"EFFECT OF DIABETES ON OPERATIVE OUTCOME OF LAPAROSCOPIC CHOLECYSTECTOMY: A ONE YEAR CASE SERIES STUDY AT TERTIARY CARE HOSPITAL, BELGAUM"

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ENDORSEMENT

This is to certify that the dissertation entitled **"EFFECT OF DIABETES ON OPERATIVE OUTCOME OF LAPAROSCOPIC CHOLECYSTECTOMY: A ONE YEAR CASE SERIES STUDY AT TERTIARY CARE HOSPITAL, BELGAUM"** is a bonafide research work done by **CANDICATE REG NO. BH0113007.**

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LIST OF ABBREVIATIONS USED

ACR	-	American College of Radiology
AD	-	Anno Domini
AIDS	-	Acquired immunodeficiency syndrome
ALT	-	Alanine aminotransferase
AST	-	Aspartate aminotransferase
B.C.	-	Before Christ
BMI	-	Body mass index
BP	-	Blood pressure
CBD	-	Common bile duct
CCK	-	Cholecystokinin
CDC	-	Centre for Disease Control and Prevention
CI	-	Confidence interval
cm	-	Centimeters
CT	-	Computed tomography
DCCT	-	Diabetes Control and Complications Trial
DIDA	-	Diisopropyl iminodiacetic acid
DM	-	Diabetes mellitus
e.g.,	-	For example
ERCP	-	Endoscopic retrograde cholangiopancreatography
EUS	-	Endoscopic Ultrasound
FPG	-	Fasting plasma glucose
GB	-	Gall bladder
GSD	-	Gallstone disease
h	-	Hours

HbA1c	-	Glycosylated haemoglobin
HBS	-	Hepatobiliary scintigraphy
HIDA	-	Hepatobiliary iminodiacetic acid
hrs	-	Hours
ICU	-	Intensive care unit
IGT	-	Impaired glucose tolerance
Kg/m^2	-	Kilogram per square meter
LC	-	Laparoscopic cholecystectomy
mg	-	Milligrams
mg/dL	-	Milligram per deciliter
mm Hg	-	Millimeters of mercury
mm	-	Millimeters
mmol/l	-	Millimole per liter
MRCP	-	Magnetic resonance cholangiopancreatography
MRI	-	Magnetic resonance imaging
mRNA	-	Messenger ribonucleic acid
NGSP	-	National Glycohemoglobin Standardization Program
NIH	-	National Institute of Health
OGTT	-	Oral glucose tolerance test
p	-	Probability
RR	-	Relative risk
SD	-	Standard deviation
TPN	-	Total parenteral nutrition
US	-	United States
USA	-	United States of America

VIP	-	Vasoactive intestinal polypeptide
viz.	-	Namely
vs	-	Versus
WHR	-	Waist hip ratio

ABSTRACT

Background and objectives

Diabetes is reported to be a risk factor for gallstone formation and these patients are generally more prone to operative and post-operative morbidities. This study was aimed to find intra-operative difficulties and complications during laparoscopic cholecystectomy in diabetics and non diabetics.

Methodology

This one year case series was carried out in the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum. A total 60 patients (30 diabetics and 30 non diabetics) undergoing elective laparoscopic cholecystectomy from January 2014 to December 2014 were studied and the operative difficulties during the surgery and complications encountered were noted. In patients with diabetes, the mean duration of diabetes was 9.08 ± 5.15 years and most of the patients (60%) were on oral hypoglycaemic agents and had moderate glycaemic control (43.33%).

Results

The male to female ratio was 1.30:1 and 56.67% of the patients were males in diabetic as well as and non diabetic group. Among the patients with diabetes, 60% were aged between 46 to 60 years compared to 23.33% in non diabetics ($p<0.001$). Other pre operative characteristics including clinical presentation duration of symptoms, history of other associated diseases and vitals were comparable in diabetic and non diabetics patients ($p>0.050$). Significantly higher number of patients in diabetic group underwent open pneumoperitoneum

(40% vs 16.67%; p=0.045). Statistically significant difference was noted with regard to the appearance of gall bladder, adhesions, dissection of Calot's triangle, releasing adhesions, intra operative bleeding, grasping of gallbladder, removal of gallbladder from liver bed, extraction of specimen, drain placement and conversion (p<0.050). The operative time was significantly higher in patients with diabetes mellitus (103.00 ± 26.54 vs 78.83 ± 19.06 minutes; p<0.050).

Conclusion and interpretation

Diabetes mellitus is significantly associated with several operative difficulties and prolonged surgical time during laparoscopic cholecystectomy.

Keywords

Diabetes mellitus; Laparoscopic cholecystectomy; Operative difficulties;

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INTRODUCTION

Cholecystitis is defined as inflammation of the gallbladder. Ninety percent of cases involve stones in the gallbladder (that is, calculous cholecystitis), with the other 10% of cases representing acalculous cholecystitis.[1]

Gallstones can occur anywhere within the biliary tree, including the gallbladder and the common bile duct. Gallstones are hard, pebble-like deposits. Gall stones vary in their composition, majority being cholesterol and remaining being mixed and pigmented.[2]

About 10% to 15% of the adult western population has gallstones. Between 1% and 4% become symptomatic in a year.[1] More than half a million cholecystectomies are performed per year in the United States alone. Regional differences exist in the cholecystectomy rates.[3] In India, the prevalence of gallbladder diseases is increasing and hence the cholecystectomies have also been progressively increasing.[4]

Symptoms of gall stone diseases are pain in the right upper abdomen, fever, jaundice, bloating, clay-colored stools, nausea and vomiting. Further complications of gallbladder disease include gallstone pancreatitis, gallstone ileus, biliary cirrhosis and carcinoma gallbladder. Gallstones may be as small as a grain of sand or they may become as large as an inch in diameter, depending on how long they have been forming. A stone blocking the opening from the gallbladder or cystic duct usually produces symptoms of biliary colic.[2]

Laparoscopic cholecystectomy provides a safe and effective treatment for most patients with symptomatic gallstones and is the treatment of choice for cholelithiasis. It has now become the most common operation performed on the biliary tree. Since the introduction of laparoscopic cholecystectomy, the number of cholecystectomy performed in the United States has increased from 5 to 7 lakhs/year. The advantages of laparoscopic cholecystectomy are earlier return to bowel function, less postoperative pain, good cosmesis, shorter length of hospital stay, earlier return to full activity, and decreased overall cost.[5]

Due to some technical problems and constraints, open Cholecystectomy is still widely used and 5 to 15% of laparoscopic operations inevitably turn into open Cholecystectomy. As a result operating time, costs and morbidity are increased. Conditions such as acute cholecystitis, gangrene, empyema of the gallbladder, obesity, pregnancy and previous upper abdominal surgery were previously considered as contra indications for laparoscopic cholecystectomy. These conditions are today known as risk factors of laparoscopy and only make this procedure harder. These risk factors are the causes of conversion of Laparoscopic Cholecystectomy to open Cholecystectomy.[6]

From a surgical point of view, diabetes is risk factor for gallstone formation, and complications. Furthermore, diabetic patients are generally more prone to operative and post-operative complications than their normal counterparts. Diabetes mellitus is a chronic and potentially disabling disease which is reaching an epidemic proportion and had become a major threat to global public health.[1] Diabetes Mellitus has evolved into a global epidemic and India has the second largest population with diabetes. Diabetes caused 4.9 million deaths in 2014 and every seven seconds a

person dies from diabetes or its complication. Based on the recent statistics of International Diabetes Association it is estimated that worldwide 387 million people have diabetes and by 2035 this will rise to 592 million. The prevalence in India is over 65 million and these figures are expected to increase to over 100 million by 2030.[7,8,9]

Diabetic patients are prone for many medical disorders. Therefore, the side effects of such disorders can be intensified with surgery. In addition, stress caused by surgery, trauma and infection lead to an increase in the production of the anti-insulin catabolic hormones. This consequence also adds to the morbidity caused by diabetes.[6]

Increased incidence of intra operative complications during laparoscopic cholecystectomy are seen in diabetic patients due to severe inflammation and distortion of anatomy. As a result operation time, costs and morbidity are increased in diabetics. Hence diabetes may be considered as an independent risk factor for intraoperative complications for laparoscopic cholecystectomy.[6]

However, morbidity and mortality from gallstones in the diabetic patients in comparison with non-diabetics have always been controversial. Previous studies have detected increased complications while others have proposed no such difference. Considering these facts the present study was undertaken to see whether the presence of diabetes is associated with increased intra-operative complications of laparoscopic cholecystectomy so as to predict the complications that may be encountered intra-operatively which will help to take precautions to achieve best possible outcome.

OBJECTIVES

Aims

The present study was aimed to find out the effect of diabetes on intra-operative complications of laparoscopic cholecystectomy.

Objectives

1. To find out whether diabetes is a risk factor for operative difficulties in patients undergoing laparoscopic cholecystectomy.

2. To propose strategies to prevent the intraoperative complications.

REVIEW OF LITERATURE

Historical aspects

Archeological excavations have proved the presence of gall stones in young Egyptian women which shows that humans have suffered from cholelithiasis for more than 2000 years.[10]

Greek physician Alexander Trallianus first described gallstones as the calculi within the bile ducts. In the 16th century, Vesailius and Fallopius described gallstones found in the gall bladder of the dissected human bodies.[12] The first interaction of gallstones and surgeons occured in 1687. Stal Pert Von Der Wiel, during operating a patient with peritonitis accidentally found gallstones.[3]

Jean-Louis Petit is known as the founder of gall bladder surgery. He described the removal of gallstone and drainage of the gall bladder by creating fistula in patients with empyema gallbladder in 1733.[13] In 1859, J. L. W Thudichum introduced elective cholecystostomy in two stages.[14,15] In the first stage, sewing the inflamed gall bladder to the anterior abdominal wall was done by making a small incision, which was used as a route for the removal of gall stone later. Dr John Stough Bobbs from Indianopolis, Indiana during operating on a patient with ovarian cyst On July 15, 1867, found an inflamed and adherent sac filled with "several solid ordinary rifle bullet" like structures. After opening the sac, it was incidentally found to be the gall bladder packed with multiple gallstones. He removed the gallstones, closed the defect in the gall bladder and left the gall bladder in situ (cholecystostomy).[16]

Marion Simms was credited for designing, perfecting and performing the first cholecystostomy on a 45-year-old woman with obstructive jaundice in 1878.[17] It paved the way for Theodor Kocher for performing the first successful cholecystostomy in June 1878.[15-17] Carl Johann August Langenbuch[17] described these measures to be only temporary and not a definite solution for gallstones. In those years, Zambecarri in 1630 and Teckoff in 1667 from two animal experiments explained that the gall bladder was not essential to life.[17] Also, physicians had the opinion that the gall bladder itself is responsible for formation of stones. Langenbuch practised the technique of cholecystectomy by cadeveric dissection. On July 15, 1882 he successfully performed cholecystectomy in a 43-year-old man who was suffering from the disease for 16 years.[17]

An audit performed in 1886 showed 39 cholecystotomies with a mortality of 27% against 8 cholecystectomies with a mortality of 12%. By the turn of the century it was established that cholecystectomy could provide permanent relief from pain as compared to cholecystostomy which gave a permanent fistula and did not relieve pain.

In the late 19th century, before the modern era of cholecystectomy, Langenbuch explained gall stone pathology and performed the first successful cholecyctectomy.[11] On June 9, 1901 Langenbuch died because of complicated appendicitis but he showed the path for further advanced and modified biliary surgeries.[17]

Surgical Anatomy

The gallbladder is pyriform in shape and is located in the gallbladder fossa on the inferior surface of right lobe of liver. It projects from the right end of the porta hepatic to the inferior border of liver.[18] Gallbladder is attached to the liver by the connective tissue, ranging from being completely covered by the peritoneum to being connected to the liver by a short mesentry.

It is 7 to 10 cm long, 3 cm broad at its widest and has 30-50ml capacity. It is divided as fundus, body and neck. The fundus, extends down, forwards and to the right. It is visible below the inferior border of liver and comes in contact with the anterior abdominal wall at the junction of the ninth right costal cartilage and the lateral edge of the right rectus abdominus muscle. Posteriorly it is related to transverse colon. The body is directed medially, towards the right end of the porta hepatis and it is continuous with neck. It is related above to the liver, below to the transverse colon and further back to the first and upper end of second segment of duodenum.

The neck is narrow, directed upwards and forwards and then abruptly backwards and downwards, joins the cystic duct. Thin areolar tissue containing cystic artery connects the neck to the liver. The mucosa of the neck shows a spiral valve which gives its surface a spiral grove when the neck is distended. Hartmann's pouch (originally described by Broca) is a small recess going down and backwards.

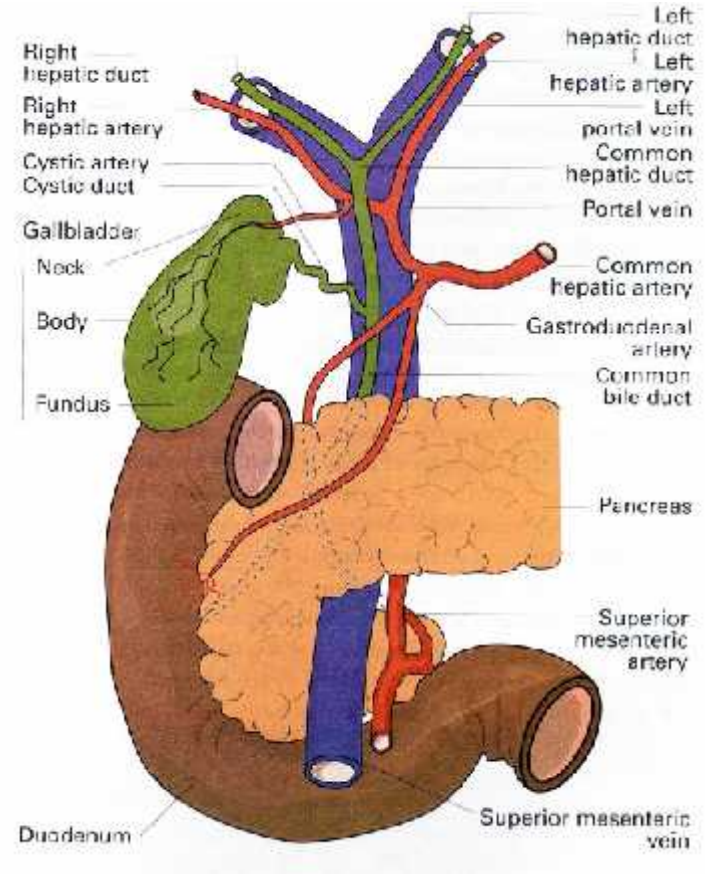


Figure 1. Surgical anatomy of biliary tract[20]

The cystic duct is 3 to 4 cm long; projecting backwards, downwards and medially. It begins from the neck of the gallbladder and joins the common hepatic duct to form the common bile duct. The junction is located just below the porta hepatis. But may occur at a lower level, where the cystic duct lies along the right edge of lesser omentum. Its mucosa shows 5-10 concentric folds projecting obliquely in regular succession, like a spiral valve, referred as the "valve of Heister".[18-21]

Arterial Supply of the Gallbladder:[18]

Cystic artery, branch of right hepatic artery is the major blood supply of the gall bladder. The gall bladder also receives many small vessels from hepatic bed.

The cystic artery cross the posterior surface of common hepatic and cystic ducts and comes to lie on the neck of the gall bladder, after which it runs downward forwards and divides into superficial and deep branches. The cystic artery gives branches to the hepatic ducts and to the upper part of the common bile duct. The lower part of the bile duct is supplied by several branches from the posterior superior pancreatico-duodenal artery. The right hepatic artery supplies branches to the bile duct.

Variations in the cystic artery's origin are of surgical interest. In 800 specimens Anson (1963) observed the following incidences, origin from the right hepatic artery 63.9%, the hepatic trunk 26.9%, left hepatic 5.5% gastroduodenl 2.6%,superior pancreaticoduodenal 0.3%, right gastric 0.1%, coelic trunk 0.3%, and superior mesenteric 0.8%. Accessory cystic artery If present, may be the branch of the common hepatic or one of its branches while the cystic artery supplies the the hepatic ducts and upper part of common bile duct. The cystic artery is an end artery and its occlusion leads to the gangrene of the gall bladder.[22]

Venous Drainage of the Gallbladder:[18]

The venous drainage of the gall bladder may vary considerably. Those from its upper surface run directly into the liver through the fossa of the gallbladder to join the hepatic veins. Those from the rest of the gall bladder join to form one or more cystic veins on its neck. Rarely a single or double cystic vein drains directly into right branch of the portal vein. They do not accompany the cystic artery.

Lymphatic Drainage[18]

The lymphatic drainage the gall bladder is of significant importance in 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 at the junction of cystic and common hepatic ducts. Efferent vessels from the nodes pass in the free edge of the lesser omentum and drain into the celiac group of preaortic nodes.

The sentinel node may attain a considerable size and may distort the normal anatomy in patients with acute cholecystitis or gallbladder carcinoma. The subserosal lymphatic vessels of the gall bladder also drain into the subcapsular lymphatic channels of liver, which is responsible for the frequent spread of carcinoma of gallbladder to the liver.

Nerve Supply[18]

The wall of the gall bladder is richly innervated with both sympathetic and parasympathetic nerve fibers, accompanying the hepatic artery and its branches. Parasympathetic fibers originate from the hepatic branch of anterior vagal trunk. They stimulate contraction of the gall bladder and relax the ampullary sphincter. Sympathetic fibers originate from the cell bodies in the celiac ganglia, with the pre-ganglionic cells in the lateral horn of the spinal cord segments, T7-T9 and they inhibit contraction. Autonomic plexus is situated in the muscular and sub mucous layers. Fibers from the right phrenic nerve communicate with celiac plexus and reach the gallbladder via hepatic plexus. It explains the “referred pain at right shoulder” in the gall bladder diseases. The biliary tract pain usually starts in the right

hypochondrium and epigastrium and may radiate round to the back in the infrascapular region, in the area of distribution of spinal nerve T7-T9.

Triangles of cholecystectomy

Jean – Francois Calot defined a triangular anatomical area formed by the common hepatic duct medially, the cystic duct inferiorly and the cystic artery superiorly in 1891. The previous concept is of the Calot's triangle has its upper limit not the cystic artery but the inferior surface of the live which is now known as hepatocystic triangle.[23] This triangle is of considerable surgical importance because a number of important structures pass through it. Therefore it should be identified by the surgeons to prevent the damage to extrahepatic biliary system.[24]

Common anomalies and variations

1. Absent gall bladder – extremely rare, autopsy incidence of 0.03% have been reported.[18]

2. Variation in size and shape of gall bladder.
    a. Bilobed gall bladder.
    b. Fundule divertculum.
    c. Phrygian cap.
    d. Hour glass gall bladder.

3. Variation in position - left sided gall bladder, floating gall bladder.

4. Double gall bladder, duplication of gall bladder - two separate cavities and two separate cystic ducts with an incidence of approximately 1 in 4000. In a

pathological process such as cholelithiasis and cholecystitis one organ may get involved while the other is spared.[25]

5. Other anomalies related to gall bladder
    a. Intra-hepatic gall bladder
    b. Diverticulum's of body or neck of gall bladder
    c. Accessory peritoneal fold due to congenital adhesions.

Floating gall bladder is seen when there is increase in the peritoneal attachment; seen in 5% of patients and susceptible for torsion, resulting in the gangrene or perforation of the gallbladder.[18]

Rarely cystic duct may be absent. Two or more cystic ducts may combine. The junction of the cystic duct and common hepatic ducts may vary in its level from the porta hepatis to behind or even below the duodenum's first part. In the low insertion of the duct, these two may be connected by fibrous tissue. Accessory hepatic ducts may arise, most frequently from the right lobe of liver and join the main hepatic duct and rarely may drain in the cystic duct itself.[21]

Physiology of gall bladder[20,21,24]

The primary function of gall bladder is to concentrate the bile by absorption of water and sodium so that it acquires greater digestive power. The gallbladder and bile duct walls are well adopted for the function of storing and secreting bile into the duodenum during the process of digestion. The concentrating power of the gallbladder makes the storage in small amount possible. 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 regulated by the intestinal migratory myoelectric complex in fasting state. During refilling it intermittently contracts and secretes pulses of bile into the duodenum. This constant fluctuation in the bile stasis and flow prevents stone formation.

Gallbladder tone is governed by both vagus and circulating peptides. During cephalic phase of digestion vagal stimulation causes gallbladder contraction. During interdigestive period, vagal neurons and circulating polypeptides mediate the contraction. Vasoactive intestinal polypeptide [VIP] released by vagal neurons inhibits gallbladder contraction and causes post prandial gallbladder filling. Gallbladder motility is inhibited by truncal vagotomy and by chronic fasting.

The gallbladder exhibits;

1. Tonic contractions
2. Rhythmic contractions

Constitution of bile

Bile at the point when it leaves the liver is composed of 97% of water, 1 to 2% of bile salts and 1% of bile pigments, cholesterol and fatty acids. The understanding of the constituents of bile is necessary as they have a great impact in the etiology of cholelithiasis.

Bile acids and bile salts:

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

Bile pigments

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

Lipids

The normal bile contains cholesterol, fatty acids and phospholipids. Cholesterol content of the bile is normally 0.04 to 0.16%. It is present in the free state and its concentration is more in gall bladder bile. Normally the cholesterol and bile salts ratio varies between 1:20 to 1:30.

