

“How Hot Is Too Hot to Handle”: A Retrospective Analysis of “Hot Cholecystectomy” at a Tertiary Care Centre

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ABSTRACT

Introduction: Acute Cholecystitis (AC) can either be managed by Laparoscopic Cholecystectomy (LC) during an acute attack, termed as “Hot Cholecystectomy”, or can be managed conservatively with antibiotics followed by LC after 6-8 weeks, termed as “Interval Cholecystectomy”. Although various studies have now established beneficial role of emergency LC, the timing of early cholecystectomy is still a topic of debate.

Aim: To study clinical outcome in patients of emergency LC and compare it with duration of attack of AC.

Materials and Methods: This is a retrospective review of patients undergoing LC at Department of General and Laparoscopic Surgery of Max Superspeciality Hospital, Patparganj Industrial area, Delhi. Patients who were treated by emergency LC (Group

A, n=121) were compared to those who had undergone elective LC (Group B, n=168). Emergency LC patients were divided into three groups based on duration of AC: <3 days (Group Aa, n=50), 4-7 days (Group Ab, n=42), >7 days (Group Ac, n=29).

Results: Mean operative time, duration of hospital stay and use of drain was higher and rate of conversion (1.6%) and complication (1.6%) was low in Group A. Degree of inflammatory changes, duration of stay and operative time was significantly more in Group Ac as compared to Group Aa and Group Ab but conversion rate and complication rates were similar.

Conclusion: Hot Cholecystectomy, although technically more challenging is safe and effective with no mortality and similar rate of complication, irrespective of the duration of symptoms.

Keywords: Acute cholecystitis, Lap cholecystectomy, Timing of cholecystectomy

INTRODUCTION

Cholelithiasis is the most common pathology affecting Gall Bladder (GB). It affects 10-25% of population, with varying rates seen in different geographical regions. They can be asymptomatic or can present with dyspeptic symptoms, biliary colic or different complications, most prominent of which is AC. The management protocol for AC has been evaluated a lot in the recent past. It can either be managed by LC during an acute attack, termed as “Hot Cholecystectomy” or can be managed conservatively with antibiotics followed by LC after 6-8 weeks, termed as “Interval Cholecystectomy”. In the past, because of oedema, exudate, adhesions with adjoining structures, friability of tissues, distorted anatomy [1], hypervascularity, or congestion seen during acute inflammation, the complication rates were thought to be, as well as found to be, high in emergency LC [2]. However, with increasing experience in field of laparoscopy, various studies have now reported beneficial role of emergency LC with no increase in morbidity [3-8].

On the other hand, interval LC was seen to be associated with 20% to 26% risk of failure of conservative management or development of early complications, necessitating an urgent and technically demanding cholecystectomy [7,9,10]. Also, 15% to 20% of patients needed readmission for recurrent symptoms while waiting for surgery [6,10,11]. Conservative management of AC allows maturation of acute inflammation, neovascularisation, fibrosis, and contraction of tissue planes, making the dissection more difficult. Therefore, surgeons may find shrunken, fibrotic GB with fibrosis at Calot's region during interval LC [12,13]. The total cost of interval LC is also higher, as patients had longer total length of hospital stay because of initial admission for conservative treatment [3,4,5,8].

Still many centres practice the concept of interval LC, believing it to be a safer option. The timing of hot cholecystectomy is also a topic of debate among surgeons. Some studies have reported increased rate of complication and conversion to open cholecystectomy after 72 hours of acute attack [14,15], whereas, some have reported

similar rate in patients operated even after 72 hours [13,16,17]. Understandably, more and more institutions are doing emergency LC and that too after 72 hours of acute symptoms. Whereas, there are centres which still follow golden rule of 72 hours, and take up the patients, presenting after 72 hours, for interval LC. Therefore, the study was carried out with an aim to study clinical outcome in patients of emergency LC and compare it with duration of attack of AC.

MATERIALS AND METHODS

This is a retrospective review of patients who had undergone LC, elective and emergency, at Department of General and Laparoscopic Surgery of Max Superspeciality Hospital, Patparganj Industrial area, Delhi, between May 2017 to November 2017. All procedures performed in studies, involving human participants, were in accordance with the Ethical standards of the institutional and/or National Research Committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The permission of Institutional Ethics Committee, for waiver of consent in view of retrospective nature of study, was taken via Ref. no. RS/MSSH/BMDRC/GENSURG/EC/18-08 dated 14th April, 2018.

