



ORIGINAL RESEARCH PAPER

General Surgery

SEVERITY ASSESSMENT AND MANAGEMENT OF ACUTE CHOLECYSTITIS- A CLINICAL STUDY

KEY WORDS: Acute Cholecystitis, Tokyo Guidelines, Severity assessment.

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ABSTRACT

This hospital based prospective observational study was conducted in the General Surgery Department of Assam Medical College & Hospital for a period of one year (June '16- May'17). The objective of this study was to evaluate the severity and outcome of treatment in various grades of acute cholecystitis. Diagnosis was done on the basis of Tokyo Guidelines for Acute Cholecystitis with severity grading and management accordingly. Data analysis was done using appropriate statistical tools. A total of 91 patients participated in the study, out of which 45 patients were in Grade I, 41 patients in Grade II and 5 patients in Grade III. Twenty three patients underwent operative intervention (22 in Grade I and 1 in Grade II) and remaining 68 patients were treated conservatively. The results were similar with the studies conducted by Cheng et al, Ambe et al, Kabul Gurbalak et al and Yucel Yusbasioglu et al.

INTRODUCTION

Acute cholecystitis (Greek, *cholecyst* = gallbladder, combined with the suffix *itis* =inflammation) can be defined as an acute inflammatory condition of the gallbladder, often attributable to gallstones; but many factors such as ischemia, motility disorders, direct chemical injury, infections by microorganism, protozoan and parasites, collagen disease, and allergic reactions are also involved.¹ Acute cholecystitis is the most common complication of gallbladder stones, and one of the most frequently seen acute surgical diseases.² It can broadly be divided into Acute Calculous Cholecystitis and Acute Acalculous Cholecystitis.

Gallstones represent a common health problem (6.5-15%) in the Western population.³ Approximately 1-4% of these patients develop complications mainly acute cholecystitis (AC) related to the gallbladder stone.⁴ Jean-Louis Petit in 1733 mooted the project of attacking the diseased gallbladder surgically. The realization and demonstration that gallbladder could be removed safely heralded the era of modern day surgical management of gallbladder disease. After a good many experimental operations on dogs in which the gall-bladder was deliberately removed, Carl Langenbuch, of Berlin performed the first cholecystectomy in humans in June of 1882.⁵

AIMS AND OBJECTIVES

1. To assess the severity of disease in patients presenting with acute cholecystitis based on Tokyo guidelines for acute cholecystitis.
2. To observe the outcome of operative and non-operative treatment in various grades of acute cholecystitis.

REVIEW OF LITERATURE

Alexander of Tralles (525-605), a physician of the Byzantine Empire, left the earliest known writings on gall stones, describing calculi in human livers.⁶ The first interaction of gallstones and surgery dates back to 1687 when Stal Pert Von Der Wiel, while operating a patient with purulent peritonitis accidentally found gallstones.⁷ Jean-Louis Petit, the founder of gall bladder surgery in 1733 suggested removal of gallstone and drainage of the gall bladder, thus creating fistula in patients with empyema, which he successfully performed in 1743.⁷ Carl Johann August Langenbuch (1846-1901) was the first surgeon, in 1882, to propose that the gall-bladder might on occasion be excised. Langenbuch's open cholecystectomy remained the gold standard for symptomatic cholelithiasis for over a century. The only major change in the operation was the introduction of operative cholangiography for the detection

of common bile duct stone by Mirizzi.⁸ In the last two decades of 20th century, the introduction of laparoscopic techniques to perform cholecystectomy has revolutionized this procedure.⁹ Prof Dr Erich Mühe of Germany performed the first laparoscopic cholecystectomy (LC) on September 1985. In September 1992, a NIH consensus conference held in Bethesda concluded that LC was the treatment of choice for gall bladder lithiasis.¹⁰ The prevalence of gall stone disease varies with age, sex, ethnic groups and geographical areas. The female prevalence of gall bladder disease in the American Indians and Pima Indians is as high as 60% - 70%, Chile 37% while in UK and in the USA it is 6% - 12% and 11% respectively. China and Japan have a very low prevalence rate of 5%.¹¹ The estimated prevalence of gallstone disease in India was 2-29% with marked differences in North and South India. It is seven times more common in North than in South India.^{12,13}

