

CLINICAL PROFILE AND EVALUATION OF OUTCOMES OF SYMPTOMATIC GALLSTONE DISEASE IN THE SENIOR CITIZEN POPULATION



Thesis

Submitted to

All India Institute of Medical Sciences, Jodhpur

In partial fulfilment of the requirement for the degree of

Master of Surgery (MS)

General Surgery

June, 2022

AIIMS, Jodhpur

Dr. Anupam Singh Chauhan

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DECLARATION

I hereby declare that this project titled “**Clinical Profile And Evaluation Of Outcomes Of Symptomatic Gallstone Disease In The Senior Citizen Population**” is the bonafide record of my original research. It has not been submitted to any other institution for the award of any degree or diploma. Information derived from the published or unpublished work of others has been duly acknowledged in the text.

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-Dr. Anupam Singh Chauhan

“If I have seen further than others, it is by standing upon the shoulders of giants.”

- Sir Issac Newton

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LIST OF ABBREVIATIONS

Abbreviation	Definition
CBD	Common Bile Duct
CT	Computed Tomography
CI	Confidence Interval
CECT	Contrast Enhanced Computed Tomography
EC	Early Cholecystectomy
EL	Exploratory Laparotomy
ERCP	Endoscopic retrograde cholangiopancreatography
GB	Gallbladder
GSD	Gallstone Disease
IC	Interval Cholecystectomy
INR	International Normalised Ratio
LFT	Liver Function Test
MRCP	Magnetic resonance cholangiopancreatography
MRI	Magnetic resonance imaging
NOM	Non-operative Management
OPD	Out Patient Department
PT	Prothrombin Time
SGOT	Serum glutamic oxaloacetic transaminase

SGPT	Serum glutamic pyruvic transaminase
SM	Surgical Management
SSI	Superficial Surgical Infection
TSH	Thyroid Stimulating Hormone
T4	Thyroxine
USG	Ultrasonography
VAS	Visual Analogue Scale
WBC	White Blood Cells

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SUMMARY

SUMMARY OF THE PROJECT

Background: About 10% to 15% of the world's population is suffering from cholelithiasis¹. The incidence and severity of symptomatic cholelithiasis increase with age. There is often a delay in presentation, leading to complicated disease, diagnostic delay, and increased morbidity. There is a paucity of studies on the presentation and management of cholelithiasis in elderly persons from the western part of India. This study aimed to observe the spectrum of presentation and management of symptomatic cholelithiasis in senior citizens, i.e., in patients over 60 years.

Objectives: The primary objective of this study was to describe the presentation, diagnosis and intraoperative findings of symptomatic gallstone disease in patients aged over 60 years. The secondary objectives of this study were to find the association of gallstone disease with age, sex, and comorbidities, including diabetes mellitus, hypertension, and thyroid disorders.

Methods: All patients above the age of 60 years presenting to the surgical outpatient and emergency departments from January 2020 to July 2021 with symptomatic gallstone disease were included. Details of history, physical examination, blood investigations, and imaging of the abdomen (ultrasonography and MRCP, when indicated) were recorded. Patients were managed as per the advice of the treating consultant. Details of management and outcomes, including hospital stay, mortality, and morbidity, were noted.

Results: A total of 76 patients were evaluated in this study, of which 73.7% were female. The mean age was 70.8 ± 1.7 years. The majority of patients (63.2%) were admitted through the outpatient department (OPD). Most common presenting complaint was pain abdomen (96.1%). Clinical jaundice was noted in 9.2%. Complicated GSD was found more commonly in the female population (57.1%). Complicated GSD was more commonly found in patients with diabetes ($p=0.075$) and hypothyroidism ($p=0.057$). No association of age with intraoperative complications was noted ($p = 0.446$).

Conclusion: Cholecystectomy can be performed in elderly patients with reasonable mortality and morbidity. The incidence of postoperative complications does not increase with increasing age in patients aged over 60 years.

INTRODUCTION

INTRODUCTION

Symptomatic gallstone disease is found in about 10% to 15% of the world's population.¹ As the age increases the prevalence of gallstone disease increases from 8% to 50% in patients older than 70 years of age.² Women over the age of 70 years have the highest prevalence³. Gallstone-related complications like cholecystitis, choledocholithiasis, biliary pancreatitis are known to increase as age increases.⁴⁻⁶

The current standard of treatment of symptomatic gallstone disease in elderly patients is laparoscopic cholecystectomy. Studies have shown that old age is not a risk factor for poor outcome in patients undergoing cholecystectomy.^{7,8}

However, there is still reluctance of patients and relatives, and even among some anaesthetists and surgeons, to proceed with laparoscopic cholecystectomy in elderly and old patients^{4,9}. There has not been any significant research in the Indian subcontinent in the senior citizen population in this regard. The aim of this study is to reduce this knowledge gap by evaluating the presentation, management and outcomes of treatment in the senior citizen population diagnosed with symptomatic gallstone disease.

AIM & OBJECTIVES

AIM AND OBJECTIVES

- **AIM**
 - To assess how symptomatic gallstone disease is managed in senior citizen population and to evaluate the association between old age and surgical treatment.

- **Objectives**
 - **Primary Objective**
 - To assess how symptomatic gallstone disease presents in senior citizen population.
 - To assess how symptomatic gallstone disease is diagnosed in senior citizen population.
 - To evaluate the intra-operative findings of the gallbladder and gallstones.

 - **Secondary Objective**
 - To evaluate preoperative USG and MRCP findings.
 - To evaluate the association of gallstone disease and constants and variables like gender, and co-morbid conditions like diabetes mellitus, hypertension and functional thyroid diseases.

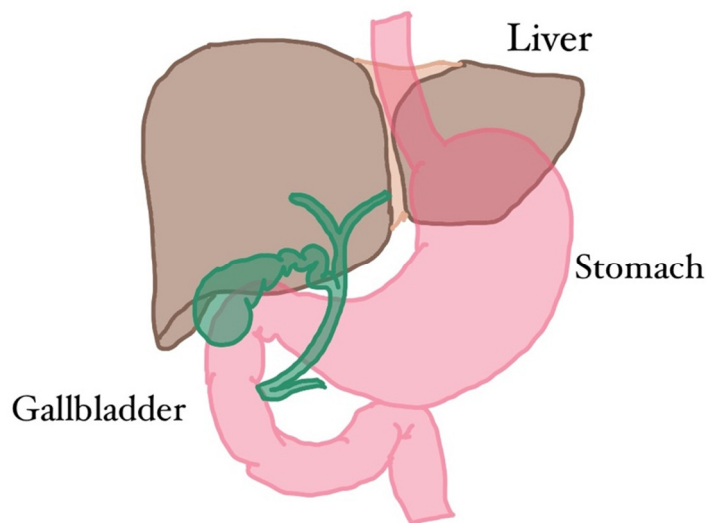
REVIEW OF LITERATURE

REVIEW OF LITERATURE

Basic anatomy

Gallbladder is a blind-ending flask-shaped blue-grey coloured diverticulum attached to the bile duct by cystic duct. Its main function is the storage and concentration of bile. It is usually firmly attached to the segment 4 and 5 of the right lobe of the liver¹⁰. In adults, its size ranges from 7 cm to 10 cm in length, volume varies from 25 to 50 ml. It usually lies in a shallow fossa on the visceral surface of the right lobe of the liver and is covered by the peritoneum from the liver. The fossa could rarely be deep and almost whole of the gall bladder could be buried into it, called intrahepatic gallbladder. It can rarely be suspended from liver by a fold of peritoneum. In this case, there is risk of torsion of the gall bladder, or can be connected to duodenum by an extension of free edge of the lesser omentum called cysto-duodenal ligament.¹¹⁻¹³

Figure 1: Anatomy of gallbladder in relation to stomach and liver



Gall bladder varies in shape and size. Fundus can be mobile and elongated and rarely fundus can fold over body forming a cap like structure called 'Phrygian cap'. Other anatomical variations include duplication with or without double cystic duct, agenesis and ectopic location, most commonly on the left side. These variations are rarely present but are particularly important if the patient has to undergo surgery for gallbladder or gallstone diseases^{10,14,15}.

Cystic duct is a 2-4 cm long tubular structure of diameter 2-3 mm. It drains the gall bladder into common hepatic duct forming the common bile duct¹⁶. In most of the individuals, the cystic duct joins the middle third of the combined length of common hepatic duct and common bile duct¹⁷, but can also join proximal or distal part of common bile duct. It usually joins the common bile duct from the right lateral aspect but can also join from anterior, posterior, medial aspect or can spiral around the common bile duct. It can also run parallel to CBD for a variable distance in the free edge of lesser omentum¹⁸. Rarely there could be double or absent (gallbladder drains directly to CBD) cystic duct or it can receive an anomalous hepatic duct from segment 5 of the liver¹⁰. These variations are rare but possess great importance in surgery.

Common bile duct is formed by the junction of the cystic duct and common hepatic duct at the porta hepatis. Its length varies from 6-8 cm in adults with luminal diameter of no more than 7 mm¹⁹, this diameter increases slightly with age. The common bile duct can be divided into supraduodenal, retroduodenal and pancreatic segment. Supraduodenal segment is the most accessible during cholecystectomy.

Etiology of gallstone disease

Gallstone formation has a multifactorial etiology from age, gender, race to obesity, rapid weight loss, drugs, pregnancy and triglyceridemia. Based on these factors – four major pathways are known that cause gallstone formation.

- Supersaturation of cholesterol in bile
- Cholesterol precipitation and crystallization
- Impaired gallbladder functions like contraction, motility
- Impaired bile reabsorption in bowel.²⁰

Supersaturation of cholesterol in bile

As the age increases, the chances of detection of gallstone also increases.²¹ The prevalence of gallstone disease is 7% to 11% in patients less than 50 years of age. This percentage increases up to 30% in patients of 60-70 years of age group and can reach as high as 50% in patients with age over 90 years.²⁰ The amount of cholesterol also increases as the age increases.²² Because of increased age, there is hypomotility of gallbladder because of sclerotic changes in the wall of the gallbladder which leads to decreased blood supply.²⁰

Estrogen is also a well-known risk factor which causes increased cholesterol excretion in to the bile and thus females have higher prevalence of gallstone disease than men. Multiparous women, postmenopausal women on hormone replacement therapy (HRT) and men with cirrhosis all tend to have a higher risk for gallstone disease.²⁰ Being overweight and obese is also a major risk factor for gallstone formation. There is increased synthesis and excretion of cholesterol in population with increased weight.²⁰ Even in patients who had undergone bypass surgery for obesity, there is a 50% risk of developing gallstone disease within 6 months of surgery.²⁰ Long term use of drugs like estrogen, prednisolone, azathioprine, oral contraceptives are also well known risk factors for gallstone formation.^{23,24}

Cholesterol precipitation and crystallization

One of the most essential and well-studied pronucleators is mucin-glycoprotein gel. Mucins are high-molecular-weight glycoproteins with oligosaccharide side chains connected by O-glycosidic connections to the apomucin backbone's serine or threonine residues. Mucins are classified into two types: gel-forming and membrane-associated. Bile mucin is composed of two primary domains: one rich in serine, threonine, and proline, which contains the majority of the covalently attached carbohydrates, and another non-glycosylated domain rich in serine, glutamic acid, glutamine, and glycine, which binds hydrophobic ligands such as bilirubin. Mucin is constantly secreted by the gallbladder mucosa; nevertheless, its secretion increases when lithogenic bile is present. Secretory mucins create gels and may increase the viscosity of bile.

Impaired gallbladder functions

Gallbladder stones are known to occur when there is delayed contraction, poor absorption and impaired secretion. It also occurs in larger gallbladder volume. Increase in gallbladder volume causes impaired gallbladder motility and stasis of bile which causes precipitation of stones. Certain physiological conditions like pregnancy or pathologies like anemia, celiac diseases are well known causes of gallbladder dysmotility and risk factors for gallstone diseases.

Impaired bile reabsorption in bowel

In patients suffering from severe malabsorption syndromes like Crohn's there is risk of more than 25% in terms of formation of stones. In cases of patients with subtotal or hemicolectomies have increased risk of gallstones formation.

Composition of gallstones

There are three main types of stones: cholesterol stones (about 75%); pigment stones and mixed stones. They are mostly made of cholesterol, bilirubin and bilirubin salts, calcium carbonate and mucin glycoprotein.

Clinical features

Gall stones can present as asymptomatic gallstones, biliary colic, acute cholecystitis, and acute choledocholithiasis. Initially, asymptomatic patients with gallstones have a 10% risk of developing symptoms within 5 years, and a 25.8% chance of developing symptoms within 10 years.²⁵ They can also present as cholangitis and in forms of biliary pancreatitis and as gallstone ileus.²⁶ These are usually benign form of gallstone diseases. They can also be concurrently found with gallbladder carcinoma.

The most common presentation of gallstone disease is with biliary pain. A comparison of observation versus surgery in patients with symptomatic, non-complicated gallstone disease revealed that 20% of patients in the observation group had recurrent biliary pain requiring hospital admission.²⁷ Older people are also significantly more likely than younger patients to present with complications such as acute cholecystitis (40% versus 18%), gallstone pancreatitis (19% versus 6%) and common bile-duct stones (21% versus 5%).²⁸

Patient can a spectrum of symptoms from most being asymptomatic to gallbladder perforation. Individuals can complain of epigastric or right upper quadrant pain that is termed as biliary colic. It can last up to 5 to 6 hours.²⁹ Patients can also complaint of pain in the right shoulder or subscapular region, nausea, vomiting, bloating sensation, diarrhoea. In the presence of gallstones in the common bile duct – greasy and foul smelling stool (steatorrhea) may be described by the patient.

When the gallstone disease becomes complicated the patient can present with severe pain abdomen radiating to the back with increased frequency of vomiting and are diagnosed to have biliary pancreatitis. When the biliary colic is lasting more than 6 hours and there is

presence of fever with increased white blood cells count then the patient might be suffering from cholangitis or acute cholecystitis.^{30,31}

On examination there can be tenderness in the right upper quadrant of the abdomen. There is inspiratory arrest on deep palpation known as the positive Murphy's sign. This is a common finding in case of acute cholecystitis. The patient can also have fever and tachycardia. The presence of jaundice depends on the presence of gallstones in the common bile duct.^{31,32}

Diagnostic methods

Gallstone disease can be provisionally diagnosed on the basis of history and physical examination but should be confirmed with laboratory analysis and radiological imaging. Leucocytosis, liver function tests should be followed closely.³³

Ultrasound of the abdomen is usually the first and the investigation of choice in the initial workup of the disease. It is able to give information like the thickness of the gallbladder, presence of pericholecystic fluid along with absence or presence of gallstones as small as 2 mm in diameter. The sensitivity and specificity can be as high as 90%.^{34,35}

If there is a discrepancy in the diagnosis or if the patient requires further investigation one can go with the contrast enhanced computed tomography (CT) of the abdomen. It is able to give the similar information as that given by ultrasound but may not be able to identify stones as they are isodense with bile.³⁶

Magnetic resonance cholangiopancreatography (MRCP) is able to give finer details of the gallbladder especially the cystic duct. It is also a useful investigation when assessing stones in the common bile duct.³⁷

Patients who have undergone all the above mentioned investigations with equivocal results can be advised for cholescintigraphy. In case of cholecystitis there is absence of radionuclide in the gallbladder. It is able to provide the functional information of the gallbladder but not the anatomical and cannot identify gallstones.^{38,39}

One of the rarely advised investigations for the gallstone disease is oral cholecystography where the patient is asked to consume an iodinated contrast (iopanoic acid) orally one day prior to their test. This contrast is released in the gallbladder and is able to visualise the

gallstones, polyps or sludge. When the gallbladder is inflamed as in case of cholecystitis, gallbladder will not be seen in the scan.^{40,41}

Types of gallstone disease

Acute and chronic calculus cholecystitis

When the cystic duct gets blocked by a gallstone or sometimes by biliary sludge then it can lead to the inflammation of the gallbladder known as acute calculus cholecystitis. When there is repeated temporary pain, it is more likely due to chronic calculus cholecystitis also known as biliary colic. Acute calculus cholecystitis usually requires urgent surgical intervention along with use of antibiotics before the gallbladder wall becomes ischemic, necrosed or worse - perforates. There are multiple methods of classification of acute calculus cholecystitis, but the most commonly used is the Tokyo Guidelines and the American Association for the Surgery of Trauma (AAST) Emergency Surgery Guidelines (Table 1)^{42,43}

Choledocholithiasis

Gallstones in the common bile duct are usually silent are found indecently in 10% of the patients undergoing biliary imaging. CBD stones are characterized into primary and secondary stones based on their origin. If the stones are formed in the CBD then they are called primary and if they pass from the gallbladder to the CBD then they are termed as secondary stones. Primary CBD stones are usually brown stones are common in the Asian population when compared to the western world. In the west, secondary stones are more common. CBD stones can manifest as jaundice, biliary colic, with darkened urine and pale stool. In the presence of fever and sepsis the patient will show characteristics of cholangitis.^{44,45}

