"OBSERVATIONAL STUDY OF EFFECT OF CO2 PNEUMOPERITONEUM ON LIVER FUNCTION FOLLOWING LAPAROSCOPIC CHOLECYSTECTOMY"

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LIST OF ABBREVIATIONS.

AB	-	ALBUMIN
AGR	-	ALBUMIN-GLOBULIN RATIO
ALP	-	ALKALINE PHOSPHATASE
ALT (SGPT)	-	ALANINE AMINOTRANSFERASE (SERUM GLUTAMIC-
AST (SGOT)	-	ASPARTATE AMINOTRANSFERASE (SERUM
CT	-	COMPUITED TOMOGRAPHY
DB	-	DIRECT BILIRUBIN
GB	-	GALLBLADDER
GL	-	GLOBULIN
		GLUTAMIC OXALOACETIC TRANSAMINASE)
IDB	-	INDIRECT BILIRUBIN
LC	-	LAPAROSCOPIC CHOLECYSTECTOMY
LFT	-	LIVER FUNCTION TEST
		PYRUVIC TRANSAMINASE)
TB	-	TOTAL BILIRUBIN
TP	-	TOTAL PROTIEN
USG	-	ULTRASONOGRAPHY

ABSTRACT

BACKGROUND:-

Laparoscopic surgery has revolutionized modern surgical practices by offering minimally invasive alternatives to traditional open procedures, enhancing patient outcomes and recovery times. Utilizing carbon dioxide (CO_2) pneumoperitoneum to create a working space within the abdominal cavity, laparoscopic techniques have become standard for various surgeries including cholecystectomy. Despite its advantages, CO_2 insufflation at pressures above 14 mmHg and prolonged operative durations can lead to transient alterations in liver function tests (LFTs), notably elevations in serum liver enzymes such as AST and ALT. These changes, though often clinically insignificant in patients with normal hepatic function, prompt questions regarding their mechanism, clinical relevance, and potential mitigation through modified surgical techniques. This study investigates the prevalence and clinical implications of such enzyme elevations post-laparoscopic cholecystectomy, aiming to contribute to the understanding and management of liver function changes associated with CO_2 pneumoperitoneum in surgical settings.

MATERIAL AND METHODS:-

The study will span one year from September 2022 to August 2023. Patients aged 18-60 years with cholelithiasis, calculous cholecystitis undergoing elective laparoscopic cholecystectomy, will be included. Exclusion criteria encompass chronic liver disease, pregnancy, and other complicating factors. LFTs will be assessed pre-operatively and on days 1, 2, and 7 post-operatively. Data was collected using routine investigations (CBC, LFT, coagulation profile) and stored in MS Excel. Statistical analysis has been performed using MS Excel, employing repeated measures, ANOVA to assess intra-group changes in LFTs.

RESULTS:-

The study population predominantly consisted of patients aged 40-50 years (28.125%) and male (59.375%). The majority were diagnosed with cholelithiasis (75.0%). Analysis of LFTs revealed non-significant differences in TB, DB, IDB, TP, ALT, AST, and ALP between pre-operative and post-operative periods across all measured time points (POD 1, 2, and 7). However, significant reductions were observed in AB ($p<0.001$), GL ($p<0.01$), and AGR ($p<0.05$) from pre-operative to post-operative periods.

CONCLUSION:-

This study highlights the stable nature of TB and DB levels following laparoscopic cholecystectomy, indicative of preserved liver function. The significant decreases in AB and GL levels underscore potential physiological responses to surgical stress or altered nutritional intake, possibly affecting immune and inflammatory pathways. Changes in ALP levels suggest considerations for liver function and bone health post-surgery. Continued monitoring of these parameters is crucial for optimizing patient recovery and overall management.

KEYWORDS:- Laparoscopic Cholecystectomy, Liver function tests, Total Bilirubin, Direct Bilirubin, Albumin, Globulin, Alkaline phosphatase.

