among patients with mild cholecystitis, 87.5% had ESR levels between 14–18 mm/hour, and 12.5% had levels between 19–38 mm/hour. In moderate cases, 93.33% had ESR levels of 19–38 mm/hour, whereas 6.67% had levels of 39–50 mm/hour. All severe cases had ESR levels between 39–50 mm/hour. The mean ESR values increased with disease severity: 14.76±3.54 mm/hour in mild, 36.78±2.35 mm/hour in moderate, and 47.45±2.97 mm/hour in severe cholecystitis (Table 5).

Table – I: Baseline characteristics of study population (*n*=130)

Variables	Mean±SD
Comorbidity, n(%)	24 (18.46)
BMI (kg/m2)	25.7 ± 5.1
Hemoglobin (gr/dl)	12.5 ± 2.6
WBC x 103 mL	11.8 ± 3.7
Total bilirubin (mg/dl)	1.56 ± 1.28
ALT (IU/L)	50.6 ± 51.4
AST (IU/L)	55.3 ± 61.7

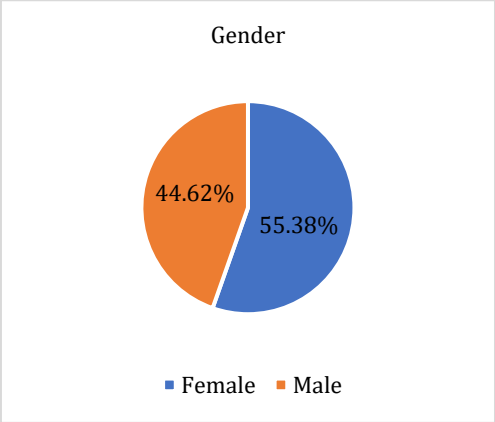

Figure – 1: Distribution of patients by gender (*n*=130)

Table – II: Age distribution of participants (*n*=130)

Age (years)	Mild cholecystitis (n=80)		Moderate cholecystitis (n=30)		Severe cholecystitis (n=20)		P-value
	n	%	n	%	n	%	
<30	16	20.00	2	6.67	4	20.00	0.027
31-40	30	37.50	2	6.67	2	10.00	
41-50	24	30.00	12	40.00	4	20.00	
51-60	6	7.50	8	26.67	8	40.00	
>60	4	5.00	6	20.00	2	10.00	

Table – III: Association of grade of acute cholecystitis with USG findings (*n*=130)

USG	Mild cholecystitis (n=80)		Moderate cholecystitis (n=30)		Severe cholecystitis (n=20)		Total		P-value
	n	%	n	%	n	%	n	%	
Gall bladder wall thickness									
<4 mm	80	100	24	80	14	70	118	90.77	0.02
>4 mm	0	0	6	20	6	30	12	9.23	
CBD diameter									
<6 mm	76	95	22	73.33	12	60	110	84.62	0.005
>6 mm	4	5	8	26.67	8	40	20	15.38	
Number of stone									
Single	72	90	26	86.67	10	50	108	83.08	0.014
Multiple	8	10	4	13.33	10	50	22	16.92	
Size of stone									
<1 cm	8	10	2	6.67	8	40	18	13.85	0.052
>1 cm	72	90	28	93.33	12	60	112	86.15	
Impacted stone at neck of GB									

ISSN: 2663-9491 e-ISSN: 2789-6897

Absent	80	100	26	86.67	10	50	116	89.23	0.001
Present	0	0	4	13.33	10	50	14	10.77	
Bile spillage									
Absent	80	100	20	66.67	2	10	102	78.46	0.001
Present	0	0	10	33.33	18	90	28	21.54	

Table – IV: Association of grade of acute cholecystitis with CRP (*n*=130)

CRP (mg/l)	Mild cholecystitis (n=80)		Moderate cholecystitis (n=30)		Severe cholecystitis (n=20)		P-value
	n	%	n	%	n	%	
<1	80	100.00	0	0.00	0	0.00	0.001
1-6	0	0.00	20	66.67	0	0.00	
>6	0	0.00	10	33.33	20	100.00	
Mean±SD	0.646±0.231		5.300±1.76		13.78±4.48		

Table – V: Association of grade of acute cholecystitis with ESR (*n*=130)

Serum ESR (mm/hour)	Mild cholecystitis (n=80)		Moderate cholecystitis (n=30)		Severe cholecystitis (n=20)		P-value
	n	%	n	%	n	%	
14-18	70	87.50	0	0.00	0	0.00	0.001
19-38	10	12.50	28	93.33	0	0.00	
39-50	0	0.00	2	6.67	20	100.00	
Mean±SD	14.76±3.54		36.78±2.35		47.45±2.97		