Treatment of cholecystitis depends on the severity of the condition and the presence or absence of complications. Controversy still exist whether to do an early or delayed cholecystectomy for AC. An English surgeon, Walton, in 1923, first advocated early operation for the disease.¹⁴ In the early 1930's a number of American surgeons began questioning the advisability of conservative management, and advocated early surgical intervention.^{14,15,16} Devid Mc Cubbrey and Thurston Thieme (1959) in their study conducted at St. Joseph Mercy Hospital advocated conservative management for AC. Vuori (1962) in his study said that with regard to mortality, incidence of postoperative complications, post-operative elevation of body temperature, and duration of postoperative hospitalization, there were no statistically significant differences between early and delayed cholecystectomy for AC. Therefore the author considers the operation advisable as early as possible with regard to the duration of the disease and the age of the patient providing, however that adequate shock, electrolyte fluid balance and other necessary treatment is given preoperatively and that there are no strong contraindications.¹⁷ Papi C et al had done a meta-analysis in 2004 by including 12 randomized trials (9 addressing OC and 3 LC) in which early and delayed cholecystectomy were compared. In both open and laparoscopic trials, rates of mortality, morbidity, common bile duct injury and retained common duct stones were similar in both groups; 13 % of the patients of delayed group had persistent and recurrent symptoms while awaiting elective surgery and underwent urgent surgery.¹⁸ Lau H et al (2005) in a total of four clinical trials comprising 504 patients concluded that the safety and efficacy of early and delayed-interval LC for AC were

comparable. Because evidence suggested that early LC reduced the total length of hospital stay and the risk of readmissions attributable to recurrent AC, it is therefore a more cost-effective approach for the management of AC.¹⁹

Mitchell L. et al (1983) described the major complications that occur early, either during or soon after operation and that occur late, weeks to years after the surgical procedure. Among the complications discussed significant are bile duct injury and wound infection.²⁰ The most significant common complication is injury to the bile duct, for which the greatest risk factor is inexperience.²¹ S Duca et al (2003) in their study observed that the main operative incidents encountered were hemorrhage (224 cases, 2.3%), iatrogenic perforation of the gallbladder (1517 cases, 15.9%) and common bile duct (CBD) injuries (17 cases, 0.1%). The main postoperative complications were bile leakage (54 cases), hemorrhage (15 cases), sub-hepatic abscess (10 cases) and retained bile duct stones (11 cases). Ten deaths were recorded (0.1%).²² Asif et al (2009) from their study stated that early cholecystectomy in acute cholecystitis is a safe and cost effective procedure with fewer complications, better cosmetically and facilitates early return to work.²³ Wang CH et al (2014) in a retrospective study investigated recurrence rates of AC and analyzed factors associated with recurrence after antibiotic treatment in adult AC patients. The study included 226 patients [mean age: 62.2 years; 144 men (63.7 %)]. The rate of recurrence of AC in patients who received antibiotics alone was low. The recurrence rate was higher within 100 days of AC.²⁴ Ludwig K et al (2002) in his prospective study on patients' outcome following laparoscopic vs. open cholecystectomy evaluated the postoperative course of 135 patients who underwent LC or OC in 1999. Patients in the LC-group returned to work after an average of 24.7 days, compared with 42.2 days following OC. The study suggested an additional advantage in surgical outcome after LC, in comparison to OC. The laparoscopic approach is the preferable procedure to treat especially older and co-morbid patients.²⁵

The Guidelines for Management:

The Tokyo guidelines for the management of acute cholangitis and cholecystitis were published in 2007 and revised in 2013 to provide clinical guidelines for the diagnosis and treatment of AC. The guidelines recommend that patients with mild cholecystitis (Grade I) should undergo early laparoscopic cholecystectomy, whereas patients with severe cholecystitis (Grade III) appropriate organ support in addition to initial medical treatment is necessary followed by urgent or early gallbladder drainage. Elective cholecystectomy can be performed after the improvement of the acute inflammatory process. For moderate cholecystitis (Grade II), the first-line management is delayed/elective laparoscopic cholecystectomy after initial medical treatment with antimicrobial agent. In non-responders to initial medical treatment, gallbladder drainage should be considered.²⁶

MATERIALS AND METHODS

In this study an endeavor has been made to assess the severity of AC and its management using Tokyo Guidelines and to see how this affects the outcome of disease management.

This hospital-based observational study was conducted in the surgical wards of the Department of General Surgery and Pediatric Surgery in Assam Medical College and Hospital, Dibrugarh, Assam over a period of one year (from June 2016 to May 2017).

The study process began after getting approval from the ethics committee of the institute. The collected data were reviewed and analysed at the end of study period. An informed consent was obtained from all patients for the use of their data in the study. Each and every case was clinically

examined and a detailed history of the patients was recorded. Necessary laboratory and radiological investigations were carried out. A final diagnosis of acute cholecystitis was made by using the Tokyo Guidelines (2013).

