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Effectiveness of Tokyo Guidelines in Diagnosis and Assessment of Severity of Acute Cholecystitis

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ABSTRACT

Background: Acute cholecystitis (AC) is an acute inflammation of the gallbladder wall. During the course of AC, concurrent complications such as acute cholangitis and biliary pancreatitis, may occur. So, further diagnostic workup and suitable therapeutic methods are required. **Objective:** This prospective study aimed to determine the validity of the new "Tokyo 2018 (TG18)" guidelines for diagnosing and assessing the severity of AC, as well as to define the outcome. **Subjects and methods:** One hundred individuals with symptoms of AC participated in this study. Every participant underwent a general examination and history taking. Also, abdominal examination was done to assess the presence of right upper quadrant (RUQ) mass/pain/tenderness and Murphy's sign, followed by radiographic and lab tests. The AC severity assessment criteria and TG18 diagnosis were used.

Results: The percentages of patients with tachycardia, tachypnea, Murphy sign and RUQ mass were considerably higher in the grades II + III group in comparison with the grade I group (0.005, 0.005, <0.001 and <0.001 respectively). In addition, the averages of systolic and diastolic blood pressures in the grades II + III group were significantly less than in grade I ($p < 0.001$ for both). The mean temperature was significantly elevated in the grades II + III group than in the grade I ($p < 0.001$ for both). The comparison between the AC grading groups regarding the intervention and outcome and no significant difference was recorded.

Conclusion: There were no clear-cut standards for diagnosing AC, with the exception of a few well-known clinical symptoms, such as Murphy's sign. The TG18 guidelines are therefore helpful for therapy, severity rating and early diagnosis all of which reduce patient morbidity and mortality.

Keywords: Acute Cholecystitis, TOKYO 18, Diagnosis, Severity.

INTRODUCTION

Acute cholecystitis (AC) is an acute inflammation of the gallbladder that typically linked to gallstones existing in the cystic duct or in the gallbladder neck [(1)]. Mainly, AC is linked to additional factors, including as ischemia, motility problems, direct chemical injury and infections [(2)]. About 90% to 95% of the causes of acute cholecystitis are attributed to cholecystolithiasis, with acalculous cholecystitis making up the remaining 5% to 10% [(3)]. The majority of gallstone patients do not have any symptoms. Nevertheless, approximately 1% to 2% of those who do not experience any symptoms do so annually. Up until the age of fifty, women are three times more likely than men to get acute cholecystitis [(4)].

During the course of AC, concurrent complications, such as acute cholangitis, and biliary pancreatitis, may occur, so further diagnostic workup and suitable therapeutic methods are required. The diagnosis of AC is relatively simple after clinical, laboratory, and imaging examination [(5)].

Prior to 2007, there were no clinical diagnostic criteria or treatment flowcharts for AC, and hospitals all over the world carried out their own unique treatments in different ways. The Tokyo Guidelines 2007 (TG07) are the initial version of the diagnostic criteria and severity grading for AC that were developed by international experts at the Tokyo Consensus Meeting [(6)]. Tokyo Guidelines (TG13) became the gold standard for AC worldwide after the update of the TG07 guidelines in 2013. The TG13 made decisions regarding the degree of severity, treatment flowcharts, bundles, and antibiotic selection in addition to the diagnostic criteria [(7)]. However, TG13 did not address concerns such as physical status or other predictors when selecting a treatment pathway based on severity.

The TG18 guidelines provide a re-designed flowchart based on recent clinical recommendations, notably the evidence presented following the introduction of TG13. Local indicators of inflammation, such as Murphy's sign, mass, pain, and tenderness, as well as systemic indicators of inflammation, such as fever, raised C-reactive protein, high WBCs count and imaging abnormalities typical of AC, are included in the TG18 diagnostic criteria for AC [(8)]. Thus, this study aimed to evaluate the validity of the new "Tokyo guidelines" in the diagnosing and assessing of the severity of AC. Also, to define the outcome morbidity and mortality.

SUBJECTS AND METHODS

Subjects: This prospective study was carried out on 100 patients presented with manifestation of AC admitted to Emergency Hospital, Mansoura University, Mansoura, Egypt within the period from March 2024 to March 2025.

Inclusion criteria: Patients aged ≥ 18 of both sexes with right upper quadrant (RUQ) pain with suspicious of AC.

Exclusion criteria: Patients aged ≤ 18, pregnant ladies and patients who do cholecystostomy or Endoscopic retrograde cholangiopancreatography.

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The TG18 guidelines were applied for the diagnosis and management of the AC cases, Figure (1).

