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Clinical spectrum and management outcome in gallbladder perforation-a sinister entity: Retrospective study from Sub-Himalayan region of India

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ABSTRACT

Objective: Gallbladder perforation is an infrequent entity seen among surgical patients. Rare occurrence owes to difficulty in diagnosing gallbladder perforations. The aim of the present study was to determine the optimal management strategy that may decrease the morbidity and mortality associated with this potentially life-threatening condition.

Material and Methods: This was a retrospective study from hospital health records wherein the experience of 40 consecutive patients with gallbladder rupture, either spontaneous or secondary to both benign conditions and malignancy, was noted at a tertiary care hospital over 48 months from February 2017 till January 2021. The etiology, clinical presentation, and treatment given were analysed.

Results: Out of 40 patients included, 23 were females and the majority of patients were more than 45 years of age. Twelve patients responded to intravenous antibiotics and analgesics alone while five required an ultrasound-guided pigtail catheter drainage due to non-improving clinical condition. The failure of expectant management led to a delayed laparotomy in seven patients while four patients required emergency laparotomy because of generalized peritonitis. An elective cholecystectomy was offered to 12 patients with cholecystoenteric fistulae after diagnostic laparoscopy in the same admission. Thirty-eight patients were discharged in stable condition and doing well at 30-day follow-up.

Conclusion: Gallbladder perforation is seen more commonly in acute calculous cholecystitis compared to other conditions. It is more evident when the treatment of acute calculous cholecystitis is delayed by more than 6-8 weeks. The spectrum of clinical presentation varies from mild pain and vomiting to generalized peritonitis. The patient often requires a step-up approach to control the ongoing sepsis for an improved outcome.

Keywords: Acute calculous cholecystitis, secondary gallbladder rupture, gallbladder perforation, acalculous cholecystitis, biliary peritonitis

INTRODUCTION

Gallbladder perforation (GBP) is a less encountered clinical condition owing to its infrequent occurrence and difficulty in diagnosis. More often, diagnosis of GBP is established during surgery. The treatment strategy is yet not clear and has been primarily focused on emergency surgery. Though emergency surgery is performed with curative intent but is associated with high mortality.

Historically, in 1934, Niemeier worked upon these gallbladder perforations and introduced a three-tier classification system for this rare condition. Niemeier classified GBP into three types based on the duration of perforation (1).

Type 1: Acute free perforation- into the peritoneal cavity without any protective adhesion.

Type 2: Sub-acute perforation- perforation walled off by adhesions from the peritoneal cavity with surrounding abscess.

Type 3: Chronic perforation- having fistulous communication between the gallbladder and bowel.

The most commonly seen GBP is type 2 (46%) followed by type 3 (40%) and lastly, type 1 (10%). The mortality rate in GBP is reported to be as high as 12-42% irrespective of the type of perforation (2).

Anderson has added another category of Gallbladder perforation (3):

Type 4: Perforation with cholecysto-biliary fistula.

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Table 1. Summary of the studies reporting more than 15 patients with their different type of perforation

Study	Number of patients	Age (years)	Perforation type			Cholelithiasis	Mortality
			I	II	III		
Lennon, 1983	32	67	37.5%	53.1%	9.4%	84.4%	12.5%
Wig, 1984	27	50	44.4%	7.4%	48.1%	88.9%	11.1%
Menakuru, 2004	31	68	2.9%	4.5%	2.6%	93.5%	9.7%
Derici, 2006	16	70	44.8%	44.8%	12.5%	-	12.5%
Stefanidis, 2006	30	60	70%	30%	-	-	-
Ergul, 2008	37	64	32.4%	56.8%	10.8%	-	10.8%
Date, 2012	19	72	47.4%	47.4%	5.3%	78.9%	0%
Present study	40	54	10%	60%	30%	72.5%	5%

Many case series have been published to date, some studies enrolling more than 15 patients are mentioned below (Table 1).

We aimed at presenting our clinical experience in gallbladder perforations.

MATERIAL and METHODS

Setting

This study was conducted in a tertiary care academic institution from the Sub-Himalayan region in Uttarakhand, India. The Institutional Ethics Committee at All India Institute of Medical Sciences Rishikesh had approved the study with Letter No-AIIMS/IEC/21/167. All patients were admitted under the Department of General Surgery and treated in the same specialty. The treating team provided standard care until discharge from the hospital and also followed them at 30 days post-discharge in the outpatient department. When no 30-day follow-up was planned, patients were contacted over phone calls about the follow-up status.

Sample Size

Forty consecutive patients with the diagnosis of gallbladder perforation from health records searched between February 2017 and January 2021 (48 months).

Inclusion and Exclusion Criteria

Patients of all age groups and both sexes were enrolled in the study. All patients included had been diagnosed for gallbladder perforation either radiologically by the institute radiology team with contrast-enhanced computed tomography (CECT) abdomen or intra-operatively by the treating team.

Data Acquisition and Management

All patient-related data was acquired by formative proforma and entered in Microsoft Excel 2019. All statistics are represented in the form of a bar graph using Microsoft excel.

Study Parameters

Baseline patient demographic profile, comorbidities, and clinical symptoms at presentation were recorded. An abdominal ultrasound was the initial imaging modality used to evaluate the hepatobiliary tree. All patients subsequently underwent CECT Abdomen (patients with acute kidney injury were hydrated to bring down the creatinine level) and perforations were graded as intrahepatic, intraperitoneal (free or localized), and hollow viscous communications. All cases were further evaluated with magnetic resonance cholangiopancreatography (MRCP) to rule out any downstream bile duct pathology. The treatment strategies were categorized as expectant, drainage under radiological control, and surgery. After initial resuscitation, if the patient had frank generalized peritonitis, an emergency laparotomy was undertaken. Expectant management (intravenous antibiotics, fluids, and analgesics) was adopted in patients having localized peritonism. The patients who did not improve clinically over subsequent 24 h after expectant management were offered ultrasound-guided pigtail catheter drainage for the intraabdominal collection. A delayed laparotomy to control the ongoing sepsis was the last resort in patients not responding even 48h after draining the collections. Those patients in the expectant or drainage group who improved clinically were planned for interval cholecystectomy. All patients with cholecystoenteric fistulae were offered diagnostic laparoscopy followed by exploration through a right subcostal incision (extended to the left side depending on desired exposure). The 30-day follow-up and status at discharge were marked on Karnofsky performance status.