Mucin

Its main constituent is mucealbumin and it increases in obstructive and inflammatory conditions of the biliary tract. It forms the cementing substance in gall stones. The functions of bile are brought about by the bile acids and are digestion and absorption of fats and fat soluble vitamins, mild laxative effects on the intestine

and also an antiputrefactive effect by their bacteriostatic property on intestinal flora. Bile salts are the best cholerectics.

Entero Hepatic Circulation

Following normal fatty meals, pancreatic lipase causes emulsification of the cleavage products from triglyceride hydrolysis results in the incorporation of fat into micelles. Absorption of fat occurs primarily in the upper intestine, whereas little absorption occurs in the lower third of the small intestine. In the ileum there are specific high affinity binding sites which are responsible for the active absorption of bile acids. Due to the efficiency of this absorptive process, less than 5% of the daily excreted bile reaches the colon. After absorption, bile acids enter the portal vein and are returned to liver. The efficiency of the hepatic removal of bile acids accounts for the extremely low peripheral blood levels normally found. The 95% return rate of bile acids to the liver has two consequences. First, most of the bile acids excreted in bile are actively recycled than being newly synthesized. Second bile acids exerts a feedback inhibition that regulates estrogens, cholesterol and fat soluble vitamins.

Laparoscopic anatomy

The advent and popularity of Laparoscopic cholecystectomy has changed the look and understanding of the gallbladder anatomy mainly of the Calot's triangle. The term ‘laparoscopic anatomy’ is now described in anatomy texts. The different anatomical ‘laparoscopic view’ of the gallbladder and the structures around it, mainly the Calot's triangle after retraction intra-operatively leads to the distortion of anatomy. The Calot's triangle gets flattened in real instead of opening.[26] The

posterior dissection of the Calot's triangle during a laparoscopic cholecystectomy changes the view of biliary anatomy and adds to its distortion.[26]

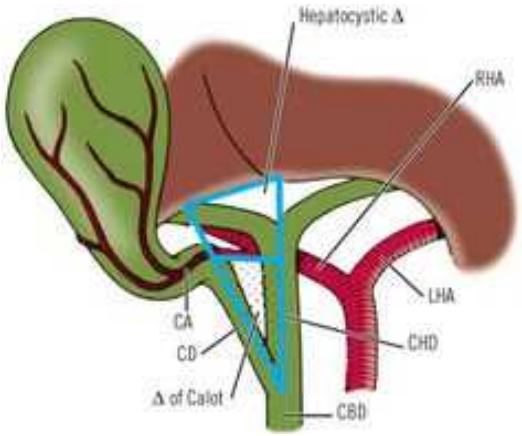


Figure 2. Callot's triangle

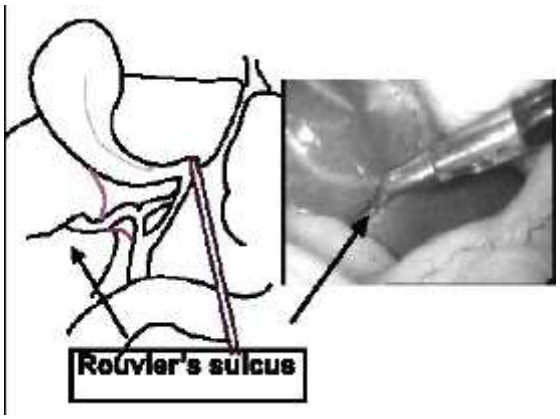


Figure 3. Rouviere's sulcus[26]

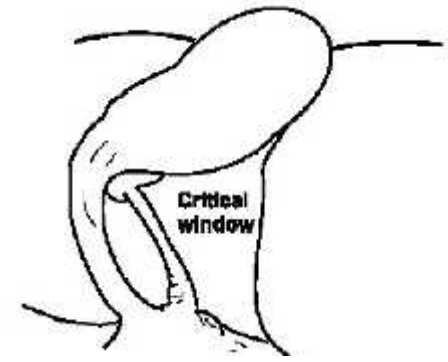


Figure 4. The critical view of safety window[26]

The Rouviere's sulcus is a narrow linear depression on the liver and is located at the level of the porta hepatis near the entry of right pedicle into the liver. It is clearly seen during the posterior dissection. The guidelines describe the safe dissection at the level anterior to this sulcus in order to prevent bile duct injury. Moreover, it is an 'extrabiliary' reference point so is unaffected due to bilary pathology. Similarly, a clear delineation of the point where cystic duct emerges from the gallbladder as well as the clear dissection in the space between the liver and the gallbladder (safety window or critical view) is an important measure in preventing intraoperative injury to the bile duct.[26]

Epidemiology

Cholecystitis is inflammation of the gallbladder. Ninety percent of cases occur due to stones in the gallbladder known as calculous cholecystitis, while remaining 10% cases represents acalculous cholecystitis.[1]

Gallstones cause significant morbidity in developed countries, affecting 10% to 15% of the adult population. 20 to 25 million Americans have gallstones or might develop at the later age.[27,28] With around 1.8 million reported cases every year, gallstone disease is a leading cause for hospital admissions due to gastrointestinal diseases.[27]

Gallstone disease also has inherent risks. Trials have shown an increased overall mortality from gallstone diseases, especially in Americans and Pima Indians.[28-30]

Due to the increase in the incidence of gallstone disease, a concomitant increase is seen in gallstones related complications.[31]

Age distribution for cholecystitis

The incidence of cholecystitis rises with increasing age. At least 10% of adults have gallstones. The prevalence varies with age, sex, and ethnic group. There is an increasing prevalence with age, after the age of 60 about 10 to 15% of men and 20 to 40% of women have gallstones.[12]

Sex distribution for cholecystitis

Gallstones are seen two to three times more commonly in female population. Increased levels of progesterone during pregnancy may lead to biliary stasis, responsible for increased incidences of gallbladder disease in pregnant females. Acalculous cholecystitis is more commonly seen in elderly men.[32]

Prevalence of cholecystitis by race and ethnicity

Cholelithiasis is the major risk factor for cholecystitis. Scandinavian descent, Pima Indians, and Hispanic populations show an increased prevalence of cholelithiasis, while it shows decreased incidence in sub-Saharan African and Asian population. In the United States, white people suffer from gallstones more commonly than black people.[33,34]

The prevalence of gallstones is especially high in the Scandinavian countries and Chile. Among Native Americans, Mexican Americans and American Indians, especially the Pima tribe, have an increased predisposition to gallstone formation.[33]

Gallstone disease in India

Although well documented by authors in India, the data has not received much attention in the West. In literature of Medicine and Gastroenterology published from the West, India is included along with countries which have low incidence of gallstones. The prevalence of gallstone disease varies in different parts of India.[4] Malhotra in 1966 conducted an epidemiological study in Indian Railway employees and it showed that North Indians had seven times higher prevalence of gallstones as compared to South Indian employees. In northern states including Kashmir where good epidemiological studies have been performed, a very high and increasing prevalence were reported.[35-39] Khuroo from Kashmir reported a prevalence of 6.12% (men 3.07% and women 9.6%) the prevalence increasing progressively to reach a peak in the sixth decade.[40] The prevalence rate is significantly higher in multiparous women.[38] There was no correlation noted with diet, obesity or socioeconomic status.[36]

A different picture arises from data available from south India. Jayanthi et al[40] reported that mixed and pigment stones were more common compared to cholesterol stones in Tamilnadu. They found no correlation with demographic features or social customs. An interesting observation that needs confirmation is an association with high consumption of tamarind. There is no scientific explanation for this observation. The overall prevalence of gallstones in Tamilnadu appears to be lower than in the North. However cholecystectomy once an extremely uncommon surgery in south India has become very frequent reflecting either a real increase in the prevalence of the disease, better diagnosis because of ease of diagnosing stones by abdominal ultrasound or the availability of Laparoscopic cholecystectomy.[4]

Clinical aspects of gallstone disease

Asymptomatic/Silent gallstones

Gallstones are very common. 10% to 20% of Americans suffer from stones in their lifetime.41 Most of them will remain asymptomatic. Upto 80% of the population will never develop biliary pain or complications due to gallstones such as acute cholecystitis, cholangitis, or pancreatitis.[42] Thus, most gallstones are clinically "silent," and found incidentally during abdominal ultrasonography done due to other reasons. Asymptomatic patients, may eventually develop symptoms like biliary pain requiring treatment, but the risk is very low, around 2% to 3% every year, 10% by 5 years.[28,43,44] 1% to 2% every year may develop complications due to gallstones.[28,41] Hence, expectant management is an appropriate choice for silent gallstones. The exception is the population with high risk for developing biliary complications:[28]

- Large gallstones (>3 cm) or gallbladder filled with stones. It carries a high risk for development of carcinoma gallbladder. It is an indication for prophylactic cholecystectomy.

- Patients suffering from Sickle cell disease are at high risk for developing pigment gallstones. Prophylactic cholecystectomy should be considered because complications due to gallstones are difficult to distinguish from the clinical picture of a sickle cell crisis or complications due to it like infarction of the liver or spleen. When performed early, in an elective setting, cholecystectomy reduces the surgical risks, but still shows a mortality rate at 1% [45]

- Patients receiving solid organ transplantation like heart, lung, kidney or pancreas- stem cell (bone marrow) transplantation has its own risk for cholelithiasis and biliary sludge formation, more problematic are the consequences of solid organ transplantation in which gallstones develop frequently and lead to symptoms and complications like cholecystitis, more commonly in the first 2 years.[46] Liver transplantation is an exception as cholecystectomy is performed at the time of hepatectomy.

- Abdominal surgery, being done for other pathology may benefit from cholecystectomy at the same setting, for patients with high risk for formation of gallstone and its complications. Prophylactic cholecystectomy should be considered in morbidly obese patients undergoing bariatric surgery.[47]

Symptomatic gallstone disease

Most gallstones are asymptomatic, hence it is necessary to define symptoms of gallstone disease like biliary pain and associated complications, also nonspecific abdominal symptoms like dyspepsia and bloating. Biliary pain shows a particular pattern.[28] The established criteria defines biliary pain to be episodic, severe pain located in the upper abdomen which lasts more than 30 minutes and its associated features such as nocturnal onset; nausea and vomiting; radiating through to the back. Avoiding an unnecessary cholecystectomy has becomes critically relevant with the increasing rates of surgery.[28]

Aacalculous (functional)gallbladder disease

The etiology of biliary pain is an increased intraluminal pressure due to the contraction of gallbladder against the outlet obstruction. In calculous cholecystitis,

the obstruction is caused by a stone in the cystic duct while in acalculous cholecystitis (functional gallbladder disease, gallbladder dyskinesia), the pain may be either due to obstruction in the cystic duct or because of lack of co-ordination between gallbladder contraction and sphincter of Oddi relaxation. An impaired gallbladder emptying can be reliably diagnosed by cholecystokinin-cholescintigraphy.[48]

The frequency and management of acalculous gallbladder disease is still unclear. Even though the exact frequency of functional gallbladder disease is unknown, increase in the rates of cholecystectomy for such cases definitely would affect the surgical rates. Thus, there is no enough evidence to support a role for cholecystectomy in functional gallbladder disease at present.[3,28]

Etiology

Risk factors for calculous cholecystitis are the same for cholelithiasis and include the following:[49]

- Female sex
- Certain ethnic groups
- Obesity or rapid weight loss
- Drugs (especially hormonal therapy in women)
- Pregnancy
- Increasing age

Acalculous cholecystitis is seen in pathologies leading to biliary stasis, and include the following:[50]

- Critical illness
- Major surgery or severe trauma/burns
- Sepsis
- Long-term total parenteral nutrition (TPN)
- Prolonged fasting

Other pathologies leading to acalculous cholecystitis such as:

- Cardiac diseases like myocardial infarction
- Sickle cell disease
- *Salmonella* infections
- Diabetes mellitus
- HIV positive patients with associated cytomegalovirus, cryptosporidiosis, or microsporidiosis infection

Immuno-compromised patients have a higher risk of developing cholecystitis from various infectious sources.

Risk factors

Obesity

Incidence of gallstones is higher in markedly obese people and in those who lose weight rapidly. There is little agreement about the effect of dietary components on the risk of gallstones. Fasting is normally associated with increased biliary cholesterol saturation and this phenomenon persists or even become more accentuated in case of obesity. A clinical study showed an increased risk for gallstones formation associated with being even moderately overweight. Obesity also reduces gallbladder emptying.[32]

Estrogen and cholesterol lowering agents

Elevated estrogen levels in pregnancy, in patients receiving hormone replacement therapy and oral contraceptive pills are associated with raised cholesterol levels in bile and reduced gallbladder motility, both of which can lead to gallstones. Drugs that lower cholesterol levels in the blood lead to an increase in the cholesterol levels secreted in bile. This in turn can increase the risk of cholesterol gallstones. Clofibrate increases the biliary cholesterol and results in formation of the gall stone. Patients who are taking clofibrates are at an increase risk for cholecystectomy. During rapid weight loss, the metabolism of fat is accelerated, which increases the secretion of biliary cholesterol from liver, which can cause gallstones.[12]

Diabetes mellitus

Gallbladder atony added to autonomic neuropathy may favour stone formation in super saturated bile.[11] It has been stated that the diabetes patients have higher incidence of gallstone disease and are particularly prone to complications from there gallstones. There is an increased incidence of complications in case of other co-morbidities like cardiovascular disease and renal insufficiency.[51]

Fasting

Fasting decreases gallbladder motility leading to bile overconcentration with cholesterol, which can lead to gallstones formation. No clear relationship has been proved between diet and gallstone formation. However, low-fibre, high-cholesterol diets, and diets high in starchy foods may also contribute to gallstone formation. Wayne et al have concluded from their study that a dietary soluble fibre psyllium

inhibits cholesterol stone formation by reducing the biliary cholesterol saturation index. Gallstones are more frequent in type 4 hyperlipidaemia.[52]

Cirrhosis of the liver

Patients with cirrhosis have 3 times greater risk for gallstones than the normal population. The stones are usually of pigment type and probably results from the chronic haemolysis. Cholecystectomy when performed in cirrhotic patients is associated with increased morbidity and mortality.[10]

Vagatomy

Early clinical studies suggested that truncal vagatomy was associated with two fold increase in the incidence of gallstones, other studies have failed to confirmed this hypothesis. While ultrasonography suggested that truncal vagatomy is associated with dialated gallbladder. Nerve fibres from both vagal nerves merge to form the hepatic plexus which supplies parasympathetic motor nerves to the extra hepatic biliary system. A number of studies have investigated the effect of vagal stimulation and vagatomy on gallbladder contractability, but the results are generally has been inconclusive.[12]

Total parenteral nutrition and gallstone formation

A number of large clinical studies have confirmed the etiological relationship between TPN and gallstone formation in both children and adult. Symptomatic gallstone disease forms in approximately 45% of patients who are maintained on long term TPN. Ultrsonographic studies have helped to identify the scientific basis for gallstone formation and have our attention on the relationship between alter

gallbladder motor activity, decrease stimulation for gallbladder contraction and the formation of sludge and ultimately biliary lithiasis.[28]

Inflammatory bowel disease

Patients with ileal dysfunction which is more saturated with cholesterol and patients with jejuno-ileal operation are associated with increased risk of gallstone formation. When the ileum is diseased or removed absorption of bile salts is impaired and a significant lose of bile salts will occur, as result of loss of bile salts there will be relative increase in cholesterol leading to the gall stone formation.[54]

Miscellaneous

The prevalence of gallstones in thalassaemia is about 10%, in sickle cell disease is 10% to 40%, and in hereditary spherocytosis is 43% to 66%. Pigment gallstones are reported in 58% of patients with homozygous sickle disease and in 17% of the patients with heterozygous type.[55] Hormonal changes during pregnancy and alteration of gallbladder motility by progesterone are thought to be responsible for the development of gallstones in women. There is no increased risk of morbidity if surgical therapy for biliary disease is carried out in the second trimester.[56]

Children with cystic fibrosis have increased risk of gallbladder disease. There is a controversy over an association between the gallstone and colorectal cancer and gastric cancer.[57] There is association between hiatus hernia and diverticular disease of the colon and gallstone. Over 70% of patients who develop gallbladder carcinoma have gallstones. Larger gallstones (>3mm) are associated with increased incidence of carcinoma gallbladder.[58]

Diagnosis

Diagnostic tests[4]

- Abdominal Ultrasonography: Single most useful test to evaluate gallstones, CBD size and stones.
- Endoscopic Ultrasound (EUS): Excellent to evaluate CBD stone, size. Expensive. Not easily available.
- ERCP: As solely a diagnostic test it has lost its value. Can be used to do sphincterotomy, therapeutically
- HIDA, DIDA, Radioisotope Scans: Accurate identification of cystic duct obstruction. Diagnosis of acute cholecystitis.
- CT Abdomen: Not ideal. Radiation. Not indicated in pregnancy
- MRI/MRCP: MRCP does not require contrast. It can be safely used in 2nd/3rd trimester of pregnancy. Reduces the number of invasive ERCPs.

Delay in the diagnosing acute cholecystitis is related to increased morbidity and mortality, especially in patients in intensive care unit (ICU) who develop acalculous cholecystitis. Early diagnosis and investigations helps in avoiding poor outcomes.[22]

Differential diagnosis[20,21]

- Cholelithiasis
- Choledocholithiasis
- Biliary Colic
- Biliary Disease

- Cholangitis
- Gallbladder Cancer
- Gallbladder Tumors
- Gastric Ulcers
- Acute gastritis
- Cholangiocarcinoma
- Appendicitis
- Acute Mesenteric Ischemia
- Abdominal Aortic Aneurysm

Approach

The workup for cholecystitis includes laboratory investigations, radiograms, ultrasonography abdomen, computed tomography (CT), magnetic resonance imaging (MRI), hepatobiliary scintigraphy (HBS), and endoscopy.

Laboratory investigations[59]

Laboratory investigations are not reliable in diagnosing cholecystitis, but the following findings may be useful in the diagnosis:

- Increased leukocyte count may be associated with cholecystitis.
- Increased bilirubin and alkaline phosphatase levels are indicative of common duct obstruction..
- Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels are raised in case of hepatitis, cholecystitis or obstruction in the common bile duct.
- Rise in alkaline phosphatase levels is seen in 25% cases of cholecystitis.

Imaging

The 2010 American College of Radiology (ACR) Criteria offer states the imaging recommendations as follows:[60]

- Ultrasonography is the initial investigation of choice for the diagnosis of cholelithiasis, acute cholecystitis.
- CT is a secondary investigation which can rule out extrabiliary pathologies and complications of cholecystitis i.e. gangrene, perforation, empyema.
- MRI with intravenous gadolinium-based contrast is also secondary imaging test which confirms the presence of acute cholecystitis.
- Plain MRI eliminates the risk of radiation exposure and is indicated in pregnant women with failure of ultrasonography to diagnose the pathology.

Radiography

Gallstones may be visualized in plain X-ray abdomen only in 10-15% patients.

Ultrasonography

Ultrasonography has 90-95% sensitivity in diagnosing cholecystitis and specificity of 78-80%. It has more than 95% sensitivity and specificity in diagnosing gallstones larger than 2 mm.[61,62]

Ultrasonography in acute cholecystitis may show the following findings: pericholecystic collection, gallbladder wall thickness more than 4 mm, and ultrasonographic Murphy's sign.[63]

Ultrasonography shows the best results when performed after fasting for at least 4 hours as the gallbladder is distended and bile-filled allowing clear visaulization of gallstones.[64]

Computed tomography and magnetic resonance imaging

Computed tomography and magnetic resonance imaging have greater than 95% sensitivity and specificity in the diagnosis of acute cholecystitis.[65] CT scan and MRI (unlike ERCP) are noninvasive, but they dont have any therapeutic value.

Findings which suggest the presence of cholecystitis are wall thickening (>4 mm), pericholecystic collection, subserosal oedema, presence of intramural gas, and breach in the mucosa.

Hepatobiliary scintigraphy (HBS)[59]

HBS has around 95% accuracy in detecting acute cholecystitis. It shows 90-100% sensitivity and 85-95% specificity. In the scintigraphy, the biliary tree with gallbladder is visualized within 30-45 minutes. Morphine increases the accuracy of HBS in case of non-visualization of the gallbladder as it increases the resistance to biliary flow through the sphincter of Oddi, which helps in filling of the gallbladder provided that the cystic duct is patent.

Endoscopic retrograde cholangiopancreatography

ERCP delineates the biliary anatomy in patients with common bile duct obstruction. Sahai et al mentioned in their study that ERCP was more useful than endoscopic ultrasonography (EUS) and intraoperative cholangiography in patients

with high risk of formation of stone in the common bile who underwent laparoscopic cholecystectomy.[66]

Disadvantages of ERCP are high cost and it requires a trained operator. It is also associated with complications like pancreatitis, in 3-5% patients.