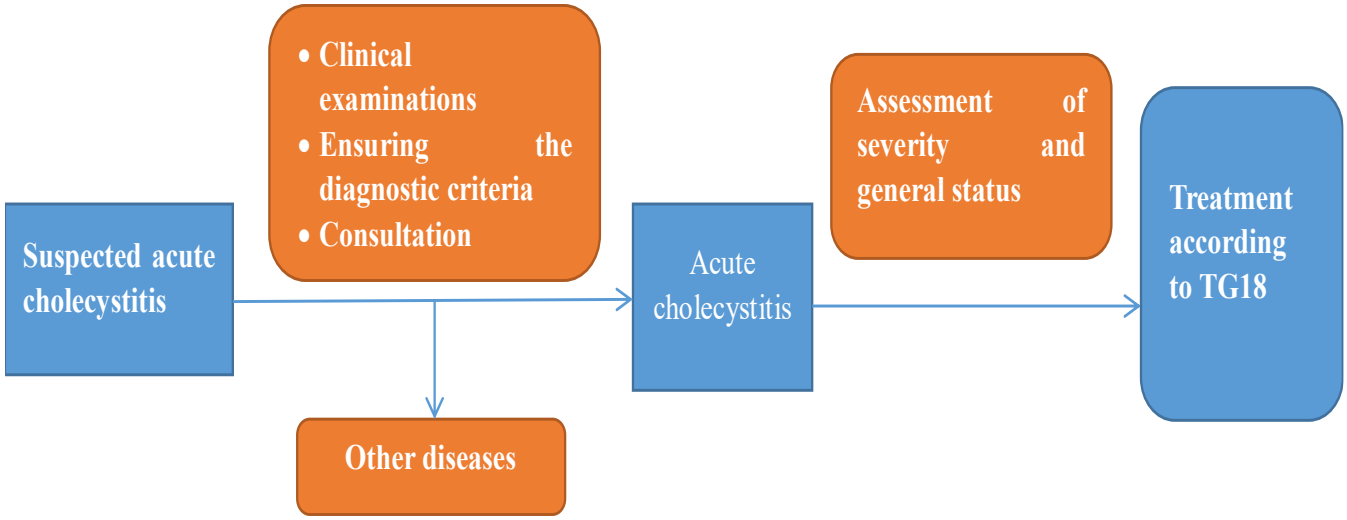

Figure (1): TG18 flowchart for the diagnosis and management of AC.

METHODS

Medical history and clinical examinations:

Full history was obtained from all participants. The general and abdominal examinations were applied to assess the presence of RUQ mass/pain/tenderness and Murphy's sign. The BMI was calculated by the formula: BMI = weight (kg)/Height in squared meter (m^2).

Radiological and lab investigations:

Ultrasound abdomen and pelvis, CT abdomen and pelvis with contrast and magnetic resonance cholangiopancreatography (MRCP) if required. Complete blood picture (CBC), CRP, liver function tests (ALT, AST, albumin and bilirubin), kidney function tests (creatinine and urea), prothrombin time (PT), partial thromboplastin time (PTT) and amylase and lipase. TG18 criteria for AC diagnosis and severity assessment were as displayed in table (1). Documentation of outcome involved hospital stay duration, criteria of ICU admission and survival (mortality and morbidity).

Ethical approval: An acceptance was gained from Institutional Research Board at Faculty of Medicine, Mansoura University (code no. MS.24-02-2707) and complied with The Helsinki Declaration. An informed written consent was gained from each patient.

Statistical analysis

Based on early studies, the sensitivity of the TG18 was 91%. The G* power was used to calculate sample size [9], a priori: computed required sample size was 60 subjects, using α error 5% and a power of 80%. Data analysis was performed by (SPSS Inc., PASW Statistics for Windows version 26). The normality of the data distribution was assessed by performing the Kolmogorov–Smirnov test. Numerical data were described using mean ± standard deviation (SD) for normally distributed data. Non-numerical data were described using frequency and percentage.

Student t-test (t) was applied to explore the statistical significance of the difference between two study group means. Unpaired Student t-test was applied to compare the means of two independent groups. A *p*-value is regarded significant if ≤ 0.05 at the confidence interval of 95%.

Table (1): TG18 guidelines of acute cholecystitis

TG18 diagnostic criteria for AC	
A. Inflammatory local signs	A-1 Murphy's sign
	A-2 RUQ pain/mass/tenderness
B. Inflammatory systemic signs	B-1 Fever B-2 ▲CRP B-3 ▲WBC counts
C. Imaging	C-1 Gallbladder thickeness > 5mm C-2 Enlarged Gallbladder C-3 Debris Echo C-4 Ultrasonographic Murphy's Sign C-5 Gas imaging C-6 Pericholecystic fluid
Suspected diagnosis: One item in A + One item in B Definite diagnosis: One item in A + One item in B+C	
Severity assessment criteria for AC:	
Grade III: (AC + Any of following organ dysfunction:(	.1 Cardiovascular system: Hypotension requiring treatment with dopamine>/= 5µg/kg/min or any dose of Noradrenaline. .2 Neurological: Decreased level of consciousness .3 Renal: Oliguria/ creatinine > 2 mg/dl .4 Respiratory: PaO2/FiO2 ratio < 300 .5 Hepatic: PT-INR > 1.5 .6 Hematological: Platelet< 1,00,000/mm^3
Grade II: presence of any of the following :	.1 ▲WBC > 18,000/mm^3 .2 Palpable tender mass in RUQ .3 Duration of symptoms > 72 hours .4 Marked local inflammation(gangrenous or emphysematous cholecystitis/pericholecystic or hepatic abscess/biliary peritonitis)
Grade I:	Doesn't meet the criteria of grade III/ II.

RESULTS

The socio-demographic information of 100 acute cholecystitis (AC) cases is presented in table (2). The cohort consisted of 33% males and 67% females. The mean age was 45.88 ± 8.58 years, ranging from 27 to 61 years. Regarding the occupation, 57% of patients were urban residents and 43% were rural residents.

Table (2): Socio-demographic data of the studied cases

	All Cohort N = 100	
Age (years)		
Mean ± SD.	45.88 ± 8.58	
Age groups (years)	**n**	**%**
<40	22	22.0
40 – 50	48	48.0
>50	28	28.0
Sex		
Male	33	33.0
Female	67	67.0
Occupation		
Urban	57	57.0
Rural	43	43.0

The anthropometric measures of the entire cohort showed that the mean weight was 72.39 ± 8.7 kg, ranging from 59.0 to 100.0 kg. The mean height was 169.0 ± 6.0 cm, ranging from 159.0 to 181.0 cm. The mean BMI was 25.29 ± 2.69 kg/m^2 and classified according to the value of BMI into normal (18.5 - < 25), overweight (25 - < 30) and obese (> 30) (Figure 2).

