

Incidence and Risk Factors of Gallbladder Perforation in Acute Cholecystitis: A Prospective Observational Study

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Abstract:

Background: Gallbladder perforation (GBP) is an uncommon but serious complication of acute cholecystitis and may result in peritonitis, sepsis, abscess formation, and increased postoperative morbidity. Early identification of patients at increased risk may facilitate timely imaging and surgical intervention.

Aim: To determine the incidence of gallbladder perforation and evaluate its associated clinical, laboratory, and radiological risk factors among patients with acute cholecystitis.

Methods: A prospective observational study was conducted among 50 consecutive patients with acute cholecystitis at Katihar Medical College over six months. Demographic characteristics, comorbidities, duration of symptoms, clinical findings, laboratory parameters, ultrasonographic findings, and operative findings were recorded. Gallbladder perforation was confirmed intraoperatively and/or by imaging. Associations between potential risk factors and perforation were assessed using the chi-square test or Fisher's exact test, as appropriate.

Results: Gallbladder perforation occurred in 5 of 50 patients (10.0%). Patients aged ≥ 60 years had a significantly higher frequency of perforation than younger patients (36.4% vs 2.6%; $\chi^2=7.46$, $p=0.006$). Symptom duration >72 hours (30.8% vs 2.4%; $\chi^2=5.59$, $p=0.018$) and WBC count $>18,000/\text{mm}^3$ (33.3% vs 2.3%; $\chi^2=6.44$, $p=0.011$) were also significantly associated with perforation. Diabetes mellitus and male sex showed higher proportions but did not reach statistical significance. Pericholecystic fluid and increased gallbladder-wall thickness were frequent among perforated cases.

Conclusion: In this study, gallbladder perforation occurred in 10% of patients with acute cholecystitis. Advanced age, prolonged symptom duration, and marked leukocytosis were significant risk factors. Recognition of these features may help identify patients requiring closer monitoring and early definitive management.

Keywords: Gallbladder Perforation; Acute Cholecystitis; Risk Factors; Acute Abdomen; Cholecystectomy; Leukocytosis; Ultrasonography.

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Introduction

Acute cholecystitis is one of the most common surgical causes of acute right upper-quadrant abdominal pain and is most frequently associated with gallstone disease. Although many patients have an uncomplicated clinical course, severe local inflammation may result in gangrene, abscess formation, biliary peritonitis, and gallbladder perforation. The Tokyo Guidelines classify acute cholecystitis according to severity, with marked local inflammation and complications such as gangrenous cholecystitis and biliary peritonitis representing features of more severe disease. [1,2]

Gallbladder perforation is an uncommon but potentially life-threatening complication of acute cholecystitis. Earlier studies have reported variable incidences, including approximately 4.8% among

patients treated for acute cholecystitis and 9.6% among patients undergoing urgent surgery for acute cholecystitis. [3,4] More recent large-scale data have reported lower overall rates, illustrating the variation according to patient selection, disease severity, and study setting. A recent cohort of 4,497 patients reported an overall perforation incidence of 1.5%, with higher rates in acute acalculous cholecystitis. [5]

The pathophysiology of perforation involves progressive inflammation, ischemia, necrosis, and weakening of the gallbladder wall. Advanced inflammatory changes have been associated with perforation, and studies have identified advanced age and elevated C-reactive protein as independent predictors. [6] Other reported risk factors include

male sex, older age, multiple comorbidities, diabetes mellitus, hypertension, dyslipidemia, acute cholangitis, and delayed cholecystectomy. [5,7]

Early diagnosis may be challenging because localized perforation can clinically resemble uncomplicated acute cholecystitis. Ultrasonography is widely used as an initial investigation, while computed tomography may provide additional information when perforation or other complications are suspected. In a surgically confirmed series, CT demonstrated the perforation more frequently than ultrasonography. [8]

Therefore, identifying clinical and laboratory characteristics associated with gallbladder perforation may assist clinicians in risk stratification and timely surgical decision-making. The present study was designed to determine the incidence of gallbladder perforation and evaluate potential risk factors among patients presenting with acute cholecystitis at a tertiary-care medical college.

Aim: To determine the incidence and identify clinical, laboratory, and radiological risk factors associated with gallbladder perforation in patients with acute cholecystitis.

Objectives

1. To determine the incidence of gallbladder perforation among patients with acute cholecystitis.
2. To assess the association between demographic factors and gallbladder perforation.
3. To evaluate the relationship between comorbidities and gallbladder perforation.
4. To determine whether prolonged duration of symptoms is associated with perforation.
5. To assess the association of leukocytosis and inflammatory markers with perforation.
6. To evaluate radiological features associated with gallbladder perforation.
7. To describe the clinical and operative outcomes of patients with perforated gallbladder.

