“A CLINICAL AND MICROBIOLOGICAL STUDY OF GALLSTONE DISEASE”

A DISSERTATION SUBMITTED TO THE TAMILNADU
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M.S. (GENERAL SURGERY)

DEPARTMENT OF GENERAL SURGERY

TIRUNELVELI MEDICAL COLLEGE

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This is to certify that the dissertation entitled **"A CLINICAL AND MICROBIOLOGICAL STUDY OF GALLSTONE DISEASE"** is a bonafide research work done by **Dr.M.Gobinath.,** Postgraduate M.S. student in Department of General Surgery, Tirunelveli Medical College & Hospital, Tirunelveli, in partial fulfilment of the requirement for the degree of M.S. in GENERAL SURGERY.

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PROTOCOL TITLE : A CLINICAL AND MICROBIOLOGICAL STUDY OF GALL STONE DISEASE.

PRINCIPAL INVESTIGATOR: Dr. M. GOBINATH, MBBS

DESIGNATION OF PRINCIPAL INVESTIGATOR: POST GRADUATE IN GENERAL SURGERY

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Dear , Dr. M. Gobinath, The Tirunelveli Medical College Institutional Ethics Committee (TIREC) reviewed and discussed your application during the IEC meeting held on 05.08.2016.

THE FOLLOWING DOCUMENTS WERE REVIEWED AND APPROVED

1. TIREC Application Form ☐
2. Study Protocol ☐
3. Department Research Committee Approval ☐
4. Patient Information Document and Consent Form in English and Vernacular Language ☐
5. Investigator's Brochure ☐
6. Proposed Methods for Patient Accrual Proposed ☐
7. Curriculum Vitae of the Principal Investigator ☐
8. Insurance /Compensation Policy ☐
9. Investigator's Agreement with Sponsor ☐
10. Investigator's Undertaking ☐
11. DCGI/DGFT approval ☐
12. Clinical Trial Agreement (CTA) ☐
13. Memorandum of Understanding (MOU)/Material Transfer Agreement (MTA) ☐
14. Clinical Trials Registry-India (CTRI) Registration ☐

THE PROTOCOL IS APPROVED IN ITS PRESENTED FORM ON THE FOLLOWING CONDITIONS

1. The approval is valid for a period of 2 year/s or duration of project whichever is later
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This is certify that this dissertation work title **"A CLINICAL AND MICROBIOLOGICAL STUDY OF GALLSTONE DISEASE"** of the candidate **Dr.M.Gobinath.,** with registration Number **221511354** for the award of **M.S.** in the branch of **GENERAL SURGERY.** I personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion page and result shows **0 percentage** of plagiarism in the dissertation.

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INTRODUCTION

Gallstones were first described in the fifth century by a Greek Physician Alexander Trallianus, who wrote about calculi within the bile ducts. Cholesterol gallstones have been described as early as in second and third centuries A.D. There are also some descriptions of stone in the biliary system in the Greek literature in the fifth century AD as well as in the Persian literature in tenth century. Around this time epidemiological association also began to be noted. In 1755 Haller observed in opercula pathologica that gallstones occurred most frequently in some countries. He also observed that all stones were more common in persons with physical inactivity and sedentary life. The natural history of gallstones was not considered in great detail until surgery became an option in the treatment of gallstones. The first cholecystostomy was done by John Stouhg Bobbs, an Indiana Surgeon on June 15, 1867. Karl Langen Buch of Berlin performed the first cholecystectomy in June 1882. The common bile duct exploration was first carried out by Kummel in 1884 and first performed successfully by Thomfom in 1889.

Gallstone disease is very common in most developed countries. In United States it is estimated that about 5,00,000 cholecystectomies are being performed every year and about 10,000 deaths are related to this disease[18].

The prevalence of gallstone disease in Europe is reported to be 5% to 15%, according to several ultrasonographic surveys[35-38]. In Asian countries, the prevalence of gallstone disease ranges from 3% to 10%[51]. According to recent studies, the prevalences of gallstone disease were 3.2% in Japan[39], 10.7% in China[40], 7.1% in Northern India [19], and 5.0% in Taiwan[41].

Despite this plethora of specimens, the knowledge of their nature, etiology and prevention of this disease is very limited.In our country, the incidence of cholelithiasis is increasing considerably. Here too, the prevalence of gallstone disease is not uniform, with the northern parts of India registering maximum number of cases, when compared to South India. This may be attributed to the difference in life style and food habits. In general, North Indian people eat foods rich in fat, low fibre diet and less carbohydrate. This type of food habits closely follow the Western pattern and this explains the high incidence of cholelithiasis in North India.

Although this disease has a low mortality rate, its economic and health impact is significant due to its high morbidity. In fact, Gall stone disease is one of the most common abdominal conditions for which patients in developed countries are admitted to hospitals and this frequency has increased in Western countries since the 1950s. However, since the introduction of lap cholecystectomy in early 90s, which is considered a safe treatment for Gall

stone disease, a possible unjustified increase in surgical procedures has been observed. Therefore, there is the need for more knowledge of the epidemiological characteristics of Gall stone disease in order to better identify therapeutic strategies.

Human bile though sterile normally, can become infected in biliary tract obstruction due to entry of microorganisms through various routes like papilla of vater or hematogenous leading to bactobilia.[33] In a study from Karachi, out of 100 patients undergoing cholecystectomy 36 (36%) patients were having bactobilia.[10] Gomes et al reported a prevalence of bactobilia in 20 (20%) patients with organisms such as *Escherichia coli* (*E.coli)* (40%), *Klebsiella* (35%), *Salmonella* (20%) and *Shigella* (20%) who underwent cholecystectomy.[33]

In another study from United Kingdom, 20 (15.6%) out of 128 patients were found to have culture detected microorganisms[42] .The pathogenesis of bile infection is incompletely understood, with the prevailing theories not fully explaining all the observations[43-45]. There is relatively sparse data, both local & international on the prevalence of the infection in patients undergoing cholecystectomy[46] .The conservative & prophylactic treatment therefore is based on best guess basis[33].

The rationale of this study was to determine the current trend of

bacteriology and their sensitivity to common antibiotics in our population with symptomatic cholelithiasis. The results of this study will be used to develop guidelines and recommendations for the rationale use of antibiotics. The results of this study will be shared with all surgeons and general practitioners in the periphery to help them identify the type of antibiotic to be administered to patients with symptomatic cholelithiasis before referring them to tertiary care. This will help us in reducing the morbidity associated with cholelithiasis

AIM AND OBJECTIVES

1. To study age, sex incidence, clinical presentation and various treatment modalitites adopted for gall stone disease.

2. Bacteriological analysis of bile collected from all cases subjected to cholecystectomy in our study so as to identity commonest type of organism associated with gall stones and their antibiotic sensitivity.

REVIEW OF LITERATURE

Studies by Stewart et al and Smith et al [1] state that bacteria were found in the majority of black and brown pigmented gallstones concluding that the bacterial infection is the primary factor in both black and brown pigment gallstone pathogenesis

In comparing black and brown pigment stones, Cetta et al[2] found positive bile culture in 25% patients with black gallstones and 100% patients with brown pigment gallstones.

Kaufman[5] and associates confirmed the role of bacteria in the formation of gallstones. In their study, bacteria were identified only within the calcium bilirubinate — protein matrix of brown pigment stones. He also conclude that black and brown pigment stones have different pathogenic mechanisms and that bacterial infection is important only in the formation of brown pigment stones.

In a review of biliary bacteriology in 200 consecutive patients with gallstone disease, Tabata and Nakyama[6] found very high incidence of infection in brown pigment stones. In contrast, very low bacterial incidence was associated with cholesterol stones and so-called black stones--sometimes called pure pigment stones. Regardless of the kind of stones present in the

common duct, the incidence of bacteria was found to be increased.

Fransesco Cetter M. documented that bile infection by E.coli is a preceding factor in brown stone formation

Attila Csendes[22] & Patricio Burdiles found out that no bacteria is seen in the bile culture studies of control groups, when compared to bile culture study of patients with gallstone disease.

Makki[7] expressed the classic theory of the pathogenesis of calcium bilirubinate gallstone formation in which he emphasized the role of infection of the stagnated bile and the enzymatic hydrolysis of bilirubin glucoronide into free bilirubin and glucoronic acid. This free unconjugated bilirubin which is insoluble in water, then combines with calcium in the bile to produce a calcium bilirubinate matrix

Infection has been documented at the time of gallstone removal in more than 90% brown gallstones. Bile infection by E.coli precedes rather than follows brown gallstone formation.

Goldfarb et al found that patients with sickle cell disease and haemolytic anaemia are at risk of development of gallstones (pigmented) and many patients become symptomatic.

Shyamal Kumar Gosh et al showed a female preponderance for Gall stone disease.

In a study by Michael Rosen et al, Laparoscopic cholecystectomy were performed in 1347 patients. Out of this 71 patients required conversion to open surgery. Obese patients with cholelithiasis have an increased chance of conversion to open surgery. Patients with multiple co- morbid diseases have more chances of failure of laparoscopic cholecystectomy

Nakeeb and co-workers established that genetic factors were responsible for at least 30% symptomatic gallstone disease.

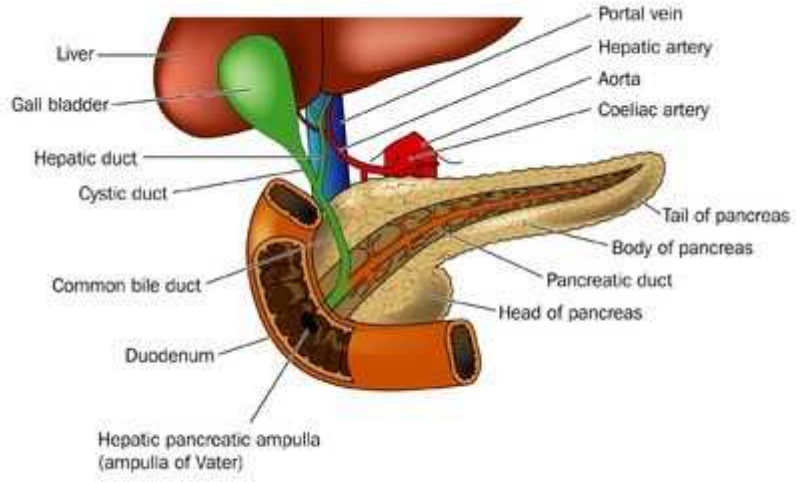
SURGICAL ANATOMY OF THE BILIARY TREE

Embryology

Liver develops from an endodermal bud that arises from the ventral aspect of the gut, at the point of junction between foregut and midgut. This bud grows into the ventral mesogastrium and passes through it into septum transversum. It enlarges and soon shows a division into a larger cranial part called ‘Pars Hepatica’ and a smaller caudal portion called ‘Pars Cystica’. The pars cystica gives origin to the gallbladder and the cystic duct. The part of hepatic bud proximal to the pars cystica forms the bile duct. [47]

Gross Anatomy

The biliary tract begins as a series of tiny blind ending channels formed by specialized structures in cell membrane of adjacent hepatocytes. It continues into ductules lined by single layer of cuboidal cells and extends into larger ductules with a muscular wall. These join to form interlobar ducts, which in turn empties into hepatic ducts. Ducts from the right and left lobes of the liver join to form the common hepatic duct.[48]



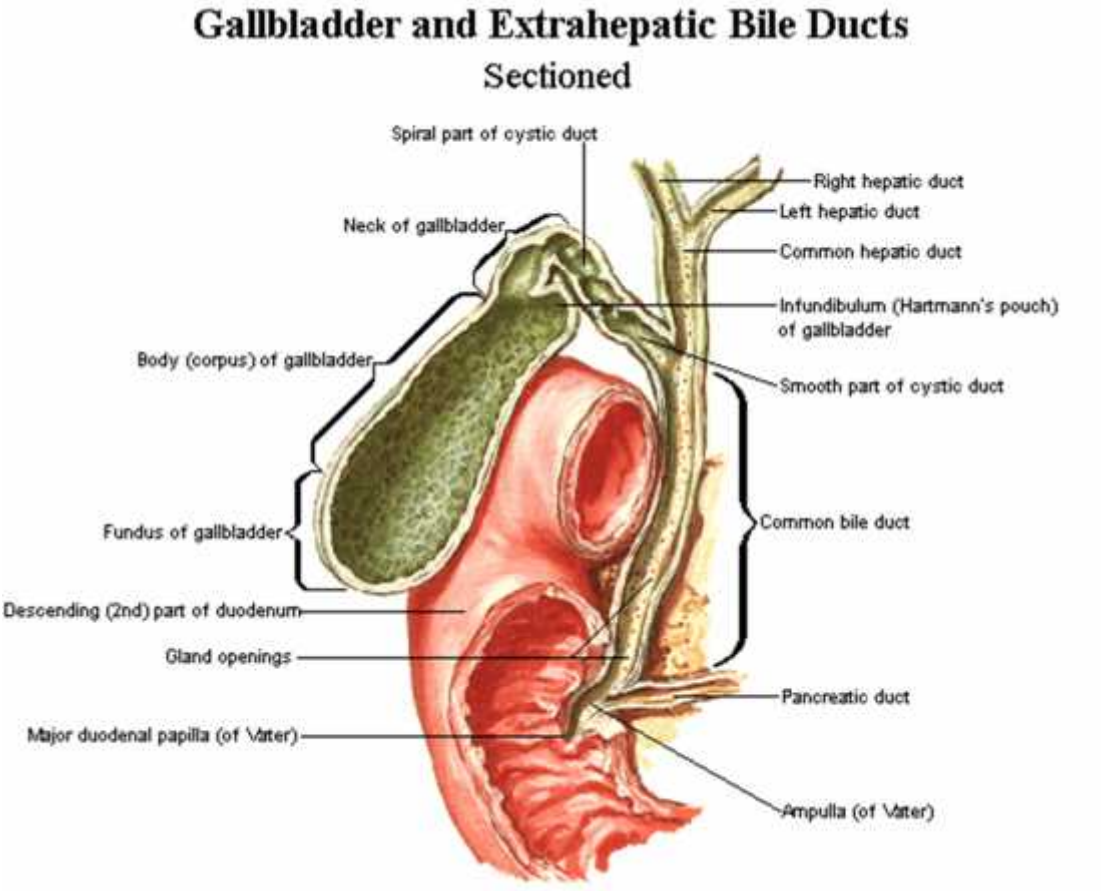
Hepatic ducts:

The right and left hepatic ducts emerge from the respective lobes of the liver in the porta hepatis. After a short course the hepatic ducts unite to form the common hepatic duct. The common hepatic duct is about 4cm long and descends within the free margin of the lesser omentum. It is joined on the

right side by the cystic duct from the gall bladder to form the common bile duct.

Common Bile duct:

The bile duct is about 3 inches (8 cm) long. In the first part of it's course it lies in the free margin of the lesser omentum in front of the opening into the lesser sac. Here it lies in front of the right margin of the portal vein and on the right of the hepatic artery. In the second part of it's course it is situated behind the first part of duodenum to the right of the gastroduodenal artery. In the third part of its course it lies in a groove on the posterior surface of the head of the pancreas. Here the bile duct comes in contact with the main pancreatic duct.



Ampulla of Vater:

The bile duct ends below by piercing the medial wall of the second part of the duodenum about half down its length. It is usually joined by the main pancreatic duct and together they open into a small ampulla in the duodenal wall called the ampulla of vater. The ampulla opens into the lumen of the duodenum by means of a small papilla, the major duodenal papilla. The terminal parts of the both ducts and the ampulla are surrounded by circular muscle, known as the sphincter of oddi. Occassionally the bile and pancreatic ducts open seperately into the duodenum. [48]

Gall Bladder

The Gall bladder is a pear shaped sac lying on the under surface of the liver. It has a capacity of about 30 to 50 ml and stores bile, which it concentrates by absorbing water. The gall bladder is divided into fundus, body and neck. The fundus is rounded and usually projects below the inferior margin of the liver, where it comes in contact with the anterior abdominal wall at the level of the tip of the ninth right Costal Cartilage. The body lies in contact with the visceral surface of the liver and is directed upward, backward and to the left. The neck becomes continuous with the cystic duct, which turns into the lesser omentum to join the right side of the common hepatic duct, to form the common bile duct.

Cystic duct

The Cystic duct is about 3.8cm long and connect the neck of gall bladder to the common hepatic duct to form the bile duct. It is somewhat "S" shaped and descends for a variable distance in the right free margin of the lesser omentum. The mucous membrane of the cystic duct is raised to form a spiral fold that is continuous with a similar fold in the neck of the gall bladder. The fold is commonly known as "Spiral Valve of Heister".