Study Objectives

The primary objective was an overall, 30-day outcome for different treatment strategies. The secondary objective was to evaluate the various etiology, age, and sex-based incidence of gallbladder perforation.

RESULTS

- The patient's age ranged from 20-80 years in the study and the mean age of patients with gallbladder perforation was 54.15 years (Figure 1).

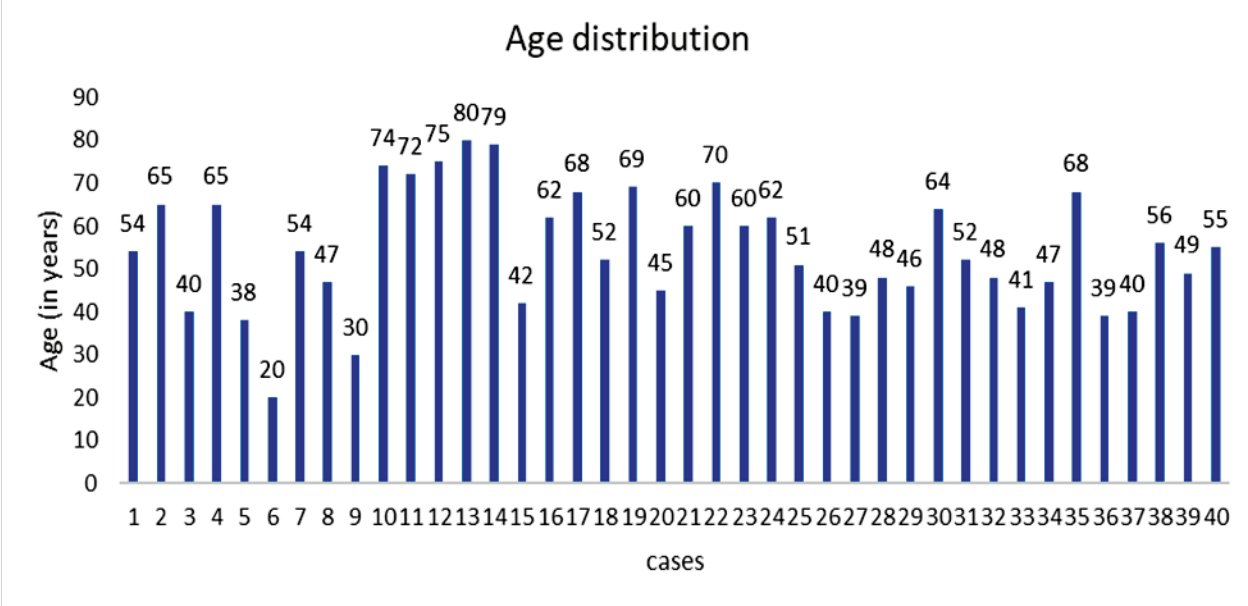

Figure 1. Bar diagram showing the age distribution of gallbladder perforations.

Figure 2. Bar diagram showing comorbid illness in gallbladder perforation.

- The majority of patients with gallbladder perforation were females (female: male ratio 23:17), though literature suggests that the perforation is more common in male patients.
- The most common comorbid illness seen in the study population was diabetes mellitus (30%) followed by leptospirosis, typhoid, and dengue infections (Figure 2).
- The most common clinical presentation was abdominal pain (90%), and fever (75%). Four patients with Type I gallbladder perforation presented with frank peritonitis and underwent emergency laparotomy after initial resuscitation.
- There were different etiologies seen for gallbladder perforations; the majority were secondary to cholelithiasis (72.5%), malignancy (12.5%), choledocholithiasis with bile duct stricture (10%), one case each of empyema gallbladder and emphysematous cholecystitis (Figure 3).
- The patients enrolled in the study were treated according to their clinical status (Table 2). 57.5% of the patients underwent exploration and cholecystectomy (emergency/

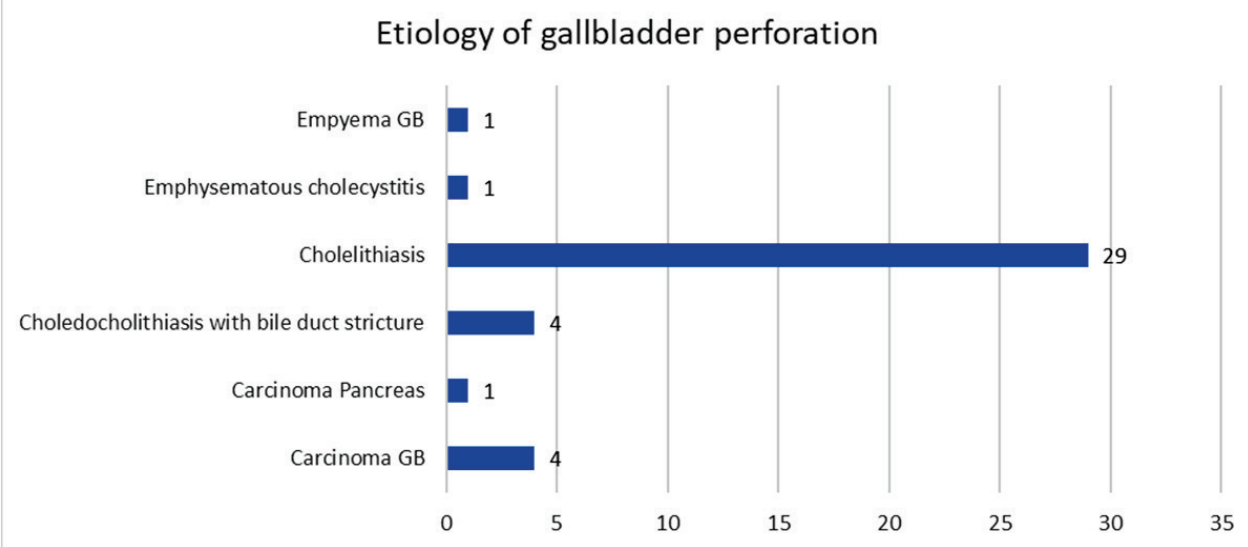

Figure 3. Bar diagram showing different etiologies of gallbladder perforation.

