“A CLINICAL STUDY ON PREVALENCE OF HYPOTHYROIDISM IN DIAGNOSED CASES OF GALL STONES ”

A DISSERTATION SUBMITTED TO THE TAMILNADU

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In partial fulfillment of the requirement for the degree of

M.S. (GENERAL SURGERY)

BRANCH - I

DEPARTMENT OF GENERAL SURGERY

TIRUNELVELI MEDICAL COLLEGE

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PROTOCOL TITLE: A CLINICAL STUDY ON PREVALENCE OF HYPOTHYROIDISM IN DIAGNOSED CASES OF GALL STONES

PRINCIPAL INVESTIGATOR: Dr.P.DINESHKUMAR MBBS

DESIGNATION OF PRINCIPAL INVESTIGATOR: POST GRADUATE STUDENT

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Dear , Dr.P.Dineshkumar, MBBS., The Tirunelveli Medical College Institutional Ethics Committee (TIREC) reviewed and discussed your application during the IEC meeting held on 25.11.2016.

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	☐
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13.	Memorandum of Understanding (MOU)/Material Transfer Agreement (MTA)	☐
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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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3

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ABBREVIATIONS

GB – GALL BLADDER

CBD- COMMON BILE DUCT

SO- SPHINCTER OF ODDI

CCK- CHOLECYSTOKININ

USG- ULTRASONOGRAM

CT- COMPUTED TOMOGRAPHY

MRCP- MAGNETIC RESONANCE CHOLANGIOPANCREATOGRAPHY

ERCP- ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY

TSH- THYROID STIMULATING HORMONE

TR- INTRANUCLEAR THYROID RECEPTORS

LDL- LOW DENSITY LIPOPROTEIN

HDL- HIGH DENSITY LIPOPROTEIN

TPO- THYROID PEROXIDASE

CHAPTER 1

INTRODUCTION

1.1 BACKGROUND[1,2,3]

The possible explanations to relate the Gall stone disease with Hypothyroidism are:

1) Disturbance of lipid metabolism in hypothyroidism causes increase in serum cholesterol level which leads to supersaturation of bile with cholesterol. It leads to change in composition of bile and formation of cholesterol stones.
2) Recent studies demonstrated low bile flow in hypothyroid patients. It leads to stagnation of bile in gall bladder and it allows more time for nucleation process for gall stone formation.
3) Sphincter of oddi has thyroid hormone receptors and thyroxine has direct prorelaxing effect on the sphincter smooth muscle cell.
4) In hypothyroidism, the effect of UDP glucuronyl transferase get decreased. So the conjugation of bilirubin gets affected. Increase in unconjugated bilirubin result in formation of pigment stones.
5) In animal model (Rabbits), thyroxine usage dissolves the fatty diet induced gall stones.[3]

1.2 AIM:

The aims of this study are

1) To study the prevalence of hypothyroidism in patients diagnosed with cholelithiasis/ choledocholithiasis.
2) To assess if thyroid profile is warranted in patients with biliary stone disease.

CHAPTER 2

REVIEW OF LITERATURE

2.1 EMBRYOLOGY [4,5,6,7]:

The gall bladder, bile ducts and liver begins to develop during 4th week of embryonic life as a ventral bud from the most caudal aspect of foregut. This bud is called hepatic diverticulum, and it grows between the layers of ventral mesentery.

The hepatic diverticulum has 2 components: pars hepatica and pars cystica.

Pars hepatica is the most cranial component , gives rise to liver, intra hepatic bile ducts and common hepatic duct.

Pars cystica is the most caudal component, gives rise to cystic diverticulum. The cystic diverticulum is the analge of gall bladder and cystic duct.

The original hepatic diverticulum elongates to form common bile duct.

These structures begins as solid cords. Establishment of lumen throughout the biliary tract occurs at 8 week of gestation.

2.2 GROSS ANATOMY:

The gall bladder is a thin walled, slate-blue colored, sac like, globular or pear shaped hollow viscus organ with a capacity of about 50ml. It measures about 7.5cm to12.5cm in length and 3cm in breadth at its widest part. It lies in a fossa in the right lobe of liver on its visceral surface just adjacent to the caudate lobe. It is attached to liver by a loose areolar tissue, rich in small blood vessels and lymphatics. The extra hepatic portion of the gallbladder is covered by peritoneum. Fewer than 10% of the gallbladder is covered by peritoneum and is attached to the liver by a narrow mesentery from the undersurface of liver.

The gallbladder typically lies in close proximity to duodenum, pylorus, hepatic flexure of right colon and right kidney. Its anatomical subdivisions are fundus, body and neck that terminates in a narrow infundibulum. Fundus is the rounded, blind portion of gallbladder that extends for a short distance beyond the sharp lower border of liver. It is directed downwards, forwards and to the right to occupy a cystic notch in the margin of liver. When the gall bladder is full, the fundus comes in contact with the parietal peritoneal layer of the anterior abdominal wall just behind the right 9th costal cartilage where the transpyloric plane crosses the right costal margin, at the lateral border of right rectus sheath. The fundus of gall bladder lies just to the left of hepatic flexure. It is generally the least well

vascularised portion of the gallbladder and therefore is more susceptible to ischemic changes, including perforation.

The body constitutes the majority of gallbladder, directed upwards and backwards and to the left towards the right end of porta hepatis. It is in relation by its upper surface with the liver; by its undersurface with the right part of transverse colon and further back with the superior part of duodenum and the upper end of the descending part.

The neck is a narrow portion of the upper end of gallbladder that lies between the body and cystic duct region. It curves upwards and forwards, and then turning abruptly backwards and downwards, becomes continuous with cystic duct. When the liver is in normal position, the neck of gall bladder lies at a higher level than its fundus and against the free edge of lesser omentum. At its point of continuity with cystic duct there is a constriction. The neck is attached to the liver by a areolar tissue in which the cystic artery is embeded.

The infundibulum is a small bulbous diverticulum of gall bladder, typically lying on the inferior surface of the right wall of neck of the gallbladder, and it projects downwards and backwards towards the duodenum. This is often termed as Hartmann's pouch has been widely regarded as a constant feature of normal gallbladder.

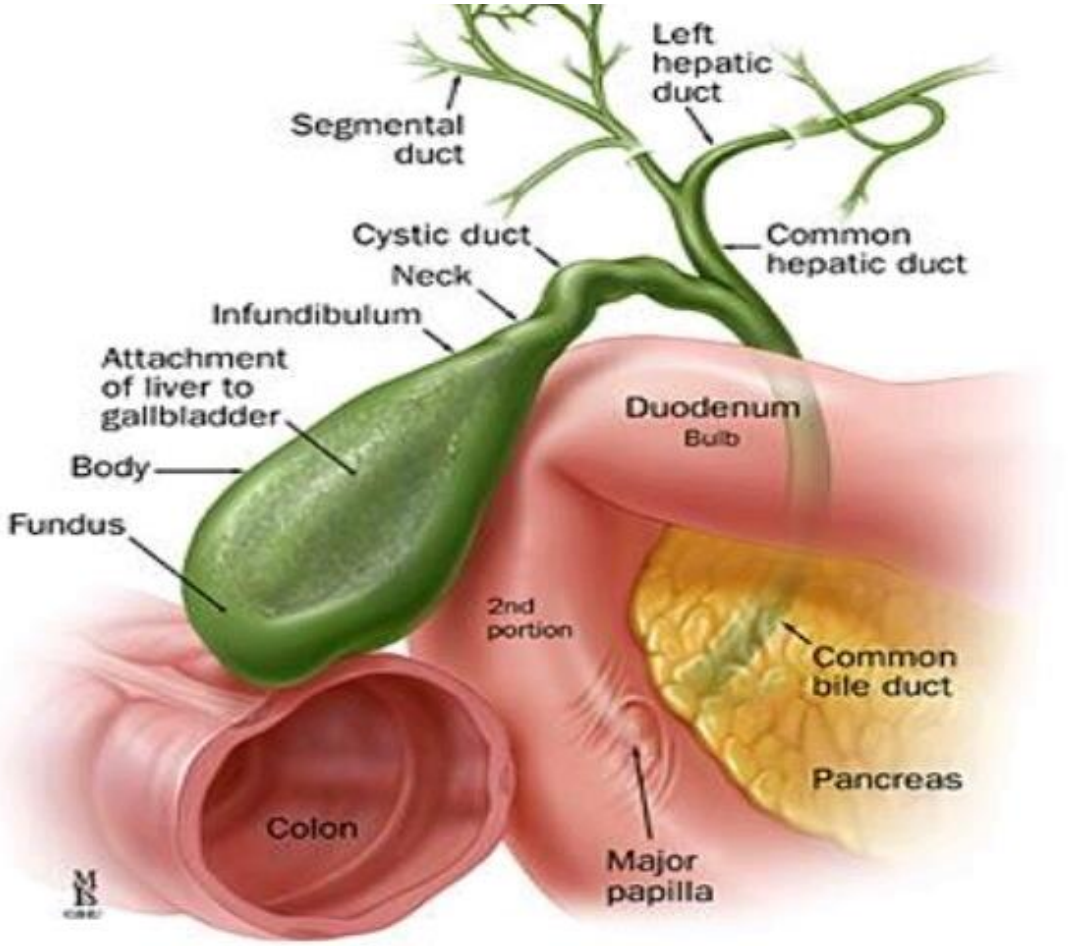

Fig 1: overall arrangement of intrahepatic and extra hepatic biliary tree

The cystic duct is a tubular structure, which connects the gall bladder to common bile duct. It is a continuation of the neck and is 2cm to 3cm in length and 2mm to 3mm in diameter. It passes downwards, backwards and to the left from the neck of gallbladder towards the porta hepatis. It joins with the common hepatic duct between the two layers of peritoneum, that forms the free edge of the lesser omentum about 1cm above the duodenum and anterior to the right hepatic artery and its cystic branch. Cystic duct runs parallel to common hepatic duct for a short distance and adheres with it.

Calot's triangle is the space bounded by cystic duct inferiorly; common hepatic artery medially; cystic artery superiorly. This was described by Jean francois calot in 1891. It is a surgical landmark while doing cholecystectomy to avoid damage to the extra hepatic biliary system

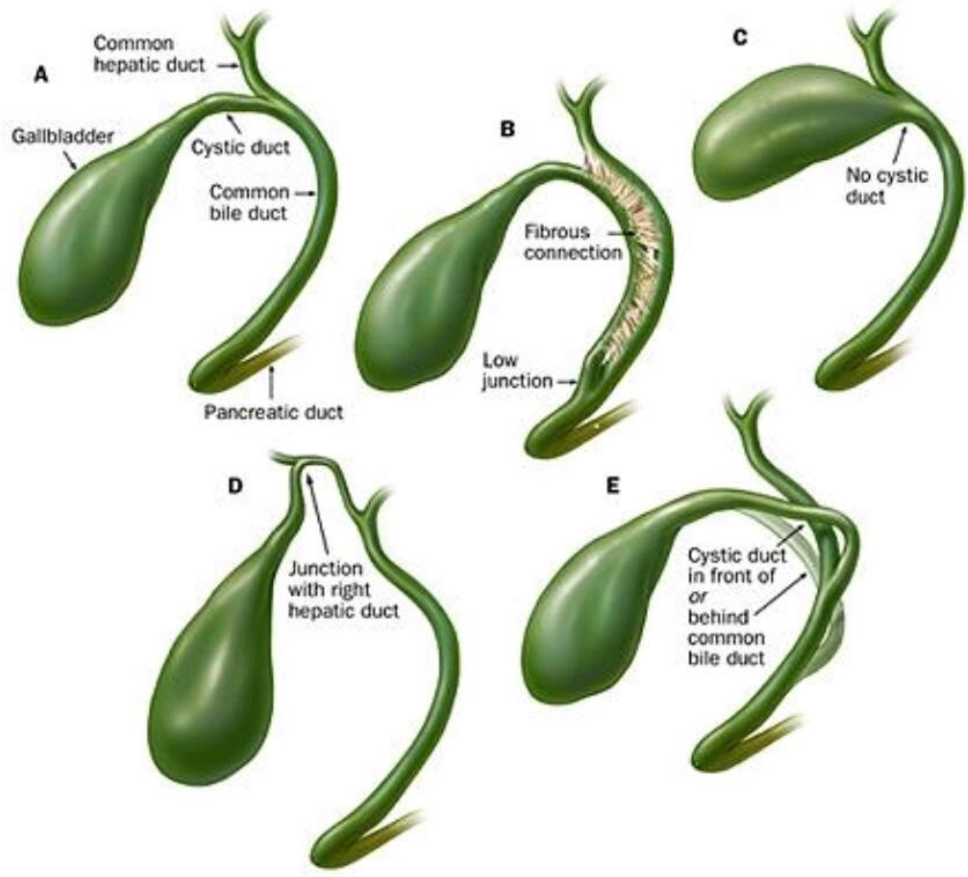

Fig 2: Anatomical variations of cystic duct

The common bile duct, about 7.5cm in length and it is formed by the union of cystic and common hepatic ducts. It lies within the hepato duodenal ligament, to the right of the hepatic artery and anterior to the portal vein. It is divided into four parts. The supraduodenal portion, about 2.5cm in length, runs in the free edge of lesser omentum. The retro

duodenal portion lies behind the second part of duodenum. The infra duodenal portion lies in a groove on the neck of pancreas. The intra duodenal portion passes obliquely through the wall of second part of the duodenum and opens into the duodenum on the summit of papilla of vater. This structure surrounds the orifice of bile duct and is composed of duodenal tissue and muscular elements which makes the sphincter of oddi. Typically, there is a common channel, which both the pancreatic and distal common bile duct joining, which opens through single orifice into the duodenum. This common channel is believed to be quite important in the pathogenesis of gall stone pancreatitis.

2.3 HISTOLOGY:

Histologically the gall bladder consists of three distinct layers: serosal, fibromuscular and mucosal layer. The serosal layer is derived from peritoneum and it completely invests the fundus, but covers only the inferior surface and sides of the body and neck of gall bladder. Beneath it has subserosal layer of areolar tissue. The fibromuscular layer is a thin layer of fibrous tissue, mixed with nonstriated muscular fibres; these are in loose bundles disposed in longitudinal, circular and oblique directions; arranged in a criss cross manner, being particularly well developed in the neck. The mucosal layer is loosely connected with the fibromuscular layer. This layer contains indentations of the mucosa that sink into the muscle

coat, these are called crypts of Luschka. The epithelium consists of a single layer of columnar cells. The mucosa in neck secrete mucus but mainly it has absorptive function.

In the cystic duct, the mucosa is elevated into 5 to 12 cresentric folds, called as, “Valves of Heister”. They appear to play an important role in the passage of bile into and out of gall bladder. Microscopically the layers of bile duct appear similar to that of gall bladder. The outer fibromuscular layer has strong connective tissue fibers with scant muscular elements, its density increases in the more distal segments of the duct. The mucosa is composed of a single layer of columnar epithelium. Electron microscopic studies have demonstrated the presence of microvilli and cilia in the apical membrane of the ductal cells. These structures are thought to be important in the mixing and motor activities of the duct.

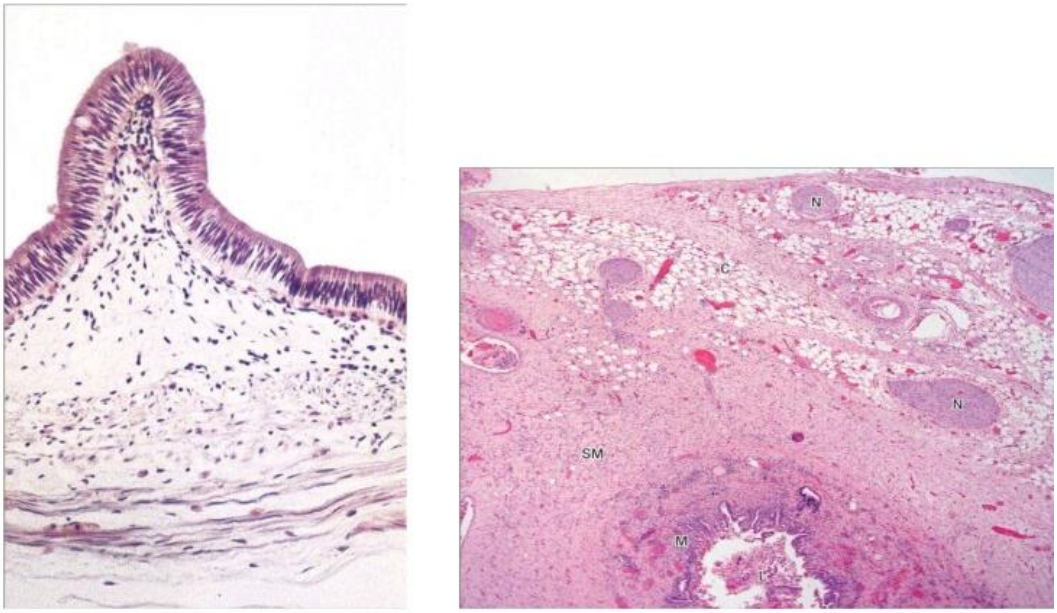

Fig 3: Histology of gall bladder

2.4 ARTERIAL SUPPLY:

The major blood supply of the gall bladder is through the cystic artery, which is typically a branch of right hepatic artery. The gall bladder also receives many small vessels from its hepatic bed. Branches from cystic artery supplies the common bile duct (upper part) and hepatic duct. The lower part of the bile duct receives branches from the posterior superior pancreatico-duodenal artery. The right hepatic artery gives branches to the middle part of the bile duct.

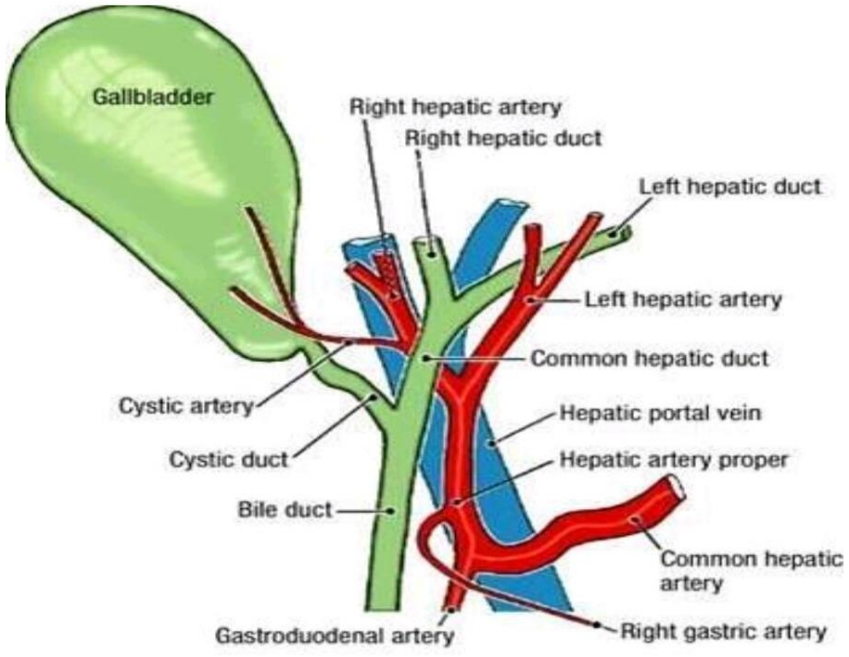

Fig 4: Normal anatomy of cystic artery

2.5 VENOUS DRAINAGE:

The veins draining the gall bladder vary considerably. Those from its upper surface lies in the areolar tissue between the gallbladder and liver and it runs directly into the liver through the fossa of gallbladder to join with the hepatic veins. Those from the rest of the gall bladder join to form one or more cystic veins on its neck, and these commonly enter into liver, either directly or after joining with the veins draining the hepatic ducts and upper part of the bile duct.