Calot's triangle:

Calot's triangle is an anatomic landmark which is bounded by the

common hepatic duct on the left, cystic duct below and inferior surface of the liver above.

The contents of the triangle are the cystic artery, often the right branch of the hepatic artery and occasionally a bile duct. If there is a replaced or accessory common or right hepatic artery, it usually runs behind the cystic duct to enter the Calot's triangle.

Dissection of Calot's triangle during cholecystectomy is of significance from the fact that the ignorance of this contents and its varied anatomy may cause unexpected haemorrhage or biliary injury and may result in bile duct injury during efforts to secure hemostasis.

COMPOSITION OF BILE

Constituents	**Liver Bile (pH) - 8 to 8.6**	**Gall Bladder Bile (pH)-7 to 7.6**
Water	97.5 g/dl	92 g/dl
Bile Salts	1.1 g/dl	6 g/dl
Bilirubin	0.04 g/dl	0.3 g/dl
Cholesterol	0.1 g/dl	0.3 - 0.9 g/dl
Fatty Acids	0.12 g/dl	0.3 -1.2 g/dl
Lecithin	0.04 g/dl	0.3 g/dl
Sodium Ion	145 mEq/L	130 mEq/L
Potassium Ion	5 mEq/L	12 mEq/L
Calcium Ion	5 mEq/L	23 mEq/L
Chloride Ion	100 mEq/L	25 mEq/L
Bicarbonate Ion	28 mEq/L	10 mEq/L

PHYSIOLOGY OF THE BILE

Bile acid Secretion: Bile is secreted in two stages

i) The first phase of secretion is by the principal hepatocytes. This secretion contains large amount of bile acids, cholesterol and other organic constituents. It is secreted into minute bile canaliculi that lie between the hepatic cells. The canaliculi empty into terminal bile ducts and then into progressively larger ducts, finally reaching hepatic duct and common bile duct,

ii) The second phase of secretion is a watery solution of sodium and bicarbonate ions secreted by secretory epithelial cells that line the ductules and ducts.

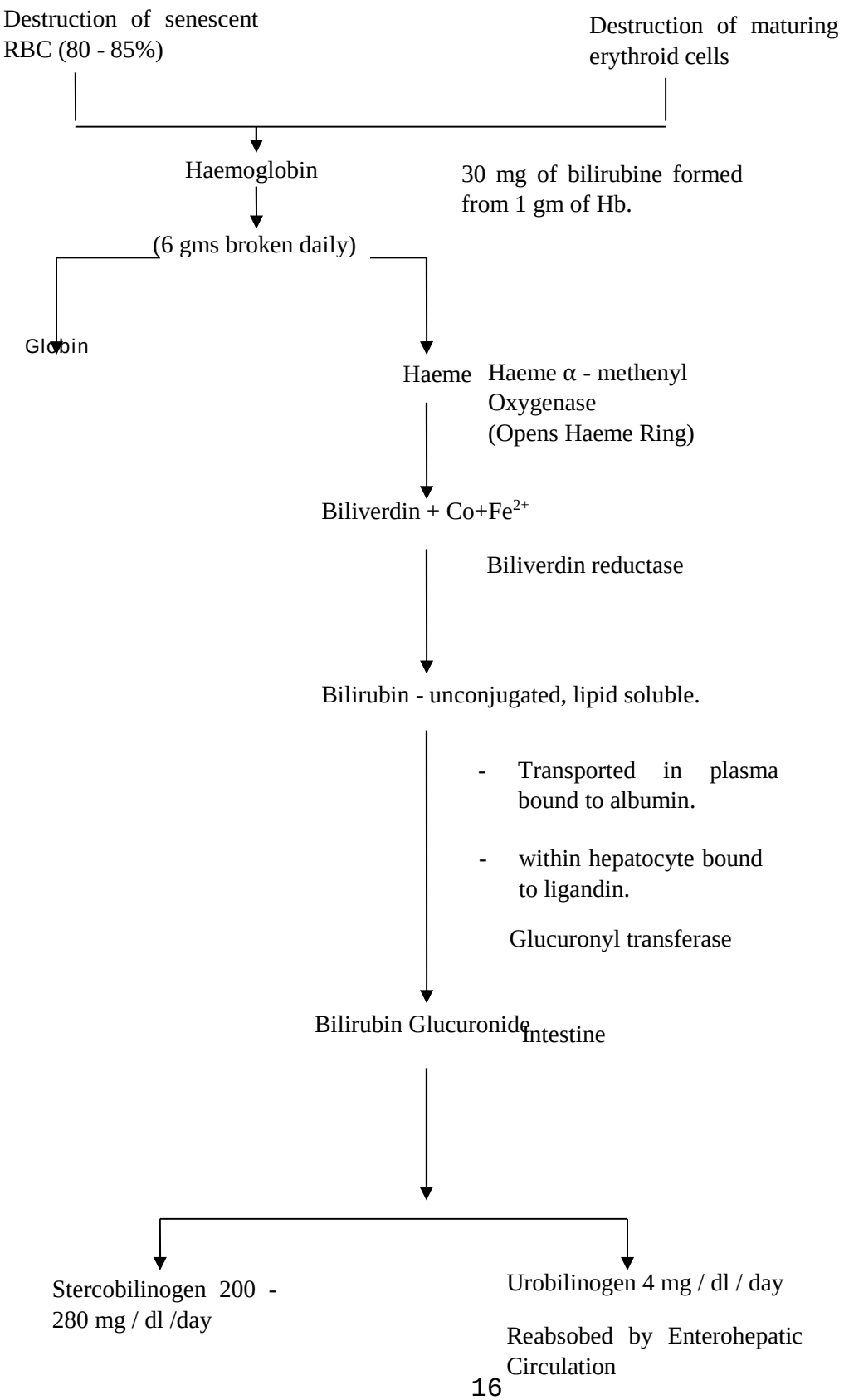
The normal bile secretion is between 600 and 1000 ml/day. The second phase of secretion sometimes increases the total quantity of bile by as much as an additional 100%.

Bile Acids

Bile acids are the major organic constituents of bile accounting for approximately 50% of the solid components. They are related structurally to cholesterol from which they are synthesized by liver. Cholesterol in the liver is converted into cholic acid and chenodeoxycholic acid through several intermediate steps of which 7α hydroxylase is the rate limiting enzyme. These

acids, called primary bile acids are then conjugated with glycine and taurine

METABOLISM OF BILIRUBIN



which are then secreted into the bile. In the intestines, by the action of bacterial enzymes deconjugation and dehydroxylation takes place resulting in the formation of secondary bile acids. Thus cholic acid is converted to deoxycholic acid and chenodeoxy cholic acid to lithocholic acid and absorbed.

Bile Pigments

Bilirubin and biliverdin are the two major bile pigments present in the body. During breakdown of haemoglobin in the reticulo-endothelial system, bilirubin is formed and transported to the liver. In the hepatocytes, the bilirubin is conjugated by the enzyme UDP glucuronyl transferase and excreted into the bile which is responsible for the characteristic gold yellow color of the bile.

In the terminal ileum and the colon, the bilirubin is deconjugated by the specific bacterial enzymes (beta-glucuronidases) and the pigment is reduced to urobilinogens. Most of the urobilinogen is excreted in the faeces as urobilins whereas a small portion of the urobilinogens is reabsorbed and reexcreted through the liver to constitute the entero hepatic urobilinogen cycle.

Storage and concentration of the bile in the Gall Bladder

The bile that is formed in the biliary canaliculi is transported by intra and inter lobular biliary ductules to the extra hepatic biliary system.

Most of the time during fasting, the gall bladder is readily distensible and the sphincter of Oddi maintains the closure of the terminal bile duct. Thus bile secreted by the liver flows into the gall bladder.

The descripency between the amount of bile secreted by the liver and the amount stored in the gall bladder is accounted for by the gall bladder's ability to concentrate bile. The concentration of the bile salts, bile pigments and other large water soluble molecules may increase 5 to 20 times as a result of water and electrolyte absorption.

The concentration of micelles also increases during the absorption of water and electrolytes. The presence of micelles, which have minimal osmotic activity, permits the high concentration of electrolytes, bile salts, phospholipids and cholesterol to be isotonic in gall baldder bile.

Acidification of the bile is another function of the gall bladder which is exemplified from the fact that the pH of the hepatic bile changes from 8 to 7 in the gall bladder bile.

Expulsion and transport of bile from gallbladder to lumen of the intestine.

Most bile secretion occurs during the digestion of meals. The secretion of the bile into the duodenum is mediated both by humoral and neural mechanisms.

When food enters the mouth, the resistance of the sphincter of Oddi decreases. Fatty acid and the amino acids in the duodenum causes release of cholecystokinin(CCK) from I cells of the upper intestinal mucosa, which causes gall bladder contraction. Substances that cause contraction of gallbladder are called cholagogues.

The production of the bile is increased by stimulation of the vagus nerve. Substances that increase the secretion of bile are known as choleretics. Bile salts themselves are among the most important physiological choleretics.

CCK relaxes the sphincter of Oddi and there by allows the bile to enter the duodenum. Thus the flow of bile from the gall bladder to the duodenum occurs in a synchronous fashion with the spincter of Oddi relaxing and the gall bladder contracting to facilitate bile flow.

Stimulation of the parasympathetic nerves causes an increase in bile flow and contraction of the gall bladder. Stimulation of the sympathetic nerves has the opposite effect. Bile flow beigns shortly after eating and may

be part of cephalic phase of the digestion.

Enterohepatic Circulation

About 90-95% of bile salts, which are secreted, are absorbed back from the small intestine. They then enter the portal blood and pass back to liver and resecreted into the bile. On an average these salts are circulated about 18 times before being excreted. The remaining 5 - 10% of bile salts enter the colon and are converted to salts of deoxycholic acid and lithocholic acid. A small fraction of the bile salts about 500 mg/day escapes absorption and is therefore eliminated in the faeces.

Function of Bile

1 .Bile salts helps in digestion and absorption of fats and fat soluble vitamins.

2.Neutralization of acids.

3.Facilitates excretion of drugs, toxins, bile pigments and various inorganic substances.

4. Large quantities of cholesterol present in the bile are solubilized in ‘micelles’, allowing cholesterol to be transported without precipitation in bile.

Effects of Cholecystectomy:

After cholecystectomy

i) Bile from the liver empties slowly but continuously into the intestine, allows sufficient digestion of fats to maintain good nutrition.

However diets rich in fats causes indigestion.

ii) Bile ducts become dilated to accommodate some of the bile which is continuously secreted by the liver. Therefore if tone of sphincter of oddi is high, it causes gradual rise of pressure in biliary passage, when this pressure exceeds secretary pressure of liver cells, it interferes with bile secretion. If tone is low, it causes dribbling of bile into intestine when it is not needed and results in wastage of bile.

DEMOGRAPHIC AND EPIDEMIOLOGIC CONSIDERATIONS

Incidence

The incidence of biliary calculus disease varies widely throughout the world. Approximately 10% of the population in United States has documented cholelithiasis. The incidence of gall stone disease in Asia is considerable and constitutes a problem of enormous. The highest prevalence is found in the Pima Indian tribe of Arizona with total and female prevalences of 49% and 73% respectively. The lowest prevalence is seen in Africans.[51,52]

A decade ago, it was generally viewed that over 90% of gall stone patients in the United States had cholesterol stones. More recent studies would suggest that there is a trend towards an increasing of pigment gall stones. Most patients in the far east including India have pigment stones.

Age

Epidemiologic studies have clearly demonstrated a linear relationship between increasing age and the prevalence of cholelithiasis. The percentage of cholesterol present in bile and the cholestrol saturation are significantly increased in elderly women compared with young subjects. Moreover the gall bladder sensitivity to cholecystokinin (CCK) the primary stimulus for gall bladder contraction decreases with age.

Gender and Hormones

It is a well known fact that gall stone disease is more prevalent among women than men. Recent studies have shown that gender disparity is because of the hormones. Progesterone causes decreased gall bladder emptying and concomitant increase in absolute and residual gall bladder volume after contraction.

Estrogen causes decreased activity of the hepatic enzyme responsible for the conversion of cholesterol to bile acids resulting in a decrease in bile acid synthesis and secretion.

Obesity

Obesity has long been recognized as a risk factor for the formation of cholesterol gall stones. Epidemiological evidence suggests that there is a two to three fold increase in the incidence of cholelithiasis among morbidly obese

patients.[50]

Diabetes

Clinical experience has long suggested that patients with diabetes mellitus have an increased risk of developing gall stones as compared to non diabetics. A rational explanation for this finding is derived from the observation that diabetic patients have bile that is usually supersaturated with cholesterol and impaired gall bladder motor activity.[50]

Cirrhosis

Though the exact frequency with which cholelithiasis occurs in patients with alcohol induced cirrhosis remains unclear, autopsy studies have shown increased incidence of gall stones in cirrhotic patients. Interestingly, these stones are mostly pigment in nature.

Vagotomy

Although early clinical studies suggested that truncal vagotomy is associated with a two fold increase in the incidence of gall stones, other studies have failed to confirm this hypothesis.

Total parenteral nutrition

Total parenteral nutrition (TPN) given on a long term basis predisposes to both acalculous and calculous cholecystitis. Ultrasonographic studies have demonstrated altered gall bladder motor activity, decreased stimulation for

gall baldder contraction and the formation of sludge and ultimately biliary lithiasis.

Putting together, below is a list of risk factors to gallstone prevalence and symptomatic gall stone disease.

I. Female sex 2. Obesity 3. Advancing Age 4. Genetics and ethnic factors 5.Highly refined, fibre depleted high animal fat diet 6.Diabetes mellitus. 7.Ileal disease and resection 8.Hemolytic states 9.Infection of the biliary tract. 10.Parasitic Infestations 11. Cirrhosis 12.Cystic Fibrosis 13.Pregnancy 14. Oral contraceptive. 15.Drugs - Clofibrate, thiazides. 16.TPN. 17.Truncal Vagotomy. 18. Cholestasis of any cause.

CLASSIFICATION OF GALLSTONES

Gallstones may be classified based on :

1. Anatomical site in biliary tree
2. Chemical composition - according to predominant component.

1. CLASSIFICATION BASED ON ANATOMICAL SITE IN BILIARY TREE [53]

1. Gallbladder Stones: The most frequent site of stone formation with cholesterol being commoner in western communities and pigment stones in Asian population[49].

2. Duct Stones: - Intrahepatic bile duct stones

- Extrahepatic bile duct stones — Primary, Secondary.
- Recurrent bile duct stones

Majority of bile duct stones originate in the gall bladder and migrate into bile duct and are usually associated with cholelithiasis. These are the secondary bile duct stones.

Primary bile duct stones are those that originate exclusively in the bile ducts. These may be intrahepatic or extrahepatic. Bile duct stones found in patients with agenesis of gallbladder provide absolute proof of their origin. Incidence of primary duct stones is controversial and varies from *4%* (Saharia et at 1977) to 56% (Madden 1973).

Stones are classified as primary duct stones if they meet the following criteria.

- Previous cholecystectomy with or without common duct exploration.
- At least two years asymptomatic period after initial biliary tract surgery.
- Characteristic morphological features, soft, friable, light brown stones or sludge in common duct.
- Absence of a long cystic duct stump or biliary stricture following previous surgery.

Saharia et al have confirmed abnormal dilatation of bile duct observed by others and suggested stasis, changes in bile composition and infection as

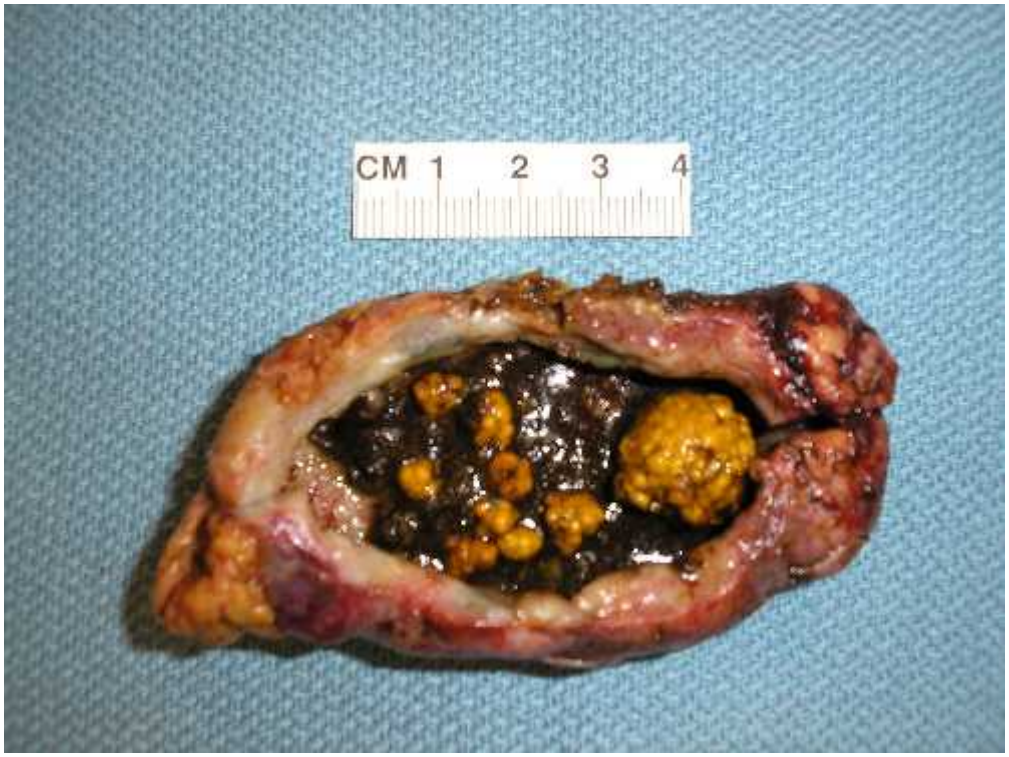
their cause for formation.