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INTRODUCTION

Laparoscopic surgery has rapidly emerged as one of the most popular and commonly performed alternative to traditional surgical procedures in recent years, especially with the availability of skilled and competent laparoscopic surgeons. It has changed the face of general surgery with a goal to perform standard, classical open surgical procedures via laparoscope to make the operative procedure more patient-friendly. [1]

Early mobilisation, shorter hospital stay, fewer scars (i.e., better cosmetic results), decreased blood loss, reduced risk of infections, and faster recovery are some of the advantages that have led to its increased use due to its minimally invasive and scarcely unpleasant access procedure. two to four]

Diagnostic and therapeutic surgical techniques that were previously only accessible by laparotomy are now available with laparoscopic surgery, which provides better access to the coelomic cavity. For several surgical indications, including diagnostic laparoscopy, total laparoscopic hysterectomy, laparoscopic cholecystectomy, and laparoscopic hernioplasty, it is the gold standard and first option. Laparoscopic surgery has many benefits, but it also comes with risks because of the significant physiological changes that take place during the process. Several factors contribute to the physiological changes that occur during laparoscopy. These include the following: the pressure effect of gas instilled into a closed cavity, the systemic effects of the gas, the patient's positioning during surgery (the reverse trendenlenberg position), the anaesthetic used, and the patient's cardiopulmonary status. Almost universally, CO2 is instilled, absorbed, or embolised. One of the requirements for laparoscopy is a functioning cavity [6]. The use of carbon dioxide in positive pressure pneumoperitoneum is a popular method for creating this cavity. Swiss gynaecologist Richard Zollikofer initially suggested using carbon dioxide for pneumoperitoneum creation in 1924 as an alternative to filtered air or oxygen. This was due to carbon dioxide's non-combustibility, rapid absorption, and reduced risk of explosion, all of which allowed for electrocoagulation to be performed during surgery. "Pneumoperitoneum with carbon dioxide has an effect on regular bodily functions [7]. The peritoneal cavity is an ideal place for its absorption into the bloodstream. It raises the concentration of vasopressin and catecholamines in the blood. A number of negative consequences on the cardiovascular system can result from a higher diaphragm and intra-abdominal pressure, including a decrease in cardiac output, an increase in arterial pressure, and hypertension and tachycardia due to increased systemic and pulmonary vascular resistance. The circulatory, respiratory, and coagulation systems are among those that could be impacted. Eight and nine

When it comes to less invasive surgical procedures, laparoscopic cholecystectomy (LC) ranks high. The tenth On September 12, 1985, the first laparoscopic cholecystectomy was conducted by Prof. Dr. Med Erich Mühe of Böblingen, Germany. the eleventh

Knowledge on the challenges of these surgeries and awareness of all possible problems has unquestionably increased since the advent of the minimally access cholecystectomy approach approximately 33 years ago. Less tissue stress, fewer intra-abdominal adhesions, less post-operative pain, shorter hospital stays, early return to work, better cosmetic results, and overall enhanced quality of life are some of the main advantages of minimally access cholecystectomy. [12] The laparoscopic approach is now the gold standard for gall bladder removal, accounting for over 90%

of all procedures. Set the intra-abdominal pressure during laparoscopy at 1514 mm Hg to provide good visualisation and exposure of the operation field. For people who are not overweight, an intra-abdominal pressure of 5 mmHg or below is considered normal. During laparoscopic cholecystectomy, a brief increase in intra-peritoneal pressure due to CO2 insufflation appears to be having minimally harmful effects. [1]

Bile leak and clinically significant changes to liver function tests are two of the main post-procedure concerns. Recent research has demonstrated that anaesthetic drugs and intra-operative circulatory failure can cause a temporary increase in liver function tests that do not have any real-world consequences. When a bile leak is suspected during the postoperative phase, these factors must be taken into account. 1, 13

