



## Use of Tokiyo Classification in Acute Cholecystitis

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### ABSTRACT

**Objectives:** To determine frequency of severity of acute cholecystitis by using Tokyo Guidelines. **Study design:** Descriptive, cross sectional **study Settings:** Surgical Unit-2, Holy Family Hospital, Rawalpindi. Study duration: ovember 2024 to April 2025. **Materials & Methods:** Total 152 patients between the ages of 20 and 40 years who had acute Cholecystitis were included, regardless of gender. Chronic cholecystitis with CBD stones, cholecystectomy due to biliary acute pancreatitis, liver disease, and prior abdominal surgery were not included, nor GB polypoid lesion and GB cancer. Severity of AC was assessed by according to the TGs. Patients were managed as per hospital protocol. **Results:** The study's participants ranged in age from 40 to 80, with a mean age of  $47.95 \pm 9.20$  years. Ninety-six (63.16%) of the patients were between the ages of 41 and 60. With a male to female ratio of 1:1.5, 61 (40.13%) of the 152 patients were male and 91 (59.87%) were female. Mean BMI was  $27.36 \pm 2.94$  kg/m<sup>2</sup>. In our study, there were 88 (57.89%) Grade I, 46 (30.26%) were Grade II and 18 (11.85%) were Grade III in accordance with the TGs. **Conclusion:** This study found that the prevalence and severity of acute cholecystitis can be ascertained using the Tokyo Guidelines.

### INTRODUCTION

Around the world, acute cholecystitis (AC) is a prevalent condition that accounts for a significant percentage of hospital admissions and elective surgeries. AC, also called ascending cholangitis, is a serious medical condition caused by a bacterial infection of the biliary tract. Most instances are caused by obstruction of the common bile duct (CBD).<sup>1</sup> Partial or total biliary obstruction can result from a variety of processes, each of which has unique underlying risk factors that affect the morbidity and mortality of AC. It is estimated that the overall current mortality rate for AC is between 5.2% and 7.2%.<sup>2</sup>

Acute cholecystitis care begins with diagnosis, and early diagnosis should result in treatment and reduced mortality and morbidity. Accurately diagnosing both normal and unusual situations requires certain diagnostic criteria.<sup>3</sup> Imaging studies, laboratory testing, and clinical presentation are used to diagnose AC.<sup>4</sup> A number of attempts have been made to establish a consistent method for describing the severity of diseases by creating an evidence-based grading scale. The Tokyo guidelines established the first contemporary grading system for acute cholecystitis in 2007, and it underwent additional

revisions in 2013. According to the Tokyo recommendations, leukocytosis, local inflammatory response, and end-organ dysfunction are among the physiologic responses that determine whether acute cholecystitis is mild, moderate, or severe. Establishing diagnostic standards for acute cholecystitis in order to direct therapeutic treatment was the main objective of the Tokyo guidelines.<sup>5</sup> Mild GB inflammation is described by Grade I, moderate gallbladder inflammation by Grade II, and severe gallbladder inflammation—which is frequently linked to organ failure—by Grade III. Clinically, the TGs can be used to propose a therapy plan and categorize the severity of AC disease.<sup>6</sup>

According to a study that evaluated the severity of AC using the Tokyo Guidelines, 217 patients in total were split into three groups based on the severity of their conditions. According to the TGs, there were 146 (67.28%) Grade I, 51 (23.5%) Grade II, and 20 (9.22%) Grade III.<sup>7</sup>

This study sought to determine the severity of AC in compliance with the Tokyo Guidelines, given the variability and complexity of the grading system for acute cholecystitis. The study will enable the clinicians to assess the severity of disease. The early identification of severity

will help to formulate the treatment plan accordingly to reduce morbidity and mortality in patients with AC.