2.6 LYMPHATIC DRAINAGE:

The lymphatics draining the gall bladder tend to be more important for both inflammatory and malignant disease of gall bladder. The lymphatic channels from the subserosal and submucosal plexus drain into cystic lymph node of Lund- the sentinel lymph node, which lies in the fork created by the junction of cystic duct and common hepatic ducts and to a node situated at the anterior border of epiploic foramen. Efferent vessels from these nodes pass through the free edge of lesser omentum to the celiac group of preaortic nodes. The subserosal lymphatic vessels of the gall bladder have connection with the subcapsular lymphatic channels of

liver, and it accounts for the frequent spread of carcinoma of gallbladder to the liver.

2.7 NERVE SUPPLY:

The wall of the gall bladder is richly innervated by both sympathetic and parasympathetic nerve fibers, which pass along the hepatic artery and its branches. Parasympathetic fibers, mainly from the hepatic branch of anterior vagal trunk, stimulates contraction of the gall bladder and relaxes the ampullary sphincter. Sympathetic fibers from the celiac ganglia, with the preganglionic cells in the lateral horn of the spinal cord segments, T7-T9 inhibits contraction of gall bladder. Autonomic plexus of the nerve lies in the muscular and sub mucosal layers. Fibers from the right phrenic nerve, through communication between phrenic and celiac plexus, appear to reach the gallbladder via hepatic plexus explaining the referred "shoulder pain" in the gall bladder pathology.

2.8 PHYSIOLOGY OF GALL BLADDER [7,8,9]:

The primary function of gall bladder is to concentrate the bile by absorption of water and sodium to acquire the greater strength and digestive power. The gallbladder and bile ducts are well adopted for the function of storing and secreting bile into the duodenum during digestion. The flow of bile in and out of the gallbladder is determined by contraction and relaxation of the sphincter of Oddi. The normal gallbladder is rarely static. Continuous cycles of partial emptying and refilling is governed by the intestinal migratory myoelectric complex between meals. During relaxation and refilling it intermittently contracts and expels pulses of bile into the duodenum. This constant fluctuation prevents formation of stone. Gallbladder tone is modulated by both vagus and circulating peptides. During cephalic phase of digestion stimulation of vagus is responsible for gallbladder contraction. During interdigestive period, the vagal neurons and circulating polypeptides mediates the contraction. Vasoactive intestinal polypeptide [VIP] released by vagal neurons inhibits gallbladder contraction and mediates post prandial filling of gall bladder. Its motility gets inhibited by truncal vagotomy and by chronic fasting.

2.9 BIOCHEMISTRY OF BILE:

Bile as it leaves the liver is composed of 97% of water, 1 to 2% of bile salts, 1% of bile pigments, cholesterol and fatty acids. The knowledge of the chemistry of the constituents of bile is essential as they have a great importance in the etiology of cholelithiasis.

Bile acids and bile salts: The bile acids of the human bile are glycocholic acid and taurocholic acids which are conjugated products of glycine and cystine with cholic acid respectively. Bile acids are present in bile as bile salts in the form of sodium glycocholate and sodium taurocholate. Human bile consists approximately 70 to 75% glycocholate and 25% of taurocholate.

Bile pigments: The biliary pigments are bilirubin and biliverdin. .Bilirubin is the chief pigment in the human bile. Biliverdin is the exudative product of bilirubin and is present in small quantity in human bile. The pigment forms about 15 to 20% of total solids in liver bile. They are derived mainly from hemoglobin and a small amount from chromoprotiens.

Lipids: The normal bile contains fatty acids, cholesterol and phospholipids. Cholesterol normally occurs to the extent of 0.04 to 0.16% in liver bile. It is present in the free state and its concentration is more in

gall bladder bile. Normally the ratio between the cholesterol and bile salts varies between 1:20 to 1:30.

Mucin: Its main constituent is mucealbumin. It increases in obstructive and inflammatory conditions of the biliary tract pathology and it forms the cementing substance in gall stones.

TABLE 1: COMPOSITION OF BILE

	LIVER BILE	GALL BLADDER BILE
Water	97.5g/dl	92g/dl
Bile salts	1.1g/dl	6g/dl
Cholesterol	0.1g/dl	0.3 to 0.9 g/dl
Bilirubin	0.04g/dl	0.3g/dl
Fatty acids	0.12g/dl	0.3 to 1.2g/dl
Lecithin	0.04g/dl	0.3g/dl
K+	5mEq/L	12mEq/L
Na+	145.04 mEq/L	130mEq/L
Cl-	100mEq/L	25mEq/L
Ca++	5mEq/L	23mEq/L
HCO3-	28mEq/L	10mEq/L

2.10 Entero Hepatic Circulation:

Following normal fatty meal, emulsification of cleavage products from triglyceride hydrolysis by pancreatic lipase results in the incorporation of fat molecules into micelles. Absorption of fat takes primarily in the upper small intestine, whereas bile acids undergo little absorption until the distal third of the small intestine is reached. In the ileum, there exists specific high affinity binding sites for the active absorption of bile acids. Due to the efficiency of this absorptive process, less than 5% of daily excreted bile reaches the large bowel. Upon absorption, bile acids enters the portal vein and return to liver. This 95% return rate of bile acids to the liver has two consequences. First, most of the bile acids excreted through bile are actively recycled rather than newly synthesized. Second bile acids exert a feed back inhibition that regulates estrogen, cholesterol, and fat soluable vitamins.

2.11 FUNCTIONS OF THE GALLBLADDER:

1. Reservoir of bile: During the intercibal period, the sphincter of Oddi is closed and the bile excreted by the liver is directed to the gallbladder. After food, the resistance to flow through sphincter of Oddi is reduced, the gallbladder contracts and bile enters the duodenum. Narcotic drugs such as morphine and pethedine increases sphincter tone , whereas anticholenergic and glyceryl trinitrate decrease the tone.

2. Concentration of bile: By active absorption of sodium, water, chloride, bicarbonate by the gall bladder into the bloodstream and to a lesser extent into the lymphatics, the liver bile which enters the gallbladder becomes concentrated 5 to 10 times with a corresponding increase in the proportion of bile pigments, bile salts, cholesterol and calcium it contains. In disease, the gallbladder instead of absorbing fluids pours fluids rapidly. The absorption of the bile salts gets enhanced while more of calcium and cholesterol is seen in the lumen. Here lies the relationship between inflammation of the gall bladder and the stone formation. It is said that the desquamated epithelium forms the nucleus of the gall stone, the increased amount of calcium and cholesterol crystals forms the raw material, while the increased absorption of bile salts results in the precipitation of cholesterol molecules.

3. Secretion of the mucus: The gallbladder secretes 20ml of thick viscid mucus per day. Allegedly this mucus protects the mucosa from the lytic action of the bile and facilitates the flow of thick bile through the cystic duct. The colourless fluid found in the hydrops of the gallbladder and the so called white bile found in choledochal obstruction, severe cholangitis and toxic hepatitis is not bile at all but is a mucinous secretion containing calcium carbonate with no bile salts and bile pigments.

4. Excretion of cholesterol: The presence of cholesterol esters in the layers of the gallbladder in the pathological entity like strawberry gallbladder or cholesteroses of gallbladder led some physiologists to ascribe the function of excretion of cholesterol molecules by gallbladder. Others say that diffuse collection of cholesterol in the layers of gallbladder is an evidence of abnormal absorption of lipid molecules. Thus there has been much difference of opinion as to whether cholesterol is absorbed or excreted.

5. Pressure regulation: Gallbladder equalizes the pressure difference within the biliary tract by virtue of its power of absorption of bile. This is brought about by the fact that the quantity of bile secreted in 24hours is about 20 times or greater than could be stored in the gallbladder. The less of its action in equalizing the pressure within the biliary duct system is probably leading to the dilatation of the biliary ducts, which so frequently follows cholecystectomy.

6. Change in the reaction of bile: The hepatic bile is distinctly alkaline with a pH of 7.1 to 8.5 whereas bile that reaches the duodenum is almost neutral with a pH of 5.5 to7.7. This is due to bicarbonate ions being reabsorbed by gallbladder.

2.12 GALL STONES:

The basis for classification of gall stone has generally been related to stone composition or structure, because analysis of these gall stone characteristics are simple.

The broadest classification of stones is into 3 categories [10]

1. Cholesterol
2. Pigment
3. Mixed.

RISK FACTORS FOR GALLSTONES [13]

- Risk increases with age
- Obesity
- Female sex
- Race and Ethnicity
- Heredity
- Parity
- Rapid Weight Loss
- Medications: Estrogens, Oral contraceptives, Clofibrate and octreotide
- Cystic fibrosis
- Intravenous Hyper alimentation

- Cirrhosis
- Hemolysis
- Diabetes Mellitus
- Vagotomy
- Hyperlipidemia

CHOLESTEROL STONE PATHOGENESIS:

The distinction between the cholesterol and pigment types can be made by inspection of a stone and chemically[13]. It also has the merits of distinguishing those gallstones which should respond to medical dissolution therapy (cholesterol gallstone) and those that will not.

Biliary vesicles, nonmicellar carriers of cholesterol on bile:

Vesicles which are unilamellar spherical structures made of cholesterol crystals, phospholipids and little if any bile salts are substantially larger than simple micelles or mixed micelles but much smaller than layered crystals. Vesicles which are relatively stable in dilute bile such as hepatic bile and when the concentration of bile salts are relatively low. Transformation of vesicles to mixed micelles occurs in the lumen of gallbladder with high bile salt concentration. If the cholesterol to phospholipids ratio is less than 1:2 then they are

relatively stable and if the ratio raises above 1 then vesicles become insoluble and fuse to form a larger multi lamellar vesicles called liquid crystals. These liquid crystals are inherently unstable and form a solid cholesterol monohydrate crystals. [15]So these vesicles will serve as the primary source of cholesterol during nucleation.

CHOLESTEROL SATURATION OF BILE:

1. The most common mechanism is increased cholesterol secretion with normal bile salt and phospholipids secretion and this mechanism occurs in obese patients and many non obese patients.

2. Decreased secretion of bile salts coupled with normal secretion of cholesterol occurs in patients with ileal resection.

3. Both excess secretion of cholesterol and decreased secretion of bile salts.

Excessive cholesterol secretion may be due to.

- An increase in the activity of rate limiting enzyme HMG Co-A reductase.

- Decrease in cholesterol esterification or inhibition of cholesterol acyl transferase

- Decrease in the activity of 7 alpha-hydroxylase rate limiting enzyme for synthesis of primary bile salts

- Increased lipoprotein uptake by the lumen with OCP use

CHOLESTEROL SOLUBILITY IN BILE:

The relative proportions of cholesterol, bile salts, phospholipids in the bile are important in determining the maximal solubility of cholesterol. The degree of saturation of bile with cholesterol can be quantified by Cholesterol saturation index CSI or lithogenic index. At the boundary of micellar zone, bile is saturated and CSI is 1.00 or 100% supersaturated bile has a CSI of above 1.00 and unsaturated bile a CSI below 1.00. Patients with cholesterol gallstones were thought to have bile composition that fell outside the micellar zone on triangular phase diagrams and normal patients have bile composition within the zone.

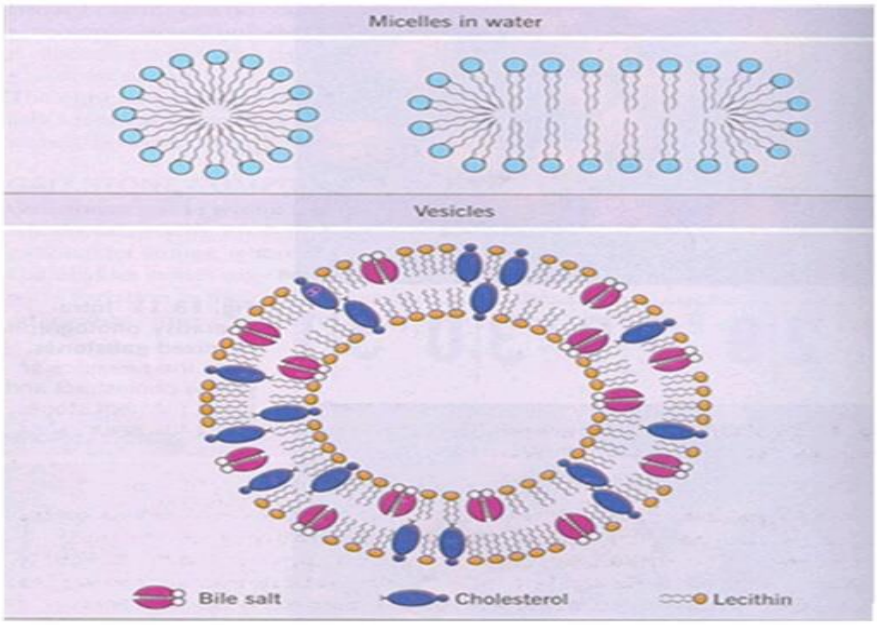

FIG 5A: BILIARY CHOLESTEROL CARRIERS

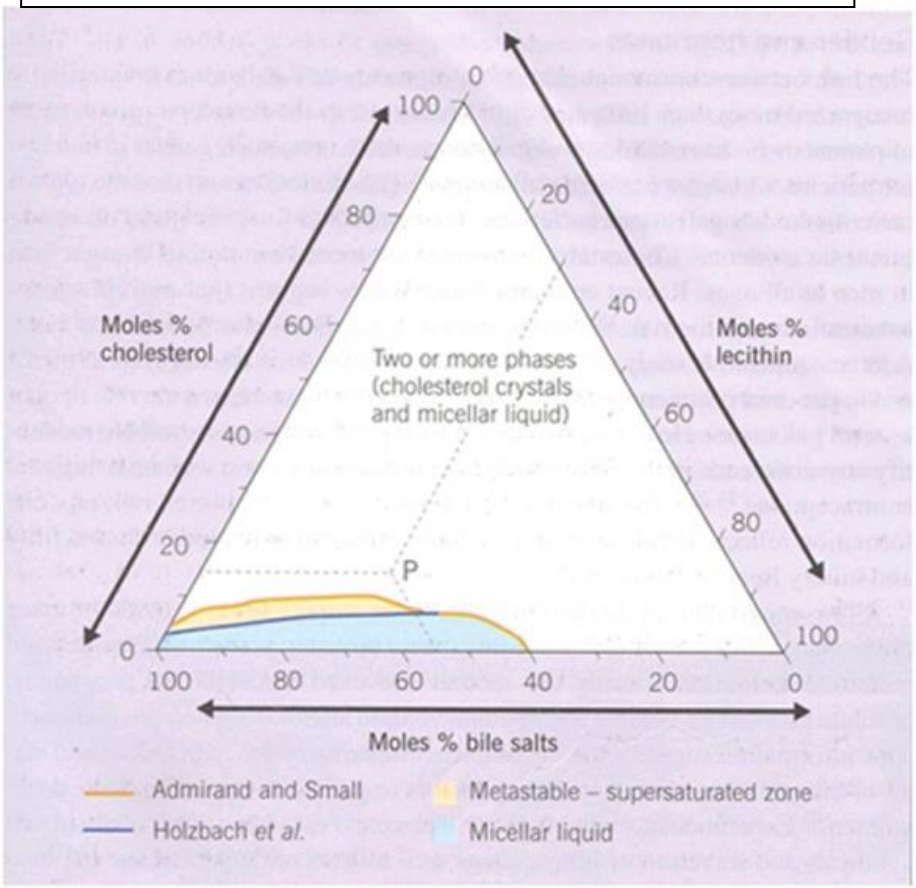

FIG 5B: BILIARY CHOLESTEROL SATURATION

NUCLEATION:

Nucleation of solid cholesterol monohydrate crystals form a supersaturated bile. Nucleating and anti nucleating factors may influence this process at one or more points.

Nucleating factors:

- Glycoprotein nucleating factor with an apparent molecular mass of 130 Kda that binds to conanavalin [16]

- Gallbladder mucin: Mucin can promote nucleation in a model bile system.[17]

Antinucleating factors:

Apolipoprotein A-I and A-II could prolong the nucleation time of supersaturated bile.

Influence of gallbladder concentration: Nucleation time is shorter in patients with cholesterol stones with well concentrated bile.

Morphology of Cholesterol Stones:

Cholesterol stones constitute more than 80% of gall stones in the western world. They are mainly composed of crystals of the cholesterol molecules.

Stones can be almost pure cholesterol and contain cholesterol monohydrate crystals agglomerated by a mucin glycolprotein matrix. Minor components of cholesterol stones contains unconjugated bilirubin and small quantity of calcium phosphate [11]. Cholesterol stones are light brown in colour, smooth or faceted, single or multiple and on cross section show a laminated and or crystalline appearance[12]. Cholesterol gall stones may be diagnosed when they are small in size and on cholecystography or ultrasonography demonstrates the floating stones with some shadowing without internal echoes. Calcium salts form the nidus in the center of the stone. They may also be dispersed rather evenly throughout the stone or in a lamellar fashion or ring like distribution throughout the periphery[13.]

FIG 6 MORPHOLOGY OF GALL STONES

PATHOGENESIS OF BLACK PIGMENT GALL STONES:

Factors associated with pathogenesis of black gall stones are[10]

- Chronic liver disease
- Ileal resection
- Chronic hemolysis

- Total parenteral nutrition
- Vagotomy

Black pigment stones are made of insoluble polymer of calcium bilirubinate. Bile is sterile and unconjugated bilirubin may be formed because of increased bilirubin in bile as a consequence of above mentioned causes . Other factors included are excess of calcium in bile or stasis and glycoprotein secretion[18], acidification defect- possibly as a result of inflammation, or by the buffering capacity of sialic acid and sulfate moieties of the mucus gel. The buffering effect facilitates the super saturation of calcium carbonate and phosphate.[12]

Increased production of unconjugated bilirubin can result from increased production of bilirubin which occurs in hemolysis or alcoholism and is associated with black pigment gall stone formation. Conditions that increase the colonic bile salt concentration such as ileal disease have been hypothesized to favour the resorption of unconjugated bilirubin and subsequent hypersecretion into bile.