Histological findings

Early changes are the presence of edema and venous congestion. Findings specific for chronic cholecystitis are mucosal fibrosis or flattening and appearance of chronic inflammatory cells. Rokitansky-Aschoff sinuses are seen in 56% of the cases and are result of increased hydrostatic pressure. Focal necrosis along with neutrophils may also be present. Complicated cases may show gangrene or perforation of the gallbladder.[19]

Complications of Gallstone Disease

- Pancreatitis
- Cholecysto-enteric fistula, gallbladder perforation
- Gallstone ileus
- Mirizzi Syndrome
- Emphysematous cholecystitis
- Gangrene of the gallbladder
- Choledocholithiasis, cholangitis
- Porcelain gallbladder-intra mucosal calcification of gallbladder wall can occur with or without gallstones

Management

Non-surgical

Drug dissolution therapy

The efficacy of ursodeoxycholic acid in preventing gallstone formation is proved. A prospective study studied the rate of gallstone formation in 152 patients who underwent bariatric surgery (which is a known risk factor for gallstone formation) the daily intake of 500 mg of ursodeoxycholic acid versus placebo, for six months. The researchers found that gallstone formation occurred significantly lesser after intake of ursodeoxycholic acid compared to placebo at 12 months (3% *v* 22%) and at 24 months (8% *v* 30%).[67,68]

However, ursodeoxycholic acid is not useful after the formation of stones. A prospective randomized placebo controlled double blind study done in the Netherlands studied 177 patients with gallstones planned for cholecystectomy and it was found that ursodeoxycholic acid was not helpful in resolution of the biliary symptoms.[69]

Percutaneous drainage

Percutaneous cholecystostomy is efficacious as a treatment for biliary sepsis in patients who are unfit for surgery. In a retrospective study of 55 patients, percutaneous transhepatic cholecystostomy was successful in 98%; 95% of them recovered well and discharged.[70]

Surgical

Open cholecystectomy pioneered by Langenbuch had remained the gold standard for symptomatic gallstones for over a century. The only major change occurred in the surgery when Mirizzi introduced the technique of intra-operative cholangiography for the detection of common bile duct stone over 60 years ago.[16]

The term trocar was introduced in 1706. It was thought to be derived from the word "trocarter troise-quarts", which means a three-faced perforator enclosed in a metal canula. A German gynaecologist, Dimitri OH, in 1901 performed the first endoscopic examination (ventroscopy). Bernheim from the United States was the first surgeon who published his experience in laparoscopy named as "organoscopy" in the Annals Of Surgery,1911.[16]

Kelling in 1923 presented before the German surgical society his experience of diagnostic laparoscopy. That was the beginning of the era of minimally invasive surgery.[16]

Kalk, known as the "father of modern laparoscopy" refined the technique of laparoscopy by introducing the faroblique (135 degrees) lens system along with a separate pneumoperitoneum needle in 1929. Veress in 1938 developed a needle which had a spring-loaded obturator allowing its safe and atraumatic insertion followed by peritoneal insufflation. Kurt Semm, in 1966 was the first one to perform omental adhesiolysis, tumour biopsy, bowel suturing and incidental appendicectomy.[16]

Hasson introduced the technique of trocar placement under direct vision in 1978. It cleared much of the doubts among general surgeons regarding laparoscopic surgery.[71]

Mouret from France[72] was the first surgeon to perform the first human laparoscopic cholecystectomy. In March 1987 when he was performing a gynaecologic laparoscopy for a woman who was also suffering from gallstones, he examined the subhepatic area. He found a relatively free and supple gall bladder and decided to remove it laparoscopically rather than doing an open procedure for it. He removed the gallbladder successfully using laparoscopic technique and the recovery of the patient was uneventful.[72]

In the USA, the procedure was being welcomed and adopted within two years and also there was an increased demand for it among the patients. In September 1992, laparoscopic cholecystectomy was declared as the treatment of choice for cholelithiasis in a NIH consensus conference held in Bethesda .[73]

Laparoscopic versus open surgery

A Cochrane review in which laparoscopic cholecystectomy was compared with open cholecystectomy showed no differences in view of mortality, intra-operative complications or operative time. However, patients undergoing laparoscopic cholecystectomy had a significantly shorter hospital stay (difference, −3 days (95% confidence interval −3.9 days to −2.3 days)) and quicker convalescence (−22.5 days (−36.9 days to −8.1 days)). These results were in favor of laparoscopic cholecystectomy than open cholecystectomy.[67]

Laparoscopic cholecystectomy in high risk patients

High risk patients undergoing laparoscopic cholecystectomy differ from the patients with no existing co- morbidities. To assess the safety of laparoscopic cholecystectomy, different high risk patients who were the candidates for laparoscopic cholecystectomy were studied. These studies included the patients having diabetes mellitus, cardiopulmonary diseases, renal diseases, sickle cell diseases, liver cirrhosis, pregnancy and the elderly. The results showed that laparoscopic cholecystectomy is a safe procedure and is recommended as the procedure of choice, provided that it is done cautiously and skilfully in case of high risk patients. The outcomes of this procedure studied were the intra-operative bile duct injury, effect of pneumoperitoneum on cardiopulmonary system and other complications were outweighed by the benefits of the surgery. High risk patients undergoing open cholecystectomy carries high morbidity and mortality in comparison with laparoscopic cholecystectomy. Laparoscopic cholecystectomy has lesser number of contraindications and recent studies focused on the modification of the technique in terms of the indications and the risk factors for the procedure.[74]

DIABETES MELLITUS

Diabetes Mellitus, a metabolic disorder caused by multiple etiologies and characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both.[75]

Historical Review

Diabetes is perhaps as old as mankind. Awareness of symptoms related to diabetes and recognition of the disorder was confined to a few geographic and cultural locations in the Ancient Era (up to 600 AD).[76]

The earliest mention of diabetes like illness characterized by polyuria can be traced to Egyptian Papyrus dating back to around 1550 B.C. The sweet taste of diabetic urine was noted in the 5th and 6th century AD by the Indian physicians and in the 17th century by Thomas Willis. The term 'Diabetes mellitus', an allusion to the honeyed taste of urine, was first used in the late 18th century by John Rollo and others, to distinguish it from other polyuric states in which urine was tasteless.[76]

In 1893, Edovard Laguesse named the pancreatic islets after Paul Langerhans, who had described them in 1869, and suggested that they produced a glucose lowering substance. Then this hypothetical hormone was named 'insulin' by Jean de Meyer in 1909, over a decade before its discovery.[76]

Insulin was discovered at the University of Toronto in 1921, through collaboration between Frederick G. Banting, Charles H. Best, James B. Collip and J.J.R. Macleod. Insulin was extracted from chilled pancreas in an acid / ethanol mixture; the extracts were found to lower blood glucose levels in pancreatectomized dogs and were first tested in a human diabetic in January 1922.[76]

Epidemiology

Worldwide

366 million people were estimated to have DM in 2011 and by 2030 the value will raise upto 552 million. The number of population diagnosed to have type 2 DM is rapidly increasing in all the countries, 80% of them are from low and middle-income countries. In 2011, 4.6 million deaths were due to diabetes. By the year 2030, the estimated number of people with diabetes would be 439 million. The incidence of diabetes mellitus varies substantially in various geographical regions due to variations in the environmental and lifestyle risk factors.[77]

Centre for Disease Control and Prevention (CDC) in 2011 stated that about 25.8 million people in the US are affected by diabetes (7.8% of the population) with 90% to 95% of them have type 2 diabetes.[78]

All around the world, age-standardized prevalence rates of diabetes is 9.8% in men and 9.2% in women respectively with regional disparity. A high prevalence was found in South Asia, Central Asia, North Africa, Latin America, the Caribbean and the Middle East.[79]

Indian scenario

India is often referred as the diabetes capital of the world. It is currently experiencing an epidemic of type 2 diabetes mellitus and has the largest number of diabetic patients. The International Diabetes Federation 2009 report reveals that the total number of diabetic subjects in India is 50.8million.[14]

Disparity was observed in urban areas as the prevalence of diabetes ranges from 5.9% to 12.1% (North India: 8.6% to 11.6%; South India: 13.5% to 19.5%).[80,81] Rural India is also found to have a high prevalence of diabetes (about 2.0% to 10.0%).[80] A systematic review in tribal population of India observed a ranging prevalence of diabetes, 0.7% to 10.0%, with a final estimate of 5.9%.[81]

A review[81] showed higher prevalence of diabetes (19.78%) in Karnataka as well as another study[82] also showed higher prevalence of diabetes (12.5%) in Kerala, South India. In Karnataka, the prevalence of diabetes was found to be more in women (22.04%) compare to men (16.06%).[81]

Indians are more susceptible to risk factors for diabetes like age, obesity (BMI) mainly the central obesity (WHR). Despite of having low BMI compared to other ethnic groups, BMI is strongly related with glucose tolerance in indians.[83]

Current criteria for the diagnosis of diabetes[84]

- HbA1C ≥6.5%. The test should be performed in a laboratory using a method that is National Glycohemoglobin Standardization Program (NGSP)-certified and standardized to the Diabetes Control and Complications Trial (DCCT) assay
- Fasting plasma glucose (FPG) ≥126 mg/dl (7.0 mmol/l). Fasting is defined as no caloric intake for at least 8 h, or
- 2-h plasma glucose ≥200 mg/dl (11.1 mmol/l) during an oral glucose tolerance test (OGTT).
- In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dl (11.1 mmol/l)

WHO Diabetes criteria - Interpretation of Oral Glucose Tolerance Test (1999)[85]

Glucose levels	**NORMAL**		**Impaired fasting glycaemia (IFG)**		**Impaired glucose tolerance (IGT)**		**Diabetes Mellitus (DM)**	
Venous Plasma	Fasting	2hrs	Fasting	2hrs	Fasting	2hrs	Fasting	2hrs
(mmol/L)	<6.1	<7.8	≥ 6.1 & <7.0	<7.8	<7.0	≥7.8	≥7.0	≥11.1
(mg/dL)	<110	<140	≥110 & <126	<140	<126	≥140	≥126	≥200

Diabetes mellitus and gallstone disease

Several studies have shown increased incidence of gallstone disease in diabetic patients. In 2001, a study conducted in University of Erciyes, Turkey found that operative complications of laparoscopic cholecystectomy in diabetics with symptomatic gallstones were significantly higher than non-diabetics. Their conversion rate was 7.1% in diabetics compared to 2.8% in non-diabetics. However, the comparison of operative time was not significant.[86]

Gallstones are frequently found in diabetic patients, especially in women with type 2 diabetes mellitus. The pathogenesis of gallstones is multifactorial. Cholesterol supersaturation, presence of crystal nucleation, and impaired gallbladder motility are the main promoting factors. Type 2 diabetics always tend to be obese and have hypercholesterolemia, and visceral neuropathy damaged in diabetics may lead to impaired gallbladder emptying.[87]

It is proposed that, higher volumes of fasting gallbladder and residual gallbladder, and lower levels of plasma cholecystokinin (CCK) protein, and CCK-A receptor mRNA expression in the diabetic groups than in controls, suggesting that impaired gallbladder motility exists in diabetic patients.[87]

Numerous studies that looked into the prevalence of gallstone in a diabetic population showed an increased association.

A cross-sectional study in the United States from 1976-1984 including 121,700 female had drawn a conclusion that a higher intake of carbohydrates, dietary glycemic load, and glycemic index increased the risk of cholecystectomy.[88]

A population-based cohort study from 2000-2008, which included 60,734 diabetic patients, and 48,116 controls showed that the diabetic group exhibited significantly higher risk of GSD.[89]

Another cross-sectional study in Iran between August 2005 and April 2007, which included 599 patients, had a similar conclusion.[90]

Several more studies had been carried out in Japan,[91] Italy,[92] Libya,[93] and Iraq,[94] and so forth. All these studies found a positive association between diabetes and risk of GSD. However, not all authors agree on it. Population-based studies on Puma Indians and Mexican Americans of the United States did not find any relation between the 2 diseases.[95,96]

In 2005, a study conducted in Singapore, found that mere presence of diabetes with uncontrolled blood sugar levels (HbA1c >6) is related to presence of severe inflammation leading to severe adhesions formation which distorts the anatomy like in case of patients who had previous upper abdominal surgeries. Patients who underwent conversion to open procedure were also found to have significantly increased number of post-operative complications.[97]

Several plausible mechanisms may explain the significantly positive association between diabetes mellitus and gallstones formation. The most important link between gallstones and diabetes mellitus is found to be obesity. Diabetics who are obese had more risk of gallstone formation. Diabetics diagnosed to have gallstones had higher values of fasting insulin, lower values of total- and low-density lipoprotein cholesterol (LDL) and lower values of high density lipoprotein cholesterol (HDL) compared to diabetics who did not have gallstones. It was suggested that maturity-onset diabetes is associated with supersaturated bile.[87]

Some other studies proposed that volume of the gallbladder in diabetics was significantly more than in the control group. Gallbladder motility was significantly less in diabetics as a result of autonomic neuropathy than in the non-diabetics. Autonomic neuropathy superadded to impaired gallbladder motility leads to bile stasis and results in cholesterol gallstone crystal formation and further gallstone growth.[98]

Laparoscopic cholecystectomy in patients with diabetes mellitus and gallstone disease

Laparoscopic Cholecystectomy has become the gold standard treatment for gallstones for many years. Complications that may arise with laparoscopic cholecystectomy can be categorized into intraoperative and post-operative complications, which can be further subdivided into early and late complications. Intra-operative complications such as bleeding, bile duct injury, biliary leak, bowel perforation, if cannot be controlled, may necessitate the conversion to open cholecystectomy.

Other reasons to convert to open procedure would be due to technical problems such as dense adhesions, inflammation, and difficult anatomy. Also, operative findings such as gangrenous cholecystitis or empyema may also require the conversion.

However, there are few studies reporting outcomes of laparoscopic cholecystectomy in patients with diabetes mellitus.[99]

In 2000, Lyass et al.[100] studied several factors that may affect the outcome of lap cholecystectomy. Their results showed that diabetes was one of the factors that significantly increased post-op morbidity, but did not increase the length of hospital stay after lap cholecystectomy. Study showed an increased length of hospitalization in diabetics post lap cholecystectomy.

In 2001, a study conducted in university of Erciyes, Turkey,[86] found that operative and postoperative complications of lap cholecystectomy in diabetics with symptomatic gallstones were significantly higher than non-diabetics. Their conversion to open rate was 7.1% in diabetics compared to 2.8% in non-diabetics. However, the comparison of operative time and length of hospital stay were not significant.

In 2006, a study conducted by Ibrahim et al.,[97] in Singapore, found that the mere presence of diabetes does not appear to increase the risk of conversion to open, however they found an association between poorly controlled diabetes (elevated HbA1c >6) with an increased risk for converting to open cholecystectomy.

Simopoulos et al.[101] in 2005, found a significant positive correlation between male gender, age more than 60, previous upper abdominal surgery, and diabetes with increased rate of conversion to open cholecystectomy.

In 2007, Cheng et al.,[102] from Taiwan studied prolonged hospital stay following laparoscopic cholecystectomy with the major complications, specifically in relation with pulmonary disease in the elderly. No other comorbidity was found to have a direct impact on the duration of hospitalization.

A study done in 2010 at king Faisal University, Alhofuf, Saudi Arabia,[103] found no difference in the operative outcome of laparoscopic cholecystectomy in diabetics compared with that in non- diabetics in relation to conversion to open procedure and operative time. However, the length of hospital stay was significantly different in both groups. Study also showed higher rates of gall bladder perforation and bile leak as well as increased adhesions in diabetics than non-diabetics. They observed higher incidences of conversion to open procedure in diabetics (16.7%) than non-diabetics (2.1%). However, the difference in time of operation was not significant.[104]

Paajanen et al.,[105] from Kipio University hospital, Finland studied the post-operative outcome of laparoscopic cholecystectomy and its conversion to open procedure in diabetic and non-diabetic patients in 2010. The results of the study showed that 16% of the diabetic patients underwent conversion to open cholecystectomy while only 7% of non-diabetic controls required the conversion. They also suggested the association between co- morbidities like diabetes and renal disease and a higher risk of complications.

In a study[106] done at California, it was found that in patients undergoing laparoscopic cholecystectomy, mortality and morbidity was higher in diabetics than non-diabetics. Diabetics were associated with more emergency cholecystectomy, intraoperative complications, conversion from laparoscopic to open procedure and poorer outcome compared with result in non-diabetics.

Similar study[105] done at Mikkeli, Finland on operative outcomes of laparoscopic cholecystectomy in diabetics showed that diabetes is associated with increased risk of operative complication with conversion rate of 16% in diabetics and 7% in non-diabetic controls.

A study[94] done at Rome, Italy suggested that the gallbladder in diabetic patients undergoes structural changes(supersaturated bile, increased fasting gallbladder volume with reduced motility and hypotonic gallbladder) which leads to advanced inflammatory changes and hence increased operative complications.

In 2013, study[107] done at Bern, Switzerland found increased rates of peri-operative complications in diabetics compared to non-diabetics.

In a similar study[108] done at Tehran, Iran it was found that among all risk factors associated with laparoscopic cholecystectomy, only diabetes caused significant increase in complications, significantly adhesions and gangrene.

METHODOLOGY

This study was done in the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum.

Study design

The study design was case series.

Study period and duration

This study was done for a period of one year from January 2014 to December 2014.

Place

This study was conducted under the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum a tertiary care teaching hospital attached to KLE University's Jawaharlal Nehru Medical College, Belgaum.

Source of Data

Patients undergoing elective laparoscopic cholecystectomy during the study period were enrolled.

Sample size

The present study comprised of 60 patients who were divided into two cohorts of 30 each based on diabetic history as diabetics and non diabetics.

Sampling procedure

The sample size was determined based on the following parameters.

- The prevalence of diabetes from the previous similar studies that is, in patients undergoing laparoscopic cholecystectomy was found to be 16.1%.[99]
- Total numbers of laparoscopic cholecystectomies done during the year 2012 at KLES Dr. Prabhakar Kore hospital, Belgaum were 216.

Hence,

n = Number of laparoscopic cholecystectomies x prevalence

= 200 x 16 /100

= 32 ≈ 30

Hence the sample size of 30 each in diabetic and non diabetic group was planned by simple random sampling (every third case was enrolled).

Selection criteria

Inclusion

- All patients undergoing elective laparoscopic cholecystectomy.
- Patients aged more than 18 years.

Exclusion

- Those who are recently diagnosed with diabetes (<5 years).
- Patients not willing to participate in the study and does not give written informed consent.
- Patients undergoing emergency cholecystectomy.

Ethical clearance

Prior to the commencement, the study was approved from the Institutional Ethical Committee, Jawaharlal Nehru Medical College, Belgaum.

Informed Consent

The patients fulfilling selection criteria were detailed about the purpose of this study. A written informed consent was obtained prior to the enrolment (Annexure I).

Method of collection of data

Demographic data including age and gender were noted. Patients were interviewed for the past history regarding comorbid conditions, treatment history and surgical history along with presenting complaints. Clinical presentation like symptoms of pain abdomen, vomiting and fever were recorded. Further these patients were subjected to clinical examination for vitals and systemic examination including abdominal examination. These findings were recorded on a predesigned proforma (Annexure II).

Investigations

Patients were subjected to the following investigations.

- Coagulation profile
- Random blood sugar (RBS)
- Fasting blood sugar levels (FBS)
- Glycosylated haemoglobin (HbA1c)

- Liver function tests (LFT)

Radiological assessment

All the patients were subjected to ultrasound and computed tomography was done wherever indicated.

Cohorts

The patients were classified in two groups that is, diabetic and non-diabetic based on their medical history. The medical history was obtained through case records and the history of diabetes mellitus was confirmed from medication records for any antidiabetic medications. The blood sugar level measurements were done to confirm the presence of diabetes (those having fasting serum glucose level > 126 mg/dl or more and random serum glucose level 200 mg/dl or more).[84,85]

Procedure

Laparoscopic cholecystectomy at our hospital is performed by experienced consultant surgeons.

Pre-operative work-up

Pre-operative work up is done for all patients on the day of admission which include serum glucose levels, liver function tests, coagulation profile, preoperative abdominal ultrasound to confirm diagnosis, to look at the site of stones, to measure wall thickness, and look for evidence of inflammation. All the patients were also assessed pre-operatively by anaesthetists to evaluate co-morbidities, and fitness for surgery.

Laparoscopic cholecystectomy

Procedure of laparoscopic cholecystectomy

Position

Classical supine position with the patient in 30^0 reverse trendelenburg tilt.

Nasogastric tube is used to ensure complete gastric deflation during the procedure, since a distended stomach and duodenal cap can obscure the operative field. The urinary bladder is emptied by a catheter prior to creation of pneumoperitoneum. If catheterization not done, it is important to percuss the suprapubic region to exclude a distended urinary bladder before inserting the Veress needle.

Part preparation and draping done in the standard manner.

Access to peritoneal cavity

1. Closed peritoneal insufflation
2. Open laparoscopy using the modified Hasson's cannula.

Closed pneumoperitoneum

This technique entails the initial creation of a carbon dioxide pneumoperitoneum using veress needle and electronic insufflators. Veress needle most often inserted at the subumbilical site

A 10 m port is inserted at the subumbilical region, through which the camera (30^0) is introduced. Following this the abdomen is inspected. After inspection, three

more ports inserted under vision. 10mm left upper paramedian, placed 1cm lateral to linea alba and 3 cm below the left costal margin (to avoid the falciform ligament), 5 mm right upper midclavicular, 5 mm right lower axillary.