delayed/elective) in the index admission, 30% responded to intravenous antibiotics and analgesics (expectant management) alone while 12.5% of the patients required ultrasound-guided pigtail catheter drainage to control the ongoing sepsis (Figure 4). All patients of the expectant and drainage group were planned for a definitive procedure at 6-8 weeks after a thorough evaluation.

- The study witnessed all Niemeier types of gallbladder perforation (Figure 5). The majority of patients were of type 2 perforation (60%) followed by Type 3 (30%), and type 1 (10%).
- The operating time ranged from 90 to 150 minutes. The estimated blood loss was 100 to 300 ml. Given the severe inflammation around hepatoduodenal ligament and dense adhesions in the calot's triangle area, it was only possible to do subtotal cholecystectomy in patients undergoing laparotomy in the same admission. The patients who had distal bile duct obstruction underwent additional T-tube drainage.
- Twenty-six percent (n= 10) of the patients had surgical site infection post laparotomy, approximately 60% (n= 24) of the patients had postoperative atelectasis and fever related to laparotomy. The mean hospital stay was 12 days for Type 1 perforation, four days for type two perforation, and seven days for Type 3 perforation.
- 95% (n= 38) of patients were discharged from the hospital and a follow-up after 30 days revealed their healthy status. Five percent (n= 2) of the patients could not survive the disease. Thirty-five percent (n= 14) of the patients had ICU stay with a mean duration of 4.5 days, the majority of ICU admissions were seen in patients undergoing laparotomy for gallbladder perforation (n= 12).

DISCUSSION

Gallbladder perforation has variable clinical presentation and thus difficult to diagnose clinically. This entity is seen in male patients more commonly, though uncomplicated acute cholecystitis is common in females. In the present study, gallbladder perforation was seen as more common in females (23:17) (4).

The most common site of gallbladder perforation is the fundus owing to the most distal blood supply (Figure 6) (5). Gallbladder perforation is seen as a complication in only 1-4% of cholecystitis but 90-95% of gallbladder perforation are seen secondary to cholelithiasis (3,5). The current study demonstrated cholelithiasis as the lead etiology seen in 70% of gallbladder perforations. Mean duration for gallbladder perforation after acute cholecystitis was 4-8 weeks, which is per the literature (4).

In a systematic review by Ravindra S. date et al., it has been observed that Type 2 perforation is the most common gallbladder perforation as evident in our study also (2). Four patients had intrahepatic abscess due to gallbladder rupture towards the liver bed (Figure 7).

The management of gallbladder perforation depends on the patient's clinical status. In our study, 57.5% of the perforations were managed surgically while 30% of patients responded to expectant management, and 12.5% of the patients required an ultrasound-guided pigtail catheter drainage of the pericholecystic collection. All Type 1 (10%) perforations were diagnosed intra-operatively (Figure 8) after an exploration was performed given generalized peritonitis at presentation, and supported by a preoperative CT that revealed pneumoperitoneum and free

Table 2. Summary of the enrolled patients in the current study

S. No.	Age (years)	Sex	Type of GBP	Treatment approach used	Morbidity & Outcome
1)	54	Female	II	Expectant management → Ultrasound guided pigtail drainage	Discharged
2)	65	Female	II	Expectant management → Ultrasound guided pigtail drainage	Postoperative atelectasis; Discharged
3)	40	Male	I	Emergency laparotomy	Postoperative atelectasis and surgical site infection; Discharged
4)	65	Female	II	Expectant management → Ultrasound guided pigtail drainage → Delayed laparotomy	Postoperative atelectasis and surgical site infection; Discharged
5)	38	Male	II	Expectant management	Discharged
6)	20	Male	I	Emergency laparotomy	Postoperative atelectasis; Discharged
7)	54	Female	II	Expectant management → Ultrasound guided pigtail drainage → Delayed laparotomy	Postoperative atelectasis and surgical site infection; Discharged
8)	47	Male	III	Elective cholecystectomy	Postoperative atelectasis; Discharged
9)	30	Male	II	Expectant management	Discharged
10)	74	Male	II	Expectant management → Ultrasound guided pigtail drainage → Delayed laparotomy	Postoperative atelectasis and surgical site infection; Discharged
11)	72	Male	II	Expectant management → Ultrasound guided pigtail drainage → Delayed laparotomy	Postoperative atelectasis; Multiorgan dysfunction syndrome; Mortality
12)	75	Female	II	Expectant management	Discharged
13)	80	Male	II	Expectant management → Ultrasound guided pigtail drainage	Postoperative atelectasis; Discharged
14)	79	Male	II	Expectant management → Ultrasound guided pigtail drainage → Delayed laparotomy	Postoperative atelectasis and surgical site infection; Discharged
15)	42	Female	II	Expectant management	Discharged
16)	62	Male	II	Expectant management → Ultrasound guided pigtail drainage	Postoperative atelectasis; Discharged
17)	68	Female	I	Emergency laparotomy	Postoperative atelectasis and adult respiratory distress syndrome; Mortality
18)	52	Male	II	Expectant management → Ultrasound guided pigtail drainage → Delayed laparotomy	Postoperative atelectasis; Discharged
19)	69	Male	III	Elective cholecystectomy	Postoperative atelectasis; Discharged
20)	45	Female	III	Elective cholecystectomy	Postoperative atelectasis; Discharged
21)	60	Female	III	Elective cholecystectomy	Discharged
22)	70	Female	III	Elective cholecystectomy	Postoperative atelectasis and surgical site infection; Discharged
23)	60	Female	II	Expectant management	Discharged
24)	62	Female	III	Elective cholecystectomy	Postoperative atelectasis; Discharged
25)	51	Female	III	Elective cholecystectomy	Postoperative atelectasis and surgical site infection; Discharged
26)	40	Female	III	Elective cholecystectomy	Postoperative atelectasis and surgical site infection; Discharged
27)	39	Female	III	Elective cholecystectomy	Discharged

