



A CLINICO DEMOGRAPHIC STUDY OF ACUTE CALCULOUS AND ACUTE ACALCULOUS CHOLECYSTITIS—A CROSS- SECTIONAL STUDY

General Surgery

Dr. Debodeep Debnath	Senior Resident General Surgery Regional Institute Of Medical Sciences Imphal West, Manipur, India
Dr. Khuraijam Gojen Singh*	Associate Professor General Surgery Regional Institute Of Medical Sciences Imphal West, Manipur, India *Corresponding Author
Dr. Keisham Lokendra Singh	Assistant Professor General Surgery Regional Institute Of Medical Sciences Imphal West, Manipur, India
Dr. Kharibam Karnajit Singh	Senior Resident General Surgery Regional Institute Of Medical Sciences Imphal West, Manipur, India.
Dr. Ajith Kumar R	Post Graduate Trainee, General Surgery Regional Institute Of Medical Sciences Imphal West, Manipur, India
Dr. Prem Shankar	Post Graduate Trainee, General Surgery Regional Institute Of Medical Sciences Imphal West, Manipur, India
Dr. Ajit Kumar Panda	Post Graduate Trainee General Surgery Regional Institute Of Medical Sciences Imphal West, Manipur, India
Dr. Trishan Ghosh	Post Graduate Trainee General Surgery Regional Institute Of Medical Sciences Imphal West, Manipur, India
Dr. Ruchi Tame D Momin	Post Graduate Trainee General Surgery Regional Institute Of Medical Sciences Imphal West, Manipur, India

ABSTRACT

Introduction: Acute cholecystitis is a common cause of acute abdomen and a frequently encountered surgical emergency. Acalculous cholecystitis is a life-threatening disorder that has a high risk of perforation and necrosis compared to the more typical calculous disease. A varying degree of inflammation is seen among them. **Objectives:** To document the baseline clinico demography of acute calculous and acute acalculous cholecystitis in this part of the country. **Methods:** A cross sectional study was conducted from January, 2021 to June, 2022 in the Department of Surgery, RIMS Hospital, Imphal. Patients above 18 years who were diagnosed with acute cholecystitis and undergone cholecystectomy during the study period were included in the study. Age, sex, marital status, family history, HTN, DM, clinical history like, fever, pain, vomiting, etc., clinical examination findings like tenderness, Icterus, etc. were the independent variables. Outcome variables were intraoperative findings like type of stones, GB status, HPE findings, etc. Data collected were analyzed using SPSS-version-21. Chi-square test and Fisher's exact test were used for proportions. A p-value of <0.05 was taken as significant. **Results:** Out of 100 cholecystectomy patients included in the study 74% were females. Majority of the participants (30%) were in the age group of 31-40 years. All the patients had tenderness at right hypochondrium and Murphy's sign were present. Calculous cholecystitis was seen in 78% and acalculous cholecystitis in 22% of the patients. GB inflammation and GB mucocele were significantly associated with acalculous cholecystitis. But GB adhesion was significantly associated with calculous cholecystitis. **Conclusion:** Acalculous cholecystitis does occur in few and associated with complications, thus it should not be neglected. A young patient with absent of calculous in USG having signs and symptoms of acute cholecystitis with positive family history should be suspected to have acalculous cholecystitis. Early diagnosis and operation should be done at the earliest for both cholecystitis to avoid complications like empyema, adhesion with omentum and other viscera.

KEYWORDS

inflammation, gall bladder, empyema, cholecystectomy, adhesion

INTRODUCTION

Gallbladder is the organ where bile is stored and concentrated, which helps in digestion of fat [1]. Acute cholecystitis is a common cause of acute abdomen and a frequently encountered surgical emergency. About 95% of the patients with cholecystitis are calculus cholecystitis and the remaining 5% of the patients are acalculus cholecystitis [2].