Diagnostic Criteria

- Local signs of inflammation: Murphy's sign, pain/tenderness/mass in RUQ
- Systemic signs of inflammation: fever, elevated CRP and WBC
- Imaging: Ultrasound, CT, MRI

Severity grading

Grade I: Mild acute cholecystitis

- Acute cholecystitis in an otherwise healthy patient
- Mild inflammatory changes of the gallbladder* e.g., edematous cholecystitis

Grade II: Moderate acute cholecystitis

- Clinical symptoms > 72 h
- Palpable mass in the RUQ
- Positive Murphy's sign
- WBC > 18,000 /dl
- Marked gallbladder inflammation* e.g., gangrenous cholecystitis

Grade III: Severe acute cholecystitis

- Acute cholecystitis with at least one of the following organ dysfunction
- Cardiovascular: hypotension requiring catecholamine
- Pulmonary: PaO₂/CO₂ low ratio, Serum Creatinine > 2.0 mg/dl
- Neurological: Decreased level of consciousness
- Hepatic: INR > 1.5
- Hematologic: Platelet count < 100,000/dl
- Severe gallbladder inflammation* e.g., necrotizing cholecystitis

RUQ right upper quadrant, CRP C - reactive protein, WBC white blood count, CT computed tomography, MRI magnetic resonance imaging *expected extent of gallbladder inflammation

Operative treatment: Out of 91 patients, operative treatment with early cholecystectomy was done in 23 patients and conservative treatment in 68 patients. Out of 23 operated cases, 6 had undergone laparoscopic cholecystectomy, 17 open cholecystectomy (One conversion).

Conservative treatment included: (1) Bed rest, (2) Nil by mouth, (3) Nasogastric aspiration, (4) Fluid and electrolytes by intravenous route, (5) Antibiotics, (6) Analgesic, (7) Monitoring (Continuous observation of the patients pulse rate, temperature, rigidity, lump and tenderness in the abdomen). The response of the patient to conservative treatment or developments of any complications were noted till the discharge of the patient.

The complications were noted under following headings:

- (1) Abscess formation, empyema, (2) Increase in size of the lump and impending perforation, (3) Development and/or increase in jaundice, (4) Onset of septicemia, (5) Development of pancreatitis, (6) Other complications due to prolonged bed rest e.g. (i) Leg vein thrombosis & (ii) Basal pneumonia and lung function Patients who were put for early cholecystectomy were observed and their intraoperative findings and post-operative development of complications, if any were noted.

Postoperative complications were noted under following headings:

- (a) Wound infection, (b) Respiratory tract infection, (c) Bleeding from drain site, (d) Prolonged ileus, (e)

Hyperpyrexia, (f) Subphrenic collection, (g) Biliary fistula or leak

Outcome: Outcome of the patients depending on their severity assessment was based on their mode of management as mentioned below:

- Non-operative management
- Development of complications
- Recurrence of symptoms before interval cholecystectomy
- Operative management (open/ laparoscopic cholecystectomy)
- Duration of hospital stay
- Development of complications if any (minor/ major/ expired)

FOLLOW UP:

Both group of patients i.e. conservative and operative patients were followed up for a period ranging from 1 to 6 months from the date of discharge. Patients with recurrence of symptoms before planned interval cholecystectomy were readmitted, observed and followed up. Patients who had undergone planned cholecystectomy were also followed up for the same duration.

Statistical Analysis:

The data is presented in terms of percentage and Mean ± S.D. Results and observations are illustrated with bar-diagrams, pie-diagrams and histograms wherever applicable. Statistical significance was tested by means of one way ANOVA test and unpaired t-Test. *p*-value of <0.05 was considered to be statistically significant. All data analysis was performed with the help of Microsoft Excel.

Terminology & Classifications used in the study:

- **Socioeconomic Status:** They were classified into 5 classes based on Modified Kuppuswamy scale. It includes education of the head of the family, occupation of head of the family and family income per month from all sources and divides them into upper (I), upper middle (II), lower middle (III), upper lower (IV) and lower (V) class groups.
- **Early Cholecystectomy:** Cholecystectomy done at the time of index admission
- **Delayed Cholecystectomy:** Interval Cholecystectomy

RESULTS, OBSERVATIONS AND DISCUSSION

Age Distribution: Acute cholecystitis is common in the fourth decade of life and is rare in children. Studies conducted by Litler *et al* (1952)²⁷, Schweiz *et al* (1994)²⁸, Sushant Kumar *et al* (2015)²⁹ have corroborated these findings.

In our study we found that the maximum incidence was in the 40-49 year age group (28.57%) followed by 30-39 year group (27.47%). The lowest age was of an 8 year old male whereas the highest age was a 74 year old female. The mean age was found to be 39.9 years. Thus it can be interpreted that the present study is at par with other published world literature.