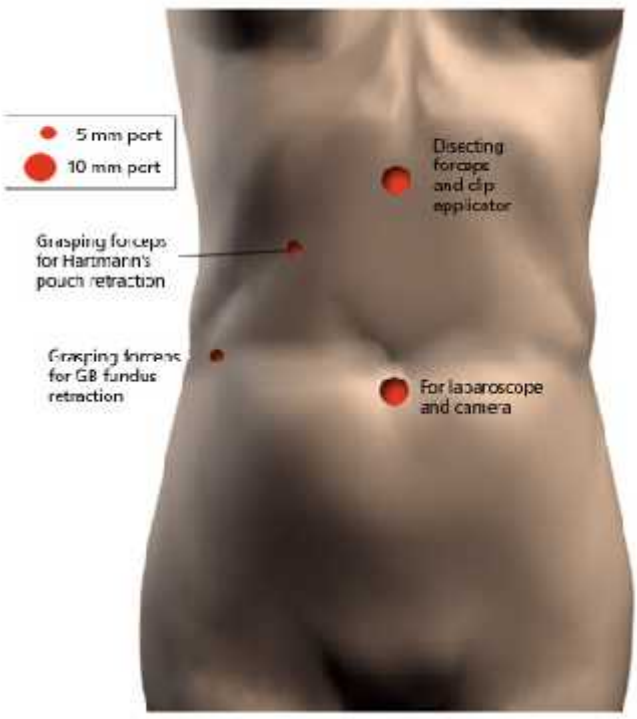


Figure 5. Laparoscopic cholecystectomy ports

The cystic pedicle is exposed by grasping the gallbladder fundus which is lifted in a lateral direction and rolled backwards to expose the subhepatic pouch. A second atraumatic grasper is applied to the neck which is lifted upwards and anteriorly. The cystic pedicle outlines the margins of the triangle of Calot and contains between its superior and inferior leaves the cystic duct (usually anteriorly), the cystic artery (above and behind the duct) and the cystic lymph node of Lund which is loosely attached to the neck of the gallbladder between the duct and artery. The prominent anterior free edge of the cystic pedicle is formed as the peritoneum folds over the cystic duct. The dissection of the pedicle is carried out using scissors,

or atraumatic graspers and the superior leaf of the pedicle is divided. Once the cystic duct and artery are well exposed, the cystic duct is clipped at the gallbladder end and cut followed by the cystic artery. The dissection is carried out between the loose fibrous layer which separates the gallbladder from the subjacent fascia covering the liver bed. Once separation of gallbladder is complete, the organ is held and extracted through the upper 10 mm port. Care is taken to avoid spillage of contents into the peritoneal cavity. After this final inspection is done to look for any oozing, haemostasis is achieved. All ports are removed under vision after decompressing the abdominal cavity to evacuate the carbon dioxide. Ports are closed using vicryl port closure for the rectus sheath and skin using ethilon. Sterile dressing applied.

Post operative assessment

Following the surgical procedure an operative note is recorded, that includes the duration of operation, and any complications that were encountered during the procedure. The gallbladder specimen was sent for histopathological evaluation. Patients are then transferred to the surgical ward or the surgical ICU at our hospital depending on their condition.

Outcome variables

The patients were evaluated for operative outcome for the following parameters according to the data obtained from the predesigned proforma which was filled by the operating surgeon.

- Method of creating pneumoperitoneum
    - Closed (using Verres needle)
    - Open.

- Appearance of gallbladder
    - Simple and uncomplicated (non thickened and uninflammed with clear anatomy)
    - Enlarged and inflamed
    - Impacted.
    - Shrunken and fibrotic.
    - Thickened gall bladder
    - Sessile gall bladder
- Adhesions
    - Absent (no adhesions).
    - Mild (covering only neck of gallbladder, fundus clearly visible).
    - Moderate (covering gallbladder).
    - Severe (buried gallbladder).
- Anatomy of Calot's triangle
    - Clear.
    - Minimal dissection required.
    - Moderate dissection required.
    - Not possible to clarify (frozen calot's triangle).
- Releasing the adhesions (adhesionolysis)
    - Easy (flimsy adhesions).
    - Difficult (thick adhesions but permitting visualization of anatomy).
    - Unsafe dissection.

- Gall bladder stone
    - Solitary.
    - Multiple.
    - Gall bladder packed with stones.
- Intra-operative bleeding[109]
    - Mild (normal).
    - Moderate (causing tachycardia > 100 /minute without drop in blood pressure).
    - Severe (causing tachycardia >100 /minute with > 10 mm Hg drop in blood pressure).
- Site of bleeding
    - From calot's triangle (from cystic artery).
    - From gall bladder.
    - From liver bed.
- Grasping gall bladder
    - Easy.
    - Difficult.
- Removal of gallbladder from liver-bed
    - Easy (time taken <20 minutes).
    - Difficult (time taken >20 minutes).
- Extraction of Gall bladder (need for extending the incision)
    - Yes
    - No

- Complications
    - Yes
        - Bile spillage.
        - Stone spillage.
        - Uncontrolled bleeding.
        - CBD injury.
        - Bowel injury.
    - No
- Need for drain placement
    - Yes
    - No
- Duration of surgery:
    - Minutes (from skin incision to skin closure).

The data regarding these variables was documented by the operating surgeon. After collecting the data, difference in the operative outcome of two cohorts that is, diabetic and non-diabetic was measured.

Statistical analysis

The data obtained was coded and entered in Microsoft Excel Spreadsheet (Annexure III). The categorical data was expressed as rates, ratios and percentages and comparison was done using chi-square test or Fisher's exact test. Continuous data was expressed as mean ± standard deviation. A 'p' value of less than or equal to 0.05 at 95% confidence interval was considered as statistically significant.

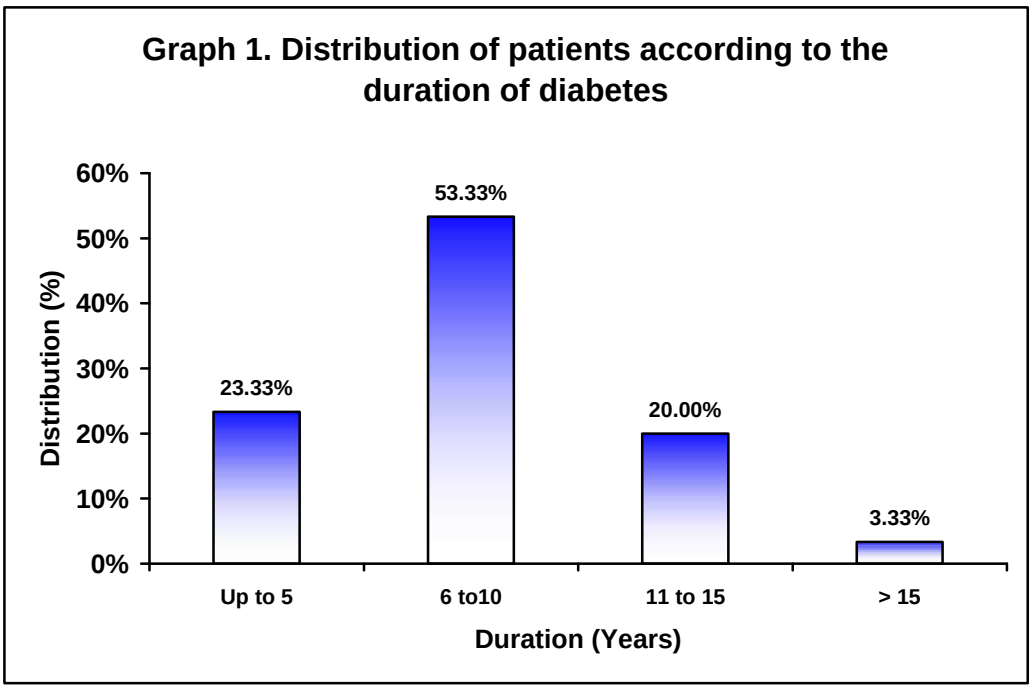
RESULTS

The present one year case series was done in the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum from January 2014 to December 2014. A total 60 patients undergoing elective laparoscopic cholecystectomy during the study period were studied. These patients were divided into two cohorts of 30 each as diabetics and non diabetics and monitored for difficulties / complications during surgery.

The data obtained was analysed and the final observations were tabulated as below.

Table 1. Distribution of patients according to the duration of diabetes

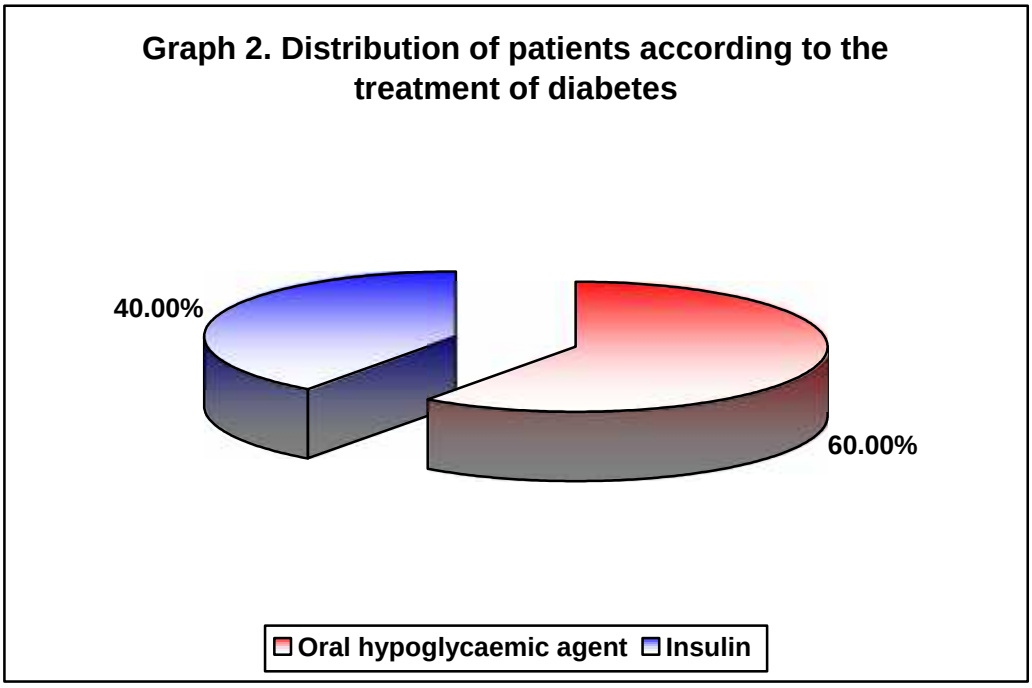
Duration (Years)	Distribution	
	Number	**Percentage**
Up to 5	7	23.33
6 to 10	16	53.33
11 to 15	6	20.00
> 15	1	3.33
Total	**30**	**100.00**



In the present study out of 30 diabetic patients, 53.33% of the patients had diabetic duration between 6 to 10 years. The mean duration was 9.08 ± 5.15 years and the median duration was 8 year (Range 5 to 30 years).

Table 2. Distribution of patients according to the treatment of diabetes

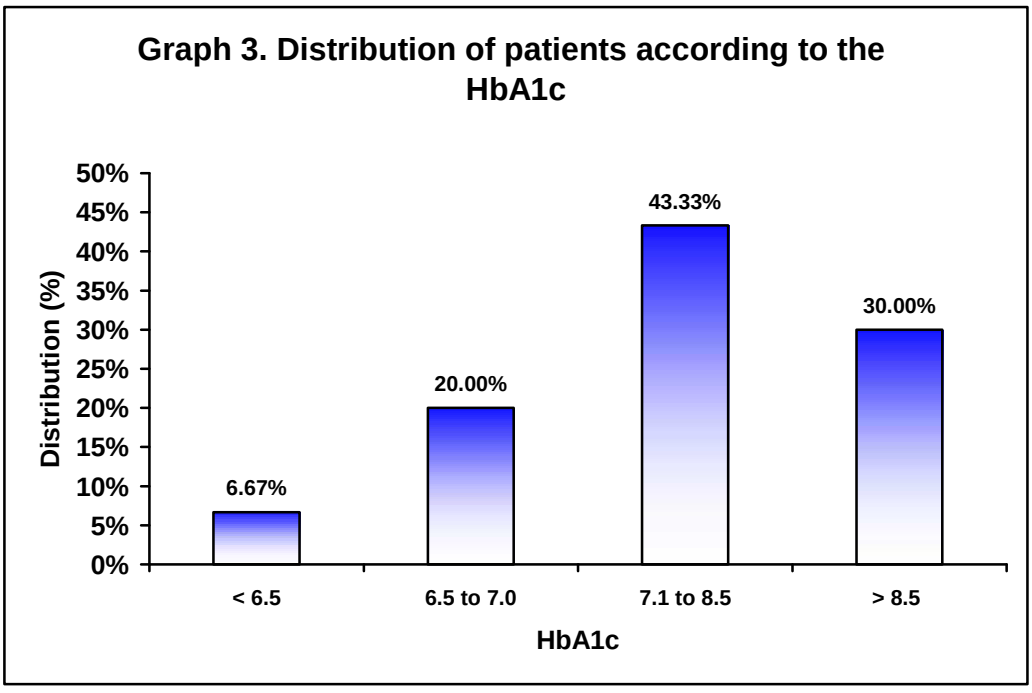
Treatment	Distribution	
	Number	**Percentage**
Oral hypoglycaemic agent	18	60.00
Insulin	12	40.00
Total	**30**	**100.00**



In the present study 60% of the diabetic patients reported treatment with oral hypoglycaemic agents while 40% were on insulin.

Table 3. Distribution of patients according to the HbA1c

HbA1c levels	Distribution	
	Number	**Percentage**
< 6.5	2	6.67
6.5 to 7.0	6	20.00
7.1 to 8.5	13	43.33
> 8.5	9	30.00
Total	**30**	**100.00**

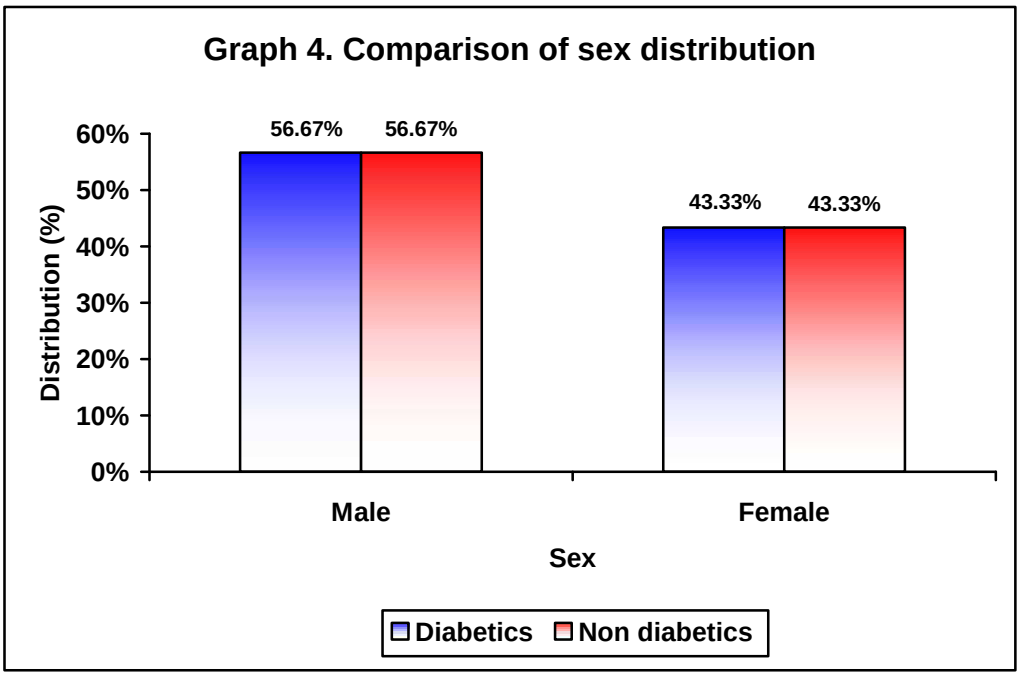


In the present study 43.33% of the patients had HbA1c levels between 7.1 to 8.5 and > 8.5 levels were noted in 30% of the patients.

Table 4. Comparison of sex distribution

Sex	Diabetic history				Total	
	Diabetics		Non diabetics			
	No.	%	No.	%	No.	%
Male	17	56.67	17	56.67	34	56.67
Female	13	43.33	13	43.33	26	43.33
Total	**30**	**100.00**	**30**	**100.00**	**60**	**100.00**

p = 1.000

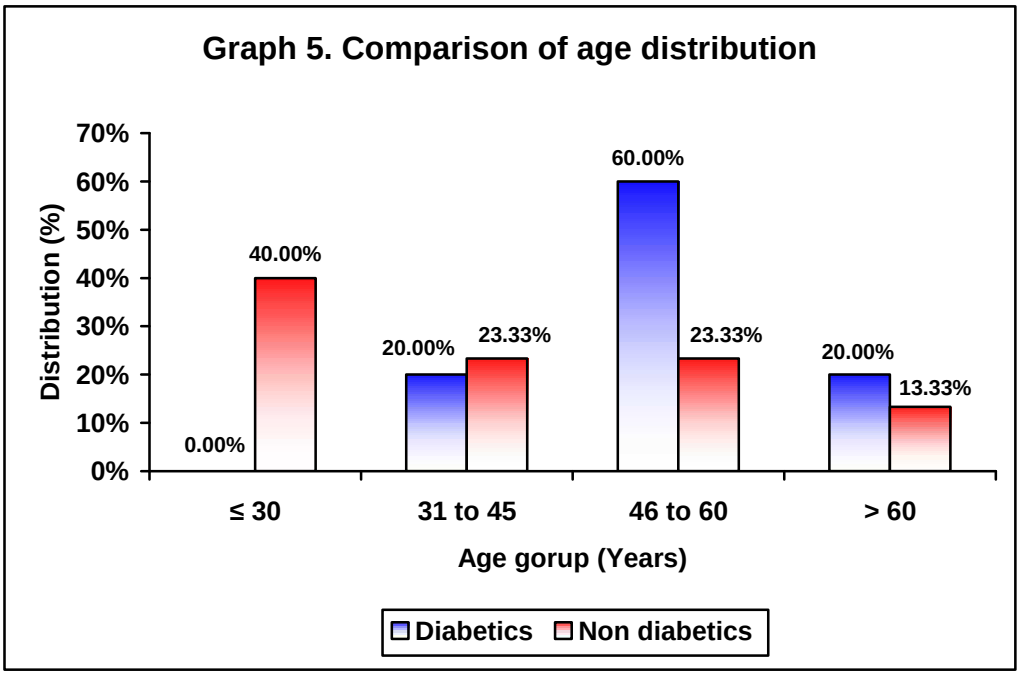


In this study 56.67% of the patients each in diabetic and non diabetic group were males with male to female ratio of 1.30:1 (p=1.000)

Table 5. Comparison of age distribution

Age group (Years)	Diabetic history				Total	
	Diabetics		Non diabetics			
	No.	%	No.	%	No.	%
≤ 30	0	0.00	12	40.00	12	20.00
31 to 45	6	20.00	7	23.33	13	21.67
46 to 60	18	60.00	7	23.33	25	41.67
> 60	6	20.00	4	13.33	10	16.67
Total	**30**	**100.00**	**30**	**100.00**	**60**	**100.00**

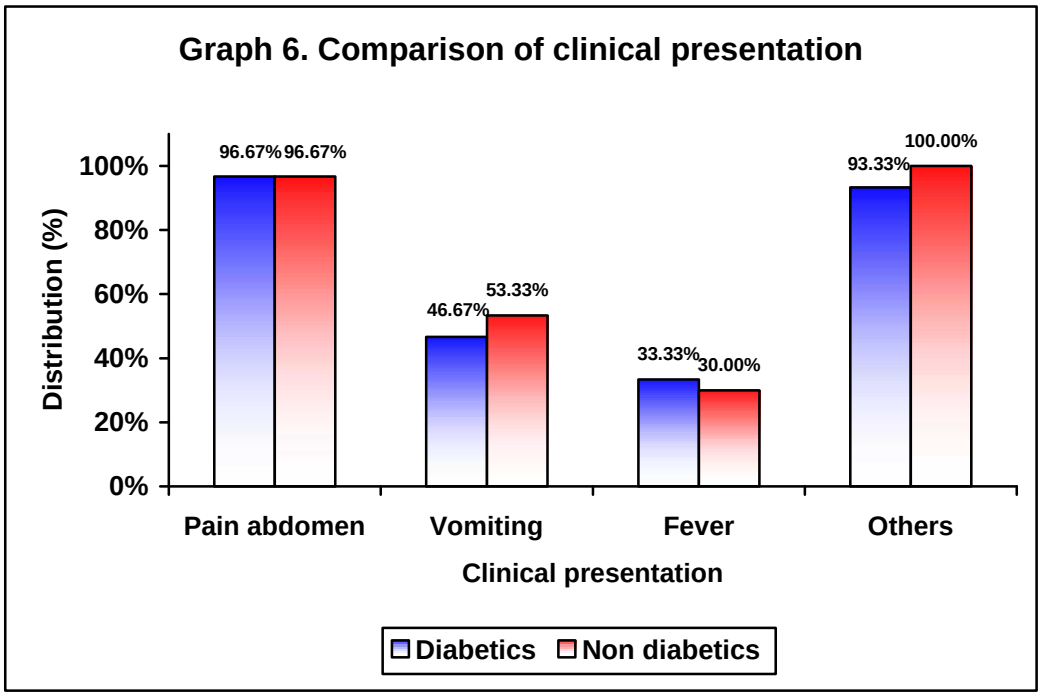
p<0.001



In this study among the patients with DM, 60% were aged between 46 to 60 years compared to 23.33% in non diabetics. This difference was statistically significant (p<0.001).