Postoperative liver function tests in patients who have had laparoscopic cholecystectomy have shown 'unexplained' differences, according to several anecdotal reports. [14] Once thought to be an incidental observation, the rise in liver enzyme readings following an uncomplicated lap cholecystectomy is now widely recognised as a sign of transitory hepatic malfunction. No one has yet explained the therapeutic relevance of these enzyme level shifts, but fresh worries about the pulmonary and cardiovascular effects of pneumoperitoneum have emerged. Pneumoperitoneum can temporarily reduce blood flow to the liver, which can lead to problems with breathing, heart failure, or kidney failure, such as hypercapnia or high intra-abdominal pressure [15]. On pages 16 and 17, It has been demonstrated that pneumoperitoneum, because to its pressure and duration, raises levels of liver enzymes. 1, 18

Although the portal venous pressure typically ranges from 7 to 10 mmHg and accounts for about half of the liver's blood flow, a pneumoperitoneum that is 14 mmHg and filled with carbon dioxide might produce temporary hepatic ischemia in LC. The tenth Consequently, these alterations may have unintended consequences in individuals whose liver function is already impaired. Potential substitutes that should be investigated include gasless abdominal wall lift and low-pressure pneumoperitoneum procedures. [1]

People with hepatic insufficiency should be cautious before having laparoscopic cholecystectomy as, according to Guven HE et al., differences in liver enzymes do not seem to be clinically significant. The year 19 Research by Morino et al. on the effects of pneumoperitoneum at constant pressure during the course of an operation revealed that AST and ALT level rises become more pronounced after 60 minutes. In [20],

Patients undergoing surgery with high pressure pneumoperitoneum (14 mmHg) had considerably greater elevations of AST and ALT than those undergoing surgery with low pressure (7 mmHg), according to a randomised trial by Hasukic et al. that compared the effects of low and high pressure pneumoperitoneum on liver functions. [13] Excluding other potential confounding variables such liver tissue injury and bile system manipulations, studies comparing enzyme variations in LC and other laparoscopic procedures were also conducted to learn about the impact of a pneumoperitoneum on liver enzymes.

Although the exact process by which alter enzymatic alterations occurs remains a mystery, Halevy proposed a number of plausible hypotheses. There are a number of factors that can lead to liver damage, such as high intra-abdominal pressure, low portal vein and hepatic artery flow, high liver function test (LFT), the compressive force of the gall bladder retracting, a momentary twist of extrahepatic ducts, diathermy-induced damage to the liver parenchyma, the unintentional severing of supplying or right branch arteries, and the existence of multiple causes. Elevated LFT and reduced hepatic perfusion can result from these causes.

Recent research has indicated that blood liver enzyme levels rise sharply after laparoscopic surgeries; this may be due to changes in hepatic and splanchnic circulation; so, our study aimed to address this hypothesis. The severity of the increase in serum levels of these liver enzymes is proportional to the pressure that is generated, which is why high-pressure pneumoperitoneum is more common. 1, 2, 10,

Patients with normal hepatic function should not be concerned if there is a transient increase in liver enzymes after laparoscopic cholecystectomy; this increase often resolves on its own. We ask, "Is there any clinical significance of these changes in liver function tests?" and "Is there any role of laparoscopic technical modifications to prevent these changes?" in response to the clinical observation that most patients with previously normal hepatic function have significantly changed serum levels of certain hepatic enzymes. In addition, research on how carbon dioxide pneumoperitoneum-assisted laparoscopic surgery affects liver enzyme alterations in India is lacking.

In light of the aforementioned, the current study set out to provide empirical evidence that CO2 insufflation more than 14 mmHg, along with a protracted duration of operation, would cause transitory alterations to liver function tests. The purpose of this study was to identify the frequency, clinical relevance, and relevance of unexplained variations in liver enzymes after laparoscopic cholecystectomy during the postoperative recovery period.