## MATERIALS AND METHODS

The Department of Surgery, Surgical Unit-2, Holy Family Hospital, Rawalpindi, conducted this descriptive cross-sectional study between November 2024 and April 2025. After being approved by the institutional ethical review committee, 152 patients who satisfied the inclusion criteria were selected via non-probability sequential sampling. The informed consent of each patient will be sought. Using the Tokyo Guidelines, a sample size of 152 cases was established with a 95% confidence level, a 4.6% margin of error, and a 9.2% frequency of grade III severity of acute cholecystitis.<sup>7</sup> All patients with acute cholecystitis aged 20–60 years were enrolled, regardless of gender. The diagnosis is made by combining ultrasonographic criteria (dimpled, thickened gallbladder, positive sonographic Murphy's sign, and pericholecystic fluid collection) with clinical criteria (WBC count > 10 × 10<sup>9</sup>/l, fever over 37, and soreness in the right upper quadrant). Chronic cholecystitis with CBD stones, liver illness, previous abdominal surgery, cholecystectomy for biliary acute pancreatitis, and GB polypoid lesion, or GB malignancy, were among the exclusion criteria.

Clinical information and demographics were documented. According to the operational definition, acute cholecystitis was identified. In accordance with the operational definition, the TGs evaluated the severity of AC. AC in a healthy adult with no organ failure and modest inflammatory alterations in the GB was classified as grade I (mild). AC that was associated with any of the following conditions was categorized as moderate, or grade II: symptoms that persist for more than 72 hours; a severe local inflammation (e.g., emphysematous cholecystitis, biliary peritonitis, hepatic abscess, gangrenous cholecystitis, or pericholecystic abscess); a palpable sore mass in the right upper abdomen quadrant; and an elevated WBC count (>18,000/mm<sup>3</sup>). AC that was linked to any one of the following organs or systems malfunctioning was classified as grade III (severe): hypotension that needs to be treated with dopamine over 5 ug/kg per minute or with any amount of norepinephrine; reduced consciousness; PaO<sub>2</sub>/FiO<sub>2</sub> ratio less than 300; creatinine greater than 2.0 mg/dL, oliguria; PT-INR > 1.5; and platelet count < 100,000/mm<sup>3</sup>. Patients were treated in accordance with hospital policy. Every piece of information was entered into a pre-made proforma.

SPSS V-25 was used to enter all of the data. For every quantitative variable, including age, weight, height, and BMI, the mean and standard deviation were determined. For every qualitative variable, including gender, comorbidities such diabetes, ischemic heart disease, COPD/asthma, chronic renal impairment, and the severity of AC, frequency and percentage were computed. To account for effect modifiers such age, gender, BMI, and comorbidities, stratification was employed. According to the post-stratification chi-square test, a significant P-value was defined as less than 0.05.

## RESULTS

The study's participants ranged in age from 40 to 80, with

a mean age of 47.95 ± 9.20 years. Ninety-six (63.16%) of the patients were between the ages of 41 and 60. With a male to female ratio of 1:1.5%, 61 (40.13%) of the 152 patients were male and 91 (59.87%) were female. On average, the BMI was 27.36 ± 2.94 kg/m<sup>2</sup>. Table I displays the distribution of patients with additional confounding variable.

In our study, there were 88 (57.89%) Grade I, 46 (30.26%) were Grade II and 18 (11.85%) were Grade III in accordance with the TGs (Figure 1). Stratification of severity of acute cholecystitis with respect to age, gender, BMI and comorbidities is shown in Table 2.

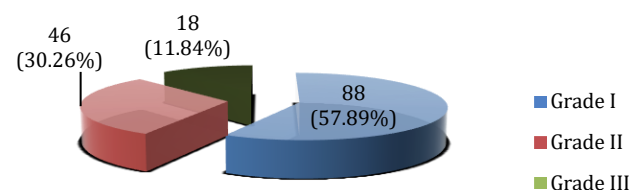
**Table 1**

*Distribution of Patients with Variables (n=152)*

Variables	Frequency	%age	
Age (years)	20-40	56	36.84
	41-60	96	63.16
Gender	Male	61	40.13
	Female	91	59.87
BMI (kg/m <sup>2</sup> )	≤25	67	44.08
	>25	85	55.92
DM	Yes	63	41.45
	No	89	58.55
IHD	Yes	36	23.68
	No	116	76.32
COPD/asthma	Yes	25	16.45
	No	127	83.55
CRF	Yes	17	11.18
	No	135	88.82

**Figure 1**

*Frequency of Severity of Acute Cholecystitis by Using Tokyo Guidelines (n=152).*



**Table 2**

*Stratification of Severity of Acute Cholecystitis with Respect to Age, Gender, BMI and Comorbidities.*