Cholangitis

Bile is naturally sterile but due to obstruction of the common bile duct by a stone, the bile can become infected and leads to cholangitis. The patient may present with fever, jaundice and pain abdomen – together referred to as Charcot's Triad. This can be found in up to 75% of the patients. In the presence of septic shock and delirium it takes the shape of Reynaud's Pentad. Secondary biliary cirrhosis results from prolonged CBD obstruction. Cholangitis requires urgent stone removal by ERCP and use of antibiotics.^{45,46}

Table 1: Classification of acute calculus cholecystitis Tokyo Guidelines and the American Association for the Surgery of Trauma (AAST) Emergency Surgery Guidelines^{42,43}

Grade III (severe) acute cholecystitis
“Grade III” acute cholecystitis is associated with dysfunction of any one of the following organs/systems:
1. Cardiovascular dysfunction: hypotension requiring treatment with dopamine ≥ 5 $\mu\text{g/kg}$ per min, or any dose of norepinephrine
2. Neurological dysfunction: decreased level of consciousness
3. Respiratory dysfunction: $\text{PaO}_2/\text{FiO}_2$ ratio < 300
4. Renal dysfunction: oliguria, creatinine > 2.0 mg/dl
5. Hepatic dysfunction: PT-INR > 1.5
6. Hematological dysfunction: platelet count $< 100,000/\text{mm}^3$
Grade II (moderate) acute cholecystitis
“Grade II” acute cholecystitis is associated with any one of the following conditions:
1. Elevated WBC count ($> 18,000/\text{mm}^3$)
2. Palpable tender mass in the right upper abdominal quadrant
3. Duration of complaints > 72 h ^a
4. Marked local inflammation (gangrenous cholecystitis, pericholecystic abscess, hepatic abscess, biliary peritonitis, emphysematous cholecystitis)
Grade I (mild) acute cholecystitis
“Grade I” acute cholecystitis does not meet the criteria of “Grade III” or “Grade II” acute cholecystitis. It can also be defined as acute cholecystitis in a healthy patient with no organ dysfunction and mild inflammatory changes in the gallbladder, making cholecystectomy a safe and low-risk operative procedure

Biliary pancreatitis

Small sized migratory gall stones can get lodged in the pancreatic duct and leads elevation of the pancreatic duct pressure leading to inflammation of the pancreas in about 4%-8% of the patients suffering from gallstone disease. Smaller the size of the stone, more will be chances of biliary pancreatitis. Gallstones with a diameter around 4 mm are more prone to cause biliary pancreatitis compared to 9 mm and above stones which are more commonly associated with obstructive jaundice. Early intervention with ERCP has proven to reduce the morbidity associated with biliary pancreatitis. Future recurrences are avoided with the same hospitalization cholecystectomy.^{47,48}

Gallstone ileus

One of the rarer presentation (0.3-0.5%) and complication of gallstone disease is called gallstone ileus which is a misnomer since it causes obstruction of the gastrointestinal tract. It is more common in elderly women. Gallstones of size more than 4 cms are usually the main risk factor. Due to continuous pressure of such a large stone in the gallbladder, it leads to formation of a fistulous tract between the gallbladder and the GI tract. Most commonly the obstruction is in the distal ileum or ileo-cecal junction. If the obstruction takes place in the duodenum or gastric outlet then it is known as Bouveret Syndrome which has an incidence of 4%.^{49,50}

Mirizzi Syndrome

Mirizzi syndrome is one of the rarer complications of chronic gallstone disease of the gallbladder, and is usually found in women of age ranging from 50 to 70 years of age. Due to chronic impaction of stone to the gallbladder wall, it leads to chronic inflammation of the wall. Overtime it causes necrosis of the wall to the common bile duct which leads to formation of a cholecysto-duodenal fistula. The most common presentation of Mirizzi syndrome is obstructive jaundice sometimes associated with right upper quadrant pain. Csendes classified Mirizzi syndrome into five categories which are as follows:

Treatment modalities

When managing a case of gallstone disease four major aspects needs to be looked into – reducing the pain and inflammation associated with the gallbladder, managing the systemic

illness, avoiding injury to the gallbladder and other complications and preventing future recurrences.

Supportive care

Stabilizing a patient coming to emergency by properly hydrating the patient with intravenous fluids, providing adequate analgesia, proper antibiotics and correction of electrolytes goes long way into a better prognosis of the patient. Even after this the patient will require definitive treatment.

Cholecystectomy

Cholecystectomy is the treatment of choice in case of gallstone diseases. Cholecystectomy is the removal of gallbladder either by laparoscopic, which is considered the standard of care, robotic or open. Cholecystectomy is considered the gold standard treatment as it permanently removes the primary cause of the disease. Though it is the standard of care it should not be done where there is acute inflammation as the operative site can be friable, infected and increases the risk of mortality to as high as 19%.^{51,52}

Laparoscopic cholecystectomy is associated with lesser post-operative pain, smaller incisions and faster recovery when compared to open cholecystectomy. Usually there are no contraindications of laparoscopic cholecystectomy other than in patients who can't tolerate general anaesthesia, has portal hypertension or coagulopathy.⁵³

When there is active inflammation or infection in the gallbladder, then interval cholecystectomy can be planned in the next 4 to 6 weeks till the inflammation reduced and the chance of iatrogenic injury reduces. There is a chance of recurrence of symptoms in 20% of patients in the waiting period. This strategy is no longer favored in case of lower risk patients with acute presentation.^{54,55}

Cholecystostomy

Cholecystostomy is a good temporary method to drain the gallbladder in case of severe sepsis with cholecystitis. This helps to reduce the toxic load and also avoid iatrogenic injury. Once the offending cause is temporarily diverted and the condition of the patient improves then cholecystectomy can be planned. About 80% success rate was seen in patients in whom

gallstone removal via the cholecystostomy was done but there is a high risk (20%) of recurrence of symptoms within 1 year.^{56,57}

ERCP

Endoscopic retrograde cholangiopancreatography is a very useful diagnostic and therapeutic modality in case of gallstone disease. An endoscope is passed up to the second part of duodenum which allows access to biliary and pancreatic ducts. Contrast material can be then injected the ducts for radiologic visualization. Biopsy or brush biopsy of a lesion can also be done. Other than being a diagnostic modality, it has become a more useful therapeutic modality by which sphincterotomy, biliary or pancreatic stent placement and stone removal can be done. ERCP is indicated in cases of obstructive jaundice, to diagnose peri-ampullary lesions, for manometry for sphincter of Oddi, biliary stent for strictures, removal of gallstones from the CBD. Sphincterotomy is indicated where there is dysfunction of the sphincter of Oddi, or presence of stenosis or difficulty in stenting of bile duct, removal of stones or periampullary growth. With the help of ERCP, more than 75% of the patients have complete clearance of CBD stones in their index procedure, and this number increases up to 90% in the second setting.⁵⁸

ERCP is also associated with a 6.8% incidence of complications. Most common complication post-ERCP is pancreatitis, followed by cholangitis and cholecystitis. Gastrointestinal bleeding can also happen post ERCP.^{59,60}

CBD exploration

If clearance of choledocholithiasis was not possible or complete via ERCP then CBD exploration can be done along with cholecystectomy. CBD exploration can be performed by the open technique or laparoscopically. Preference of open CBD exploration is that palpation of the CBD can be done and the stones can be “milked” back into cystic duct or the gallbladder. If the stone is not palpable then a choledochotomy can be done, a catheter can be introduced and flushed with saline to push the stone. Once there is complete clearance of stones from the CBD, then a T-Tube can be placed and a cholangiogram can be done to confirm the findings before closure.

With the advancement of laparoscopic surgeries, surgeons now prefer laparoscopic exploration of the CBD with a choledoscope or ureteroscope, where similar steps can be done and the stone can be removed with the help of a wire basket.

Laparoscopic exploration of the CBD with cholecystectomy is comparable to ERCP done after laparoscopic cholecystectomy in relation to the patient's outcome, hospital stay and overall expenditure.^{58,61}

Mora-Guzman I et al. conducted a study in 2020 where they found that more than a third of elderly patients could present with a recurrence within 2 years after initial non-operative management of gallstone disease. They concluded that early cholecystectomy should be considered at index admission in order to prevent recurrence. They reviewed a consecutive series of patients, older than 65 years, admitted for a gallstone-related disease and treated with a non-operative management between January 2010 and December 2013. They analysed comorbidities, clinical data, diagnosis, management, recurrence, and its treatment. The study included 226 patients. Mean age was 80.4 ± 7.2 years, 127 (56%) were female. The main causes of index hospitalization were acute cholecystitis (58%) and biliary pancreatitis (18.1%). After 2 years of follow-up, the recurrence rate was 39.8%; mean time to recurrence was 255.2 ± 42.1 days, 81% of patients recurred within 1 year. Bile duct disease implied a higher recurrence rate than the gallbladder disease group (52% vs 33%, $p < 0.001$). Subjects with two or more diagnoses during index admission presented higher recurrence rate (32% vs 49%, $p < 0.001$).⁶²

In 2019, Antonino A et al. conducted a retrospective study where they performed 1227 cholecystectomies and analysed the outcomes of laparoscopic cholecystectomy in the elderly population. 351 out of 1227 patients were 65-79 years of age and 65 were 80 years of age or older. Only 65 patients (5.3%) of 1227 patients underwent primary open cholecystectomy. The incidence was of about 3.7% in the young population and 9.2% in the elderly. The conversion to open rate was 1.2% more in the older group but there was no significant difference between the two groups. Laparoscopic cholecystectomy was performed in emergency setting in 10.3% of young patients and in 13.8% of elderly group. They concluded that laparoscopic cholecystectomy is a feasible and safe procedure in elderly patients and might be performed during the same hospitalization like definitive treatment of gallstone disease.⁶³

In 2017, Yokota Y et al. conducted a study where they concluded that the results of laparoscopic surgery in elderly(≥ 80 years) are comparable to the younger population(< 80 years). Out of 351 patients, 52 (14.8%) and 299 (85.2%) were categorized as older and younger, respectively. No significant differences between the two groups were found in operation time, intraoperative blood loss, or conversion rate to open surgery. Incidence of postoperative complications and duration hospital stay also were also similar.⁷

According to a 2016 study by **Lupinacci RM et al.**, as life expectancy rises around the world and the prevalence of gallstones rises with age, the number of very elderly individuals requiring gallstone disease treatment is rising. The purpose of this study was to examine the outcomes of cholecystectomy in patients aged 80 and up with various clinical presentations. This was a retrospective research involving 81 people aged 80 and over. Indications for surgery were stratified into three groups: outpatients (symptomatic chronic cholecystitis), inpatients (complicated gallstone diseases), and urgent patients (acute cholecystitis). Age, sex, the American Society of Anaesthesiologists score, surgical indication, length of hospital stay, morbidity, and death were all examined. The patients' average age was 83.9 years (range: 80–94 years). There were 34 men (42 percent). Thirty individuals underwent surgery for acute cholecystitis. Patients in the urgency group were admitted to the ICU more frequently, required a longer hospital stay, and had more comorbidities, with a 32% death rate. There were no differences between inpatients and outpatients, with both having low morbidity, no death, and the same postoperative duration of stay. More than 80% of the patients required surgery due to severe gallstone disease. Although the results of semi-elective cholecystectomy patients were similar to those of outpatients, individuals with acute cholecystitis had exceedingly high morbidity and fatality rates.⁵

Bergman S et al. In 2010, researchers conducted a study to examine changes in the management of symptomatic gallstone disease among different aged groups and to assess the relationship between older age and surgical treatment. This retrospective chart review at a single institution included all patients 65 and older who had their first hospital visit for symptomatic gallstone disease between 2004 and 2008. The patients were divided into three age groups: group 1 (65–74 years old), group 2 (75–84 years old), and group 3. (age, ≥ 85 years). The patient's features and presentation at the initial hospital visit, as well as the surgical and other nonoperative procedures performed over a one-year follow-up period, were described. To investigate the influence of age on surgery, logistic regression was used. Data

from 397 patient charts were assessed: 182 in group 1, 160 in group 2, and 55 in group 3. Cholecystitis was the most common diagnosis in groups 1 and 2, whereas cholangitis was the most common diagnosis in group 3. Elective admissions to a surgical ward were most common in group 1, whereas urgent admissions to a medical ward were most common in group 3. Elective surgery was performed at the first visit for 50.6% of group 1, for 25.6% of group 2, and for 12.7% of group 3, with a 1- year cumulative incidence of surgery of 87.4% in group 1, 63.5% in group 2, and 22.1% in group 3. Inversely, cholecystostomy and endoscopic retrograde cholangiopancreatography (ERCP) were used more often in the older groups. Increased age (odds ratio [OR], 0.87; 95% confidence interval [CI], 0.84–0.91) and the Charlson Comorbidity Index (OR, 0.80; 95% CI, 0.69–0.94) were significantly associated with a decreased probability of undergoing surgery within 1 year after the initial visit. Even in the elderly population, older patients presented more frequently with severe disease and underwent more conservative treatment strategies. Older age was independently associated with a lower likelihood of surgery.⁶⁴

Lord A. et al conducted a metanalysis in 2019 where they also concluded that laparoscopic cholecystectomy is a safe option in the elderly. Studies comparing laparoscopic cholecystectomy in >80s with younger patients were included. Twelve studies including 366,522 patients were included. The elderly group had more complicated gallbladder disease and also had more co-morbidities and a higher ASA grade. The risk of morbidity was lower in the younger group (RR 0.58 (95% CI 0.58-0.59)) with a slightly lower risk of conversion (RR 0.96 (0.94-0.98)). Length of stay was significantly longer for the elderly patients. Differences in mortality and bile duct injury were non-significant in all but one study.⁸

Schlottmann F. et al performed a retrospective, population based analysis in 2019, where they found that elderly patients undergoing cholecystostomy for acalculous and calculous acute cholecystitis have higher incidences of post-procedural morbidity and mortality. This was also associated with a longer length of hospital stay, when compared to cholecystectomy. Patients of age more than 65 years of age, getting admitted for acute cholecystitis and undergoing cholecystostomy or cholecystectomy were included in the study. A total of 200,915 patients were included. 7516 underwent cholecystostomy and 193,399 underwent cholecystectomy. Patients undergoing cholecystostomy were more likely to have post-procedural infection (OR 2.25; 95% CI 2.07, 2.45), bleeding (OR 1.28; 95% CI 1.19,

1.37), and inpatient mortality (OR 9.27; 95% CI 7.95, 10.81). On average, cholecystostomy patients stayed 1.25 days longer (95% CI 1.14, 1.37) in hospital after the procedure.⁶⁵

Heesewijk A. et al conducted a study in 2019 where they found that in elderly patients, the complication and mortality rate following cholecystectomy is more than what was reported before. It was a retrospective analysis of 565 patients who underwent cholecystectomy. Focus of the analyses was on postoperative complications and its predictors. The study population was divided in two cohorts; aged <70 and ≥70 years. More complications were found in patients aged ≥70 years. More elderly patients were admitted to the intensive care, respectively 4.0% and 14.1% (P = 0.045). Hospital mortality was 6% in patients aged ≥70 years vs 0.6% in patients <70.⁶⁶

In 2018, **Joliat G. et al.** concluded that delayed cholecystectomy can be a good option to emergency cholecystectomy in elderly individuals with acute cholecystitis. Following percutaneous draining, 18 patients (64%) underwent delayed cholecystectomy. In the percutaneous drainage group, postoperative morbidity was 39% (7/18), and one patient died. Elderly patients who had delayed cholecystectomy following percutaneous drainage (n = 18) had a longer median hospital stay (10 days against 3 days, P = .001) and had worse postoperative complications (7/18 versus 6/53, P = .015) than those who had delayed cholecystectomy after antibiotic therapy (n = 53). draining is associated to a higher complication risk and a longer hospital stay. The goal of this study was to look at how we now treat older patients with acute cholecystitis. Between 2006 and 2015, all patients over the age of 70 with acute cholecystitis treated largely with antibiotics with or without percutaneous drainage and delayed cholecystectomy were evaluated retrospectively. A total of 105 elderly patients with acute cholecystitis were treated with delayed cholecystectomy. Antibiotics were used alone in 93 individuals at initially. Twenty-eight patients required percutaneous drainage, either due to requirement (n = 12) or due to antibiotic treatment failure (n = 16). Due to failure of percutaneous drainage or antibiotic treatment, nine patients (32%) and 11 patients (12%) underwent an emergency cholecystectomy. Eighteen patients (64%) underwent delayed cholecystectomy after percutaneous drainage. Postoperative morbidity was 39% (7/18) after delayed cholecystectomy in the percutaneous drainage group, and 1 patient died. Compared to delayed cholecystectomy after antibiotic treatment (n = 53), elderly patients who underwent delayed cholecystectomy after percutaneous drainage (n =

18) had longer median hospital stay (10 days versus 3 days, $P = .001$) and higher postoperative complications (7/18 versus 6/53, $P = .015$).⁶⁷