Study Groups

Group A: The patients who had undergone emergency LC for AC were included in this group. The diagnosis of AC was re-confirmed based on the presence of at least two of the following criteria:

- Acute upper abdominal pain and Murphy's sign [18];
- Fever >37.5°C and white blood cell count >11,000 cells per cubic mm;
- Ultrasound findings of thick-walled gallbladder, ultrasound Murphy's sign, and pericholecystic fluid, in the presence of gallstones.

Based on duration of AC, authors further divided the Group A (emergency cholecystectomy) into three subgroups:

- Group Aa: ≤ 72 hours from onset of attack;
- Group Ab: 72 hours to ≤ 7 days from onset of attack;
- Group Ac: > 7 days from onset of attack.

Group B: The patients who had undergone elective LC for symptomatic gallstone disease were included in Group B. Diagnosis of symptomatic gallstone disease was defined by following symptoms, in presence of ultrasonographic report of Gall stones:

- Biliary Colic defined by pain right hypochondrium, lasting less than six hours and not requiring admission;
- Dyspeptic symptoms

Only the cases operated by five senior surgeons of the hospital were included. All cases were done by standard four port technique. Patients with no gallstones, incomplete records, obstructive jaundice, cholangitis or Common bile duct calculi, those undergoing emergency LC for biliary pancreatitis and those with prior history of AC/pancreatitis or previous upper abdominal surgery were excluded from study. Also, patients who could not be operated within 24 hours of admission were excluded from study to have a uniform total length of stay being unaffected by preoperative stay.

Following parameters were retrieved from records of patients:

- Baseline characteristic like age, sex, presenting complaints, co morbid conditions etc.,
- Blood investigations and ultrasonography report;
- Preoperative and postoperative antibiotics use;
- Intraoperative findings were reviewed including duration of surgery and use of drain;
- Duration of stay (preoperative and postoperative)
- Conversion to open and biliary leak (Intraoperatively or diagnosed postoperatively)

Intraoperative findings were divided into four groups:

- **Nil:** no oedema or adhesion to GB;
- **Oedema:** tissue planes around GB are oedematous irrespective of adhesions;
- **Mild adhesion:** Minimal adhesion, easily separable, tissue planes at calot's intact;
- **Dense adhesion:** difficult adhesion requiring meticulous dissection, tissue planes at calot's not identifiable.

STATISTICAL ANALYSIS

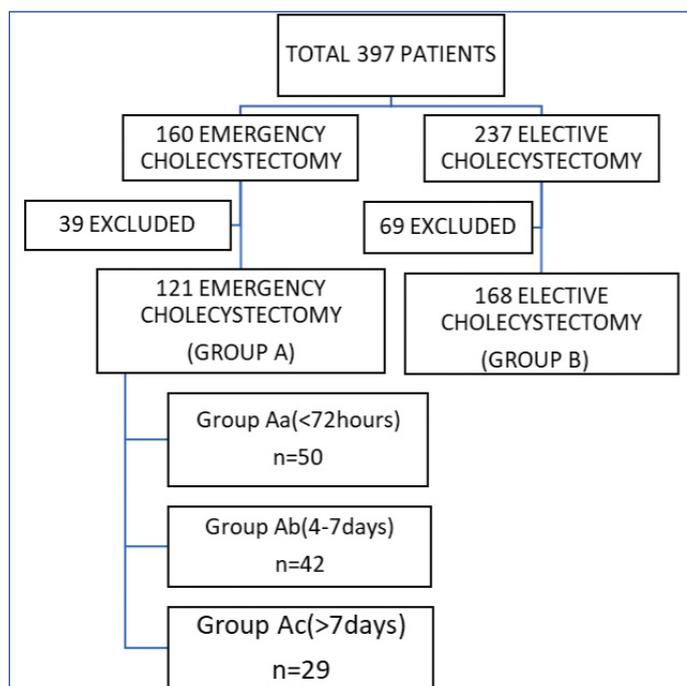
Data were represented as means for continuous data and proportions for parametric data. Mean was assessed using Student's t-test and parametric data were assessed using chi-square test. A p-value of 0.05 was taken as a cut-off for significance of tests.

RESULTS

During the period of seven months, 160 patients had undergone emergency LC. Out of these, five had past history of AC or pancreatitis, 10 were for acute pancreatitis, 10 had obstructed biliopathy, four had previous upper abdomen surgery and 10 patients had incomplete records. Remaining 121 were reviewed as Group A as shown in [Table/Fig-1]. The duration of onset of symptoms ranges from 1-13 days.