Variables	Grade I (n=88)	Grade II (n=46)	Grade III (n=18)	P-value	
Age (years)	40-60	38 (67.86%)	15 (26.79%)	03 (5.35%)	0.081
	61-80	50 (52.08%)	31 (32.29%)	15 (15.63%)	
Gender	Male	35 (57.38%)	18 (29.51%)	08 (13.11%)	0.923
	Female	53 (58.24%)	28 (30.77%)	10 (10.99%)	
BMI (kg/m <sup>2</sup> )	≤25	37 (55.22%)	23 (34.33%)	07 (10.45%)	0.607
	>25	51 (60.0%)	23 (27.06%)	11 (12.94%)	
DM	Yes	29 (46.03%)	25 (39.68%)	09 (14.29%)	0.043
	No	59 (66.29%)	21 (23.60%)	09 (10.11%)	
IHD	Yes	18 (50.0%)	12 (33.33%)	06 (16.67%)	0.453
	No	70 (60.34%)	34 (29.31%)	12 (10.34%)	
COPD/asthma	Yes	13 (52.0%)	08 (32.0%)	04 (16.0%)	0.724
	No	75 (59.06%)	38 (29.92%)	14 (11.02%)	
CRF	Yes	10 (58.82%)	05 (29.41%)	02 (11.76%)	0.996
	No	78 (57.78%)	41 (30.37%)	16 (11.85%)	

## DISCUSSION

Gallstones blocking the GB neck or cystic duct are typically the cause of AC, which is characterized as an inflammation of the GB. Gallstones are the most common cause, although there are other potential contributing factors as well, including ischemia, motility issues, and bacterial infections. The treatment options for AC, which resembles this clinical condition, include conservative measures or temporary drainage during the acute phase. However, surgical resection is the only way to treat a GB that has been harmed by inflammation.<sup>8</sup> Despite the prevalence of AC, prior to 2007, there were no set standards for clinical practice, diagnosis criteria, or severity assessment.<sup>9</sup>

In this study, we determined the frequency of severity of acute cholecystitis by using Tokyo Guidelines. Ninety-six (63.16%) of the patients were between the ages of 41 and 60. With a male to female ratio of 1:1.5%, 61 (40.13%) of the 152 patients were male and 91 (59.87%) were female. Studies by Rao et al., Herman et al., Hanif et al., Ganey et al., and Moreaux et al. revealed similar findings.<sup>10-13</sup> Of the patients, 55.92% had underlying obesity (BMI $\geq$ 25 kg/m<sup>2</sup>), and 41.42% had diabetes mellitus. These results aligned with what Palanivelu et al. and Liu et al. found in their investigation.<sup>14,15</sup>

In both clinical practice and research, TGs are utilized globally for the diagnosis and management of AC. According to the TGs, 88 (57.89%) of the participants in our study were in Grade I, 46 (30.26%) were in Grade II, and 18 (11.85%) were in Grade III. According to a study that evaluated the severity of AC using the Tokyo Guidelines (TGs), 217 patients in total were split into three groups based on the severity of their conditions. According to the TGs, there were 146 (67.28%) Grade I, 51 (23.5%) Grade II, and 20 (9.22%) Grade III.<sup>7</sup>

An further study<sup>16</sup> examined 112 patients with a male to female ratio of 1:3.5. 63.4% of patients had comorbidities, and the largest percentage of patients were in the 45–59 age range. Of the patients, only 21.4% had disturbed LFT. Using the Tokyo criteria, the severity of each patient's sickness was evaluated (TG 13). Mild illness affected 64 individuals (57.1%), moderate illness affected 43 patients (38.4%), and severe illness affected 5 patients (4.5%). Conservative care resulted in improvements for 95 patients, or 84.8% of the total. Open surgical intervention was required for three patients of the severe grade. One patient passed away during the recovery phase. The majority of patients spent an average of 3.8 days in the hospital, which is less than one week. The majority of mild-to-moderate illness patients were under 60. Females were more likely to have all severity levels.<sup>16</sup>

The distribution of TG severity grade was reported by Yokoe et al. as 36.4%, 46.0%, and 17.6% of patients were diagnosed with Grade I, II, or III, respectively.<sup>17</sup> This severity rating is comparable to that of the current study's AAC patients. Furthermore, they reported death rates from