Table 2. Summary of the enrolled patients in the current study (continue)

S. No.	Age (years)	Sex	Type of GBP	Treatment approach used	Morbidity & Outcome
28)	48	Male	II	Expectant management	Postoperative atelectasis; Discharged
29)	46	Female	III	Elective cholecystectomy	Discharged
30)	64	Female	III	Elective cholecystectomy	Postoperative atelectasis and surgical site infection; Discharged
31)	52	Male	II	Expectant management	Discharged
32)	48	Female	I	Emergency laparotomy	Postoperative atelectasis; Discharged
33)	41	Female	III	Elective cholecystectomy	Discharged
34)	47	Female	II	Expectant management	Discharged
35)	68	Male	II	Expectant management → Ultrasound guided pigtail drainage	Postoperative atelectasis; Discharged
36)	39	Female	II	Expectant management	Discharged
37)	40	Male	II	Expectant management	Discharged
38)	56	Female	II	Expectant management → Ultrasound guided pigtail drainage → Delayed laparotomy	Postoperative atelectasis and surgical site infection; Discharged
39)	49	Male	II	Expectant management	Discharged
40)	55	Female	II	Expectant management	Discharged

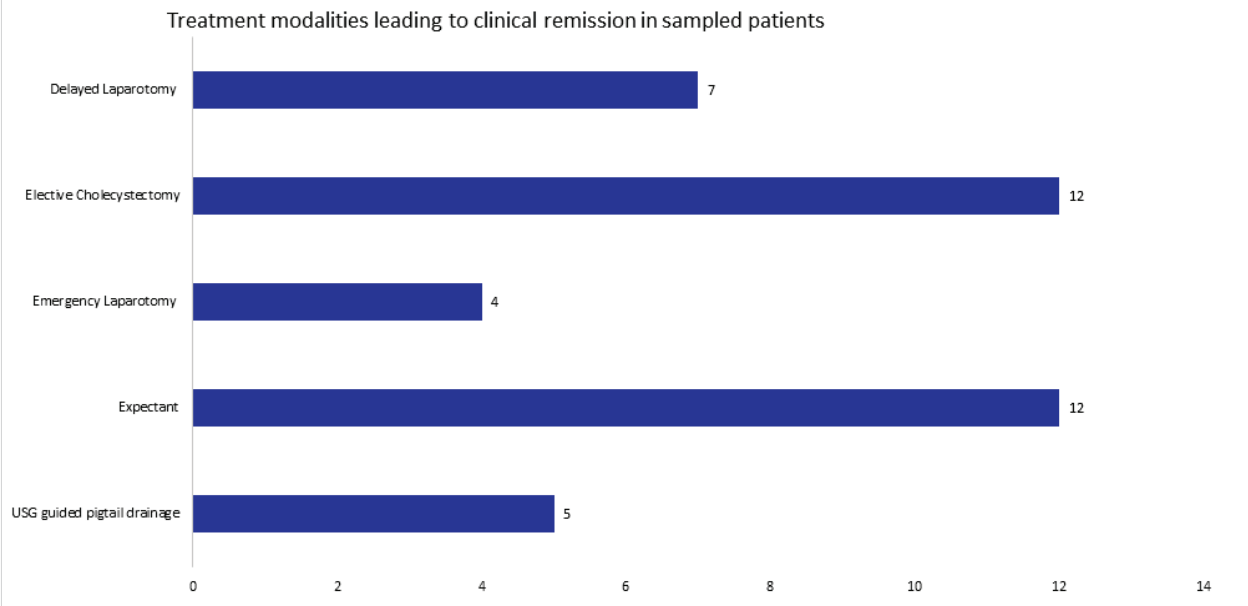

Figure 4. Bar diagram showing different treatment modalities that led to clinical remission in the sampled patients.

fluid (NCCT was ordered in patients with acute kidney injury). Ultrasound abdomen revealed a spectrum of findings like thickened gallbladder, rent in gallbladder wall (Figure 9), pericholecystic fluid, or a contracted gallbladder. Ultrasound sensitivity for detecting gallbladder perforation is nearly 70% and thus CECT is needed for an accurate diagnosis (6). The diagnosis of Type 2 and 3 perforations were made after a contrast-enhanced CT scan (Figures 10,11), and most of them were managed with delayed laparotomy. The magnetic resonance cholangiopancreatography confirmed the gallbladder perforation and also aided to rule out any downstream bile duct pathology (Figure 12). Only Type 2 perforations that demonstrated clinical improvement and resolving sepsis were managed with antibiotics alone strategy. There were a total of two mortalities, that occurred in the Type 1 perforation group. Mean hospital stay was 12 days for Type 1 perforation, four days for Type 2 perforation,