PATHOGENISIS OF BROWN PIGMENT STONE:

Brown pigment stones are usually found in common bile duct. Stasis and infection are invariably present. Enzymes such as glucuronidase,

phospholipase and deconjugase plays a role in forming insoluble salts such as calcium bilirubinate, calcium palmitate and calcium stearate as well as reducing cholesterol carrying capacity of bile.

Brown stones have 20% to 80% cholesterol by weight. (30% contributed by mucin glycoprotein made of bacterial glycocalyx.)[18]

Morphology of Pigment stones:

Pigment stones consist primarily of pigments (either calcium bilirubinate or pigment polymers) and other calcium salts

Pigment stones have 2 major sub sets

1. Black
2. Brown.

Black pigment gall stones contain primarily of calcium bilirubinate or pigment polymers and calcium carbonate may also be present , along with mucin[10]. Black pigment stones contain calcium salts of unconjugated bilirubin in a polymerized matrix. The additional presence of calcium phosphate molecule in the mucin matrix results in opacity of black pigment stones on plain radiographs[13].

Brown pigment gall stones also consist primarily of calcium bilirubinate but have little if any calcium carbonate or phosphate. They contain substantial amounts of calcium salts of fatty acids, usually Palmitic acid, and also contains some amounts of cholesterol[10]. The hallmark of brown pigment stones is the presence of bacterial degradation products of biliary lipids, calcium salts of fatty acids and unconjugated billirubin[14].

TABLE 2: DIFFERENCE BETWEEN BLACK AND BROWN PIGMENT STONE

BLACK PIGMENT STONE	BROWN PIGMENT STONE
Shiny black	Dull brown
Made of Polymers of calcium bilirubinate	Made of crystalline or amorphous calcium bilirubinate
Resist manual crushing	Laminated and soft
Found in gallbladder	Found in bile ducts
Bile is sterile	Bile is infected
Contains a trace of calcium palmitate, calcium carbonate and calcium phosphate	Contains 15% calcium palmitate and or stearate and traces of calcium carbonate or calcium phosphate
Contains less than 20% cholesterol	Contains 20% – 80% cholesterol

Morphology of Mixed stone:

These are stones that contain cholesterol monohydrate crystals along with varying degree of calcium components i.e. calcium carbonate, phosphate, bilirubinate, or palmitate. Most of the mixed stones are multifaceted with angular edge. A shiny greenish black colour predominates. Cut surface shows a concentric laminated structure due to rhythmical deposition of biliary constituents including cholesterol, bile pigments and calcium. When mixed stones are lobulated they are sometimes called as mulberry stones.

IMAGING STUDIES OF THE BILIARY TRACT[10] :

Only 50% of pigment stones and 20% of cholesterol stones contain enough calcium to be visible on a plain abdominal film. Plain abdominal films have greatest utility in evaluating complications of gallstones such as emphysematous cholecystitis, Cholecysto-enteric fistula and a porcelain gallbladder.

Ultrasonography: Principal imaging modality for the diagnosis of cholelithiasis Should follow a fast of atleast 8hrs because gallstones are best seen in a distended bile filled gallbladder.

Diagnosis relies on the findings of echogenic objects within the lumen of gallbladder that produces an acoustic shadow[19]. Can detect stones as small as 2mm in size with sensitivity greater than 95% and specificity greater than 95% when stones are seen with accompanying acoustic shadow. The contracted gallbladder filled with stones may give a "double arc shadow" or " wall echo shadow" sign. Distinctly less powerful for detection of stones in CBD

CT Abdomen: Less sensitive than USG abdomen . Main advantage is to study the status of extrahepatic biliary tree and adjacent structures. Used to identify CBD stones and dilatation of CBD and other biliary radicles in obstructive jaundice cases.

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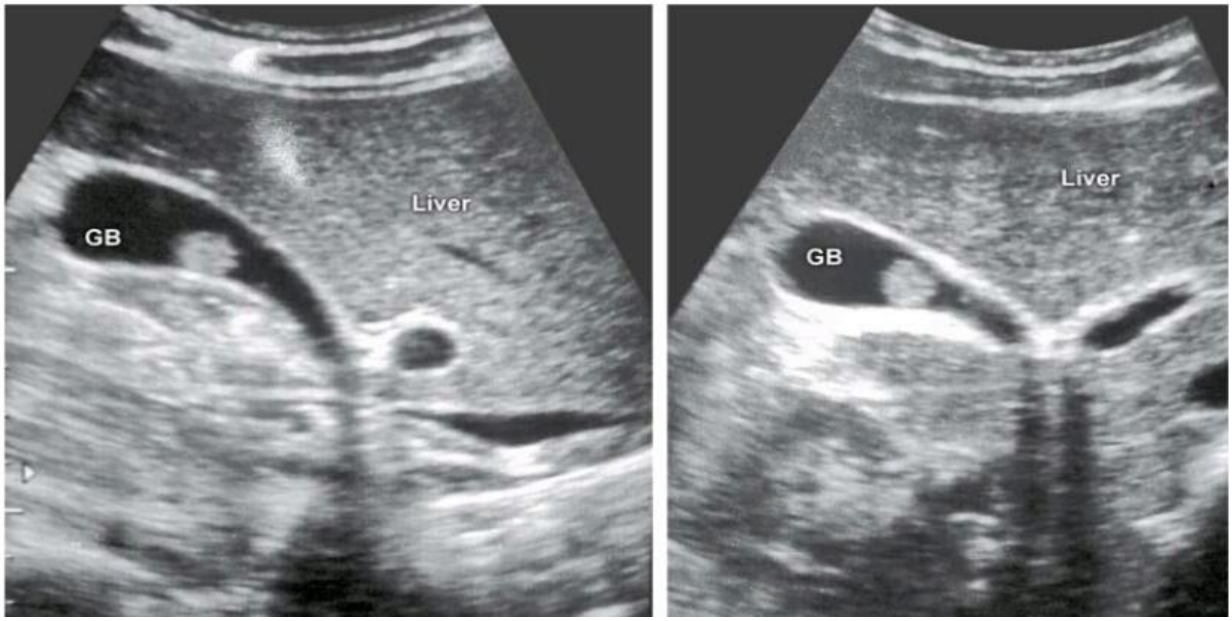


Fig 7 : ultrasound abdomen showing multiple stones in lumen of gall bladder

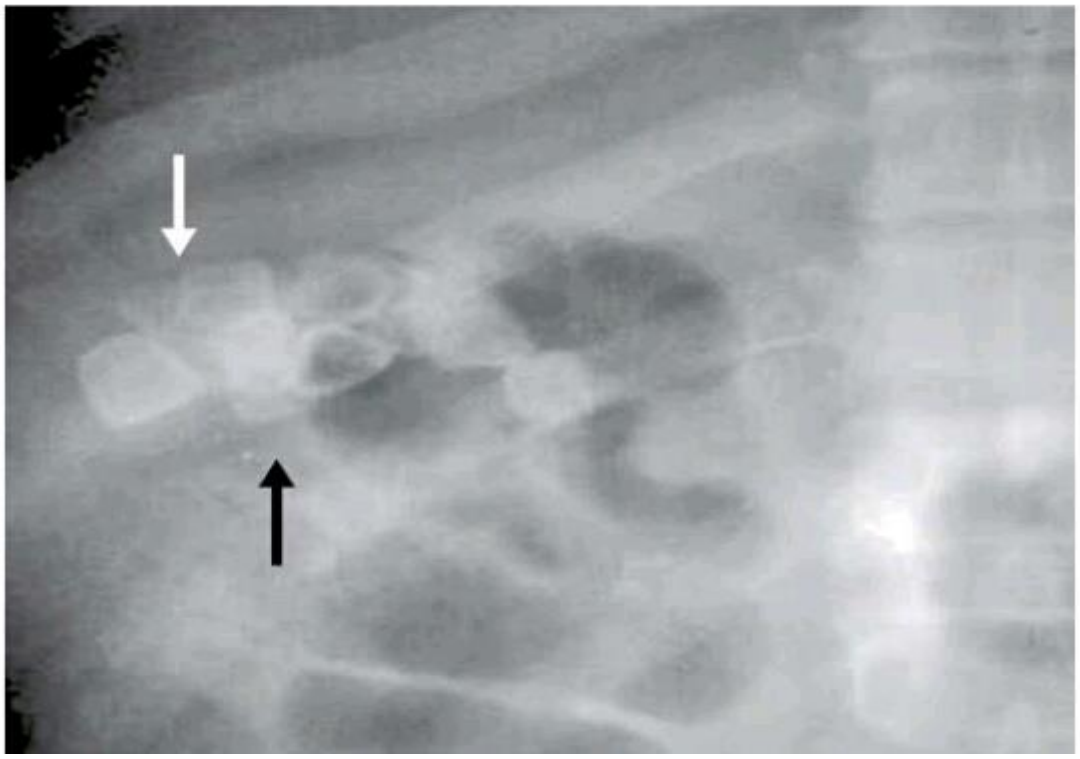


Fig 8: multiple gall stones in plain xray abdomen showing radio opaque shadow

ERCP: Is the gold standard investigation for the diagnosis of choledocholithiasis with sensitivity greater than 95%. With contrast medium flowing retrograde into the gallbladder, stones appear as filling defects detectable with sensitivity of 80%.

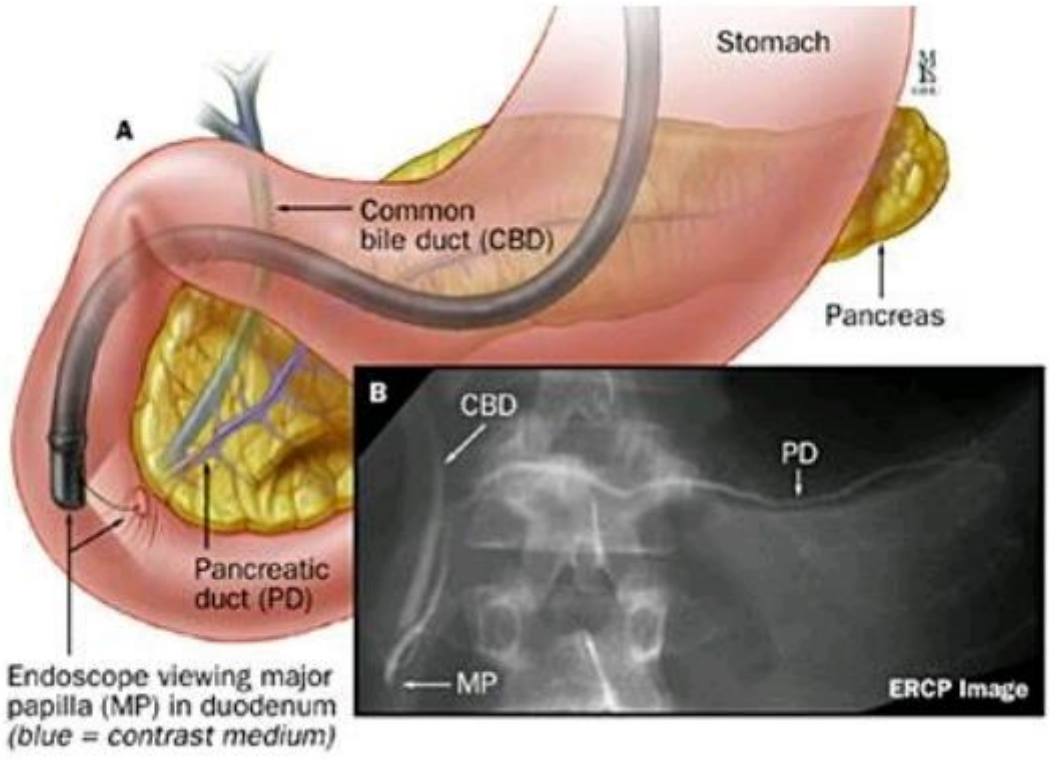


Fig 9 : ERCP- showing side endoscope picture in duodenum

Oral Cholecystography: Limited application as a secondary means of identifying stones in the gallbladder[20].

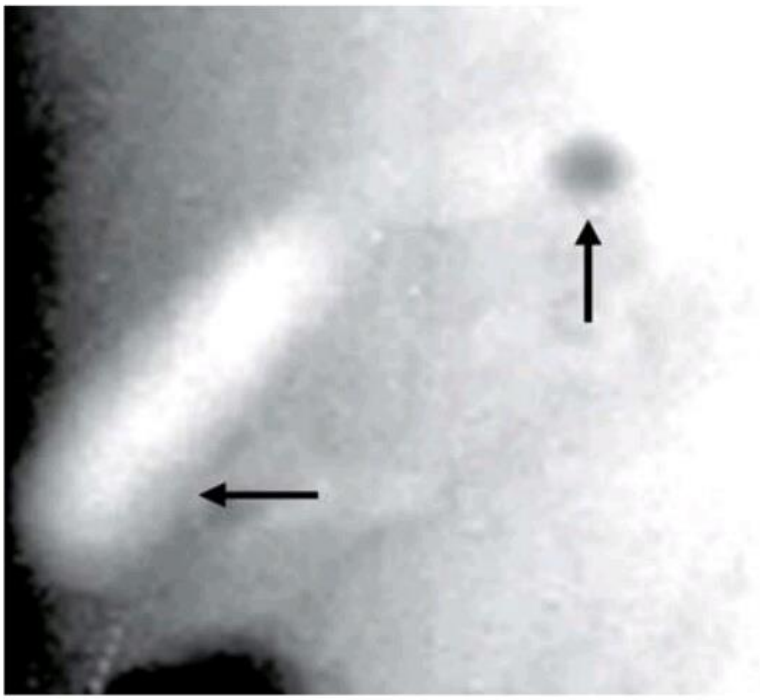


Fig 10: oral cholecystography showing smoth filling defect in the cystic duct

CT Cholangiography and MRCP: These investigations are helpful in detecting complications of gallstones such as pericholecystic fluid in acute cholecystitis, gas in the gallbladder wall in emphysematous Cholecystitis, and gallbladder perforation.

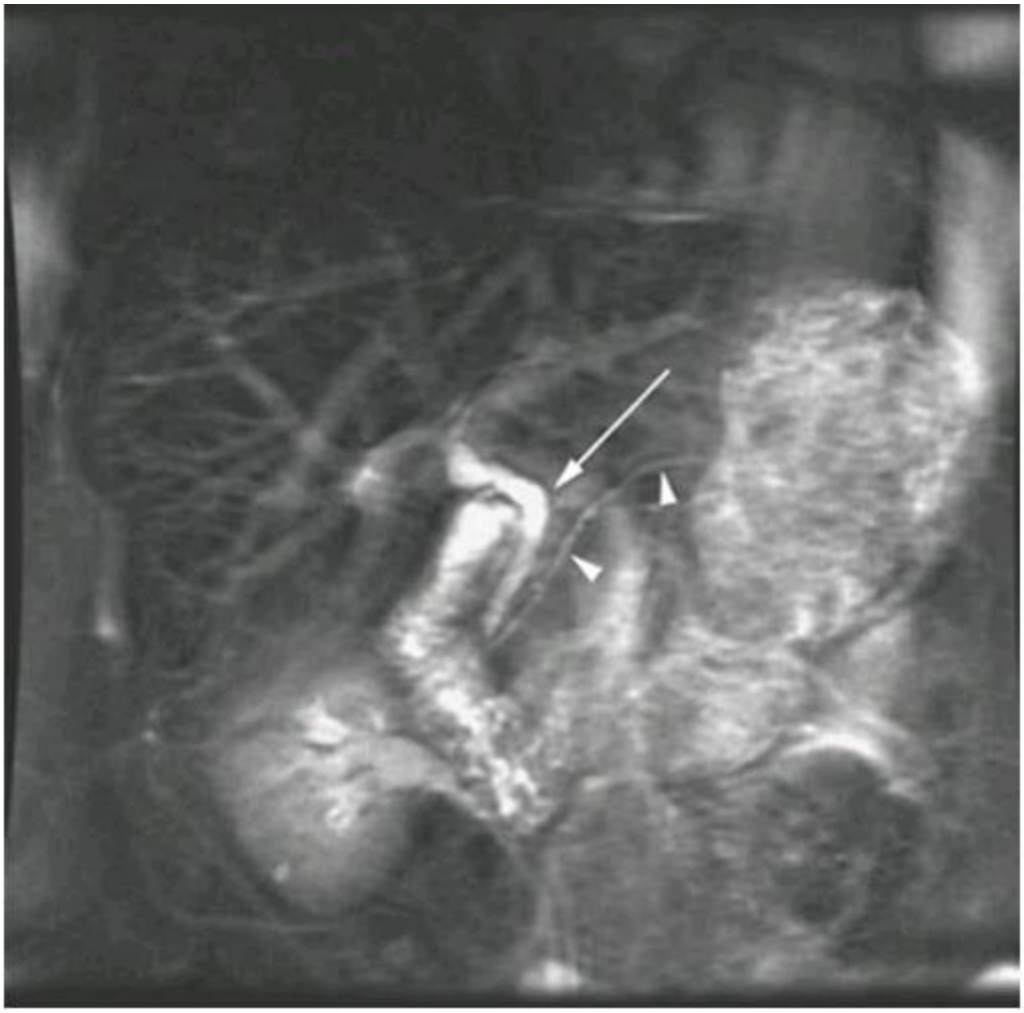


Fig11: MRCP- Shows the course of extra hepatic biliary tree

CLINICAL MANIFESTATION AND COMPLICATIONS OF GALLSTONE DISEASE:[12]

1. Asymptomatic stones

2. Stone intermittently obstructing cystic duct causing intermittent biliary colic 20%.

3. Stone impacted in cystic duct causing acute cholecystitis 10%.

4. Stone in cystic duct compressing or fistulising into common bile duct causing Mirrizzi syndrome < 0.1%.

5. Stone impacted in distal common bile duct causing jaundice, biliary colic type of pain and risk of ascending cholangitis or acute biliary pancreatitis 5%.

6. Stone eroding through the gallbladder into duodenum, resulting in cholecystoenteric fistula.

7. Long standing cholelithiasis resulting in gallbladder

8. Emphysematous cholecystitis –secondary infection of gall bladder wall with gas forming organisms.

9. Porcelain gall bladder: intramural calcification of gall bladder wall, usually associated with stones can lead to gall bladder carcinoma in approximately 20%

ELECTIVE TREATMENT OF GALLBLADDER STONES:

The choices for elective therapy of gallstones have expanded in the last several decades. Cholecystectomy is the treatment of choice for symptomatic gallstones and includes both traditional open and laparoscopic approaches. For patients who are reluctant to undergo surgery or who are at high surgical risk, oral bile salt therapy, usually with Ursodiol is an option provided the patients have some radiolucent stones in a functioning gallbladder. Elective percutaneous radiological extraction of stones from the gallbladder is rarely performed but it is an another option.[10]

Extracorporeal shock wave lithotripsy [ESWL] combined with bile salts is being utilized. It is most successful in patients with single radiolucent stones although it is also used for patients with more than one stone. Percutaneous instillation of solvents, particularly methyl tert-butyl ether [MTBE], into gallbladder lumen is being investigated because of its safety and efficacy and appears to be most useful for patients with radiolucent stones of any size or number.