Sex Distribution: The incidence of acute cholecystitis is more common in the female sex has been observed since a long time now. Many studies conducted over various places in different times have proved the association. Litler and Ellis (1952)²⁷, Kala *et al* (1977)³⁰, Indar *AA et al* (2002)³¹, Ali Nawaz Khan (2006)³² & Sushant Kumar *et al*²⁹ in all their studies have found that the incidence to be more common in female sex.

In our present study too, there was female predominance with male-female ratio of 1: 3.13 (male=24.18%, female=75.82%). The mechanism for the increased risk of gallstone disease in women is probably related to female sex hormones as parity, oral contraceptive use and hormone replacement therapy (HRT) all increase the risk of gallstone disease.^{33,34}

Case Distribution according to Severity: In our study, out of 91 patients, 45 (49.45%) patients were in Grade I, 41 (45.05%)

patients were in Grade II and 5 (5.49%) patients were in Grade III severity. The relatively higher number of patients in Grade II compared to other studies conducted by Cheng *et al* (2013)³⁵, Ambe *et al* (2015)³⁶, Kabul Gurbulak *et al* (2015)³⁷, Yucel Yuzbasioglu *et al* (2017)³⁸ was probably due to the fact that being a tertiary care medical centre, our centre had higher number of referral cases while Grade I patients were treated in peripheral hospitals. The low incidence of Grade III patients in our study calls for the necessity of further studies with the involvement of all the tertiary care centers of this region.

STUDIES	TOTAL NUMBER OF CASES	GRADE I n (%)	GRADE II n (%)	GRADE III n (%)
Cheng <i>et al</i> (2013) ³⁵	103	48, 46.6%	31, 30.09%	24, 23.3%
Ambe <i>et al</i> (2015) ³⁶	138	79, 57.25%	33, 23.9%	26, 18.8%
Kabul Gurbulak <i>et al</i> (2015) ³⁷	682	439, 64.4%	220, 32.25%	23, 3.37%
Yucel Yuzbasioglu <i>et al</i> (2017) ³⁸	236	136, 57.6%	68, 28.8%	32, 13.56%
Present Study (2016-17)	91	45, 49.45%	41, 45.05%	5, 5.49%

TABLE-1.1: SHOWING DISTRIBUTION OF SEVERITY OF AC INVARIOUS STUDIES

Age distribution according to Severity: It is an established fact that the severity of acute cholecystitis increases with increasing age. In our present study too, we found that the severity increases with increasing age. The mean age in Grade I, Grade II and Grade III were 35.42 years, 43.66 years and 49.4 years respectively.

AGE GROUP (in years)	Grade I		Grade II		Grade III		TOTAL (N)
	n	%	N	%	n	%	
<20	6	85.71	1	14.29	0	0.00	7
20-29	8	66.67	4	33.33	0	0.00	12
30-39	15	60.00	9	36.00	1	4.00	25
40-49	10	38.46	15	57.69	1	3.85	26
50-59	3	30.00	5	50.00	2	20.00	10
60-69	2	22.22	6	66.67	1	11.11	9
≥ 70	1	50.00	1	50.00	0	0.00	2
TOTAL	45	49.45	41	45.05	5	5.49	91

Table-1.2: Showing age distribution in Grade I, Grade II and Grade III acute cholecystitis.

Duration of Symptoms: In our study of 91 patients, we observed that the minimum duration of symptoms at the time of admission was 1(one) day and maximum was of 12 days. Majority of the patients (48.35%) presented in less than 3 days after onset of symptoms whereas 31.87% presented in between 4-6 days and remaining 19.78% patients presented 7 days after the onset of symptoms. The mean duration in Grade I, Grade II and Grade III severity were 2.7 days, 5.58 days and 9.8 days respectively.

Therefore it can be interpreted that the severity of acute cholecystitis increases with the increase in mean duration of symptoms which is in accordance with the study of Kabul Gurbulak *et al* (2015).³⁷

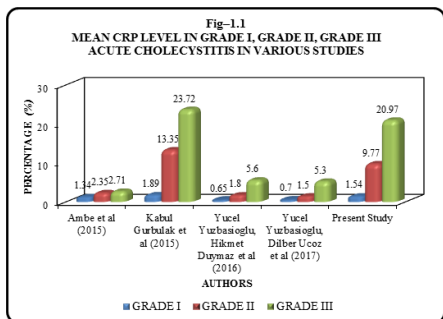
	SEVERITY OF ACUTE CHOLECYSTITIS		
	GRADE I (Mean ± S.D.)	GRADE II (Mean ± S.D.)	GRADE III (Mean ± S.D.)
Duration of Presenting Symptoms (Days)	2.71 ± 1.24	5.59 ± 1.95	9.8 ± 1.48

Table-1.3: Duration of symptoms in Grade I, Grade II and Grade III acute cholecystitis.