2. CLASSIFICATION BASED ON CHEMICAL COMPOSITION[49]

Cholesterol Gallstones: Can be single (cholesterol solitaire) or multiple (smooth or faceted, 2-4 mm in diameter, light brown) cross-section shows a laminated or crystalline appearance with a distinct dark nucleus.

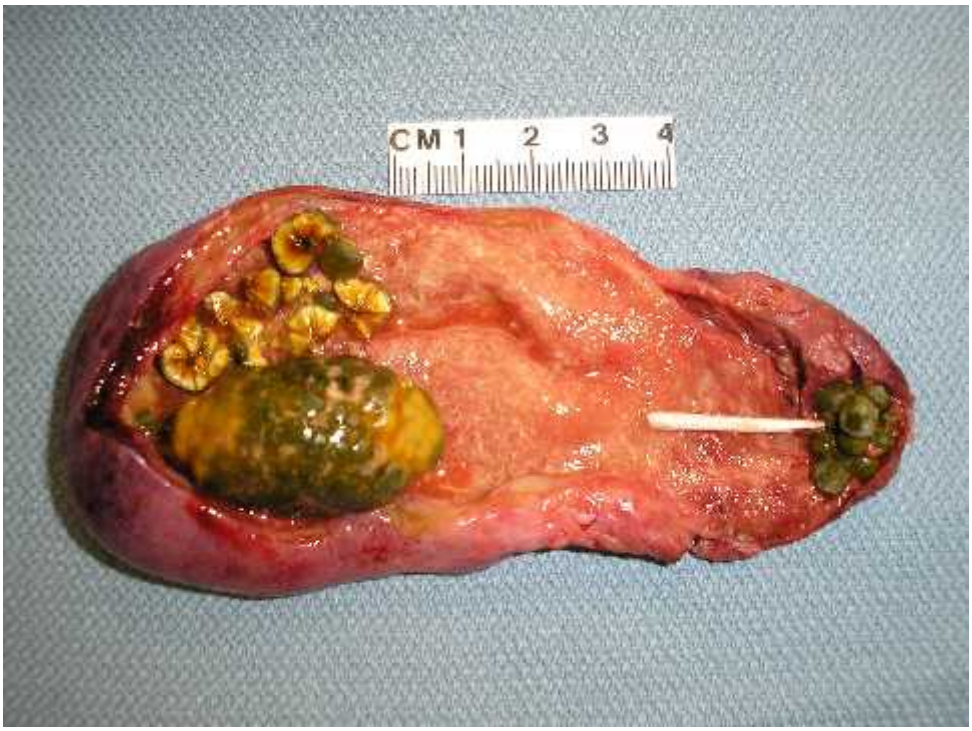
Pigment Stones: Composed almost entirely of calcium bilirubinate, usually multiple, 2-5 mm in diameter, irregular or smooth, black or brown and amorphous or crystalline. Black and brown stones differ in chemical composition and clinical association.

Sl.No	**Black**	**Brown**
1	Shiny	Dark Brown
2.	Resist manual crushing	Easily crushable
3	Found mostly in Gallbladder	Found in biliary tract
4	Bile sterile	Bile usually infected
5	Associated with hemolysis and	No such association
6	Calcium bilirubinate - 40%	Calcium bilirubinate -
7	Calcium palmitate - trace	Calcium palmitate -15%
8	Calcium Carbonate - 6%	Calcium carbonate - trace
9	Cholesterol 2%	Cholesterol 15%



CHOLESTEROL GALL STONE

PIGMENT GALL STONE



COMBINED /MIXED GALL STONES

GALLSTONE STRUCTURE AND CHEMICAL COMPOSITION

GALLSTONE STRUCTURE

Electronic microprobe analysis, X-ray diffraction and infrared spectroscopy have been used to investigate structure of gallstones.

The essential constituent of all gallstones is the matrix, a gel like substance consisting of glycoproteins. An amorphous mass of calcium, bilirubinate and protein, with or without copper ions, occurs at the centre of most cholesterol gallstones. Surrounding this core may be cholesterol crystals with or without calcium salts or deposition or discrete alternate layers of calcium bilirubinate and cholesterol. Highly calcified stones also have a central pigment. Pigment stones are amorphous conglomerates and consist primarily of bile pigments with variable amounts of calcium.

CHEMICAL COMPOSITION OF GALLSTONES

Cholesterol is the major component of cholesterol stones, in mixed stones and in small quantities in pigmented stones. In pigmented stones the cholesterol content is usually < 30%. In cholesterol stones it occurs mainly as cholesterol monohydrate crystals while in others as anhydrous cholesterol.

Bile pigment: The second commonest component of gallstones mostly bilirubin. May be present in the centre of gallstones or diffusely as in pigment stones.

Calcium: The third major component of gallstones varying from 0.2 to 5% occurs predominantly as bilirubinate but phosphate, carbonate, palmitate can also be present. Calcium content is greater in stones with low cholesterol content. Calcium is usually absent in stones with more than 80% by weight in cholesterol.

Other substances: Include inorganic ions like sodium, potassium, copper, iron, manganese, magnesium, lead, silver, nickel, chromium, phosphorous, sulphur, phosphates and organic compounds such as triglycerides, polysaccharides, phospholipids and fatty acids. Gallstones in patients on oral contraceptives for prolonged period have been shown to contain high levels of copper.

PATHOGENESIS OF GALLSTONES CHOLESTEROL GALLSTONES

Pathogenesis of cholesterol gallstones separated into 3 stages[34,].

(i) Cholesterol Saturation (ii) Nucleation (iii) Stone growth.

i) **Cholesterol Saturation** : Though the defect in the hepatic secretion of cholesterol supersaturated bile is accepted as a pre-requisite for cholesterol stone formation, of critical importance is not the absolute but the relative concentration of cholesterol to lecithin and bile acids.

Cholesterol is an organic molecule, insoluble in aqueous bile. Bile acids

are amphipathic compounds containing hydrophobic and hydrophilic polar groups. On reaching a critical concentration bile acid molecules aggregate with their hydrophilic ends oriented outwards and hydrophobic ends inwards. Lecithin molecules enter this aggregate to form “micelles”. Cholesterol molecules are transported within this micelle. When concentration of cholesterol exceeds the critical level it forms crystals in labile phase.

Bile supersaturation with cholesterol occurs when the bile salt pool is decreased or when synthesis and excretion of cholesterol is increased. It is called as lithogenic bile.

Bile Salt Pool: Reduced in most patients with gallstones to half the normal. This may result from:

a. Decreased efficiency of intestinal absorption – malabsorption in diseased states such as regional enteritis, ileal resection or bypass; cirrhosis; and use of contraceptive.

b. Increased cycling frequency: Small multiple meals - rapid enterohepatic circulation

c. Decreased steady state synthesis: Reduced activity of 7 α - hydroxylase (rate limiting enzyme for bile synthesis).

d. Abnormally sensitive feedback regulation of faecal bile acid loss.

*Hepatic cholesterol synthesis and secretion***:** Supersaturation of cholesterol

and its precipitation in bile occurs when it constitutes greater than 10% of total biliary lipids. This may be because of increase in HMGCoA reductase (3 hydroxy - 3 methol glutaryl - coA), the rate limiting enzyme for cholesterol synthesis. Obesity, lipid lowering drugs, diet, age, female sex hormones have been implicated.

Enterohepatic Circulation: Cholesterol super saturation of bile may result from enterohepatic circulation of bile salts. Factors influencing enterohepatic circulation are:

a. Phospholipids - Qualitative and quantitative changes reported in patients with gallstones. In non obese patients, phopholipids proportionately reduce with reduction in biliary salt secretion but not so in obese.

b. Stratification of bile - gallbladder during the 24 hours receives bile of varying degree of cholesterol saturation and may form layers of non-homogeneity with resultant cholesterol crystal formation. Gallbladder sensitivity to cholecystokinin may vary and some authors have found diminished emptying in patients with gallstone. Gallbladder motility has relevance in not only interrupting enterohepatic circulation and influencing bile acid pool size but also determining mixing of bile. It is of greater importance in influencing cholesterol crystal growth than influencing bile salt kinetics.

c. Metabolic functions of gallbladder: the gallbladder not only concentrates the bile but also influences its solubility. Lysolecithin derived by action of phopholipase A (mucosal enzymes) on lecithin adversely affects cholesterol solubility. Biliary lipid concentration are also affected by esterases and hydroxylases present in gallbladder mucosa.

ii) **Nucleation of cholesterol crystals:** Is the process by which cholesterol monohydrate crystals form and agglomerate. 40-80% of normal individuals have supersaturated bile suggesting additional factors for gallstone formation, nucleation being one of them. Though the nature of nucleating factor awaits definition a heat labile glycoprotein has been identified in patients with cholesterol gallstone which considerably reduces nucleating time. Increased gallbladder mucus secretion has been shown to induce gallstones and aspirin which inhibits mucous secretion reduces incidence of experimentally induced gallstones.

Specific but as yet unidentified proteins within cholesterol saturated bile may promote nucleation of gallstones. But nucleation inhibiting and promoting factors, their physiologic balance and mechanism of action are unknown and efforts to understand them are still on.

iii)Stone growth

The growth of cholesterol gallstones has been traditionally viewed as a

natural consequence of cholesterol precipitation and agglomeration. Biliary sludge which is composed of mucin, calcium, monoconjugated bilirubin and cholesetrol is now thought to be the direct precursor of gallstones.

Calcium and cholesterol gallstones: Calcium salt forms the central matrix of majority of cholesterol stones and is important in their pathogenesis. Total and ionised calcium is increased in bile of patients with cholesterol gallstone. Though the biological significance is obscure, data suggests calcium may accelerate cholesterol crystal growth. The exact mechanism of calcium increase is unknown

Pigment Stones[6,7]

Irrespective of the type of pigment stones black or brown, the final common pathway is the formation of calcium bilirubinate crystals. In the case of black pigment stones, due to excessive hemolysis, some bilirubin may escape conjugation in liver and are excreted in the bile as unconjugated bilirubin. Calcium in bile form calcium bilirubinate polymers which act as a matrix around which the pigment stone grow. Similarly in the case of brown.

pigment stones the beta - glucuronidases produced by the bacteria deconjugates the bilirubin which then combines with the calcium as mentioned above.

CLINICAL SPECTRUM OF GALLSTONE DISEASES

The Gallstone disease is not a single entity. It is a spectrum of clinical syndromes associated with biliary stone. It is as varied as the etiologies and risk factors that have been associated with the formation of gallstones. Often nonspecific, the symptoms may be acute, chronic or totally absent. [49]

Silent Gallstones

Most surveys have shown that silent gallstones heavily outnumber the symptomatic ones. Silent gallstones are diagnosed as incidental findings, commonly by abdominal radiographs and routine ultrasonography.

The current consensus regarding the management of the asymptomatic gallstones is that there is no indication for cholecystectomy except in the following situations:

1. Those who are undergoing laparotomy for some other cause and are found to have gallstones.
2. Asymptomatic patients who are acromegalic and are on long term somatostatin analogues which often produces large gall stones.
3. Patients with calcified gallbladder as they have increased risk of gallbladder cancer.
4. Diabetic patients with gallstones as they are more prone to develop symptoms and complications.

Spectrum of symptomatic gallstone disease

1. Acute cholecystitis.

2.Chronic cholecystitis.

3. Jaundice due to bile duct obstruction.

4.Cholangitis/Septicemia

5. Acute gall stone pancreatitis.

6.Biliary fistulous disease.

7. Gallstone ileus.

Acute Cholecystitis

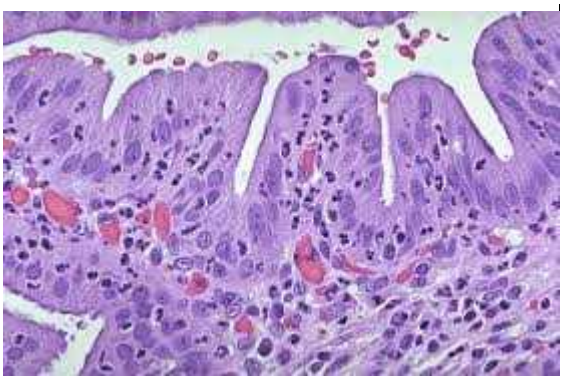
It is most commonly obstructive in nature, from the impaction of a stone in cystic duct/Hartmann's pouch. Initial inflammation is chemically induced and is followed by bacterial infection.

The clinical picture varies with the severity of the inflammatory process. In mild cases, the patient complains of right upper quadrant pain and tenderness. Pyrexia, severe pain and tenderness in the right hypochondrium effect more severe degrees of gallbladder inflammation. Murphy's sign (inspiratory arrest due to pain on inspiration during gentle palpation of the right subcostal region) is usually present. Nausea, vomiting, ileus, mild abdominal distension and toxicity are encountered in severe forms of the disease. Jaundice is present in 20-25% of patients with acute cholecystitis.

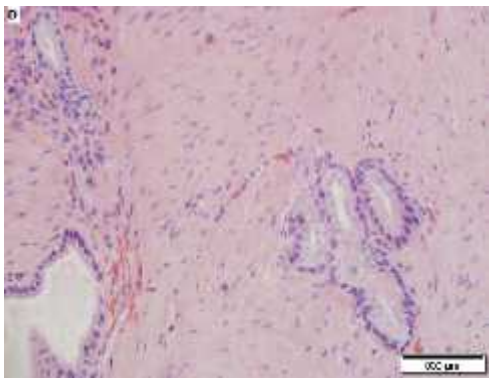
Finally the natural course of the disease follows any one of the following patterns namely: 1. Resolution - Complete. 2. Persistence of infection - Empyema of gallbladder 3. Resolution of inflammation within the gallbladder with persistence of cystic duct obstruction - mucocele 4. Gangrene Perforation - Peritonitis. 5. Fistula formation. This course of the disease is altered by medical intervention.

Chronic Cholecystitis

Chronic inflammation of the gallbladder is most commonly due to stones and the patients with chronic cholecystitis complain of recurrent attacks of epigastric or right hypochondrial pain often radiating to right side of the back. The pain is more often persistent than intermittent. Nausea and vomiting may accompany episodes of persistent pain and the severe attacks of biliary colic. Jaundice may follow an attack and indicate common bile duct obstruction by a calculus. The only reliable sign, which is frequently found on clinical examination is tenderness in the right upper quadrant.



ACUTE CHOLECYSTITIS



CHRONIC CHOLECYSTITIS

Acute biliary colic

The most common presentation for patients in symptomatic gallstones is postprandial right upper quadrant pain. It is usually precipitated by fatty or protein - rich meal. It occurs 30 to 60 minutes after eating and lasts for several hours and then diminishes. Unlike other colics, the pain of the biliary colic may be constant. It is generally felt in the right upper quadrant, but may referred to inferior medial aspect of scapula or shoulder or to the mid epigastrium. Nausea and vomiting are usually associated with biliary colic. The onset of pain is often related to the impaction of stone in the cystic duct or in the Hartmann's pouch, with obstruction to out flow of bile occurring secondarily. It is usually self limited and resolves within few hours. Frequency of attacks is unpredictable and does not have any relation to the number of stones or the size of the stone.