In 2019, **Zahur Z. et al** determined that ultrasonography can be used as an initial and baseline tool for the detection of CBD calculi because it is non-invasive, widely available, radiation-free, and inexpensive. From February to July 2015, a descriptive cross-sectional validation research was done at PAEC General Hospital in Islamabad. The study comprised patients with suspected choledocholithiasis who went to the radiology department for an ultrasonography abdomen. The researchers discovered common bile duct dilation, intrahepatic biliary channel dilatation, and direct imaging of calculus in CBD. The results of the ultrasound were compared to the results of a subsequent ERCP, which was regarded the gold standard. The diagnostic accuracy of trans abdominal ultrasonography in detecting choledocholithiasis was found to be 76.9%, with 76.2 percent sensitivity and 81.3 percent specificity.⁶⁸

In 2017, **Manning A. et al.** published a study that found that protocol-driven management of patients with suspected common duct stones reduced the number of endoscopies and length of hospitalisation while having no effect on postoperative morbidity. This strategy has the potential to reduce endoscopy-related morbidity and total costs without compromising care quality. Patient demographics, presence of pancreatitis, common duct stone risk factors, comorbidities, length of hospitalization, and surgical morbidity were compared retrospectively between protocol and baseline patients. The t-test, chi-square, and Wilcoxon rank-sum tests were used in the statistical analysis, with significance set at $p 0.05$. Each group had 56 patients, with an average age of 50.5 ± 20.88 years and 49.3 ± 20.92 years, respectively ($p = NS$). Individual and cumulative preoperative comorbidities, pancreatitis, increase of liver function tests, bilirubin, common duct size, and surgical morbidity were not significantly different between baseline and protocol individuals. In protocol patients, there were fewer endoscopies (22 vs 35; $p = 0.014$) and a shorter length of stay (2.8 vs 3.8 days; $p = 0.025$).⁶⁹

In a 2013 study, **Barlow A. et al** colleagues determined that patients with acute gallstone pancreatitis need have specific imaging, preferably MRCP, to rule out choledocholithiasis because LFTs and ultrasonography are unreliable in predicting common bile duct stones. All patients hospitalised with gallstone pancreatitis (amylase $>300\text{u/l}$) who had MRCP between

January 2008 and January 2011 were included in their study. The LFTs and radiography reports were retrieved from the appropriate computer systems. MRCP was performed on 173 patients with acute gallstone pancreatitis, and choledocholithiasis was found in 30% (52/173) of them. Although there was no significant difference in alkaline phosphatase (276 25iu/l vs 229 16iu/l, $p=0.1154$), the mean bilirubin level was substantially higher in individuals with choledocholithiasis (46 5mol/l vs 36 3mol/l, $p=0.0388$). However, abnormal bilirubin ($>21\text{mol/l}$) had a sensitivity of only 62% and a specificity of 41% for choledocholithiasis. The sensitivity and specificity of aberrant alkaline phosphatase ($>140\text{iu/l}$) for choledocholithiasis were only 75% and 37%, respectively. Although the sensitivity of biliary dilatation for choledocholithiasis was only 44% and the specificity was 79%, there was a significant relationship between biliary dilatation on ultrasonography and choledocholithiasis on MRCP ($p=0.0099$). Furthermore, there was no difference in the incidence of choledocholithiasis on MRCP between individuals with consistently disturbed LFTs and those with normal LFTs (relative risk: 1.07, 95 percent confidence interval: 0.61-1.89, $p=1.00$). On admission, 10% of patients with choledocholithiasis on MRCP had completely normal LFTs and no biliary dilatation or choledocholithiasis on ultrasonography.⁷⁰

Magnetic resonance cholangiopancreatography is a reliable evaluation tool for the detection of choledocholithiasis, according to a 2012 study by **Wong H. et al.** It lowers the possibility of misdiagnosing retained choledocholithiasis with normal biochemical predictors and prevents choledocholithiasis from being overlooked. There hasn't been a single predictor or combination of markers that has been proven to reliably include or exclude the existence of choledocholithiasis. The goal of this study was to see how well MRCP and high biochemical markers for choledocholithiasis might predict choledocholithiasis in patients with acute cholecystitis. Between September 2006 and August 2008, 57 patients with acute cholecystitis who met the Tokyo guidelines' diagnosis criteria got MRCP before surgery. Six biochemical indicators for choledocholithiasis were also assessed for their predictive values. Seven (12.28 percent) of the 57 patients developed choledocholithiasis, with three of them having CBD stones in nondilated ducts. The smallest stone found in a dilated CBD and a nondilated duct had diameters of 3.19 and 4.55 mm, respectively. During the follow-up period, none of their patients with a clear CBD on MRCP returned with symptomatic choledocholithiasis. The positive predictive values of all biochemical markers and CBD diameter were limited.⁷¹

In 2014, **Sodhi J. et al** published a study that found that people with type 2 diabetes mellitus had a greater risk of gallstone disease than the general population. This was a case-control study to investigate the prevalence of gallstones, risk factors, and relative risk in patients with type 2 diabetes mellitus compared to persons without diabetes from the general population. 377 (88.8%) of the 450 patients with type 2 diabetes mellitus who had been diagnosed for at least two years took part in the study. Ultrasonography revealed gallstones, as well as a history of cholecystectomy for gallstones. An oral glucose tolerance test was used to rule out diabetes in the controls, who were drawn from the general community. The age, gender, and BMI of the cases and controls were matched. Gallstones were found in 67 (17.7%) of the cases versus 40 (5.8%) of the controls ($p = 0.001$). Prevalence rose with age, peaking in the sixth decade (23.4 percent in cases and 4.4 percent in controls ($p = 0.001$), and was greater in women (27.9% in cases and 7.8% in controls, respectively) ($p = 0.001$). Age, female sex, BMI, multiparity, family history of GS, and high triglycerides and cholesterol with low high-density lipoprotein cholesterol were all found to be risk factors for gallstones in univariate analysis. Age (RR 1.54, CI 1.1-2.1), female sex (RR 1.6, CI 1.0-1.9), and BMI (RR 1.5, CI 1.3-2.5) were found to be independent risk factors for gallstone formation in multivariate analysis.⁷²

In 2014, **Wang W. et al** published a meta-analysis that concluded that diabetes mellitus and the risk of GSD in patients had a very significantly positive correlation. Eligible studies were searched in the PubMed and Cochrane Central databases. The aggregate combined risk estimates were then calculated using a random effect model. A total of 403,001 cases and 411,877 controls were included in the meta-analysis, which came from six case-control studies, three cohort studies, and thirteen cross-sectional investigations. Finally, statistical analyses were carried out in accordance with the study classification. 1.75 (95 percent confidence interval [CI]: 1.44-2.13, $p < 0.001$), 1.76 (95 percent CI: 1.24-2.5, $p < 0.001$), and 2.02 (95 percent CI: 1.59-2.58, $p < 0.001$) were the risk ratios for diabetes mellitus and GSD, respectively. The heterogeneity I-square test and risk ratios were unaffected by sensitivity analysis based on excluding any study.⁷³

Gallstone disease is linked to various diabetes risk factors, according to a study published in 2017 by **Lv J. et al**. The purpose of this study was to see if gallstone disease was linked to type 2 diabetes in the China Kadoorie Biobank. At the time of the study, 189,154 men and 272,059 women aged 30-79 years were eligible for analysis after removing those with

diabetes and prior history of cancer, heart disease, or stroke. Gallstone disease affected 5.7 percent of the individuals at the start of the study. A total of 4,735 men and 7,747 women were diagnosed with type 2 diabetes throughout the 4,138,687 person-years of follow-up (median, 9.1 years). The multivariate-adjusted hazard ratios (HRs) for type 2 diabetes for those with GSD were 1.09 (95 percent CI: 0.96-1.24; P = 0.206), 1.21 (95 percent CI: 1.13-1.30; P 0.001), and 1.17 (95 percent CI: 1.10-1.25; P 0.001) in men, women, and the entire cohort, respectively, compared to those without gallstone disease at baseline. There was no statistically significant difference between males and women (interaction P = 0.347). The strongest link between gallstone disease and type 2 diabetes was found among participants who had been diagnosed for at least 5 years and were still receiving treatment at the time of the study (HR = 1.48; 95 percent CI: 1.16-1.88; P < 0.001).⁷⁴

In 2019, **F. Wang et al.** published a study. Using a Mendelian randomization approach, the researchers wanted to see if there was a possible causal link between gallstone disease and the likelihood of type 2 diabetes. The Dongfeng-Tongji cohort research included 16,299 patients who had no history of cancer, heart disease, stroke, and diabetes at the start of the trial. Experienced clinicians used abdominal B-type ultrasound inspection to detect gallstone disease. The connection of gallstone disease with the risk of type 2 diabetes was investigated using a Cox proportional hazard regression model. Eight single nucleotide polymorphisms taken from previous genome-wide association studies were used to create a genetic risk score (GRS) for gallstone disease. In a Mendelian randomization analysis, the causal correlations of the gallstone disease score with type 2 diabetes were examined among 7,000 participants. From 2008 to 2013, they tracked 1,110 new cases of type 2 diabetes across a period of 73,895 person-years (median 4.6 years). The multivariate-adjusted hazard ratio of type 2 diabetes risk in those with GSD was 1.22 (95 percent confidence interval [CI], 1.03-1.45, P = 0.02), compared to those without gallstone disease. Each 1 SD (0.23) increment in the weighted GRS was associated with a 17% increment of type 2 diabetes risk (odds ratio = 1.17, 95% CI, 0.90-1.52). Without statistical significance (P = 0.25), each 1 SD (0.23) increase in the weighted GRS was linked with a 17 percent increase in type 2 diabetes risk (odds ratio = 1.17, 95 percent CI, 0.90-1.52). In conclusion, the current investigation found a positive but not a causal link between gallstone disease and the incidence of type 2 diabetes..52) without statistical significance (P = 0.25). In conclusion, the present study supported a positive but not a causal association of gallstone disease with type 2 diabetes risk.⁷⁵

In a 2003 study, **Laukkarinen J. et** found that hypothyroidism can result in delayed biliary tract emptying, as measured by quantitative (99m)Tc HIDA cholescintigraphy. In addition to the changes in bile composition and excretion rate previously suggested to occur in hypothyroidism, changes in biliary emptying may also be included in the probable causes for the increased prevalence of common bile duct stone in hypothyroidism, according to the current study. This could be owing to thyroxine's lack of a pro-relaxing impact on the sphincter of Oddi. The goal of this study was to look into human biliary dynamics in connection to thyroid gland function changes. With quantitative (99m)Tc HIDA cholescintigraphy, biliary ultrasonography, and serum determinations, eight female patients, one with untreated hypothyroidism and seven with total thyroidectomy due to thyroid cancer, were studied in hypothyroid stage and again after thyroxine replacement therapy in euthyroid stage. Throughout the two stages of the trial, each patient acted as her own control. The maximal uptake of (99m)Tc HIDA in hypothyroidism was not different from euthyroidism in quantitative (99m)Tc HIDA cholescintigraphy. In the two stages of the study, the first manifestation of radioactivity in major bile channels at the hepatic hilum remained unchanged. When compared to euthyroid stage, hepatic clearance of (99m)Tc HIDA was reduced at 45 minutes (28 percent [11-38] vs 50 percent [33-54]; $P = .028$; median and range) and at 60 minutes (55 percent [28-80] vs 69 percent [61-79]; $P = .028$; median and range), and hilum-duodenal transit time increased by 31%. In the two stages of the trial, ultrasonography revealed no alterations in the gall bladder or bile ducts. In the hypothyroid stage, serum hypercholesterolemia was also discovered.⁷⁶

Laukkarinen J. et al. conducted a study in 2007 and reported that subclinical hypothyroidism is more common in CBD stone patients compared to non-gallstone controls, validating our hypothesis that hypothyroidism may play a role in the formation of CBD stones. In this investigation, the frequency of previously undetected subclinical hypothyroidism in CBD stone patients was compared to non-gallstone controls. All patients were clinically euthyroid and had no history of thyroid function problems. CBD stones were identified using endoscopic retrograde cholangiopancreatography (group I; $n = 303$) or ruled out using a medical history, liver function tests, and ultrasonography (control group II; $n = 142$). Serum free FT(4) and TSH (S-TSH) levels were measured; S-TSH levels beyond the normal range (>6.0 mU/litre) were classified subclinical, while S-TSH levels 5.0-6.0 mU/litre were considered borderline-subclinical hypothyroidism. Subclinical and borderline-subclinical hypothyroidism were detected in 5.3 and 5.0 percent (total 10.2 percent ; 31 of

303) of CBD stone patients, respectively, compared to 1.4 percent ($P = 0.05$) and 1.4 percent (total 2.8 percent, four of 142; $P = 0.026$) in the control group. Subclinical hypothyroidism was found in 11.4 percent of CBD stone patients and 1.8 percent of control patients ($P = 0.032$), while subclinical plus borderline-subclinical hypothyroidism was found in 23.8 percent of CBD stone patients and 1.8 percent of control patients ($P = 0.012$).⁷⁷

H. Ajdarkosh et al. conducted a study in 2013 and discovered a link between thyroid disorders and the prevalence of bile duct stones. The purpose of this study was to assess the thyroid function pattern in patients with common bile duct (CBD) stones. This case-control study enrolled 151 individuals with preliminary CBD stone diagnoses who underwent ERCP (cases). The control group consisted of healthy people who met the study criteria and were treated at the same facility. Ultrasonography was performed on the control group to rule out any asymptomatic bile duct stones. An allocated physician completed a questionnaire that comprised demographic and anthropometric data. All participants had their blood drawn in the morning after fasting for 12 hours in order to determine serum total thyroxine (T4) and serum thyroid stimulating hormone (TSH) (TSH). TSH levels in patients were higher (2.59 4.86mg/dl) than in the control group (2.53 4.13 9mg/dl). Serum TSH levels more than 5 MU/L were reported in 30.6 percent of cases with subclinical hypothyroidism compared to 22.5 percent of controls [OR: 1.53; 95 percent confidence interval (CI): 0.968-2.438]. Hypothyroidism was found in 10.8% of the control group and 11.3 percent of the patients (OR: 1.87; 95 percent CI: 0.578-2.043).⁷⁸

MATERIALS & METHODS

MATERIALS AND METHODS

METHODS:

Study Design

Hospital-based prospective observational study

Study Setting

This study was conducted in patients who were more than the age of 60 years of age at the time of admission and presented with symptomatic gallstone disease to the Department of General Surgery, AIIMS Jodhpur.

Participants

All patients who underwent elective laparoscopic cholecystectomy for symptomatic gall stones in the Department of General Surgery, AIIMS Jodhpur were recruited for study based on inclusion and exclusion criteria as mentioned below

Inclusion Criteria

- Patients were are part of the senior citizen population (>60 years of age⁷⁹)
- Patient who were diagnosed to have symptomatic gallstone disease
- Patient's with gallstones and polyps
- Any patients with symptoms suggestive gallstone-induced pancreatitis, cholangitis and obstructive jaundice.
- Any patients with USG suggestive of CBD stones
- Patients who gave informed consent.

Exclusion Criteria

- Any patients with symptoms suggestive non-gallstone induced pancreatitis, cholangitis and obstructive jaundice
- Patients with a diagnosis of carcinoma gallbladder
- Patient in whom MRI is contraindicated (e.g. Pacemaker)
- Patient who were claustrophobic and were afraid to undergo MRI.
- Uncooperative patients and patients not giving consent for participation in the study.

Sample Size Calculation

All patients in the time span of 1.5 years from Jan 1st, 2020 to July 31st, 2021 were included in the study

Study Duration

Jan 1st, 2020 to Dec 31st, 2021

Study Procedure

Cases were recruited based on inclusion and exclusion criteria. Informed written consent was obtained. All patients were subjected to full history taking, general and abdominal examination, haemoglobin, total leucocyte count, platelet count, liver function tests, Hb1Ac, thyroid function test, ultrasound abdomen and MRCP as required. In patients who had associated CBD stones, ERCP and stone retrieval were done if indicated and followed by laparoscopic cholecystectomy. Intra-operative findings of the surgery were noted. Gallbladder and gallstones were sent for pathological analysis and their final histopathological analysis was noted. Patients were followed up for a period of 2 weeks after surgery. Investigations like haemoglobin, total leucocyte count, platelet count, liver function tests, thyroid function test will be repeated on follow-up if required. Eventually all the data were combined and analysed.

Statistical analysis

Data were entered and analysed using SPSS version 28. The nominal data were described using frequency and percentages and compared using the chi square test or Fischer Exact test. The ordinal Data was described using Median and Interquartile Range (IQR) and compared using the Mann-Whitney U test. The continuous data were described using mean +/- SD and compared using unpaired t-test. P-value of <0.05 will be considered as statistically significant.