Level of CRP in relation to Severity:

C-reactive protein (CRP) is an annular (ring-shaped), pentameric protein found in blood plasma. It is an acute phase reactant protein. It reflects the intensity of the pathological process, and hence is a good indicator of the severity of inflammation. Tokyo Guidelines incorporated CRP as one of the parameters in the diagnosis of acute cholecystitis. In our study we found that the mean CRP levels in Grade I, Grade II and Grade III acute cholecystitis were 1.54 mg/dl, 9.77 mg/dl and 20.97 mg/dl respectively. It was statistically significant (p value <0.01). It was observed that there was rise of CRP level in accordance with the severity of acute cholecystitis.

The present study supports the value of CRP as an important and reliable predictor in assessing the severity of acute cholecystitis. Its value increases with increasing severity and so it is a strong and reliable marker. This finding has also been established by studies of Ambe *et al* (2015)³⁷, Kabul Gurbulak *et al* (2015)³⁸, Yucel Yuzbasioglu *et al* (2016)³⁹ and Yucel Yuzbasioglu, Dilber Ucoz *et al* (2017)³⁸.



Duration of Hospital stay in relation to Severity:

In our present study we found that the mean length of hospital stay in Grade I, Grade II and Grade III acute cholecystitis patients were 7.53 days, 8.29 days and 13.8 days respectively which was statistically significant (p value <0.05). Hospital stay increases with increasing severity. This is in accordance with the other studies and we can opine that Tokyo guidelines are very much helpful in assessing the severity of patients with acute cholecystitis.

MANAGEMENT:

The Tokyo guidelines for the management of acute cholecystitis were published in 2007 and revised in 2013 to provide clinical guidelines for the diagnosis and treatment of acute cholecystitis. The guidelines recommend that patients with mild cholecystitis (Grade I) should undergo early laparoscopic cholecystectomy, whereas patients with severe cholecystitis (Grade III), urgent or early gall-bladder drainage is essential in addition to organ support and medical treatment. For moderate cholecystitis (Grade II), the management is medical treatment initially. If it doesn't respond to medical treatment urgent or early gall-bladder drainage is required. In our study we found that out of 91 patients 68 patients received medical treatment and the remaining 23 patients received operative management. Out of those operated, 17 patients underwent open cholecystectomy (One conversion) and 6 patients underwent laparoscopic cholecystectomy. It was observed that the open cholecystectomy patients were older than the laparoscopic group (34.29 ± 13.44 years vs. 19 ± 13.78 years). The mean duration of hospital stay is 9.64 ± 4.09 days vs. 6.0 ± 0.89 days in the open and laparoscopic group respectively. Nowadays early laparoscopic cholecystectomy is suggested as the first line treatment in acute cholecystitis.^{40,41} However, in spite of all these published literatures, the rate of early cholecystectomy in patients with acute cholecystitis is significantly low (15-40%).^{42,43,44}

In our institute, the preferred protocol is medical treatment followed by interval cholecystectomy in AC. However in the

present study, 23 (25%) patients had undergone early cholecystectomy as per Tokyo guidelines with excellent results.

MANAGEMENT	NUMBER (n)	PERCENTAGE (%)
Conservative	68	74.72
Operative		
Laparoscopic Cholecystectomy	6	6.59
Open Cholecystectomy	17	18.68
(1 Converted to Open Cholecystectomy)		
TOTAL	91	100.00

Table-1.4: Distribution of patients in terms of operative and non-operative management.

Study	Total Patients	Non-operative Management n (%)	Operative management	
			Open Cholecystectomy n (%)	Laparoscopic Cholecystectomy n (%)
Cheng <i>et al</i> (2013) ³⁵	103	67 (65.04%)	13 (12.62%)	23 (22.33%)
Sert I, Ipekci <i>et al</i> (2017) ⁴⁶	142	-	76+19=95 (66.9%)	47 (33.09%)
Present Study (2016-17)	91	68 (74.72%)	16+1=17 (18.68%)	6 (6.59%)

Table1.5: Number of Patients with Operative & Non operative Management in various series

Outcome of Operated cases:

