

A Clinical study of Acute Cholecystitis in the light of Tokyo Guidelines

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Abstract

Background: Acute Cholecystitis is a very common disease encountered in the Surgery department. Despite the relevant frequency of acute cholecystitis, the diagnosis and management of acute cholecystitis remains a major challenge. The Tokyo Guidelines provides diagnostic criteria and severity grading for acute cholecystitis.

Aims and Objectives: to study the clinical manifestations and to stratify the patients of Acute Cholecystitis according to their severity in the light of Tokyo Guidelines, and also to study about the different modalities of treatment.

Materials and Methods: A total of 100 patients with diagnosis of Acute Cholecystitis were included. A detailed history taking and clinical examination was performed in the suspected cases and necessary investigations were done. The Tokyo Guidelines were used to diagnose and confirm the cases of Acute Cholecystitis and the patients were categorized into Mild, Moderate and Severe groups on the basis of the Tokyo Guidelines. Early cholecystectomy was performed in 26 patients, whereas the other 74 patients were treated conservatively and postoperative complications were recorded and assessed. The patients undergoing conservative treatment were called for interval cholecystectomy after 4-6 weeks.

Results: The most common age group is between (41-50) years. There was female preponderance. Pain in the right

upper quadrant was present in all the patients. Positive Murphy's sign could be elicited in 92 patients. Fever was present in only 42 patients during initial presentation. Ultrasonography was done in all the cases which gave evidence of acute cholecystitis. Most of the patients presented within 5 days of onset of symptoms. The mean values of period of hospital stay increased with the increase in severity of the disease. There was a rise in CRP level with the increase in severity of acute cholecystitis. Majority of the patients could be categorized as mild and moderate severity whereas only 5% of cases were Severe. All the grade III cases were treated conservatively. Out of the total 43 case of Grade II, only 2 cases were operated. Out of the 24 case of Grade I, that underwent surgery, 6 developed wound infections in the postoperative period, while 1 had bleeding from drain site. Another 1 in this group had bile leak, which however resolved spontaneously. No mortality was recorded.

Summary and Conclusion: Acute cholecystitis is a common problem mostly arising out as a sequelae of gallstones¹. The Tokyo Guidelines has provided us with a pragmatic approach for the diagnosis and management of acute cholecystitis, which can be implemented as an institutional protocol to ensure uniformity in management of this common problem for the benefit of the patients.

Keywords: Acute cholecystitis, Tokyo guidelines, Murphy's sign

Introduction

Acute Cholecystitis is acute inflammation of the gall bladder that is usually precipitated by the presence of gall stones¹. Till 2006, there were no clearly defined criteria for the diagnosis and evaluation of this condition². The Tokyo Guidelines were published in 2007³. But later studies revealed that these guidelines were not sensitive enough to identify potentially life threatening cases of acute cholecystitis. So with an aim to remove such drawbacks, the guidelines were amended in 2013 (TG-13)⁴. The same criteria were adopted as it is in 2018 (TG-18)⁵ [Table 1]. These criteria also help us to grade the disease into mild, moderate and severe forms which enables better management of acute cholecystitis. With the advent of these criteria, it has become the need of the time to approach this commonly encountered surgical problem in a more scientific and practical way.

Table 1: TG 13/TG 18 diagnostic criteria for Acute Cholecystitis⁵

A. Local signs of inflammation etc.

(1) Murphy's sign, (2) RUQ mass/pain/tenderness

B. Systemic signs of inflammation etc.

(1) Fever, (2) elevated CRP, (3) elevated WBC count

C. Imaging findings

Imaging findings characteristic of acute cholecystitis

Suspected diagnosis: one item in A + one item in B

Definite diagnosis: one item in A + one item in B + C

CRP C-reactive protein, RUQ right upper abdominal quadrant, WBC white blood cell

Aims and Objectives

The present study is an attempt to study the clinical manifestations and to stratify the patients of Acute Cholecystitis according to their severity in the light of

Tokyo Guidelines, and also to study about the different modalities of treatment.

Materials and Methods

This study was conducted in the Department of General Surgery in Assam Medical College and Hospital. A total of 100 patients with diagnosis of Acute Cholecystitis were included in the study. A detailed history taking and clinical examination was performed in the suspected cases and necessary investigations were done. The Tokyo Guidelines were used to diagnose and confirm the cases of Acute Cholecystitis.