Figure 2: Intraoperative photograph of a patient undergoing laparoscopic cholecystectomy for cholelithiasis



Figure 3: Intraoperative photograph of a patient undergoing early laparoscopic cholecystectomy for acute calculus cholecystitis

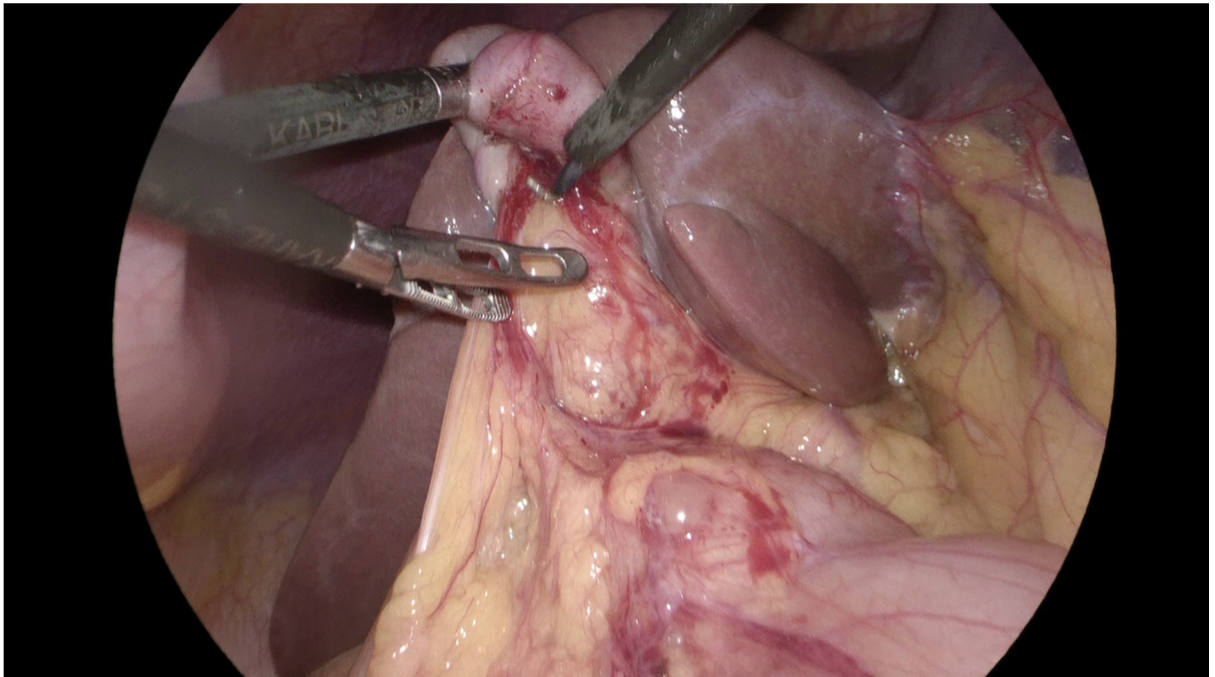
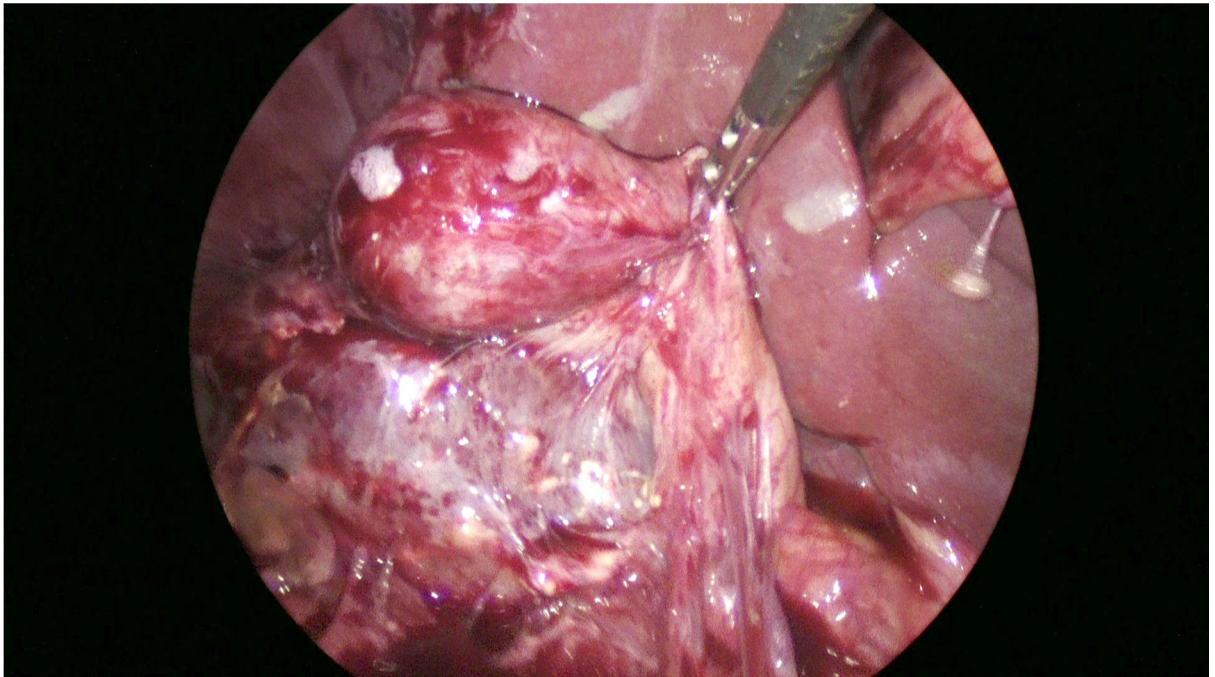


Figure 4: Intraoperative photograph of a patient undergoing interval laparoscopic cholecystectomy for acute calculus cholecystitis



Figure 5: Intraoperative photograph of a patient undergoing interval laparoscopic cholecystectomy post ERCP stenting for biliary pancreatitis



RESULTS

RESULTS

In the period of 1.5 years from 1st of January 2020 to 31st July 2021, a total of 76 patients were recruited in the study who all matched the inclusion criteria of this study.

Out of 76 patients, 26.3% were male , and 73.7% were females. About 97.4% of the study population was married. Only 13.2% of the study population were literate and 9.2% were self-employed. The study population also suffered from co-morbidities like diabetes mellitus(19.7%), hypertension(30.3%) or had thyroid disorder(9.2%). Around 15.8% had a history of smoking and 30.3% had a history of alcohol consumption. 63.2% of the study population were admitted in the hospital through the out-patient department (OPD) while 36.8% were admitted through the emergency department.(Table 2)

Table 2: Demographic Details Of The Study Population

Demographic variables		n (%)
Gender	Male	20 (26.3)
	Female	56 (73.7)
Age (years)	70.8 ±1.7	
Marital status	Married	74 (97.4)
	Unmarried	2 (2.6)
Educational status	Illiterate	66 (86.8)
	Literate	10 (13.2)
Occupation	Employed	7 (9.2)
	Unemployed	69 (90.8)
Comorbidities	Diabetes Mellitus	15 (19.7)
	Hypertension	23 (30.3)
	Thyroid Disorder	7 (9.2)
	Smoker	12 (15.8)
	Alcoholic	23 (30.3)
Admission	OPD	48 (63.2)
	Emergency	28 (36.8)
ASA	1	20 (35.1)
	2	15 (26.3)
	3	21 (36.8)
	4	1 (1.8)
	5	0 (0)

The most common presenting complaints were pain abdomen (96.1%) with dyspepsia (60.5%) and vomiting (55.3%). Some of the patients also complained of loss of appetite (47.4%) and back pain (32.9%). The least common symptoms were fever (23.7%) and yellowish discoloration of the skin (9.2%). On clinical evaluation, 41.6% of patients had a positive Murphy's Sign and 22.1% of the patients had abdominal distention. An abdominal lump was only found in 5.2% of the patients.(Table 3)

Table 3: Signs And Symptoms Of The Patients

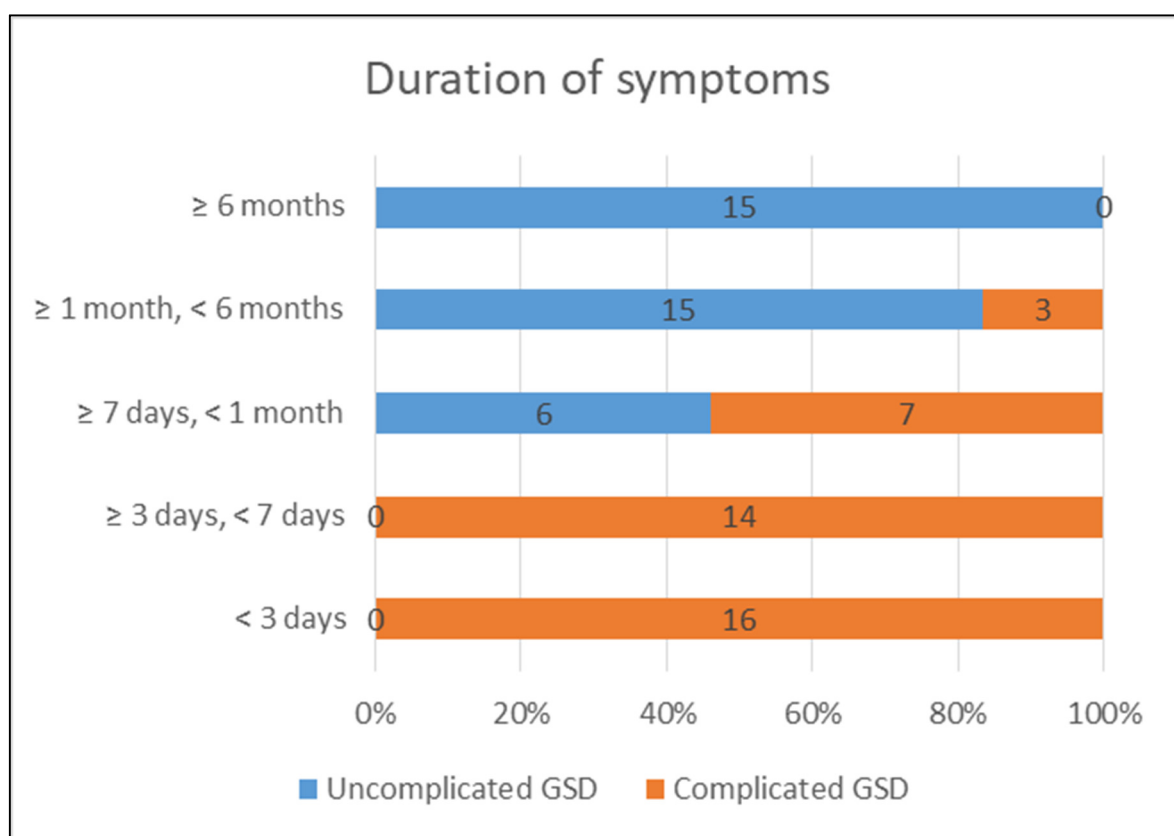
Signs and Symptoms	n (%)
Presenting complaints	
Pain abdomen	73 (96.1)
Dyspepsia	46 (60.5)
Vomiting	42 (55.3)
Loss of appetite	36 (47.4)
Back pain	25 (32.9)
Fever	18 (23.7)
Yellowish discoloration of skin	7 (9.2)
Signs	
Murphy's sign	32 (41.6)
Abdominal distension	17 (22.1)
Palpable gallbladder	4 (5.2)

Uncomplicated GSD (biliary colic) presented with a trend towards longer duration of history whereas complicated GSD (acute calculus cholecystitis, choledocholithiasis, biliary pancreatitis, cholangitis) presented to the hospital with a shorter duration of history. (Table 4) (Figure 6)

Table 4: Duration of Symptoms (Pearson Chi square 53.013, p value <0.001)

Duration	Clinical Presentation		p-Value
	Uncomplicated GSD	Complicated GSD	
	n	n	
< 3 days	0	16	<0.001
≥ 3 days, < 7 days	0	14	
≥ 7 days, < 1 month	6	7	
≥ 1 month, < 6 months	15	3	
≥ 6 months	15	0	

Figure 6: Duration of symptoms



Out of 76, 74 patients underwent ultrasonographic evaluation of the abdomen where the following gallbladder findings were noted. 47.3% of the 74 patients had thickened gallbladder wall. 37.8% of the patients had presence of pericholecystic fluid. 81.1% of the patients had multiple gallstones in the gallbladder while only 17.6% patients had single stone. The average size of the single stone was 10.65 mm whereas the average size of the multiple stones were 6.85 mm. 20.3% of the 74 patients had dilated CBD (≥ 8 mm), out of these only 4 patients CBD stones that were identified on ultrasound. The average size of the CBD stones was 7.84 mm. (Table *Table 5*)

Table 5: Ultrasonographic findings of Gallbladder

Ultrasonographic findings of Gallbladder		No. of patients	Percentage
Gall bladder wall thickness (mm)	≤ 3	39	52.7
	> 3	35	47.3
Pericholecystic fluid	Present	28	37.8
	Absent	46	62.2
No. of stone in Gallbladder	No stone	1	1.4
	Single	13	17.6
	Multiple	60	81.1
Stone size (mean)	Single (mm)	10.6	-
	Multiple (mm)	6.8	-
CBD diameter (mm)	< 8	59	79.7
	≥ 8	15	20.3
CBD stone	Single	3	4.1
	Multiple	1	1.4
CBD stone size mean (mm)		7.84	-

Out of 75 ultrasonographic evaluations, one study was not able to find the presence of gallstones. More than 80% patients had multiple gallstones and had presented more commonly with biliary colic, acute calculus cholecystitis and choledocholithiasis. (Table 6)

Table 6: CORRELATION OF GALLSTONES TO CLINICAL PRESENTATIONS
(Pearson Chi-Square 9.518)

Clinical presentation	Number of Gallstones in Gallbladder			Total	p- Value
	No stone	Single	Multiple		
	n (%)	n (%)	n (%)	n (%)	
Biliary Colic	0 (0.0)	8 (21.1)	30 (78.9)	38 (48.7)	0.246
Acute Calculous Cholecystitis	0 (0.0)	3 (15.0)	17 (85.0)	20 (25.6)	
Cholelithiasis with choledocholithiasis	0 (0.0)	0 (0.0)	5 (100.0)	5 (6.4)	
Biliary Pancreatitis	1 (10.0)	3 (30.0)	6 (60.0)	10 (12.8)	
Cholangitis	0 (0.0)	0 (0.0)	2 (100.0)	2 (2.6)	
Total	1 (1.3)	14 (18.7)	60 (80.0)	75 (100.0)	-

Various blood investigations were done on admission. 56.6% of patients had anemia, 31.6% had leucocytosis. On evaluating the liver function tests – 34.2% had deranged SGPT with only 25% with deranged SGOT. 10.5% of the study population had hyperbilirubinemia and 27.6% had increased ALP. Lipase and amylase were increased in 22.4% and 13.2% of the study population respectively. 68.5% of the patients were found to have a predilection towards diabetes. More than 50% of the population studies had hypothyroidism. (Table 7)

Table 7: BLOOD INVESTIGATIONS

Blood Investigations		n (%)
Anaemic	Yes	43 (56.6)
	No	33 (43.4)
Leucocytosis	Present	24 (31.6)
	Absent	52 (68.4)
SGPT	Increased	26 (34.2)
	Normal	50 (65.8)
SGOT	Increased	19 (25)
	Normal	57 (75)
ALP	Increased	21 (27.6)
	Normal	55 (72.4)
Hyperbilirubinemia	Present	8 (10.5)
	Normal	68 (89.5)
Lipase	Increased	17 (22.4)
	Normal	59 (77.6)
Amylase	Increased	10 (13.2)
	Normal	66 (86.8)
Thyroid Function Test	Normal	33 (43.4)
	Hypothyroidism	40 (52.6)
	Hyperthyroidism	3 (4)
HbA1c	Normal	26 (34.2)
	Prediabetic	20 (26.3)
	Diabetic	30 (39.5)

Benign gallstone diseases were classified into a spectrum of 5 clinical presentations – acute calculous cholecystitis, biliary colic, cholelithiasis with choledocholithiasis, biliary pancreatitis and cholangitis. The most common presentation was biliary colic (49.4%) followed by acute calculus cholecystitis (27.3%), while the least common was cholangitis (2.6%) and cholelithiasis with choledocholithiasis (6.5%). The incidence of biliary pancreatitis was higher (22.9%) in patients aged 60-69 years compared with those aged 70 years and above. Although the difference was not statistically significant, there was a trend towards significance. (Table 8, Table 9) (Figure 7)