BILE SALT THERAPY

The most widely used non surgical treatment for stones in the gallbladder is administration of an oral bile salt, either Chenodiol or

Ursodiol. Ursodiol is used far more extensively than Chenodiol. The combination of both is sometimes used for Bile salt therapy is a potential alternative to cholecystectomy for patients at high operative risk. However the use of bile salt need not be limited to such high risk patients. Others may benefit from bile salt therapy, such as those who wish to avoid surgery or those whose symptoms are exceedingly mild.

Dissolution of gallstones with Chenodiol:[21]

Chenodiol (chenodeoxycholic acid) was the first bile salt reported to dissolve gallstones. Chenodiol is a dihydroxy bile salt that normally accounts for about one third of the human bile salt pool. Administration of chenodiol in sufficient doses results in secretion of hepatic bile that is unsaturated with cholesterol. Unsaturated hepatic bile enters the gallbladder, where it can bathe the surface of gallstones. Miscelles in unsaturated bile can absorb cholesterol from the surface of cholesterol gallstones, gradually diminishing their size and eventually, under optimal circumstances, completely dissolving them. Chenodiol did not achieve any degree of widespread use and is rarely used as monotherapy. Its major drawbacks are dose related side effects. The two most common are diarrhoea and elevation of serum amino transferase levels. Chenodiol is occasionally used in combination with Ursodiol for gallstone dissolution [usually at the dosage of 5-7.5 mg/kg/day each]

Dissolution of gallstones with Ursodiol:[21]

Ursodiol is a naturally occurring dihydroxy bile salt that accounts for approximately 1% to 2% of the total human bile salt pool. The safety and ease of administration of Ursodiol make it the first non surgical option to consider when an alternative to cholecystectomy is sought. Ursodiol has been used most extensively as monotherapy for dissolution of cholesterol gallstones but has also been increasingly used after fragmentation of gallstones by ESWL. Ursodiol dissolves gallstones by solubilizing cholesterol from the surface of the stones. Ursodiol administration results in the conversion of bile supersaturated with cholesterol to unsaturated bile. In addition to desaturation, it has the unique property of promoting the formation of a liquid crystal mesophase [phospholipids plus cholesterol] in bile. Chenodiol does not do so. Liquid crystals can form in the presence of bile that is saturated with cholesterol. Liquid crystals are less dense than bile and are expelled from the gallbladder as it empties. The proportion of Ursodiol in the bile rises maximally during therapy to 55% to 60% and levels off there after 2 weeks, even with higher doses.The optimal dosage of Ursodiol is 8 to 10mg/kg/day. A strict linear relationship does not exist between

the dose and complete stone dissolution. Doses as low as 3 to 5mg/kg/day have resulted in stone dissolution. Doses above 10mg/kg/day do not result in higher dissolution rate.

EXTRA CORPOREAL SHOCKWAVE LITHOTRIPSY:

Use of ESWL for the treatment of the gallstones followed its successful application for kidney stones. A major impetus for the development of gallstone lithotripsy was the limited success of gallstone dissolution using the bile salts ursodiol and chenodiol, which may require 2 years or more and has an overall success rate of about 30 %.

Fragmentation of gallstones into small particles can aid in overcoming problems of big stones by increasing the surface area /volume ratio and disrupting localized areas of calcium salts. Shockwaves that are used in lithotripsy are complex acoustic waves that typically have a single pressure spike of sharp upstroke with gradual relaxation. The amplitude of shockwaves used therapeutically is in the range of 600 to 1000 bars.

The finer the fragmentation of stone, the more effectively the fragments can be dissolved by bile salts or emptied by the gallbladder. Optimal fragment size after ESWL is 3mm or less. Fragmentation of multiple gallstones is less successful than that of single stone. The two potential mechanisms for gallstone fragments clearance are gallbladder

emptying of fragments and dissolution by oral bile salt therapy. Fragments may be rapidly cleared through gallbladder emptying in a few patients. However, dissolution of fragments by oral bile salt therapy is the principle mechanism for their disappearance in the majority of patients.

Symptomatic patients with a patent cystic duct are the most important prerequisites. Single radiolucent stones 20mm or less in diameter are optimal for ESWL therapy. Fragment clearance is directly proportional to initial gallstone number and size. Best results are for one stone of 20mm or less, and approximately 50% to 70% of such patients become stone free after 6 months.

Complications of ESWL include hematuria, skin petechiae or ecchymoses and asymptomatic elevation of serum aminotransferase or amylase values in some patients. Delayed problems include transient mild biliary pain, presumably as a result of fragment passage, occurring in 30% to 50% of patients within 6 to 12 months after ESWL. Serious complications occur infrequently and include pancreatitis and common bile duct obstruction.

CONTACT DISSOLUTION THERAPY:[10]

Infusion of a chemical agent directly into the gallbladder or bile ducts in an attempt to dissolve gallstones is known as contact dissolution

therapy. Solvents can be delivered through indwelling T-tube catheters, percutaneous transhepatic biliary tube, nasobiliary catheters or percutaneous cholecystostomy tubes. Commonly used dissolution agents are monoctanoin and methyl tert-butyl ether.

SURGICAL THERAPY:[22]

Cholecystectomy has become most common general surgical procedure now. Around 650,000 cholecystectomies are performed annually in the USA.

Indications for the cholecystectomy include

- Biliary colic
- Acute cholecystitis
- Chronic cholecystitis
- Complications of gall stone disease
- Asymptomatic gallstones larger than 2cms

OPEN CHOLECYSTECTOMY:

Open cholecystectomy carries an overall mortality of around 0.17% with mortality rates for patients under and over 65yrs of age being 0.03% and 0.5% respectively .

Technique: Open cholecystectomy is typically performed through a right sub costal incision 2-3cms below the right costal margin. Satisfactory access can also be gained through a midline laparotomy incision. Two techniques are available for open cholecystectomy

- Ante grade method (fundus first method)
- Retrograde method

Retrograde cholecystectomy begins with dissection in the Calot's triangle to identify the cystic duct as it enters the infundibulum of gallbladder. Once identified the cystic duct is mobilised and divided and cystic duct stump is suture ligated. Cystic artery is similarly identified and ligated. If the Calot's triangle demonstrates considerable edema and inflammation in the presence of acute cholecystitis, ante grade cholecystectomy is generally safer and advocated to minimize the chances of inadvertent CBD or hepatic duct injury.

Ante grade cholecystectomy starts at the fundus, dividing the peritoneal attachments of the gallbladder to the liver and mobilizing the gallbladder from the gallbladder fossa. Once identified the cystic duct is mobilised and divided and cystic duct stump is suture ligated. Cystic artery is similarly identified and ligated.

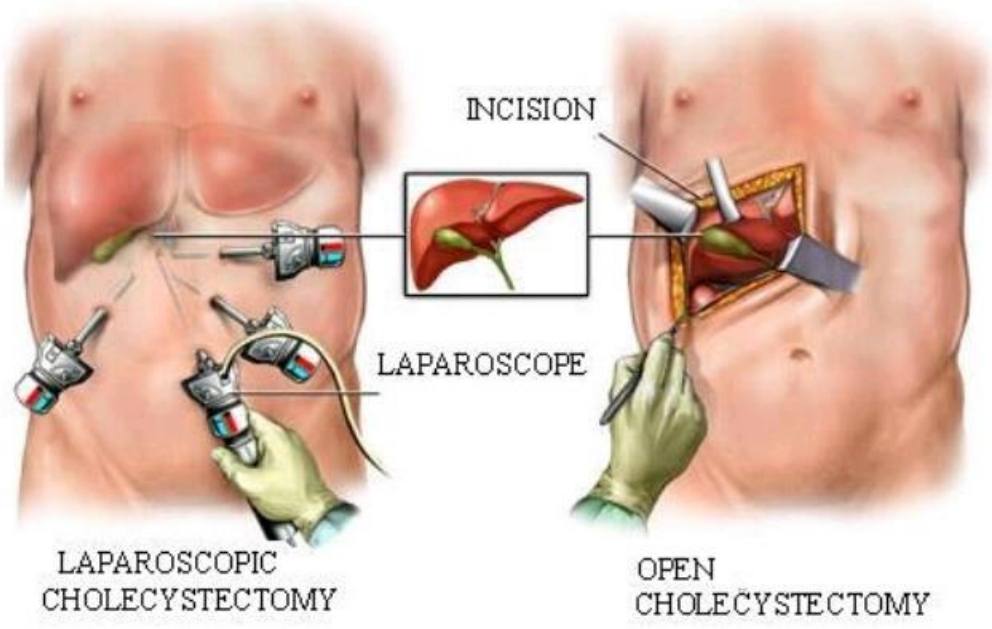


FIG 12: LAPAROSCOPIC AND OPEN CHOLECTSTECTOMY

LAPAROSCOPIC CHOLECYSTECTOMY:

Although laparoscopic cholecystectomy first reported in 1988, it has rapidly become the standard of care in many parts of the world for patients with gallstone disease. The key to laparoscopic cholecystectomy is to create a satisfactory pneumoperitoneum and expose the triangle of calot. Thereafter the principles of safe cholecystectomy are the same as those used for open retrograde cholecystectomy. The cystic duct and artery must be clearly visualized. Anatomic variation in the position of ductal and arterial structures must be sought to avoid ductal injury and vascular compromise.

The indications for laparoscopic choliangiography include

- CBD dilatation
- History of jaundice
- Hyper amylasemia
- Abnormal liver function tests
- Palpable duct stones

Indications to convert to open cholecystectomy:

- Inability to identify key anatomical structures
- Marked inflammations with adhesions to adjacent viscera
- Hemorrhage
- Bile duct injury
- Discovery of unexpected pathology

Common Bile Duct Exploration:

Common bile duct stones that are detected intraoperatively on intraoperative cholangiography or ultrasonography may be managed with laparoscopic choledochal exploration as a part of the laparoscopic cholecystectomy procedure. Patients with common bile duct stones detected preoperatively, but in whom endoscopic clearance was either not

available or unsuccessful, should also have their ductal stones managed during the cholecystectomy. If the stones in the duct are small, they may sometimes be flushed into the duodenum with saline irrigation via the cholangiography catheter after the sphincter of Oddi has been relaxed with glucagon. When the duct has been cleared, the cystic duct is ligated and cut and the cholecystectomy completed. Occasionally, a choledochotomy, an incision into the common bile duct itself, is necessary. The flexible choledochoscope is then passed into the duct for visualization and clearance of stones. The choledochotomy is sutured with a T tube left in the common bile duct with one end taken out through the abdominal wall for decompression of the bile ducts. By managing common bile duct stones at the time of the cholecystectomy, the patients can have all of their gallstone disease treated with one invasive procedure. It does, however depend on the available surgical expertise.

2.13 THYROID HORMONES:

PHYSIOLOGY OF THYROID METABOLISM:[23,24,25,26,27,28]

Thyroid function is closely related to the iodine metabolism because the hormones produced by the thyroid gland-thyroxine and tri-iodothyronine contain high proportion of iodine. The effect of these two hormones are qualitatively very similar but differ dramatically in their time and course of action. Thyroid hormones play an important role in

the regulation of growth, brain development, and for maintaining metabolism and functional activity of most organs.

Iodine metabolism:

The normal thyroid gland contains approximately 5000-8000 µg of iodine, only about 1 percent being inorganic iodide. The normal daily intake of iodine in food and water is about 150 µg. All iodine is converted into iodide in the gut and in this form, it is completely and rapidly absorbed into the blood.

Synthesis of thyroid hormones:

Left: TSH binds its receptor and promotes thyroid hormone production. Circulating I- is taken up at the basolateral membrane via the sodium-iodide symporter, NIS. Intracellular I- accumulates and moves across the apical membrane by a process believed at least partially to be mediated by Pendrin, thereby providing this essential element for hormone synthesis.

Middle: Tg is produced by the thyroid epithelial cells, processed along the synthetic pathway and released into the follicular lumen.

Top: H_2O_2, required for the coupling of I- and Tg, is generated by $DUOX_2$ at the apical membrane.

Reaction of these components is catalysed by TPO; I- is coupled to many tyrosine residues within Tg, of which only a select number are hormonogenic. Tyrosine residues can be either mono- or di-iodinated. TPO also facilitates coupling of these residues to form precursor to T3 (mono- + di-iodinated) and T4 (2 × di-iodinated).

Right: Outline of endocytosis and processing of the pro-hormone. Some Tg is proteolysed at the apical surface by externalized cathepsins prior to uptake Internalized Tg is proteolysed by cathepsins within lysosomes.T3 and T4 exit basolaterally in a process at least partially mediated by MCT8, a monocarboxylic acid transporter of the SLC16 family . Un-utilized iodotyrosines are further degraded by iodotyrosine dehalogenases and recycled.[25]

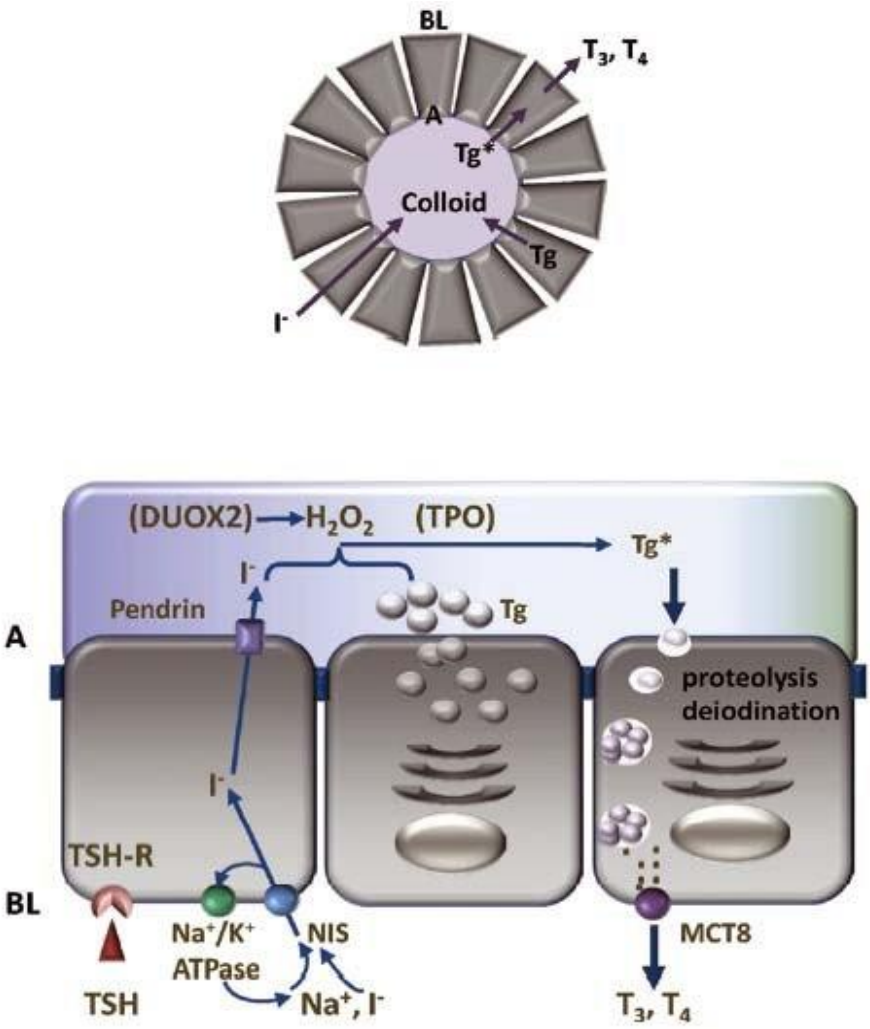


FIG 13: SYNTHESIS OF THYROID HORMONES

Storage: After synthesis, the thyroid hormones are stored in thyroglobulin. Each molecule of thyroglobulin contains one to three molecules of thyroxine, and an average of one tri-iodothyronine molecule for every 14 molecules of thyroxine. In this form the thyroid hormones are often stored in the follicles for several months. Release of T4 and T3

The thyroid gland is unique within the endocrine system in having a large extracellular space, the follicular lumen used for storage of the hormones and their precursors. The thyroid is unique among the endocrine glands by virtue of the large store of hormones that it contains and the slow-rate at which the hormone is released.

In the thyroid gland, the organic iodine is constituted as follows, T4 constitutes approximately 35 per cent, T3 – 5 percent and iodothyrosines (DIT & MIT) about 60 per cent.

The apical surface of thyroid cells send pseudopodia like extensions around the colloid. The proteinases present in the lysosomal enzymes digest the thyroglobulin molecules to release T3 and T4 which diffuse through the basement membrane into the blood.

Transportation, turnover and metabolism of thyroid hormone:

In the blood, T4 and T3 are almost entirely bound to plasma proteins such as thyroxine binding globulin (TBG), thyroxine binding pre-albumin (TBPA) and thyroxine binding albumin (TBA). Normally 99.98% of the T4 in the plasma is protein bound. The free T4 level is only above 2ng/dL. There is very little T4 in the urine. Of the 0.15 g/dL of normally found T3 in plasma, 0.2% (0.3 ng/dL) is free. The remaining 99.8% is protein bound. Homeostatic regulation of thyroid function is directed towards the maintenance of free thyroxine rather than total hormone concentration. Half-life of thyroxine (T4) is 6 days and T3 has a half life of 1-3 days.

The thyroid gland has a storage reserve of approximately three weeks. TBG molecular weight – 60,000D with a half life of about 5 days. It has a high affinity but low capacity for T4 – which is 2-6 times greater than for T3. TBPA molecular weight 50,000D with half life of about 2 days. Can bind much T4 and little T3. Albumin has low affinity but high capacity for T4 and T3 binding.

The function of protein binding of thyroid hormones may be to help, to reduce the proportion of free hormones in the blood which inturn reduces loss by kidney and liver maintaining the plasma level of free hormones T4 is more firmly bound to plasma proteins so it is

more stable than T3 in the body. T4 is a extracellular hormone, while T3 penetrates tissue fluids and cells rapidly. T3 is quicker acting and more potent than T4. T4 is very largely converted to T3 by deiodination – so, it acts as a prohormone.

There are several routes of T4 metabolism, the major route (85 percent) is deiodination to T3 (monodeiodination at 5' position) or to reverse T3 (monodeiodination at the 5 position) in the liver, kidney and other sites. Other routes include conjugation to form glucuronides and sulphates and alteration of alanine side chain to form acetic or propionic acid.

PHYSIOLOGICAL EFFECTS OF THYROID HORMONES ON DIFFERENT BODILY MECHANISMS

The principal effects of thyroid hormone is to increase the metabolic effects of most tissues of the body (with few exceptions such as brain, retina, spleen, testes and lungs). The growth rate of young persons is greatly increased. Many specific events occurs in the cells throughout the body under the influence of thyroid hormones. But the basic mechanisms leading to all these effects is still largely unknown.