The patients with associated choledocholithiasis or pancreatitis, as well as other patients of acute abdomen without any evidence of gallstone disease were excluded from the purview of this study. Patients diagnosed as chronic cholecystitis were also excluded from the study. All the 100 patients received inpatient care in the hospital. Laboratory investigations, imaging studies including ultrasonography of abdomen was done in all the patients. The investigative findings along with clinical correlation was used to categorize the patients into Mild, Moderate and Severe groups on the basis of the Tokyo Guidelines [Table 2].

Table 2: TG18/TG13 severity grading for acute cholecystitis⁵

Grade III (severe) acute cholecystitis

“Grade III” acute cholecystitis is associated with dysfunction of any one of the following organs/systems:

1. Cardiovascular dysfunction: hypotension requiring treatment with dopamine ≥ 5 $\mu\text{g}/\text{kg}$ per min, or any dose of norepinephrine
2. Neurological dysfunction: decreased level of consciousness

3. Respiratory dysfunction: PaO_2/FiO_2 ratio <300
4. Renal dysfunction: oliguria, creatinine >2.0 mg/dl
5. Hepatic dysfunction: PT-INR >1.5
6. Hematological dysfunction: platelet count <100,000/mm³

Grade II (moderate) acute cholecystitis

“Grade II” acute cholecystitis is associated with any one of the following conditions:

1. Elevated WBC count (>18,000/mm³)
2. Palpable tender mass in the right upper abdominal quadrant
3. Duration of complaints >72 h^a
4. Marked local inflammation (gangrenous cholecystitis, pericholecystic abscess, hepatic abscess, biliary peritonitis, emphysematous cholecystitis)

Grade I (mild) acute cholecystitis

“Grade I” acute cholecystitis does not meet the criteria of “Grade III” or “Grade II” acute cholecystitis. It can also be defined as acute cholecystitis in a healthy patient with no organ dysfunction and mild inflammatory changes in the gallbladder, making cholecystectomy a safe and low-risk operative procedure.

During the study period, early cholecystectomy was performed in 26 patients, whereas the other 74 patients were treated conservatively with antibiotics, analgesics and correction of fluid and electrolytes. This group of patients were kept nil orally and nasogastric aspiration was done.

The patients were monitored on a regular basis and observed for any development of complications like empyema, impending perforation, jaundice, pancreatitis, septicaemia and other pulmonary complications.

Out of the total of 26 patients, laparoscopic cholecystectomy was done in 8 cases whereas the other 18 cases underwent open cholecystectomy. A drain was put in the subhepatic space in all the cases irrespective of the procedure. The patients were followed up postoperatively for the development of any complications like bleeding, wound infection, biliary leak, fever, subphrenic abscess, respiratory tract infections etc. All such complications were managed accordingly.

All the discharged patients were advised to come for follow up. The patients undergoing conservative treatment were called for interval cholecystectomy after 4-6 weeks. Patients undergoing surgical treatment were followed up for a period of 6 months.

Results and Observations

The results and observations in the present study were recorded and is displayed with the help of following tables and figure:

Age Incidence

Table 3: Distribution of cases among different age groups in the present study

Age Group	Number	Percentage (%)
Less than 20	6	6
20-30	13	13
31-40	28	28
41-50	31	31
51-60	11	11
61-70	8	8
More than 70	3	3

Acute cholecystitis was found to be more common in 41-50 years group in our study. The disease was found to be less common above 70 years of age.

Sex Distribution

Table 4: Sex Distribution in the present study

SEX	Number of patients	Percentage
Male	24	24
Female	76	76

Female preponderance was noted in the present study.76% of the total patients were females. Male female ratio was 1: 3.16

Presenting features

All the patients in the present study had pain in the right upper quadrant. Positive Murphy’s sign could be elicited in 92 patients. Fever was present in only 42 patients during initial presentation. Ultrasonography was done in all the cases which gave evidence of acute cholecystitis in the form of oedematous gall bladder wall, presence of gall stones, pericholecystic fluid. Laboratory tests like CRP and WBC count helped in establishing the diagnosis on the basis of Tokyo Guidelines.

Table 5: Common presenting features of acute cholecystitis

Presenting Features	Number of Patients
Pain in Right upper quadrant	100
Tenderness in Right upper quadrant	84
Mass in Right upper quadrant	18
Murphy’s sign	92
Fever	42

Duration of Symptoms

Table 6: Duration of symptoms among the patients in present study

Duration of symptoms(in days)	Number of patients	Percentage
Less than 5 days	52	52
5—7 days	32	32
More than 7 days	16	16

Majority of our patients reported within 5 days of onset of symptoms, whereas only 16% of the patients reported after 7 days.