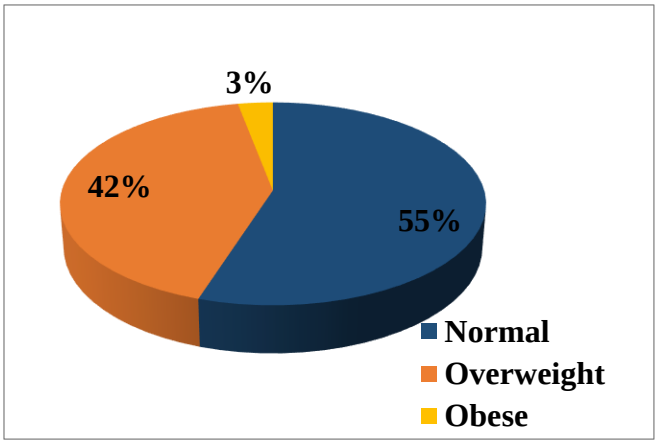

Figure (2): Body mass index of the studied AC patients

In terms of the past medical history of all of the AC cases, 30% of the cases had diabetes, 19% had hypertension 18% had dyslipidemia and 1% had hyperparathyroidism. Among the studied cases, 10% are smokers and 2% had a previous history of abdominal surgeries. Regarding the clinical presentation, 25% of patients presented with fever, 82%

with abdominal pain, 15% with tachycardia, 15% with tachypnea, 42% with vomiting, 5% with jaundice, 5% with confusion, 3% with dark urine and 2% with light-colored stool, as shown in figure (3).

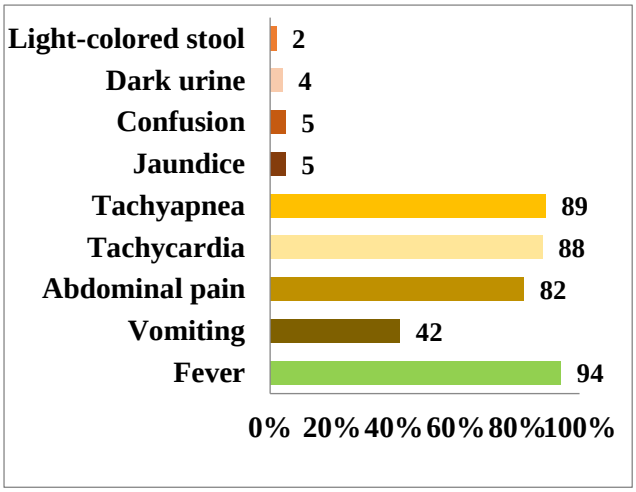

Figure (3): Clinical presentation of the studied cases.

The abdominal examination revealed that 70% of patients had Murphy sign, and 88% had right upper quadrant (RUQ) mass and 89% had RUQ tenderness. The pelvic/ abdomen ultrasound examination showed that 70% of patients had stone/retained debris, 88% had enlarged gallbladder, 89% had thickening in the gallbladder wall, 32% had pericystic fluid and 86% had soreness, as shown in table (3).

Table (3): Radiological examinations of the studied cases

	All Cohort (N = 100)	
	No.	**%**
Pelvic/ Abdomen US		
Stone/retained debris	70	70.0
Enlarged gallbladder	88	88.0
Thickening of gallbladder wall (>3mm)	89	89.0
Pericystic fluid	32	32.0
Soreness	86	86.0
Computed Tomography		
Gas bubbles	6	6.0
Not performed	94	94.0
MRCP		
Stone	2	2.0
No finding	3	3.0
Not performed	95	95.0

Computed tomography was performed for 6 patients and all of them had gas bubbles. Also, MRCP was performed for 5 of the patients (stones were found in 2 of them while no finding was detected in the other 3 patients). Laboratory investigations were performed for all the studied AC patients, as shown in table (4).

Table (4): Laboratory investigations among the studied AC patients

	All Cohort N = 100	
WBCs ($\times 10^9$/L)	10.0 (4.3 – 20.0)	
WBCs ($\times 10^9$/L)	**No.**	**%**
<10	49	49.0
10 – 18	45	45.0
>18	6	6.0
CRP (mg/L)	5.0 (2.0 – 90.0)	
INR	1.1 (1.0 – 2.0)	
PTT (sec)	30.5 (25.0 – 46.0)	
Urea (mg/dl)	31.0 (16.0 – 62.0)	
Creatinine (mg/dl)	1.0 (0.70 – 1.4)	
Cholesterol (mg/dl)	160 (115 – 299)	
Cholesterol	**No.**	**%**
<160	49	49.0
160 – 200	33	33.0
>200	18	18.0
Total bilirubin (mg/dl)	1.03 (0.5 – 9.0)	
Total bilirubin	**No.**	**%**
<1	30	30.0
1 – 5	65	65.0
>5	5	5.0
Direct bilirubin (mg/dl)	0.15 (0.1 – 7.9)	
Direct bilirubin	**No.**	**%**
<0.3	83	83.0
0.3– 3.0	12	12.0
>3.0	5	5.0
ALT (U/L)	28.0 (18.0 – 80.0)	
ALT	**No.**	**%**
≤40	91.0	91.0
>40	9	9.0
AST (U/L)	28.0 (17.0 – 75.0)	
AST	**No.**	**%**
≤40	92	92.0
>40	8	8.0
Albumin (g/dl)	4.26 (3.6 – 5.11)	
ALP (U/L)	200.0 (100.0 – 380.0)	
ALP	**No.**	**%**
≤280	95	95.0
>280	5	5.0
GGT (U/L)	25.0 (10.0 – 75.0)	
GGT	**No.**	**%**
≤50	95	95.0
>50	5	5.0
Amylase (U/L)		
Amylase	**No.**	**%**
≤80	86	86.0
>80	14	14.0
Lipase (U/L)	31.0 (19.0 – 98.0)	
Lipase	**No.**	**%**
≤60	91	91.0
>60	9	9.0