Table 6. Comparison of clinical presentation

Clinical presentation	Findings	Diabetic history				Total		p value
		Diabetics		Non diabetics				
		No.	%	No.	%	No.	%	
Pain	Present	29	96.67	29	96.67	58	96.67	0.754
abdomen	Absent	1	3.33	1	3.33	2	3.33	
	Total	**30**	**100.00**	**30**	**100.00**	**60**	**100.00**	
Vomiting	Present	14	46.67	16	53.33	30	50.00	0.606
	Absent	16	53.33	14	46.67	30	50.00	
	Total	**30**	**100.00**	**30**	**100.00**	**60**	**100.00**	
Fever	Present	10	33.33	9	30.00	19	31.67	0.781
	Absent	20	66.67	21	70.00	41	68.33	
	Total	**30**	**100.00**	**30**	**100.00**	**60**	**100.00**	
Other	Bloating	19	63.33	26	86.67	45	75.00	0.101
	Nausea	1	3.33	0	0.00	1	1.67	
	Bloating & nausea	8	26.67	4	13.33	12	20.00	
	Absent	2	6.67	0	0.00	2	3.33	
	Total	**30**	**100.00**	**30**	**100.00**	**60**	**100.00**	

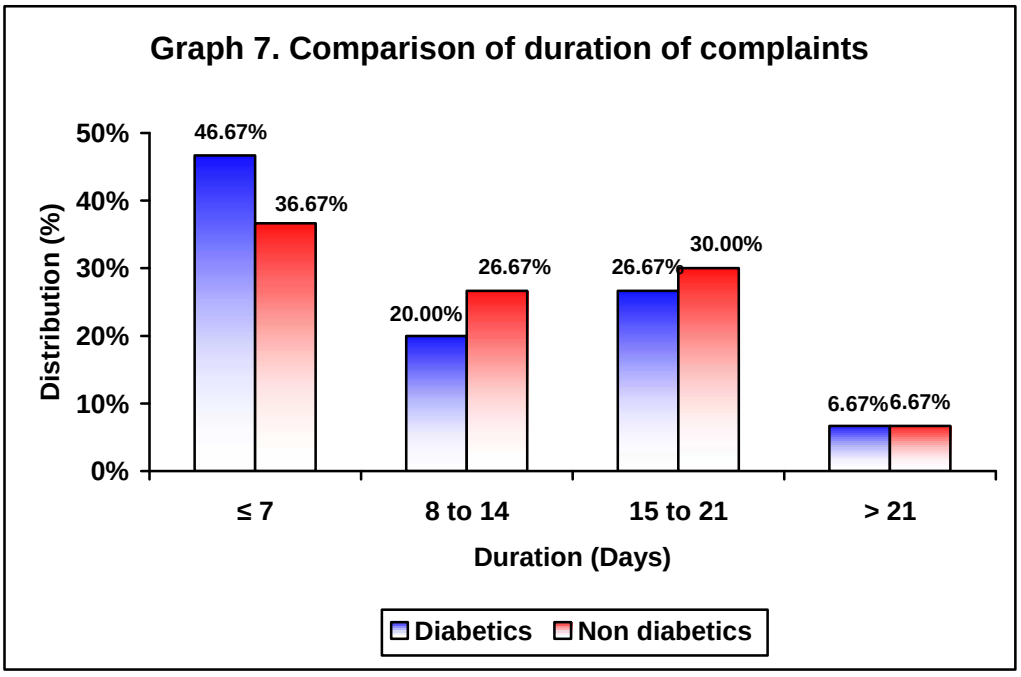


In the present study clinical presentation of pain abdomen, vomiting and fever were comparable among diabetic and non diabetics patients (p>0.050). Bloating was noted in 86.67% of the non diabetics compared to 63.33% of the diabetic patients but the difference was statistically not significant (p=0.101).

Table 7. Comparison of duration of complaints

Duration (Days)	Diabetic history				Total	
	Diabetics		Non diabetics			
	No.	%	No.	%	No.	%
≤ 7	14	46.67	11	36.67	25	41.67
8 to 14	6	20.00	8	26.67	14	23.33
15 to 21	8	26.67	9	30.00	17	28.33
> 21	2	6.67	2	6.67	4	6.67
Total	**30**	**100.00**	**30**	**100.00**	**60**	**100.00**

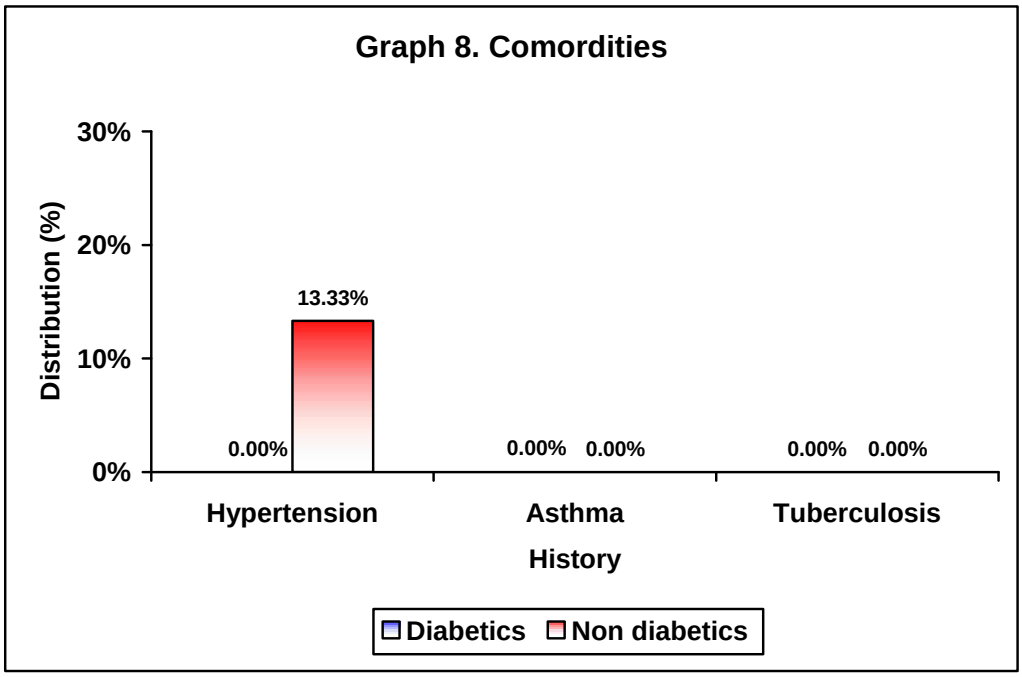
p = 0.917



In the present study 46.67% of the patients with DM had ≤ 7 days duration of symptoms compared to 36.67% of the patients who did not had history of DM. However, this difference was statistically not significant (p=0.917).

Table 8. Comorbidities

History	Findings	Diabetic history				Total		p value
		Diabetics		Non diabetics				
		No.	%	No.	%	No.	%	
Hypertension	Present	0	0.00	4	13.33	4	6.67	**0.056**
	Absent	30	100.00	26	86.67	56	93.33	
	Total	**30**	**100.00**	**30**	**100.00**	**60**	**100.00**	
Asthma	Present	0	0.00	0	0.00	0	0.00	-
	Absent	30	100.00	30	100.00	60	100.00	
	Total	**30**	**100.00**	**30**	**100.00**	**60**	**100.00**	
Tuberculosis	Present	0	0.00	0	0.00	0	0.00	-
	Absent	30	100.00	30	100.00	60	100.00	
	Total	**30**	**100.00**	**30**	**100.00**	**60**	**100.00**	

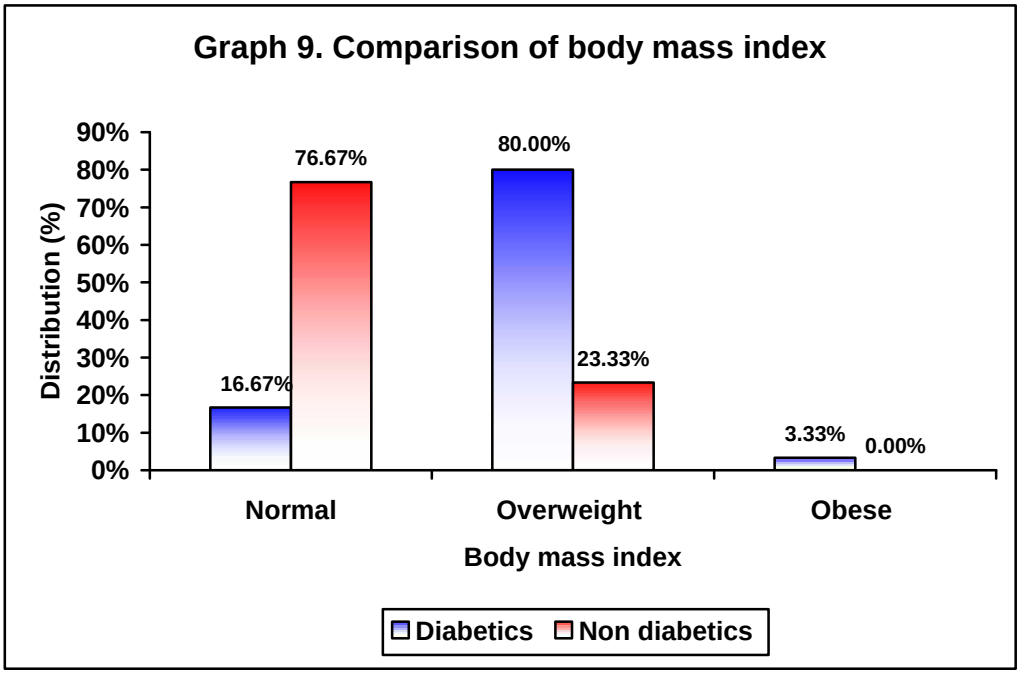


In the present study history of hypertension was noted in 13.33% of the patients among non diabetics (p=0.056).

Table 9. Comparison of body mass index

Body mass index (Kg/m^2)	Diabetic history				Total	
	Diabetics		Non diabetics			
	No.	%	No.	%	No.	%
Normal (< 25.00)	5	16.67	23	76.67	28	46.67
Overweight (25.00 to 29.99)	24	80.00	7	23.33	31	51.67
Obese (≥ 30)	1	3.33	0	0.00	1	1.67
Total	**30**	**100.00**	**30**	**100.00**	**60**	**100.00**

p<0.001

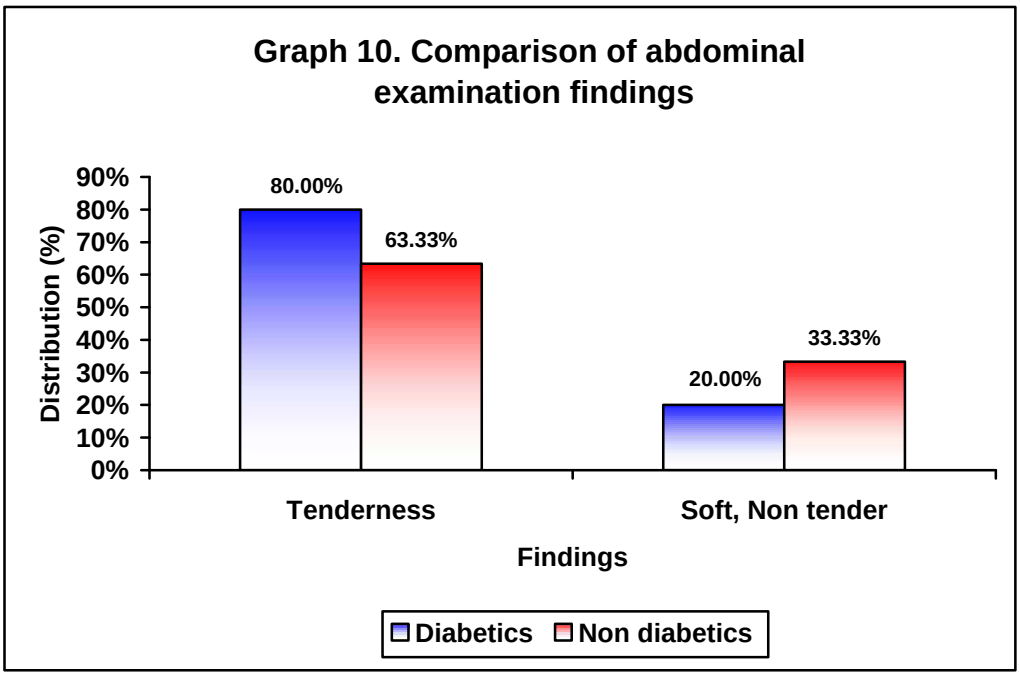


In this study significantly higher number of diabetic patients were overweight (80%) compared to non diabetic patients (23.33%) (p<0.001)

Table 10. Comparison of abdominal examination findings

Findings	Diabetic history				Total	
	Diabetics		Non diabetics			
	No.	%	No.	%	No.	%
Tenderness	24	80.00	19	63.33	43	71.67
Soft, non tender	6	20.00	10	33.33	16	26.67
Total	**30**	**100.00**	**29**	**96.67**	**59**	**100.00**

p = 0.211



In the present study 80% of the diabetics had tenderness compared to 63.33% of the non diabetic patients (p=0.211)

Table 11. Comparison of clinical characteristics among diabetic and non diabetic patients

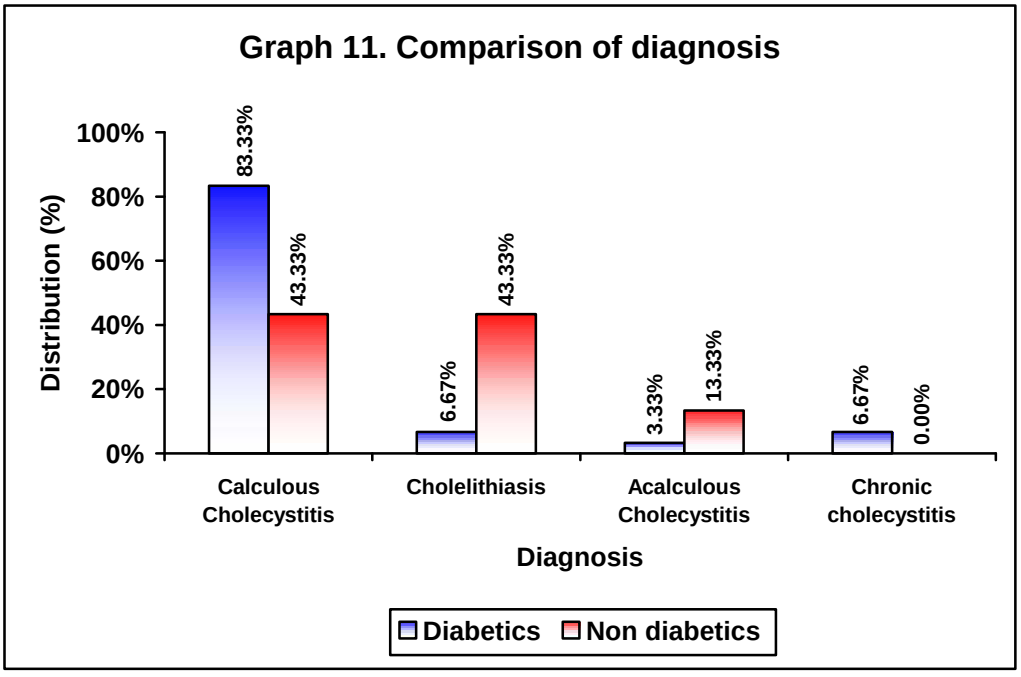
Variables	Diabetic history				
	Diabetics		Non diabetics		p value
	Mean	SD	Mean	SD	
Age (Years)	53.63	8.87	41.20	17.03	**0.001**
Duration of complaints (Days)	10.53	6.98	10.87	7.10	0.855
Duration of DM (Years)	9.08	5.15	-	-	-
Pulse rate (/minute)	87.73	8.51	84.13	6.52	0.071
Systolic BP (mm Hg)	125.67	10.06	122.33	10.73	0.219
Diastolic BP (mm Hg)	79.00	7.59	75.00	5.72	**0.025**
Fasting blood sugar (mg/dL)	130.90	41.76	91.53	13.21	**<0.001**
Random blood sugar (mg/dL)	220.43	78.69	140.47	20.35	**<0.001**
HbA1c	8.08	1.83	-	-	-

The comparison of clinical characteristics among diabetic and non diabetic patients is as depicted in table 11. It was observed that, the mean age, diastolic blood pressure levels, fasting and random blood sugar levels were significantly high in patients with DM ($p<0.050$).

Table 12. Comparison of diagnosis

Diagnosis	Diabetic history				Total	
	Diabetics		Non diabetics			
	No.	%	No.	%	No.	%
Calculous Cholecystitis	25	83.33	13	43.33	38	63.33
Cholelithiasis	2	6.67	13	43.33	15	25.00
Acalculous Cholecystitis	1	3.33	4	13.33	5	8.33
Chronic Cholecystitis	2	6.67	0	0.00	2	3.33
Total	**30**	**100.00**	**30**	**100.00**	**60**	**100.00**

p = 0.001

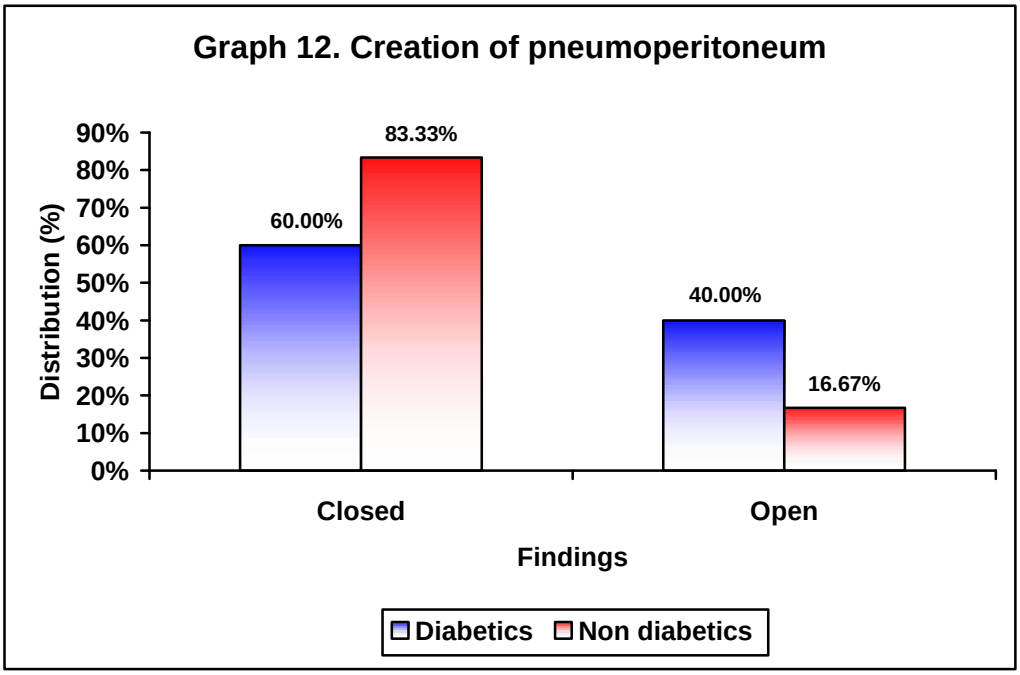


In the present study among the patients with history of DM, 83.33% had calculous cholecystitis compared to 43.33% in non diabetic patients and this difference was statistically significant (p=0.001).

Table 13. Creation of pneumoperitoneum

Findings	Diabetic history				Total	
	Diabetics		Non diabetics			
	No.	%	No.	%	No.	%
Closed	18	60.00	25	83.33	43	71.67
Open	12	40.00	5	16.67	17	28.33
Total	**30**	**100.00**	**30**	**100.00**	**60**	**100.00**

p = 0.045



In this study significantly higher number of patients in diabetic group underwent open pneumoperitoneum (40%) compared to non diabetic patients (16.67%) (p=0.045).

Table 14. Appearance of gallbladder

Appearance	Diabetic history				Total	
	Diabetics		Non diabetics			
	No.	%	No.	%	No.	%
Simple and uncomplicated	8	26.67	18	60.00	26	43.33
Enlarged and Inflamed	12	40.00	11	36.67	23	38.33
Impacted	6	20.00	1	3.33	7	11.67
Shrunken, Fibrotic	2	6.67	0	0.00	2	3.33
Thickened wall of GB (>4 mm)	1	3.33	0	0.00	1	1.67
Sessile gall bladder	1	3.33	0	0.00	1	1.67
Total	**30**	**100.00**	**30**	**100.00**	**60**	**100.00**

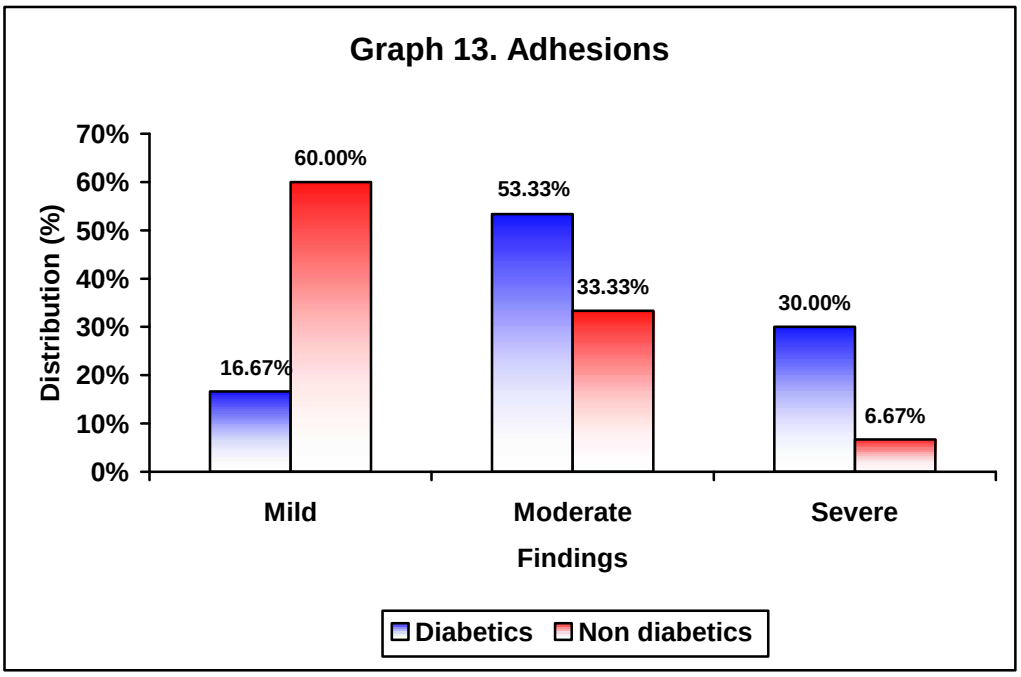
p=0.043

In the present study simple and uncomplicated gall bladder (non thickened and uninflammed with clear anatomy) was noted in 26.67% of the diabetics and 60% of the non diabetics. The appearance of gall bladder was enlarged and inflamed in 40% of the patients with diabetes compared to 36.67% of the non diabetics. This difference was statistically significant (p=0.043).