Mitchell L. *et al* (1983) describe the major complications that occur early, either during or soon after operation and that occur late ranging from weeks to years after the surgical procedure. Among the complications discussed, significant are bile duct injuries and wound infection.⁴⁵ S Duca *et al* (2003) in their study observed that the main operative incidents encountered were hemorrhage (224 cases, 2.3%), iatrogenic perforation of the gallbladder (1517 cases, 15.9%) and common bile duct (CBD) injuries (17 cases, 0.1%). The main postoperative complications were bile leakage (54 cases), hemorrhage (15 cases), sub-hepatic abscess (10 cases) and retained bile duct stones (11 cases). Ten deaths were recorded (0.1%).⁴⁷

In our study we found that out of 23 operated cases, 22 cases were operated in Grade I severity and only 1 case in Grade II severity. Other hand, all the patients from Grade III severity received conservative approach of management with good response. While no complication was detected in the Grade II category, 6 patients in Grade I developed wound infections while 1 one of them had bleeding from drain site and 1 had biliary leakage. The patient with bleeding from drain site had her problem resolved when one suture was placed in the drain site, while the other with biliary leakage had spontaneous recovery within a week. Wound infections were considered as minor complications whereas bleeding and biliary leakage was considered as major complications. There was no mortality in all the grades of severity. Hence it can be interpreted that early operative intervention can be carried out according to the management protocol of Tokyo Guidelines with the least complication rate.

Follow up:

In our present study of 91 patients, 68 patients received medical management while 23 patients received surgical management at the time of index admission. The patients undergoing both non-operative and operative management were followed up for a period of one to six months. All the

operated patients showed excellent recovery without any significant morbidity during their follow up. Whereas in the non-operative group six patients had recurrence of symptoms (two each in Grade I, Grade II and Grade III respectively) after their discharge, requiring re-admission. These patients were again treated by non-operative management initially followed by interval cholecystectomy. No significant morbidity and mortality were noted in that group too.

Limitations:

In our department, acute cholecystitis is generally managed with either emergency or planned cholecystectomy. The alternative treatment options like percutaneous cholecystostomy were not used. Thus it remains a limitation as to how PC would have influenced the outcomes of patients with severity grade II/III.

CONCLUSION

Acute cholecystitis is one of the commonest surgical problems encountered in day to day life. The most common cause of acute cholecystitis is cholelithiasis. It is more common in the female sex and in their forties. Before the introduction of Tokyo Guidelines, there was no consensus over diagnosis and evaluation of acute cholecystitis. A definite management protocol was also lacking. Tokyo Guidelines for the diagnosis and severity assessment of the disease together with its well defined management strategy filled the void. Our study was conducted on the basis of this guideline. In our study, maximum number of patients were in Grade I severity followed by Grade II. Being a tertiary care medical centre, our institute usually gets severely ill patients and that explains the relative increase in the number of patients in Grade II as compared to other studies. The severity of the disease was more in the male gender and it showed increasing trend with increasing age. The mean duration of hospital stay also showed increasing trend with increasing severity of the disease. CRP is found to be an important and reliable predictor for diagnosis and severity assessment of AC. Early cholecystectomy showed excellent outcome. The Tokyo Guidelines may be adopted as an institutional protocol for the management of Acute Cholecystitis.

ABBREVIATIONS:

AC: Acute Cholecystitis, OC: Open Cholecystectomy, LC: Laparoscopic Cholecystectomy, PC: Percutaneous Cholecystostomy, SD: Standard Deviation, ANOVA: Analysis of Variance, NIH: National Institute of Health, UK: United Kingdom, USA: United States of America.

ETHICAL CLEARANCE: TAKEN.

CONFLICT OF INTEREST: NONE.

REFERENCES

1. Kimura Y, Takada T, Strasberg SM, Pitt HA, Gouma DJ, Garden OJ, Buchler MW, Windsor JA, Mayumi T, Yoshida M, Miura F, Higuchi R, Gabata T, Hata J, Gomi H, Dervenis C, Lau WY, Belli G, Kim MH, Hivano SC and Yamashita Y, TG13 current terminology, etiology, and epidemiology of acute cholangitis and cholecystitis. *Journal of Hepato-Biliary-Pancreatic Sciences*, 2013 Jan;20(1):8-23
2. Strasberg SM. Clinical practice. Acute calculous cholecystitis. *N Engl J Med*. 2008;358(26):2804-11
3. Shaffer EA. Gallstone disease: Epidemiology of gallbladder stone disease. *Best Pract Res Clin Gastroenterol* 2006; 20: 981-996
4. Haldestam I, Enell EL, Kullman E, Borch K. Development of symptoms and complications in individuals with asymptomatic gallstones. *Br J Surg* 2004; 91: 734-738.
5. History of Gall-Bladder Surgery. *The British Medical Journal*, March 4, 1939. 464
6. Thudicum JMW. Part 1: historical introduction. In: Robinson JO, ed. *Silvergirl's surgery: biliary tract*. Austin, Texas: Silvergirl, 1985:4-13.
7. Beal JM. Historical perspective of gall stone disease. *Surg Gynecol Obstet* 1984; 158:81
8. Mirizzi P L. Operative cholangiography. *Lancet* 1938; 2:366-9.
9. De Utpal. Evolution of cholecystectomy: A tribute to Carl August Lagenbuch. *Indian Journal of Surgery*, Vol. 66, No. 2, Mar-Apr 2004, 97-100.
10. NIH Consensus Conference: Gallstones and laparoscopic cholecystectomy. *JAMA* 1993; 269: 1018-24.
11. Stinton LM, Shaffer EA. Epidemiology of Gallbladder Disease: Cholelithiasis and Cancer. *Gut Liver*. 2012; 6(2): 172-87.
12. Mohan H, Punia R, Dhawan S, Ahal S, Sekhon M. Morphological spectrum of