Early laparoscopic cholecystectomy (ELC) was performed for 92% of patients, delayed laparoscopic cholecystectomy (DLC) was performed for 8% of patients and gallbladder drainage (GBD) was carried out for one patient prior to the DLC**.** Post-surgical complications were found in 6 patients (2 with ecchymosis, 2 with hernia and 3 with bile duct injury). The 3 patients who had bile duct injury following the ELC were converted to open cholecystectomy. After the follow up of all the patients for 30 days, there was no mortality table (5).

Table (5): Severity grading, management and outcome of AC patients

	All Cohort (N = 100)	
Grade of severity	**No.**	**%**
Mild	30	30.0
Moderate	65	65.0
Severe	5	5.0
Intervention	**No.**	**%**
ELC	91	91.0
DLC	8	8.0
DLC+GBD	1	1.0
Intervention time after onset	48.0 (24.0 – 120.0)	
Intervention time after onset	**No.**	**%**
<24 hours	0	0.0
24 – 72 hours	92	92.0
>72 hours	8	8.0
ICU admission	**No.**	**%**
Yes	5	5.0
No	95	95.0
Post-surgical complications	**No.**	**%**
Ecchymosis.	2	2.0
Hernia	1	1.0
Bile duct injury	3	3.0
Not found	95	95.0
Conversion to open cholecystomy	**No.**	**%**
Yes	3	.0
No	97	97.0
Mortality	**No.**	**%**
Present	0	0.0
Absent	100	100.0

Table (6) detailed the comparison between AC grades regarding the socio-demographic data, history and the clinical presentation of AC cases (grade I vs. grades II+III), in which the BMI, the percentage of smokers and patients with history of hypertension were considerably elevated in the grades II + III group than grade I group ($p < 0.001$, 0.04 and 0.04 respectively).

The percentages of patients with tachycardia, tachypnea, Murphy sign and RUQ mass were considerably raised in the grades II + III group than the grade I (0.005, 0.005, <0.001 and <0.001 respectively).

Table (6): Comparison of socio-demographic data, history and clinical presentation between the AC grading groups

	Grade I (N = 30)		**Grades II + III (N = 70)**		**p-value**
Age (years)	45.4 ± 9.51		46.86 ± 5.88		*0.44*
Sex	**No.**	**%**	**No.**	**%**	
Male	21	70.0	46	66.0	*0.67*
Female	9	30.0	24	34.0	
Occupation	**No.**	**%**	**No.**	**%**	
Urban	11	36.7	32	45.7%	*0.40*
Rural	19	63.3	38	54.3%	
Smoking	**No.**	**%**	**No.**	**%**	
Yes	0	0.0	10	14.2	*0.04**
No	30	100.0	60	85.8	
BMI	24.51 ± 2.12		27.11 ± 2.93		*<0.001**
Dyslipidemia	**No.**	**%**	**No.**	**%**	
Yes	6	20.0	12	17.1	*0.71*
No	24	58.0	58	82.9	
Hypertension	**No.**	**%**	**No.**	**%**	
Yes	2	6.7	7	10	*0.04**
No	28	93.3	53	90	
Diabetes	**No.**	**%**	**No.**	**%**	
Yes	12	40	18	25.7	*0.09*
No	16	60	52	74.3	
Fever /chills	**No.**	**%**	**No.**	**%**	
Yes	10	33.3	15	21.4	*0.20*
No	20	66.7	55	78.6	
Vomiting	**No.**	**%**	**No.**	**%**	
Yes	15	50	28	40	*0.45*
No	15	50	39	60	
Abdominal pain	**No.**	**%**	**No.**	**%**	
Yes	24	80.0	58	82.8	*0.73*
No	6	20.0	12	17.2	
Tachycardia	**No.**	**%**	**No.**	**%**	
Yes	0	0.0	15	21.4	*0.005**
No	30	100.0	55	78.6	
Tachyapnea	**No.**	**%**	**No.**	**%**	
Yes	0	0.0	15	21.4	*0.005**
No	30	100.0	55	78.6	
Jaundice	**No.**	**%**	**No.**	**%**	
Yes	0	0.0	5	7.0	*0.13*
No	30	100.0	65	93	
Confusion	**No.**	**%**	**No.**	**%**	
Yes	0	0.0	5	7.0	*0.13*
No	30	100.0	65	93	
Dark urine	**No.**	**%**	**No.**	**%**	
Yes	0	0.0	4	5.7	*0.18*
No	30	100.0	66	94.3	
Light-colored stool	**No.**	**%**	**No.**	**%**	
Yes	0	0.0	2	2.8	*0.34*
No	30	100.0	68	97.2	
Murphy signs	**No.**	**%**	**No.**	**%**	
Yes	0	0.0	70	100.0	*<0.001**
No	30	100.0	0	0.0	
RUQ mass	**No.**	**%**	**No.**	**%**	
Yes	19	63.3	70	100.0	*<0.001**
No	11	36.7	0	0.0	
RUQ tenderness	**No.**	**%**	**No.**	**%**	
Yes	21	70.0	67	95.7	*p=0.19*
No	9	30.0	3	4.3	

*: significant if ($p<0.05$).