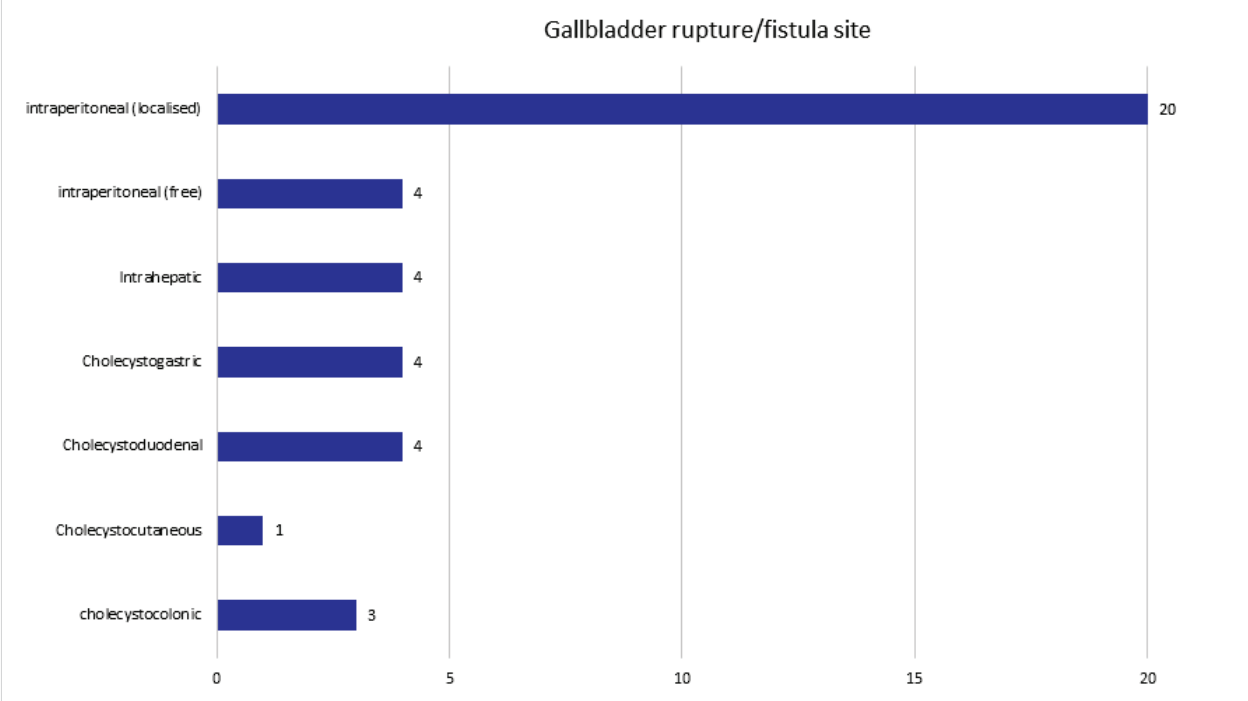

Figure 5. Bar diagram showing the gallbladder rupture/fistulization site.

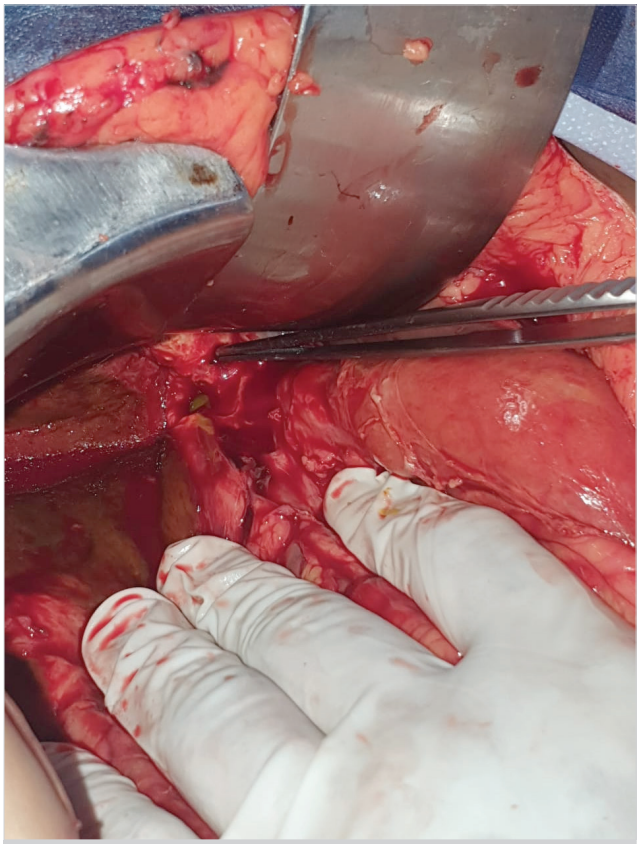

Figure 6. Intraoperative photograph showing perforation over the fundus of the gallbladder - pointed by the instrument.

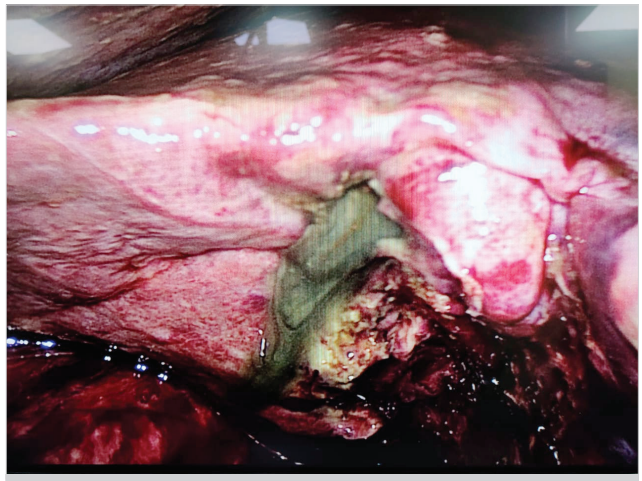

Figure 7. Laparoscopic view of an intrahepatic rupture of gallbladder perforation.

and seven days for Type 3 perforation. The antibiotics used were third-generation cephalosporin preferably cefoperazone and metronidazole as per the Surgical Infection Society of North America (SIS) and Infectious Disease Society of America (IDSA) (7,8).