1) Effect on protein synthesis

Thyroid hormones increases the protein synthesis in almost all tissues of the body in experimental animals.

2) Effect on cellular enzyme systems

Thyroid hormones increases the level of more than 100 intra-cellular enzymes. As an example, one enzyme, alpha-Glycerophosphate dehydrogenase can be increased to an activity six times of its normal level.

3) Effect on mitochondria

Thyroid hormones increases the number and size of mitochondria in most cells of the body.

4) Effect on cellular cyclic AMP

Thyroid hormones increases cyclic AMP in perhaps all cells of the body, especially so in muscle cells. Therefore, some believe that the primary action might be to activate adenylcyclase which in turn increases the formation of cyclic AMP.

5) Effect on bone growth and calcium metabolism

Thyroid hormones increases the growth of bone. These hormones also cause rapid closure of epiphyses. Osteoclastic activity in the bones is increased. Greater than normal quantities of calcium and phosphate are excreted in the urine and gastrointestinal tract.

6) Effect on carbohydrate metabolism

Thyroid hormones increases the uptake of glucose by all cells, glycolysis, gluconeogenesis and glucose absorption from gastro-intestinal tract.

7) Effect on fat metabolism and vitamin metabolism

All aspects of fat metabolism enhanced under the influence of thyroid hormones and also increased need for vitamins

8) Effect on basal metabolic rate and body weight

In hyperthyroidism basal metabolic rate can increase as much as 100 per cent above normal and decreases body weight despite increased appetite. On the other hand, when no thyroid hormone is produced, basal metabolic rate falls almost to one half the normal, that is the basal metabolic rate becomes 30 to 50 per cent.

9) Effect on cardiovascular system

The following effects occur in the cardiovascular system in hyper- thyroidism and the opposite effects occur in hypothyroidism.

a) Increased blood flow and increased cardiac output.

b) Increase in the heart rate.

c) Slight increase in blood volume.

d) Increase in pulse pressure.

10) Effect on respiratory system

Thyroid hormones increase the rate and depth of respiration.

11) Effect on gastrointestinal tract

Increase in absorption of products of digestion, motility of gastrointestinal tract and the appetite.

12) Effect on central nervous system and sleep

Thyroid hormones increase the rapidity of cerebration. Thyroid hormone seem to increase synaptic activity but does not influence the peripheral nerve activity. Excess thyroid hormones cause difficulty in sleep.

13) Effect on muscle

Excess of thyroid hormones cause the fine muscle tremors 10-15 times per second.

2.14 Hypothyroidism:

Hypothyroidism is one of the common problem encountered by both the sexes women>men. The incidence of hypothyroidism in women found to be 350/10,0000 annually. The usual prevalence of subclinical hypothyroidism above 60 years females is found to be 20%.

Hypothyroidism is defined as decrease in the level of circulating thyroid hormones with increase in the level of circulating TSH. It may be due to pathology in hypothalamus, pituitary or thyroid gland itself. The rate of all metabolic process gets reduced.

Clinical symptoms :

1) Hair loss
2) Easy fatiguability
3) Lethargy
4) Memory disturbances
5) Intolerance to cold
6) Loss of appetite
7) Increase in weight
8) Hoarseness of voice
9) Hearing impairment

10) Body pain

11) Constipation

12) Menstrual irregularity

Clinical signs include:

1) Coarse and thin hair

2) Skin: dry and cold

3) Macroglossia

4) Slow speech

5) Anemia

6) Decrease in heart rate

7) Hypertension

8) Delayed deep tendon reflexes

9) Ascites

10) Pleural and pericardial effusions

11) Pedal edema

12) vitiligo

13) In children, hypothyroidism leads to growth and mental retardation.

LAB FINDINGS:

1) Increase in serum cholesterol level
2) Anemia
3) Clinical hypothyroidism: increased TSH; decreased free T3 and T4 with clinical features of hypothyroidism
4) Subclinical hypothyroidism: increased TSH; Normal free T3 and T4 and the patient is mostly asymptomatic
5) In case of hypothyroidism due to autoimmune thyroiditis, anti-thyroperoxidase antibody may present.

The treatment of hypothyroidism is Thyroxine supplementation. Mostly the hypothyroid patients need lifelong thyroxine supplementation.

2.15 Prevalence of Hypothyroidism in biliary stone patients:

For past years, several studies were conducted to report an correlation between hypothyroidism and gall stones.

A retrospective study conducted on 2001 (Inkinen et al.) on patients above 60 yrs of age.[2] It was found that CBD stone patients had more prevalence of hypothyroidism (11%) when compared to non biliary stone patients (2%). They also compared the prevalence of hypothyroidism in Gall stones patients without CBD stone found to be 6%. They also found no

difference in the frequency of other diseases between these groups. This finding suggested the correlation between gall stones and hypothyroidism is not only due to alteration in cholesterol metabolism but also due to other factors like low bile flow in hypothyroidism.

A prospective study[29] conducted in 2007 (Laukkarinen et al) showed that even subclinical hypothyroidism is more common in biliary stone disease. They studied the prevalence of subclinical hypothyroidism in clinically euthyroid biliary stone patients and they compared with non biliary stone patients. Prevalence of subclinical hypothyroidism in biliary stone patients found to be 5.3% and in control patients found to be 1.4% . In more than 60 yrs females, prevalence of subclinical hypothyroidism found to be 11.4% in biliary stone patients and in control patients it was found to be 1.8%.

In 2010, medical registry based large study conducted from finland (Laukkarinen et al)[30] confirmed the relationship between gall stones and hypothyroidism. In this study, the prevalence of gall stones in hypothyroid patients compared with age, sex and area of residence adjusted glaucoma patients (control) were studied. Patients with other diseases were excluded from the study. Out of 14,334 patients in each group, 23% in hypothyroid cohort and 16% in control cohort had treated for gall stones. These groups did not differ statiscally in number of gall stone treatments. But 56% of gall

stone treated patients were found in hypothyroid cohort compared with glaucoma cohort. This suggest that stone formation may start during the untreated period of hypothyroidism. This hypothesis is supported by increased prevalence of both clinical and subclinical hypothyroidism in gall stone patients.

TABLE 3: Results from various studies:

STUDY	YEAR	NO. OF PATIENTS	RESULTS
Conducted in MCH Trivandrum	2015	93 gall stone patients	Sub clinical hypothyroidism present in 13%. Goiter present in 7.6% cases. Higher proportion of hypothyroidism with gall stones were noted in females (83.3%) compared with males (7.6%)
P sundeshwari et al , GRH Madurai	2014	200 gall stone patients	18 patients had subclinical hypothyroidism and 6 patients had clinical hypothyroidism . prevalence of hypothyroidism in gall stones found to be 12%
Conducted by Aishwin saravanakumar in Coimbatore	2016	50 gall stone patients	24% of gall stone patients had clinical/ subclinical hypothyroidism
Conducted in PGIMS, Rohtak	2017	200 gall stone patients	10.5% had subclinical hypothyroidism and 3.5% had clinical hypothyroidism. Prevalence of hypothyroidism in gall stones found to be 14%

2.16 Mechanism of Formation of Gallstones in Hypothyroidism:

There are many factors that may account to the formation of biliary stones in hypothyroidism.

In hypothyroidism, the decrease in

the level of thyroxine

➢ causes decrease in cholesterol metabolism[31] leads to supersaturation of cholesterol in bile, which in decreases the motility, contractility and filling of gallbladder, which leads to retention of cholesterol crystals and formation of gall stones.

➢ reduces the secretion of bile from liver resulting in decreased clearance of precipitates from the biliary ducts.[32]

➢decreases the sphincter of oddi relaxation leads to impaired bile flow. Stagnation of bile causes formation of stones[33, 34, 35,36]

Thyroid hormones act through interaction with their nuclear receptors which are expressed in a target tissue.[37,38,39,40,41] In human, the Sphincter of oddi has both TR β1 and β2. Actions of thyroid hormones are mostly intracellular which requires transport of thyroid hormones across plasma membrane. Newly detected thyroid transporters are

monocarboxylate transporter 10 (MCT10), MCT8, and organic anion transporting polypeptide 1C1 (OATP1C1).[42,43]

Hypothyroidism Reduces Bile Flow into the Duodenum:

In a study conducted in rats, hypothyroidism causes sphincter of oddi contraction and decreased the rate of bile flow to duodenum whereas in hyperthyroidism the bile flow was increased. Similarly, in a prospective study conducted in humans[35,36], hepatic clearance of bile was significantly reduced and bile flow had a tendency to decrease in the hypothyroid stage after thyroidectomy, when compared to the euthyroid stage in the same patients. In this study , the uptake of radioactivity in large bile ducts were found to be similar in both hypothyroid and euthyroid stages but in the hypothyroid stage the bile flow to duodenum is reduced. This is due to changes in composition of bile and hypomotility of gallbladder, and non relaxation of sphincter of oddi.

Mechanisms by Which Thyroxine Mediates SO Relaxation:

The experiments studied using α- and β- receptor blockers, NO synthesis blocker, and with tetrodotoxin (eliminates the nerve function) proved that the thyroxine- induced relaxation of Sphincter of oddi is not mediated through neural effects. Human Sphincter of oddi has TR β1 and

β2. The presence of Thyroid receptors in sphincter of oddi[34] is necessary but is no sufficient evidence that thyroid hormone exerts its prorelaxant effect through hormone-receptor ligand complex action. However, the experiments with thyroxine showed that the underlying cellular events require a certain time lag, which supports the theory that part of the action of thyroid hormone is TH-TR mediated. The binding of thyroxine with nuclear receptor is fast event, whereas the resulting transcription and translation is time consuming, and this explains the not immediate relaxation of sphincter of oddi by thyroxine and this effect is mediated by regulatory proteins which are synthesized as a result of thyroxine-mediated gene expression. The prorelaxant effect of thyroxine is probably partly mediated via partly via binding to nuclear receptors and partly via transporter proteins, subsequently leads to opening of K+ channel results in hyperpolarisation, which closes the cell membrane Calcium channels, reduces Ca2+ influx, and results in decreased contraction of the Sphincter of oddi smooth-muscle cell.[44,45,46]

2.17 Clinical Implications:

In summary, several recent studies "documented the association between hypothyroidism, or subclinical hypothyroidism, and biliary stones.

The higher prevalence of hypothyroidism in biliary stone patients compared to gallbladder stone patients suggests the reasons are not only due to changes in the cholesterol metabolism, or decreased bile excretion rate, but particularly alteration in the function of sphincter of oddi that may account the correlation of gall stones and hypothyroidism. It remains to be investigated whether known hypothyroid patients whose gallbladder removed for gall stones are at an higher risk to develop CBD stones when compared to normal euthyroid individuals or not. The initial formation of bile cholesterol crystals may start during the undiagnosed/ untreated period of hypothyroidism, and the stones may continue to develop even after starting of thyroxine replacement therapy. It is possible that thyroxine replacement therapy is not adequate in all patients to maintain the normal Sphincter of oddi function, causing the increased risk of CBD stone formation. Studies shown that subclinical hypothyroid patients have alteration in the serum cholesterol level and prone to develop on cardiovascular disturbances, neuromuscular symptoms and this can be prevented by early replacement treatment with thyroxine, and it can be assumed that subclinical hypothyroid patients may also benefit from gall stone formation by early treatment with thyroxine. *In conclusion patients who are presenting with gallstones,*

especially females >40 years of age, may have subclinical hypothyroidism. So, clinicians should be perform thyroid profile in all gall stone patients.

CHAPTER 3

MATERIALS AND METHODS

3.1 Type of study : Cross- sectional study

3.2 Study approval : Prior to commencement of this study - Thesis & Ethical Committee of Tirunelveli Medical College, Tirunelveli had approved the thesis protocol.

3.3 Place of study : Tirunelveli medical college Hospital

3.4 Period of study : Duration starting from December 2016 to August 2018

3.5 Sample size : 100 cases

3.6 Selection of patients:

a) Sampling method- Purposive.

b)**Inclusion criteria**- Patients with symptomatic or asymptomatic cholelithiasis/ choledocholithiasis or both.

c) **Exclusion criteria** - Patients with previous history of hypothyroidism on treatment

3.7 Investigations: USG abdomen

Thyroid function test and USG thyroid

Lipid profile

CT abdomen if indicated

Liver function test

3.8 Study procedure:

Method of selecting cases was non-random, purposive. After admission clinical history was taken and physical examination was conducted on all patients who were admitted in General surgery department with features of Gall stone disease. Basic investigations were done, followed by imaging studies. About the disease nature and the possible line of management were explained to the patients. All the required information about this study was explained to the patients and their valid guardian. Informed written consent was taken from the patients and their guardian who are willing to participate in this study. Detailed history was obtained from the study group to establish proper diagnosis. Thorough physical examination was done in all cases. Data collection sheets were filled by the investigator himself. All of the preoperative factors related to the Gall stone disease were

noted down in the data sheet. After proper evaluation and pre-op preparation, patients who required surgical management were taken up for surgery. Strict aseptic precautions were followed during surgery. Meticulous techniques were practiced . The surgery procedure and related peroperative factors were observed and recorded in the data collection sheet . After completing the collection of data it was compiled in a systematic way. Those who were found to be hypothyroid were started thyroxine supplementation therapy.

3.9 Operational definitions:

Cholelithiasis : presence of stones in gall bladder or CBD either single or multiple which are visualised by ultrasound abdomen/CT abdomen.

Choledocholithiasis : presence of stones in the common bile duct which are visualised by imaging methods.

Clinical Hypothyroidism : Decrease in level of circulating thyroid hormones with increased TSH.

Sub-clinical Hypothyroidism: Normal T4 with slightly raised TSH.

Jaundice : Those with S. bilirubin > 1.2 mg/ dl were recorded as jaundiced. Hypercholestrolemia : an excess of cholesterol in the bloodstream.

ERCP (Endoscopic Retrograde CholangioPancreatography): Procedure has both diagnostic and therapeutic value for pathology in the gallbladder, biliary system, pancreas, and liver.

Types of operations: were recorded during each operation.

3.10Variables studied:

i. Age

ii Sex

iii. Co-morbidities

iv. Lipid Profile

v. Ultrasonogram and CECT findings

vi. Thyroid function test

vii. USG thyroid

viii. Type of operation

3.10Ethical consideration

All the patients and legal guardians were given an explanation of this study and about the investigations and operative procedures with their own merits and demerits, expected results, and possible complications. If he/she agreed, then the case had been selected for this study. This study did not involve any additional investigation or any significant risk to the patient. It did not cause economic burden to the patients. The study was approved by the institutional ethical committee board prior to commencement of data collection. Informed consent was taken from all patients and their guardians.

3.11 Data collection

Data were collected by pre-tested structured questionnaire. Data were collected from all the cases by direct interview after getting informed written consent from them and from their legal guardian.

3.12 Data analysis

Data analysis was done both manually and by using computer. Calculated data were arranged in systemic manner, presented in various table and figures and statistical analysis was made to evaluate the objectives of this study with the help of Statistical Package for Social Science (SPSS).

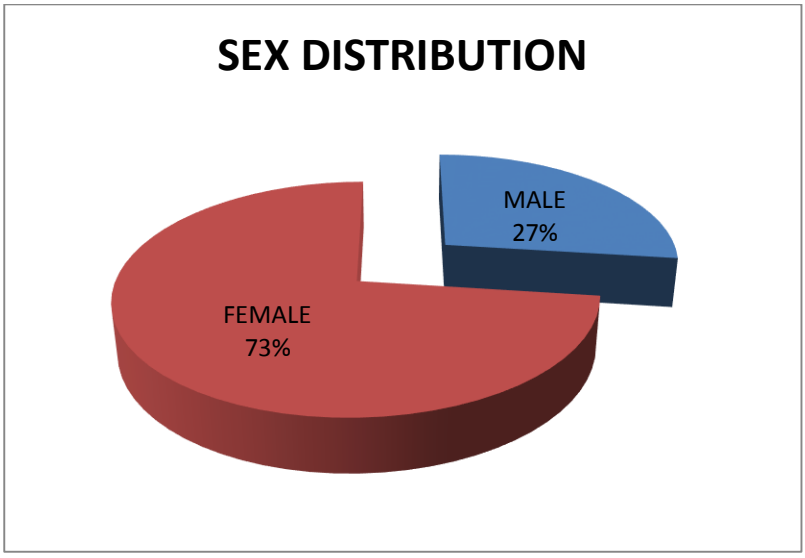
CHAPTER 4

RESULTS

This cross sectional study was carried out to determine the prevalence of hypothyroidism/ sub-clinical hypothyroidism among patients who admitted with either cholelithiasis or choledocholithiasis or both. One hundred patients fulfilling the inclusion criteria from Surgery department of Tirunelveli Medical College Hospital during the period of December2016 to August 2018 were selected. All cases were evaluated clinically. Only essential investigations necessary for diagnosis and preoperative assessment were done before operations. All patients underwent thyroid function test in addition. The patients of both sexes and different ages were included in this study. The results obtained are as follows.

TABLE 4: SEX DISTRIBUTION OF GALL STONE PATIENTS

SEX	NO. OF PATIENTS	PERCENTAGE
MALE	27	27%
FEMALE	73	73%
TOTAL	100 Patients	100%

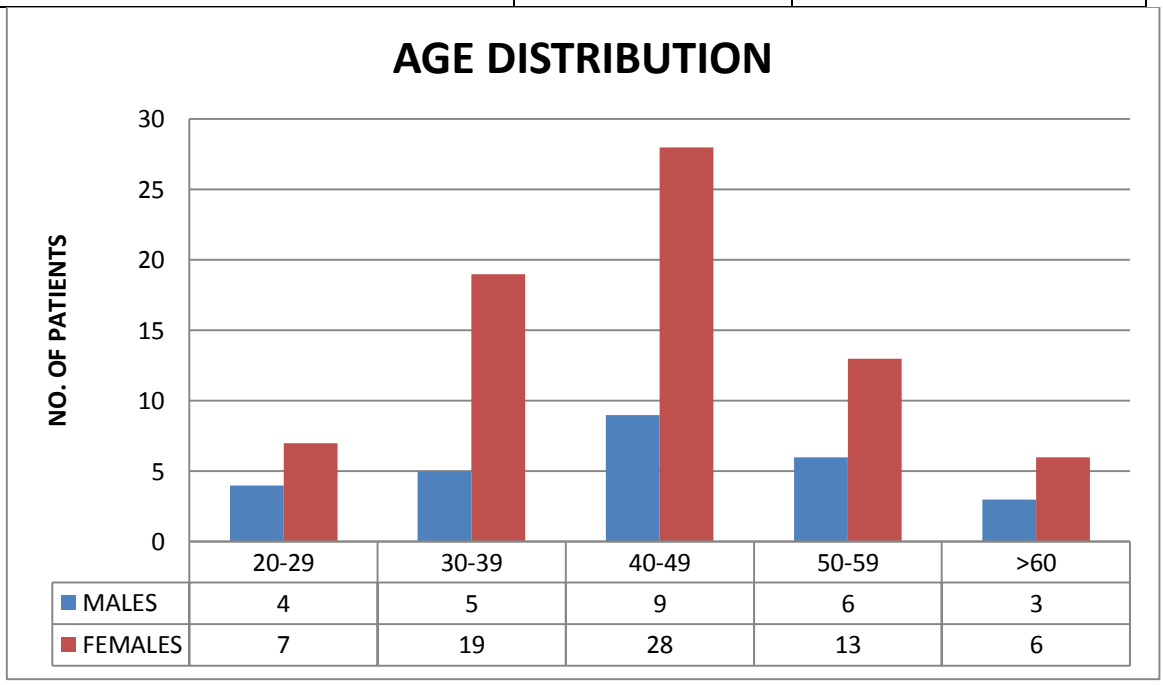


MALE: FEMALE Sex Ratio: 1:2.7

Gall stone disease found to be 2.7 times more common in females than males.