Table (7) outlined a comparison between grade I and grades II + III groups regarding the results of clinical and radiological examinations as well as management and outcome of the studied cases.

The averages of SBP and DBP in the grades II + III group were substantially less than grade I (p<0.001 for both). The mean temperature was significantly higher in the grades II + III group than in the grade I group (p<0.001 for both).

Moreover, results of laboratory investigations showed that the direct bilirubin level was substantially elevated in the grades II + III group in comparison with the grade I group (p<0.001). The comparison between the AC grading groups regarding the intervention and outcome, no significant difference was recorded.

Table (7): Comparison of general examination, radiological and lab investigations between the AC grading groups

	Grade I (N = 30)		**Grades II + III (N = 70)**		**p-value**
HR (beat/min)	86.8 ± 7.31		86.34 ± 13.31		0.80
RR (breath/min)	16.1 ± 2.12		17.4 ± 3.83		0.08
SBP (mmHg)	121.41 ± 4.12		110.1 ± 16.69		<0.001*
DBP (mmHg)	75.26 ± 10.98		80.55 ± 3.07		<0.001*
Temperature (°C)	37.56 ± 0.60		38.0 ± 0.69		0.002*
WBCs ($\times 10^9$/L)	10.0 (4.3 – 19.5)		9.85 (4.3 – 20.0)		0.13
CRP (mg/L)	5.05 (2.0 – 12.0)		5.0 (2.0 – 90.0)		0.46
Cholesterol (mg/dl)	160 (115 – 299)		160 (115 – 299)		0.46
Total bilirubin (mg/dl	1.01 (0.5 – 1.15)		1.04 (0.5 – 9)		0.08
Direct bilirubin (mg/dl	1.01 (0.1 – 0.33)		0.66 (0.1 – 7.9)		<0.001*
ALT (U/L)	26 (18 – 41)		30.5 (18 – 80)		0.11
AST (U/L)	26 (17 – 41)		31 (18 – 75)		0.13
ALP (U/L)	200 (100 – 277)		200 (100 – 380)		0.93
GGT (U/L)	25 (10 – 36)		26.5 (10 – 75)		0.52
Amylase (U/L)	62.5 (50 – 87)		63 (44 -215)		0.10
Lipase (U/L)	30 (19 – 59)		33 (20 -98)		0.19
Enlarged gallbladder	**No.**	**%**	**No.**	**%**	
Yes	20	66.7	65	92.8	<0.001*
No	10	33.3	5	7.2	
Thick gallbladder wall (>3mm)	**No.**	**%**	**No.**	**%**	
Yes	10	33.3	56	78.8	<0.001*
No	20	66.7	14	21.2	
Pericystic fluid	**No.**	**%**	**No.**	**%**	
Yes	11	36.7	21	30	0.49
No	19	63.3	49	70	
Soreness	No.	%	No.	%	
Yes	24	80.0	62	88.5	0.57
No	6	20.0	8	11.5	
Intervention time after onset	48.0 (24.0 – 72.0)		48.0 (24.0 – 120.0)		0.10
Intervention	**No.**	**%**	**No.**	**%**	
ELC	30	100.0	61.0	87.0	0.12
DLC	0	0.0	8.0	11.4	
DLC+GBD	0	0.0	1.0	1.6	
Post-surgical complications	**No.**	**%**	**No.**	**%**	
Yes	3	10.0	2	2.8	0.13
No	27	90.0	68	97.2	
ICU admission	**No.**	**%**	**No.**	**%**	
Yes	0	0.0	5	7.0	
No	30	100.0	65	93.0	
Conversion to open cholecystomy	**No.**	**%**	**No.**	**%**	
Yes	0	0.0	3	4.2	0.24
No	30	100.0	67	95.8	

*: significant if (p<0.05).

DISCUSSION

As a potentially fatal surgical emergency, acute cholecystitis requires early detection and the swift implementation of suitable therapeutic measures [(1)]. Prior to January 2007 release of TG07 guidelines, which were subsequently revised in 2013 and 2018, there were no global practical guidelines that focused only on treating AC.

The main aim was to evaluate validity of new TG18 guidelines in diagnosis and assessment of severity of acute cholecystitis. The secondary aim was to define outcome morbidity and mortality of acute cholecystitis. This study was made on 100 patients with AC evaluated using the TG 18 guidelines.

Gallstone diseases are more prevalent in women, as the literature review discussed. Similar findings were seen in our study group, where females were predominate (67%) and the majority (48%) were in the middle age range, or between the fourth and fifth decades, with a mean age of 45.88 ± 8.58 years, ranging from 27.0 to 61.0 years. Patients' residences were similar, with 43% of patients living in rural areas and 57% of patients living in metropolitan areas. The age-related disparities between genders were confirmed in various investigations. In a study by **Demirkan *et al.*** [(10)], the gender difference between the young and elderly patient groups was significant in the diagnosis of AC. In the younger group, the female to male ratio was 2.25, while in the older group, it was 0.71 (p=0.016)**.** Young female patients had a greater diagnostic rate of AC than young male patients, however this difference diminishes with age. According to **Völzke *et al***. [(11)], women are two to three times more likely than males to have gallstones, and their risk of developing gallstone disease is highest during their reproductive years. Men and women experience nearly equal rates of new gallstone development after the fifth decade**.** Estrogen causes bile to become supersaturated with cholesterol via increasing biliary cholesterol production. Consequently, a number of risk variables, including female gender, pregnancy, estrogen medication, and oral contraceptives, have an impact on gallstone formation. Women obviously have a larger incidence rate of AC than younger men, but this difference goes away as people age, most likely due to these variables [(12)]**.** Furthermore, **Sangma and Marak** [(13)] found that the age group of 41–60 years had the highest incidence of 45%, followed by 21–40 years (37%), 61–80 years (13%), and 0–20 years (5%). Their descriptive study sought to identify the different modes of clinical presentation and etiological factors of AC. Similarly, a female/male ratio of 2.6:1 indicated the female predominance in the sex-wise distribution**.**