DISCUSSION

Acute cholecystitis is a common inflammatory condition of the gallbladder, often requiring timely diagnosis and severity assessment to guide treatment. Biomarkers like CRP and ESR have emerged as valuable tools for evaluating inflammation. This study aims to estimate the severity of acute cholecystitis using CRP and ESR levels, aiding in early risk stratification and management. The mean body mass index (BMI) was 25.7 ± 5.1 kg/m^2, which indicates that a significant portion of patients were overweight, a known risk factor for gallstone formation and subsequent cholecystitis. This aligns with findings from the CHOLECOVID study, which reported a mean BMI of 27.1 ± 5.3 kg/m^2 among AC patients, underscoring the association between higher BMI and gallbladder disease[14]. In this study, the mean hemoglobin level was 12.5 ± 2.6 g/dL, The white blood cell (WBC) count averaged 11.8 ± 3.7 × 10^3/mL, indicative of a mild leukocytosis commonly observed in inflammatory conditions like AC. This is consistent with the study by Zgheib et al., which found that WBC counts were significantly higher in patients with moderate or gangrenous cholecystitis compared to those with milder forms[15]. Liver function tests revealed elevated levels of total bilirubin (1.56 ± 1.28 mg/dL), alanine aminotransferase (ALT) (50.6 ± 51.4 IU/L), and aspartate aminotransferase (AST) (55.3 ± 61.7 IU/L). These elevations may reflect biliary obstruction or hepatic inflammation associated with AC. Zgheib et al. reported similar findings, with mean total bilirubin levels of 1.82 mg/dL, ALT of 110.9 IU/L, and AST of 164.4 IU/L in patients with AC and concomitant common bile duct stones (CBDS), that highlights the impact of biliary obstruction on liver enzymes[15]. In our study of acute cholecystitis patients, most participants were middle-aged with the 41–50 age. Females slightly outnumbered males (55.38%). Although no significant association was found between gender and disease severity, older age was linked to more severe cholecystitis (p=0.02). These findings align with those of Gurbulak et al., who reported a female predominance and increasing severity with age (p<0.05)[16]. Similar age trends were noted by Muhammad et al. (mean age 40.32 years, 75% female) [17], Sakalar et al. (mean age 59.87 years, severity correlated with age but not gender)[18], and Park et al., who observed that patients with more severe disease were significantly older (p<0.05)[19]. The Tokyo Guidelines highlight key USG indicators of acute cholecystitis (AC), including probe tenderness in the area of gall bladder, GB wall thickness >4 mm, enlarged gall bladder, impacted gall stones, presence of debris or pericholecystic fluid collection and sonolucent layer in GB wall[20]. In our study, USG was performed in all cases. We observed GB wall thickening (>4 mm) in 9.23%, CBD dilation (>6 mm) in 15.38%, multiple stones in 16.92%, impacted stones at the GB neck in 10.77%, and bile spillage in 21.54%. Most stones (86.15%) were >1 cm. Significant associations were found between AC severity and GB wall thickening, CBD dilation, multiple and impacted stones, and bile spillage (p<0.05), though stone size was not significantly associated (p>0.05). Supporting studies reported GB wall thickening in 47.3%, multiple stones in 81.1%, and CBD dilation in 20.3% of cases[21]. Indar et al. also found USG findings correlated with moderate AC severity (p<0.05)[22]. Another study noted increasing abnormal USG features with severity but without statistical significance[23]. According to the Tokyo Guidelines, CRP is used for diagnosing AC, but not for grading its severity. In our study, all severe cases had CRP >6 mg/L, while mild cases had CRP <1 mg/L. The mean CRP levels were 0.646 mg/L (mild), 5.30 mg/L (moderate), and 13.78 mg/L (severe), showing a significant correlation with disease severity (p<0.05). ESR, an acute-phase reactant, has limited clarity in diagnosing and grading AC. According to our study, higher ESR levels significantly associated with increased disease severity (p<0.05). ESR ranged from 14–18 mm/hr in 53.85% of cases, 19–38 mm/hr in 29.23%, and 39–50 mm/hr

in 16.92%. Our results from CRP and ESR are comparable with the findings of Gurbulak et al.[24]. Despite these findings, ESR is a non-specific marker influenced by many conditions, such as infections, autoimmune diseases, and pregnancy. Our results suggests that ESR increases with inflammatory burden, although its diagnostic accuracy is limited.

Limitations of the study:

- The cross-sectional design did not allow for evaluation of long-term outcomes such as complications, recurrence, or mortality.
- Although exclusion criteria were applied, other unmeasured comorbid conditions might have influenced CRP and ESR levels, potentially introducing bias.
- Severity classification relied on clinical and imaging findings without histopathological confirmation, which may lead to interobserver variability.

CONCLUSION

CRP and ESR levels show a clear and statistically significant correlation with the clinical severity of acute cholecystitis. CRP levels below 1 mg/L were consistently associated with mild disease, while values exceeding 6 mg/L strongly predicted severe inflammation. Similarly, higher ESR levels aligned with increasing severity grades. These markers, due to their accessibility and cost-effectiveness, can be valuable adjuncts to clinical and radiological assessment, especially in resource-limited settings. Future studies with larger sample sizes and multicenter participation are recommended to validate these cut-off values and further refine severity prediction tools for acute cholecystitis.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee.

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