A total of 237 patients had undergone elective LC for Gallstone disease (biliary colic, dyspeptic symptoms, history of attack of AC and acute pancreatitis). Out of this 15 had history of obstructed biliopathy/ERCP, 20 had ERCP in same admission, 17 had history of AC or pancreatitis (admitted for interval cholecystectomy), six had previous upper abdomen surgery and 11 patients had incomplete records. Remaining 168 were reviewed as Group B as shown [Table/Fig-1].

Both groups were comparable in terms of age, sex distribution and presence of comorbidities like diabetes, hypertension, heart disease, hypothyroid etc. The results are tabulated in [Table/Fig-2].



[Table/Fig-1]: Distribution of study population.

Variables	Group A (n=121)	Group B (n=168)	p-value
Age (years)	47 \pm 2.54	46.85 \pm 2.07	0.93
Sex			0.57
Male (%)	39 (32.23%)	49 (29.17%)	
Female (%)	82 (67.77%)	119 (70.83%)	
Co morbidities:			
Nil (%)	77 (63.63%)	99 (58.9%)	0.418
Diabetes (%)	21 (17.35%)	22 (13.09%)	0.315
Hypertension (%)	20 (16.53%)	32 (19.05%)	0.583
Hypothyroid (%)	15 (12.4%)	18 (10.07%)	0.657
Others (%)	9 (7.44%)	19 (11.3%)	0.2723
Intraoperative:			
Dense adhesion (%)	37 (30.57%)	15 (8.9%)	<0.00001
Mild adhesion (%)	2 (1.65%)	16 (9.5%)	
Oedema (%)	78 (64.46%)	0	
Nil (%)	0	137 (81.54%)	
Gangrenous GB (%)	3 (2.48%)	0	
Contained GB perforation (%)	1	0	
Others:			
Thick Walled GB (%)	18 (14.88%)	25 (14.88%)	0.99
Empyema (%)	23 (19%)	2 (1.2%)	
Mucocele (%)	5 (4.13%)	7 (4.17%)	
Surgery time (min)	68.22 \pm 5.4	53.04 \pm 2.83	<0.00001
Duration of Stay (days)	2.71 \pm 0.25	2.03 \pm 0.03	<0.00001
Use of drain (%)	34 (28.1%)	6 (3.6%)	<0.00001
Cholecystostomy (%)	2 (1.6%)	0	
Conversion to open Cholecystectomy (%)	2 (1.6%)	0	
Retrograde Cholecystectomy (%)	5 (4.13%)	2 (1.19%)	
Bile leak (%)	2 (1.6%)	0	

p-value <0.05 is significant

[Table/Fig-2]: Demographic profile and intraoperative parameters of Group A and Group B.

Authors further divided the emergency cholecystectomy group into three subgroups:

- Group Aa: ≤ 72 hours from onset of attack;
- Group Ab: 72 hours to ≤ 7 days from onset of attack;
- Group Ac: > 7 days from onset of attack.

All groups were comparable in terms of age, sex distribution and presence of co-morbidities like diabetes, hypertension, heart disease, hypothyroid etc. Results are tabulated in [Table/Fig-3,4].

Variables	Group Aa (n=50)	Group Ab (n=42)	Group Ac (n=29)	p-value
Range (days)	1-3	4-7	8-13	
Sex				
Male (%)	21 (42%)	9 (21.42%)	9 (31%)	0.11
Female (%)	29 (58%)	33 (78.6%)	20 (69%)	
No of Co morbidities:				
Nil (%)	33 (66%)	25 (59.5%)	19 (65.5%)	0.792
Diabetes (%)	6 (12%)	8 (19.04%)	7 (24.14%)	0.365
Hypertension (%)	7 (14%)	7 (16.67%)	6 (20.7%)	0.742
Hypothyroid (%)	6 (12%)	6 (14.3%)	3 (10.4%)	0.879
Others (%)	2 (4%)	4 (9.53%)	3 (10.4%)	0.477
Intraoperative				
Oedema (%)	41 (82%)	30 (71.43%)	7 (24.14%)	<0.00001
Dense (%)	7 (14%)	10 (23.8%)	20 (69%)	<0.00001
Empyema (%)	8 (16%)	12 (28.6%)	9 (31%)	0.34
Perforated GB (%)	0	0	1	
Gangrenous GB (%)	2	1	0	
Others				
Use of drain (%)	6 (12%)	8 (19%)	20 (69%)	<0.00001
Cholecystostomy (%)	1	1	0	
Conversion to open cholecystectomy (%)	1 (2%)	1 (2.38%)	0	
Retrograde cholecystectomy (%)	1	1	3	
Bile leak (%)	-	1 (2.38%)	1 (3.4%)	
p-value <0.05 is significant				

[Table/Fig-3]: Demographic profile and intraoperative parameters of three subgroups of patient undergoing emergency LC.