The symptoms onset of AC before diagnosis had a median duration of 48 hours, ranging from 24.0 to 120.0 hours. Over forty percent of AC patients presented 72 hours following symptom onset, while 56% of patients sought medical attention between 24 and 72 hours following symptom onset, which agrees with **Shridhar *et al*.** [(14)]**.**

From the entire studied patient, 94% of them were febrile at the time of presentation. The most prevalent symptoms in the study group were rapid breathing, pulse rate, and RUQ discomfort, while upper quadrant soreness over the right hypochondrium was the most common clinical sign evoked (89%), followed by RUQ mass and Murphy's sign in 88% and 70% of them respectively. As previously reported, localized tenderness, guarding, and rebound tenderness in the RUQ, as well as a positive Murphy's sign were consistent and suggestive of AC. In a research conducted by **Kune and Gill** [(15)]**,** 40% of patients had a palpable gallbladder**. Roslyn and Zinner** [(16)] reported that sensitive masses in the right hypochondrium occurred in 10 to 20% of cases**. Sangma and Marak** [(13)] reported that all AC patients experienced right hypochondrial discomfort, along with fever (94%). Other symptoms included upper abdominal dyspepsia (84%), vomiting (76%), nausea (44%) and jaundice (6%). On examination, they found tenderness in the right hypochondrium in all the patients with positive Murphy's sign in 95% of them**. Shridhar *et al.*** [(14)] reported that the study group's most common symptom was acute upper abdominal discomfort, while AC patients' most common clinical sign was RUQ soreness. In addition, over half of the patients in the cholecystitis group were feverish at the time of presentation, and 65% of patients had Murphy's sign. However, our findings in the current series were closely associated with those reports**.** Moreover, a study conducted by **Yokoe *et al.*** [(17)] showed that the diagnostic accuracy was significantly higher when the Tokyo Guidelines were used than when Murphy's sign was used**.**

In our work, 30% of the AC patients were diabetics, 19% were hypertensive and 18% had dyslipidemia. Hypercholesterolemia was also observed, where 18% of patients had cholesterol level > 200 mg/dl. **Coaston *et al.*** [(18)] reported that class 3 obsesses was related to high rates of conversion to open than class 1–2 (4.6 vs 3.8 %; $p < 0.001$) In the current study, obesity was noticed among the patients as 42% of the classified as overweight and 3% as obese, according to their body mass index**.**

Also, in the present work, we recorded that 10% of patients were smokers. A meta-analysis carried out by **Aune *et al.*** [(19)] provides evidence of an increased risk of gallbladder disease associated with tobacco smoking. The summary relative risk (RR) was 1.19 for current smokers, 1.10 for former smokers and 1.15 for ever smokers. In the dose–response analysis the summary RR was 1.11 for ten cigarettes/day and there was a dose-dependent direct proportion with increasing number of cigarettes smoked per day**.**

Likewise, the findings in the study by **Sangma and Marak** [(13)], they related disorders with AC, which were hypertension (13%), DM (3%), and recurrent appendicitis (2%)**.** Furthermore, in the present

investigation, 89% of the study population in cholecystitis group had thickening of gallbladder wall > 3 mm, which was the most consistent finding in the initial screening ultrasound, followed by an enlarged gallbladder in 88% of patients. Similar to our results, **Shridhar *et al.* [14],** who aimed to investigate the usefulness of TG 18 recommendations in diagnosing AC, found that > 66% of the cholecystitis group had an enlarged gallbladder, followed by 50% of patients with a thicker gallbladder wall**.**

In our research, the most important laboratory result was the elevated WBCs count, with 45% of patients had WBCs count (10 – 18) × 10^9/L. The CRP ranged among the AC patients from 2 to 90 mg/L. **Sangma and Marak [13]** reported the presence of leucocytosis of (10- 15) ×10^9/L in 60% of case **[13].** The diagnostic criteria for AC include inflammatory markers. Raised peripheral WBC and CRP, are routinely applied by clinicians to help diagnosis, severity ranking, and forecast the progression and surgical complications in the therapy of AC **[20].** Tokyo guidelines state that test results for the diagnosis of AC must include CRP, which rises quickly in inflammatory states **[21].** These indicators do have certain limits, leukocytosis, for instance, is a non-specific indicator of sepsis, and individuals with severe sepsis, diabetes, elderly patients, and immunocompromised patients may paradoxically have lower WBC counts **[22].** Forty three percent of AC patients (n = 31/72) had normal WBC counts, according to a retrospective study by **Yazici *et al.* [23].** Furthermore, a WBC count of > 9.7 x 10^9/L has only 64% sensitivity and 47% specificity for diagnosing AC, according to a retrospective study conducted by **Hwang *et al.* [24]** on 107 patients treated with emergency cholecystectomy **[24].** It has been demonstrated that CRP is a discriminative marker superior to WBC to detect AC **[25].** However, according to **Lee *et al*. [26]**, only 55.1% to 65.3% of patients have elevated CRP**.** According to **Yazici *et al.* [23]**, normal CRP levels were present in 34.7% of AC patients**.** CRP has been shown in multiple studies to be a strong predictor of the severity of gallbladder inflammation. AC patients with high levels of CRP were observed to have a greater rate of conversion from laparoscopic to open procedures **[27, 28].**