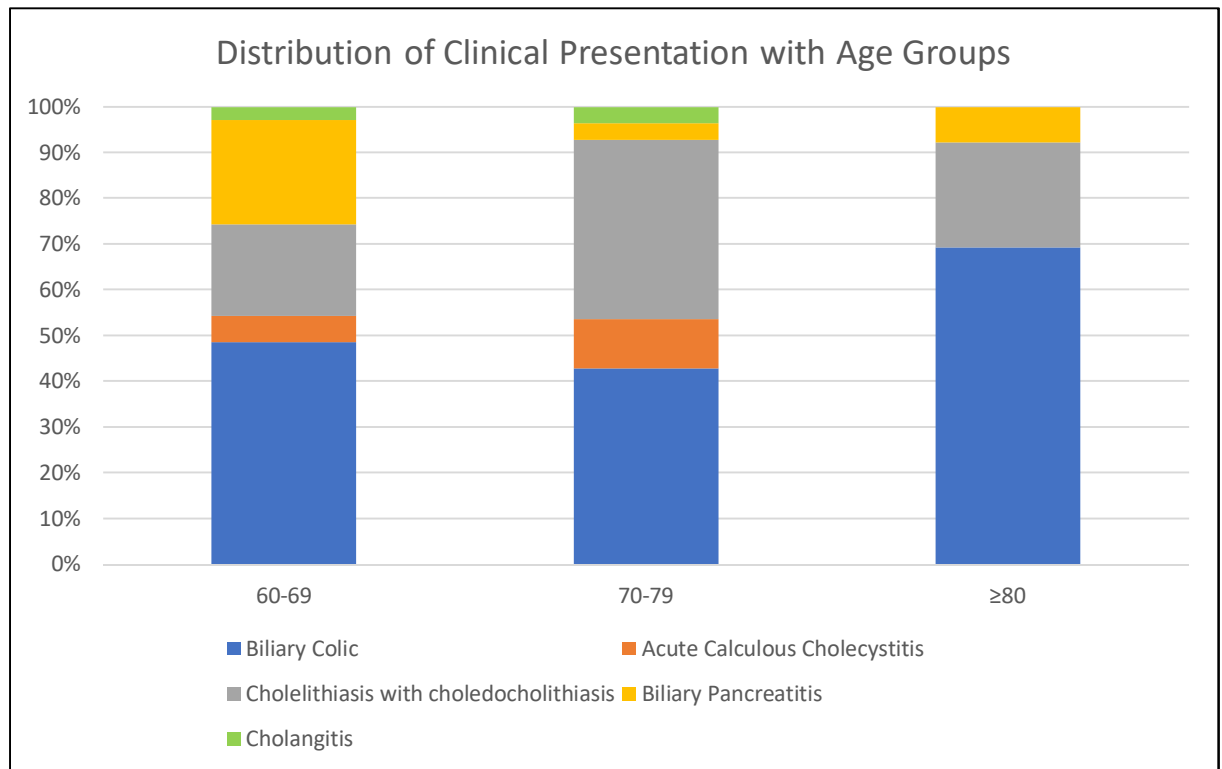
Table 8: Clinical Presentation of Gallstone Disease (Pearson Chi-Square Test)

Clinical presentation	Age (years)			Total n (%)	p-value
	60-69	70-79	≥80		
	n (%)	n (%)	n (%)		
Biliary Colic	17 (48.6)	12 (42.9)	9 (69.2)	38 (50)	0.283
Acute Calculous Cholecystitis	7 (20)	11 (39.3)	3 (23.1)	21 (27.6)	0.217
Cholelithiasis with choledocholithiasis	2 (5.7)	3 (10.7)	0 (0)	5 (6.6)	0.419
Biliary Pancreatitis	8 (22.9)	1 (3.6)	1 (7.7)	10 (13.2)	0.064
Cholangitis	1 (2.9)	1 (3.6)	0 (0)	2 (2.6)	0.796
Total	35	28	13	76	-

Table 9: Distribution of gallstone disease by different age groups (Pearson Chi-Square Test)

Clinical presentation	Age (years)			Total n (%)	p-value
	60-69	70-79	≥80		
	n (%)	n (%)	n (%)		
Uncomplicated GSD	16 (44.4)	11 (30.6)	9 (25.0)	36 (100.0)	0.195
Complicated GSD	19 (47.5)	17 (42.5)	4 (10.0)	40 (100.0)	
Total	35 (46.1)	28 (36.8)	13 (17.1)	76 (100.0)	-

Figure 7: Distribution of Clinical Presentation with Age Groups

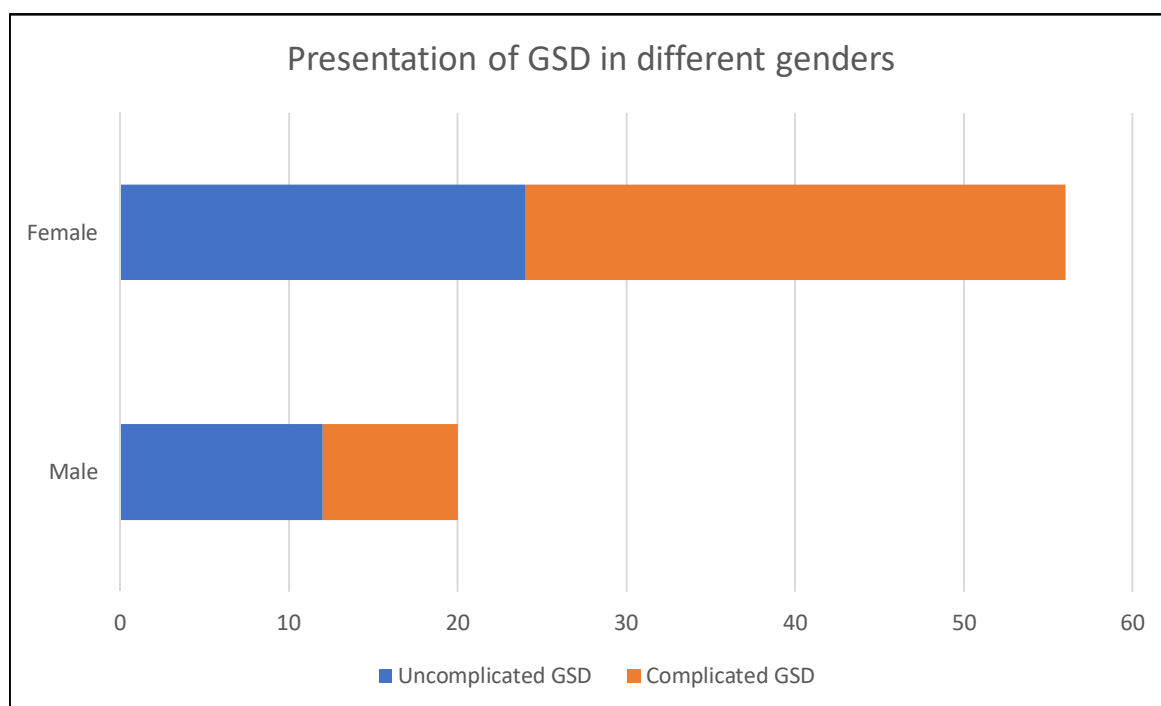


Uncomplicated gallstone disease (biliary colic) was found to be more common in the male population as compared to the female population, where complicated gallstone disease (acute calculus cholecystitis, cholelithiasis with choledocholithiasis, biliary pancreatitis, cholangitis) were found to be more common. (Table 10)(Figure 8)

Table 10: Correlation of clinical presentation of GSD with age (Fisher Exact Test)

Clinical presentation	Gender		Total	p-Value
	Male	Female		
	n (%)	n (%)	n (%)	
Uncomplicated GSD	12 (60.0)	24 (42.9)	36 (47.4)	0.204
Complicated GSD	8 (40.0)	32 (57.1)	40 (52.6)	
Total	20 (100.0)	56 (100.0)	76 (100.0)	-

Figure 8: Correlation of clinical presentation of GSD with age



Out of 76 patients 43.4% were found to be euthyroid, 52.6% were found to be suffering from hypothyroidism but only 4% were found to have hyperthyroidism. Statistically there was no significant difference found between the thyroid status of the patient and the clinical presentation but there was a significantly higher incidence of biliary pancreatitis that was associated with hypothyroidism. Patients who had diabetes were more associated with complicated GSD (60.9%), though it was found not to be statistically significant. (Table 11) (Figure 9, Figure 10)

Table 11: Correlation Between Thyroid Disorders And Gallstone Clinical Presentations
(Fisher Exact Test*; Pearson Chi Square Test**)

Co-morbidities		Clinical presentation		Total	p-Value
		Uncomplicated GSD	Complicated GSD		
		n (%)	n (%)	n (%)	
Thyroid Disorders	Euthyroid	18 (54.5)	15 (45.5)	33 (100.0)	0.057*
	Hypothyroidism	15 (37.5)	25 (62.5)	40 (100.0)	
	Hyperthyroidism	3 (100.0)	0 (0.0)	3 (100.0)	
Hypertension	Hypertensive	9 (39.1)	14 (60.9)	23 (100.0)	0.343**
	Normotensive	27 (50.9)	26 (49.1)	53 (100.0)	
Diabetes	Diabetic	18 (39.1)	28 (60.9)	46 (100.0)	0.075**
	Not-diabetic	18 (60.0)	12 (40.0)	30 (100.0)	

Figure 9: Correlation of Thyroid Disorders with GSD

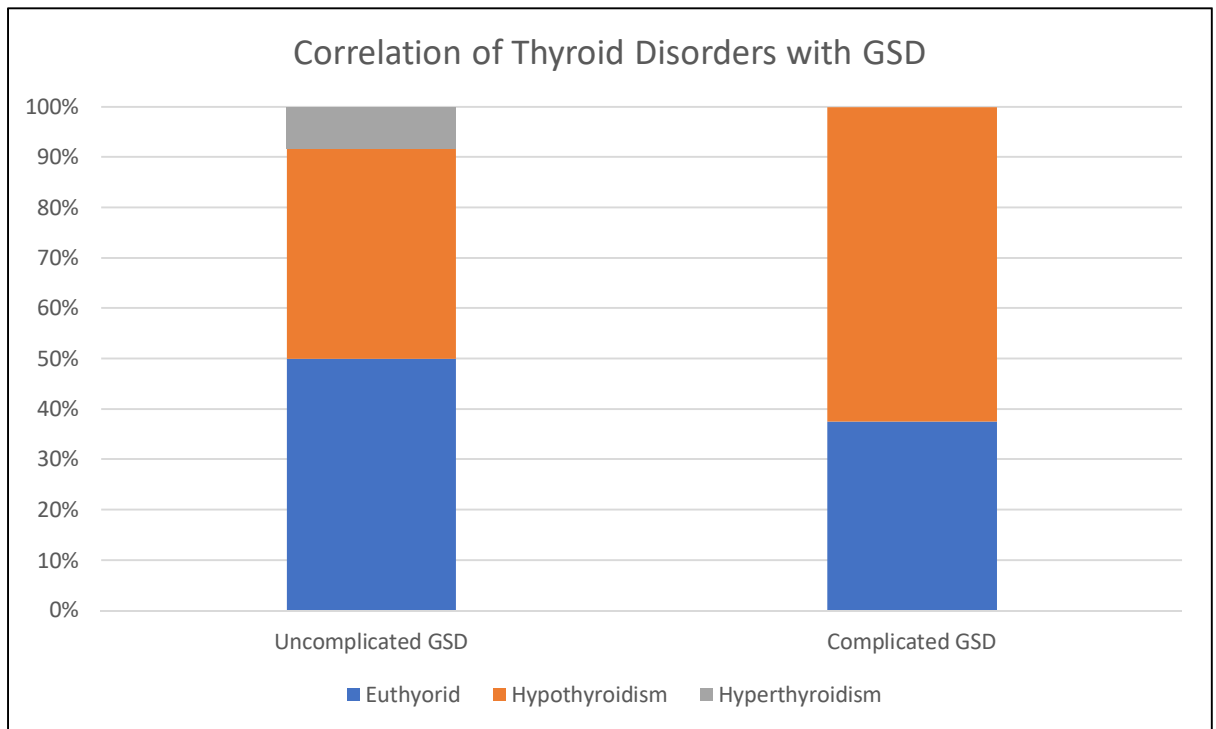
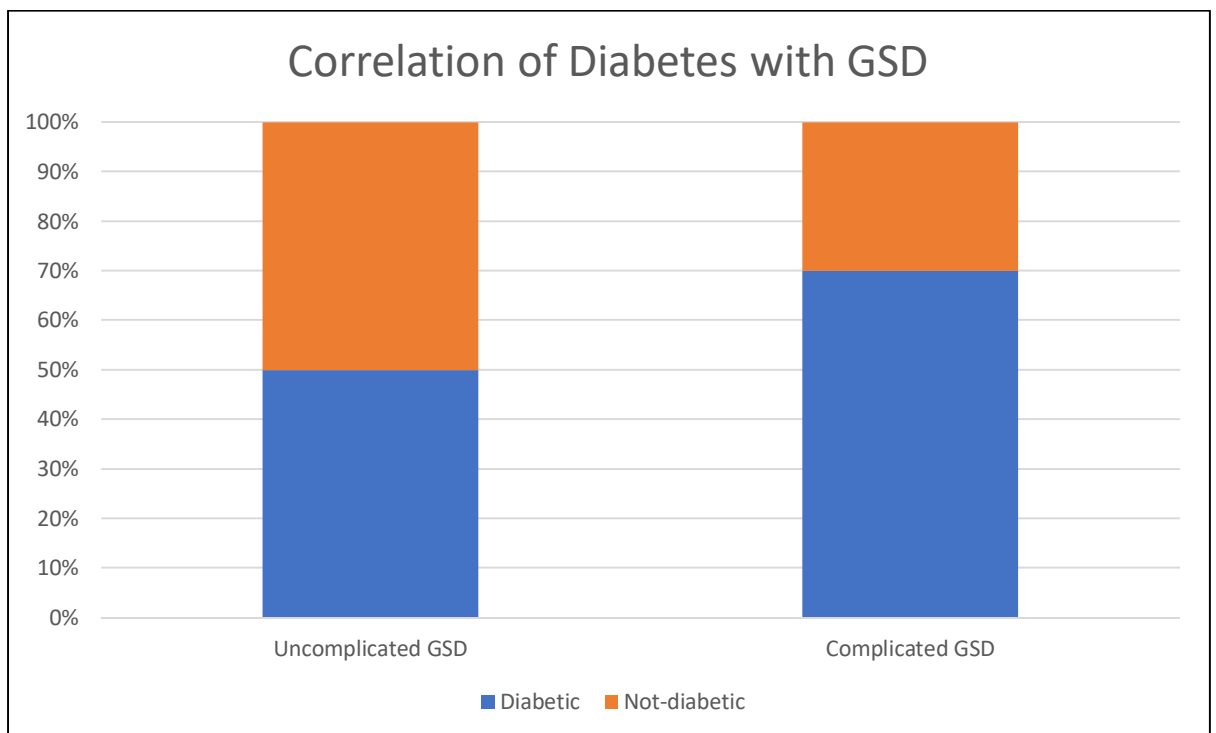


Figure 10: Correlation of Diabetes with GSD



Fifteen patients underwent MRCP, of which 11 patients were found to have a dilated CBD (≥ 8 mm), and seven patients were found to have either CBD stone or sludge in the CBD.