Severity of acute cholecystitis

Table 7: Grades of severity of acute cholecystitis among the patients in the present study

Severity	Number of patients	Percentage
Grade I (Mild)	52	52
Grade II (Moderate)	43	43
Grade III (Severe)	5	5

In our study, majority of the patients could be categorized as mild and moderate severity whereas only 5% of cases were Severe. The more severe cases were found in the elderly age group.

Period of Hospital stay and its relation to severity of acute cholecystitis

Table 8: Relation between severity of cholecystitis and hospital stay of patients

Grade of severity	Mean duration of stay(days)	Minimum days	Maximum days
Grade I	7.23	5	10
Grade II	10.12	8	15
Grade III	14.8	12	20

We found that the mean values of period of hospital stay increased with the increase in severity of the disease. The mean duration of hospital stay for the mild patients was

7.23 days, but the severe category of patients had to stay for a longer time (14.8 days).

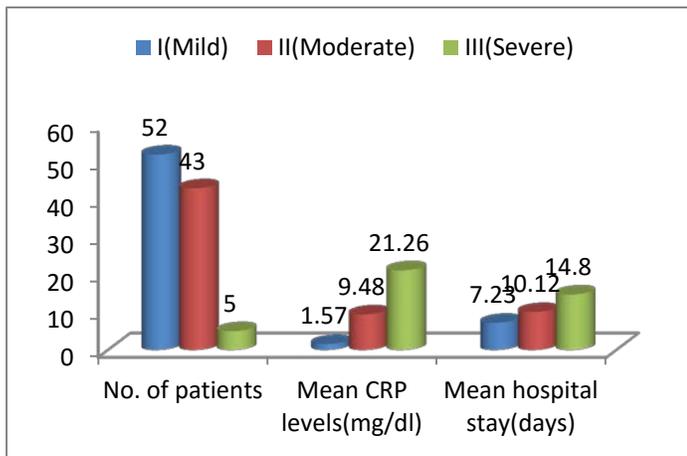
CRP level in relation to severity

Table 9: CRP levels in relation to severity among the patients in our present study

Severity Grade	Mean CRP value(mg/dl)	Standard Deviation
Grade I	1.57	0.68
Grade II	9.48	5.14
Grade III	21.26	4.87

The mean values of the CRP levels of the Grade I cases was found to be 1.57mg/dl, whereas Grade II and Grade III cases had mean values of 9.48mg/dl and 21.26 mg/dl respectively. The p value was <0.01 and so the data can be accepted as statistically significant. Thus, it was observed that there was a rise in CRP level with the increase in severity of acute cholecystitis.

Figure 1: Column chart showing number of patients in different grades of severity along with their relation with CRP level and mean hospital stay



Mode of Treatment

Most of the patients in the present study were treated conservatively. Out of the 26 patients, who were operated, laparoscopic cholecystectomy was done in 8 patients, whereas open cholecystectomy performed in 18 patients.

The remaining 74 patients received conservative treatment.

Complications

Table 10: Postoperative Complications in relation to severity

Grade of Severity	Total no of operated patients	No of patients with Major complications	No of patients with Minor complications	No of patients without any complications
Grade I	24	2	6	16
Grade II	2	0	0	2
Grade III	0	0	0	0

All the grade III cases were treated conservatively. Out of the total 43 case of Grade II, only 2 cases were operated and they were discharged without any complications.

Out of the 24 case of Grade I, that underwent surgery, 6 developed wound infections in the postoperative period, while 1 had bleeding from drain site. Another 1 in this group had bile leak, which however resolved spontaneously. No mortality was recorded in the present study.

Discussion

Acute cholecystitis is found to be more common after 40 years of age. Studies carried out by Sushant Kumar et al (2013) reported highest incidence of acute cholecystitis in the 3rd and 4th decades of life⁶. Dr Thomas H Lewis (2015) from the United States has also reported similar findings⁷. In our study of 100 patients, maximum incidence was found in 41-50 year age group (31%) and second common in 31-40 groups (28%) which is consistent with earlier studies.

Various studies have reported female preponderance of acute cholecystitis. Kala et al⁸ (1977), Indar et al⁹ (2002), Ali Nawaz Khan¹⁰ (2006), E.Fialkowski et al¹¹ (2008) and Sushant Kumar et al⁶ (2013) all have found higher incidence of the disease in females with average female to male ratio of 3:1. In our study, 76 females and

24 males out of the 100 cases, which is similar to these findings?

Pain in the right upper quadrant with or without tenderness is the most common presentation of acute cholecystitis. Positive Murphy’s sign could be elicited in 92% of cases in the present study which is consistent with Singer et al (1996) who had reported a sensitivity of 97%¹².Fever was present in only 42 patients which is similar to the finding of P J Gruber et al (1996) who has reported that 71% of acute cholecystitis patients to be afebrile¹³.