TABLE 5: AGE DISTRIBUTION OF GALL STONE DISEASE:

AGE GROUP IN YEARS	MALE	FEMALE
20-29	4	7
30-39	5	19
40-49	9	28
50-59	6	13
>60	3	6
Total	27	73



Gall stones found to be most common in the age group of 40-49 years in both sexes.

TABLE 6 CO-MORBIDITIS:

CO-MORBIDITIS	NO. OF PATIENTS
Diabetes	8
Hypertension	3
Diabetes+ Hypertension	4
Diabetes+ CAD	6
Hypertension+ CAD	2
Bronchial asthma	2
Old PTB	1
DM+ HTN+ CAD	1

TABLE 7 :USG ABDOMEN FINDINGS:

USG abdomen findings	No. Of patients
Multiple GB calculi	67
Single GB calculi	24
GB+ CBD calculi	6
CBD calculi	3

TOTAL- 100 patients

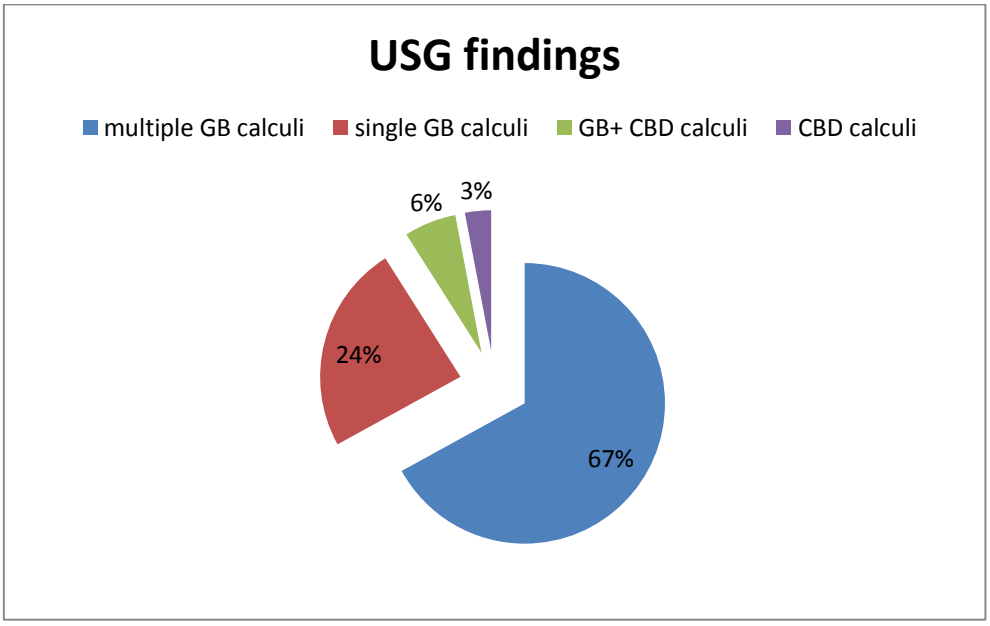


TABLE 8. MANAGEMENT OF BILIARY STONES:

PROCEDURE	NO.OF PATIENTS
Laparoscopic cholecystectomy	73
Open/ lap converted open cholecystectomy	18
Open cholecystectomy + CBD exploration	5
ERCP	2
ERCP+ Lap cholecystectomy	2

In 100 gall stone patients, 21 patients were found to be hypothyroid. 4 patients were males; 17 patients were females

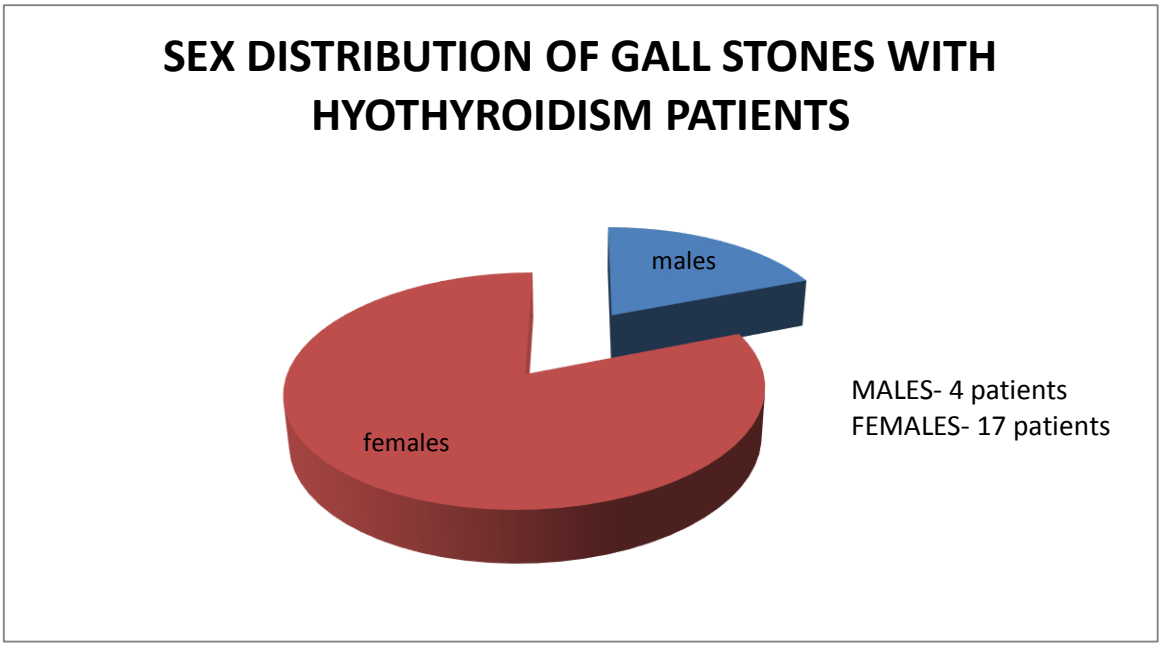


TABLE 9: AGE DISTRIBUTION OF PATIENTS WITH GALL STONES AND HYPOTHYROIDISM

AGE GROUP IN YEARS	MALE	FEMALE
20-29	0	0
30-39	1	1
40-49	2	9
50-59	1	5
>60	0	2

TOTAL- 21 Patients

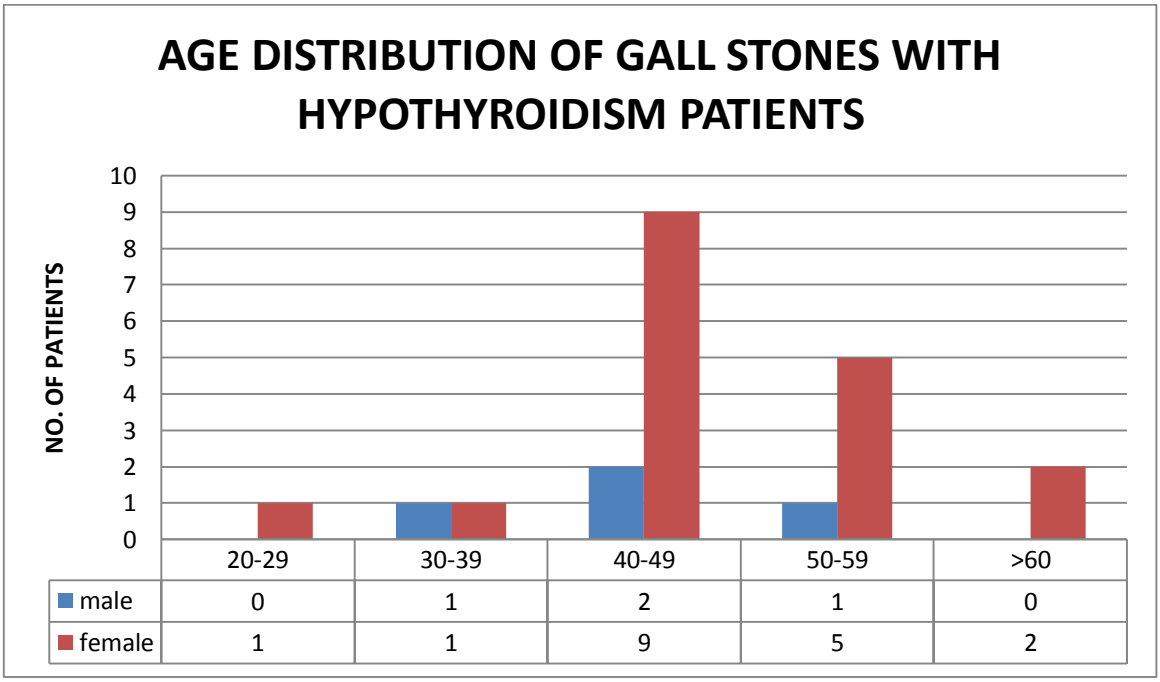


TABLE 10: STATUS OF HYPOTHYROIDISM

Thyroid status	Male	Female	Total
Sub-clinical hypothyroidism	4	14	18
Clinical hypothyroidism	0	3	7

Total – 21 patients

TABLE 11: THYROID EXAMINATION (CLINICAL+ USG THYROID)

SEX	GOITER	WITHOUT GOITER
Males	Nil	4
Females	5	12
Total	5	17

Among 21 hypothyroid patients, 5 patients had goiter, 17 patients were had clinically not enlarged thyroid gland.

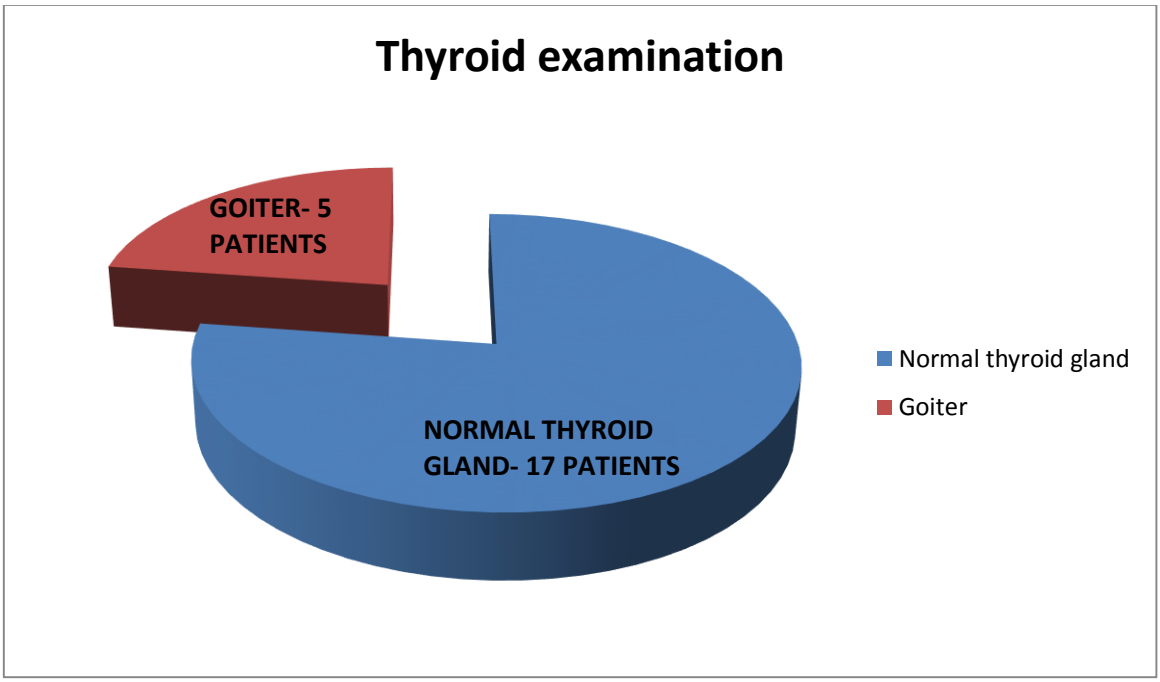


TABLE 12: FNAC OF GOITER

FNAC REPORT	**NO. OF PATIENTS**
Colloid goiter	3
Nodular goiter	2

All hypothyroid patients were started with thyroxine supplementation

TABLE 13: SERUM CHOLESTEROL LEVEL AND GALL STONES

SERUM CHOLESTEROL LEVEL IN mg/dl	GALL STONES NO. OF PATIENTS	GALL STONES+ HYPOTHYROIDISM
<150	21	1
150-200	34	6
>200	45	14
TOTAL	100 patients	21 patients

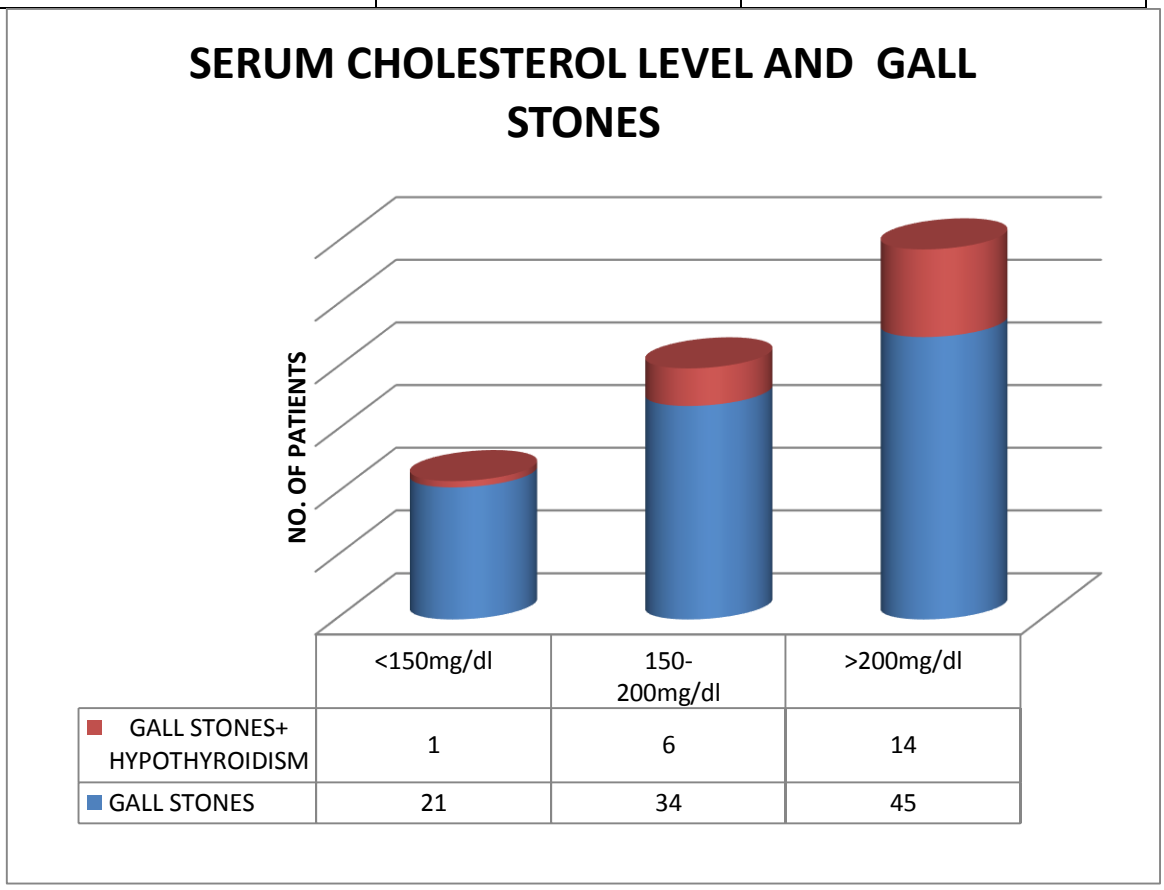
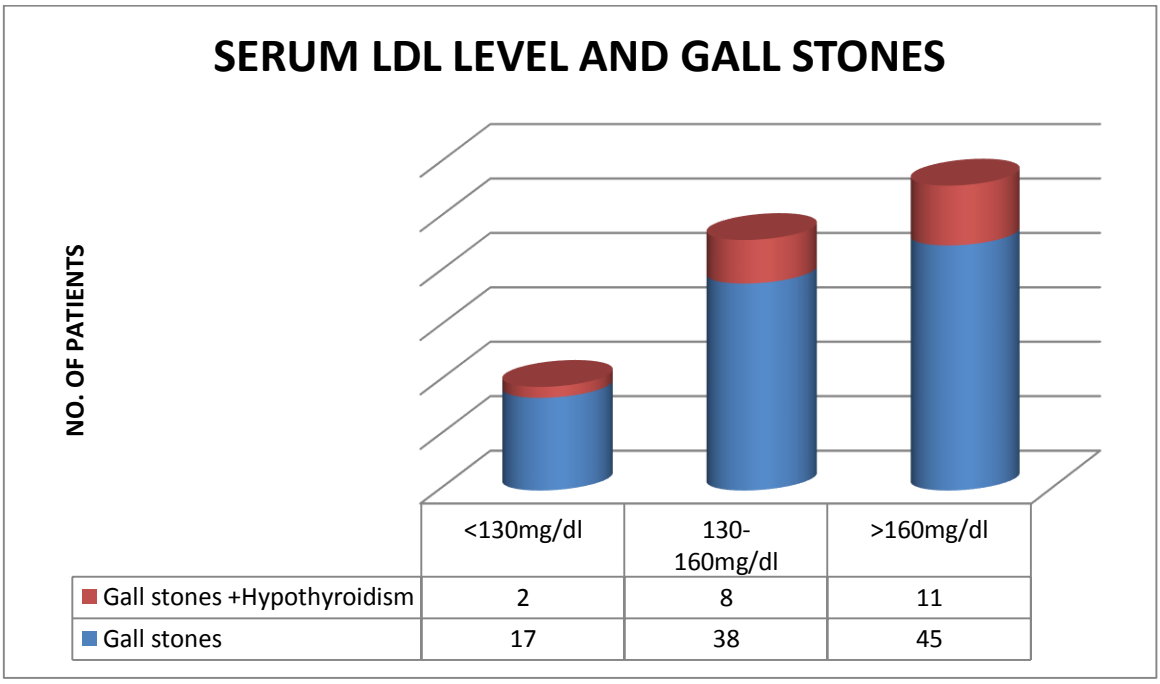


TABLE 14: SERUM LDL LEVEL AND GALL STONES

SERUM LDL LEVEL IN mg/dl	No. of gall stone patients	No. of gall stones with hypothyroidism patients
<130mg/dl	17	2
130-160 mg/dl	38	8
>160mg/dl	45	11
Total	100 patients	21 patients



CHAPTER 5

5.1 DISCUSSION:

This cross sectional study was conducted in 100 selected patients with either gall stones or CBD stones or both in Department of General surgery, Tirunelveli medical college. This study was carried out with a view to identify the prevalence of hypothyroidism in patients with extra hepatic biliary lithiasis in view of identifying its importance as a causative factor and to add the thyroid function test as a part of routine workup in biliary stone patients.