The most common comorbid illness observed in our study was diabetes mellitus followed by infections including leptospirosis, typhoid, and dengue (3:2:1) which has been reported in the literature. Typhoid is one of the leading causes of bowel perforation among the tropical population. *Salmonella* as the etiology of gallbladder perforation is rare (9). Our study also witnessed

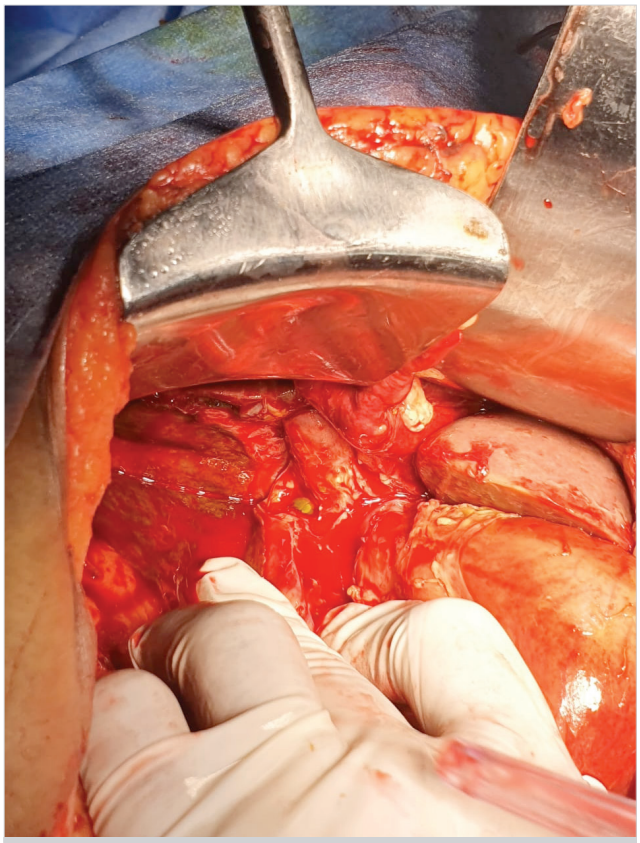

Figure 8. Type 1 Gallbladder perforation with bile leak seen on exploration.

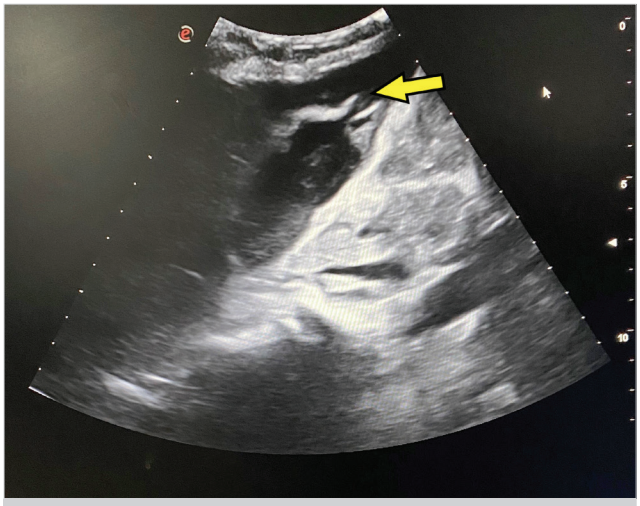

Figure 9. Ultrasound showing rent in the gallbladder wall depicted by yellow arrow.

two patients with spontaneous gallbladder rupture with typhoid as a comorbid illness. The pathophysiology of gallbladder perforation in typhoid is not well understood. Perforation in typhoid illness could be due to thrombosis of blood vessels, immune-compromised state, or severe inflammation. Different

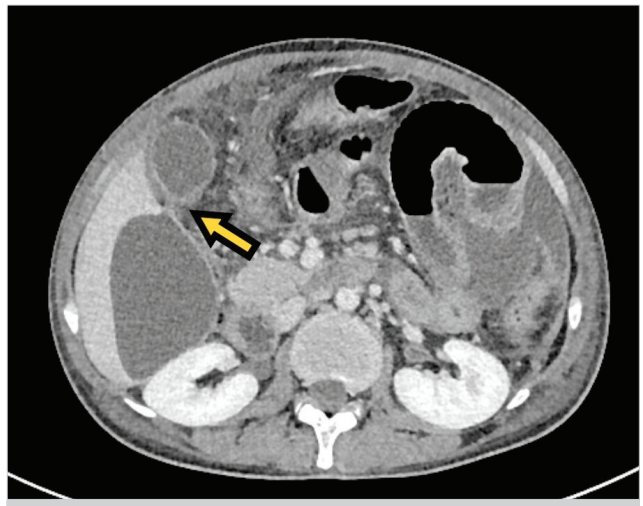

Figure 10. Axial section of abdominal tomography showing gallbladder perforation with thickened gallbladder wall and pericholecystic fluid.

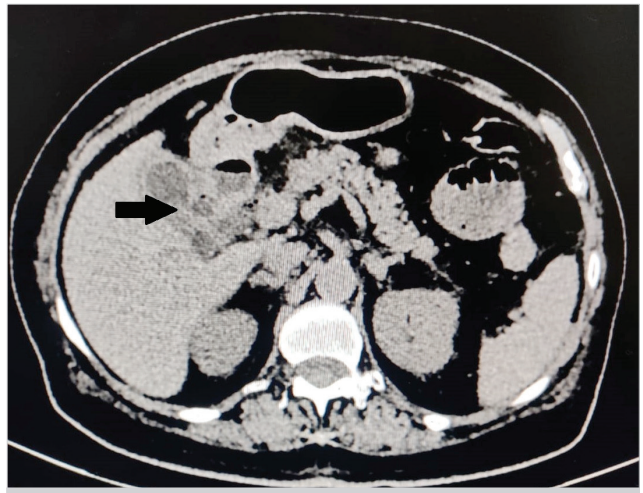

Figure 11. Computed tomography scan of the abdomen showing suspicious communication between the gallbladder and first part of duodenum depicted by horizontal black arrow in axial view.

tissue injury factors such as hemolysin, endotoxin, and lipase release tend to have complex interactions, resulting in capillary vasculitis and loss of red blood cells via swollen junctions and fenestra, resulting in ischemic necrosis.