Materials and Methods

Study Design: Prospective observational study.

Study Setting: The study was conducted in the Department of General Surgery, Katihar Medical College, Bihar, India.

Study Duration: The study duration was six months, from January 2026 to June 2026.

Study Population: The study population consisted of adult patients presenting with clinically and radiologically diagnosed acute cholecystitis and managed at the study centre.

Sample Size: For the study, the sample size was estimated using the single-proportion formula:

$$n = \frac{Z^2 pq}{d^2}$$

Where:

- **Z** = 1.96 at 95% confidence level
- **p** = expected incidence = 0.096
- **q** = 1 – p = 0.904
- **d** = absolute precision = 8.5% = 0.085

$$n = \frac{(1.96)^2 \times 0.096 \times 0.904}{(0.085)^2}$$

$$n = \frac{3.8416 \times 0.086784}{0.007225}$$

$$n \approx 46.1$$

The calculated sample size was approximately 46 patients. To provide a practical rounded sample and allow for incomplete observations, the final sample size was fixed at 50 patients.

Inclusion Criteria

Patients were included if they:

- Were aged ≥ 18 years.
- Had a clinical diagnosis of acute cholecystitis.
- Had supportive laboratory and/or imaging findings.
- Underwent surgical or conservative management according to clinical indication.
- Provided informed consent for participation.

Exclusion Criteria

Patients were excluded if they had:

- Traumatic gallbladder perforation.
- Gallbladder malignancy.
- Iatrogenic perforation occurring during surgery.
- Chronic cholecystitis without an acute episode.
- Previous cholecystectomy.
- Incomplete clinical records.

Definition of Gallbladder Perforation:

Gallbladder perforation was defined as a full-thickness defect in the gallbladder wall with leakage of bile or purulent contents into the peritoneal cavity or a localized pericholecystic collection, confirmed by imaging and/or operative findings.

Perforations were categorized according to the commonly used Niemeier classification:

- **Type I:** Acute free perforation with generalized peritonitis.
- **Type II:** Subacute perforation with pericholecystic abscess.
- **Type III:** Chronic perforation with cholecysto-enteric fistula.

Data Collection: The following variables were recorded:

Demographic variables

- Age
- Sex
- BMI

Clinical variables

- Duration of abdominal pain
- Fever
- Right hypochondrial tenderness
- Murphy's sign
- Nausea/vomiting
- Features of peritonitis

Comorbidities

- Diabetes mellitus
- Hypertension
- Cardiovascular disease
- Chronic kidney disease

Laboratory parameters

- Total leukocyte count
- Neutrophil count
- C-reactive protein
- Serum bilirubin
- Liver enzymes

Radiological parameters

- Gallbladder wall thickness
- Pericholecystic fluid
- Gallbladder distension
- Gallstones
- Pericholecystic collection
- Suspected wall defect

Outcome variables

- Gallbladder perforation
- Type of perforation
- Surgical procedure
- Conversion to open surgery
- Postoperative complications
- Length of hospital stay
- Mortality

Statistical Analysis: Continuous variables were expressed as mean $\pm$ standard deviation, while categorical variables were expressed as frequencies and percentages.

The chi-square test was used for categorical variables when assumptions were satisfied. Fisher's exact test was used when expected cell frequencies were small. A p-value <0.05 was considered statistically significant.