The diagnosis was confirmed on the basis of the criteria of the Tokyo Guidelines. Further they were also used to categorize the patients into Grade I (Mild), Grade II (Moderate) and Grade III (Severe).Out of the total 100 patients,52 patients were Mild,43 were Moderate and only 5 cases were Severe or Grade III .

Table 11: Severity of cholecystitis reported by various studies

Various Studies	Grade I (%)	Grade II (%)	Grade III (%)
Lee et al (1993) ¹⁴	68.5%	25.5%	5.9%
Yokoe et al (2012) ³	48.8%	45.8%	5.2%
Esin K Gurbulak et al(2015) ¹⁵	64.4%	32.2%	3.3%
Present Study	52.0%	43.0%	5.0%

Thus it is evident from the above table (Table: 10), that the findings observed in the present study are comparable to that of the previous authors.

In the present study, the maximum duration of hospital stay was observed among the Grade III patients (Mean— 14.8 days),by which it can be concluded that severe cases as categorized on the basis of Tokyo Guidelines had to stay longer in the hospital.

Esin K Gurbulak et al (2015) have reported mean CRP levels of 18.96 mg/l in Grade I, 133.51 mg/l in Grade II and 237.23 mg/l in Grade 3¹⁵. Yucel Yuzbasioglu (2016) from Turkey has reported mean CRP levels of 0.7mg/dl in Grade I, 1.5mg/dl in Grade II and 5.3 mg/dl in Grade III patients¹⁶. In the present study also a similar trend of increase in CRP level with increase in severity is observed.

The Tokyo Guidelines have recommended early cholecystectomy for Grade I cases, while the severe or Grade III cases had to be managed by some form of gall bladder drainage, in addition to medical treatment of associated abnormalities⁵. The Grade II cases are to be initially managed by medical treatment and those that do not respond to medical therapy would be subjected to gall bladder drainage. In the present series early cholecystectomy was performed in 24 out of the 52 grade I cases with good results. The other 28 cases presented late and hence treated conservatively and subsequently offered interval cholecystectomy as per institutional protocol. 2 cases in Grade II required intervention while all others responded to conservative treatment. All the 5 Grade III cases responded to medical therapy. Laparoscopic cholecystectomy was done in 8 cases whereas 18 cases underwent open cholecystectomy.

S.Duca et al (2003) has reported bile leakage as the most common major complication after gallbladder surgery¹⁷. Other complications reported are bleeding; wound infection and subhepatic abscess .K .A. Talpur et al (2010) has reported 1.67% to be the incidence of biliary leaks after cholecystectomy¹⁸. M Radunovic has reported bleeding (3.64%),biliary leaks (1.89%) and wound infection (0.94%) as the common complications¹⁹.In the present series, only 1 patient had bile leak and 1 had bleeding from drain site which is comparable with previous studies. The slightly higher incidence of wound

infection may be explained by the greater number of open cholecystectomy in the present series as opposed to laparoscopic cholecystectomy in the previous studies. There was no mortality in the present series.

Summary and Conclusion

Acute cholecystitis is a common problem mostly arising out as a sequelae of gallstones. The age old saying that “Gall stones are common in fatty fertile female of forty or fifty” also holds good for acute cholecystitis. Most of these patients present to the clinician with right upper quadrant pain. Tenderness in the area and more so a positive Murphy’s sign helps us to arrive at a diagnosis. The Tokyo Guidelines, that was a result of a discussion among some global experts in Tokyo, later modified in 2013, and accepted again in 2018, now gives us a set of criteria to establish the diagnosis on the basis of clinical, laboratory and imaging findings. It also helps us to categorize the patients into grades of severity and most of the cases of acute cholecystitis are Grade I or Mild variety. It is evident that laboratory findings like CRP level can be correlated with the increase in severity of the disease. Most of the Grade I patients can be treated with early cholecystectomy if they present early. Grade II and Grade III patients may require some form of surgical intervention, but again a majority of patients respond well to initial conservative treatment and can be managed later with interval cholecystectomy. Regarding complications, biliary leak remains the major concern as it may account for increase in morbidity. Wound infection rates have decreased considerably with laparoscopic cholecystectomy being practiced as the gold standard of treatment.

To conclude the Tokyo Guidelines has provided us with a pragmatic approach for the diagnosis and management of acute cholecystitis, which can be implemented as an

institutional protocol to ensure uniformity in management of this common problem for the benefit of the patients.

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