Other causes of gallbladder perforation mentioned in the literature are trauma, viral infection, and pneumonia. The incidence of gallbladder perforation in trauma post blunt injury is less than 2% (10).

Type 3 gallbladder perforation (Figure 13) is categorized as chronic perforation leading to fistulous communication between the gallbladder and adjacent bowel (mostly duodenum, stomach, and transverse colon) (11,12). The most common cholecystoenteric fistula is between the gallbladder and duo-

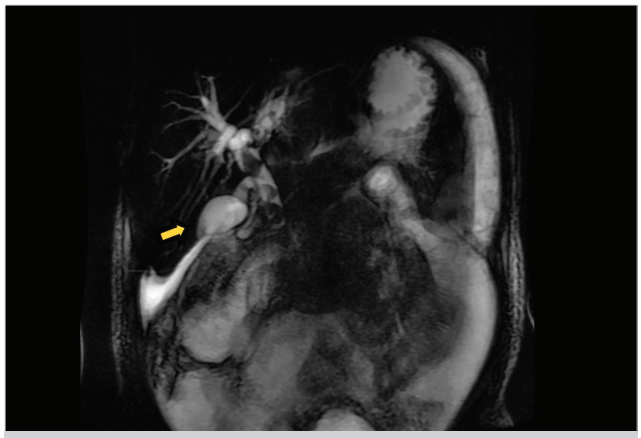

Figure 12. Magnetic resonance cholangiopancreatography scan showing gallbladder perforation with bile leak in the coronal view.

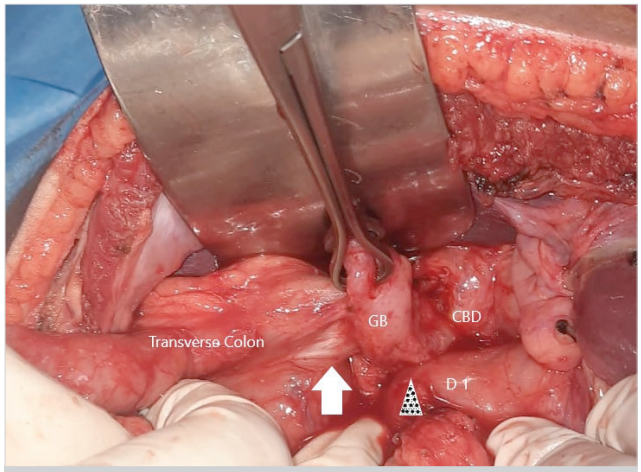

Figure 13. Intraoperative photograph of a Type 3 perforation with vertical white arrow showing fistulous communication between the gallbladder and transverse colon and dotted arrow-head showing adhesions between the gallbladder and first part of the duodenum.

denum due to its proximity (13). Twelve out of 40 cases in our study had Type 3 perforation having communication with the stomach, duodenum, and transverse colon (4:4:3). All of these perforations are seen secondary to cholelithiasis. The pathogenesis of cholecystoenteric fistula is due to an obstructing stone in the gallbladder neck or cystic duct causing ischemic necrosis and perforation of the gallbladder (Figure 14) forming a walled-off abscess. This abscess perforates in the adjacent bowel lumen forming a fistulous communication. These cholecystoenteric fistulae seldom cause gallstone ileus, though it is a known entity (12,13).

Ultrasound has proven to be 100% successful in the diagnosis of cholecystitis, but based on ultrasound, no definitive indication can be made of cholecystoenteric fistula. Although CECT may not be able to diagnose cholecystoenteric fistula as such, it helps to rule out malignant conditions or suspected lymphadenopathy and can provide a reasonably straightforward route

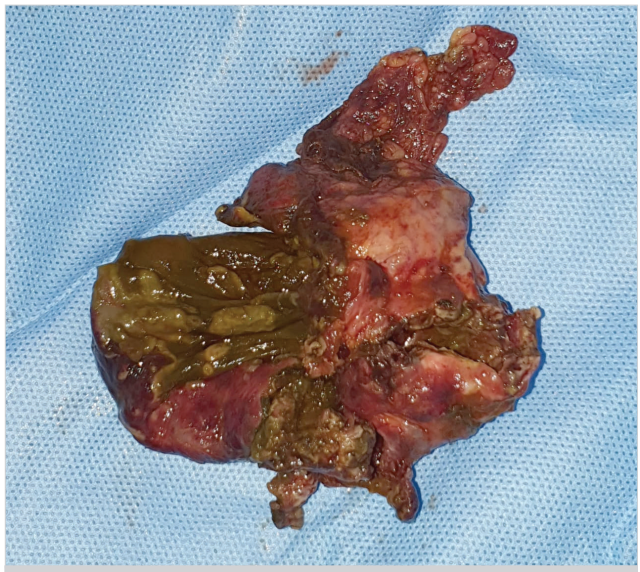

Figure 14. Resected specimen of the ruptured gallbladder.