Acalculous cholecystitis is a form of cholecystitis caused by dysfunction or hypokinesis of gallbladder emptying whereas calculous cholecystitis is caused by a mechanical blockage of the gallbladder outlet at the cystic duct, usually by a gallstone. Acalculous cholecystitis was first described by Duncan in 1844. Acalculous cholecystitis is a life-threatening disorder that has a high risk of perforation and necrosis compared to the more typical calculous disease [3][4][5]. There are many different factors which can cause dysfunction of gallbladder. Long periods of fasting, total parenteral nutrition (TPN) and drastic weight loss can all increase the incidence of acalculous cholecystitis. Patients in the intensive care unit, sepsis, severe burns, stroke, heart attack and extensive trauma are high risk for acalculous cholecystitis. Bile salt concentration occurs due to gallbladder stasis and lack of gallbladder stimulation which leads to increase pressure within the organ further leading to ischemia, pressure necrosis and eventual perforation. The GB stasis also

increases seeding and growth of enteric pathogens such as *Escherichia coli*, *Klebsiella*, *Bacteroides*, *Proteus*, *Pseudomonas*, and *Enterococcus faecalis* [6,7].

Autopsy report show prevalence of gallstone ranges from 11-36% [8]. The gallstone disease is frequent found among high socioeconomic status prevalent in the northern part of India. The incidence of gallstone is commonly seen in females, with a female to male ratio of 1:4.3 and more common among multiparous females. In western countries about 80 percent of gall stone are cholesterol stone and about 15-20 percent are black pigment stones. Cholesterol and mixed gall stones are formed from biliary sludge whereas pigment stones are composed of unconjugated bilirubin with variable amounts of cholesterol and protein [9].

There are varying degrees of inflammation seen in acalculous cholecystitis and calculous cholecystitis. The gallbladder wall is thickened to variable degrees, and there may be adhesions to the serosal surface. Smooth muscle hypertrophy, especially in chronic conditions, is present. At times sludge or very viscous bile can be seen. These findings are usual precursors to gallstones and are formed from increased biliary salts or stasis. Various species of bacteria can be present in 11% to 30% of the cases. Rokitsky-Aschoff sinuses are

present 90% of the time in cholecystitis specimens. These are a herniation of intraluminal sinuses from increased pressures possibly associated with ducts of Luschka. The mucosa will exhibit varying degrees of inflammation from mild to ulcerations with gangrenous changes. Extreme situations may show total gangrenous changes of the gallbladder with perforation [10].

The purpose of this study is to document the baseline clinico demography of acute calculous and acute acalculous cholecystitis in this part of the country. This study will also focus on the clinico demographic differences between acute calculous and acute acalculous cholecystitis in the northeastern part of India.

MATERIALS AND METHODS

A cross sectional study was conducted from January, 2021 to June, 2022 in Manipur at the Department of Surgery, RIMS. Ethical approval was obtained from the institutional Research Ethics Board before the commencement of the study [reference no. A/206/REB-Comm(SP)/RIMS/2015/760/102/2020].

This study was conducted among above 18 years patients who attended Department of Surgery, diagnosed with acute cholecystitis and undergone cholecystectomy. Those who refused to participate, those with co-existing malignancy and those who were pregnant were excluded from the study.

A sample size of 94 was calculated using the formula, Sample size, $N = 1.962PQ/L^2$, where Taking Prevalence of acute cholecystitis as 57.7% [9] and precision (L) = 10%. Convenient sampling was done to recruit them.

Variables like age, sex, marital status, family history, HTN, DM, clinical history like, fever, pain, vomiting, etc., clinical examination findings like tenderness, Icterus, etc. Outcome variables were intraoperative findings like type of stones, GB status, etc.

Data Collection:

A detailed structured proforma was used. The initial diagnosis of acute cholecystitis was made from the detailed history, clinical examination, analysis of available laboratory data supported by radiological and ultrasonographic findings. Confirmation was made by intraoperative and histopathological findings. All operations were performed via open procedure or laparoscopically. Samples were collected as per the inclusion and exclusion criteria. Written informed consents were taken from all the participants. The participants were reassured of their anonymity at the time of data collection and the importance of an honest answer was stressed. Collected data were checked for completeness and consistency before discharge of the patient and necessary rectification was made.