AIMS AND OBJECTIVES

- To interpret the results of liver function following laparoscopic cholecystectomy due to Co2 pneumoperitoneum

REVIEW OF LITERATURE

Laparoscopic surgery has prompted significant shifts in how surgical disorders are approached in the current era. We are now reviewing almost all procedures for the possibility of converting them to laparoscopic technique as a result of the "Minimally invasive surgery" (MIS), which has evolved into "Minimal Access Surgery" (MAS).

CHOLECYSTECTOMY:

Cholecystectomy is the surgical removal of gall bladder.

Acute and chronic cholecystitis, acalculous cholecystitis, empyema gall bladder, mucocele of gall bladder, typhoid carriers, gallstone pancreatitis, and symptomatic gallstones are among the indications. Gall bladder polyps larger than 1 cm are also in the list of indications.

People with diabetes, impaired immune systems, those getting organ transplants, those with congenital hemolytic anaemia, those having bariatric surgery, and those with porcelain gall bladders are the ones who have prophylactic cholecystectomy.

Patients who are not suitable for general anaesthesia, those who have coagulation abnormalities, those who are suspected of having gall bladder cancer (since the surgery could lead to metastases at the port site), and those who are unwilling to undergo the laparoscopic procedure are all considered absolute contraindications of laparoscopic cholecystectomy.8

Pregnancy, cardiac problems, pulmonary issues, portal hypertension (due to the possibility of many venous collaterals), liver cirrhosis (because to the brittleness of the liver), and prior upper abdominal procedures (due to dense adhesions) are relative contraindications.

Cholecystectomy complications can include troublesome Calot's dissection, thick adhesions, perioperative haemorrhage from the liver bed or pedicle, and abnormalities of the cystic duct and cystic artery.

Infection, sub phrenic abscess, cystic artery, and liver bed haemorrhage are post-cholecystectomy complications. The hepatic duct or common bile duct could sustain an accidental injury. Rare but potentially life-threatening complications include bile leakage, biliary fistula formation, or stricture formation. When there are a lot of adhesions, it might cause harm to the colon, duodenum, or mesentery.

HISTORY OF LAPAROSCOPIC CHOLECYSTECTOMY

In the history of surgery few procedures have so rapidly changed the surgeon’s way of thinking and acting as has Laparoscopic cholecystectomy. It has been the true detonator of the laparoscopic revolution in digestive surgery.

- **1882- Carl Langbuch** from Germany performs the first cholecystectomy.
- **1980- Semm** performs first laparoscopic appendectomy.
- **1984- Erich Muhe** designs the galloscope (laparoscope for cholecystectomy)
- **1985- Sept 12- Erich Muhe performs the first laparoscopic cholecystectomy.**

- Uses pistol grip scissors, pistol grip applier and hemoclips.
- Uses Verres technique to create pneumoperitoneum.

- **1986- Muhe** presents the case before the German Surgical society and is rejected by them.
- **1987- Lyon** performs his first laparoscopic cholecystectomy in France.
- **Moureta** general surgeon performed a Laparoscopic cholecystectomy and few months later showed video tape of his technique in Paris 1987.
- In **1988** in Paris, **Dubois and Co-workers** – tried the laparoscopic method. During the same year, technique of internal lithotripsy for re- moving gallstones with a laparoscopic access was developed.
- **1988- First laparoscopic cholecystectomy in USA.**
- For the first time in the United States, a videotape of laparoscopic cholecystectomy using intra corporeal lithotripsy technique Endoscopic Surgeons in Louisville, Kentucky in April 1989.
- **1990- Perissat, Dubios, Cushieri** acknowledged by SAGES for having performed Laparoscopic Cholecystectomy
- **1992- Muhe receives GSS anniversary award** as acknowledgement for his contribution.
- As early as 1992, laparoscopic cholecystectomy had become the procedure of choice to remove gallbladder with calculi for two main reasons, constant improvement of results and simplification of technique.
- **1997- Navarra et al** performs the first single incision laparoscopic surgery.
- 1999- Muhe presents "THE FIRST LAPAROSCOPIC

CHOLECYSTECTOMY'' in TEXAS in STORZ conference ascertaining his place in history as the first person to have performed laparoscopic cholecystectomy

- The explosive success of laparoscopic cholecystectomy-initiated revolution within us. At present nearly all abdominal surgeries can be performed laparoscopically.