- gallstones disease in 1100 cholecystectomies in North India. *Ind J Surg*. 2005;67(3):140-2
13. Parkash A. Chronic cholecystitis and cholelithiasis in India. *IntSurg*. 1968;49:79-85.)
14. Heuer, G. J.: *The Surgical Aspects of Acute Cholecystitis*. *Ann. Surg.*, 105:758, 1937.
15. Graham, H. F.: *The Value of Early Operation for Acute Cholecystitis*. *Ann. Surg.*, 93:1152, 1931
16. Mentzer, S. H.: *The Acute Gallbladder Manifesting Few Signs or Symptoms*. *Surg., Gynec. & Obst.* 55:709, 1932.
17. Vuori EE. *Ann Chir Gynaecol Fenn*. Radical or expectant therapy of acute cholecystitis. 1962; 51:331-41.
18. Papi C, Catarci M, D'Ambrosio L, Gili L, Koch M, Grassi GB, Capurso L. Timing of cholecystectomy for acute calculous cholecystitis: a meta-analysis. *Am J Gastroenterol*. 2004 Jan; 99(1):147-55.
19. Lau H, Lo CY, Patil NG, Yuen WK. Early versus delayed-interval laparoscopic cholecystectomy for acute cholecystitis: a metaanalysis. *Surg Endosc*. 2006 Jan; 20(1):82-7.
20. *Surgical Clinics of North America, Complications of Cholecystectomy*. *Surgical Clinics of North America Volume 63, Issue 6, December 1983, Pages 1191-1204*
21. Lee VS, Chari RS, Cucchiario G, Meyers WC. Complications of laparoscopic cholecystectomy. *Am J Surg*. 1993 Apr; 165(4):527-32.
22. S Duca, O Bala, N Al-Hajjar, C Iancu, IC Puia, D Munteanu, and F Graur. *Laparoscopic cholecystectomy: incidents and complications. A retrospective analysis of 9542 consecutive laparoscopic operations*. *HPB (Oxford)*. 2003; 5(3):152-158.
23. Asif Quereshi, Jahanjaib Haider, Adnan Aziz, Early laparoscopic cholecystectomy for acute calculous cholecystitis: What is the optimal timing? *Journal of Surgery Pakistan (International)* 17 (1) Jan-Mar, 2012
24. Wang CH, Chou HC, Liu KL, Lien WC, Wang HP, Wu YM. Long-term outcome of patients with acute cholecystitis receiving antibiotic treatment: a retrospective cohort study. *World J Surg*. 2014 Feb; 38(2):347-54
25. Ludwig K, Patel K, Wilhelm L, Bernhardt J. Prospective study on patients' outcome following laparoscopic vs. open cholecystectomy. *Zentralblatt für Chirurgie*, 01 Jan 2002, 127(1):41-46.
26. Miura F, Takada T, Strasberg SM, Solomkin JS, Pitt HA, Gouma DJ, Garden OJ, Buchler MW, Yoshida M, Mayumi T, Okamoto K, Gomi H, Kusachi S, Kiriyaama S, Yokoe M, Kimura Y, Higuchi R, Yamashita Y, Windsor JA, Tsuyuguchi T, Gabata T, Itoi T, Hata J, Liau KH; Tokyo Guidelines Revision Committee. TG13 flowchart for the management of acute cholangitis and cholecystitis. *J Hepatobiliary Pancreat Sci*. 2013 Jan; 20(1):47-54
27. Lidler Ellis CR, *Brit J. Surg.* 1952; 68: 753-57
28. Bhanasali SK cholecystitis and cholecystitis (an appraisal of clinico-surgical experiences with 228 cases). *J Postgrad Med (serial online)* 1980; 26: 74
29. Sushant Kumar, Pranaya Kunal, Deepak Kumar Yadav, A comparative study of symptomatic and radiologic findings in cases of gallbladder disease undergoing cholecystectomy. *International Journal of Recent Trends in Science and Technology*, August 2015; 16(1):66-69
30. Kala ZS, Wani NA, Matoo GM, MisgerMs and Rasid PA, 1977, *In J. Surg.* 33:530-32
31. Indar AA et al, *BMJ* 2002; 325:639-643 (21 Sept)