Out of these 11 patients, 9 underwent ERCP stenting and stone retrieval, 8 underwent laparoscopic cholecystectomy and one underwent exploratory laparotomy. (Table 12)

Table 12: Findings of biliary tree on MRCP

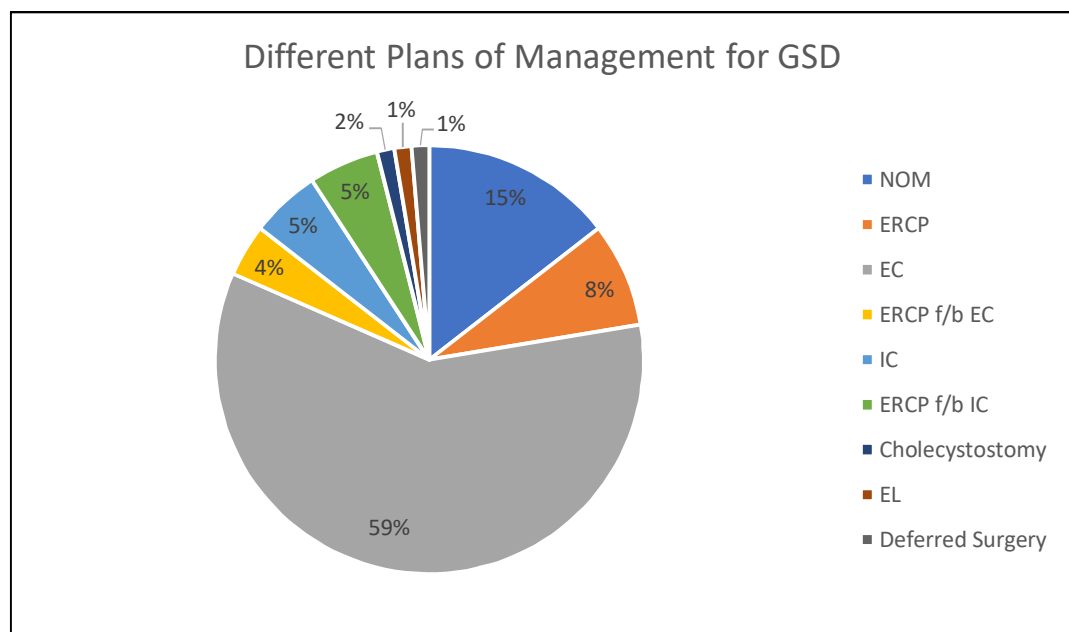
MRCP Details		No. of patients	Percentage
Gallbladder stone number	Single	1	6.7
	Multiple	14	93.3
Stone size mean (mm)	Single	3	-
	Multiple	7	-
CBD diameter (mm)	<8	4	26.7
	≥ 8	11	73.3
CBD stone	No stone	8	53.3
	Single	2	13.3
	Multiple	1	6.7
	Sludge	4	26.7

Patients were managed via various modalities based on the condition of the patients, requirement of endoscopic intervention and informed consent of the patient. About 75% of the study population underwent some type of surgical intervention. 11 patients were managed initially non-operatively and were planned for interval cholecystectomy, but due to Covid-19 pandemic these patients were lost to follow-up. Due to uncontrolled diabetes, surgery of one patient was deferred and the patient was ultimately lost to follow-up. (Table 13, Figure 11)

Table 13: Different management plans for GSD

Management	n (%)
Non Operative Management	11 (14.5)
ERCP	6 (7.9)
Early Cholecystectomy	45 (59.2)
ERCP followed by Early Cholecystectomy	3 (3.9)
Interval Cholecystectomy	4 (5.3)
ERCP followed by Interval Cholecystectomy	4 (5.3)
Cholecystostomy	1 (1.3)
Exploratory Laparotomy	1 (1.3)
Deferred Surgery	1 (1.3)
Total	76 (100.0)

Figure 11: Different Plans of Management for GSD



Majority of the patients included in this study underwent some kind of surgical procedure irrespective of age either in the index admission or in re-admission. More than 90% of the uncomplicated GSD underwent some kind of surgical intervention. 3 of the patients who had uncomplicated GSD were admitted in during the Covid-19 Pandemic of 2020, were infected by the said virus and thus their surgery was deferred. These patients were later lost to follow up. There was a trend today's surgical management based on the type of GSD, though it was not statistically significant. (Table 14, Figure 12, Figure 13)

Table 14: Management based on age and clinical presentation (Pearson Chi Square Test)

Age And Clinical Presentation		Management		Total	p-Value
		NOM	SM		
		n (%)	n (%)	n (%)	
Age Group (year)	60-60	9 (25.7)	26 (74.3)	35 (46.1)	0.001
	70-79	8 (28.6)	20 (71.4)	28 (36.8)	
	≥80	2 (15.4)	11 (84.6)	13 (17.1)	
Clinical Presentation	Uncomplicated GSD	3 (8.3)	33 (91.7)	36 (47.4)	0.657
	Complicated GSD	16 (40.0)	24 (60.0)	40 (52.6)	

Figure 12: Management plans in different age groups

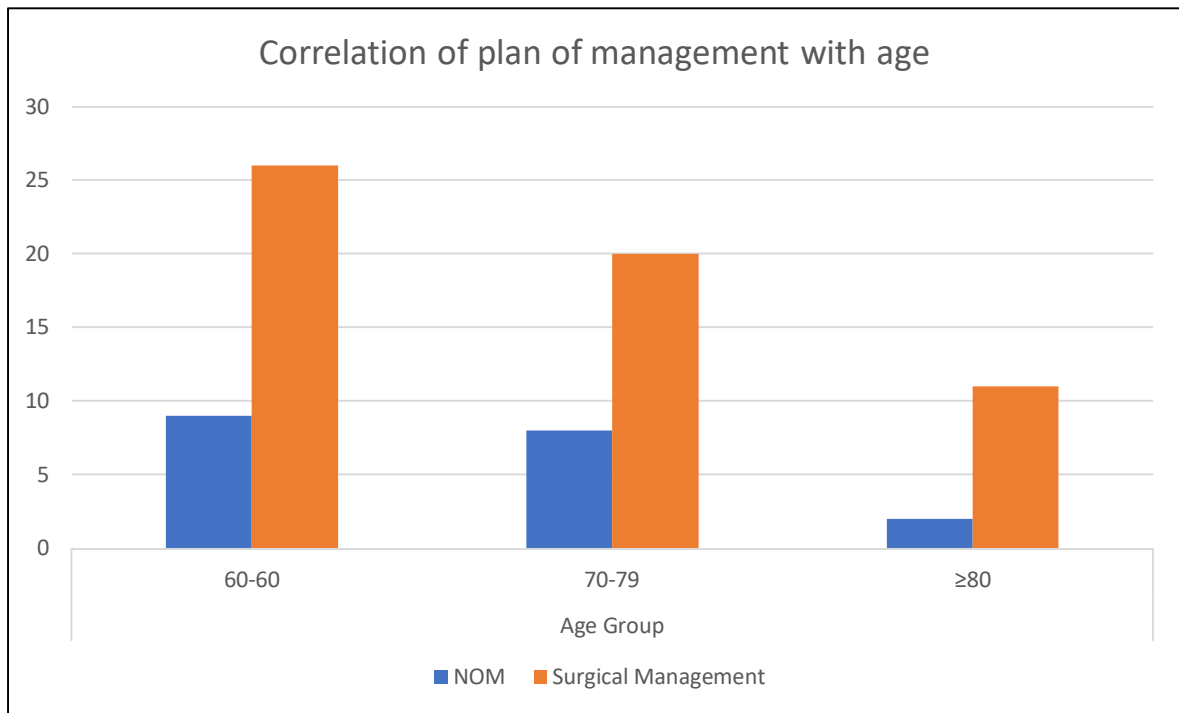
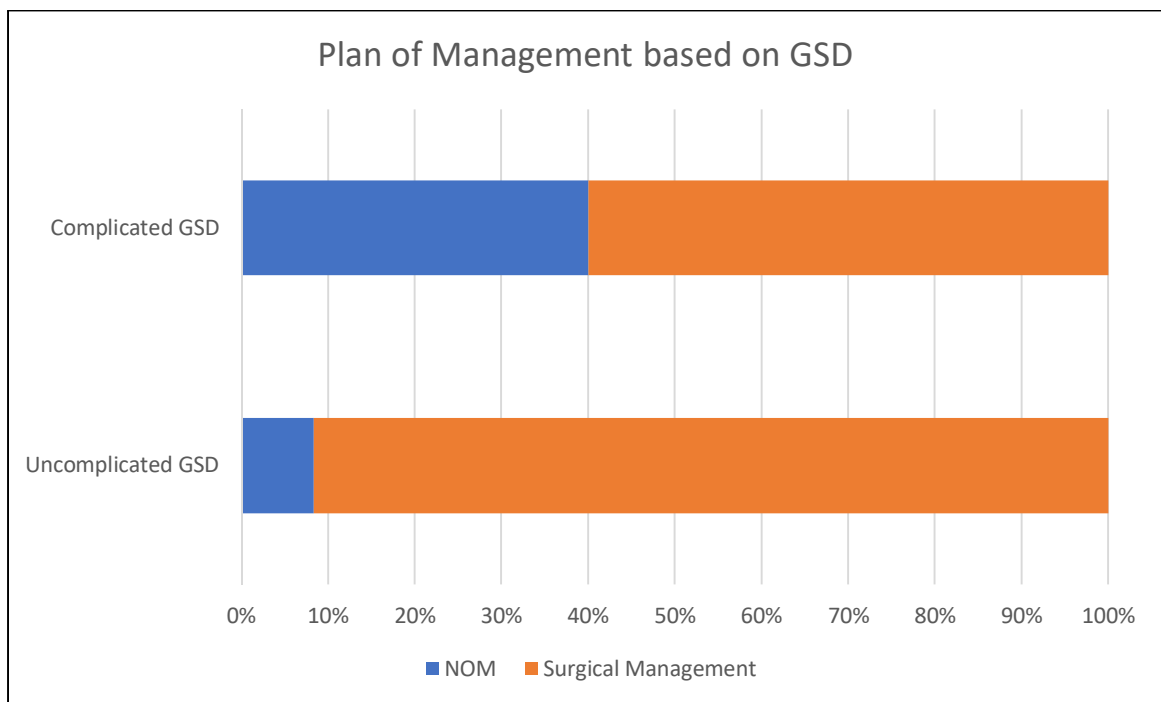


Figure 13: Plan of Management based on GSD

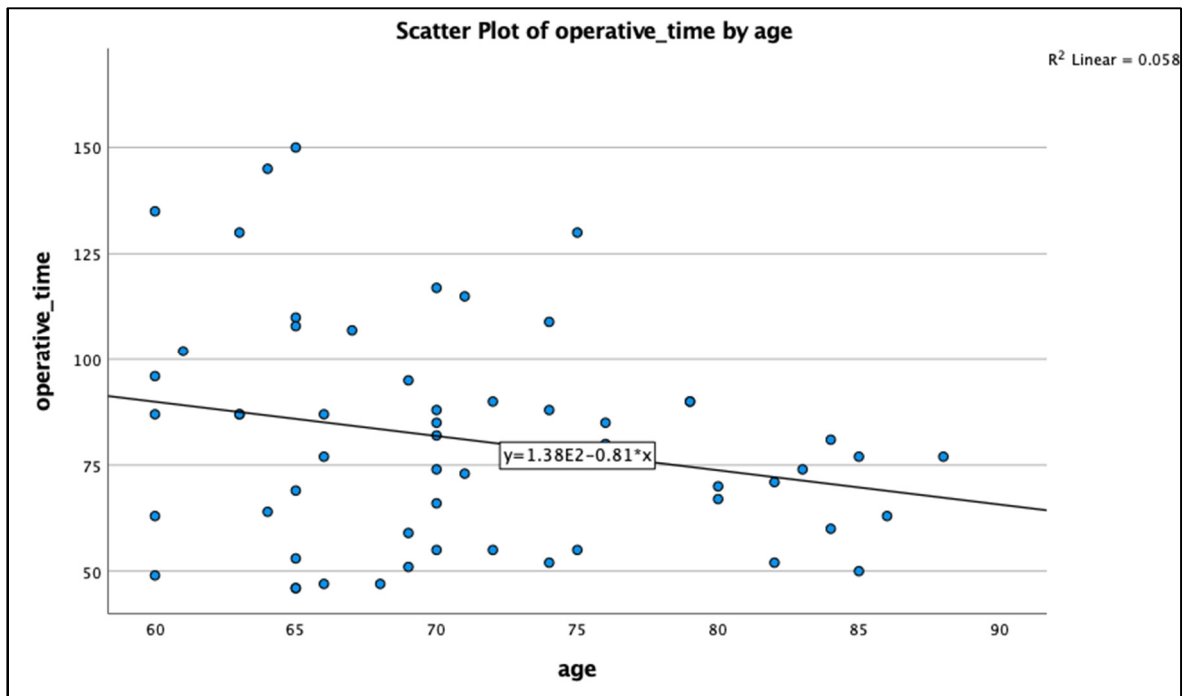


Out of 76 patients, 57 were operated. The patients were divided into three sub-groups based on age. There was no significant difference found in between the groups in terms of presence of adhesions, distension or contraction of gallbladder, occurrence of complications, conversion rate or use of drains in various age groups. There was also no significant difference in the mean operative time among the three groups, but there was a trend towards shorter duration of surgery as the age increases. (Table 15, Figure 14)

Table 15: Operative Details vs Age groups (Pearson Chi Square Test)

Operative Details		Age (yrs.)			Total	P value
		60-69	70-79	≥80		
		n (%)	n (%)	n (%)	n (%)	
Adhesions	Present	11 (42.3)	11 (55.0)	4 (36.4)	26 (45.6)	0.547
	Absent	15 (48.4)	9 (45.0)	7 (63.6)	31 (54.4)	
Gallbladder status	Distended	16 (64.0)	12 (60.0)	7 (63.7)	35 (61.4)	0.959
	Contracted	9 (36.0)	8 (40.0)	4 (36.3)	21 (36.8)	
Complication	Occurred	2 (7.7)	4 (20.0)	2 (18.2)	8 (14.0)	0.446
	None	24 (92.3)	16 (80.0)	9 (81.8)	49 (86.0)	
Conversion	Yes	3 (11.5)	3 (15.0)	0 (0.0)	6 (10.7)	0.417
	None	22 (88.5)	17 (85.0)	11 (100.0)	50 (89.3)	
Abdominal drain	Used	5 (19.2)	10 (50.0)	3 (27.3)	18 (31.6)	0.079
	Not used	21 (80.8)	10 (50.0)	8 (72.7)	39 (68.4)	
Operative time (Mean & SD)		84.5±32.14	83.9±21.81	67.4±10.23	-	-
Drain Removal (Mean & SD)		2.5 ±1.096	2.5 ±1.42	1.3 ±0.53	2.3±0.9	-

Figure 14: Operative time vs Age



There was a statistically significant result noted in terms of presence of adhesions and the gross presentation of gallbladder when the patients were divided into two groups based on their clinical presentation. The mean operative time as well as the mean day of drain removal was also significantly less in the patients suffering from uncomplicated GSD. (Table 16)

Table 16: Clinical Presentation vs Operative Details (Pearson Chi Square Test)

Operative Details		Clinical presentation		Total n (%)	p-Value
		Uncomplicated GSD	Complicated GSD		
		n (%)	n (%)		
Adhesions	Present	7 (21.2)	19 (79.2)	26 (45.6)	<0.001
	Absent	26 (78.8)	5 (20.8)	31 (54.4)	
Gallbladder status	Distended	28 (84.8)	7 (29.2)	35 (61.4)	<0.001
	Contracted	5 (15.2)	17 (70.8)	22 (38.6)	
Intraoperative Complication	Occurred	6 (18.2)	2 (8.3)	8 (14.0)	0.291
	None	27 (81.8)	22 (91.7)	49 (86.0)	
Conversion	Yes	2 (6.1)	4 (17.4)	6 (10.7)	0.177
	None	31 (93.9)	19 (82.6)	50 (89.3)	
Abdominal drain	Used	7 (21.2)	11 (45.8)	18 (31.6)	0.048
	Not used	26 (78.8)	13 (54.2)	39 (68.4)	
Operative time (mean; mins)		69.8 ±7.1	96.5 ±9.7	-	-
Drain Removal (mean; days)		1.1 ±0.5	3.1 ±1.3	-	-

When the operative details were evaluated based on the different management plans, adhesions were found to be more common on patients who had undergone ERCP and those who underwent interval cholecystectomy. Similarly, gallbladder was found to be contracted in the same group of patients. Because of this there was a significant increase in the operative time and day of removal of drain in the post-operative period. (Table 17)

Table 17: Management vs Operative Details (Pearson Chi Square Test)

Operative Details		Management					Total n (%)	p- Value
		EC	ERCP + EC	IC	ERCP + IC	EL		
		n (%)	n (%)	n (%)	n (%)	n (%)		
Adhesions	Present	15 (33.3)	2 (66.7)	4 (100.0)	4 (100.0)	1 (100.0)	26 (45.6)	0.007
	Absent	30 (66.7)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	31 (54.4)	
GB Status	Distended	34 (75.6)	0 (0.0)	1 (25.0)	0 (0.0)	0 (0.0)	35 (61.4)	<0.001
	Contracted	11 (24.4)	3 (100.0)	3 (75.0)	4 (100.0)	1 (100.0)	22 (38.6)	
Complication	Occurred	6 (13.3)	0 (0.0)	1 (25.0)	1 (25.0)	0 (0.0)	8 (14.0)	0.832
	None	39 (86.7)	3 (100.0)	3 (75.0)	3 (75.0)	1 (100.0)	49 (86.0)	
Conversion	Yes	4 (8.9)	1 (33.3)	1 (25.0)	0 (0.0)	0 (0.0)	6 (10.7)	0.377
	None	41 (91.1)	2 (66.7)	3 (75.0)	4 (100.0)	0 (0.0)	50 (89.3)	
Abdominal drain	Used	10 (22.2)	2 (66.7)	3 (75.0)	2 (50.0)	1 (100.0)	18 (31.6)	0.044
	Not used	35 (77.8)	1 (33.3)	1 (25.0)	3 (50.0)	0 (0.0)	39 (68.4)	
Operative time (mean; mins)		75.8 ±7.4	123.3 ±23.7	109.3 ±14.6	110.3 ±3.9	135	-	-
Drain Removal (mean; days)		2.1 ±1.5	3.5 ±0.7	3.3 ±2.2	2 ±0.7	-	-	-

There was a major difference seen in the numbers of days the patient stayed in the hospital post-operatively, when they were managed differently by various approaches. The mean hospital stay post-early cholecystectomy was about 2 days, which increased significantly to 15 days with ERCP intervention. The mean post-operative stay post interval cholecystectomy was about 3 days and with ERCP intervention of about 2 days, but total number of days the patient spent in the hospital had a mean of about 17 days for interval cholecystectomy compared to 21 days for interval cholecystectomy with ERCP. (Table 18)

Table 18: Hospital stay vs Different plans of management

Management	Post op stay (Mean±SD)	Total stay (Mean±SD)
EC	1.93±2.08	5.88±4.37
EC with ERCP	15.33±15.94	21.66±18.44
IC	3.25±2.63	17.5±7.85
ERCP f/b IC	2.00±0.81	21.5±7.32
Cholecystostomy	7.00±0.00	9.00±0.00
Open Cholecystectomy	3.00±0.00	53.00±0.00