Table 15. Adhesions

Findings	Diabetic history				Total	
	Diabetics		Non diabetics			
	No.	%	No.	%	No.	%
Mild	5	16.67	18	60.00	23	38.33
Moderate	16	53.33	10	33.33	26	43.33
Severe	9	30.00	2	6.67	11	18.33
Total	**30**	**100.00**	**30**	**100.00**	**60**	**100.00**

p = 0.001

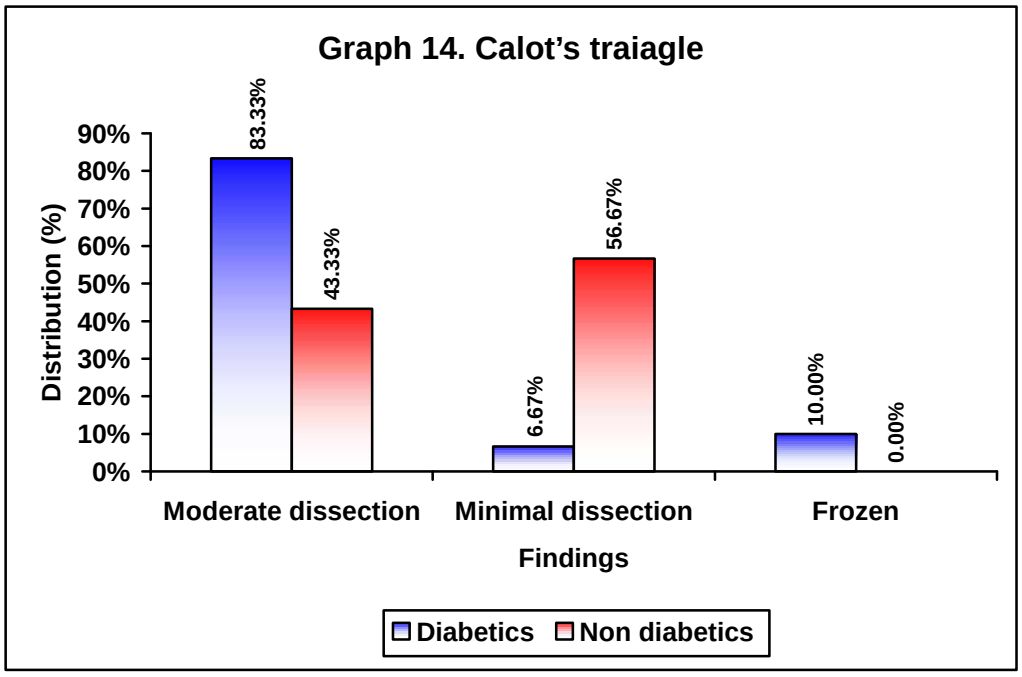


In this study significantly higher number of patients with severe and moderate adhesions were noted among 30% and 53.33% of the patients with history of DM compared to 6.67% and 33.33% in non diabetics respectively (p=0.001)

Table 16. Calot's triangle

Findings	Diabetic history				Total	
	Diabetics		Non diabetics			
	No.	%	No.	%	No.	%
Moderate dissection	25	83.33	13	43.33	38	63.33
Minimal dissection	2	6.67	17	56.67	19	31.67
Frozen	3	10.00	0	0.00	3	5.00
Total	**30**	**100.00**	**30**	**100.00**	**60**	**100.00**

p<0.001

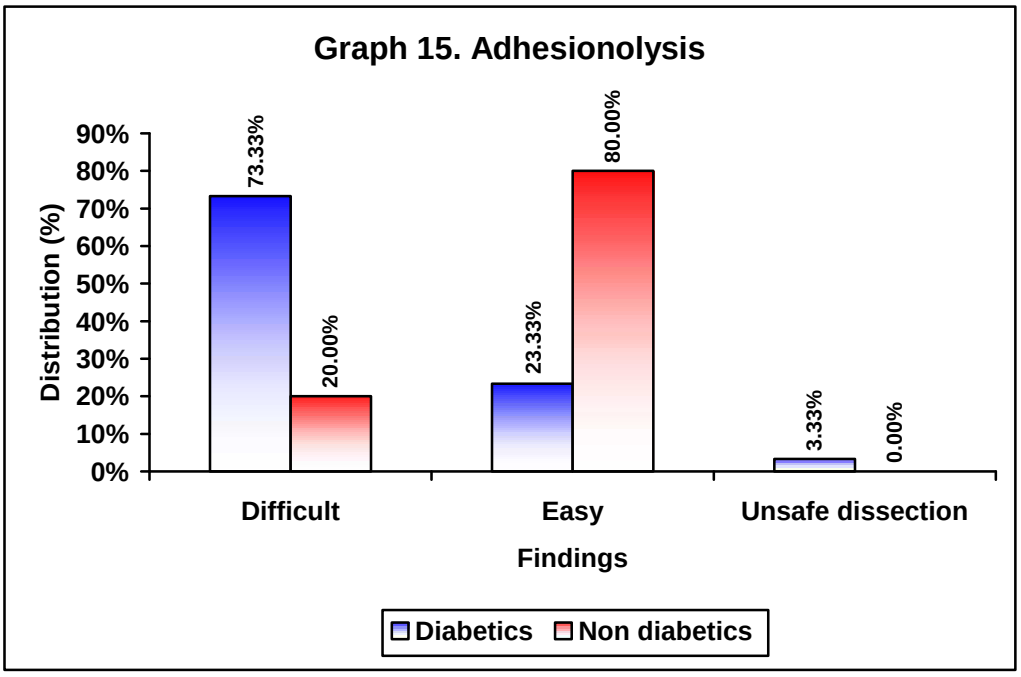


In the present study significantly higher number of patients with history of DM (83.33%) required moderate dissection compared to non diabetic patients (43.33%) (p<0.001).

Table 17. Adhesionolysis

Findings	Diabetic history				Total	
	Diabetics		Non diabetics			
	No.	%	No.	%	No.	%
Difficult	22	73.33	6	20.00	28	46.67
Easy	7	23.33	24	80.00	31	51.67
Unsafe dissection	1	3.33	0	0.00	1	1.67
Total	**30**	**100.00**	**30**	**100.00**	**60**	**100.00**

p<0.001

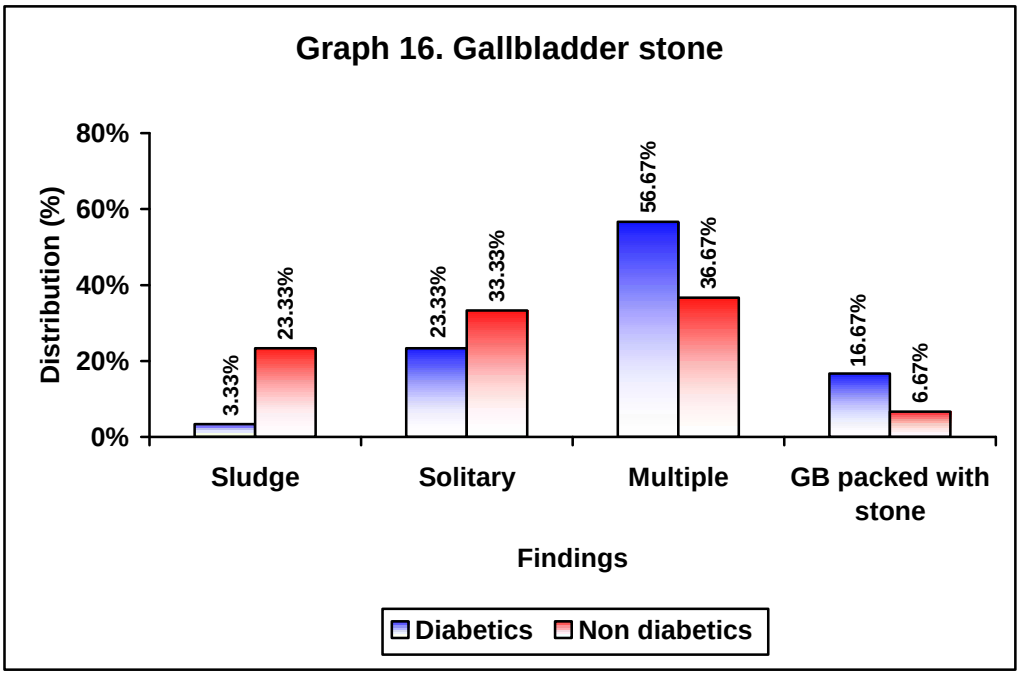


In this study releasing adhesions was difficult in significantly higher number of diabetic patients (73.33%) compared to non diabetics (20%) (p<0.001).

Table 18. Gallbladder stone

Findings	Diabetic history				Total	
	Diabetics		Non diabetics			
	No.	%	No.	%	No.	%
Sludge	1	3.33	7	23.33	8	13.33
Solitary	7	23.33	10	33.33	17	28.33
Multiple	17	56.67	11	36.67	28	46.67
GB packed with stone	5	16.67	2	6.67	7	11.67
Total	**30**	**100.00**	**30**	**100.00**	**60**	**100.00**

p = 0.054

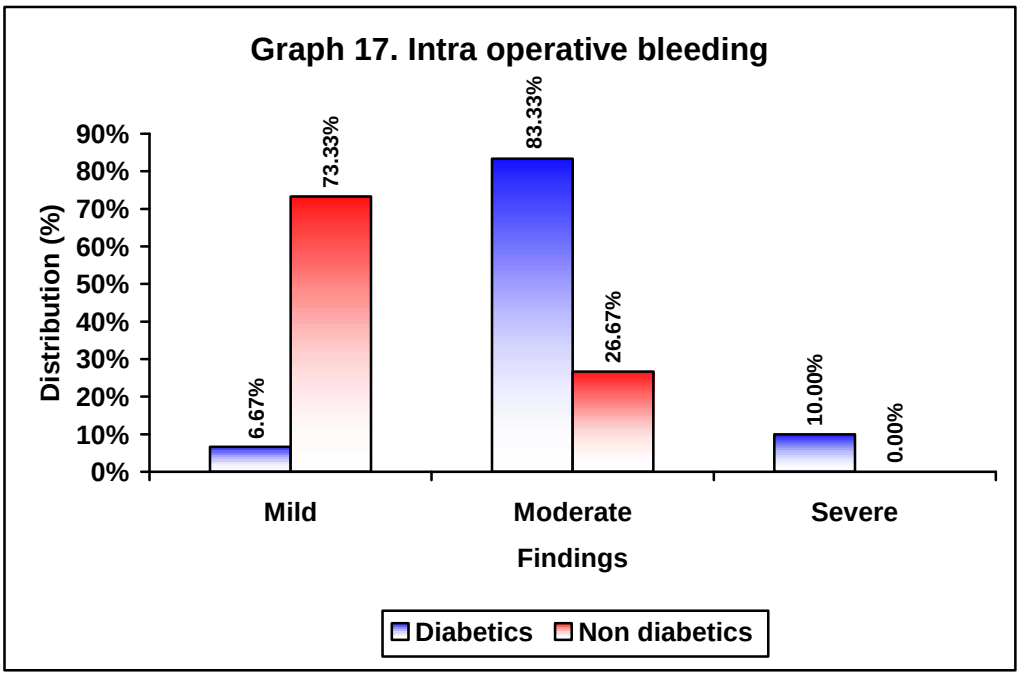


In the present study multiple gall bladder stones were noted in 56.67% of the patients with diabetes mellitus compared to 36.67% of the non diabetic patients. However this difference was statistically not significant (p=0.054)

Table 19. Intra operative bleeding

Findings	Diabetic history				Total	
	Diabetics		Non diabetics			
	No.	%	No.	%	No.	%
Mild	2	6.67	22	73.33	24	40.00
Moderate	25	83.33	8	26.67	33	55.00
Severe	3	10.00	0	0.00	3	5.00
Total	**30**	**100.00**	**30**	**100.00**	**60**	**100.00**

p<0.001

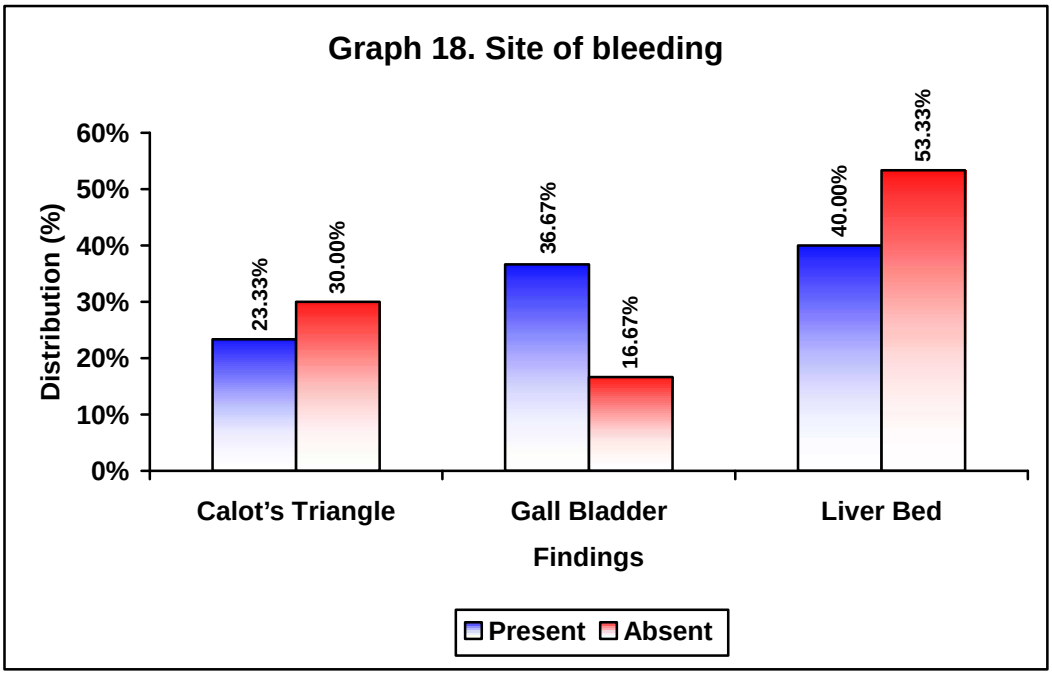


In this study significantly higher number of patients with diabetes mellitus had moderate (83.33% vs 26.67%) and severe (10% vs none) intra operative bleeding compared to non diabetics (p<0.001).

Table 20. Site of bleeding

Findings	Diabetic history				Total	
	Present		Absent			
	No.	%	No.	%	No.	%
Calot's Triangle	7	23.33	9	30.00	16	26.67
Gall Bladder	11	36.67	5	16.67	16	26.67
Liver Bed	12	40.00	16	53.33	28	46.67
Total	**30**	**100.00**	**30**	**100.00**	**60**	**100.00**

p = 0.215

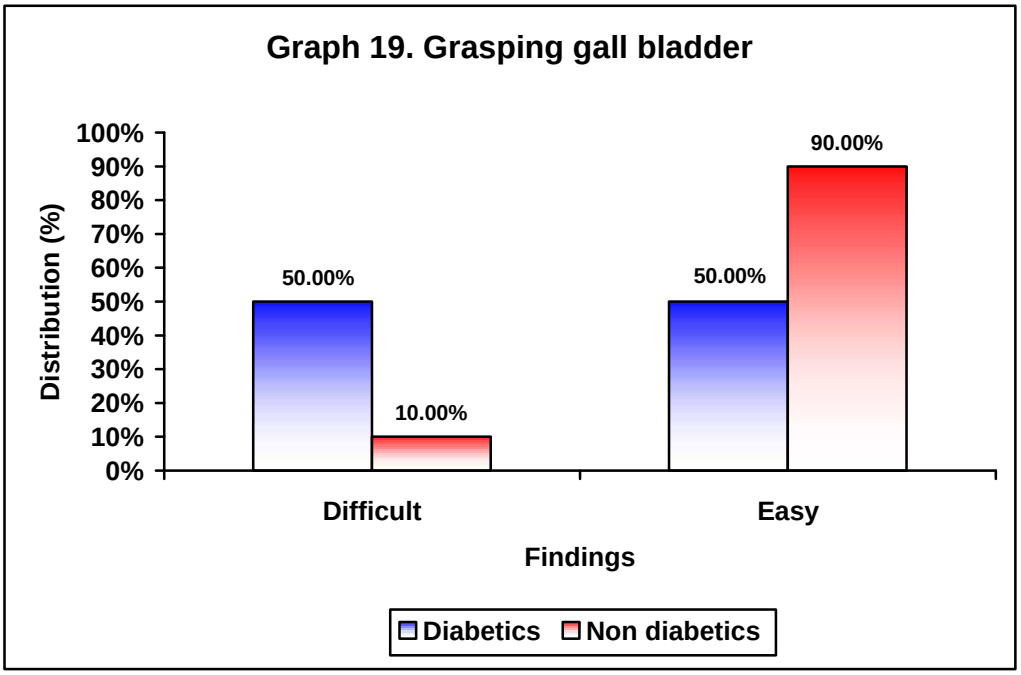


In the present study the site of bleeding was comparable among the diabetics and non diabetic patients (p=0.215).

Table 21. Grasping gall bladder

Findings	Diabetic history				Total	
	Diabetics		Non diabetics			
	No.	%	No.	%	No.	%
Difficult	15	50.00	3	10.00	18	30.00
Easy	15	50.00	27	90.00	42	70.00
Total	**30**	**100.00**	**30**	**100.00**	**60**	**100.00**

p = 0.001

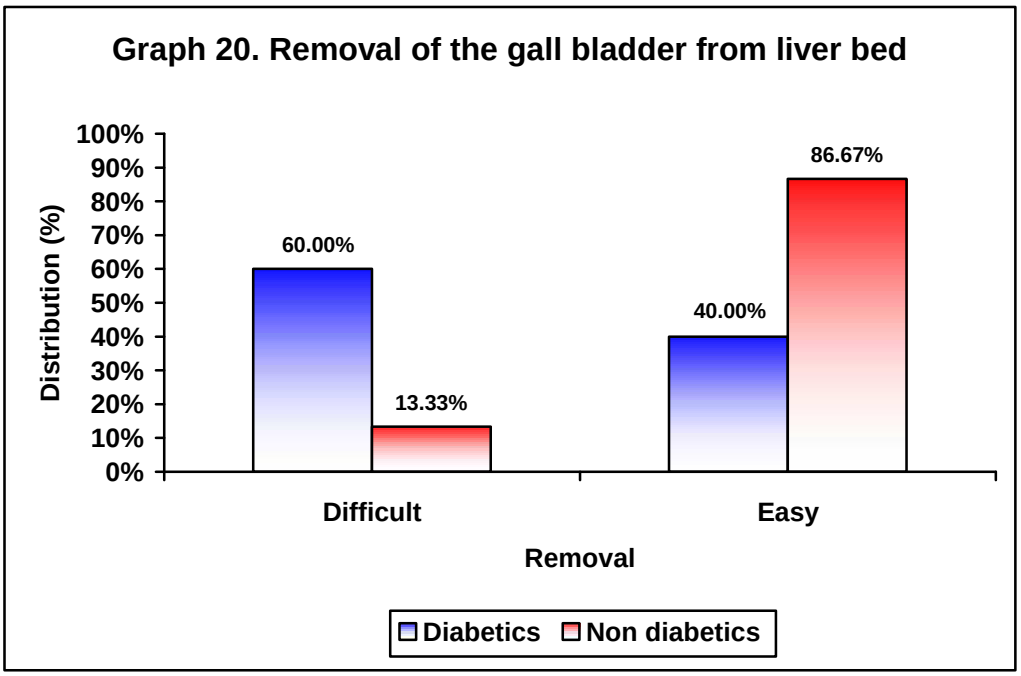


In this study the grasping of gallbladder was difficult in significantly higher number of patients with diabetics compared to non diabetics (50% vs 10%; p=0.001)

Table 22. Removal of the gall bladder from liver bed

Removal	Diabetic history				Total	
	Diabetics		Non diabetics			
	No.	%	No.	%	No.	%
Difficult	18	60.00	4	13.33	22	36.67
Easy	12	40.00	26	86.67	38	63.33
Total	**30**	**100.00**	**30**	**100.00**	**60**	**100.00**

p<0.001

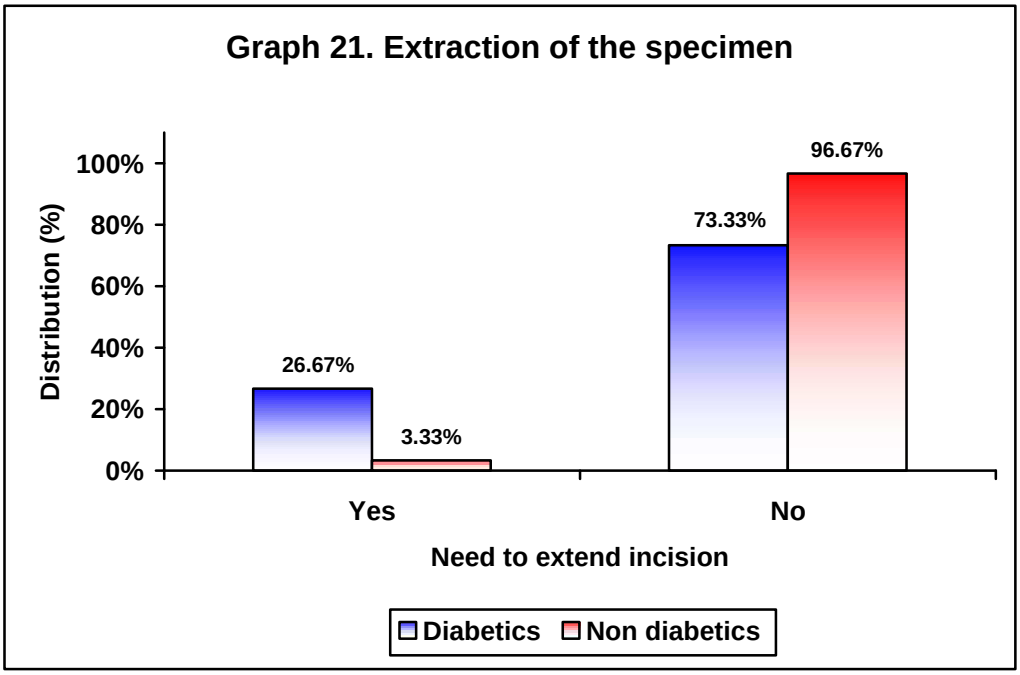


In the present study the removal of gall bladder was difficult in 60% of the patients with diabetes mellitus compared to 13.33% of the non diabetic patients. This difference was statistically significant (p<0.001).