There are majorly four types of laparoscopic surgery:

1. *Laparoscopic Appendicectomy*
2. *Laparoscopic Cholecystectomy*
3. *Diagnostic Laparoscopy*
4. *Laparoscopic Ovariectomy*

ANATOMY OF GALL BLADDER

The gall bladder is a pear or pyriform shaped organ of size 7.5 – 12 cm, with a normal capacity of about 5 ml that lies in close proximity to the liver (its inferior surface).

Gallbladder is located in the gallbladder fossa of inferior surface of right lobe of liver and covered by layer of peritoneum.

The gallbladder is divided anatomically into

- Fundus
- Body
- Neck (or) infundibulum through which bile drains into cystic duct which joins the common bile duct.

The arterial supply of the gallbladder is by the cystic artery, which is a branch of the right hepatic artery.

The venous drain is through the cystohepatic veins. These are multiple in number and are unnamed.

Lymphatic drainage is mainly through the lymph node of Lund.

Parasympathetic supply is through the right vagus and sympathetic through T7-9.

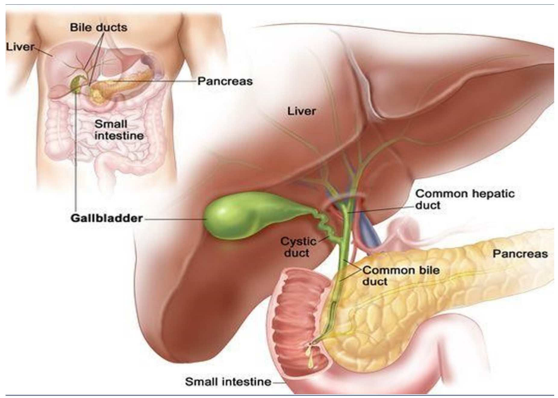


Figure 1. Anatomy of gall bladder

In order to ligate and sever the cystic duct and cystic artery, the Calot's triangle is a crucial landmark during cholecystectomy. The common hepatic duct forms the medial side of the Calot's triangle, while the inferior liver surface and the cystic duct comprise the superior and lateral sides.

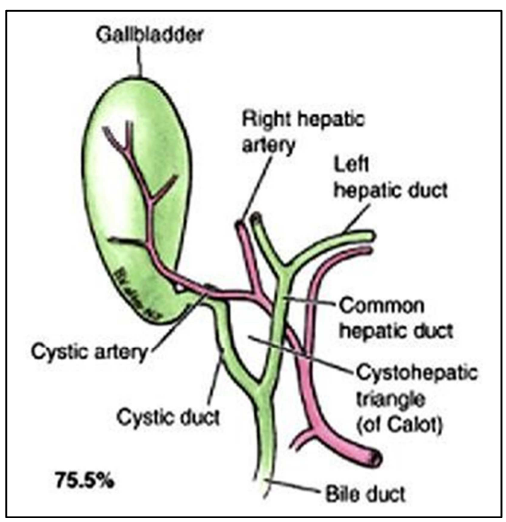


Figure 2. The Calot’s triangle

Lymph node of Lund and cystic artery make up the contents of Calot's triangle. Thirty to fifty millilitres is the typical gallbladder volume. However, the size may grow substantially when an impediment is present. Typically, you won't be able to feel the gallbladder. When the gall bladder is palpable, it may indicate a blockage in the common bile duct or, less frequently, the cystic duct.

PHYSIOLOGY

Gallstones are the most common biliary pathology. More than 85% of patients are asymptomatic who needs expectant line of management.