On histopathological evaluation of the gallbladder, 86.1% were found to have features suggestive of chronic cholecystitis, xanthogranulomatous cholecystitis being the second most common diagnosis on biopsy (8.8%). The most common type of stone found was of mixed cholesterol type (61.4%), followed by brown (22.8%) and black (15.8%). (Table 19, Figure 15, Figure 16)

Table 19: Histopathological Analysis

Histopathological analysis		No. of patients	Percentage
Histopathological Evaluation	Chronic Cholecystitis	49	86.1
	Xanthogranulomatous Cholecystitis	5	8.8
	Follicular Cholecystitis	1	1.8
	Hyperplastic Cholecystitis with intestinal metaplasia	1	1.8
	Necrosed gallbladder	1	1.8
Stone type	Black	9	15.8
	Brown	13	22.8
	Mixed cholesterol	35	61.4

Figure 15: Histopathological Diagnosis

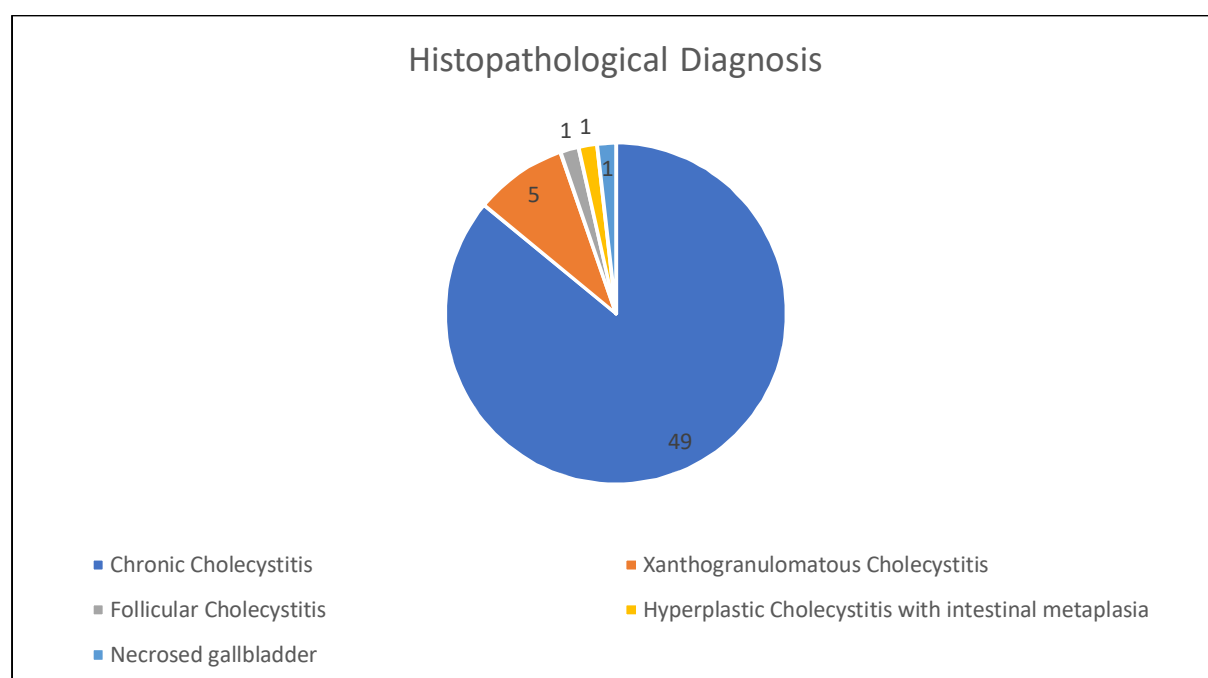
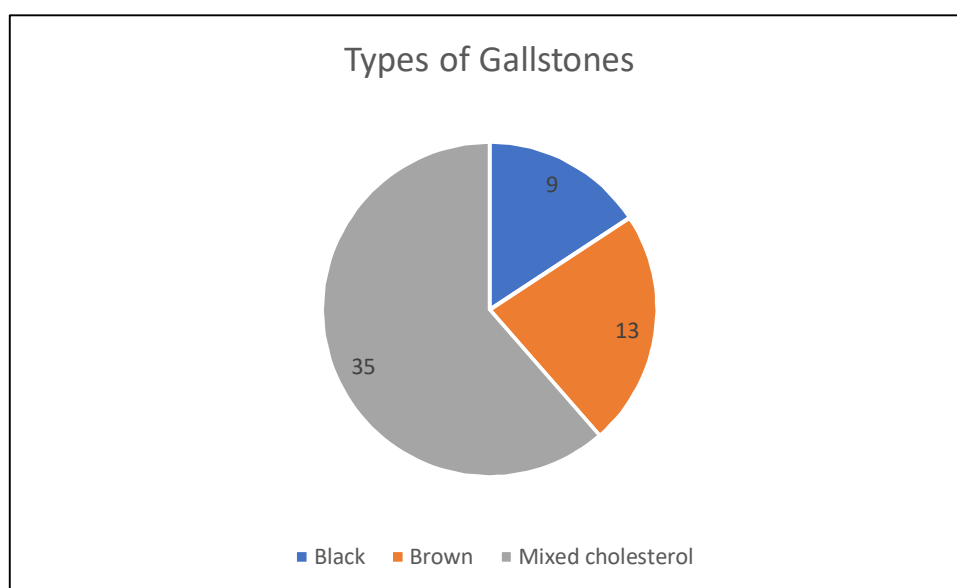


Figure 16: Types of Gallstones



There was no statistical difference found among the sub-groups of age based on the VAS score, presence of fever, SSI, recurrence of jaundice or any change in lifestyle of the patient on follow up. Though more than 70% of the patients who came for follow up had an improved lifestyle. (Table 20)

Table 20: Review on follow up of patients (Pearson Chi Square Test)

Review on follow-up		Age Groups			Total	p-Value
		60-69	70-79	≥80		
		n (%)	n (%)	n (%)	n (%)	
VAS (mean)		1.73	2.1	1.6	1.81	0.516
Fever	Present	2 (7.7)	1 (5.0)	0 (0.0)	3 (5.3)	0.631
	Absent	24 (92.3)	19 (95.0)	11 (100.0)	54 (94.7)	
SSI	Present	4 (15.4)	4 (20.0)	1 (9.1)	9 (15.8)	0.726
	Absent	22 (84.6)	16 (80.0)	10 (90.9)	48 (84.2)	
Jaundice	Present	1 (3.8)	1 (5.0)	0 (0.0)	2 (3.5)	0.763
	Absent	25 (96.2)	19 (95.0)	11 (100.0)	55 (96.5)	
Lifestyle	Decreased	5 (14.3)	9 (32.1)	2 (15.4)	16 (21.1)	0.367
	Improved	21 (60.0)	10 (35.7)	9 (69.2)	40 (52.6)	
	No change	0 (0.0)	1 (3.6)	0 (0.0)	1 (1.3)	
	Death	1 (2.9)	0 (0.0)	0 (0.0)	1 (1.3)	
	Lost to follow up	8 (22.9)	8 (28.6)	2 (15.4)	18 (23.7)	

DISCUSSION

DISCUSSION

One of the objectives of this study was to assess how a senior citizen who might be suffering from gallstone disease presents to the hospital. In this cohort, it was found that there was a higher incidence of gallstone disease in females. Similar findings were found in other studies like **Agrusa et al.**, **Nilesen et al.** and **Berger et al.**^{63,80,81} where the incidence of gallstone disease was found more in female than male; however the difference in incidence was less when compared to that of this study. In a few of the studies like **Fukami et al.** and **Yokota et al.** the incidence of gallstone disease was found to be more in males when compared to females.^{7,82} Interestingly, the male population of this study was found to have more of uncomplicated gallstone disease where as complicated gallstone disease was more common in the female group. On the contrary, in the study by **Bailey et al.**, males suffered more from complicated gallstone disease. One of the possible reasons given by them for this could be that the males tend to attend hospitals less than females.⁸³

Though no previous studies have been found comparing the prevalence of symptoms, the most common presenting complaint of the patients was pain abdomen, usually biliary colic. The least common complaint was yellowish discoloration of the skin. Jaundice is not common in the elderly because, as the age increases, the diameter of the common bile duct also increases, which might have a role in the easy passage of gallstones through the duct without causing jaundice. Due to this, symptoms associated with common bile duct stones were also seen less. Similar results were found in the study by **Hu et al.**⁸⁴

In this study, it was found that patients more than the age of 80 years of age tended to have uncomplicated gallstone disease when compared to the younger sub-group. This can again be attributed to the fact that as age increases, the diameter of the common bile duct also increases, and complications like choledocholithiasis, pancreatitis, and cholangitis usually take place due to the impaction of the stone in the duct. Due to this fact, there was a higher incidence of biliary pancreatitis in the younger group when compared to the elder group. Alternatively, in the study by **Fukami et al.**, acute cholecystitis was more prevalent in the elderly population (>80 years).⁸²

Even though no significant association was found among the different clinical presentations of gallstone disease, there was a slightly positive trend towards the patient being pre-diabetic

and diabetic. In previous studies like **Lv et al.**, a ten-year prospective study, there was a strong correlation between diabetes and gallstone disease incidence. Similar results were found in **Sodhi et al.** and **Wang et al.** All these studies were not able to confirm the direct casualty of gallstone disease by the presence of diabetes, but because of a similar list of risk factors like obesity insulin resistance, they were only able to conclude a correlation. Diabetes is known to decrease the mobility of the gallbladder because of diabetic neuropathy, increased fasting volume of the gallbladder, compared to non-diabetic patients, and is also a risk factor for bile stasis and thus gallstone formation. In our study, it was seen that prediabetic and diabetic states were associated with complicated gallstone disease. Further research can be done in this regard.^{72,74,85}

More than 50% of the cases presenting with symptomatic gallstone disease suffered from hypothyroidism. Our study showed a strong correlation between common bile duct stone and hypothyroidism. This association was also seen in studies like **Song et al.**, **Ajdarkosh et al.** and **Laukkarinein et al.**^{77,86,87} suggested that T4 has pro-relaxation action on the sphincter of Oddie, and in hypothyroidism, there are increased chances of stagnation of bile in the common bile duct, thus leading to the formation of stones. Hypothyroidism is also associated with the formation of cholesterol stones. These two actions are known to increase the risk of stone formation.^{77,86,87} To diagnose gallstone disease, with the help of presenting history of the patient and clinical examination, radiological and blood investigations were required. The most common complaint of the patient was pain abdomen associated with dyspepsia and vomiting. About 40% of the total cases presented to the hospital with an acute history, out of which only 13 patients were diagnosed with acute cholecystitis, 10 had biliary pancreatitis, and 2 had cholangitis. Studies like **Magnuson et al.** similar results were found when comparing the elderly population to the younger one, though the incidence of acute calculus cholecystitis was lesser in our study.²⁸

Out of 76 patients, 75 had undergone abdominal ultrasonography where 74 patients were found to have either one or multiple gallstones in the gallbladder. The one patient where no gallstones were found on ultrasound, was diagnosed to have biliary pancreatitis and had undergone CECT of the abdomen based on their history, clinical findings, laboratory reports and presence of a dilated CBD on ultrasound. This patient underwent ERCP stenting and retrieval of stones/sludge. 11 patients also underwent MRCP when the diagnosis and the anatomy of the biliary system needed further evaluation. Grossly the findings of the

ultrasound and MRCP were somewhat similar, though there was an underreporting of about 30% in terms of the diameter of the CBD. This further weakens the use of MRCP in the case of gallstone diseases, where ultrasound can provide major information required to diagnose the disease.^{88,89}

Blood samples were also sent to augment the differential diagnosis and as part of the pre-operative evaluation. A quarter of these patients were found to have increased SGPT/SGOT levels; 90% of these were borderline increased and did not change our management plan. 10% of the patients had hyperbilirubinemia, whereas 22% were diagnosed with a stone in the common bile duct, keeping these tests as screening tests other than for diagnosis.

Once the diagnosis of either complicated or uncomplicated gallstone disease was made, the appropriate management plan was made for each patient based on their clinical status and after discussing the plan with the patient and their family members. Out of 76 patients, only 57 patients underwent surgical intervention. Out of the remaining 19 patients who did not, 18 were optimised in their primary admission and were planned for interval cholecystectomy but lost to follow-up because of the ongoing Covid-19 pandemic of 2020. Out of these 19 patients, one underwent cholecystostomy and was also planned for IC.

In the 57 patients who were operated on, there was no significant difference seen in the intraoperative findings of the patients in different age groups. Because there was no difference in difficulty level based on the operative time, we can concur that the patient's age is not a risk factor for a “difficult” surgery. Similar results have been noted in studies like **Loureiro et al.**, **Trust et al.**, **Agrusa et al.**, and **Fukami et al.**, where they all concluded that in a hemodynamically stable patient, with features suggestive of mild acute cholecystitis, or even mild biliary pancreatitis, age has no effect on the outcomes of the laparoscopic cholecystectomy and should be considered as the primary modality when treating the senior citizens.^{63,82,90,91}

In a study by **Simopoulos et al.**, the average conversion rate for laparoscopic cholecystectomy to open cholecystectomy for patients aged more than 60 years of age was about 9.4%, which was a similar finding – 10.5%. The most common reason for conversion found in our study was adhesions. Even though they concluded that age is a risk factor for conversion and other studies by **Fried et al.** and **Sanabria et al.**, there was no significant

difference in the different sub-groups in our study. This might be because most patients of ages >80 years had presented with uncomplicated gallstone disease.^{92–94}

Interestingly, this study found that patients older than 80 years of age had fewer cases that had adhesions, contracted gallbladder, and even had lesser incidence of complications and lower conversion rate. This was probably because this group of patients was suffering from a milder form of gallstone disease. Because of this, the mean operative time for this age group was also less.

As expected, there was a higher incidence of adhesions in complicated gallstone disease due to active and or chronic inflammation associated with the condition that led to higher chances of gallbladder being contracted. Even though there was a 14% incidence of intra-operative complications, iatrogenic perforation of the gallbladder during dissection was the most common one; none of these iatrogenic perforations were converted to open. The most common reason for conversion was to prevent iatrogenic injury due to dense adhesions in the operative site. There was a trend seen towards placing a drain in the abdomen, and the most common reasons were to check for any bile leak from the distal cystic duct stump and drain out any peritoneal contamination.

In our study, it was found that patients who underwent interval cholecystectomy had a 100% incidence of the presence of adhesions, this can be attributed to the fact that these patients were initially suffering from complicated gallstone disease, and because of increased localized inflammation, dense adhesions were found in the surgery. Similarly, patients who underwent early laparoscopic surgery with ERCP intervention also had a higher incidence of adhesions due to similar reasons. Moreover, for this reason, there were increased chances of complications, conversion rate, and increased use of drains in the surgery. Studies like **Serna et al.**⁹⁵ concluded that there is no difference in early cholecystectomy and interval cholecystectomy outcomes in cases of mild to moderate acute cholecystitis. Studies like **Fuks et al.**⁹⁶ went on further to conclude that the outcomes of early cholecystectomy in patients less than the age of 75 years had a similar result compared to patients more than 75 years of age. However, **Nikfarjam et al.**⁹⁷ had asserted that elder patients (> 80 years) had a worse post-operative prognosis when compared to their younger counterparts and hence should be managed optimally before taking to the operating theatre in acute settings. Though in our study, there was a trend towards lesser operative time in early cholecystectomy for acute cholecystitis, when compared to interval cholecystectomy, further research is required to

validate this observation further. On histopathological evaluation, similar findings were noted compared to studies like **Khan S et al.** Interestingly, in this study, the incidence of xanthogranulomatous cholecystitis was less than half of what was found in our study. The worldwide incidence of xanthogranulomatous cholecystitis is about 1-3%, whereas, in India, it is about 8.8% which matched our data. There have been several theories as to why India has such a high number of cases of xanthogranulomatous cholecystitis; the most accepted one is the high number of cases of gallstone disease in India. Dedicated research can find the true root cause of these findings.^{98,99}

Gallstones most commonly seen in cholelithiasis are of cholesterol (mixed and pure) type (60%), followed by composite (21%), black pigmented (8.5%) and brown pigmented (6.5%) stones. Though the incidence of mixed cholesterol stones in our study was found similar to this, the number of pigmented gallstones were more than double, for black, and triple, for brown.¹⁰⁰

CONCLUSION

CONCLUSION

Persons aged more than 60 years of age can present with both complicated and uncomplicated gallstone disease. Gallstone disease, in the presence of hypothyroidism or diabetes mellitus, presents in a much for complicated form. Earlier surgical intervention in form of laparoscopic cholecystectomy can be beneficial to the patient if diagnosed with gallstones. Patients of this age group may not be over investigated if a benign pathology is suspected.

In case of mild acute cholecystitis and mild biliary pancreatitis, early cholecystectomy can be the intervention of choice and age should not be a limiting factor for the surgery.