Most of the Gall stone patients were in the age group of 40-49 years.

Among this patients, 27% were males; 73% were females.

Male to female ratio: 1:2.7. Females were the predominant group.

On analysing the co- morbid factors, Diabetes was the predominant co- morbidity associated with Gall stones.

On evaluation of patients with USG abdomen , 67% had multiple gall bladder calculi, 24% had single gall bladder calculi, 6% had both gall bladder and CBD calculi, 3% had CBD calculi.

Patients were managed with both laparoscopic and open procedures. 73 patients underwent laparoscopic cholecystectomy, 18 patients were treated

with open/ lap converted open cholecystectomy. The reason for conversion of laparoscopic to open procedure were adhesions, bleeding and technical issues. 4 patients of both gall bladder and CBD calculi and 1 patient of CBD calculi underwent open cholecystectomy with CBD exploration. 2 patients of both gall bladder and CBD calculi underwent ERCP+ laparoscopic cholecystectomy. 2 patients of CBD calculi treated with ERCP.

In 100 gall stone patients , 21 patients were found to be hypothyroid (21%).79 patients (79%) found to be Euthyroid.

Among 21 hypothyroid patients, 4 patients (4%) were males and 17 patients (17%) were females.

Most of gall stone patients with hypothyroidism were found to be in the age group of 40-49 years of age.

18 patients (18%) had subclinical hypothyroidism and gall stones. 3 patients (3%) had clinical hypothyroidism).

Thyroid examination by clinical and USG examination showed 5 patients had goiter. Others had no clinically enlarged thyroid gland.

FNAC done for that 5 goiter patients showed 3 had colloid goiter and 2 had nodular goiter.

All hypothyroid patients were started with thyroxine supplementation therapy (T. Thyroxine 100 microgram OD in empty stomach).

Most of gall stone patients (45%) had raised serum cholesterol and LDL level.

5.2 LIMITATIONS OF THE STUDY:

1) Small sample size.
2) Assessment of composition of gall stones not done.
3) Assessment of mobility of biliary tract not done to demonstrate decreased rate of bile flow in hypothyroid patients.

Eventhough this study has some limitations, it has some credentials in reflecting the facts regarding prevalence of hypothyroidism in gall stone patients and its positive correlation with gall stone disease.

5.3 RECOMMENDATION

The recommendation made from this study is Evaluation of thyroid function test should be a part of general workup in patients with biliary stone disease especially in female patients

CHAPTER 6 CONCLUSION

This cross sectional study was conducted in Department of General surgery, Tirunelveli medical college hospital. It can be concluded from the findings of this study that hypothyroidism is a probable risk factor for development of Gall stones especially in middle aged females. Undetected and untreated hypothyroidism in such patients will result in complications. Clinicians should be aware of possible hypothyroid background and consider examining the thyroid profile atleast in females over 40 years of age, in which group the prevalence of clinical and sub clinical hypothyroidism is the highest.

BIBLIOGRAPHY:

1) Cicala M, Hibib FI, Fiocca F, Pallota N, Corazziari E, Gut 2001. Increased sphincter of oddi basal pressure in patients affected by gallstone disease: a role of biliary stasis and colicky pain; 48:414-417
2) Inkinen G,S& J, Norback I, 2001. Association between common bile duct stones and treated hypothyroidism, hepatogastroenterology; 47:919-921
3) Vassilakis JS, Nicolopoulos N, 1981. Dissolution of gall stones following thyroxine administration . 28; 60-61
4) G. A. G .Decker, D.J.Duplessis, J.A.Myburgh:.The liver and biliary system: Lee Mc Gregor's synopsis of surgical anatomy, K .M.Varghewse company, India1996, Chap 6, pp88-98.
5) R.M.H. McMinn, Liver and biliary tract; R.M.H. McMinn, Last's Anatomy regional and applied, Churchill Livingstone, 9th editon, 1994, chap5, pp342-350.
6) Susan Standring: Gall bladder and biliary tree; Susan Standring, Harold Ellis, Jeremiah C Healy, David Johnson, Andrew Williams, Patricia Collins et al: Gray's anatomy, The anatomical basis of clinical practice, Elsevier Churchill Livingstone, 39th edition, 2005,chapter 86,. Pp 1227-1230.
7) R.C.G.Russel:Gallbladder and bileducts; R.C.G.Russel, Norman.S.Williams Bulstrode.J.K.C: Bailey and Love's short practice of surgery; Arnold publication,24th edition, 2004, chap65, pp1094-1096.

8) Steven.A.A, Henry.A.T: Biliary tract; Coutney.M.T, Beauchamp.D.R, Evers.M.B, Mattox.L.K: Sabiston text book of surgery: Saunders Elsevier, 17th edition, vol2, .chap 52, pp-1599-1600.

9) Margret, Oddsdottir and John.G.Hunter:Gall bladder and the extra hepatic biliary system; F.Charles Brunicardi, Dania.K.Anderson ,Timothy.R.B.Uliar,David. L.Dunn, John.G.Hunter, Raphel.E.Pollock: Schwartz's principles of surgery;
McGraw- Hill Medical publication, 8th edition, 2005, chap 31, pp 1187-1191.

10) Peter. F.Mallet, Dale.J.Rosenberg: Cholelithiasis ,Gallstone pathogenesis, Natural history, Biliary pain and Nonsurgical therapy; Hall Brich, Schaffer, Berk: Bockus Gastroenterology, W. B. Saunders company publication,5th edition,1995, vol-3, chapter .139, pp-2674-2728

11) Joanne.M.Donovan: Physical and metabolic factors in gall stone pathogenesis; Allen.D.Cooper: Gastroenterology clinics of North America; W.B.Saunders company, vol 28, no.1.march 1999. Pp75-97.

12) Jay.D.Horton. and Lyman.E.Bilhartz: Gall stone disease and its complications; MarkFeldman, Lawrence.S.Friedma, Marvin.H.Sleisenger: Sleisenger and Fordtran's Gastro intestinal and liver disease, Pathophysiology/Diagnosis/Management, Saunders company, 7th edition, 2002, vol 1, chap55, pp1065-1081.

13) Malet P.F, Takabayashi a Trotman B.W: Black and Brown pigment Gallstones Differ in micro structure and micro composition. Hepatology 2: 1984, pp227-234,

14) Cetta FM: Bile infection documented as initial event in in the pathogenesis of brown piment biliary stones. Hepatology 6:1996, 482-489

15) Lusp, Park.H.Z,Madani.H., Partial characterizations of a non micellar system of cholesterol solubilization in bile, AMJ Physiology 1987:252; pp 374-380.

16) Groenak, Ottenhoff.R, Jansen.P.L.M: Effect of cholesterol nucleation-promoting activity on cholesterol solubilization in model bile, Journal Lipid ras,1989:30; pp 51-58.

17) Levy P.F, Smith..B.F, Lamontt.J.T Human gall bladder mucin accelerates in vitro nucleation of cholesterol in artificial bile; Gastroenterology, 1984; 87: pp 270-275.

18) J.A.D. Boucher: Gallstones. Formation and Epidemiology L.H.Blumgart: Surgery of the Liver and Biliary tract, Churchill Livingstone, 2nd edition, 1994, vol 1, chap 38, pp 555-556

19) Scanlan.K.A: Sonographic artifacts and their origins; AJRAMJ Roentgenology, 1991, 156: pp 1267.

20) Shea.JA Berlin.J.A, Escarce.J.J: Revised estimates of diagnostic test sensitivity and specificity in suspected biliary tract disease; Arch Internal Med,1994:154; pp 2573.

21) Jinl.G.S, Salen.G, Colalillo.A; Ursodeoxy cholic acid: A safe and effective agent for dissolving cholesterol gall stones .Ann Internal Medicine Journal 1982;97;pp 351-356.

22) A. James Moser and Joel. J .Roslyn:.Gall bladder and Biliary tree; John .D. Corson, Robin. C.N.Williamson, J.Andrew Bradley, Howard .R.

Champion, ALbbert. E. Gram,J.Michael Dixon et al.: SURGERY; Mosby international limited, first edition, 2001,section 3, chapter 13 pp 13.1-13.26.

23) Maussier Errico D, Putigannce. Clinical and laboratory assessment. Thyrotoxicosis. RAYS 1999;24(2):263-72.

24) Guyton AC, Hall JE. The Metabolic Hormones. 12th ed. In: Text book of Medical Physiology. New Delhi: Elsevier; 2006. pp. 931-43.

25) Ganong WF. The thyroid gland. 23rd ed. In: Review of Medical Physiology. London: McGraw-Hill; 2010. pp. 301-5.

26) Ledingham IM, Mackay C. Thyroid. 3rd ed. In: Jamieson and Kay's Text book of Surgical Physiology. New York: Churchill Livingstone; 1978. pp. 72-81.

27) Keele CA, Neil E, Joels N. The thyroid. 13th ed. In: Samson Wright's

Applied Physiology. New Delhi: Manzarkhan; 2003. pp. 537-45.

28) The Author. Journal Compilation @ 2011. The Physiological Society.

J Physiol 589.24 Thyroid Iodide Efflux 5929-5939.

29) J Laukkarinen, G.Kiudelis, M.Lempinen et al., "Increased prevalence of subclinical hypothyroidism in common bile duct stones", journal of clinical endocrinology and metabolism, vol 92, no.11, pp 4260,200730) J Laukkarinen, J.Sand, V.Autio and I.Nordback, "Bile duct stone procedures are frequent in patients with hypothyroidism. A large , registry-based, cohort study in finland, "Scandinavian Journal of Gastroenterology, vol 45, no.1, pp70-74,2010

31)J.P.Andreini, W.F.Prigge, C.Ma and R.L.Gebhard, “vesicles and mixed micelles in hypothyroid rat bile before and after thyroid hormone treatment; evidence for a vesicle transport system for biliary cholesterol secretion,” Journal of lipid research, vol 35, no.8, pp.1405-1412,1994

32) F. J. Field, E. Albright, and S. N. Mathur, “Effect of dietary cholesterol on biliary cholesterol content and bile flow in the hypothyroid rat,” *Gastroenterology*, vol. 91, no. 2, pp. 297–304, 1986.

33) J. Inkinen, J. Sand, P. Arvola, I. Porsti,¨ and I. Nordback, “Direct effect of thyroxine on pig Sphincter of Oddi contractility,” *Digestive Diseases and Sciences*, vol. 46, no. 1, pp. 182–186, 2001.

34)J. Laukkarinen, J. Sand, S. Aittomaki¨ et al., “Mechanism of the prorelaxing effect of thyroxine on the sphincter of Oddi,” *Scandinavian Journal of Gastroenterology*, vol. 37, no. 6, pp. 667–673, 2002.

35) J. Laukkarinen, P. Ko¨obi,¨ J. Kalliovalkama et al., “Bile flow to the duodenum is reduced in hypothyreosis and enhanced in hyperthyreosis,” *Neurogastroenterology and Motility*, vol. 14, no. 2, pp. 183–188, 2002.

36) J. Laukkarinen, J. Sand, R. Saaristo et al., “Is bile flow reduced in patients with hypothyroidism?” *Surgery*, vol. 133, no. 3, pp. 288–293, 2003.

37) C. K. Glass and J. M. Holloway, “Regulation of gene expression by the thyroid hormone receptor,” *Biochimica et Biophysica Acta*, vol. 1032, no. 2-3, pp. 157–176, 1990.

38) M. A. Lazar and W. W. Chin, “Nuclear thyroid hormone receptors,” *Journal of Clinical Investigation*, vol. 86, no. 6, pp. 1777–1782, 1990.

39) V. K. K. Chatterjee and J. R. Tata, “Thyroid hormone receptors and their role in development,” *Cancer Surveys*, vol. 14, pp. 147–168, 1992.

40) M. A. Lazar, “Thyroid hormone receptors: multiple forms, multiple possibilities,” *Endocrine Reviews*, vol. 14, no. 2, pp. 184–193, 1993.

41) W. W. Chin, “Molecular mechanisms of thyroid hormone action,” *Thyroid*, vol. 4, no. 3, pp. 389–393, 1994.

42) J. Jansen, E. C. H. Friesema, C. Milici, and T. J. Visser, “Thyroid hormone transporters in health and disease,” *Thyroid*, vol. 15, no. 8, pp. 757–768, 2005.

43) H. Heuer and T. J. Visser, “Minireview: pathophysiological importance of thyroid hormone transporters,” *Endocrinology*, vol. 150, no. 3, pp. 1078–1083, 2009.

44)K. W. Park, H. B. Dai, K. Ojamaa, E. Lowenstein, I. Klein, andW. Sellke, “The direct vasomotor effect of thyroid hormones on rat muscle resistance arteries,” *Anesthesia and Analgesia*, vol. 85, no. 4, pp. 734–738, 1997.

45)A. R. Shepard and N. L. Eberhardt, “Molecular mechanisms of thyroid hormone action,” *Clinics in Laboratory Medicine*, vol. 13, no. 3, pp. 531–541, 1993.

46)B. G. Allen and M. P. Walsh, “The biochemical basis of the regulation of smooth-muscle contraction,” *Trends in Biochem-ical Sciences*, vol. 19, no. 9, pp. 362–368, 1994

DATA COLECTION CHART

QUESTIONAIRE

Patient details:

Name:

Age:

sex:

IP No.

ON ADMISSION:

Main Complaints :

Symptoms of Gallstone/CBD stones

H/o right upper quadrant pain :

H/o vomiting :

H/o dyspepsia :

H/o fever :

H/o jaundice :

Symptoms of Hypothyroidism

H/o weight gain :

H/o weakness/ lethargy :

H/o intolerance to cold :

H/o constipation :

H/o swelling of face or limbs :

H/o loss of hair / dry skin :

Co – Morbid Illness :

Significant Past History :

CLINICAL EXAMINATION:

Pulse: BP: RR: Temp:

Pallor: Icterus:

CVS: RS:

P/A:

Thyroid examination:

INVESTIGATIONS:

Hemogram:

Renal Function Test:

Liver Function Test:

BT/CT: Blood Grouping: Fasting Lipid Profile:

ECG: CXR:

USG Abdomen: CT Abdomen:

USG Thyroid: FNAC Goiter:

Thyroid profile: T3 -- T4 -- TSH —

Operative Procedure:

FOLLOW UP:

S.NO.	NAME	AGE	SEX	IP NO.	symptoms of Hypothyroidism					comorbidities	Thyroid examination	LFT		Lipid profile	TFT			USG Abdomen			Procedure	Remarks		
					cold intolerance	loss of appetite/ weight gain	Hair Loss	Constipation	Menstrual Disturbances			total bilirubin	direct bilirubin	chol/Tgl/LDL/HDL	T3 (ng/ml)	T4 (microgm/dl	TSH (micro IU/ml)	GB Calculi	CBD Calculi	No. Of Calculi			FNAC	THYROID MANAGEMENT
1	PEER AVULIYA	52	M	63457	-	-	+	-	-	DM	N	1	0.3	225/185/165/34	1.6	7.2	0.6	+	-	multiple	lap chol	Euthyroid		
2	MARI	25	F	67423	-	-	-	-	-	NIL	N	0.9	0.2	142/168/145/46	0.8	4.9	1	+	-	single	lap chol	Euthyroid		
3	PETCHI AMMAL	44	F	66534	-	+	-	+	-	DM	N	4.8	3.6	173/163/155/42	0.7	5.1	16.3	+	+	multiple	open chol/ CBD exp	Subclinical hypothyroid		Thyroxine
4	MADASAMY	33	M	67458	-	-	-	-	-	NIL	N	1.2	0.4	165/155/145/40	0.7	5.2	4.8	+	-	multiple	lap chol	Euthyroid		
5	NAKOORAMMAL	66	F	69865	-	-	-	-	-	NIL	N	1.2	0.3	253/165/172/42	1.3	7	0.9	+	-	multiple	open chol	Euthyroid		
6	CHELLAMMAL	43	F	67547	-	-	-	-	+	NIL	N	6.3	4.9	192/165/152/41	1.9	8.6	4	-	+	single	ERCP	Euthyroid		
7	ANANTHAN	27	M	70987	-	+	-	-	-	NIL	N	0.9	0.3	135/115/120/45	0.6	5.2	1.2	+	-	multiple	lap chol	Euthyroid		
8	VELLATHAI	58	F	71267	-	-	-	-	-	DM+HTN	N	0.8	0.2	234/167/178/42	1.6	6.5	0.8	+	-	multiple	lap chol	Euthyroid		
9	BHUVANESWARI	28	F	72341	-	-	-	-	-	NIL	N	1.2	0.2	135/160/126/51	1.3	5.1	0.7	+	-	single	lap chol	Euthyroid		
10	BALA ARASI	44	F	74532	-	+	-	-	+	NIL	Goiter	1	0.2	167/150/145/51	0.7	4.9	14.4	+	-	multiple	lap chol	Subclinical hypothyroid	colloid goiter	Thyroxine
11	MUPPIDATHY	46	F	79865	-	-	-	-	-	OLD PTB	N	1.2	0.4	138/154/142/43	1.3	4.4	0.6	+	-	multiple	lap chol	Euthyroid		
12	KOTHAI AMMAL	56	F	124	-	+	-	+	-	NIL	N	0.9	0.2	289/167/170/40	1.5	5.1	0.8	+	-	single	lap chol	Euthyroid		
13	MUTHU VINAYAGAM	48	M	678	-	+	+	-	-	HTN	N	0.9	0.4	168/155/145/45	0.6	4.9	18.6	+	-	multiple	lap chol	Subclinical hypothyroid		Thyroxine
14	CHITRA	35	F	1267	-	-	-	-	+	NIL	N	1.3	0.3	159/126/138/52	1.6	7.8	2.2	+	-	single	lap chol	Euthyroid		
15	ANNAI AMMAL	54	F	1543	-	-	-	-	-	NIL	N	1.2	0.3	234/175/185/38	1.9	8.2	0.8	+	-	multiple	lap chol	Euthyroid		
16	SELVI	34	F	1784	-	-	-	-	-	NIL	N	1	0.2	162/137/141/48	1	5.2	1.4	+	-	multiple	open chol	Euthyroid		
17	MOOKANDI	35	M	1985	-	-	-	-	-	NIL	N	5.7	4.2	175/145/135/45	0.9	5.1	17.2	+	+	multiple	open chol/ CBD exp	subclinical hypothyroid		Thyroxine
18	CHELLAMMAL	56	F	10965	-	-	-	-	-	DM	N	0.9	0.2	253/156/178/42	1.5	7	0.8	+	-	multiple	lap chol	Euthyroid		
19	AYYAR	58	M	10764	-	+	-	-	-	DM+OLD CAD	N	0.9	0.3	220/195/145/35	0.7	5.2	20.3	+	-	single	lap chol	Subclinical hypothyroid		Thyroxine
20	JOTHI	35	F	10342	-	-	-	-	+	NIL	N	1.2	0.3	195/154/168/42	1.8	7.2	0.9	+	-	multiple	lap chol	Euthyroid		
21	RAHAMATH NISHA	29	F	11432	-	-	-	-	-	NIL	N	1	0.2	142/134/121/52	1.6	6.7	1.4	+	-	multiple	lap chol	Euthyroid		
22	ANAND MUTHURAJ	28	M	11763	-	-	-	-	-	NIL	N	1.2	0.2	125/135/135/40	1.8	5.6	5.3	+	-	single	lap chol	Euthyroid		
23	MALAI APPAN	44	M	11343	-	+	+	-	-	DM	N	0.8	0.2	225/195/170/45	0.9	7.2	2.4	+	-	multiple	lap chol	Euthyroid		
24	SERMAKANI	32	F	12653	-	-	-	-	-	NIL	N	0.8	0.3	154/123/142/56	0.7	6	2.1	+	-	multiple	lap chol	Euthyroid		
25	VELAMMAL	65	F	11232	-	-	-	-	-	DM	N	1	0.2	309/195/198/35	0.9	5.1	0.9	+	-	multiple	lap chol	Euthyroid		
26	LAKSHMI	37	F	12897	-	-	+	-	-	NIL	N	1.1	0.3	213/154/165/48	1.4	7.1	0.7	+	-	single	open chol	Euthyroid		
27	SARASWATHI	43	F	14563	-	+	-	-	-	DM	N	1.2	0.4	165/154/148/52	1.1	10.2	0.6	+	-	multiple	lap chol	Euthyroid		
28	BALA AMMAL	53	F	14897	+	+	-	+	-	NIL	Goiter	1.1	0.2	231/195/178/53	0.2	4	20.2	+	-	multiple	open chol	Hypothyroid	nodular goiter	thyroxine
29	MUTHU AMMAL	63	F	14325	-	-	-	-	-	NIL	N	0.9	0.2	245/179/165/41	1.6	7.9	0.6	+	-	multiple	lap chol	Euthyroid		
30	KAVI PRIYA	35	F	15764	-	-	-	-	+	NIL	N	0.8	0.2	135/143/142/43	1.2	8.9	0.7	+	-	multiple	lap chol	Euthyroid		
31	MARIYA PREMA	47	F	15098	-	-	-	-	-	NIL	N	0.9	0.3	174/155/138/49	1.1	6.4	0.9	+	-	Single	lap chol	Euthyroid		
32	THANGAMMAL	52	F	16097	-	+	-	-	-	BA	N	5.1	3.8	216/186/174/42	1.2	5.9	0.8	-	+	Single	CBD expl	Euthyroid		
33	KUMAR	36	M	16532	-	-	-	-	-	NIL	N	1.2	0.3	135/115/125/45	0.6	5.1	0.7	+	-	multiple	lap chol	Euthyroid		
34	POONKODI	37	F	17865	-	-	-	-	-	NIL	N	1.1	0.2	165/145/149/51	1.2	5.2	0.9	+	-	multiple	lap chol	Euthyroid		
35	PARVATHI	42	F	18436	-	+	-	-	-	NIL	N	1.2	0.4	254/178/187/37	1.6	7.2	0.7	+	-	multiple	open chol	Euthyroid		
36	SELVI	41	F	18321	-	-	-	-	-	NIL	N	1	0.2	168/143/146/48	1.1	5.2	4.8	+	-	multiple	lap chol	Euthyroid		
37	RAMASAMY	64	M	19087	-	-	-	-	-	DM+OLD CAD	N	1.1	0.2	245/195/170/41	1.2	8.3	2.4	+	-	single	open chol	Euthyroid		
38	NAZEER BEGAM	54	F	21157	-	+	-	-	-	NIL	N	1.2	0.3	265/176/196/36	0.8	5	19.4	+	-	multiple	lap chol	Subclinical hypothyroid		thyroxine
39	INDIRA	33	F	21455	-	-	-	-	-	NIL	N	6.7	4.8	155/165/143/57	1.3	7.3	4.2	+	+	multiple	open chol/ CBD exp	Euthyroid		
40	LAKSHMI	27	F	21897	-	-	-	-	-	NIL	N	1.1	0.3	132/154/126/52	1.4	6.5	2.3	+	-	multiple	open chol	Euthyroid		
41	PADMAVATHI	32	F	24656	-	+	-	-	-	NIL	N	1.2	0.2	135/126/122/45	0.6	4.9	18.3	+	-	single	lap chol	subclinical hypothyroid		thyroxine
42	MUTHUAMMAL	42	F	25432	-	-	-	-	-	NIL	N	1.1	0.2	168/154/142/51	1.1	6.1	0.9	+	-	multiple	lap chol	Euthyroid		
43	MARIMUTHU	42	M	26789	-	-	-	-	-	NIL	N	1.2	0.3	155/160/155/45	1.3	6.7	2.6	+	-	multiple	lap chol	Euthyroid		
44	THANGARAJ	47	M	26908	-	-	-	-	-	DM+HTN	N	1.2	0.3	165/150/145/43	1.5	5.9	3.2	+	-	multiple	open chol	Euthyroid		
45	AYYAPAN	62	M	26743	-	+	-	+	-	DM+OLD CAD	N	0.9	0.2	225/195/190/33	1.6	5.1	2.2	+	-	multiple	lap chol	Euthyroid		
46	NELLAI VADIVU	43	F	27805	-	-	-	-	-	NIL	N	0.9	0.2	225/176/178/39	1.2	6.3	4.3	+	-	multiple	lap chol	Euthyroid		
47	SUBBAMMAL	45	F	27604	-	-	-	-	-	NIL	N	0.9	0.2	234/186/174/40	1.4	5.7	3.6	+	-	multiple	lap chol	Euthyroid		
48	PERACHI	36	F	28904	-	-	-	-	-	NIL	N	1.2	0.2	165/142/148/46	1.3	6.7	4.1	+	-	single	open chol	Euthyroid		
49	THANGA PUSPAM	46	F	28643	-	-	-	-	-	NIL	N	1.1	0.3	223/165/168/43	1.5	8.1	0.9	+	-	multiple	lap chol	Euthyroid		
50	KUMAR	46	M	28621	-	-	+	+	-	NIL	N	1.2	0.3	173/165/145/48	0.9	4.7	20.1	+	-	multiple	lap chol	Subclinical hypothyroid		thyroxine
51	RAJA AMMAL	43	F	29046	-	-	-	-	-	NIL	N	0.9	0.2	224/178/189/42	1.2	7.3	0.8	+	-	multiple	open chol	Euthyroid		
52	TAMIL SELVI	34	F	30097	-	-	-	-	-	NIL	N	0.9	0.2	231/187/181/40	1.6	6.9	3.7	+	-	multiple	lap chol	Euthyroid		
53	NALLA KANNU	53	M	31157	-	+	-	-	-	HTN+OLD CAD	N	1.4	0.3	315/195/190/38	1.2	8.2	4.3	+	-	single	lap chol	Euthyroid		
54	MARIAMMAL	56	F	32114	-	-	-	+	-	DM+OLD CAD	N	1.2	0.2	297/197/210/32	0.6	5.1	19.2	+	-	multiple	open chol	Subclinical hypothyroid		thyroxine
55	LAKSHMI	27	F	32565	-	-	-	-	-	NIL	N	0.9	0.2	165/145/147/49	1.1	5.6	4.9	+	-	multiple	lap chol	Euthyroid		
56	LATHA	43	F	32678	-	-	-	-	-	NIL	N	1.1	0.3	172/183/143/51	0.9	6.2	2.1	+	-	multiple	lap chol	Euthyroid		

S.NO.	NAME	AGE	SEX	IP NO.	symptoms of Hypothyroidism					comorbidities	Thyroid examination	LFT		Lipid profile	TFT			USG Abdomen			Procedure	Remarks		
					cold intolerance	loss of appetite/ weight gain	Hair Loss	Constipation	Menstrual Disturbances			total bilirubin	direct bilirubin	chol/Tgl/LDL/HDL	T3 (ng/ml)	T4 (microgm/dl	TSH (micro IU/ml)	GB Calculi	CBD Calculi	No. Of Calculi			FNAC	THYROID MANAGEMENT
57	MURUGAN	45	M	32656	-	-	-	-	-	NIL	N	1.2	0.4	165/155/140/43	1.7	5.8	3.7	+	-	multiple	lap chol	Euthyroid		
58	JEYALAKSHMI	46	F	33354	+	+	-	+	-	NIL	Goiter	1.4	0.4	223/192/174/42	0.3	2.1	23.1	+	-	multiple	lap chol	Hypothyroid	COlloid goiter	thyroxine
59	MUTHU SELVI	47	F	33453	-	-	-	-	-	NIL	N	0.9	0.2	212/156/165/48	1.6	7.3	5.6	+	-	single	lap chol	Euthyroid		
60	MAHA LAKSHMI	38	F	32334	-	-	-	-	-	NIL	N	1.1	0.2	132/112/117/52	1.8	5.8	4.6	+	-	multiple	lap chol	Euthyroid		
61	VIJAYA	42	F	34548	-	-	-	+	+	NIL	N	5.7	3.8	174/156/152/49	0.7	5.1	16.7	+	+	multiple	ERCP+lap chol	Subclinical hypothyroid		thyroxine
62	VADIVU	56	F	34212	-	-	-	-	-	DM	N	0.9	0.2	154/136/142/52	1.2	7.6	2.3	+	-	multiple	lap chol	Euthyroid		
63	MUTHUSAMY	38	M	35427	-	-	-	-	-	NIL	N	0.9	0.2	258/195/173/42	1.1	6.7	3.4	+	-	single	open chol	Euthyroid		
64	RAJESHWARI	37	F	35765	-	-	-	-	-	NIL	N	1.2	0.2	135/156/120/52	1.4	7.3	2.5	+	-	single	lap chol	Euthyroid		
65	BALAN	52	M	35763	-	-	-	-	-	HTN+OLD CAD	N	1.2	0.3	315/203/194/37	1.2	6.8	4.1	+	-	multiple	lap chol	Euthyroid		
66	PETCHI	53	F	36753	-	+	-	+	-	HTN	N	1.1	0.2	224/165/168/47	0.2	2.7	19.8	+	-	multiple	lap chol	Hypothyroid		thyroxine
67	PREMA	41	F	37545	-	-	-	-	-	NIL	N	1.1	0.2	141/126/126/51	0.9	5.6	0.9	+	-	multiple	lap chol	Euthyroid		
68	ROHINI	46	F	36542	-	-	-	-	-	NIL	N	1.1	0.3	234/156/168/48	1.4	6.9	3.1	+	-	single	open chol	Euthyroid		
69	SORNAKANI	32	F	35753	-	-	-	-	-	NIL	N	1.3	0.4	183/154/148/48	1.6	7.3	2.1	+	-	multiple	lap chol	Euthyroid		
70	MANI RAJ	37	M	36752	-	-	-	-	-	NIL	N	0.9	0.2	264/195/188/37	0.9	5.6	2.1	+	-	multiple	lap chol	subclinical hypothyroid		thyroxine
71	VELAMMAL	66	F	37314	-	+	+	-	-	NIL	N	0.9	0.3	163/145/151/47	0.8	5.1	14.4	+	-	single	lap chol	subclinical hypothyroid		thyroxine
72	ANTHONY	28	M	38976	-	-	-	-	-	NIL	N	1.1	0.3	131/123/115/49	1.1	5.3	3.1	+	-	multiple	lap chol	Euthyroid		
73	CHINNA PONNU	28	F	30976	-	-	-	-	+	NIL	N	7.8	5.2	142/135/121/52	1.1	6.7	2.1	+	+	multiple	open chol/CBD exp	Euthyroid		
74	MYDEEN BEEVI	46	F	31232	-	-	-	-	-	BA	N	0.9	0.3	245/187/195/45	0.6	4.8	16.3	+	-	single	open chol	Subclinical hypothyroid		thyroxine
75	ULAGAMMAL	57	F	37897	-	-	-	-	-	NIL	N	1.1	0.3	165/154/143/49	1.6	7.2	0.8	+	-	multiple	lap chol	Euthyroid		
76	MARIYAPPAN	64	M	38764	-	-	-	-	-	NIL	N	0.9	0.2	235/197/205/36	1.1	5.3	3.1	+	-	single	lap chol	Euthyroid		
77	VALLI	42	F	38097	-	+	-	+	-	DM+HTN	N	0.9	0.3	298/195/187/40	1.3	6.1	4.1	+	-	multiple	lap chol	Euthyroid		
78	RAJESHWARI	31	F	28124	-	-	-	-	-	NIL	N	1	0.2	132/142/112/52	1.1	5.7	2.1	+	-	multiple	open chol	Euthyroid		
79	JEYA SUDHA	43	F	38342	-	-	-	+	-	NIL	N	0.9	0.2	155/158/149/44	0.5	4.6	18.2	+	-	multiple	lap chol	Subclinical hypothyroid		thyroxine
80	MEENATCHI	53	F	32135	-	-	-	-	-	DM	N	1.1	0.2	278/165/175/45	1.2	6.3	2.7	+	-	single	lap chol	Euthyroid		
81	SANKARA LINGAM	56	M	38976	-	-	+	-	-	NIL	N	8.1	6.7	215/155/195/37	0.9	5.6	1.2	-	+	single	ERCP	Euthyroid		
82	MUTHU SELVI	47	F	38654	-	+	-	-	-	NIL	N	1.1	0.3	267/185/176/37	0.9	6.2	3.1	+	-	multiple	lap chol	Euthyroid		
83	ESAKKI AMMAL	35	F	39087	-	-	-	-	-	NIL	N	1.2	0.4	138/150/121/52	1.1	7.6	3.7	+	-	multiple	lap chol	Euthyroid		
84	SHANTHI	46	F	39867	-	-	-	-	-	NIL	N	1.2	0.3	165/154/141/42	1.4	7.2	0.9	+	-	single	lap chol	Euthyroid		
85	AMBIKA	42	F	39125	-	+	-	-	+	NIL	Goiter	1.4	0.4	265/186/178/41	1.1	5.2	15.6	+	-	multiple	lap chol	subclinical hypothyroid	nodular goiter	thyroxine
86	SHEIK MOHAMED	52	M	40005	-	-	-	-	-	DM+HTN	N	1.2	0.3	256/175/172/44	1.4	6.9	2.1	+	-	multiple	open chol	Euthyroid		
87	VEERA AMMAL	65	F	40012	-	+	-	-	-	DM+OLD CAD	N	1.1	0.4	298/165/176/43	1.1	5.2	16.1	+	-	single	lap chol	Subclinical hypothyroid		thyroxine
88	UTHRA	43	F	40564	-	-	-	-	-	HTN	N	1.2	0.2	135/143/121/52	1.3	6.2	4.6	+	-	multiple	lap chol	Euthyroid		
89	PON MARI	36	F	40521	-	-	-	-	-	NIL	N	1.2	0.3	165/171/142/47	1.2	6.7	4.3	+	-	multiple	lap chol	Euthyroid		
90	GANESAN	46	M	40653	-	-	-	-	-	NIL	N	1.3	0.4	223/169/184/42	1.1	5.8	3.4	+	-	single	lap chol	Euthyroid		
91	KANAGA RAJ	42	M	40123	-	-	-	-	-	NIL	N	1.1	0.2	256/188/176/43	1.6	5.2	1.8	+	-	single	lap chol	Euthyroid		
92	SHANMUGA VADIVU	48	F	40234	-	-	-	+	-	NIL	N	0.9	0.2	194/174/153/45	0.9	4.6	16.1	+	-	multiple	lap chol	Subclinical hypothyroid		thyroxine
93	BAKKERAL BANU	63	F	40432	-	-	+	-	-	DM+HTN+CAD	N	0.9	0.2	314/237/216/30	1.2	5.8	2.1	+	-	multiple	open chol	Euthyroid		
94	SARASWATHI	32	F	40657	-	-	+	-	-	NIL	N	1.2	0.3	214/160/164/45	1.4	6.7	2.3	+	-	multiple	lap chol	Euthyroid		
95	KARPAGA VALLI	48	F	40784	-	+	-	+	-	NIL	Goiter	9.3	6.7	135/159/115/45	1.2	5.1	16.7	+	+	multiple	ERCP+lap chol	Subclinical hypothyroid	colloid goiter	thyroxine
96	XAVIER	44	M	41238	-	-	-	-	-	NIL	N	0.9	0.2	165/155/140/42	0.9	5.2	2.1	+	-	single	lap chol	Euthyroid		
97	PARAMESHWARI	26	F	41234	-	-	+	-	-	NIL	N	0.9	0.3	145/115/124/55	1.4	5.7	1.2	+	-	multiple	lap chol	Euthyroid		
98	KARUNAKARAN	26	M	41543	-	-	-	-	-	NIL	N	1.3	0.4	132/115/100/50	1.5	6.7	0.9	+	-	multiple	open chol	Euthyroid		
99	ARPUTHA MARY	54	F	41532	-	+	-	+	-	DM+OLD CAD	N	1.2	0.3	215/176/168/48	0.6	4.9	15.5	+	-	multiple	lap chol	Subclinical hypothyroid		thyroxine
100	SORNA KILI	34	F	41674	-	-	-	-	-	NIL	N	0.9	0.2	165/145/143/48	0.9	5.6	6.8	+	-	multiple	lap chol	Euthyroid		

DM	DIABETES MELLITUS
HTN	HYPERTENSION
OLD PTB	OLD PULMONARY TUBERCULOSIS
CAD	CORONARY ARTERY DISEASE
BA	BRONCHIAL ASTHMA
CHOL	SERUM CHOLESTEROL
TGL	SERUM TRIGLYCERIDE
LDL	LOW DENSITY LIPOPROTEIN
HDL	HIGH DENSITY LIPOPROTEIN
LAP CHOL	LAP CHOLECYSTECTOMY
OPEN CHOL	LAP CONVERTED OPEN/OPEN CHOLECYSTECTOMY
T3	REF RANGE: 0.5-2.0 ng/ml
T4	REF RANGE: 4.4-11.6 microgm/dl
TSH	REF RANGE: 0.5-7.0 microIU/ml