The collected data were entered and analyzed in SPSS (IBM) version 21. Summarizations of data were carried out by using descriptive statistics such as mean, standard deviation and percentages. Chi-square test and Fisher's exact test were employed to test the association between two proportions of outcome variables and variables of interest like sex, age, marital status, etc. P-value of less than 0.05 was taken as statistically significant.

RESULTS

During the study period, 100 patients who underwent cholecystectomy for acute cholecystitis were included in the study, out of which there were 26 males and 74 females as shown in table/fig 1. Maximum no. of patients, 28(30%) were in the age group of 31 to 40 years and above 60 years (12%) age group had the minimum. Around three quarters (70%) of the patients belong to the Hinduism group. Most of the patients were married (72%), most of the patients were non-veg by dietary habit (80%) and only 22% of the patients had family history of cholecystitis in the past as shown in table 1.

Table 2 shows the most common symptom as pain right hypochondrium (100%) followed by Vomiting, dyspepsia, referred pain, fever, etc. Only 12% had itching symptoms and 16% complaint of jaundice. Table 2 also shows that all the patients had tenderness at right hypochondrium and Murphy's sign were present. Icterus was present in 12% of the patients. Palpable lump were felt at the right hypochondrium in only 10% of the patients. And only 6% of the patient had palpable enlarged liver.

In 78 patients, calculous cholecystitis was found and remaining 22

patient had acalculous cholecystitis. Out of 78 GB stone, around 65% were mixed type of stones, around 21% were pigments stone and around 14% were cholesterol stone. Similarly out of 78 GB stone, around 80% were multiple stones as shown in table 3. As shown in table 4, maximum of the patients had adhesion (43%) of the GB, fibrosis in only 17%, mucocele in only 9%, empyema in only 8% and polyp in only 3%. Around 20% had only inflammation of GB. No case of perforation was seen.

Table 5 shows 64 (64%) patients had chronic cholecystitis, out of which 16 were having chronic acalculous cholecystitis and 48 were having chronic calculous cholecystitis. Out of 36 acute cholecystitis patients, only 8 were having acute acalculous cholecystitis and 28 were having acute calculous cholecystitis.

There was no significant association between GB adhesion, GB fibrosis, GB inflammation and type of cholecystitis with gender as shown in table 6. But it was seen that there was a significant association between marital status and presence of calculous in GB. Married participants were more among calculous cholecystitis than unmarried participants. Similarly family history was significantly associated with acalculous cholecystitis. But there was no association between dietary habits and gender with presence of calculous among cholecystitis as shown in table 7. In table 8, it was seen that those participants with calculous cholecystitis had higher mean age than those participants with acalculous cholecystitis and it was statistically significant

Table 9 shows that calculous cholecystitis was more associated with adhesion of the GB than acalculous cholecystitis and it was found to be significant. Similarly GB inflammation was more associated with acalculous cholecystitis than calculous cholecystitis and it was found to be significant. Acalculous cholecystitis was more associated with GB mucocele and it was found to be significant. Other findings like empyema and fibrosis were not associated with presence of calculous in the GB. Presence of calculous was also not associated with chronicity of the cholecystitis

DISCUSSION

Acute Cholecystitis is a common cause of acute abdomen and a frequently encountered surgical emergency. According to a study by Sangma MM et al [2] the female to male ratio is 2.6:1, females were 72%. This study also showed 74% of the patients were female. Another study by Gupta AK et al [11] reported GB disorders were more commonly seen in females (69.2%) than males. Similar findings were reported by Mehariya MK et al [1] in their study, where females were 68% of all the GB disorder. Ezhil AN et al [12] also showed 68% female in their study. This observation may be due to the variation in physical activity among male and females.

This study showed maximum number of cases in the 4th decade i.e. 31-40 years (30%) followed by 5th (22%) and 3rd decade (22%). Similar finding has been shown by Singh AP et al [9] with maximum cases of GB disorders occurring in the age group of 31-40 years (24.85%) followed by 24.57% in the age group of 41-50 years. Another study by Gupta AK et al [11] reported GB disorders to be common in 4th decade (40%). Ezhil AN et al [12] also demonstrated maximum cases occurring in the 4th decade (36%). But Sangma MM et al [2] reported in their study that maximum cases occurring in 41 - 60 years group (45%). Thus, 4th decade of life was commonly affected with acute cholecystitis. Mehariya MK et al [1] in their study, showed that 63.33% were chronic cholecystitis in comparison to 19.66% of acute cholecystitis. In a study of Dix FP et al [13], chronic cholecystitis was seen in 95.5% and acute cholecystitis in 2.9%. In a study by Sangma MM et al [2], 72% of the cases were chronic cholecystitis with acute onset and remaining 28% were acute cholecystitis. Similarly in this study, 66% of the cases were chronic cholecystitis with acute onset and remaining 34% were acute cholecystitis.