They are classified into

1. Cholesterol stones – Most common
2. Pigment stones which again divided into
   a. Brown pigment stones.
   b. Black pigment stones

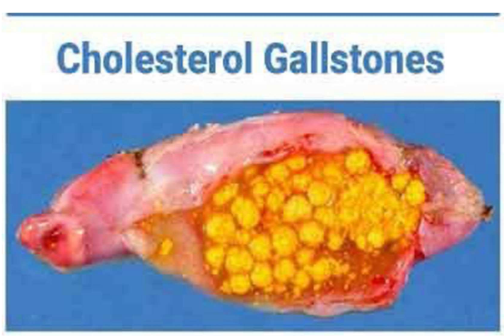


Figure 3. Cholesterol Stones

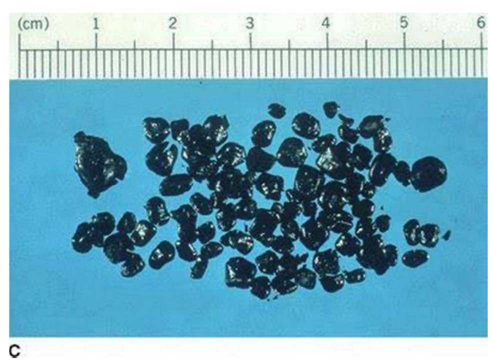


Figure 4. Pigment Stones

Factors in gallstone formation

1. Supersaturated bile – Most important.
2. Impaired gall bladder function
3. Cholesterol nucleating factors
4. Absorption and enterohepatic circulation of bile acids.

PATHOLOGY

A, D, E, and K vitamins, as well as lipids, are more easily absorbed when bile is present. In addition to bilirubin, cholesterol is excreted by the body during the digestive process. Bile salt dissolves lipids and facilitates their absorption. The liver uses bile salt and other chemicals to make phospholipids. Being extremely non-polar, cholesterol does not dissolve in either water or bile. Between 800 and 1000 millilitres (ml) of bile per day is considered normal for the liver.

Gall stones occur due to the loss of solubility of bile salt, chenodeoxycholic acid, and cholic acid. The main thing that happens is that "biliary sludge" forms. The ingredients include mucin, cholesterol crystals, and granules of calcium bilirubinate. Prolonged fasting states or complete parenteral feeding are contributing factors.

CHOLESTEROL GALLSTONES:

The multifactorial step is

- ❖ Supersaturation
- ❖ Nucleation
- ❖ Growth

Gallstones develop when the body's motor functions fail. Micelles help keep cholesterol soluble. The combination of cholesterol-phospholipid vesicles and a bile salt-phospholipid-cholesterol complex. The relative concentrations of cholesterol, bile salts, and phospholipid determine the solubility of cholesterol.

Many healthy people do not have gallstones but do have cholesterol supersaturation. As a result, when cholesterol levels are too high, the process enters a metastable state where the production of gallstones is dependent on the presence or absence of other bile components that promote or prevent the nucleation of cholesterol.

The formation and subsequent clumping together of solid crystals of cholesterol monohydrate is known as nucleation. Cholesterol and phospholipids facilitate vesicle transport to miscelles. Compared to cholesterol, phospholipid transfer is more efficient. This leads to the remaining vesicles undergoing cholesterol enrichment. The transformation of cholesterol-rich vesicles into massive monohydrate occurs. Immunoglobulin, mucin, and glycoprotein are factors that speed things up.

When the gall bladder gets injured or the biliary tree gets blocked, it causes clinical symptoms. There are two possible pathways for stone growth.

- Insoluble precipitate deposition at the bilestone interface.
- Leading to large conglomerate.

The development of stones occurs when the mobility of the gallbladder decreases.

Gallbladder stasis, malnutrition, parenteral nutrition, the aftermath of vagotomy, somatostatin-producing tumours, and somatostatin treatment are all factors that can contribute to the problem.