Xanthogranulomatous cholecystitis has been found at a higher prevalence rate in this study and other studies, but true pathogenesis of this entity is not known. Further research can be done in this regard.

This might be one of a kind study in the Indian subcontinent, a much more detailed research can be done to further remove the fear of bad outcome in “old age” from the surgeon and the anaesthesiologist.

LIMITATIONS

LIMITATIONS

1. One of the major limitations of this study was its small sample size.
2. Due to the ongoing Covid-19 Pandemic, a number of patients were lost to follow-up.
3. Due to the ongoing Covid-19 Pandemic, the average number of hospital stay was increased, as some patients required readmissions.

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ANNEXURES

ANNEXURE – 1

ETHICAL CLEARANCE CERTIFICATE



अखिल भारतीय आयुर्विज्ञान संस्थान, जोधपुर
All India Institute of Medical Sciences, Jodhpur
संस्थागत नैतिकता समिति
Institutional Ethics Committee

No. AIIMS/IEC/2020/2074

Date: 01/01/2020

ETHICAL CLEARANCE CERTIFICATE

Certificate Reference Number: AIIMS/IEC/2019-20/1003

Project title: “Clinical profile and evaluation of outcomes of symptomatic gallstone disease in the senior citizen population”

Nature of Project: **Research Project**

Submitted as: **M.S. Dissertation**

Student Name: **Dr. Anupam Singh Chauhan**

Guide: **Dr. Ashok Puranik**

Co-Guide: **Dr. Ramkaran Chaudhary, Dr. Poonam Elhence & Dr. Pawan Garg**

This is to inform that members of Institutional Ethics Committee (Annexure attached) met on **23-12-2019** and after through consideration accorded its approval on above project. Further, should any other methodology be used, would require separate authorization.

The investigator may therefore commence the research from the date of this certificate, using the reference number indicated above.

Please note that the AIIMS IEC must be informed immediately of:

- Any material change in the conditions or undertakings mentioned in the document.
- Any material breaches of ethical undertakings or events that impact upon the ethical conduct of the research.

The Principal Investigator must report to the AIIMS IEC in the prescribed format, where applicable, bi-annually, and at the end of the project, in respect of ethical compliance.

AIIMS IEC retains the right to withdraw or amend this if:


- Any unethical principle or practices are revealed or suspected
- Relevant information has been withheld or misrepresented

AIIMS IEC shall have an access to any information or data at any time during the course or after completion of the project.

On behalf of Ethics Committee, I wish you success in your research.

Enclose:

1. Annexure 1


Dr. Praveen Sharma
Member secretary
Institutional Ethics Committee
AIIMS, Jodhpur

ANNEXURE – 2
INFORMATION SHEET

Information Sheet for the patient and patient's relative

Title of Thesis: **Clinical profile and evaluation of outcomes of symptomatic gallstone disease in the senior citizen population**

Name of PG Student: Dr. Anupam Singh Chauhan

Contact No.: +91 9634059999

Before you decide whether or not you wish to participate in this study, it is important for you to understand why the research is being done and what it will involve. Please take the time to read the following information carefully and discuss it with others if you wish.

1. What is the purpose of the study?

The purpose of the study is to assess how symptomatic gallstone disease is managed in senior citizen population and to evaluate the association between old age and surgical treatment.

2. What if I don't want to take part in this study or if I want to withdraw later?

Participation in this study is voluntary. It is completely up to you whether or not you participate. You may withdraw from the study at any time and for any reason or no reason. Please tell the researcher that you wish to withdraw from the study.

3. What does this study involve?

This study will involve the patient's bed side ticket of trauma ward, post operative notes and all investigation reports.

4. Will the confidentiality of my patient's be protected?

The information about patient's will be subjected to absolute anonymity.

Thank you for taking the time to consider this study.

If you wish to take part, please sign the attached consent form.

This information sheet is for you to keep.

ANNEXURE – 3

सूचना पत्रक

रोगी और रोगी के रिश्तेदार के लिए सूचना पत्र

थीसिस का शीर्षक:- Clinical profile and evaluation of outcomes of symptomatic gallstone disease in the senior citizen population

पीजी छात्र का नाम:- डॉ. अनुपम सिंह चौहान

संपर्क संख्या:- +91-9634059999

यह तय करने से पहले कि आप इस अध्ययन में भाग लेना चाहते हैं या नहीं, यह समझना आपके लिए महत्वपूर्ण है कि यह शोध क्योंकि याजा रहा है और इस में क्या शामिल होगा। कृपया निम्नलिखित जानकारी को ध्यानपूर्वक पढ़ें और दूसरों के साथ चर्चा करें, यदि आप चाहें।

1. इस अध्ययन का उद्देश्य क्या है

इस अध्ययन का उद्देश्य यह आकलन करना है कि वरिष्ठ नागरिक आबादी में रोगसूचक पित्त पथरी रोग का प्रबंधन कैसे किया जाता है और बुढ़ापे और सर्जिकल उपचार के बीच संबंध का मूल्यांकन किया जाता है।

2. क्या होगा यदि मैं इस अध्ययन में भाग नहीं लेना चाहता हूँ या यदि मैं बाद में वापस लेना चाहता हूँ?

इस अध्ययन में भागीदारी स्वच्छिक है। यह पूरी तरह आप पर निर्भर है कि आप भाग लेते हैं या नहीं। आप किसी भी समय और किसी भी कारण से या किसी कारण से अध्ययन से वापस ले सकते हैं। कृपया शोधकर्ता को बताएं कि आप अध्ययन से हट ना चाहते हैं।

3. इस अध्ययन में क्या शामिल है

इस अध्ययन में रोगी के आघात वार्ड, पोस्ट ऑपरेटिव नोट्स और सभी जांच रिपोर्टों के बेड साइड टिकट शामिल होंगे।

4. क्या मेरे रोगी की गोपनीयता सुरक्षित रहेगी?

आपके रोगी बारे में जानकारी पूर्णतः गोपनीय रहेगी।

इस अध्ययन पर विचार करने के लिए समय निकालने के लिए आपका धन्यवाद।

यदि आप भाग लेना चाहते हैं, तो कृपया संलग्न सहमति फॉर्म पर हस्ताक्षर करें।

यह जानकारी पत्र आपके रखने के लिए है।

ANNEXURE – 4

**All India Institute of Medical Sciences
Jodhpur, Rajasthan**

INFORMED CONSENT FORM

Title of Thesis/Dissertation: **Clinical profile and evaluation of outcomes of symptomatic gallstone disease in the senior citizen population**

Name of PG Student: Dr. Anupam Singh Chauhan Tel. No. 9634059999

Patient/Volunteer Identification No.: _____

I, _____ S/o or D/o _____

R/o _____

give my full, free, voluntary consent to be a part of the study “**Clinical profile and evaluation of outcomes of symptomatic gallstone disease in the senior citizen population**”, the procedure and nature of which has been explained to me in my own language to my full satisfaction. I confirm that I have had the opportunity to ask questions.

I understand that my participation is voluntary and am aware of my right to opt out of the study at any time without giving any reason.

I understand that the information collected about me and any of my medical records may be looked at by responsible individual from _____(Company Name) or from regulatory authorities. I give permission for these individuals to have access to my records.

Date : _____

Place : _____
impression

Signature/Left thumb

This to certify that the above consent has been obtained in my presence.

Date : _____

Place : _____

Signature of PG Student

1. Witness 1

2. Witness 2

Signature

Signature

Name: _____

Name: _____

Address : _____

Address : _____

ANNEXURE – 5

All India Institute of Medical Sciences
Jodhpur, Rajasthan

सूचित सहमति प्रपत्र

Title of Thesis/Dissertation: **Clinical profile and evaluation of outcomes of symptomatic gallstone disease in the senior citizen population**

Name of PG Student: **Dr. Anupam Singh Chauhan** Tel. No. 9634059999

Patient/Volunteer Identification No.: _____

मैं, _____ एस / ओ या डी / ओ
_____ आर / ओ _____

अध्ययन का एक हिस्सा बनने के लिए मेरी पूर्ण, स्वतंत्र, स्वच्छिक सहमति दें “**Clinical profile and evaluation of outcomes of symptomatic gallstone disease in the senior citizen population**”, जिस प्रक्रिया और प्रकृति को मुझे अपनी पूरी संतुष्टि के लिए अपनी भाषा में समझाया गया हूँ। मैं पुष्टि करता हूँ कि मुझे प्रश्न पूछने का अवसर मिला है।

मैं समझता हूँ कि मेरी भागीदारी स्वच्छिक है और मुझे किसी भी कारण दिए बिना किसी भी समय अध्ययन से बाहर निकलने का मेरा अधिकार है।

मैं समझता हूँ कि मेरे और मेरे मेडिकल रिकॉर्ड के बारे में एकत्रित की गई जानकारी को _____ (कंपनी नाम) या विनियामक प्राधिकरणों से जिम्मेदार व्यक्ति द्वारा देखा जा सकता है। मैं इन लोगों के लिए मेरे रिकॉर्डों तक पहुंच की अनुमति देता हूँ

तारीख : _____

जगह: _____ हस्ताक्षर / बाएं अंगूठे का छाप

यह प्रमाणित करने के लिए कि मेरी उपस्थिति में उपरोक्त सहमति प्राप्त की गई है।

तारीख : _____

जगह: _____ पीजी छात्र के हस्ताक्षर

1. गवाह 1

2. साक्षी 2

_____ हस्ताक्षर

_____ हस्ताक्षर

नाम: _____

नाम : _____

पता: _____

पता : _____

ANNEXURE – 6
PATIENT PROFORMA

Clinical profile and evaluation of outcomes of symptomatic gallstone disease in the senior citizen population

Name:

Patient Identification Number:

Age / Sex:

Address:

1. Education status:

- ☐ Illiterate ☐ Primary school (1-5) ☐ Middle school (5-8)
☐ Higher school(9-10) ☐ Secondary school (11-12) ☐ Graduate ☐ Professional

2. Occupation:

3. Marital status: ☐ Unmarried ☐ Married

4. Chief complaints: **abdominal pain jaundice fever**

5. Total duration of illness:

☐ < 6 months ☐ 6-12 months ☐ 1-2 years ☐ >2 years

6. H/O diabetes: ☐ Yes ☐ No

If, yes→ Duration:

Treatment taken:

7. H/O Hypertension: ☐ Yes ☐ No

If, yes→ Duration:

Treatment taken:

8. H/O Thyroid illness: ☐ Yes ☐ No

If, yes→ Duration:

Treatment taken:

12. H/O smoking/ Alcohol: ☐ Yes ☐ No

If, yes→ Duration:

13. Family history:

Examination:

General physical examination: Pallor/ Icterus/ Clubbing/ Cyanosis/ Pedal edema/
Generalized lymphadenopathy

Vitals: **BP-** / mmHg **PR-** /min **RR-** /min **Temp**

Systemic examination: CVS - RS - CNS -

ABDOMEN –

INVESTIGATION SHEET -

	Date: __/__/__	Date: __/__/__
Hemoglobin		
Total leucocyte count		
Platelet		
Liver function tests		
SGPT/SGOT/ALP (IU/L)	/ /	/ /
Total bilirubin/Direct Bilirubin/Indirect Bilirubin (mg/dl)	/ /	/ /
Total protein/Albumin/Globulin (g/dl)	/ /	/ /
Thyroid Function Test		
T3/T4/TSH	/ /	/ /
Hb1Ac		-
		-

USG WHOLE ABDOMEN

Gall bladder & biliary system

1. Wall thickness
2. No. of gall stones-
3. Max size of gall stone-
4. Intra-hepatic biliary radicles
5. Cystic duct
6. Common bile duct
7. Any anomaly

Other organs

MRCP FINDINGS

- Hepatobiliary tree:-
- GB and Cystic ducts:-
- CBD:-
- MPD:-
- Any other variations:-

Perioperative outcome

Intraoperative data

- Adhesions – yes/no
- Gall bladder status
 - A. Normal
 - B. Acute inflammation
 - C. Chronic inflammation

D. Gangrenous

E. Mucocele

- Conversion to open cholecystectomy
 - Reason for conversion
 - Post conversion steps
- Operative time of laparoscopic cholecystectomy
 - A. < 1 hr.
 - B. 1 hr. to 2 hrs.
 - C. > 2 hrs.
- Abdominal drain required - yes/no
 - α. Reason for abdominal drain placement
- Abdominal Drain removed after - _____ days

Number of stones

Type of stones

- Cholesterol Stones
- Pigment Stones
 - Black
 - Brown

Postoperative data

- Bile leak/bile duct injury
- Collection in Morrison's pouch
- Length of hospital stay: <24 hrs./ 24-72 hrs./ >72 hrs.

On follow up

- Any recurrence of pain?
- Any recurrence of fever?
- Any recurrence of jaundice?
- Any infection of the surgery site?
- Any change in life style?
- Result of biopsy

ANNEXURE – 7
KEY TO MASTER CHART

sex	M	Male
	F	Female
Age group	1	≥60 - <70 years
	2	≥70 - < 80 years
	3	≥ 80 years
Clinical Presentation	1	Acute Calculous Cholecystitis
	2	Cholelithiasis with choledocholithiasis
	3	Biliary Colic
	4	Biliary Pancreatitis
	5	Cholangitis
Type of GSD	1	Uncomplicated Gallstone Disease
	2	Complicated Gallstone Disease
Mode of Admission	1	Out Patient Department
	2	Emergency Department
Symptoms	Pain Abdomen	1 = Present; 2 = Absent
	Vomiting	1 = Present; 2 = Absent
	Yellowish discolouration of skin	1 = Present; 2 = Absent
	Dyspepsia	1 = Present; 2 = Absent
	Back Pain	1 = Present; 2 = Absent
	Fever	1 = Present; 2 = Absent
	Loss of Appetite	1 = Present; 2 = Absent
Duration of symptoms	1	≤ 3 days
	2	>3 - < 7 days
	3	> 7 days - < 1 month
	4	> 1 month - < 6 months
	5	≥ 6 months

co_morbidities	Diabetes	1 = Present; 2 = Absent
	Hypertension	1 = Present; 2 = Absent
	Thyroid disorder	1 = Present; 2 = Absent
	Smoker	1 = Present; 2 = Absent
	Alcohol	1 = Present; 2 = Absent
Abdomen	Distension	1 = Present; 2 = Absent
	Murphy's sign	1 = Present; 2 = Absent
	Abdominal Lump	1 = Present; 2 = Absent
Lab Investigations	Anemia_admission	1 = Present; 2 = Absent
	leucocytosis_admission	1 = Increased; 2 = Normal
	plt_admission	1 = Increased; 2 = Normal
	SGPT_adm	1 = Increased; 2 = Normal
	SGOT_adm	1 = Increased; 2 = Normal
	alp	1 = Increased; 2 = Normal
	hyperbilirubinemia_admission	1 = Present; 2 = Absent
	Lipase_admission	1 = Increased; 2 = Normal
	Amylase_admission	1 = Increased; 2 = Normal
	Thyroid	1 = Euthyroid
		2 = Hypothyroid
		3 = Hyperthyroid
	Diabetes	1 = Diabetic
		2 = Prediabetic
		3 = Normal
Ultrasonographic Details	usg_thickness	1 = <=3mm
		2 = >3mm
	usg_pericholecystic_fluid	1 = Present; 2 = Absent
	usg_cbd_diameter	1 = <=8mm
		2 = >8mm
	Usg_cbd_stone	1 = Single
		2 = Multiple

MRCP Details	mrcp_gb_stone_number	1 = Single
		2 = Multiple
	mrcp_cbd	1 = ≤8mm
		2 = >8mm
Management	1 = NOM	
	2 = ERCP	
	3A = EC	
	3B = ERCP + EC	
	4A = IC	
	4B = ERCP + IC	
	5 = Cholecystostomy	
	6 = EL	
	7 = Deferred Surgery	
Management2	1 = NOM	
	2 = Surgery	
Intraoperative Details	intraop_adhesions	1 = Present; 2 = Absent
	intraop_gb_status	1 = Distended; 2 = Contracted
	intra_op_complication	1 = Present; 2 = Absent
	conversion	1 = not converted
		2 = converted
	abdominal_drain	1 = Used
		2 = Not used
Review on follow up	followup_fever	1 = Present; 2 = Absent
	followup_ssi	1 = Present; 2 = Absent
	followup_jaundice	1 = Present; 2 = Absent
	followup_lifestyle	1 = decreased;
		2 = improved;
		3 = no change;
		4 = death;
		5 = lost to follow up

followup_biopsy	1 = chronic cholecystitis;
	2 = chronic cholecystitis with cholesterolosis;
	3 = chronic cholecystitis with intestinal metaplasia;
	4 = Xanthogranulomatous cholecystitis;
	5 = Follicular cholecystitis;
	6 = Hyperplastic cholecystitis with intestinal metaplasia;
	7 = chronic cholecystitis with adenomatous hyperplasia;
	8 = necrosed gallbladder
Stone_type	1 = black;
	2 = brown;
	3 = mixed cholesterol

ANNEXURE – 8
MASTER CHART