Cholangitis

Acute bacterial cholangitis is a serious life-threatening emergency caused by infection of the obstructed biliary tract. In severe cases of cholangitis there is neutrophilic infiltration of the sinusoids and microabscess formation in the hepatic lobules, portal thrombosis and area of hepatic necrosis are seen. The infection is commonly caused by Gram-negative organisms. The classical triad of symptoms consists of pain in Right

hypochondrium, intermittent fever and jaundice(Charcot's triad). Complete triad seen only in 70% of cases. The liver is often enlarged. Nausea, vomiting are frequent.

Gallstone pancreatitis

Patients with biliary stone disease sometimes develop gallstone pancreatitis due to obstruction in the ampulla of vater.

Biliary Fistulous Disease

The biliary enteric fistula due to gallstone are cholecystoduodenal, cholecystogastric, choledochoduodenal, cholecystocholedochal and cholecystocolic. Of these cholecystoduodenal is the commonest.

Gallstone Ileus

2% of patients with gallstones develop gallstone ileus. It is commonly present in elderly patients due to intraluminal intestinal obstruction by a large gallstone, subsequent to a fistula either cholecystoduodenal or cholecystocolic. It presents commonly as small bowel obstruction and rarely as colonic obstruction. Most commonly terminal ileum (70%) is the site of obstruction. Colonic obstruction is due to impaction in the colon as a result of cholecystocolic fistula. It is suspected when gas is present in biliary tree or

gallstone is visualized in bowel lumen. It is very uncommon in our part of country.

Sydromes associated with gallstones

Mirizzi Syndrome - It comprises of obstructive jaundice due to stone impacted in the neck of gallbladder compressing the common hepatic duct. Depending on the severity 4 types are described.

Bourveret's Syndrome

In this rare condition, there is a duodenal obstruction due to passage of gallstone from gallbladder into duodenum through cholecystoduodenal fistula. Endoscopy will be diagnostic as well as therapeutic.

INVESTIGATIONS

Apart from the routine investigations done for the patients admitted in surgical ward, there are certain specific investigations done for the patients with gallstone disease. Few of the investigations and its implications are discussed.

Biochemical Investigations

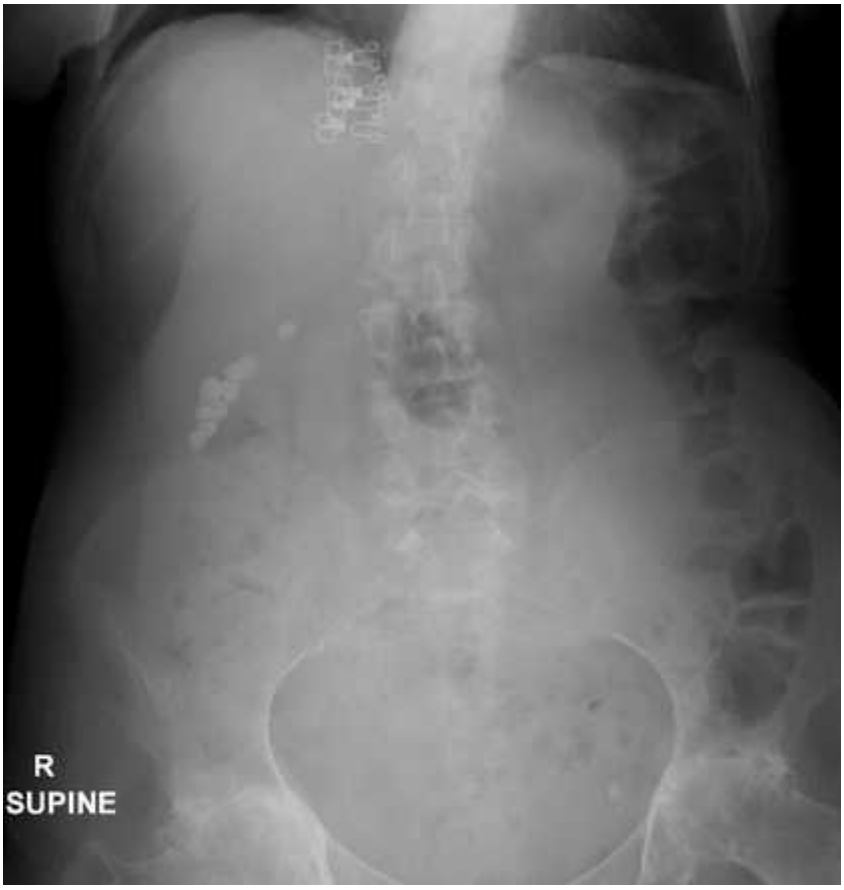
Blood Count - The count will be elevated in case of acute cholecystitis, with polymorphonuclear leucocytosis.

LFT - Bilirubin will be elevated in case of the obstruction in the biliary tract. Also the serum alkaline phosphatase and aminotransferases are elevated.

Urine Urobilinogen - Absent in case of obstructive jaundice.

X-ray Abdomen

The X-ray abdomen will show radiopaque gallstones in 10% of patients. It will also show rare cases of calcification of gallbladder called as ‘Porcelain’ gallbladder. Gas may be seen in the wall of the gallbladder (Emphysematous Cholecystitis). Gas in the gallstone is called as "Seagull" sign or "Mercedes Benz" sign.

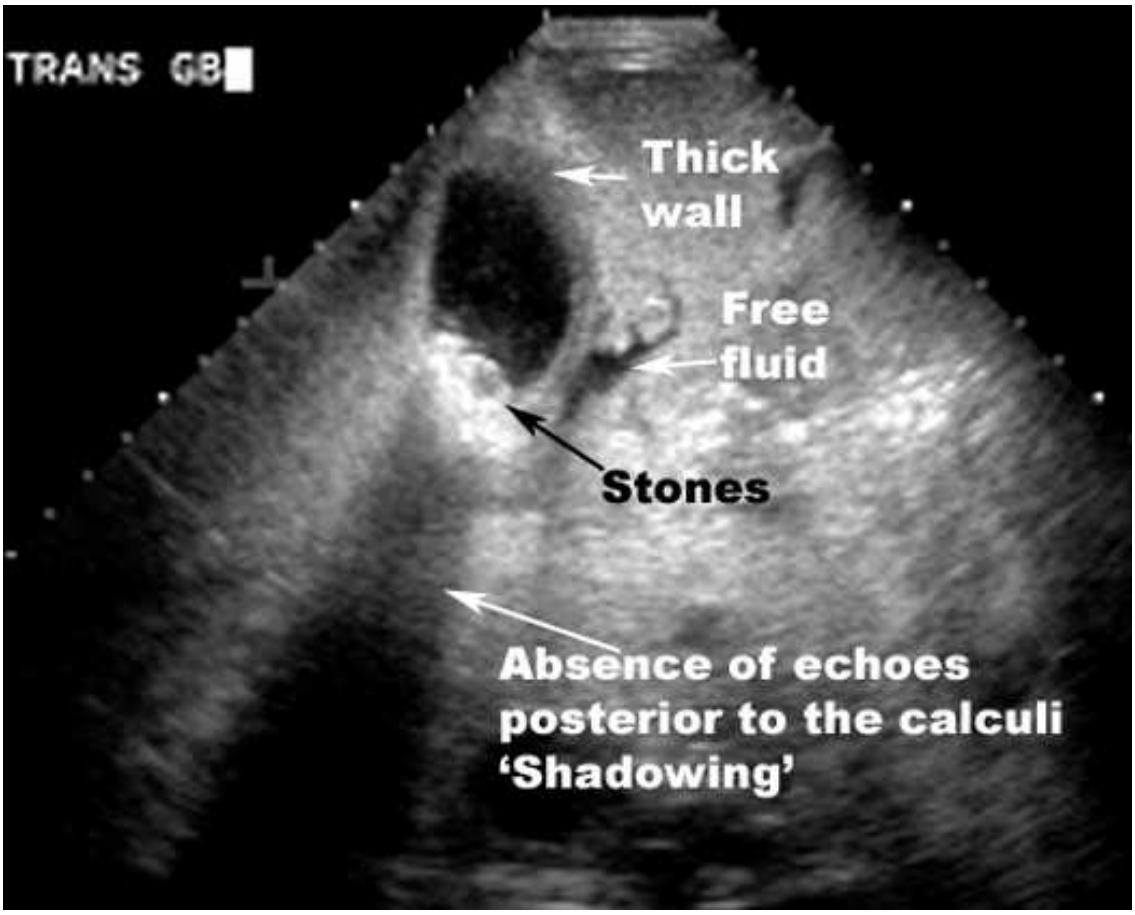


X-Ray Abdomen showing gall stones

Abdominal Ultrasonography

Ultrasonography is non-invasive and is now the standard initial imaging technique for the investigation of the patient suspected of having a gallstone, and is also the prime investigation for the patient presenting with jaundice. It will demonstrate biliary calculi., the size of the gallbladder, the thickness of the gallbladder wall, the presence of inflammation around the gallbladder, the size of the common bile duct and occasionally the presence of stones within the biliary tree. Endoscopic ultrasound using an endoscope which has a

miniature ultrasound transducer mounted on its tip is valuable for detecting stones in or obstruction of the lower bile duct. It may prove unsatisfactory for technical reasons in the following: Obesity, following previous surgery, ascites, gaseous distension of the upper abdominal viscera and distal part of CBD.



Ultrasonogram Abdomen showing gall stones

Oral Cholecystography

Iopanoic acid is taken as tablets on the night before the examination. A control radiograph is taken before the tablets are given and a series of

radiographs are taken on the following day with further films after a fatty meal. The fatty meal stimulates gallbladder contraction and reveals the adequacy of gall bladder function. This investigation has been discarded by most hospitals because of its inaccuracy except to show diverticulae and polyps, and to assess function; adequate films depend on the patient taking the tablets, and the tablets being absorbed, secreted by the liver and concentrated in the gall bladder after passing into the gallbladder through an unobstructed cystic duct. Thus, a cholecystogram that shows no concentration of contrast can result from many causes and is not diagnostic of gallstone disease

Intravenous Cholangiography

Intravenous cholangiography (biligram - meglumine ioglycamate) permits radiological visualisation of the bile ducts. The drug is given intravenously and is rapidly secreted by the liver into the biliary tree. Careful radiography with or without tomography can clearly define the ducts and the gallbladder, delineating

the presence of stones. (Not useful if bilirubin is > 3mg%)

Radio Isotope Scanning

Technetium - 99m (^{99}TC) - labelled derivatives of iminodiacetic acid (HIDA, IODIDA) are excreted in the bile and are used to visualize the biliary tree. In acute cholecystitis, the gallbladder is not seen. The technique is used

when biliary - enteric anastomoses are functioning inadequately as it will show the extent of obstruction at the anastomoses and indicate the delay in excretion.

CT Scanning and Magnetic Resonance Imaging (MRI)

Helical or spiral CT scanning can provide similar information on the biliary tree as ultrasonography but in view of cost and radiation exposure it is usually held in reserve when ultrasound examination has failed. Regarding MRI Scan, its use in the diagnosis of gall stones is limited and no specific advantage is seen with MRI when compared to CT scan.

Percutaneous Transhepatic Cholangiography (PTC)

First performed by Howard and Duvan (1937). Okuda (1974) popularized it by using fine bore chiba needle (21 guage, outer diameter 0.7 mm). It has a success rate of 99% with dilated duets and 70% in non-dilated intrahepatic biliary radicles. It is the procedure of choice in obstructive pathology. [61]

Indications

1. To differentiate obstructive from non-obstructive pathology. 2.To demonstrate calculi - number and location in CBD. 3.To demonstrate malignancy in biliary tract. 4.To decompress the biliary tree by stenting

preoperatively.

Contraindications

1. Haemorrhage. 2.Cholangitis. 3. Ascitis. 4. Hypoprothrombinemia

5. Suspicion of intrahepatic vascular tumour.

Complications

1. Liver laceration. 2.Blood bile fistula (Haemobilia). 3. Pneumothorax.

4. Bile Peritonitis

Endoscopic Retrograde Cholangio Pancreatography (ERCP)

Through a side viewing gastroduodenoscope sphincter of oddi is cannulated, dye is injected and biliary pancreatic tree is visualized. ERCP is very accurate in the diagnosis of ductal calculi but less accurate than the ultrasonography and oral cholecystography in the diagnosis of gallstones and gallbladder disease. Therapeutic wise, ERCP can be used to retrieve the CBD stones.

Magnetic Resonance Cholangio Pancreatography (MRCP)

MRCP provides useful information about the biliary calculi and it detects stones as small as 2mm in the bile duct.

Operative Cholangiography

Types : 1. Preexploratory. 2. Post Exploratory and the techniques are,

1. Cystic Duct Cholangiography. 2.CBD Cholangiography. 3.Transhepatic Cholangiography. 4.Post Exploratory Cholangiography.[62]

Operative Choledochoscopy

Bakes in 1923 had done the first choledochoscopy. At operation, a flexible fibreoptic endoscope can be passed down the cystic duct into the CBD enabling stone identification and removal under direct vision. It can be combined with X-ray image intensifier to ensure complete clearance of biliary tree. [63]

TREATMENT OF GALLSTONE DISEASE

The treatment of the gallstone disease depends on the clinical presentation. It varies from conservative medical treatment to surgery as per the need. In this chapter we discuss the clinical presentation and its treatment.

Acute Calculous Cholecystitis

It may present as acute progressive and life-threatening condition or as a mild resolving condition. In mild or resolving disease, the initial treatment consists of nasogastric suction, I.V. fluids and electrolyte correction with Broad Spectrum antibiotics and adequate analgesics. In the mean time the patient is evaluated and further treatment will be either interval cholecystectomy or early cholecystectomy. The rationale behind interval cholecystectomy is that the surgery is performed after the inflammation has subsided. Now the trend is towards the early cholecystectomy, since it has an

advantage of less hospital stay and cost of treatment without any increase in morbidity or mortality.

The acute cholecystitis is called **progressive and life threatening** when the following are seen.

i. Progression of disease despite the conservative treatment.
ii. Failure to improve within 24 hrs especially in patients above 60 yrs.
iii. Presence of an inflammatory mass in right hypochondrium.
iv. Detection of gas in the gallbladder/biliary tract.
v. Established generalised peritonitis.

In these patients, the surgical intervention is emergency and carried out under antibiotic cover (Broad Spectrum). The exact procedure depends on the operative findings. In case of tense empyema, preliminary decompression of the gallbladder contents using a mayo-ochsner suction trocar cannula inserted through purse string suture in the fundus precede the cholecystectomy. If the anatomy in obscured by the inflammation or general condition of patient is poor, a cholecystostomy is performed. In later stage an elective cholecystectomy is done. Sometimes subtotal cholecystectomy is done. In all cases bile and pus are obtained for culture and sensitivity and thorough peritoneal toileting is done. Then patient is put on appropriate antibiotics. Of late the laparoscopy has been used to manage the situation except when

established gangrene or perforation are seen, in which case open surgery is better.

Chronic Cholecystitis

Patients with chronic cholecystitis are treated by elective cholecystectomy under antibiotic cover. Now-a-days laparoscopic cholecystectomy is the gold standard treatment. In these patients intraoperative cholangiogram should be routine. If stones are detected in biliary tract they are managed by CBD exploration and extraction of stones. In certain cases nonoperative techniques of management like percutaneous contact dissolution therapy, extracorporeal shock-wave therapy, oral dissolution therapy are used if the criteria for their use is fulfilled.

In cases with jaundice due to large **bile duct obstruction,** the treatment depends on whether multiple stone or single stone at the distal end. In the earlier case cholecystectomy followed by CBD exploration with T-tube drainage is the preferred procedure. If it is single stone it may be better to remove through endoscope, followed by cholecystectomy.

In case of **cholangitis,** which is a serious life-threatening emergency caused by infection of an obstructed biliary tree. The patient is energetically treated with anti-biotics, analgesics and I.V. fluids. If not responding, emergency biliary decompression is required. Decompression may be surgical

duct exploration and stone extraction or endoscopic sphincterotomy.

In case of **gallstone pancreatitis,** the initial treatment is conservative. If not improving, then do endoscopic papillotomy and stone extraction or open surgery and relieve obstruction. If improves with conservative treatment, elective correction of cholelithiasis should be done.

It may also present as **biliary enteric fistula.** The patient is treated with cholecystectomy and closure of the fistulous communication.

It may present as intestinal obstruction. (Gallstone ileus). The treatment is as follows, in ileal obstruction, it is enterolithotomy with cholecystectomy and closure of duodenal fistula. But in colonic obstruction, the calculus is removed through a colotomy, then a cholecystostomy (cholecystectomy if patient is fit) with exteriorization of the colonic fistula as a proximal diverting colostomy.