PIGMENT GALLSTONES

Stones are formed when anions, bilirubin, palmitate, and phosphates are precipitated with calcium. In addition, pigment gallstones also contain bilirubinate and palmitate.

There are two main types of pigment stones: brown and black. Hemolytic anaemia and cirrhosis are the causes of black pigment stones. Both the total and indirect bilirubin concentrations rise in hemolytic anaemia.

The Asian population is the most usual to see brown pigment stones. Cholesterol and calcium palmitate are the building blocks. Infection and biliary motility problems are contributing causes.

COMPLICATIONS OF GALLSTONES

A. In the Gall Bladder

1. Chronic Cholecystitis
2. Acute Cholecystitis
3. Gangrene
4. Perforation
5. Empyema
6. Mucocele
7. Carcinoma

B. In the Bile Ducts

1. Obstructive Jaundice
2. Cholangitis
3. Acute Pancreatitis

C. In the Intestine

1. Acute intestinal Obstruction (Gallstone ileus)

The term "silent stone" refers to a stone that is discovered by accident during a routine checkup or an examination for another pathology; it does not cause any symptoms. If a patient does not fall into one of the following high-risk categories, prophylactic cholecystectomy may not be necessary.

- Diabetic patients
- Patients on immunosuppressive therapy
- Candidates for renal transplant
- Large gall stone more than 2 cm
- Multiple small stones
- Patients living in high-risk areas where there is increased incidence of GB carcinoma.
- Porcelain GB, Cholesterolosis GB
- Patient undergoing for abdominal surgery with incidental finding of gall stones, if general condition of the patient permits – incidental cholecystectomy may be done.

Figure 5. Cholesterolosis gallbladder

INVESTIGATIONS

1. Complete hemogram – Hb%, TC, DC, ESR
2. Urine for routine examination
3. Blood for sugar, urea, creatinine and electrolytes
4. Bleeding time, clothing time and PTT
5. Liver function test
   a. Sr. Bilirubin – Total / Direct
   b. SGOT
   c. SGPT
   d. Alkaline Phosphatase
   e. Proteins
6. Chest X-ray PA view
7. ECG
8. USG Abdomen

Figure 6. Usg of cholelithiasis

Reliable investigation for evaluation of biliary tract diseases.

LATEST ADVANCEMENTS IN CHOLECYSTECTOMY

"Larger problems meant larger incisions," the surgical community used to think.

Thanks to developments in anaesthesia, fibre optics, and instruments, the trend now is for minimally invasive surgery, which leaves little or no visible scarring.An increasingly essential goal is cosmosis. Postoperative pain, adhesions, and complications are all reduced when scarring is modest.

As a result of these investigations, new opportunities have arisen in robotic surgery, three-dimensional laparoscopy, natural orifice laparoscopy, and single-incision laparoscopy.

Stal Pert in 1687, found gall stones in a patient who underwent laparotomy for peritonitis.

Two centuries later, Langenbuch performed the first open **cholecystectomy on a patient. The open technique remained the gold standard procedure for nearly a century.** Until alternative approaches arrived and supplanted it. When further procedures, such as exploration of the common bile duct or extensive adhesions, need an open cholecystectomy, this surgical procedure is still utilised.For a brief period, minilap cholecystectomy was the norm.

Radiographic techniques, including ultrasound, helped pinpoint the exact location of the gall bladder and Calot's triangle. Right above the gall bladder's position, a smaller incision—one third the size of the normal one—is made. The incision is made deeper and dissection is performed in the Calot's triangle using retractors. The incision can be made longer if necessary in the event of complications. It is still utilised in areas where laparoscopic procedures are not yet common. In addition to patients who aren't good candidates for general anaesthesia, this method can be employed when laparoscopy fails and open surgery is necessary.

Zolliker et al. of Switzerland had suggested the use of carbon di oxide for creation of pneumoperitoneum in 1924.