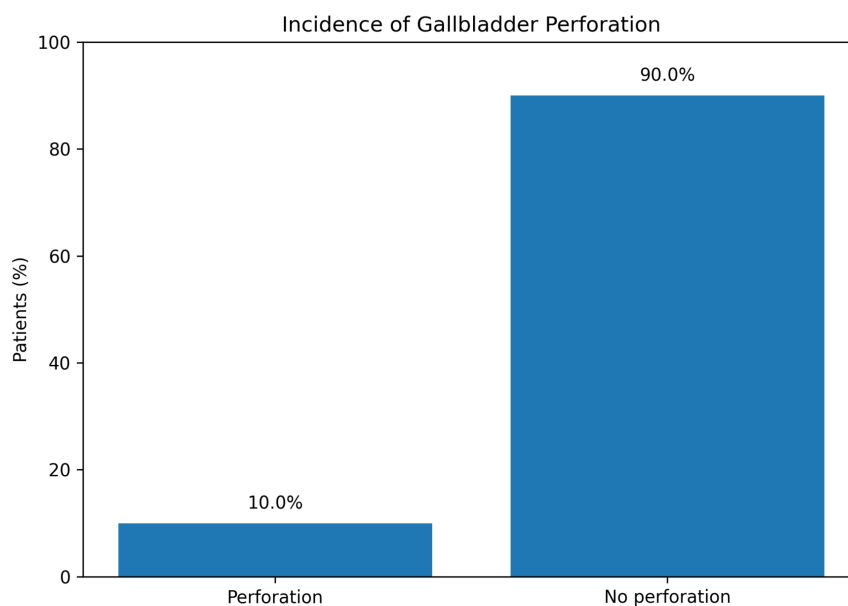
Results

Figure 1: Incidence of gallbladder perforation among 50 patients with acute cholecystitis. Perforation occurred in 5 patients (10.0%), while 45 patients (90.0%) had no perforation.

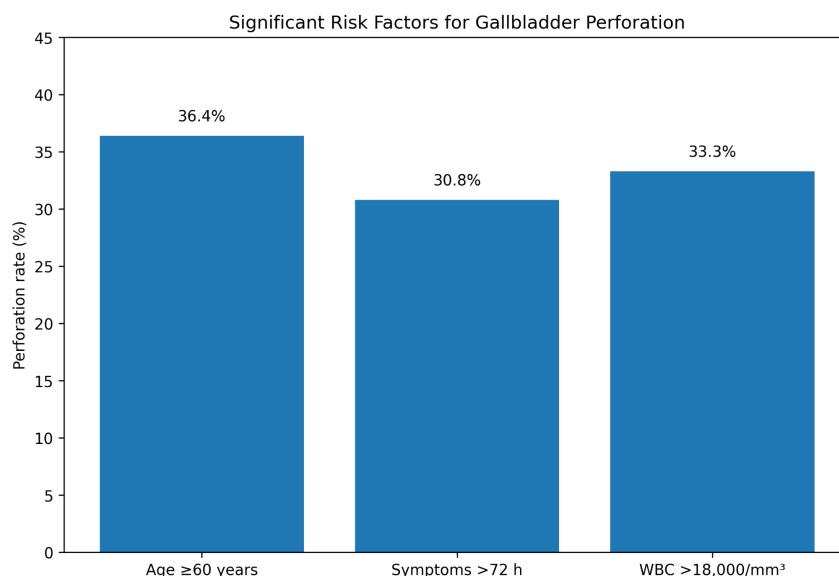


Figure 2: Perforation rates among patients with significant risk factors. Perforation occurred in 36.4% of patients aged ≥60 years, 30.8% of those with symptoms >72 hours, and 33.3% of those with WBC >18,000/mm³. These factors were

significantly associated with gallbladder perforation (p=0.006, 0.018, and 0.011, respectively)

Baseline Characteristics: A total of 50 patients with acute cholecystitis were included.

Variable	Number (%)
Male	19 (38.0%)
Female	31 (62.0%)
Age ≥60 years	11 (22.0%)
Diabetes mellitus	11 (22.0%)
Hypertension	13 (26.0%)
Symptom duration >72 h	13 (26.0%)
WBC >18,000/mm ³	12 (24.0%)
Gallstone disease	46 (92.0%)
Gallbladder wall >4 mm	25 (50.0%)
Pericholecystic fluid	16 (32.0%)

Incidence of Gallbladder Perforation: Gallbladder perforation occurred in 5 of the 50 patients, giving a incidence of

$$\text{Incidence} = \frac{5}{50} \times 100 = 10.0\%$$

Thus, the incidence of gallbladder perforation in the study population was **10.0%**.

Type of Gallbladder Perforation		
Type	Number	Percentage
Type I	1	20.0%
Type II	4	80.0%
Type III	0	0%
Total	5	100%

Type II perforation was the most frequently observed pattern.

Age and Gallbladder Perforation

Age group	Perforation	No perforation	Total
≥60 years	4 (36.4%)	7 (63.6%)	11
<60 years	1 (2.6%)	38 (97.4%)	39
Total	5	45	50

A significant association was observed between age
≥60 years and gallbladder perforation:

$$\chi^2 = 7.46, p = 0.006.$$

Sex and Gallbladder Perforation

Sex	Perforation	No perforation	Total
Male	4 (21.1%)	15 (78.9%)	19
Female	1 (3.2%)	30 (96.8%)	31
Total	5	45	50