	Group Aa vs Group Ab		Group Ab vs Group Ac		Group Aa vs Group Ac	
Age (years)	45.06 \pm 3.72	46.04 \pm 4.28	46.04 \pm 4.28	49.72 \pm 4.28	45.06 \pm 3.72	49.72 \pm 4.28
	p=0.73		p=0.11		p=0.63	
OT time (min)	63.8 \pm 7.01	63.8 \pm 8.35	63.8 \pm 8.35	82.24 \pm 13.67	63.8 \pm 7.01	82.24 \pm 13.67
	p=0.99		p=0.026		p=0.02	
Total stay (days)	2.4 \pm 0.25	2.67 \pm 0.4	2.67 \pm 0.4	3.31 \pm 0.69	2.4 \pm 0.25	3.31 \pm 0.69
	p=0.3		p=0.121		p=0.018	
p-value <0.05 is significant						

[Table/Fig-4]: Comparison of variables between three subgroups of Group A.

As per institutional protocol, antibiotic use was as follows:

- After admission, all acute cases were started on injectable cefuroxime and injectable metronidazole.
- Elective LC cases were started on injectable cefuroxime at the time of induction only.
- Both the groups were continued on same antibiotics in post operative period.

DISCUSSION

Authors analysed the records of a total of 121 emergency LC and 168 elective LC patients. Patients with previous upper abdominal surgery, ERCP or past/current obstructed biliopathy were excluded

to minimise the effect of adhesion/inflammation due to any pathology other than gall stones.

Interval LC may be challenging as conservative management of cholecystitis allows maturation of acute inflammation, neovascularisation, fibrosis and contraction of tissue planes [12]. While inflammation in the early stages may not necessarily involve the structures in Calot's triangle, chronic inflammation over the time may involve the Calot's region, obscuring anatomy and making dissection difficult, especially in region of bile duct [12,13]. Difficult dissection translates into higher risk of injury to surrounding structures, biliary injury or conversion to open with consequent increased pulmonary and stitch line complications.

Because of risk of increased fibrosis during interval LC, comparing emergency LC with interval LC, might not be a good indicator of difficulty encountered or increased morbidity during emergency LC. Thus, authors compared AC patients to Group B which had no prior history of AC, expecting as normal anatomy as possible in non-inflamed GB. However, thick-walled GB, an indirect marker of recurrent inflammation due to gallstones leading to fibrosis and wall thickening, was found to be equally distributed in both groups, signifying the effect of gall stones and subclinical infection over time irrespective of acute attacks.

Majority of patients in Group B (81%) had no inflammation or adhesion followed by 9% cases showing dense adhesion, whereas in Group A 64% patient had oedema followed by dense adhesion in 30% cases. This difference in dense adhesion between two groups was statistically significant ($p < 0.00001$), implying increased operative difficulty in Group A. Retrograde dissection, done in cases of obscured anatomy in calot's region, was also more common in Group A.

More difficult surgery, eventually means longer surgery time as also seen in present records, Group A (68.22 \pm 5.4 minutes) vs Group B (53.04 \pm 2.83 minutes), which was statistically significant ($p < 0.001$). Difficult intraoperative findings mean difficult dissection, which means more common use of drain as seen in the present records. According to study by Suter M and Meyer A, comparing Elective LC to Emergency LC (22% patients had persistent symptoms for seven days or more), surgery duration was significantly longer in Emergency LC group as compared to Elective LC (111 vs 90 minutes; $p < 0.001$) [19].

Conversion to open was done in only two cases (1.6%) in emergency group whereas no conversion was reported in the elective group. The reason for conversion in both cases was dense adhesion. According to study by Suter M and Meyer A, Emergency LC had more risk of conversion to open (4% vs 15.6%; $p < 0.001$) and the main reason was adhesions not manageable laparoscopically [19]. Whereas, Lai PB et al., reported similar conversion rate in interval (24%) and emergency LC group (21%) [5]. Rate of conversion in our study in Emergency LC is lower than reported by de Mestral C et al., (11%), Lai PB et al., (21%), Tzovaras G et al., (4.6%), Al-Mulhim AA (5%), Wang YC et al., (3.6%), Suter M and Meyer A, Hadad SM et al., (24.4%) and Sert I et al., (13.4%) [4,5,12,15,16,19,20,21], whereas studies

like Zhu B et al., and Gomes RM et al., reported no conversion in any case [13,17].