No CRP cut-off values have yet to be suggested in prior research pertaining to the disease's grading in accordance with Tokyo criteria. However, **Nikfarjam *et al.* [29]** indicated that a CRP value greater than 94 mg/L carried a risk for cholecystitis**.** In a similar vein, **Asai *et al.* [30]** found a strong association between advanced age, elevated CRP, and signs of a serious gallbladder infection and a high risk of bactobilia. The cut-off CRP value for bactobilia in their investigation was determined to be 134 mg/L**.**

In the present study, only 5% of patients were icterus with a median of total and direct bilirubin > 5 and > 3 mg/dl respectively. Also, only 5% of the studied cases had elevated ALP > 280 U/L, ALT > 40 U/L, AST > 40 U/L, GGT > 50 U/L, amylase > 80 U/L and lipase 60 U/L. **Sangma and Marak [13]** reported the presence of leucocytosis of (10 - 15) ×109/L in 60% of cases. Also, they found mild elevation of ALP and bilirubin in 30 to 40% of participants **[13].**

According to the grade of severity in the present study, 30 % of patients were in mild grade, 65% were in moderate and 5% were in severe, as per TG 18 severity assessment criteria. The intervention following the symptoms was classified into through 24 – 72 hours in 92% of patients and through > 27 hours in the other patients.

Early laparoscopic cholecystectomy (ELC) was performed for 92% of patients, delayed laparoscopic cholecystectomy (DLC) was performed for 8% of patients and gallbladder drainage (GBD) was carried out for one patient prior to the DLC. The recorded outcome displayed that the post-surgical complications were found in 7 patients (2 with ecchymosis, 2 with hernia and 3 with bile duct injury. The 3 patients who had bile duct injury following the ELC were converted to open cholecystectomy. After the follow up of all the patients for 30 days, there was no mortality. Similar observations were found by **Takada *et al.* [31]**, which showed that 45.8, 48.9 and 5.3% of patients were grade I, II, and III. Additionally, they discovered that 75% of patients with grade II cholecystitis and 69% of patients with grade I cholecystitis received conservative treatment as their initial treatment option. Additionally, 25% of grade II cholecystitis patients were treated by early surgery underwent laparoscopic cholecystectomy, which was later changed to open cholecystectomy because of intraoperative complications. During 3 days of the onset of symptoms, all patients in the grade II cholecystitis group who were in the early surgical group underwent surgery. The operated cholecystitis group experienced few post-operative problems, with one patient developing a wound infection **[31].**

In addition to being linked to technical issues during laparoscopic surgeries, obesity is a recognized risk factor for cholecystitis. This study aimed to evaluate the relationship between obesity class and laparoscopic cholecystectomy conversion to open. Gallstones impacted in Hartmann's pouch or blocking the cystic duct were discovered in 95% of cases of acute calculus cholecystitis, according to **Nathaniel *et al.* [29].** This suggests that stone obstruction of the cystic duct was most likely the main etiologic factor to the pathologic changes of acute calculus cholecystitis. They stated that only 3–4% of people had acute calculus cholecystitis.

CONCLUSION

Gallstones are often the cause of AC. In order to get the 1st line therapies for AC, which include analgesics, IV fluids, and fasting, patients should be taken to the hospital very away. Surgery (cholecystectomy) should be performed as the 1st line of therapy within 24 to 48 hours of admission (early). Although this study used an open cholecystectomy,

laparoscopic cholecystectomy is the preferred and gold standard procedure. There are no clear-cut standards for diagnosing AC, with the exception of a few well-known clinical indicators, such as Murphy's sign. Therefore, the 2018 Tokyo recommendations are useful for early AC diagnosis, severity classification, and management. Consequently, patient morbidity and death are decreased. The short follow-up period to ascertain the results is the main drawback of this study. Further studies with larger samples size from multi-centers with a longer period of follow up are recommended to reinforce our findings. Moreover, another studies could be performed to assess validity of new TG18 guidelines in diagnosis and assessment severity of acute cholangitis.