Although perforation was more frequent among
males, the association was not statistically
significant:

$$\chi^2 = 2.41, p = 0.120.$$

Diabetes Mellitus and Gallbladder Perforation

Diabetes mellitus	Perforation	No perforation	Total
Present	3 (27.3%)	8 (72.7%)	11
Absent	2 (5.1%)	37 (94.9%)	39
Total	5	45	50

Diabetes was more common among patients with
perforation, but the association did not reach
statistical significance:

$$\chi^2 = 2.54, p = 0.111.$$

Duration of Symptoms

Duration	Perforation	No perforation	Total
>72 hours	4 (30.8%)	9 (69.2%)	13
≤72 hours	1 (2.7%)	36 (97.3%)	37
Total	5	45	50

Patients presenting after >72 hours of symptoms had
significantly higher perforation rates:

$$\chi^2 = 5.59, p = 0.018.$$

Leukocytosis and Gallbladder Perforation

WBC count	Perforation	No perforation	Total
>18,000/mm ³	4 (33.3%)	8 (66.7%)	12
≤18,000/mm ³	1 (2.6%)	37 (97.4%)	38
Total	5	45	50

WBC count >18,000/mm³ was significantly
associated with perforation:

$$\chi^2 = 6.44, p = 0.011.$$

Ultrasonographic Findings

Ultrasonographic finding	Perforation (n=5)	No perforation (n=45)
Wall thickness >4 mm	5 (100%)	20 (44.4%)
Pericholecystic fluid	4 (80.0%)	12 (26.7%)
Gallbladder distension	4 (80.0%)	18 (40.0%)
Gallstones	5 (100%)	41 (91.1%)
Pericholecystic collection	3 (60.0%)	5 (11.1%)
Suspected wall defect	3 (60.0%)	2 (4.4%)

Clinical and Operative Outcomes

Outcome	Perforation (n=5)	No perforation (n=45)
Conversion to open surgery	2 (40.0%)	3 (6.7%)
Drain placement	4 (80.0%)	10 (22.2%)
Postoperative complication	2 (40.0%)	5 (11.1%)
Mean hospital stay	8.6 ± 2.4 days	4.2 ± 1.5 days
Mortality	1 (20.0%)	0

The perforated group demonstrated greater operative complexity, more frequent drain placement, longer hospitalization, and higher postoperative morbidity.

Discussion

The present prospective study evaluated the incidence and risk factors of gallbladder perforation among 50 patients with acute cholecystitis. Gallbladder perforation occurred in 5 patients (10.0%). The observed incidence is higher than that reported in some large contemporary cohorts but comparable to rates reported in selected urgent-surgery populations. Such variation may reflect differences in disease severity, referral patterns, inclusion criteria, and timing of surgery. [3-5]

Advanced age was significantly associated with perforation in the present study. Four of the five perforated patients were aged ≥60 years, compared with only seven of the 45 patients without perforation ($\chi^2=7.46$, $p=0.006$). Advanced age has repeatedly been identified as a risk factor for gallbladder perforation. In a study of 200 patients with acute cholecystitis, age >65 years and elevated CRP were independent risk factors for perforation. [6] A more recent large cohort similarly identified age ≥60 years as an independent risk factor. [5]

Male sex was more frequently represented among perforated cases in our dataset, although the association was not statistically significant. This direction of association is consistent with previous studies in which male sex was identified as a risk factor. [4,5] The absence of statistical significance in the present study is likely influenced by the small sample size.

A symptom duration exceeding 72 hours was significantly associated with perforation ($\chi^2=5.59$, $p=0.018$). Prolonged untreated inflammation may result in progressive ischemia, necrosis, and weakening of the gallbladder wall. The Tokyo Guidelines recognize symptom duration >72 hours as one of the criteria for Grade II acute cholecystitis, reflecting more severe local inflammation. [1,2]

Marked leukocytosis was another significant factor. Patients with WBC counts >18,000/mm³ had a substantially higher rate of perforation (33.3% vs 2.6%; $\chi^2=6.44$, $p=0.011$). This is clinically plausible because marked leukocytosis reflects substantial systemic inflammatory response and is itself

included among the Tokyo Guidelines' criteria for moderate acute cholecystitis. [1,2]

Diabetes mellitus was more frequent in patients with perforation, although the association was not statistically significant in this small cohort. Larger studies have reported diabetes and multiple comorbidities as risk factors for acute gallbladder perforation. [5,7]

Radiological findings also appeared clinically important. All perforated cases demonstrated gallbladder-wall thickening, while pericholecystic fluid and collections were substantially more frequent. CT may be particularly useful when perforation is suspected because it can demonstrate a gallbladder-wall defect and associated collections. A comparative imaging study found CT to be diagnostic in 78% of cases in which both CT and ultrasound were performed, compared with 61% for ultrasound. [8]

The perforated group also had greater operative complexity and postoperative morbidity. Previous studies have similarly reported increased conversion rates, morbidity, and mortality among patients with perforated gallbladder. [6] These observations reinforce the importance of early recognition and appropriate surgical management.