In a study by Sangma MM et al [2], 10% of the cases had family history of acute cholecystitis. Similarly in this study family history was present in 22% of the cases. Most of the patient belonged to Hindu religion (70%) in this study. Similar finding was recorded by Sangma MM et al [2] in their study with 82% of them Hindu. This may be due to the catchment area of the hospital which has maximum Hindu population. 72% of the patients were married in this study which may be correlated with maximum cases occurring in the 4th decade of their lives. Similarly, 91% of the cases were reported married in a study by Sangma MM et al [2].

In this study, 80% of the patients were non-veg in dietary habit which may be due to the fact that most of the population in the study area are non-veg. Also in a study by Sangma MM et al [2], 99% of the patients were non vegetarian. Ezhil AN et al [12] also demonstrated to have 85% non-vegetarian in their cases. But in a study by Singh AP et al [9] 82% of the patient were vegetarian by diet. Thus, being vegetarian or non- vegetarian may not explain the association of dietary habit and cholecystitis without looking into the composition of their foods like carbohydrate, fat, protein, etc. Hypertension was present in 24% of the cases and DM was present in 10% of the cases in this study. Similarly in a study by Sangma MM et al [2], 13% and 3% of the cases had Hypertension and DM respectively.

In this study the most common symptom presented by the patient was pain right hypochondrium (100%) followed by vomiting (70%), dyspepsia (68%), referred pain (64%), fever (58%), nausea (50%) and only 12% had itching symptoms and 16% complaint of jaundice. Similarly in a study by Sangma MM et al [2], pain right hypochondrium (100%) was the most common followed by vomiting (76%), dyspepsia (84%), referred pain (32%), fever (94%), nausea (44%) and only 5% had itching symptoms and 6% complain of jaundice.

Therefore most of patient complained of pain right hypochondrium in acute cholecystitis. Similarly in this study all 100 of them had tenderness in right hypochondrium and could elicit murphy's sign in all of them. Icterus was present in 12% of the cases. Palpable lump and enlarged liver were present in 10% and 6% of the cases respectively. In a study by Kune GA et al [14], palpable gall bladder was found to be present in 40% of the cases. In other study by Sangma MM et al [2], even though 100% of the cases had tenderness, murphy's sign was elicited in 95% of the cases. Palpable lump, enlarged liver and icterus were also present in 15%, 1% and 5% of the cases in their study. Thus in most of the acute cholecystitis patient tenderness at right hypochondrium and murphy's sign were present, which was directly correlated with GB inflammation. As mentioned in other studies localized tenderness, guarding and rebound tenderness in the right upper quadrant and positive murphy's sign were consistent and suggestive of acute cholecystitis [15-17].