AC that were very identical to those from AAC that were presented in our study. These findings align with those from a different study. Thus, it appears that the high AAC death rate reported in earlier research was exaggerated, and selection and publication bias may have been involved.<sup>18</sup>

AC starts off as a chemical irritation but is frequently made worse by intestinal bacterial invasion. While *Bacteroides fragilis* and *Clostridium* are frequently observed anaerobes, the aerobic bacteria that are most frequently found include *Escherichia coli*, *Streptococcus faecalis* and *Klebsiella*. Infections of mixed types are common. At least 60% of early-stage AC patients have bacteria, which is especially common in older people.<sup>19</sup>

Cholecystitis sequelae can be a major difficulty in clinical practice, even though acute cholecystitis often has a fair prognosis with prompt diagnosis and treatment. Increased mural ischemia or a subsequent bacterial infection can result in complications from acute cholecystitis. Significant morbidity and mortality are possible outcomes of complicated cholecystitis. Therefore, therapy and treatment approaches, such as early cholecystectomy or percutaneous gallbladder draining, depend on early diagnosis and detection.<sup>20</sup>

The preferred course of treatment for AC is laparoscopic cholecystectomy. Although the cholecystectomy alone carries a minimal surgical risk, percutaneous cholecystostomy or postponement of surgery may be necessary if the patient is unstable. A cholecystectomy can be successfully carried out within 48 to 72 hours of the commencement of the disease, during the congestive or edematous phase, therefore early surgery is advised for low-risk patients. The degree of the patient's overall health should be used to determine the surgical risk. GB drainage is a short-term, potentially life-saving procedure that can be used for individuals with severe GB inflammation and significant surgical risk. The patient may get elective surgery if their condition improves later. Like early surgery, GB draining can help avoid major AC problems.<sup>20,21</sup>

There are a number of intrinsic limitations to this study. First, as a guide for treatment, the TGs are often based on the clinical or inflammatory states of the patients. Consequently, even though the surgical condition is significant, this might not be as clinically relevant. Second, bile infections caused by carbapenem-resistant Enterobacteriaceae are presently a significant issue in Pakistan.

## CONCLUSION

This study concluded that Tokyo Guidelines can be used to determine the frequency of severity of acute cholecystitis. The early identification of severity will help to formulate the treatment plan accordingly to reduce morbidity and mortality in patients with AC.

## REFERENCES

- Adachi T, Eguchi S, Muto Y. Pathophysiology and pathology of acute cholecystitis: a secondary publication of the Japanese version from 1992. *J Hepatobiliary Pancreat Sci.* 2022;29:212-6. <https://doi.org/10.1002/jhbp.912>

- Barie P, Kao L, Moody M. Infection or inflammation: are uncomplicated acute appendicitis, acute cholecystitis, and acute diverticulitis infectious diseases? *Surg Infect.* 2023;24:99-111. <https://doi.org/10.1089/sur.2022.363>