Few modalities of treatment of gallstones are described in detail due to the importance of those procedures in the management of gallstones

OPERATIVE TECHNIQUES

OPEN CHOLECYSTECTOMY Indications for cholecystectomy

1. Presence of gallstones with symptoms and rarely without symptoms.
2. Acute of chronic cholcystitis with or without gallstones.
3. Torsion of gallbladder.

4. Following cholecystostomy

   a. As a second stage procedure

   b. Where there is persistent biliary or mucous discharge

   c. In patients with recurrent gallstones treated by non operative modality.

5. Traumatic rupture of gallbladder or cystic duct.

6. Biliary peritonitis with or without demonstrable perforation.

7. Carcinoma gallbladder, usually operable when tumour is a chance finding at laparotomy for calculus disease.

Contraindications of open cholecystectomy

1) Asymptomatic gallstones.
2) When the stones produce only minor symptoms in the poor risk, aged, feeble patients.
3) Patients with serious medical disorders.

Advantages of cholecystectomy

a. Eradication of the more specific symptoms of gallstones
b. Prevents complications of gallstones.
c. No recurrence of gallstones.
d. Procedure allows full inspection of abdominal viscera.

Disadvantages of open cholecystectomy

a. Inflicts considerable discomfort to the patient.
b. Requires hospitalization for 7 - 10 days and loss of work for upto one month.
c. About 47% of patients continue to complain of some persistence symptoms and dyspepsia. The post-cholecystectomy syndrome, attributed to:

a. Retained stones in bile duct.
b. Long cystic stump remnant.
c. Ampullary stenosis
d. Sphincter of Oddi dysfunction.

Complications

1. Haemorrhage. 2. Biliary injury and stricture. 3. Biliary fistula. 4. Post operative jaundice. 5. Accumulation of bile in right sub - phrenic (or) sub - hepatic region leads to " waltman - waiter's " syndrome. 6. Infection.

These could have been prevented or corrected at surgery but cannot be considered as outcome of surgery in every case. Increased risk of developing colonic malignancies following cholecystectomy reported by some investigations but largely not confirmed by others.

Operative Techniques

Two operative techniques are:

1. The retrograde or standard cholecystectomy.
2. “Fundus-down” or Fundus first” Cholecystectomy.

Some Golden Rules in Case of Difficulty

1) Clear identification of pylorus, duodenum, and colon is a prerequisite for a proper approach to ductal and arterial system.
2) A common duct hidden in fibrous tissue may be located by means of an aspirating syringe with a fine needle.
3) With severe inflammation in Calot’s triangle, it may be wise to open the gallbladder, extract all the stones and bile, and excise as much of the wall of the gallbladder as possible. The cystic duct opening is closed by a catgut suture from within. Any mucous membrane remaining on the hepatic bed may be cauterised.An alternative is cholecystostomy.
4) A clear identification of the common and right hepatic duct in the danger area can be done by inserting a sound upwards through a choledochotomy.

CHOLECYSTOSTOMY

This option of simple drainage of the gallbladder combined with removal of any stones is occasionally indicated.

a. If it is deemed that a cholecystectomy would be technically difficult - severe inflammatory changes rendering the anatomy obscure.
b. In poor risk patients especially when general condition is poor.

c. For a preliminary drainage of the biliary tree obstructed by tumour in patients in whom later resection is contemplated.

Usually performed via a subcostal incision under a local or general anaesthesia. A tube cholangiogram and definitive surgery is performed after an interval of 6 to 12 weeks.

PARTIAL CHOLECYSTECTOMY

A useful alternative technique to the standard procedure when the separation of the gallbladder from the common hepatic duct would be hazardous and dissection from gallbladder fossa is likely to be followed by uncontrolled bleeding. In this procedure gallbladder mucosa is cauterised.

MINICHOLECYSTECTOMY

A standard mini cholecystectomy is performed through a 5 cm midline incision using special instruments and the modern fixed retractor system for exposure. This limited exposure prevents a full abdominal exploration and hence leads to less post-operative discomfort, paralytic ileus and quicker recovery thereby

reducing the hospital stay and loss of work, which are the chief drawbacks of the standard cholecystectomy. [57]

LAPAROSCOPIC CHOLECYSTECTOMY [55,56]

Its now becoming the procedure of choice.

Indications

1. Cholelithiasis and biliary colic.

2. Symptomatic gallbladder polyps.

3. Resolving gallstone pancreatitis.

4.Symptomatic chronic cholecystitis

Contraindications

Relative: Acute cholecystitis, prior upper abdominal surgery, bleeding diathesis, common duct stones, COPD with acidosis and hypercarbia, mirizzi's syndrome.

Absolute: Acute cholangitis,severeacutecholecystitis acutepancreatitis, peritonitis, portal hypertenstion, pregnancy, serious bleeding diathesis, morbid obesity, thick walled gallbladder.

Complications

1. Bleeding - Slipped clip.

2. Bile leak.

3. Bowel injury.

4. Biliary injury.

Chemical cholecystectomy [57]

This procedure is used with cholecystolithotomy, which allows access to the gallbladder. It may become an important method of preventing stone recurrence because of the advent of non-operative procedures as a treatment modality for gallstones. It has two components: gall bladder mucosal ablation and cystic duct obstruction. A number of chemicals have shown to destroy gallbladder mucosa, but reepthelialisation takes palce from the cystic duct. Cystic duct occlusion using a bipolar electrocoagulation catheter has overcome this. Thus chemical cholecystectomy in combination with stone removal in one stage offers a theoretical option for managing gallbladder stones and preventing recurrence. However this procedure is still in the experimental stage and such an ablative iatrogenic procedure may possibly increase the likelihood of gallbladder cancer.

NON OPERATIVE TECHNIQUES EXTRACORPOREAL SHOCKWAVE LITHOTRIPSY (ESWL) FOR BILIARY STONES [58,59]

Inclusion criteria for patient selection in gallbladder stone treatment by ShockWave Lithotripsy.

1) History of biliary colic. 2) Single radiolucent gallbladder stone with a diameter 30mm as determined by ultrasound or upto 3 stones totaling a similar stone volume. 3) Opacifying gallbladder on OCG (to assure patency of cystic duct). 4) No calcification attributable to gallstone on plain abdominal

film. 5) Identification of stones and gallbladder by ultrasonography and successful focusing of shock waves.

Exclusion criteria

1) Acute cholecystitis, cholangitis, biliary obstruction. 2) Bile duct stones. 3) Gastroduodenal ulcers. 4) Acute pancreatitis. 5) Coagulopathy. 6) Vascular aneurysm, lung tissue or cysts in path of shock waves. 7) Pregnancy

The treatment of partially calcified stone (3m ring of calcium) is being investigated but not as yet considered for a routine procedure.

Morbidity and mortality following ESWL for gallstones

Hematuria (3%) petichiae at cutaneous entry site (4%), biliary pain by passage of fragments through biliary tree (35%), transient cystic duct obstruction (5%), pancreatitis (1%) mortality (0%).

Under the current criteria only 0-20% of all symptomatic and uncomplicated gallbladder stones can be treated with ESWL. The technology of ESWL for a gallstone will improve with time increasing efficacy of stone fragmentation while maintaining a low level of discomfort for the patient. Long term follow-up studies are needed to define the place of ESWL in management of gallstone.

DISSOLUTION THERAPY FOR GALLSTONES

Gallstones predominantly composed of cholesterol are theoretically

amenable to oral and topical agents. The concept is not new. In 1863, Thudicum demonstrated in vitro dissolution of gallstones using ether and turpentine. In 1873 Maurice Schiff proposed ingestion of bile salt for gallstones as a treatment. In 1937 Newbridge of Minnesota demonstrated in-vivo dissolution of gallstone on prolonged oral administration of a mixture of bile salts and olive oil. In 1972 oral administration of chenodeoxycholic acid (CDCA) were shown capable and effective as dissolution agents.

Topical infusion likewise is not a new concept Walter (in 1891) used ether to dissolve stones. Since then chloroform olive oil, ether, warm saline have beem used via T-tube in an attempt to dissolve the stones.

ORAL DISSOLUTION THERAPY [60]

Chenodeoxycholic acid and ursodeoxycholic acid are two naturally occuring bile acids used for oral dissolution of gallstones.

Criteria for patient selection

a. Any age and sex: Women in childbearing need adequate contraception.
b. Patients with mild and tolerable symptoms.
c. Patient compliance should be assured - treatment has a prolonged course.
d. Gallbladder should be functioning as demonstrated by oral cholecystography or on ultrasound
e. Stones should be radiolucent.

f. The size of the stone should be less than 15mm.

g. Patients otherwise, unfit for surgery.

Contraindications of dissolution therapy

a. Chronic liver disease.

b. Severe and prolonged symptoms

c. Nonfunctioning gallbladder.

d. Radio-opaque stones.

e. Stones greater than 2 cm in diameter.

f. Concomitant hepatobiliary disease, inflammatory bowel disease or peptic ulceration.

Oral dissolution agents

- Chenodeoxycholic acid (CDCA): Naturally occuring primary bile acid. (30-40% of bile acid pool) effective in reducing cholesterol saturation alters the composition of bile by decreasing endogenous hepatic cholesterol synthesis and exogenous expansion of bile salt pool. Suppresses activity of HMGCoA reductase a rate limiting enzyme for hepatic cholesterol synthesis. Dissolution takes palce by molecule alteration of cholesterol from crystalline form to unsaturated mixed micelles.

Dose: 12-15 mg/kg/day as a single dose at bed time with a low cholesterol diet.

Ursodeoxycholic acid (UDCA): A 7-beta hydroxy epimer of chenodeoxycholate which is a primary bile salt of bears. Absorbed from the intestine, undergoes enterohepatic circulation, and gets conjugated with glycine and taurine within the liver. Apart from mechanism of action similar to CDCA it also causes increased bile output and decreases absorption of cholesterol from the gut.

Dose: 8-10 mg/kg/day or 600 mg taken at bed time for 6-12 months.

CONTACT DISSOLUTION THERAPY

A 5 French pigtail Polyethylene catheter is inserted percutaneously into gallbladder under fluoroscopic control. Dissolution agent is repeatedly instilled and aspirated, agitating the gallbladder contents. Dissolution occurs within hours to days. The procedure is terminated by removing the catheter and inserting a gelfoam plug to prevent bile leakage. The solution should not be infused under pressure, should have a free access to the intectine and should not leak into peritoneal cavity.

Chemical Used

1. Methyl ter-butyl ether: An aliphatic ether that effectively dissolves cholesterol stones. It is toxic to CBD. Its complications include hemolysis, duodenitis, mild anaesthesia, nausea and vomiting. An inflammable and toxic compound that can cause haemorrhagic peritonitis. Complication rate

is 50%.

2. Mono-octanoic Acid: A medium chaintriglyceride effective as a cholesterol solvent. A solution buffered to pH 7.4 infused at 3-7 ml/hr would dissolve a stone in 5 days. Success rate reported between 50-80%. When infused under pressure may cause respiratory distress or if it enters the duodenum results in diarrhoea, vomiting and abdominal cramps.

Contact dissolution therapy in its present form is unlikely to have a clinical impact except in specialised centres with special equipment and requisite skill. Development of newer and safer solvents and in combination with other modalities like ESWL, transcatheter fragmentation using lasers, it may in the future find an application.

MANAGEMENT OF STONES IN THE COMMON BILE DUCT

Modem imaging technique have improved the accuracy of pre-operative diagnosis of common duct stones. In addition at the time of laparotomy operative cholangiography makes a major contribution to accurate diagnosis.

COMMON BILE DUCT EXPLORATION

Indications

1. Palpable stones in the common bile duct, most reliable and accuracy rate is 98%.

2. Jaundice with cholangitis/pancreatitis
3. Pre-operative radiographic demonstration of choledocholithiasis.
4. A stone visualised at intra-operative cholonagiography
5. A dilated CBD
6. Single faceted stone or multiple small stones in gallbladder.

Jaundice with fever and rigor is indicative of acute cholecystitis and cholangitis; when cholecystitis is excluded it is associated with choledocholithiasis in 97%. In the non jaundiced, intraoperative cystic duct cholangiography is the most reliable determinant of choledocholithiasis with an accuracy of 85-98%.

Reasons of performing routine intraoperative cholangiography.

a. Exclusion of CBD exploration in patients with clinical indications of CBD stones but at operation may not harbour stones.
b. Detection of unsuspected stones at time of surgery.
c. Preexploratory identification of number of stones, their size and location in CBD.
d. Visualization of ampullary region and biliary system.

Technical Consideration

Along the free edge of lesser omentum, peritoneum over anterolateral surface of CBD is divided, bile is collected for culture and cystic duct is

ligated. The CBD is opened in the supraduodenal portion between 2-0 chromic catgut stay sutures. Ducts are explored by means of a Desjardin's forceps, initially passed upwards into the common, left and right hepatic ducts and any stone encountered is removed, packed with gauze; then the distal part of CBD is explored. Large stones in intrapancreatic portion of the duct are removed only after mobilizing duodenum by Kocher's manoeuver. The duct is irrigated with normal saline via a Catheter to remove any sludge or debris. To complete the exploration Bakes dilators are passed through the papilla into the duodenum.

Choledochoscopy: After clearing the duct the choledochoscopy is performed using a flexible instrument to remove any missed stones and to visualize the papilla, seen as a rosette of mucosal folds. Stone may also be retrieved by balloon catheters, grasping forceps, retractable wire basket (Dormia) and double-jointed currete for disimpaction of difficult stones.

T-tube Drainage: A T-tube with limbs shortened to 1 cm length is now placed in the choledochotomy incision and the duct is sutured with absorbable suture as an interrupted suture, taking care not to include the tube in the suture. The tube should be of latex rubber or a material that promotes adhesive reaction.

Post-exploratory Cholangiography:

A post-exploratory cholangiography is performed, after cleaning the operation site of all instruments and taking care not to introduce any air bubbles, using a water-soluble radio-opaque solution. This determines any residual stones in the ductal system. The T-tube is brought out through a separate stab incision in the abdomen and connected to a bag.

The T-tube is allowed to drain into sterile bag and from 4 day onwards it is clamped 2-4 hours a day with continuous occlusion on 8^{th} or 9^{th} day. Post operative cholangiogram is performed and the tube is removed by a gentle firm traction.

ADDITIONAL BILIARY ENTERIC DRAINAGE PROCEDURES

Biliary enteric drainage procedure are not routinely recommended.

Indications

1. Multiple or primary duct stones, particularly in dilated duct in elderly patients.
2. One or several large stones within the dilated duct.
3. Unretrievable intrahepatic stones.
4. Impacted ampullary stone.

The available procedures are:

1. **Sphincterotomy:** In this operation part of the musculature

surrounding the lower, intraduodenal portion of the CBD is divided to allow exploration of the duct. In relation to choledocholithiasis its sole purpose is to provide access to the distal part of the CBD. It carries a slight risk of post-operative pancreatitis. Its advantage is that the patient has a duct draining through a competent sphincter and long term results are satisfactory.

2. **Sphincteroplasty:** In this proceudre the entire length of the musculature surounding the lower end of CBD is divided. It allows a thorough exploration and also provides free drainage of the bile through a wide opening. It is, infact, an internal choledechoduodenostomy. It is a safe and effective procedure. In this procedure the duct mucosa is sutured to the duodenal mucosa and restenosis is rare. Post operative hyperamylasemia is common, and clinical pancreatitis occurs in 1% and mortality in less than 1%.

3. **Choledochoduodenostomy:** Here a dilated common duct is anastomosed to the duodenum. Has more chance of cholangitis.

4. **Choledochojejunostomy** : It can also be done when CBD is dilated.

It has more chance of peptic disease.

Indications with regards to choledocholithiasis are:

1. Multiple common bile duct calculi. 2.Impacted distal stone in the absence of pancreatitis. 3.Intrahepatic calculi. 4.Residual stones.

Contradindications

1.Sclerosing cholangitis. 2.Decompression of pancreatic duct for pancreatitis. 3. Malignant obstruction. 4.Significant duodenal edema or inflammation because of risk of anatomic disruption.

It is the prefered procedure with a markedly dilated and infected duct, and when a previously explored duct is being dealt with and in recurrent stone.

RETAINED AND RECURENT CBD STONES

Stones within CBD may present under following circumstances

1. Discovered in the early postoperative period at the time of T tube cholangiography - residual stones.
2. Stones manifesting months or years after cholecystectomy at which time operative choledochoscopy and cholangiogram were normal - recurrent stones.
3. Intrahepatic stones migrated into CBD.