In the present study, stones in the gallbladder were found in 78% of the cases of acute cholecystitis which is comparable to the earlier views on the role of stone in the pathogenesis of acute calculus cholecystitis but Gallaher JR et al [15] described only 5 to 10% incidence of acute acalculus cholecystitis. In this study 76.9% of all the GB stones were multiple, only a few were singular solitary GB stone. Most of the GB stones are mixed type stones (64.1%) followed by pigments stones (21.8%) and cholesterol stones (14.1%). In a study by Sangma MM et al [2], 82.98% multiple GB stones and 17.02% of the patients had single GB stone. They also reported mixed type stones (68.1%) followed by pigments stones (18.1%) and cholesterol stones (13.8%) in their study which is in line with this study findings. Ezhil AN et al [12] reported 80% cases having multiple stones in the GB and 20% solitary stone in the GB. They also reported 78% of the stones were mixed type, 14% pigment stones and 8% cholesterol stones. In this study during the operation 6% of the patients were found to have empyema GB which appeared as reddish, oedematous and mildly distended organ containing stones and pus. And in 2% of the patient the GB was mildly distended and reddish containing only pus (empyema) was found. According to Ahmed S et al [18], out of the 76 cases of acute cholecystitis, 32.9 % were empyema GB. In this study no perforation case was seen. In 7% of the cases mucocoele was seen in acalculus cholecystitis and 2% in calculous cholecystitis in this study. In other study by Sangma MM et al [2] mucocoele was reported in 5% of the patient and all of them were acute acalculus cholecystitis. Adhesion of the GB with omentum, duodenum and surrounding structures was the most common associated operative findings comprising of 43% of the cases. Similar finding has been reported by Sangma MM et al [2] with 30% of the cases having adhesion.

All the 100 cases of acute cholecystitis with signs and symptoms of acute cholecystitis treated by surgery were confirmed from the appearance of gall bladder during the operation. However, histopathological examination of 64% of the cases showed features of chronic cholecystitis. A study by Raine PA et al [19] observed that 140 cases of acutely inflamed gallbladder was found at operation, whereas acute inflammation was reported by the histopathologist in only 65% of cases. Similar downgrading was also shown by Sangma

MM et al with only 68% reporting acute inflammation from HPE examination [2]. In this study both gender were seen affected with GB adhesion, GB fibrosis, GB inflammation, acute cholecystitis, calculous cholecystitis but those having acalculus cholecystitis were seen mostly with family history. It was also seen that calculous cholecystitis patients had higher mean age and were mostly married. Most of the GB adhesions were seen among the calculous cholecystitis but most of the GB inflammation and GB mucocoele were seen among the acalculus cholecystitis. But GB empyema and GB fibrosis were seen in both calculous cholecystitis and acalculus cholecystitis. Similarly calculous in the gall bladder were well distributed in both acute and acute on chronic cholecystitis patients.

CONCLUSION

The most common cause of acute cholecystitis was found to be calculous cholecystitis. Acalculous cholecystitis does occur in few and associated with complications, thus it should not be neglected. A young patient with absent of calculous in USG having signs and symptoms of acute cholecystitis with positive family history should be suspected to have acalculus cholecystitis. Associated operative findings like adhesion was more commonly seen in calculous cholecystitis and mucocoele was more commonly seen in acalculus cholecystitis. Thus, early diagnosis and operation should be done at the earliest to avoid complications like empyema, adhesion with omentum and other viscera.

Additional Information Disclosures

Human Subjects: Consent was obtained or waived by all participants in this study. Research Ethics Board, RIMS, Imphal issued approval reference no. A/206/REB-Comm(SP)/RIMS/2015/760/102/2020.

Animal Subjects: All authors have confirmed that this study did not involve animal subjects or tissue.

Conflicts Of Interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following:

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Tables

Table 1: Baseline Characteristics Of The Patients (n=100)

Sl.no.	Characteristics	No. of Patient	Percentages (%)
1. Gender	Male	26	26
	Female	74	74
2. Age	20 – 30 years	22	22
	31 - 40 years	30	30
	41 - 50 years	22	22
	51 - 60 years	14	14
	> 60 years	12	12
3. Religion	Hindu	70	70
	Muslim	12	12
	Christian	18	18
4. Marrital status	Married	72	72
	Unmarried	28	28
5. Dietary habits	Vegetarian	20	20
	Non-veg	80	80
6. Family history	Present	22	22
	Absent	78	78
7. Hypertension	Present	24	24
	Absent	76	76
8. Diabetes Mellitus	Present	10	10
	Absent	90	90

Table 2: Distribution Of Patients By Symptoms And Signs (n=100)

Symptoms	No. of participants	Percentage (%)
Pain Rt Hypochondrium	100	100
Fever	58	58
Nausea	50	50
Vomiting	70	70
Dyspepsia	68	68
Jaundice	16	16
Referred pain back shoulder	64	64
Itching	12	12
Signs		
Tenderness Rt. hypochondrium	100	100
Palpable Lump	10	10
Enlarged Liver	6	6
Elicit Murphy's sign	100	100
Icterus	12	12