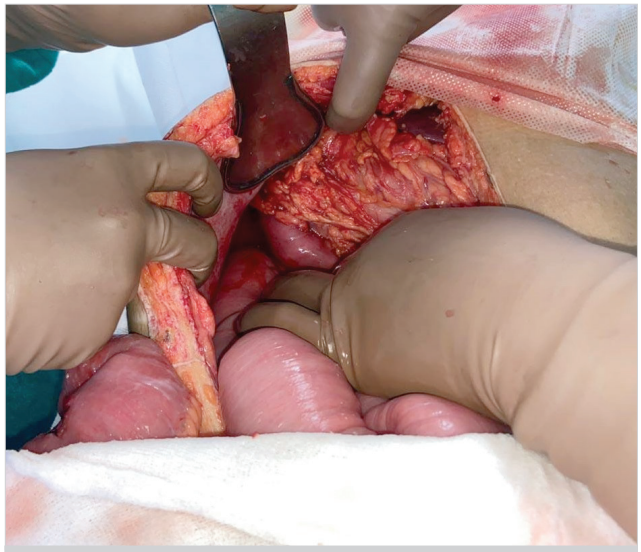

Figure 15. Omental wrapping seen around the gallbladder area on laparotomy.

through which the surgeon can move (14). Diagnostic Laparoscopy was performed in all patients to visualize the gallbladder and adjacent structures. Subsequently, all of them underwent open subtotal cholecystectomy with excision of fistulous tract and closure of the fistulous opening on the gastrointestinal side because of omental wrapping around the gallbladder and non-visualization of calot's area (Figure 15). Conservative management in asymptomatic, high-risk surgical patients has been reported (15). In the treatment of this disease, laparoscopic management can be used with continuously evolving new and improved methods, but the rate of conversion to open surgery and the cost burden is still high (16).

A single case of cholecysto-cutaneous fistula (Type 3 perforation) due to cholelithiasis was seen, with abdominal wall abscess as the clinical presentation in the present study, which has also been reported earlier (17). The treatment given was the drainage of the abdominal abscess, approx. 100 ml of bile stained purulent discharge was noticed. The underlying gallbladder malignancy was ruled out with a contrast-enhanced CT scan of the abdomen. The patient underwent open cholecystectomy and excision of the fistula tract.

Limitations

The present report contains retrospective data from health records from which association but not causation can be derived. Though there are many case series and systematic reviews in the literature for gallbladder perforation, still a guideline for managing this entity is lacking and needs to be focussed. A single-centre experience was presented. The patients with this pathology are treated based on clinical status and treatment lies on the surgeon's decision.

CONCLUSION

This study concludes with the need for rapid diagnosis and treatment of gallbladder perforation to reduce the associated morbidity and mortality. The diagnosis of Type 1 perforation is usually observed intra-operatively due to overlapping symptoms of many acute abdomen conditions (hollow viscus perforation, cholecystitis), Type 2 and 3 perforation are often made based on contrast-enhanced CT Scan. The patients with Type 1 perforation present with peritonitis and are hemodynamically unstable requiring an emergency laparotomy after initial stabilization with postoperative ICU care. The patients with Type 2 and Type 3 perforations present with chronic symptoms and can be managed with delayed surgical management. Most of the time, a subtotal cholecystectomy can only be offered given the presence of dense adhesions and severe inflammation in the region of the hepatoduodenal ligament. Niemeier, in 1934, gave an excellent classification for gallbladder perforation, but a more elaborate classification system is needed for managing this entity.

Ethics Committee Approval: The ethical approval for this study was obtained from All India Institute of Medical Sciences Institutional Ethics Committee (Date: 09.04.2021, Decision No: 167).

Peer-review: Externally peer-reviewed.

Author Contributions: Author Contributions: Concept - D.R.; Design - S.K., D.R.; Supervision - D.R., A.G.; Materials - A.G.; Data Collection and/or Processing - D.R., T.S.; Analysis and/or Interpretation - S.K., K.S.; Literature Search - D.R., J.J.C.; Writing Manuscript - D.R., S.K.; Critical Reviews -All of authors.

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ORİJİNAL ÇALIŞMA-ÖZET
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Safra kesesi perforasyonunda klinik spektrum ve tedavi sonuçları - olumsuz bir durum: Hindistan'ın Alt Himalaya bölgesinden retrospektif bir çalışma

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ÖZET

Giriş ve Amaç: Safra kesesi perforasyonu cerrahi hastalarda nadir görülen bir durumdur. Bu durumun sebebi safra kesesi perforasyonlarının tanısının zor oluşudur. Bu çalışmanın amacı, potansiyel olarak hayatı tehdit edici bu durumun yol açtığı mortalite ve morbiditeyi azaltacak optimal yönetim stratejisini oluşturmaktı.

Gereç ve Yöntem: Bu retrospektif çalışmada, Şubat 2017 ile Ocak 2021 arasındaki 48 ayda üçüncü basamak hastanede spontan veya benign ya da malign durumlara sekonder gelişen safra kesesi rüptürü ile tedavi edilen ardışık 40 hastanın hastane kayıtları incelendi. Etiyoloji, klinik görünüm ve uygulanan tedavi değerlendirildi.

Bulgular: Çalışmaya dahil edilen 40 hastanın 23'ü kadındı ve hastaların çoğunluğu 45 yaş üstüydü. On iki hasta intravenöz antibiyotik ve analjeziklere yanıt verirken beş hastaya iyileşmeyen klinik durumları sebebiyle ultrason rehberliğinde perkütan pigtail kateter drenajı uygulandı. Yedi hastaya gecikmiş laparotomi, dört hastaya ise yaygın peritonit sebebiyle acil laparotomi uygulandı. Aynı yatışta tanısal laparoskopi sonrası kolesistoenterik fistülleri olan 12 hastaya elektif kolesistektomi önerildi. Otuz sekiz hasta stabil olarak taburcu edildi ve 30 günlük takipleri normaldi.

Sonuç: Diğer durumlara kıyasla safra kesesi perforasyonu akut taşlı kolesistitte daha yaygın görülmektedir. Akut taşlı kolesistit tedavisi 6-8 hafta arasında geciktiğinde daha da yaygın hale gelir. Klinik görünüm hafif ağrı ve kusmadan yaygın peritonite kadar uzanır. Hastalar genellikle devam eden sepsisi kontrol altına almak amacıyla basamaklı yaklaşıma gerek duymaktadır.

Anahtar Kelimeler: Akut taşlı kolesistit, sekonder safra kesesi rüptürü, safra kesesi perforasyonu, taşsız kolesistit, biliyer peritonit

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