Available treatment modalities include:

1. T-tube still in-situ at the time of discovery of stone

a) Chemical dissolution via lavage down T-tube, **b)** Track of T-tube is allowed to mature for 5 weeks and stone is extracted using a steerable basket under fluoroscopy - Burhenne Technique, **c)** Endoscopic Sphincterotomy, **d)**

Operative re-exploration with a biliary enteric drainage procedure.

2. Stones manifesting after T-tube has been removed or if there is late recurrence of the stone : **a)** Endoscopic sphincterotomy, **b)**Operative reexploration of CBD with drainage procedure.

NON-OPERATIVE REMOVAL OF GALLSTONES

Endoscopic sphincterotomy and stone extraction

It is a minor procedure in patients with retained or recurrent CBD stones. A preliminary ERCP confirms the diagnosis and delineates the anatomy. A special catheter incorporating a wire connected to a diathermy is inserted into the bile duct. The placement of the catheter is radiologically screened. The wire is then tightened, causing the catheter to bow and thereby exposing the cutting system. Cutting current is then employed to make an incision in the roof of the duct and is extended upto 15-20 mm. Stones can now be extracted using balloon catheters and stone baskets.

This procedure can be performed as a Primary treatment in selected cases - elderly patients unfit for operative surgery where risk of bile duct exploration is high.

DISSOLUTION OF BILE DUCT STONES [60]

If the T-tube is in-situ chemical solutions can be infused into bile ducts in patients with retained or recurrent stones. This can also be carried out with

nasobiliary tube inserted endoscopically into the bile duct.

The solution that have been tried with acceptable degree of success include, cholic acid, mono-octanoic acid and MTBE (discussed under dissolution of gallbladder stones).

METHODOLOY

Source of data:

This study has been based on the analysis of 50 cases of cholelithiasis admitted to tirunelveli medical college hospital. The cases were collected from all the seven surgical units and the patients were followed up till the completion of the course.

Type of study:

It is a prospective study.

Inclusion criteria

All proven cases of gallstone disease who got admitted to the hospital for cholecystectomy which includes both open and laparoscopic cholecystectomy.

Exclusion criteria

1. Acute cholecystitis
2. Acute acalculus cholecystitis
3. Emphyema gall bladder
4. Mucocele of the gall bladder
5. Jaundice patients

6. Gallstones with multiple common bile duct stones (multiple CBD and intrahepatic stones).
7. Patients who were not willing for surgery

TOTAL NUMBER OF PATIENTS : 50

Proforma: Details of proforma and master chart attached in the annexure

Sample collection

Bile was collected from excised gall bladder in laparoscopic cholecystectomy. In cases of open cholecystectomy, bile was aspirated from the gallbladder of the patient using a sterile syringe (5ml). The sample was collected in sterile bottle and was transferred to microbiology laboratory. In the laboratory the bile sample was inoculated in the basal media like nutrient agar, MacConkey agar, blood agar in the temperature of 37°c and the results were read after 18-24 hours for growth of organisms. Identification of species was done using biochemical tests like indole test, citrate test, urease test, TSI test, oxidase test, gram staining, motility test. Antibiotic sensitivity testing was done after identification of the organism. Antibiotic sensitivity test was done with ceftriaxone, cefuroxime, ciprofloxacin, amoxicillin.

RESULTS

Table 1 **AGE DISTRIBUTION**

Age Group	Number of Patients	Percentage
21 -30	7	14%
31-40	11	22%
41-50	8	16%
51-60	13	26%
61-70	11	22%

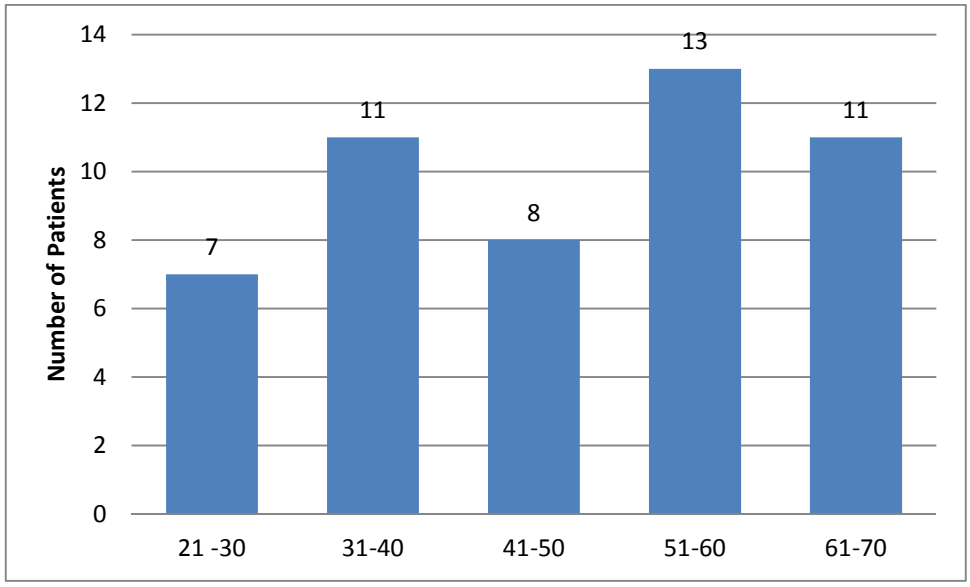


Figure 1 **AGE DISTRIBUTION**

In our study the age group of 51 – 60 years (13 cases) were more commonly affected (26%) , followed by 31-40 (22%) and 61-70 years (22%)age group.

Table 2: **SEX DISTRIBUTION**

Gender	Number of Patients	Percentage
Male	12	24%
Female	38	76%

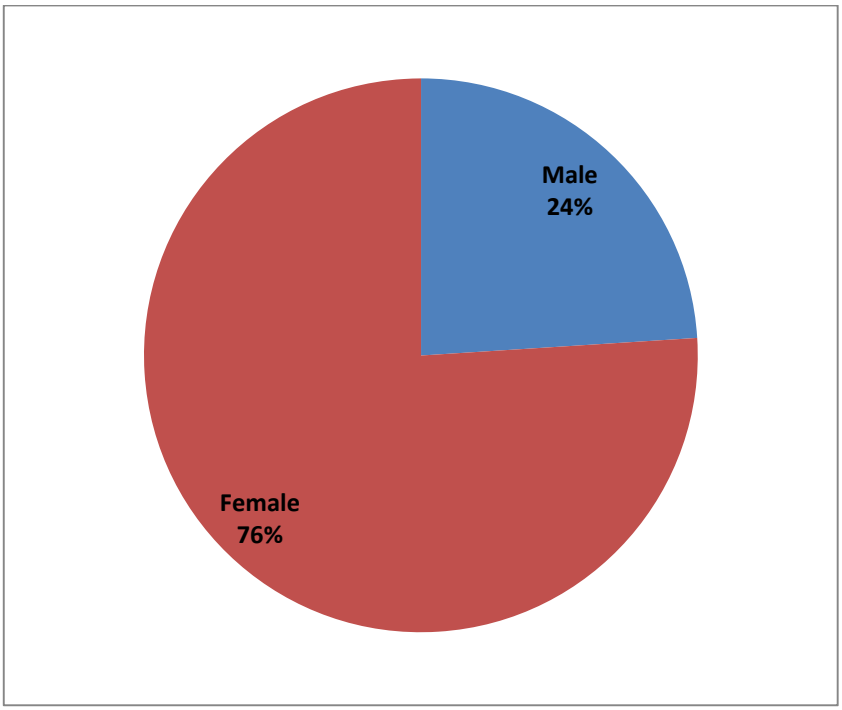


Figure 2 **: SEX DISTRIBUTION**

In our study females were more commonly affected in the ratio of 3.17 : 1.

Out of 50 patients 38 (76%) were females and males 12 cases(24%).

Table 3 **DIET DISTRIBUTION**

Diet	Number of Patients	Percentage
Vegetarian	13	26%
Mixed	37	74%

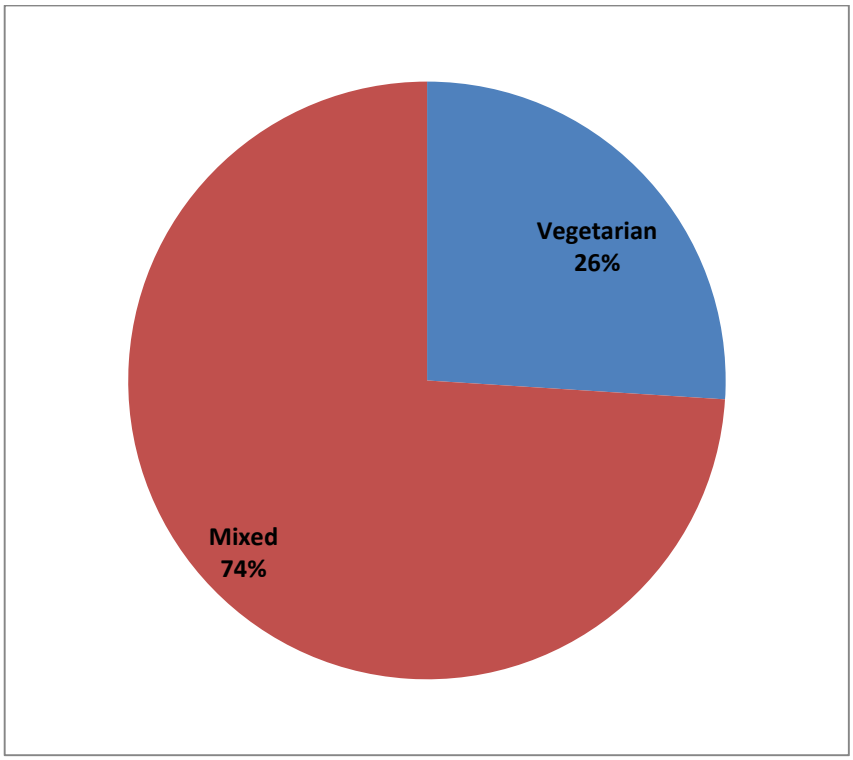


Figure 3 **DIET DISTRIBUTION**

74% cases (37 patients)consumes mixed diet while remaining were vegetarians.

Table 4 :CLINICAL PRESENTATION OF GALL STONE

Clinical Symptoms	Number of Patients	Percentage
Pain	50	100%
Fever	20	40%
Dyspepsia	16	32%
Nausea/ Vomiting	22	44%

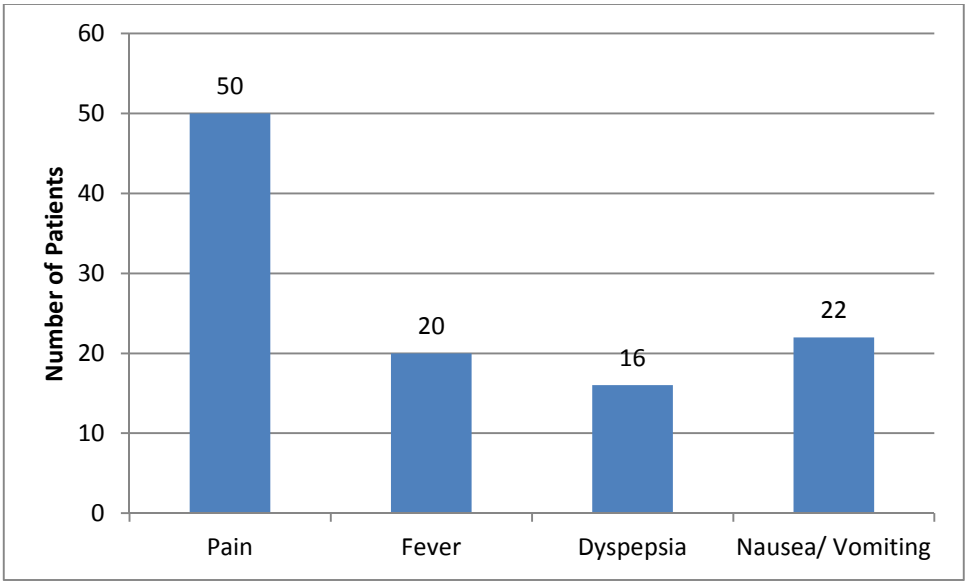


Figure 4 CLINICAL PRESENTATION OF GALL STONE

The most common clinical presentation among the cases studied was abdominal pain, all the cases studied presented with abdominal pain(100%). The second most common presentation was nausea/vomiting, which was the presenting symptom in 22 cases (44%) followed by fever 20(40%) and dyspepsia 16(32%).

Table 5 : SURGICAL TREATMENT

Surgery	Number of Patients	Percentage
Lap	39	78%
Open	8	16%
Lap converted to Open	3	6%

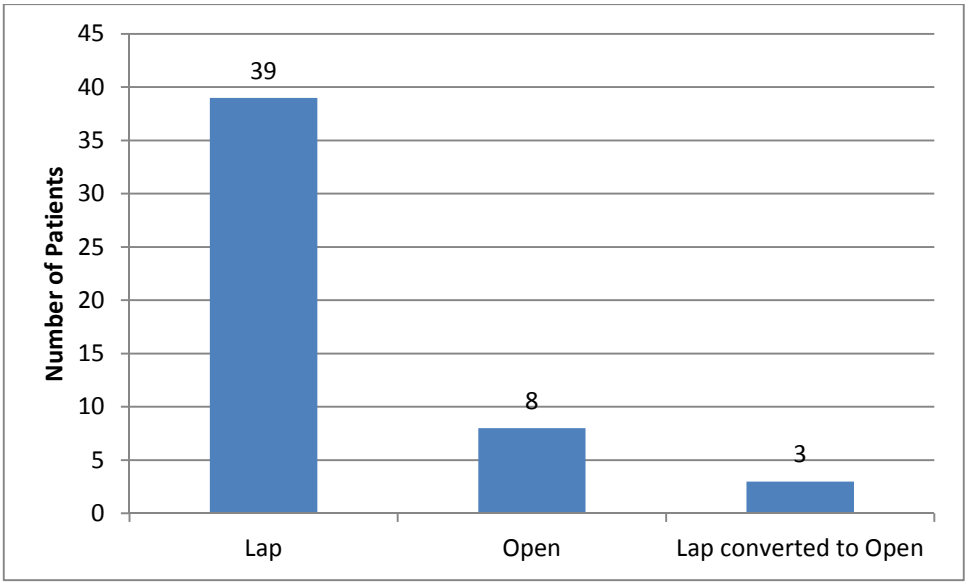


Figure 5: SURGICAL TREATMENT

The most common modality of surgery performed for our patients was laparoscopic cholecystectomy in 39 patients(78%) while remaining cases were operated by open method. 3cases(6%) were converted from laparoscopic to open cholecystectomy.

Table 6 :COLOUR OF GALL STONES

Type of Stone	Number of Patients	Percentage
Cholesterol/ Yellow stone	20	40%
Pigment/ Black stone	30	60%

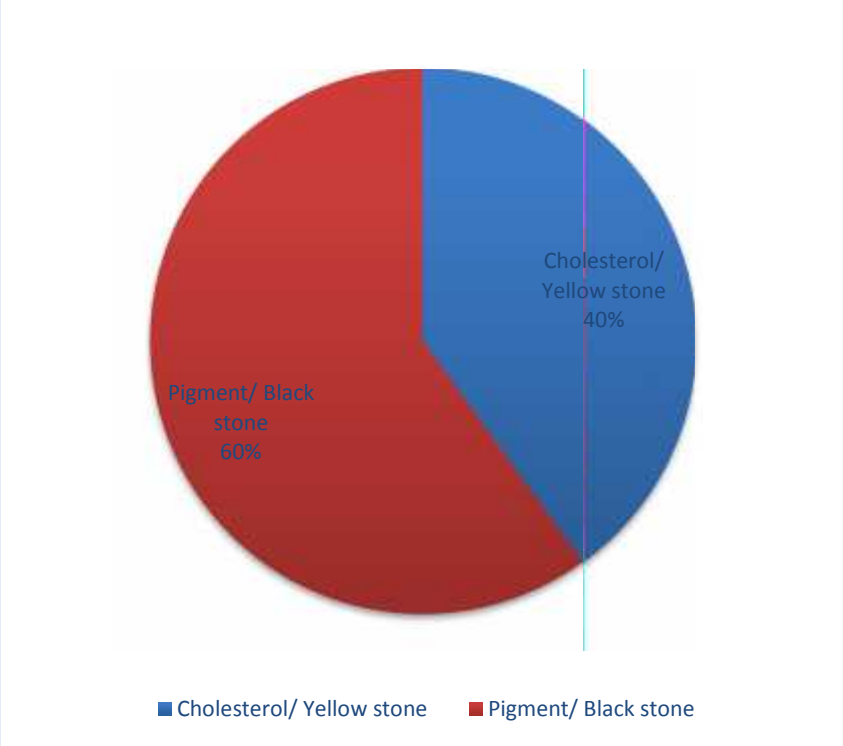


Figure 6: COLOUR OF GALL STONES

In our study most of the stones recovered from the gall bladder were Black/Pigment stones , which were found in 30 (60%) cases.