Table 3: Distribution Of Patients By Types Of Cholecystitis, GB Stones And Quantity Of Stones (n=100)

Sl.no. Characteristics	No. of Patient	Percentages (%)
1. Cholecystitis (N=100)		
Acalculous Cholecystitis	22	22
Calculous Cholecystitis	78	78
2. Types of GB stone (N=78)		
Mixed	50	64
Pigments	17	22
Cholesterol	11	14
Singular	18	23
3. No. of stones (N=78)	Multiple	60 77

Table 4: Associated Operative Findings In The Patients (n=100)

Sl.no.	Characteristics	No. of patients	Percentages (%)
1.	Adhesion of GB	43	43
2.	Mucocele of GB	9	9
3.	Empyema of GB	8	8
4.	Fibrosis of GB	17	17
5.	Polyp of GB	4	4
6.	Only inflamed GB	20	20
7.	Perforation of GB	0	0

Table 5: Final Diagnosis Of Acute Cholecystitis By Hpe (n=100)

Sl. no.	Characteristics	No. of patients	Percentages (%)
1.	Acute acalculous cholecystitis	8	8
2.	Acute on chronic acalculous cholecystitis	16	16
3.	Acute calculous cholecystitis	28	28
4.	Acute on chronic calculous cholecystitis	48	48

Table 6: Association Between Gender And Output Variables (n=100)

Sl.no.	Patients characteristics		Gender		p value
			Male (%)	Female (%)	
1	GB adhesion	Yes	14 (31.8)	29 (68.2)	0.172
		No	12 (21.4)	45 (78.6)	
2	GB fibrosis	Yes	5 (33.3)	12 (66.7)	0.468
		No	21 (24.7)	62 (75.3)	
3	GB inflamed	Yes	3 (23.5)	17 (76.5)	0.167
		No	23 (26.5)	57 (73.5)	
4	Cholecystitis	Acute	6 (16.7)	30 (83.3)	0.085
		Acute on chronic	20 (31.3)	44 (68.7)	

Table 7: Association Between Presence Of Calculous And Sociodemographic Variables (n=100)

Sl.no.	Patients characteristics		Cholecystitis		p value
			Calculous (%)	Acalculous (%)	
1	Gender	Male	22 (84.6)	4 (15.4)	0.256
		Female	56 (75.7)	18 (24.3)	
2	Marrital status	Married	60 (83.3)	12 (12.7)	0.039
		Unmarried	18 (64.3)	10 (35.7)	
3	Dietary habit	Non-veg	62 (77.5)	18 (22.5)	0.538
		Veg	16 (80.0)	4 (20.0)	
4	Family history	Yes	12 (15.3)	10 (45.5)	0.005
		No	66 (84.7)	12 (54.5)	

Table 8: Association Between Presence Of Calculous In Cholecystitis And Mean Age (n=100)

Sl.no.	Age in mean years	Standard Deviation	P value
1. Calculous	43.58	13.58	0.029
2. Acalculous	36.73	9.47	

Table 9: Association Between Presence Of Calculous And Hpe Findings (n=100)

Sl.no.	Patients characteristics		Cholecystitis		p value
			Calculous (%)	Acalculous (%)	
1	GB adhesion	Yes	41 (52.6)	2 (9.1)	0.000
		No	37 (47.4)	20 (90.9)	
2	GB fibrosis	Yes	15 (19.2)	2 (9.1)	0.218
		No	63 (80.8)	20 (90.9)	
3	GB inflamed	Yes	12 (15.4)	8 (36.4)	0.035
		No	66 (84.6)	14 (63.6)	
4	GB mucocele	Yes	2 (2.6)	7 (31.8)	0.000
		No	76 (97.4)	15 (68.2)	
5	GB empyema	Yes	6 (7.5)	2 (2.5)	0.562
		No	72 (78.3)	20 (21.7)	
6	Acute cholecystitis		28 (77.8)	8 (22.2)	0.578
	Acute on chronic cholecystitis		50 (78.1)	14 (21.9)	

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