Also, rate of open cholecystectomy or conversion of LC depends on experience of surgeon. Study by Sert I et al., reported a conversion rate of 13.4% and almost 50% of the patients were taken up directly for open cholecystectomy [21]. Authors have accepted that most of the open cholecystectomy operations were performed in the initial period of their routine early cholecystectomy experiences, implying role of surgeon's expertise.

Mean duration of stay was significantly longer for Group A (2.71±0.25 days) as compared to Group B (2.03±0.03 days), (p<0.001). This extra stay in majority of cases was due to use of drain signifying difficult surgery. The study by Suter M and Meyer A, also shows similar findings (5.5 days versus 3.4 days, p<0.001) [19].

Two cases of bile leak were seen in Group A (1.6%). One was due to Common Hepatic duct injury, managed by stenting and other was due to cystic duct stump leak managed on drain placement only. No biliary injury or leak was seen in Group B. Study by Suter M and Meyer A, reports more rate of overall complications in emergency LC but similar rate of major complications like biliary injury (2.6%) between the two groups [19]. The rate of bile leak/injury as seen in the present patients was less than reported by Tzovaras G et al., (3.1%) and Al-Mulhim AA (1.8%), Suter M and Meyer A (2.6%) [12,15,19], whereas studies like Zhu B et al., and Gomes RM et al., reported no bile injury or leak in any case [13,17].

The timing of emergency LC is also a topic of debate. The inflammatory response of AC has a well-described pathological course. In the early phase, the stages of hyperaemia and oedema predominate and this may even facilitate laparoscopic dissection of the Calot's triangle. After 72 hours, chronic inflammatory changes like adhesions, fibrosis and necrosis replaces hyperaemia and oedema. These changes are responsible for the difficulty in laparoscopic dissection of the Calot's triangle seen after 72 hours [17]. Therefore, it is expected, that after 72-96 hours of acute attack, the difficulty in surgery and consequently the complication rate should increase.

As per the present records, oedema was more commonly seen in Group Aa (82%) and Group Ab (71%) as compared to Group Ac (24%) whereas dense adhesion was more common in Group Ac (69%) as compared to Group Ab (24%) and Group Aa (14%). This difference was statistically significant (p<0.001). This signifies that as duration of attack increases, oedematous component is replaced by fibrosis. Study by Zhu B et al., (study population <72 hours after onset of AC, >72 hours after onset of AC, range 4-21 days) and González-Rodríguez FJ et al., also reported increasing difficulty in surgery beyond 72 hours due to adhesions [13,14]. Study by Catani M and Modini C, also reported that beyond 60 hours of onset of AC, operative time doubles due to increased adhesions making LC more difficult and more morbid [22]. However, study by Wang YC et al., and Gomes RM et al., (study population <72 hours after onset of AC, >72 hours after onset of AC, range 4-21 days) show that degree of inflammation at varying time of presentation may be similar [16,17]; thus, consolidating the fact that the pathological course of AC is not simply a time-dependent event but depends on a number of risk factors such as advanced age, male sex, comorbidity etc.

The severity of adhesion and inflammation may increase with duration of attack but rate of conversion was not affected as shown by Zhu B et al., and Gomes RM et al., [13,17], whereas González-Rodríguez FJ et al., (7.8% in <72 hours vs 18.4% in >72 hours, p = 0.02) and Hadad SM et al., (9.5%, 16.1%, 38.9%, and 38.6% for delays of 0-2 days, 3-4 days, 5-6 days, and >6 days from symptom onset, respectively, p≤0.001) show increasing rate of conversion with increasing duration [14,20]. A study by Tzovaras G et al., study population <72 hours, 4-7 days and >7 days, show increasing rate of conversion from Group 1 {1 (2.8%)}, Group 2 {2(3.4%)} to Group 3 {3 (8.5%)} but the result could not reach statistical significance

[12]. As per the present records, only two patients were converted to open due to dense adhesions. One belongs to Group Aa (2%) and other to Group Ab (2.38%). The rate of conversion was lower in the present study as compared to what has been reported in literature, whereas studies like Zhu B et al., and Gomes RM et al., reported no conversion in any case [13,17]. Similarly, in another two patients, both were <5 days, adhesions were so severe; it was decided against conversion to open. In these patients, LC was abandoned in favour of laparoscopic cholecystostomy.