Table 7 :BACTERIOLOGY OF BILE CULTURE IN GALL STONE DISEASE

Organism	Number of Patients	Percentage
E.Coli	11	22%
Klebseilla	6	12%
Proteus vulgaris	3	6%
Salmonella	2	4%
Shigella	1	2%
No growth	27	54%

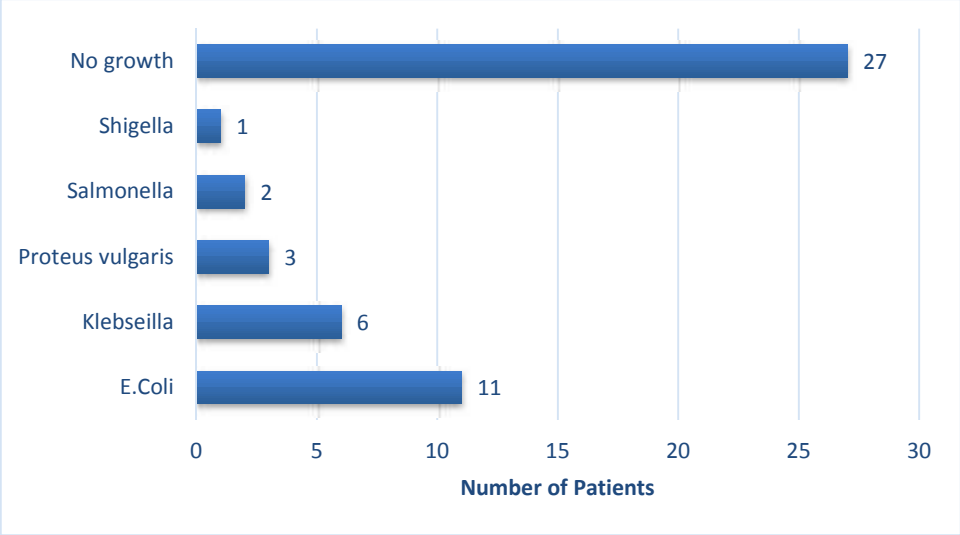
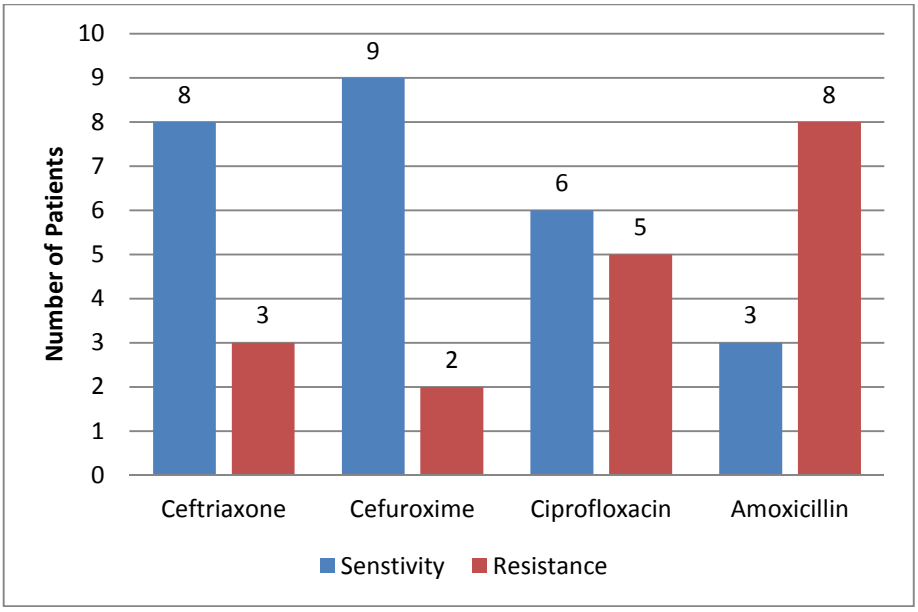


Figure7: BACTERIOLOGY OF BILE CULTURE IN GALL STONE DISEASE

Culture reports of the bile revealed organism in 23 cases(46%) while it showed no growth of organism in 27 cases(54%). E.Coli was the most common organism in 11 patients(22%) followed by Klebseilla 6 (12%),proteus vulgaris 3 (6%), salmonella 2(4%) and shigella 1(2%). Out of 23 cases with microbial growth in bile, 17 were from pigment stones and 6 were from cholesterol stones.

TABLE 8: ANTIBIOTIC SENSITIVITY FOR E.COLI

Antibiotics	Senstivity		Resistance	
	Number of Patients	Percentage	Number of Patients	Percentage
Ceftriaxone	8	73%	3	27%
Cefuroxime	9	82%	2	18%
Ciprofloxacin	6	55%	5	45%
Amoxicillin	3	27%	8	73%

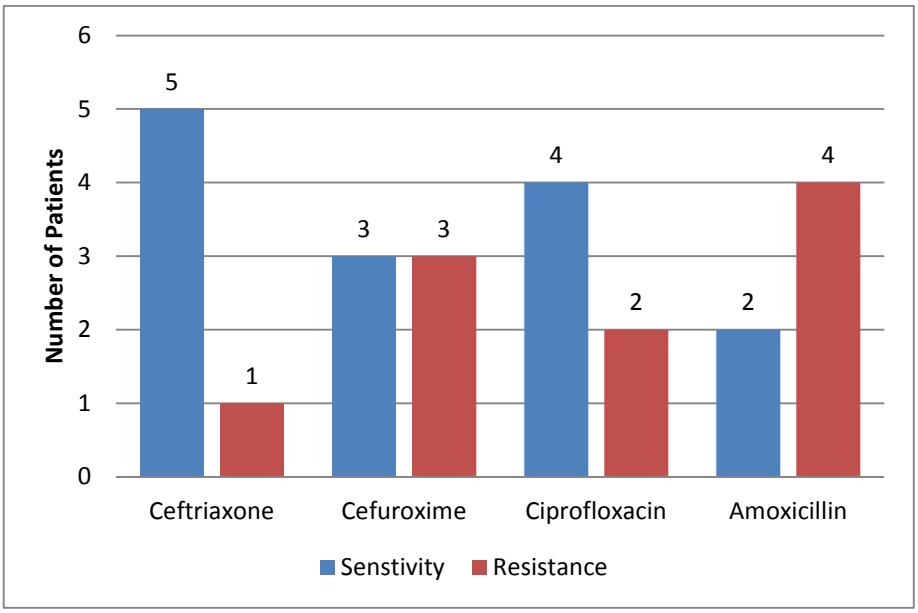


On culture and sensitivity test, E.Coli showed maximum sensitivity to cefuroxime in 9 cases(82%) followed by ceftriaxone in 8 patients(73%).

E.coli showed high resistance to amoxicillin in 8 patients (73%)followed by ciprofloxacin in 5 cases(45%)

TABLE 9: ANTIBIOTIC SENSITIVITY FOR KLEBSIELLA:

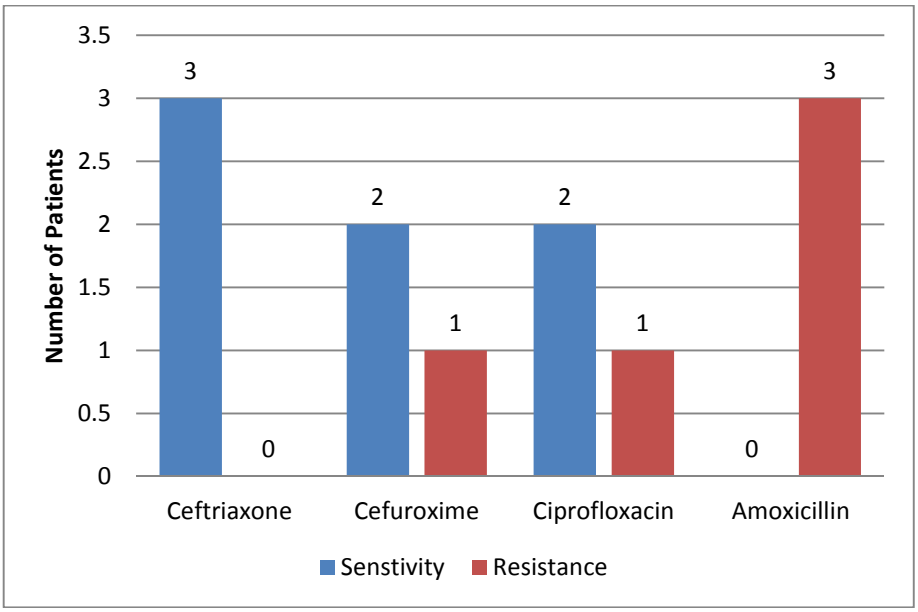
Antibiotics	Senstivity		Resistance	
	Number of Patients	Percentage	Number of Patients	Percentage
Ceftriaxone	5	83%	1	17%
Cefuroxime	3	50%	3	50%
Ciprofloxacin	4	67%	2	33%
Amoxicillin	2	33%	4	67%



Klebseilla showed high sensitivity to *Ceftriaxon*e in 5 (83%) patients. The resistance of *Klebseilla* was noted maximum to Amoxicillin which was in 24(67%) patients followed by resistance to Cefuroxime in 3 (50%).

TABLE 10: ANTIBIOTIC SENSITIVITY FOR PROTEUS:

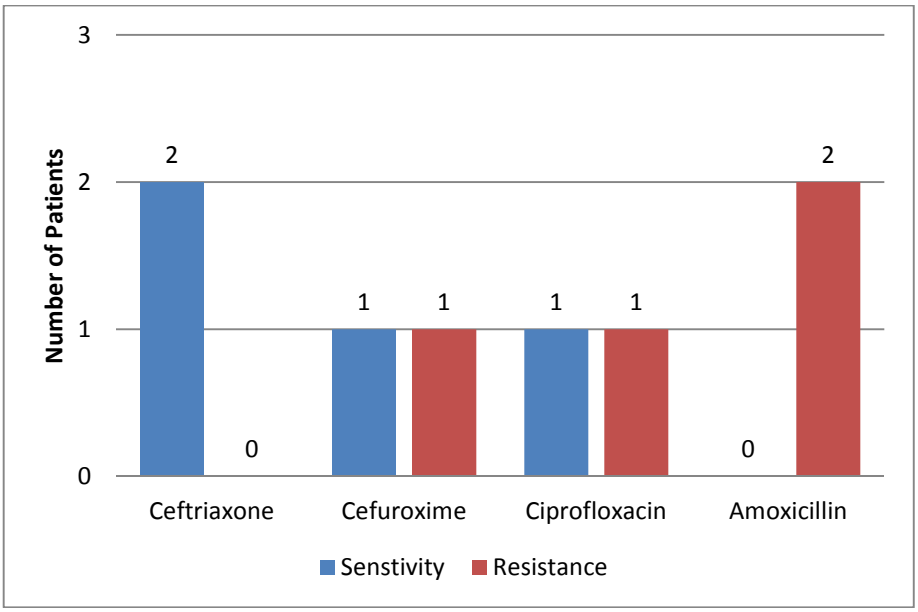
Antibiotics	Senstivity		Resistance	
	Number of Patients	Percentage	Number of Patients	Percentage
Ceftriaxone	3	100%	0	0%
Cefuroxime	2	67%	1	33%
Ciprofloxacin	2	67%	1	33%
Amoxicillin	0	0%	3	100%



In culture and sensitivity test, all 3 cases of *Proteus vulgaris* were sensitive to ceftriaxone (100%) followed by cefuroxime 2(67%) and ciprofloxacin 2 (67%). Amoxicillin resistance was noted in all cases.

TABLE 11: ANTIBIOTIC SENSITIVITY FOR SALMONELLA:

Antibiotics	Senstivity		Resistance	
	Number of Patients	Percentage	Number of Patients	Percentage
Ceftriaxone	2	100%	0	0%
Cefuroxime	1	50%	1	50%
Ciprofloxacin	1	50%	1	50%
Amoxicillin	0	0%	2	100%



Salmonella was found in bile culture of 2 patients . Both cases were highly sensitive to ceftriaxone and maximum resistance was shown to amoxicillin.

DISCUSSION

In our study the age group of 51 – 60 years (13 cases) were more commonly affected (26%), followed by 31-40 (22%) and 61-70 years (22%) age group. Females were more commonly affected in the ratio of 3.17: 1. Out of 50 patients 38 (76%) were females and males 12 cases (24%). In a study by Thapa SB. et al.[21] the total number of patients presenting with symptomatic cholelithiasis were 259. Out of these, male and female patients were 64 (24.71%) and 195 (75.29%) respectively with M:F ratio of 1:3., which was in concurrence with our study.

As per literature gall stone disease is more common in fat, fertile, female of forty. Essenhigh (1996) found this female to male ratio 2.4:1 with maximum number of cases between 60 and 70 years of age. Similar observations were given by National Academy of Medical Sciences in Nepal. However in the study of C-Y Chen et al 1995 the incidence is more common in males.

Since dietary habits place an important role in the pathogenesis of gall stones, dietary habits of the patients were analysed. 74% cases (37 patients) consumes mixed diet in our study.

The most common clinical presentation among the cases studied was abdominal pain, all the cases studied presented with abdominal pain (100%).

The second most common presentation was nausea/vomiting, which was the presenting symptom in 22 cases (44%) followed by fever 20(40%) and dyspepsia 16(32%).The observations of our study were similar to that of Multicentre Italian Study of Cholelithiasis, DIEHL et al and Kelinische waarde van et al Netharlands.

The most common modality of surgery performed for our patients was laparoscopic cholecystectomy in 39 patients (78%) while open cholecystectomy was done for 8 cases. 3 cases (6%) were converted from laparoscopic to open cholecystectomy for practical difficulties.

In our study most of the stones recovered from the gall bladder were Black/Pigment stones, which were found in 30 (60%) cases. This result similar to the observations made by Pammysinha et al.

Culture reports of the bile revealed organism in 23 cases (46%) while it showed no growth of organism in 27 cases(54%).In different studies, bacterial growth in bile culture was found to be 16-54% [11-17,22-25.]

E.Coli was the most common organism in 11 patients(22%) followed by Klebseilla 6 (12%), proteus vulgaris 3 (6%), salmonella 2(4%) and shigella 1(2%). Out of 30 cases with pigment stones, 17 showed growth (57 %) and out of 20 cholesterol stones only 6 cases (30%) showed microbial growth in bile culture. Our finding were similar to study by Abeysuriya et al [13], in which

bacterial isolates were significantly more common in pigment stone-containing bile than in cholesterol stone-containing bile. In a study by masahisa tabata[6] et al incidence of bacteria was quite high in bile pigment calcium stones and in combination stone cases . In contrast, in black stone cases, the incidence was found to be extremely low

In a study by Capoor et al [3], total of 104 bile samples were studied and bacteria were isolated in 37 samples (35.6%). The most common organisms isolated were *Escherichia coli* (11, 29.7%), *Klebsiella pneumoniae* (10, 27%), *Citrobacter freundii* (3, 8.1%), Salmonella enterica serovar typhi (3, 8.1%), *Pseudomonas aeruginosa* (2, 5.4%), *Acinetobacter* spp. (1, 2.7%), *Candida krusei* (1, 2.7%), *Staphylococcus aureus* (1, 2.7%). Polymicrobial infection of *P. aeruginosa* with *K. pneumoniae* was observed in 4 patients (3.8%).

In a study by Ballal et al [4], a total of 125 bile samples along with 25 gall stones were processed for both aerobic and anaerobic microorganisms. Bile cultures grew bacteria in 88 (70.4%) of 125 patients. Analysis of the bacterial flora showed that Escherichia coli was the most common isolate both in bile as well as in gall stones which was isolated either singly or in association with other organisms in clinical specimens. *Salmonella typhi* was isolated from 2 bile samples followed by *Klebsiella*. Maximum isolates 34 (45.4%) were seen in age groups between 51-60 years.

In a study by Ahmaad Maqsood et al[20], positive bile culture were found in only 25 out of 106 patients (23.6%) with cholecystectomy for symptomatic gallstones E. coli was the most common cultured organism in 10 (40%) patients, Klebsiella in five (20%) patients, Pseudomonas in five (20%) patients, Proteus in two (8%) patients, Staphlococcus aureus in two (8%) patients, and mixed organisms were cultured in one patient (4%). Cefoperazone with sulbactum and amikacin were the most effective antibiotics.