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REFERENCES

1. **Mencarini L, Vestito A, Zagari RM, Montagnani M** (2024): The diagnosis and treatment of acute cholecystitis: a comprehensive narrative review for a practical approach. J Clin Med., 13 (9): 2695. doi:10.3390/jcm13092695.
2. **Wang X, Niu X, Tao P *et al.*** (2023): Comparison of the safety and effectiveness of different surgical timing for acute cholecystitis after percutaneous transhepatic gallbladder drainage: a systematic review and meta-analysis. Langenbecks Arch Surg., 408 (1): 125.
3. **Escartín A, González M, Cuello E *et al.*** (2019): Acute cholecystitis in very elderly patients: disease management, outcomes, and risk factors for complications. Surg Res Pract., 55: 1–7.
4. **Tanaja J, Lopez R, Meer J (2025):** Cholelithiasis. StatPearls . https://pubmed.ncbi.nlm.nih.gov/29262107/
5. **Cianci P, Restini E (2021):** Management of cholelithiasis with choledocholithiasis: endoscopic and surgical approaches. World J Gastroenterol., 27 (28): 4536–4554. doi:10.3748/wjg.v27.i28.4536.
6. **Miura F, Takada T, Kawarada Y *et al.* (2007):** Flowcharts for the diagnosis and treatment of acute cholangitis and cholecystitis: Tokyo Guidelines. J Hepatobiliary Pancreat Surg., 14 (1): 27–34. doi:10.1007/s00534-006-1153-x.
7. **Miura F, Takada T, Strasberg SM *et al.* (2013):** TG13 flowchart for the management of acute cholangitis and cholecystitis. J Hepatobiliary Pancreat Sci., 20 (1): 47–54. doi:10.1007/s00534-012-0563-1.
8. **Seyit M, Yilmaz A, Yilmaz S *et al.* (2021):** Does the frequency of acute cholecystitis decrease during the Ramadan month? Int J Health Serv Res Policy, 6 (3): 337–344.
9. **Faul F, Erdfelder E, Lang A, Buchner A (2007):** G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods, 39: 175–191.
10. **Demirkan A, Tanrıverdi AK, Çetinkaya A *et al.* (2019):** The effect of leucocytosis, gender difference, and ultrasound in the diagnosis of acute cholecystitis in the elderly population. Emerg Med Int., 1: 6428340.
11. **Völzke H, Baumeister SE, Alte D *et al.* (2005):** Independent risk factors for gallstone formation in a region with high cholelithiasis prevalence. Digestion, 71 (2): 97–105.
12. **Novacek G (2006):** Gender and gallstone disease. Wien Med Wochenschr., 156 (19-20): 527–533. doi:10.1007/s10354-006-0346-x.
13. **Sangma MMB, Marak F (2016):** Clinicoetiopathological studies of acute cholecystitis. Int Surg J., 3 (2): 914.
14. **Shridhar M, Shivakumar M, Satish H *et al.* (2023):** Effectiveness of Tokyo Guidelines 2018 in the management of acute cholangitis and acute cholecystitis. Int J Adv Res., 11: 175–187. doi:10.21474/IJAR01/16866.
15. **Kune G, Gill G (1990):** Cholecystitis. In: Maingot's abdominal surgery. Schwartz SI, Ellis H, Husser WC (eds). Appleton & Large, London, 9th ed.
16. **Roslyn J, Zinner M (1944):** Gall bladder and extrahepatic biliary system. In: Principles of surgery. Schwartz SI, Shire FC, Husser WC (eds). McGraw-Hill, New York, 6th ed.
17. **Yokoe M, Hata J, Takada T *et al.* (2018):** Tokyo Guidelines 2018: diagnostic criteria and severity grading of acute cholecystitis (with videos). J Hepatobiliary Pancreat Sci., 25 (1): 41–54. doi:10.1002/jhbp.515.
18. **Coaston T, Vadlakonda A, Curry J *et al.* (2024):** Association of severe obesity with risk of conversion to open in laparoscopic cholecystectomy for acute cholecystitis. Surg Open Sci., 20: 1–6.
19. **Aune D, Vatten LJ, Boffetta P (2016):** Tobacco smoking and the risk of gallbladder disease. Eur J Epidemiol., 31 (7): 643–653. doi:10.1007/s10654-016-0124-z.
20. **Amirthalingam V, Low J, Woon W, Shelat V (2017):** Tokyo Guidelines 2013 may be too restrictive and patients with moderate and severe acute cholecystitis can be managed by early cholecystectomy too. Surg Endosc., 31: 2892–2900.
21. **Okamoto K, Suzuki K, Takada T *et al.* (2018):** Tokyo Guidelines 2018: flowchart for the management of acute cholecystitis. J Hepatobiliary Pancreat Sci., 25: 55–72.
22. **Yuzbasioglu Y (2017):** The role of C-reactive protein in the evaluation of the severity of acute cholecystitis. Acta Med Mediterr., 33: 475–480.
23. **Yazıcı P, Demir U, Bozdağ E *et al.* (2015):** What is the effect of treatment modality on red blood cell distribution width in patients with acute cholecystitis? Turk J Surg., 31: 1–4.
24. **Hwang H, Marsh I, Doyle J (2014):** Does ultrasonography accurately diagnose acute cholecystitis? Improving diagnostic accuracy based on a review at a regional hospital. Can J Surg., 57: 162–168.
25. **Beliaev AM, Marshall RJ, Booth M (2015):** C-reactive protein has a better discriminative power than white cell count in the diagnosis of acute cholecystitis. J Surg Res., 198: 66–72.

26. **Lee S, Chang CS, Lee T *et al.* (2010):** The role of the Tokyo Guidelines in the diagnosis of acute calculous cholecystitis. J Hepatobiliary Pancreat Sci., 17: 879–884.
27. **Teckchandani N, Garg P, Hadke N *et al.* (2010):** Predictive factors for successful early laparoscopic cholecystectomy in acute cholecystitis: a prospective study. Int J Surg., 8 (8): 623–627. doi:10.1016/j.ijsu.2010.05.014.
28. **Licciardello A, Arena M, Nicosia A *et al.* (2014):** Preoperative risk factors for conversion from laparoscopic to open cholecystectomy. Eur Rev Med Pharmacol Sci., 18(2): 60–68.
29. **Nikfarjam M (2019):** Incidence and predictors of common bile duct stones in patients with acute cholecystitis. https://doi.org/10.1111/ans.15565
30. **Asai K, Watanabe M, Kusachi S *et al.*** (2012): Bacteriological analysis of bile in acute cholecystitis according to the Tokyo Guidelines. J Hepatobiliary Pancreat Sci., 19 (4): 476–486. doi:10.1007/s00534-011-0463-9.
31. **Takada T, Strasberg S, Solomkin J *et al.*** (2013): TG13: updated Tokyo Guidelines for the management of acute cholangitis and cholecystitis. J Hepatobiliary Pancreat Sci., 20 (1): 1–7.