32. eMedicine - cholecystitis, Acute: Article by Ali Nawaz Khan, MBBS, FRCP, FRCR, Consultant Radiologist, Dept. of Diagnostic Radiology, North Manchester General Hospital, July 26, 2006. WWW.emedicine.com/Radio/topic158.htm.
33. Hart AR, Luben R, Welch A, Bingham S, Khaw KT. Hormone replacement therapy and symptomatic gallstones - a prospective population study in the EPIC-Norfolk cohort. *Digestion* 2008; 77:4-9
34. Cirillo DJ, Wallace RB, Rodabough RJ, et al. Effect of estrogen therapy on gallbladder disease. *JAMA* 2005; 293:330-9
35. Wei-Chun Cheng, Yen-Cheng Chiu, Chiao-Hsiung Chuang, Chiung-Yu Chen. Assessing clinical outcomes of patients with acute calculous cholecystitis in addition to the Tokyo grading: A retrospective study. *Kaohsiung Journal of Medical Sciences* (2014) 30, 459-465
36. Peter C. Ambe, Hildegard Christ and Dirk Wassenberg, Does the Tokyo guidelines predict the extent of gallbladder inflammation in patients with acute cholecystitis? A single center retrospective analysis. *BMC Gastroenterology* (2015) 15:142
37. Esin Kabul Gurbulak, Bunyamin Gurbulak, Ismail Ethem Akgun, Yigit Duzkoylu, Muharrem Battal, Mustafa Fevzi Celayir, Uygur Demir. Prediction of the Grade of Acute Cholecystitis by Plasma Level of C-Reactive Protein. *Iran Red Crescent Med J*. 2015 April; 17(4): e28091
38. Yucel Yuzbasioglu, Dilber Ucoz, Ferhaticme, Gullu Ercan Haydar, Huseyin Uzunosmanoglu, Recep Pekicic. The Role Of C-Reactive Protein In The Evaluation Of The Severity Of Acute Cholecystitis, *Acta Medica Mediterranea*, 2017, 33:475
39. Yucel Yuzbasioglu, Hikmet Duymaz, Ceren Sen Tanrikulu, Huseyin Cahit Halhalli, Mirac Ozturk Koc, Meral Tando an, Figen Coskun. Role of Procalcitonin in Evaluation of the Severity of Acute Cholecystitis, *Eurasian J Med* 2016; 48:162-6
40. Al-Mulhim AA. Timing of early laparoscopic cholecystectomy for acute cholecystitis. *JLS* 2008; 12:282-287
41. Fumihiko Miura, Tadahiro Takada. TG13 flowchart for the management of acute cholangitis and cholecystitis. *J Hepatobiliary Pancreat Sci* (2013) 20:47-54
42. Cameron IC, Chadwick C, Phillips J, Johnson AG. Management of acute cholecystitis in UK hospitals: time for a change *Postgraduate Medical Journal* 2004; 80:292-294
43. Casillas RA, Yeniyants S, Collins JC. Early laparoscopic cholecystectomy is the preferred management of acute cholecystitis. *Arch Surg* 2008; 143:533-537
44. Senapati PS, Bhattacharya D, Harinath G, Anmori BJ. A survey of the timing and approach to the surgical management of cholelithiasis in the UK. *Ann R Coll Surg Engl* 2003; 85:306-312
45. *Surgical Clinics of North America, Complications of Cholecystectomy*. *Surgical Clinics of North America Volume 63, Issue 6, December 1983, Pages 1191-1204*
46. Sert I, Ipekci F, Engin O, Karaoglan M, Cetindag O. Outcomes of early

- cholecystectomy (within 7 days of admission) for acute cholecystitis according to diagnosis and severity grading by Tokyo 2013 Guideline. *Turk J Surg.* 2017;33(2):080-086.
47. S Duca, O Bala, N Al-Hajjar, C Iancu, IC Puia, D Munteanu, and F Graur, Laparoscopic cholecystectomy: incidents and complications. A retrospective analysis of 9542 consecutive laparoscopic operations. *HPB (Oxford)*. 2003; 5(3):152-158