As per the records, operative time was similar in Group Aa (63.8±7.01 minutes) and Group Ab (63.8±8.35 minutes) but statistically more in Group Ac (82.24±13.67 minutes) representing difficult anatomy requiring more time. A study by Tzovaras G et al., study population <72 hours, 4-7 days and >7 days, also show similar results with surgery duration increasing significantly from Group 1 (55 minutes, range 35-90 minute) to Group 3 (72.5 minutes, range 35-120 minute, p<0.05) [12]. According to study by Al-Mulhim AA, the mean operation time was less (105±49.5 minutes) when patients were operated within 72 hours as compared to when operated >72 hours (126±56.9 minutes) (p=0.008) [15]. The study by Zhu B et al., also shows a similar result of significantly longer operative time (44.1±5.32 minutes vs. 66.4±3.05 minutes, p=0.01) in patients operated >72 hours after attack [13]. On the other hand, study by Wang YC et al., and Gomes RM et al., shows no difference in operative duration when operated before or after 72-96 hours [16,17]. In the present records, surgery duration was similar till 7 days of onset and increased duration was seen in patients with >7 days of onset.

The mean duration of stay shows significantly increasing trend from Group Aa (2.4±0.25 days), Group Ab (2.67±0.4 days) to Group Ac (3.31±0.69days). Studies by Al-Mulhim AA and Gomes RM et al., show longer mean duration of stay in >72 hours group but it failed to reach statistical significance [15,17], whereas study by Tzovaras G et al., and Zhu B et al., reported similar mean postoperative stay in all groups [12,13]. The major reason for increase in duration of stay in the present study was use of drain as shown in [Table/Fig-5]. The use of drain was more common in Group Ac (69%) as compared to Group Ab (19%) and Group Aa (12%). This difference was statistically significant (p≤0.00001). According to study by Tzovaras G et al., drain usage was more common in 4-7 days group but similar in <3 days and >7 days group, reason not given [12].

1.	Dense adhesion±empyema*	26
2.	Bile Leak [†]	2
3.	Perforated GB	1
4.	Gangrenous	3
5.	Oedema±Empyema*	3

[Table/Fig-5]: Distribution of reason for Drain use in Group A.

*: drain due to Difficult dissection; †: 1 patient of bile leak was already inserted drain intraoperatively, 1 inserted postoperatively

Only two patients reported biliary leak, both diagnosed in same hospital stay and managed non-operatively. one case was seven days duration (2.38%) and other was 10 days duration (3.4%). Study by Al-Mulhim AA reported similar findings of one case each of CBD injury and cystic duct leak, both in >72 hours group [15]. Whereas, Zhu B et al., and Gomes RM et al., did not report any bile leak or injury in any group [13,17]. According to Tzovaras G et al., no bile duct injury was seen, although bile leak was seen in two cases each, in 4-7 day (3.49%) and >7-day group (5.7%) [12].

A benefit of hot cholecystectomy, which authors could not assess in present study, is shorter total length of hospital stay as compared to interval LC [3,4,5,8]. This is because a patient of interval LC needs an initial admission for conservative management of AC, followed by readmission for LC. According to study by de Mestral C et al., total hospital length of stay was shorter by mean difference of 1.9 days [4] whereas a much higher difference has been reported by various

studies such as Gutt CN et al., (5.4 days vs 10.0 days), Lai PB et al., (7.6 days versus 11.6 days) and Agrawal R et al., (4.1 days versus 8.6 days) [3,5,8]. In the present study, 5 cases excluded from Group A and 17 cases excluded from Group B, due to past history of AC or pancreatitis, also gave history of admission for 3-4 days for conservative management, either in the centre or some other hospital. Shorter length of hospital stay translates in lower cost of treatment [3] and less number of working days being lost as compared to interval LC.

LIMITATION

The study was limited by its retrospective design and smaller sample size in AC Group greater than seven days.

CONCLUSION

Patients of AC have more difficult anatomy and LC in these patients is technically more challenging, but it is safe and effective with no mortality and low rate of complication. Also, in hands of an experienced Laparoscopic surgeon, patients of AC can be safely and effectively managed by Hot Cholecystectomy with minimal morbidity, irrespective of duration of symptoms.

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