Table 23. Extraction of the specimen

Need to extend the incision	Diabetic history				Total	
	Diabetics		Non diabetics			
	No.	%	No.	%	No.	%
Yes	8	26.67	1	3.33	9	15.00
No	22	73.33	29	96.67	51	85.00
Total	**30**	**100.00**	**30**	**100.00**	**60**	**100.00**

p = 0.025

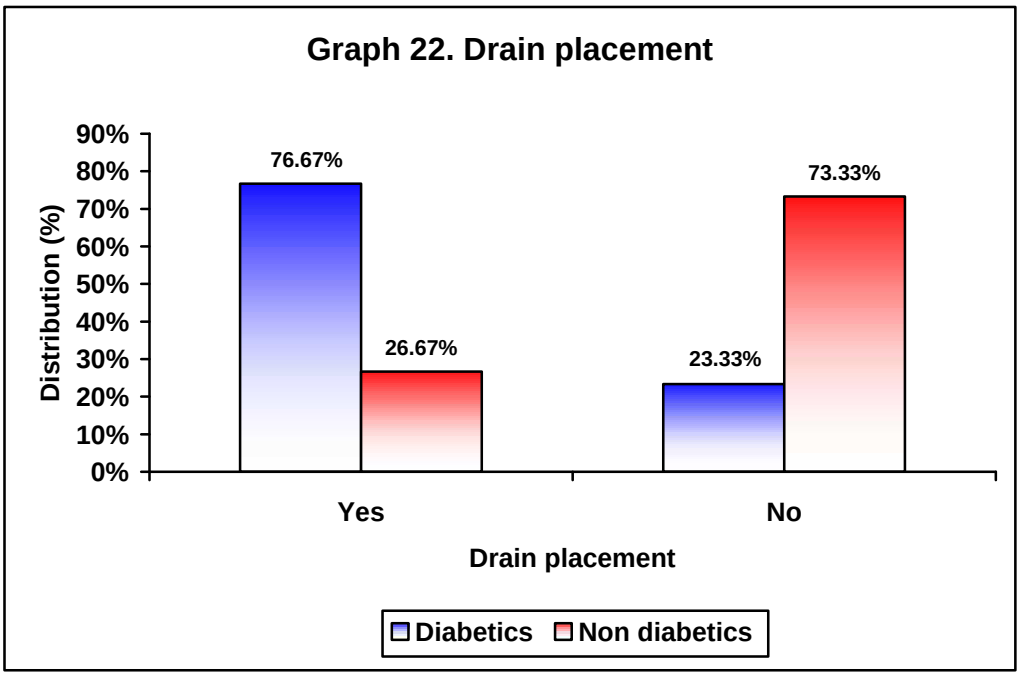


In this study maximum i.e. 26.67% of the patients with diabetes mellitus had difficult extraction of gall bladder compared to 3.33% of the non diabetic patients. This difference was statistically significant (p=0.025).

Table 24. Drain placement

Drain placement	Diabetic history				Total	
	Diabetics		Non diabetics			
	No.	%	No.	%	No.	%
Yes	23	76.67	8	26.67	31	51.67
No	7	23.33	22	73.33	29	48.33
Total	**30**	**100.00**	**30**	**100.00**	**60**	**100.00**

p<0.001

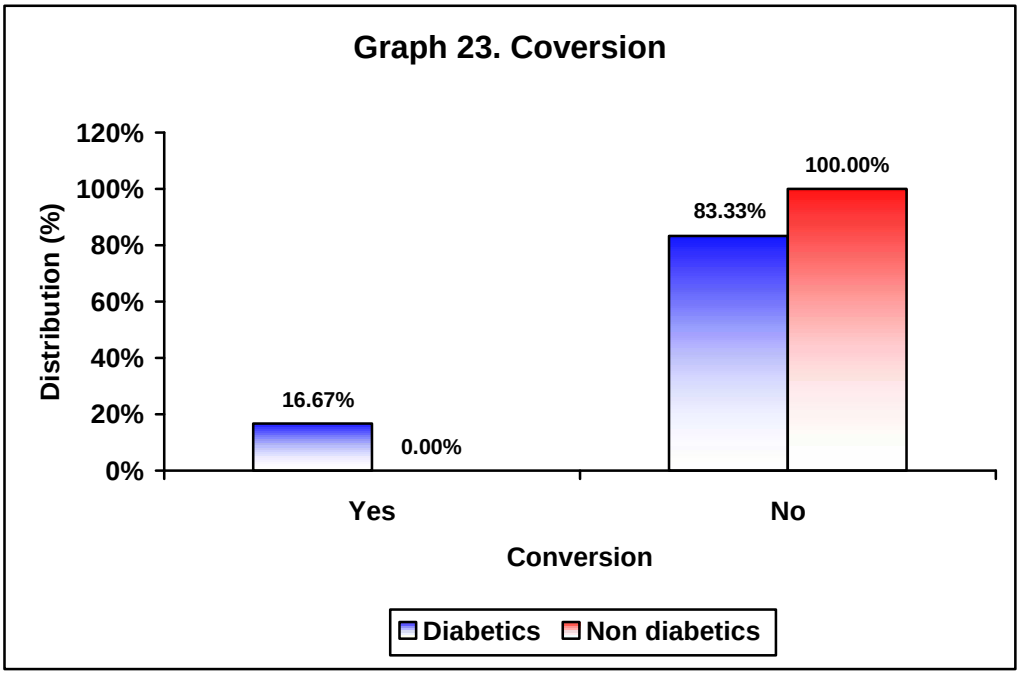


In the present study majority of the patients (76.67%) with diabetes mellitus required drain placement compared to few non diabetic patients (26.67%) (p<0.001).

Table 25. Conversion

Conversion	Diabetic history				Total	
	Diabetics		Non diabetics			
	No.	%	No.	%	No.	%
Yes	5	16.67	0	0.00	5	8.33
No	25	83.33	30	100.00	55	91.67
Total	**30**	**100.00**	**30**	**100.00**	**60**	**100.00**

p = 0.026



In this study the rate of conversion was 16.67% in patients with diabetes mellitus compared to nil in non diabetic patients. This difference was statistically significant (p=0.026).

Table 26. Distribution of patients according to the reason of conversion in diabetics

Reason	Distribution	
	Number	Percentage
Difficult dissection	2	6.66
Mucocele of the GB with difficult dissection	1	3.33
Severe Uncontrolled bleeding	1	3.33
Thickened Gall Bladder packed with stones	1	3.33
Uncontrolled bleeding and unclear anatomy	1	3.33

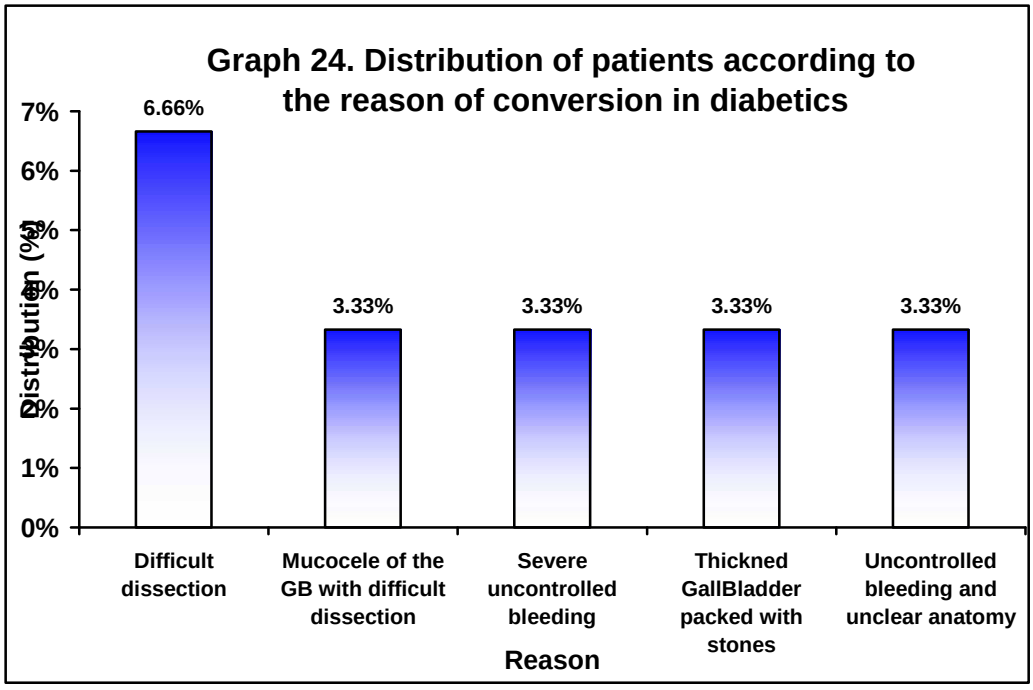
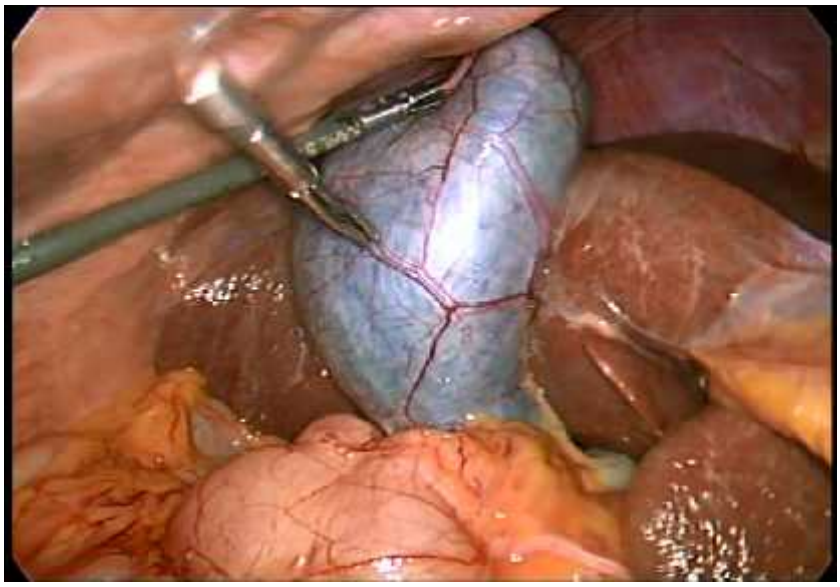


Table 26 shows the reasons for conversion in diabetic patients.

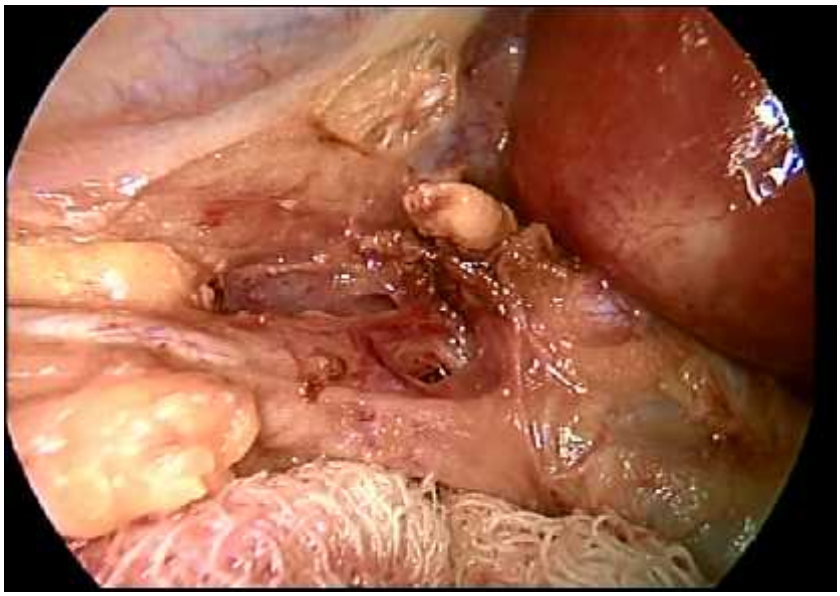
Table 27. Comparison of mean surgical time

Variables	Diabetic history				p value
	Diabetics		Non diabetics		
	Mean	SD	Mean	SD	
Surgical time (minutes)	103.00	26.54	78.83	19.06	**<0.001**

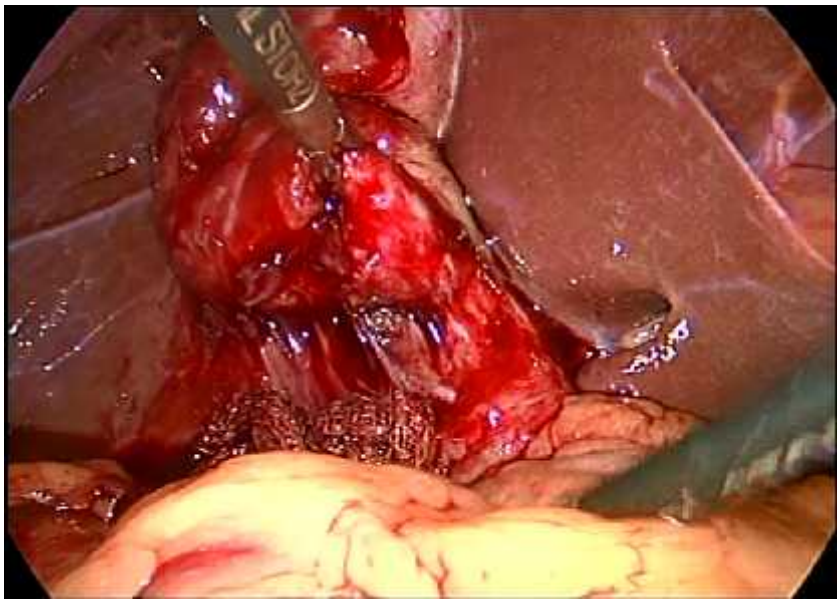
In this study the mean surgical time was significantly high in patients with diabetes mellitus that is, 103.00 ± 26.54 minutes compared to 78.83 ± 19.06 minutes in non diabetics ($p<0.001$).



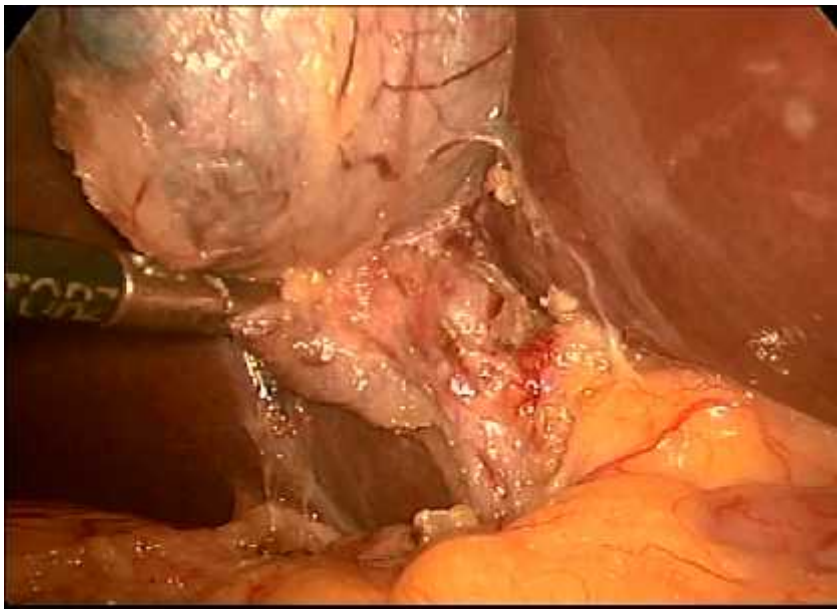
Photograph 1. Uninflamed gallblaader



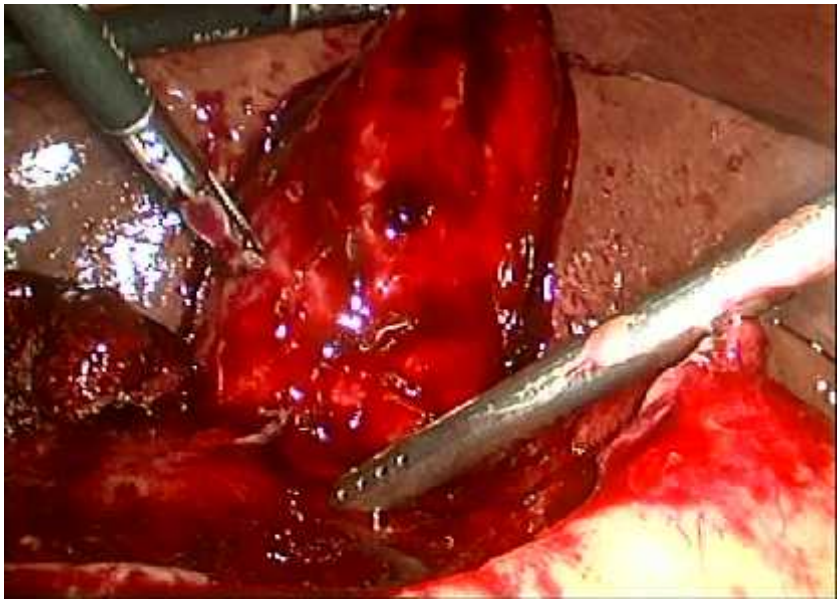
Photograph 2. Normal anatomy - Calot's triangle



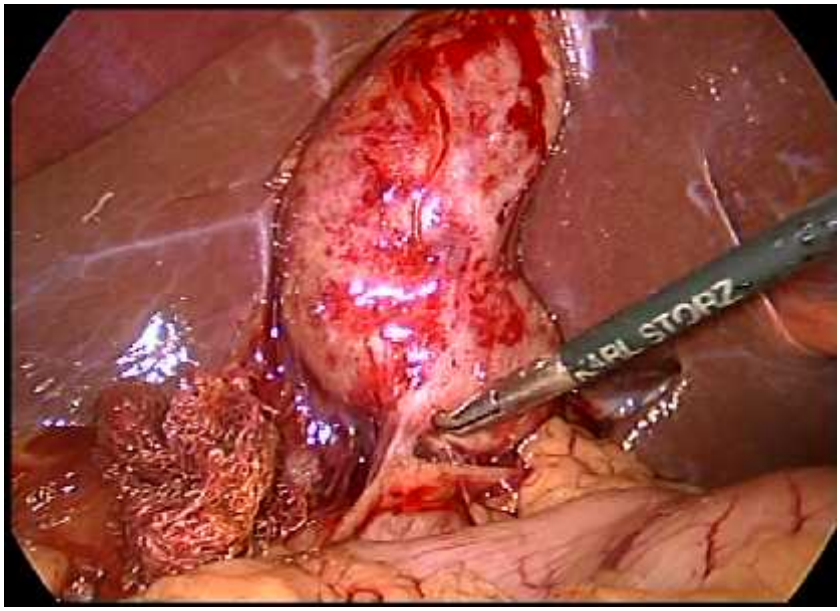
Photograph 3. Chronic cholecystitis- thickened gallbladder with frozen Calot's triangle



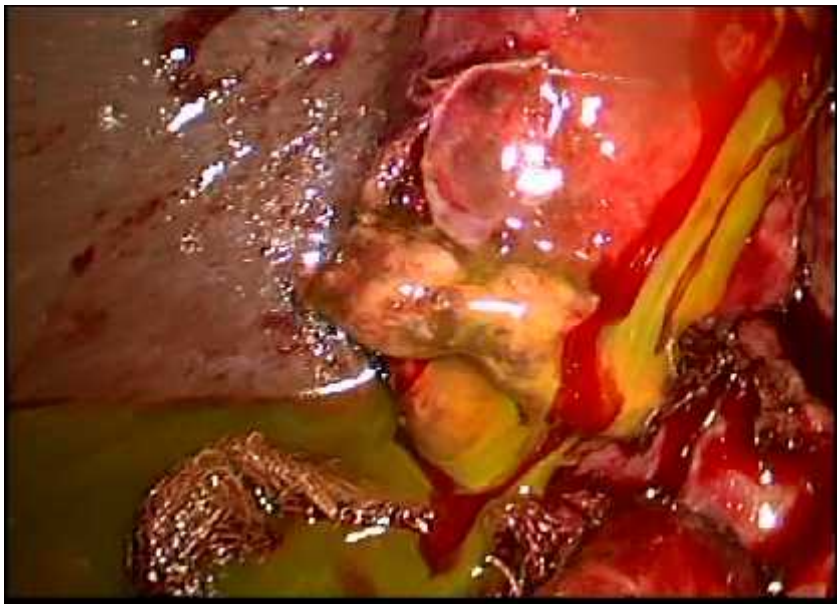
Photograph 4. Severe adhesions in Calot's triangle



Photograph 5. Severe intraoperative bleeding



Photograph 6. Mucocele gallbladder



Photograph 7. Empyema gallbladder

Photograph 8. Shrunken fibrotic gallbladder

DISCUSSION

Laparoscopic cholecystectomy has gained popularity at international level from 1987. With improved techniques, it has quickly established itself as the surgical procedure of choice for cholelithiasis. Laparoscopic cholecystectomy is minimally invasive, uses smaller incisions and allows early postoperative mobility and regain of normal health. It has morbidity incidence of 1% -3% peroperatively as compared to the 4.5% morbidity in case of open cholecystectomy. Hence it has emerged as the 'gold standard" for elective surgical treatment for gallstone disease.[110]

Diabetic patients are more prone to surgical complications due to their background diseases and therefore the rate of morbidity and mortality is higher in these patients. It is proved that diabetic patients are at high risk for gallstones formation than normal population. However, mortality and morbidity related to gallstones in the diabetic patients as compared to non-diabetics have been controversial. Previous studies have shown increased rate of complications and mortality, suggesting a prophylactic cholecystectomy in the diabetics for gallstones, while a few studies have denied such a difference. Till date, only few studies have been done in view of intraoperative complications of laparoscopic cholecystectomy in diabetics.[108] In this study, we assessed the operative findings of laparoscopic cholecystectomy in the diabetic patients in comparison with the non-diabetics, to know the operative difficulties which will help to propose the strategies for the prevention of intraoperative complications.