Our study were in contrast to study by Dhiel et al [26]and Thapa SB. et al[24] in which pseudomonas is the most common organism in bile culture.

Abeysuriya et al [13], performed a case control study of 70 bile samples (35 cholesterol and 35 pigment stones from 51 females and 19 males) from patients who underwent laparoscopic cholecystectomy for uncomplicated cholelithiasis, and 20 controls (14 females and 6 males, aged 33-70 years with a median age of 38 years) who underwent laparotomy and had no gallbladder stone shown by ultrasound scan. The bile samples were aerobically cultured to assess microflora and their antibiotic susceptibility. 38 (54%) of the 70 patients with gallstones had bacterial isolates. 9 isolates (26%) were from cholesterol stone-containing bile and

29isolates (82%) from pigment stone-containing bile (P = 0.01, t test). Twenty-eight of these 38 (74%) bile samples were shown positive only after enrichment in brain heart infusion medium (BHI) (P = 0.02, t test). The overall bacterial isolates from bile samples revealed *E. coli* predominantly, followed by *P. aeruginosa*, *Enterococcus* spp, *Klebsiella* spp. and *S. epidermidis*. There were no bacterial isolates in the bile of controls after either direct inoculation or enrichment in BHI.

In a study by sattar I et al[10] ,36 out of 100 patients with cholelithiasis had positive bile culture. The most common organism was E. coli (17 patients) followed by Klebsiella (9), Pseudomonas (6), Staphylococcus aureus (2), Salmonella (1) and Bacteroids fragalis (1) patient. In this study, most of the biliary organisms were highly sensitive to the 2nd generation cephalosporins and quinolones.

In a study by Özturk et al[31], 114 patients who underwent cholecystectomy for various reasons were included in the study. Bacterial growth was detected in the bile culture of 15 patients (13.1%). The most commonly isolated bacteria were *Enterococcus* spp (4 patients, 26.6%), *Escherichi*a *coli* (3 patients, 20%) and *Enterobacter* spp (3 patients, 20%). The bile culture positivity rate was highest in patients with acute cholecystitis combined with choledocolithiasis (3 patients, 100%). The bile culture

bacterial growth was highest in patients over 60 years of age (10 patients,27%) and in those with concomitant illness (9 patients, 23.6%). Postoperative surgical site infection was detected in only one patient; there were no surgical site infections in patients with a positive bile culture.

In another study, Bacteria isolated in gallbladder bile culture were *E. coli* (30%), *Enterobacter* sp. (15%), *Staphylococcus aureus* (10%), *Streptococcus faecalis* (15%), *Klebsiella* (5%), *Serratia* (2.5%), *Streptococcus* (2.5%), *Streptococcus* sp (20%).[32]

Although surgical intervention remains the mainstay of therapy for acute cholecystitis and its complications, however before elective or emergency cholecystectomy a period of hospitalization is required. In the current study, the empirical antibiotics were given according to recommended guidelines[8,9] and these were changed as culture and sensitivity results were available. As postoperative complication of wound infection, abscess formation or sepsis are reduced in antibiotic treated patients. In brief, for mild cases of biliary colic, the administration of non-steroidal anti-inflammatory drugs (NSAIDS) is recommended to prevent progression of inflammation (recommendation grade A). For moderate infection, agents with a narrow spectrum of activity such as cefuroxime or ciprofloxacin plus metronidazole are preferred. For severe infections, combination drugs or carbapenem are

recommended. The latter also required hydration and electrolyte correction and elimination of oral intake. In our study, on culture and sensitivity test, *E. Coli* showed high sensitivity to Cefuroxime in 9 (82%) cases followed by Ceftriaxone in 8 (73%) patients. *E. coli* showed high resistance to Amoxicillin in 8 (73%) patients followed by resistance to Ciprofloxacin in 5 (45%) patients. *Klebseilla* showed high sensitivity to Ceftriaxone in 5 (83%) patients. The resistance of *Klebseilla* was noted maximum to Amoxicillin which was in 4 (67%) patients followed by resistance to Cefuroxime in 3 (50%). *Proteus* showed high sensitivity to Ceftriaxone in 3 (100%)cases while the resistance was high to Amoxicillin 3 (100%) patients. Salmonella showed showed high sensitivity to Ceftriaxone (100%) while the resistance was high to Amoxicillin (100%).

In our series of patients, majorities of isolates were susceptible to Cefuroxime and ceftriaxone and were resistant to Amoxicillin. It seems that history of previous and recurrent hospitalization, prolong hospital stay and wide spread use of broad spectrum antibiotics has led to the selective survival and emergence of resistant organism[27,28]. Therefore, antimicrobial activity against potential causative organisms, the severity of the cholecystitis, and the local susceptibility pattern must be taken into consideration when prescribing drugs. Prior studies have observed excellent responses with piperacillin-

tazobactam and meropenem with quinolones for Gram-negative isolates and vancomycin for Gram-positive isolates being preferred.[29,30]

Therefore, antimicrobial activity against potential causative organisms, the severity of the cholecystitis, and the local susceptibility pattern must be taken into consideration when prescribing drugs.

CONCLUSION

From observation of our prospective study of 50 cases, the following conclusions were derived

- Gallstone disease is common in females than in the males and the age group was 51 to 60 years.
- All the cases presented with right hypochondriac pain. Nausea and vomiting were present in 22 cases and fever was present in 20 cases.
- Ultrasound abdomen was the main investigation to detect gall stones and MRCP to know the anatomy of common bile duct.
- In our study, 8 patients underwent open cholecystectomy, 39 patients underwent laparoscopic cholecystectomy and 3 patients underwent laparoscopy which was converted to open cholecystectomy for practical difficulties.
- 30 cases in our study showed pigment stones and 20 cases were cholesterol stones.
- 23 cases showed organisms in bile culture The most common microorganism isolated from bile culture was E.Coli (11 cases) followed by klebsiella (6 cases), proteus vulgaris (3), salmonella (2) and shigella(1).

- These organisms showed maximum sensitivity to ceftriaxone and cefuroxime. The empirical antibiotics used for the treatment of symptomatic gall stone disease must cover these common bacteria.
- Ceftriaxone and/or Cefuroxime must be a part of empirical regime as it will help in reducing the morbidity associated with symptomatic cholelithiasis.

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ANNEXURE

ANNEXURE - I PROFORMA

NAME :

AGE : I.P. No. SEX : WARD No:

RELIGION : UNIT : OCCUPATION

D.O.A. : ADDRESS

D.O.S. : D.O.D.

COMPLAINTS

1. Abdominal Pain
2. Sensation of Fullness
3. Nausea and Vomiting
4. Jaundice
5. Fever
6. Mass
7. Itching over the body
8. Appetite
9. Bowel habits
10. Colour of the urine

HISTORY OF PRESENTING ILLNESS

1. Abdominal Pain

a. Mode of onset

b. Site of pain

c. Character of pain

d. Duration of each attack

e. Radiation or referred pain

f. Effect of pressure and respiration

g. Relation to food

h. Relieving factors / Aggravating factors

2. Sensation of Fullness

3. Nausea and vomiting

4. Jaundice

a. Duration

b. Sites

c. Intensity

d. Type

e. Itching

f. Variation in intensity

g. Recurrent attacks

5. Fever

a. Duration

b. Type

c. Severity

d. Diurnal variation

e. Associated with chills and Rigors

6. Mass / Lump

a. Site

b. Mode of onset

c. Progression

d. Pain in the swelling

e. Any associated factors

f Blood disorders

PAST HISTORY

1. Jaundice with pain and fever

2. Similar attacks of pain

3. Blood transfusion

4. Vaccination

5. Drugs

6. Abdominal surgery like

7. Enteric fever

PERSONAL HISTORY

1. Diet
2. Appetite
3. Dislike for fatty food
4. Sleep
5. Alcohol amount and quantity
6. Smoking
7. Bowel habits
    a. Amount of stool
    b. Colour of stool
8. Micturition
    a. Amount of urine
    b. Colour of urine

MENSTRUAL HISTORY

1. Menarche
2. LMP
3. PARA
4. Post Partum
5. Abortion

FAMILY HISTORY

1. Jaundice

2. Gallstones

3. Diabetes

TREATMENT HISTORY OF ALLERGY

PHYSICAL EXAMINATION

1. General appearance

2. Built

3. Anemia

4. Cyanosis ±

5. Clubbing ±

6. Lymphadenopathy

7. Jaundice

8. Anasarca

9. Thrombophlebitis

10. Spider naevi

VITAL SIGNS

1. Pulse

2. Blood pressure

3. Respiratory rate

4. Temperature

ABDOMINAL EXAMINATION

Inspection

Contour

Movement of all quadrants with respiration

Skin

Engorged veins

Visible pulsations and peristalsis

Umbilicus

Hernial orifices

External genitalia

Swelling

- Site - Surface
- Size - Borders
- Shape - Movement with
- Extent - Plane of the swelling

Palpation

1. Local rise of temp/hyperaesthesia
2. Tenderness
3. Position
4. Size
5. Shape
6. Extent
7. Surface
8. Borders
9. Mobility
10. Murphy's sign ±
11. Consistency
12. Plane of the swelling

13. Liver

Size

Borders

Consistency

Surface

Mobility with respiration

14. Spleen

PERCUSSION

Light percussion of abdomen

AUSCULTATION Systemic examination

Cardiovascular System

Respiratory system

Central nervous system

PROVISIONAL DIAGNOSIS INVESTIGATIONS

1. Blood

a.HB

b.TC DC

c.CT

d. PTT

e. BT

f.PT

g. RBS

h. Blood Urea

i. Serum Cholesterol

j. Serum Creatinine

2. Urine

a. Albumin c. Microscopy

b. Sugar d. Colour

3. Liver Function tests:

a. S. Bilirubin

b. S. Alkaline Phsophate

c. S. Albumin

d. S. Globulin

e. SGOT

f. SGPT

g. Total proteins

4. Ultrasound

5. Radiological examination

6. CT Scan

DIAGNOSIS

TREATMENT

Medical

Surgical - Open

Laparoscopic

Postoperative investigations

Bile culture report

Histopathological report

Sl. No.	Name	Age	Sex	IP No	DIET	USG	CLINICAL		Surgery	Type of stone	Bile culture	Sensitive to	Resistant to
							Abd. Pain	Others					
1	Balasubramanian	54	M	56017	V	+	P	F,D,N	Lap.	P	EC	CX,CO	AM,CI
2	Selvi	33	F	47665	M	+	P		Open	C	NG		
3	Chithra	48	F	45875	M	+	P	F,N	Lap.	P	KL	CX,CI,CO	AM
4	Singaperumal	35	M	59090	V	+	P	N	Lap.	C	NG		
5	Gubilal Mary	60	F	50297	M	+	P	F,N	Lap.	P	EC	CX,CO,CI	AM
6	Sivapathiyammal	53	F	82612	M	+	P	F,D,N	Lap.	C	NG		
7	Jothi	22	F	56826	M	+	P		Open	P	NG		
8	Avudaiammal	65	F	3487	M	+	P		Lap.	P	SA	CX,CI	CO,AM
9	Esakkiammal	70	F	25671	M	+	P	N	Lap.	C	NG		
10	Shamugamaiah	61	M	53577	M	+	P	D,N	Lap.	P	KL	CX,CI	AM,CO
11	Chithra	31	F	31143	V	+	P	D,N	Lap.	C	NG		
12	Murugaiah	51	M	72328	M	+	P	F	Lap.	P	EC	CO,CI	CX,AM
13	Selvi	44	F	3495	M	+	P		Lap.	P	NG		
14	Chitharaivadivoo	65	F	10481	M	+	P	F,D,N	lap to open	P	EC	CX,CO	AM,CI
15	Chellammal	64	F	49096	M	+	P		Lap.	P	KL	CX,AM	CI,CO
16	Mookandi	44	M	47869	M	+	P		Lap.	C	EC	AM,CO,CI	CX
17	Muthuammal	64	F	53085	V	+	P	D,N	Lap.	P	NG		
18	Annapushpum	58	F	63581	M	+	P	F,N	Lap.	P	EC	CX,CO	AM,CI
19	Rahmath Nisha	24	F	59498	M	+	P	N	Lap.	P	NG		
20	Ayyar	42	M	53370	M	+	P	F	Open	C	NG		
21	Annapushpum	35	F	46358	M	+	P		Lap.	C	KL	CX,CO	AM,CI
22	Ananthammal	65	F	47709	M	+	P	D,N	Lap.	P	EC	CX,AM	CO,CI
23	Mupudathy	36	F	32572	V	+	P	F	lap to open	P	SA	CX,CO	CI,AM
24	Mari	48	F	1703	V	+	P	D	Lap.	P	NG		
25	Malaiyappan	55	M	63750	M	+	P	F	Lap.	C	NG		
26	Nachiyar	56	F	76848	M	+	P	N	Lap.	P	EC	CX,CO,CI	AM
27	Paravathi	55	F	26341	M	+	P	F,D	Open	P	NG		
28	Andal	50	F	61378	M	+	P	N	Lap.	C	NG		
29	Mallika	52	F	70582	M	+	P	F,N	Lap.	P	KL	CX,CI	AM,CO
30	Chellammal	70	F	51549	V	+	P		Open	C	NG		
31	Alaghupandian	52	M	75695	M	+	P		Lap.	P	NG		
32	Iyyammal	62	F	82345	M	+	P		Lap.	P	PR	CX,CI	AM,CO
33	Komalakumari	55	F	6141	V	+	P	F,D,N	Lap.	P	NG		

Sl. No.	Name	Age	Sex	IP No	DIET	USG	CLINICAL		Surgery	Type of stone	Bile culture	Sensitive to	Resistant to
							Abd. Pain	Others					
34	Meenaichi Selvam	32	M	57135	M	+	P	N	Lap.	P	KL	AM,CI,CO	CX
35	Arokiyarani	34	F	39961	M	+	P	F	Lap.	C	NG		
36	Thangam	43	F	25864	M	+	P	D	Open	P	NG		
37	Shyed Fathima	58	F	18025	M	+	P	D,N	Lap.	P	EC	CX,AM	CO,CI
38	Chellathai	33	F	13962	V	+	P		Lap.	P	PR	CX,CO	AM,CI
39	Velammal	60	F	33824	M	+	P	F	Open	C	SG	CX,CI,AM	CO
40	Vilotmary	62	F	48522	M	+	P	F	Lap.	P	NG		
41	Usha	26	F	67622	V	+	P		Lap.	C	NG		
42	Kanthimathi	35	F	13641	M	+	P	F,D	Lap to Open	C	EC	CO,CI	CX,AM
43	Anandh Muthuraj	24	M	62037	M	+	P		Lap.	P	NG		
44	Rani	47	F	66493	M	+	P		Lap.	C	NG		
45	Rasathi	31	F	57312	V	+	P	D	Lap.	P	NG		
46	Anthony Raj	27	M	45422	M	+	P	D,N	Lap.	C	PR	CX,CI,CO	AM
47	Subaiah	65	M	23364	M	+	P	F,N	Open	C	EC	CX,CO,CI	AM
48	Rangaammal	70	F	53972	V	+	P		Lap.	P	NG		
49	Divwan Bevi	25	F	53629	M	+	P	F	Lap.	C	NG		
50	Manjula	39	F	66379	V	+	P	F,D,N	Lap.	C	NG		

V- VEGETARIAN
M-MIXED DIET

P- ABDOMINAL PAIN
F-FEVER
D-DYSPEPSIA
N-NAUSEA / VOMITING

C- CHOLESTEROL STONES
P-PIGMENT STONES

NG - NO GROWTH
EC - ESCHERICHA COLI
KL-KLEBSIELLA
PR-PROTEUS VULGARIS
SA-SALMONELLA
SH- SHIGELLA

CX-CEFTRIAXONE
CO-CEFUROXIME
CI-CIPROFLOXACIN
AM-AMOXICILLIN

LAP.- LAPAROSCOPIC CHOLECYSTECTOMY
OPEN-OPEN CHOLECYSTECTOMY
LAP.TO OPEN- LAPAROSCOPIC CONVERTED OPEN CHOLECYSTECTOMY

ABBREVIATIONS

E.coli	–	Escherichia coli
P. aeruginosa	–	Pseudomonas aerunginosa
CBD	–	Common bile duct
CCK	–	Cholecystokinin
LFT	–	Liver Function Test
MRCP	–	Magnetic Resonance Cholangio Pancreatography
ERCP	–	Endoscopic Retrograde Cholangio Pancreatography
LAP	–	Laparoscopic
HB	–	Hemoglobin
COPD	–	Chronic Obstructive Pulmonary Disease
IV	–	Intra Venous