3. Affan RA, Noureldin AW, Jr MA. Classification and Management of Acute Cholangitis. *Panam J Trauma, Crit Care Emerg Surg.* 2022;11(3):163-8. <https://doi.org/10.5005/jp-journals-10030-1401>
4. Sperna Weiland CJ, Busch CBE, Bhalla A. Performance of diagnostic tools for acute cholangitis in patients with suspected biliary obstruction. *J Hepatobiliary Pancreat Sci.* 2022;29(4):479–86. <https://doi.org/10.1002/jhbp.1096>
5. Fugazzola P, Cobianchi L, Di Martino M. Prediction of morbidity and mortality after early cholecystectomy for acute calculous cholecystitis: results of the S.P.Ri.M.A.C.C. study. *World J Emerg Surg.* 2023;18:20. <https://doi.org/10.21203/rs.3.rs-2370414/v1>
6. Adachi T, Eguchi S, Muto Y. Pathophysiology and pathology of acute cholecystitis: A secondary publication of the Japanese version from 1992. *J. Hepatobiliary Pancreat. Sci.* 2021;29:212–16. <https://doi.org/10.1002/jhbp.912>
7. Park TY, Do JH, Oh HC, Choi YS, Lee SE, Kang H, et al. Relationship between the tokyo guidelines and pathological severity in acute cholecystitis. *J Personalized Med.* 2023;13(9):1335-41. <https://doi.org/10.3390/jpm13091335>
8. Shridhar M, Shivakumar M, Satish HT, Nutan BV, Diggi A. Effectiveness of tokyoguidelines 2018 in the management of acute cholangitis and acute cholecystitis. *Int J Adv Res.* 2023;11(05):175-87. <https://doi.org/10.21474/ijar01/16866>
9. Morikawa T, Akada M, Shimizu M, Nishida Y, Izai J, Kajioka H, et al. Current status and therapeutic strategy of acute acalculous cholecystitis: Japanese nationwide survey in the era of the Tokyo guidelines. *J Hepatobiliary Pancreat Sci.* 2024;31:162–72. <https://doi.org/10.1002/jhbp.1401>
10. Rao KS, Meghavathu G, Rao S, Prasad T. Clinical study of gallstone disease and treatment options. *J Evo Med Dental Sci.* 2015;4(79):13841-8. <https://doi.org/10.14260/jemds/2015/1972>
11. Hermann RE. "Biliary disease in the aging patients". New York: Masson; 1983: 227-32. 16. Motiwala HG. Operative technique of cholecystectomy: A study of 250 cases. Macmillan India Limited, 1991;204.
12. Ganey JB, Johnson PA, Jr, Prillaman PE, McSwain GR. Cholecystectomy: clinical experience with a large series. *Am J Surg.* 1986;151(3):352-7. [https://doi.org/10.1016/0002-9610\(86\)90466-6](https://doi.org/10.1016/0002-9610(86)90466-6)
13. Moreaux J. Prospective study of open cholecystectomy for calculous biliary disease. *Br J Surg.* 1994;81(1):116-9. <https://doi.org/10.1002/bjs.1800810142>
14. Jayanthi V, Prasanthi R, Surendran R, Palanivelu C. Epidemiology of gall stone disease. *BJH.* 2020;5:786-9.
15. Liu CM, Tung TH, Chou P, Chen VTK, Hsu CT, Chien WS, et al. Clinical correlation of gallstone disease in a Chinese population in Taiwan: Experience at Cheng Hsin General Hospital. *World J Gastroenterol.* 2006;12(8):1281-98. <https://doi.org/10.3748/wjg.v12.i8.1281>
16. Iqbal A, Shah FH, Gani M, Naqash SH, Shah MA. Assessing the severity grading of acute cholecystitis according to Tokyo guidelines 2013 and outcome of conservative management. *Int J Res Med Sci.* 2025;13:1482-7. <https://doi.org/10.18203/2320-6012.ijrms20250969>
17. Yokoe M, Takada T, Hwang TL, Endo I, Akazawa K, Miura F, et al. Validation of TG13 severity grading in acute cholecystitis: Japan-Taiwan collaborative study for acute cholecystitis. *J Hepatobiliary Pancreat Sci.* 2017;24:338–45. <https://doi.org/10.1002/jhbp.457>
18. Asai K, Iwashita Y, Ohyama T, Endo I, Hibi T, Umezawa A, et al. Application of a novel surgical difficulty grading system during laparoscopic cholecystectomy. *J Hepatobiliary Pancreat Sci.* 2022;29:758–67. <https://doi.org/10.1002/jhbp.1068>
19. Janssen ERI, Hendriks T, Natroshvili T, Bremers AJA. Retrospective analysis of non-surgical treatment of acute cholecystitis. *Surg Infect (Larchmt).* 2020;21(5):428-32. <https://doi.org/10.1089/sur.2019.261>
20. Donohue SJ, Reinke CE, Evans SL, Jordan MM, Warren YE, Hetherington T, et al. Laparoscopy is associated with decreased all-cause mortality in patients undergoing emergency general surgery procedures in a regional health system. *Surg Endosc.* 2022;36:3822–32. <https://doi.org/10.1007/s00464-021-08699-1>
21. Cook MD, Karim SA, Jensen HK, Bennett JL, Burdine LJ, Bhavaraju A, et al. Percutaneous cholecystostomy tubes versus medical management for acute cholecystitis. *Am Surg.* 2022;88:828–33. <https://doi.org/10.1177/00031348211054567>