This one year case series study was performed in the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum. Total 60 patients undergoing elective laparoscopic cholecystectomy during the study period, from January 2014 to December 2014 were studied. Two cohorts of 30 each as diabetics and non diabetics were studied for intra operative difficulties / complications.

In the present study 60% of the patients were on oral hypoglycaemic agents and 40% were on insulin. Among the diabetic patients the duration of diabetes ranged from 5 years to 30 years. The poor diabetic control as measured by HbA1c of > 8.5 was present among 30% of the patients while 43.33% of the patients had HbA1c levels between 7.1 to 8.5 suggestive of moderate diabetic control. Nearly half of the study population (53.33%) presented with duration between 6 to 10 years and the mean duration was 9.08 ± 5.15 years and the median duration was 8 years.

In this study 56.67% of patients, in both diabetic and non diabetic group were males and the male to female ratio was 1.30:1 ($p=1.000$). In patients with diabetes mellitus, significantly higher number of patients (60%) were aged between 46 to 60 years compared to non diabetics (23.33%) ($p<0.001$). The mean age was also significantly high in patients with diabetes mellitus compared to non diabetics (53.63 ± 8.87 vs 41.20 ± 17.03 years; $p=0.001$). Further the clinical presentation of pain in abdomen, vomiting and fever ($p>0.050$), duration of symptoms ($p=0.917$), history of hypertension ($p=0.052$), pulse rate ($p=0.071$) and systolic blood pressure ($p=0.219$) were comparable in diabetics compared to non diabetics. However, age distribution ($p<0.001$), mean age ($p=0.001$), diastolic blood pressure ($p=0.025$), fasting blood sugar ($p<0.001$) and random blood sugar levels ($p<0.001$) were

significantly high in patients with diabetes mellitus. Further, significantly high number of patients (80%) with diabetes mellitus had diagnosis of calculous cholecystis compared to non diabetic patients (40%) (p=0.001).

Overall, these findings suggest that, pre operative characteristics in patients with diabetes mellitus and non diabetics were comparable except age, diastolic blood pressure and diagnosis.

Creation of pneumoperitoneum is the first step of laparoscopic cholecystectomy. In this study more than one third of the diabetic patients (40%) underwent open pneumoperitoneum compared to non diabetic patients (16.67%) and statistically the difference was significant (p=0.045) may be due to obesity and surgeon's preference.

In the present study appearance of the gallbladder was simple and uncomplicated (non thickened and uninflammed with clear anatomy) in 26.67% of the diabetics compared to 60% of the non diabetics while gall bladder was enlarged and inflamed in 40% of the diabetics compared to 36.67% of the non diabetics. The other findings of gall bladder noted in diabetics were impacted (20%0, shrunken and fibrotic (6.67%) thickened gall bladder (3.3%) and sessile gall bladder (3.3%). Whereas, in non diabetics impacted gall bladder was noted in 3.3% of the patients. This suggest that, the appearance of gall bladder varies significantly in diabetic patients compared to non diabetics (p=0.043). The findings of the present study were similar to the study by Ziaee SA et al.[108] who showed that, 14.3% of the diabetics had gangrenous gall bladder as compared to 1.6% of the nondiabetics (RR: 8.7; 95% CI: 3.8-20.8).

In this study significantly higher number of patients with diabetes mellitus had severe (30% Vs 6.67%) and moderate adhesions (53.33% Vs 33.33%) compared to non diabetic patients (p=0.001). Also adhesionolysis was difficult in significantly higher number of patients (73.33%) compared to non diabetics (p<0.001). Ziaee SA et al.[108] showed that, diabetes also causes a significant increase in the risk of adhesions formation (28.6% *vs* 6.2%). Aldaqal SM. et al.[99] in their study reported that increased number of adhesions were present in 46.7% of the diabetic patients compared to 34.7% of the non-diabetics *(*p=0.775). In 2006, a study conducted by Ibrahim et al.[97] in Singapore, found an association between poorly controlled diabetes (elevated HbA1c >6) with an increased risk for conversion. They proposed an association between poorly controlled blood sugar levels and severe inflammation distorting the anatomy.[97]

In the present study significantly higher number of patients with Diabetes (83.33%) required moderate dissection compared to of non diabetic patients (43.33%) (p<0.001). The meticulous slow dissection in the present study can be due to an inflamed, thickened gall bladder and the presence of adhesions. Increased gall bladder wall thickness is related to the inflammation and fibrosis following the repeated attacks of cholecystitis and hence reflects the difficulty in understanding the anatomy intra-operatively.

In this study significantly higher number of patients with diabetes mellitus had complications of moderate (83.33% vs 26.67%) and severe (10% vs none) intra operative bleeding compared to non diabetics (p<0.001). In a study by Seyed Hosseini SV et al.[6] also, complications such as bleeding were high in diabetes patients compared to non diabetics (4 vs 1 patient; p=0.353). In another study by

Aldaqal SM et al.[99] there were total 3 (2.7%) patients who had severe intraoperative bleeding. Two of them were diabetics and one was non-diabetic (11.1% and 1.1%, with a p=0.068).

In this study the grasping of gallbladder was difficult in significantly higher number of patients with diabetics compared to non diabetics (50% versus 10%; p=0.001). The removal of gall bladder from the liver bed was difficult in significantly higher number of patients that is, 60% with diabetes mellitus compared to 13.33% of the non diabetic patients (p<0.001).

In the present study maximum i.e. 26.67% of the patients with diabetes mellitus had difficult extraction of gall bladder specimen requiring the extension of incision compared to 3.33% of the non diabetic patients. This difference was statistically significant (p=0.025). Also majority of the patients (76.67%) with diabetes mellitus required drain placement compared to few non diabetic patients (26.67%) (p<0.001). In contrast these findings, Aldaqal SM et al.[99] reported comparable outcome with regard to extraction of gallbladder and drain placement in patients with diabetes mellitus and non diabetics.

In this study the rate of conversion was 16.60% in patients with diabetes mellitus compared to nil in non diabetic patients. This difference was statistically significant (p=0.026). These findings were consistent with several other studies. A study done by Aldaqal SM et al.[99] who reported that, there was conversion of laparoscopic cholecystectomy to open procedure in 5 patients (4.5%). Out of them, 3 patients were diabetics (16.7%) and 2 were non-diabetics (2.1%) (p=0.029). In 2001, a study conducted in university of Erciyes, Turkey,[86] found that operative and

postoperative complications of laparoscopic cholecystectomy in diabetics were significantly higher than non-diabetics. Their conversion to open rate was 7.1% in diabetics compared to 2.8% in nondiabetics.

Paajanen et al.[105] from Kipio University hospital in Finland (18) studied the operative outcome of laparoscopic cholecystectomy in diabetic patients in 2010. The results of their study showed that 16% of the diabetic patients undergoing laparoscopic cholecystectomy required conversion to open procedure in comparison to 7% of the non-diabetic controls.

In this study the mean surgical time was significantly high in patients with diabetes mellitus that is, 103.00 ± 26.54 minutes compared to 78.83 ± 19.06 minutes in non diabetics ($p<0.050$). In contrast a study by Aldaqal SM et al.[99] reported comparable mean duration in diabetics (114.06±60.01) and non-diabetics (102.30 ± 40.688) ($p=0.305$). Another study by Seyed Hosseini SV et al.[6] reported the mean duration of operation on diabetic and non-diabetic patients as 57.22 ± 7.40 and 53.27 ± 11.19 minutes, respectively ($P=0.113$).

Overall the present study showed significantly higher complications in patients undergoing laparoscopic cholecystectomy with diabetes compared to non diabetics. Similar findings have been described in several other studies. A study reported a complication rate of 21% and 9% for diabetic and non-diabetic patients, respectively. According to these studies, complications in diabetics are significantly higher than non-diabetics ($P<0.05$).[111]

Rasohoff et al.[112] (1987) concluded that acute cholecystitis is more dangerous in diabetic patients than non-diabetics. Reiss[113] (1993) also concluded

that diabetic patients are more prone to surgical complications compared to other patients**.**

Till date only few studies[94,99-108] have assessed the effect of diabetes on the course of gallbladder diseases and diabetes as an independent risk factor for intra-operative complications of laparoscopic cholecystectomy. Moreover, these studies[94,99-108] have shown variable conclusions. Since both diabetes and gallstones are on the rising trend our country being important health issues, the aim of the study was to further evaluate their relationship, in order to provide the patients a better healthcare and surgical outcome.

The strength of the study is, the study included 30 cases of diabetes mellitus which is first to our knowledge and assessed various complications occurred during the laparoscopic cholecystectomy in details. However the age and certain characteristic of the study population differed significantly which would have created the bias in the study results. Further studies overcoming these pitfalls will explore the feasibility of laparoscopic cholecystectomy in patients with diabetes mellitus.

CONCLUSION

Based on the results of this study it may be concluded that, diabetes mellitus is significantly associated with several operative difficulties during laparoscopic cholecystectomy including adhesions distorting the anatomy, difficult dissection of Calot's triangle, difficult adhesionolysis, intra operative bleeding, difficult grasping of gall bladder, difficult removal of gall bladder from liver bed, need to extend the incision for extraction of specimen, drain placement and conversion to open cholecystectomy. Furthermore, diabetic patients are at risk of having multiple gall bladder stones and the operating surgeon is likely to require higher operative time.

SUMMARY

Diabetes is reported to be a risk factor for gallstone formation and these patients are generally more prone for operative and post-operative morbidities than their normal counterparts. This study was aimed to find intra-operative difficulties and complications in patients with diabetes mellitus during laparoscopic cholecystectomy compared to non diabetics.

This one year case series was carried out in the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum. A total 60 patients (30 diabetics and 30 non diabetics) undergoing elective laparoscopic cholecystectomy from January 2014 to December 2014 were studied and the operative difficulties during the surgery and complications encountered were noted.

The male to female ratio was 1.30:1 and 56.67% of the patients were males in diabetic as well as and non diabetic group. Among the patients with diabetes, 60% were aged between 46 to 60 years compared to 23.33% in non diabetics ($p<0.001$). In patients with diabetes, 53.33% of the patients had diabetic duration between 6 to 10 years (mean duration 9.08 ± 5.15 years) and most of the patients (60%) were on oral hypoglycaemic agents and had moderate glycaemic control (43.33%). Other pre operative characteristics including clinical presentation, duration of symptoms, history of other associated diseases and vitals were comparable in diabetic and non diabetics patients ($p>0.050$). Significantly higher number of patients in diabetic group underwent open pneumoperitoneum (40% vs 16.67%; $p=0.045$). Statistically significant difference was noted with regard to the appearance of gall bladder

(p=0.043), adhesions (p=0.001), dissection of Callot's triangle (p<0.001), releasing adhesions (p<0.001), intra operative bleeding (p<0.001), grasping of gallbladder (p=0.001), removal of gallbladder from liver (p<0.001), extraction of specimen (p=0.025), drain placement (p<0.001) and conversion (p=0.026). Furthermore the operative time was significantly high in patients with diabetes mellitus compared to in non diabetics (103.00 ± 26.54 vs 78.83 ± 19.06 minutes; p<0.050).

Diabetes mellitus is significantly associated with several operative difficulties and prolonged surgical time during laparoscopic cholecystectomy.

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ANNEXURE I – CONSENT FORM

CONSENT FOR PARTICIPATION IN RESEARCH STUDY

Mr. /Mrs. /Miss. _____ we are requesting you to enroll yourself in study titled **"EFFECT OF DIABETES ON OPERATIVE OUTCOME OF LAPAROSCOPIC CHOLECYSTECTOMY: A ONE YEAR CASE SERIES STUDY AT TERTIARY CARE HOSPITAL"** conducted by Dr. ***** **** *****, Post Graduate in M.S. General Surgery under the guidance of Dr. ***** ****** Professor, Department of General Surgery, Jawaharlal Nehru Medical College, Belgaum under KLE university, Belgaum.

Respected Sir/Madam,

We request you to enroll yourself to participate in our study as you are eligible for participating in the study. During the study your operative outcome will be accessed by some questions which will be answered by your operating surgeon.

Purpose of the study

This study is aimed to find out the effect of diabetes on operative outcome of laparoscopic cholecystectomy. Whether the presence of diabetes is associated with increased intra-operative complications or not will be studied. It will help the surgeon and the patients to deal with the complications.

Operative outcome of patients undergoing elective laparoscopic cholecystectomy at out institute will be studied by the investigator, Dr. *** ****** *****.

Procedure involved

If you agree to enroll yourself in my study, I will ask your present past history regarding diabetes. Then you will be clinically examined in detail and routine

investigations like Blood sugar level will be done accordingly to confirm the presence of diabetes. You will be allotted into one of the two groups- diabetic and non diabetic. After your surgery (laparoscopic cholecystectomy), your operating surgeon will be requested to fill a proforma which will give the exact picture of operative outcome.

Risks and Benefits

There is no risk involved.

Benefit-It will help in better preparation for surgery to handle risks.

Alternatives

Even if you decline the participation in the study, your operative outcomes will not be documented. Your participation in this research is voluntary. You may choose not to enroll yourself in this study. Your decision will not change present or future health care services offered to you at K.L.E.S. Dr. Prabhakar Kore Hospital. If you decide to participate you are free to withdraw at any time.

Privacy and Confidentiality

The only people to know that you are a research subject are members of the research team. No information about you or information provided by you during the research will be disclosed to other without your written permission except:

1. In emergency to protect your rights and welfare.
2. If required by law.

Institutional/sponsors policy

There is no possibility of any harm or injury during your participation in this study.

Financial Incentives for participation

No financial incentives are being offered to enrolled patients. It is purely being done with the idea of research and all the cost of the study will be borne by the investigator.

Authorization to Publish Results

When the results of the research are published or discussed, in a conference, no information will be displayed that would disclose your identity. Any information that is obtained in connection with this study and that can be identified with your identity remaining confidential.

Questions

In case you have any questions related to the study, in future or in case of study related injury or illness, you can contact Dr. **** ***** *****, Department of General Surgery, KLES Hospital and MRC, Belgaum, phone number: ***** *****. Or Dr. ***** ******, Professor, Dept Of General Surgery, KLES Hospital and MRC, Belgaum Ph: ***** *****.

If you have any queries about your rights as a study subject, you may call Dr. ***** ******, Professor, Department of Pathology and Chairman, J. N. Medical College Institutional Ethical Committee for Human Subjects Research, Phone number-***** *****, or extension **** at J.N. Medical College, Belgaum.

"EFFECT OF DIABETES ON OPERATIVE OUTCOME OF LAPAROSCOPIC CHOLECYSTECTOMY: A ONE YEAR CASE SERIES STUDY AT TERTIARY CARE HOSPITAL"

CONSENT FOR PARTICIPATION IN CASE SERIES STUDY

I, Mr. /Ms. / Mrs. _____ voluntarily agree for the participation as a subject of study. By signing this consent form I am not giving up any of my legal rights, I may withdraw from the study anytime. I am signing the consent form after having read or been read for me in vernacular language, including the risks and the benefits and having all my questions answered.

Subject Name: _____

Signature or the Left Thumb Print of Subject: _____

Date:

Witness Name: _____

Signature: _____

Date:

Investigators Name _____

Signature: _____

Date:

Place: _____

ANNEXURE II – PROFORMA

"EFFECT OF DIABETES ON OPERATIVE OUTCOME OF LAPAROSCOPIC CHOLECYSTECTOMY: A ONE YEAR CASE SERIES STUDY AT TERTIARY CARE HOSPITAL."

Principle Investigator

Dr. *** ******
Professor,
Department of General Surgery,
Jawaharlal Nehru Medical College,
K.L.E. University,
Belgaum – 590 010
.

Co Investigator

Dr. *** ***** ******
Post Graduate Student,
Department of General Surgery,
Jawaharlal Nehru Medical College,
K.L.E. University,
Belgaum – 590 010.

Name _____

Address _____

Age/Sex of the Patient: _____

In Patient Number: _____

Date of Surgery: _____

Operating Surgeon: _____

History

Chief Complaints

Past History

- History of Diabetes Mellitus/Hypertension/Asthma/Tuberculosis
- If diabetic, duration of diabetes:
- If diabetic, Drug Therapy for diabetes:
- Previous surgeries:
- Other co-morbidities:

Family History

General Physical Examination

Pulse: Blood Pressure:

Temperature:

BMI: <17.9 / 18-24.9 / 25-29.9 / 30-34.9 / >40

Systemic examination

Cardiovascular System:

Respiratory System:

Central Nervous system:

Per abdomen:

Investigations

Serum glucose level- fasting _____mg/dl HbA1c- _____U

Random _____mg/dl

Other investigations- USG / CT Abdomen / ERCP

Findings

Diagnosis

Proposed Surgery Laparoscopic cholecystectomy (elective)

Operative Outcome

1) Method of creating pneumoperitoneum

- Closed (using Verres needle).
- Open.

2) Appearance of gallbladder

- Simple and uncomplicated (non thickened and uninflammed with clear anatomy)
- Enlarged and inflamed
- Impacted.
- Shrunken and fibrotic.
- Thickened gall bladder
- Sessile gall bladder

3) Adhesions

- Absent (no adhesions).
- Mild (covering only neck of gallbladder, fundus clearly visible).
- Moderate (covering gallbladder).
- Severe (buried gallbladder).

4) Anatomy of calot's triangle

-Clear.

-Minimal dissection required.

-Moderate dissection required.

-Not possible to clarify (frozen calot's triangle).

5) Releasing the adhesions (adhesionolysis)

-Easy (flimsy adhesions).

-Difficult (thick adhesions but permitting visualization of anatomy).

-Unsafe dissection.

6) Gall bladder stone

-Solitary.

-Multiple.

-Gall bladder packed with stones.

7) Intra-operative bleeding

- Mild (normal).

- Moderate (causing tachycardia > 100 /minute without drop in blood pressure)

- Severe (causing tachycardia >100 /minute with > 10 mm Hg drop in blood pressure)

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8) Site of bleeding

-From calot's triangle (from cystic artery).

-From gall bladder.

-From liver bed.

9) Grasping gall bladder

-Easy.

-Difficult.

10) Removal of gallbladder from liver-bed

-Easy (time taken <20 minutes).

-Difficult (time taken >20 minutes).

-Perforation of gall bladder during dissection.

11) Extraction of Gall bladder/need for extending the incision

Yes / No:

12) Complications (if yes) -

-Bile spillage.

-Stone spillage.

-Uncontrolled bleeding.

-CBD injury.

-Bowel injury.

-Other. Mention:

13) Need for drain placement

Yes

No

14) Duration of surgery

_____ minutes(from skin incision to skin closure).

Time to conversion (if yes)- _____ minutes(from skin incision for Laparoscopic Procedure to skin incision for open procedure).

>90 minutes from insertion of Verres needle till Gallbladder extraction from Liver bed. Yes / No.

15) Conversion to open procedure Yes / No.

If yes, mention reason -

Signature of operating surgeon:

ANNEXURE III – KEY TO MASTER CHART

-	-	Absent
+	-	Present
A	-	Afebrile
Bl	-	Bloating
BP	-	Blood pressure
F	-	Female
GB	-	Gall bladder
HbA1c	-	Glycosylated haemoglobin
I	-	Insulin
M	-	Male
mm	-	Millimeters
mm Hg	-	Millimeters of mercury
N	-	Normal
Ns	-	Nausea
O	-	Oral hypoglycaemic agent
OB	-	Obese
OV	-	Overweight
PC	-	Pericholesystic collection
SN	-	Soft, non tender
T	-	Tenderness