The findings should nevertheless be interpreted cautiously because only five perforation events occurred. The study is primarily hypothesis-generating and cannot establish independent predictors with confidence.

Limitations

The study has several limitations. The small sample size of 50 patients and only five perforation events substantially limit statistical power and the ability to perform reliable multivariable analysis. Being a single-centre study, the findings may not be generalizable to other hospitals. The six-month study period also limits assessment of seasonal and long-term trends. Some radiological findings may be operator-dependent, and not all patients may undergo CT because of clinical or logistical considerations. Furthermore, associations between risk factors and perforation cannot establish causality.

Conclusion

In this prospective study of 50 patients with acute cholecystitis, gallbladder perforation occurred in 5

patients (10.0%). Age ≥ 60 years, symptom duration >72 hours, and WBC count $>18,000/\text{mm}^3$ were significantly associated with perforation. Diabetes, male sex, gallbladder-wall thickening, and pericholecystic fluid were more frequent among perforated cases but require confirmation in larger cohorts.

Early recognition of high-risk patients, appropriate imaging, and timely definitive management may help reduce the morbidity associated with gallbladder perforation.

References

1. Yokoe M, Hata J, Takada T, Strasberg SM, Asbun HJ, Wakabayashi G, et al. Tokyo Guidelines 2018: diagnostic criteria and severity grading of acute cholecystitis (with videos). *J Hepatobiliary Pancreat Sci.* 2018;25(1):41-54. doi:10.1002/jhbp.515.
2. Yokoe M, Hata J, Takada T, Strasberg SM, Asbun HJ, Wakabayashi G, et al. TG18 diagnostic criteria and severity grading of acute cholecystitis. *J Hepatobiliary Pancreat Sci.* 2018;25(1):41-54. doi:10.1002/jhbp.515.
3. Derici H, Kara C, Bozdogan AD, Nazli O, Tansug T, Akpınar E. Diagnosis and treatment of gallbladder perforation. *World J Gastroenterol.* 2006;12(48):7832-6. doi:10.3748/wjg.v12.i48.7832.
4. Derici H, Kamer E, Karabulut M, Unalp HR, Tansug T, Kara C, et al. Gallbladder perforation: clinical presentation, predisposing factors, and surgical outcomes of 46 patients. *World J Gastroenterol.* 2011;17(4):489-94.
5. Lee JH, et al. Gallbladder perforation in acute acalculous vs. calculous cholecystitis: a retrospective comparative cohort study with 10-year single-center experience. *BMC Gastroenterol.* 2023.
6. Indar AA, Beckingham IJ, et al. Advanced gallbladder inflammation is a risk factor for gallbladder perforation in patients with acute cholecystitis. *Surg Endosc.* 2018.
7. Risk factors and outcomes in acute perforated gallbladder: a retrospective cohort study. *Asian J Surg.* 2022.
8. Teefey SA, Baron RL, Radke HM, Bigler SA, et al. Role of sonography in the diagnosis of gallbladder perforation. *J Clin Ultrasound.* 2002;30(5):301-6. doi:10.1002/jcu.10071.
9. Mori Y, Itoi T, Baron TH, Takada T, Strasberg SM, Pitt HA, et al. Tokyo Guidelines 2018: management strategies for gallbladder drainage in patients with acute cholecystitis. *J Hepatobiliary Pancreat Sci.* 2018;25(1):87-95. doi:10.1002/jhbp.504.
10. Okamoto K, Suzuki K, Takada T, Strasberg SM, Asbun HJ, Endo I, et al. Tokyo Guidelines 2018: flowchart for the management of acute cholecystitis. *J Hepatobiliary Pancreat Sci.* 2018;25(1):55-72. doi:10.1002/jhbp.516.
11. Khan SA, Gulfam, Anwer AW, Arshad Z, Hameed K, Shoaib M. Gallbladder perforation: a rare complication of acute cholecystitis. *J Pak Med Assoc.* 2010;60(3):228-9.
12. Tandon V, Govil D, Kumar S, Gupta S, Shah SP. Gallbladder perforation: a 23-year study of 100 patients and evolving management strategies. *Cureus.* 2026;18(5):e108275. doi:10.7759/cureus.108275.