Veress designed a technique for creation of pneumoperitoneum using closed method. And Hasson introduced an open method for creation of pneumoperitoneum. These paved the way for the advent of modern laparoscopy.

Erich Muhe performed the first laparoscopic cholecystectomy in his patient when he found a relatively free gall bladder in a lady during gynecological laparoscopy, paving the way for laparoscopy in cholecystectomy.

Surgeons from over the world started trying out laparoscopic cholecystectomy after hearing about it, and before long, it had replaced the open method as the go-to procedure.

Despite numerous novel methods developed during the last 30 years, laparoscopic cholecystectomy remains the standard of care.

The four-port method is the conventional and still widely used method. For the sake of aesthetics, researchers have experimented with fewer ports and smaller ports.

The fourth trocar for liver withdrawal has been the subject of much debate about whether it is necessary for certain simple cases and whether a cholecystectomy may be performed just as quickly and easily without it.

Liver retractions no longer required ports because to the development of transabdominal sutures. During dissection at the Calot's triangle, the gall bladder can be retracted by suturing it to the anterior abdominal wall.

This gave rise to the two-port cholecystectomy. The requirement for skill and the fact that one to three sutures could be introduced kept researchers looking for a better method. A limitation of this method was that it could not be altered in situ to suit the surgeon's requirements for retraction and levelling.

Responding to these worries An specialised port called the R-port was used with the introduction of single incision laparoscopic surgery (SILS). The Rport is unique among specialty big umbilical trocars. It has three built-in holes that allow you to position three 5 mm instruments at slightly varying angles to one another. The patient only had to endure a single scar as a consequence of the open approach's ability to create a single 2.5 cm incision in the umbilicus.

Consequently, SILS is a cutting-edge procedure for MI surgery. On top of that, the specimen can be effortlessly withdrawn through the massive 2.5 cm opening. The hefty price tag of the R port is the main cause of the high surgical expense, which is the sole major downside. Natural Orifice The concept of Transluminal Endoscopic Surgery (NOTES) originated from the realisation that a 2.5 cm scar in the umbilicus would be undesirable to some patients. The use of a natural orifice for laparoscopy is being investigated for a number of surgical procedures, including trans-oral thyroidectomy.

There are a lot of cholecystectomy techniques that are being investigated right now. There are a lot of options, such as the trans-gastric, trans-anal, transvaginal, and trans-colon approaches. The process requires flexible endoscopic equipment, staplers, vaginal platforms, and colonoscopies.

There are a lot of problems with these approaches, including a steep learning curve, a higher initial investment, the risk of peritoneal infection, soiling the surgical field, and the requirement to repair a perforation surgically caused.

Thanks to its adaptability, NOTES is a rapidly evolving area that could pave the way for a brand new subfield to emerge.

LAPAROSCOPY

Laparoscopy allows the use of an endoscope to view the peritoneal cavity. A typical instrument for expanding the peritoneal cavity and keeping the abdominal wall and contents apart is the pneumoperitoneum. The abdominal organs are more plainly seen due to the pneumoperitoneum. It provides the necessary space for diagnostic and therapeutic procedures. It protects the neighbouring organs from potential damage. Maintaining a normal physiological condition is crucial for a successful and risk-free surgery.

Pneumoperitoneum:

The selection of pneumoperitoneum gas is dependent on several factors. Considerations for selecting an anaesthetic gas include the following: anaesthetic type, delivery method, gas compatibility with the body, toxicity, ease of use, safety, cost, lack of injury upon leakage, and ease of metabolism-induced excretion. Common gases include argon, carbon dioxide, nitrous oxide, air, and helium. All of these options have their own unique medicinal uses due to their own advantages and disadvantages.

Creation of pneumoperitoneum:

The development of pneumoperitoneum is a possible outcome of both of these operations. Particularly, the closed methods of Veress and the open methods of Hasson.

The Veress method, in order to induce pneumoperitoneum, makes use of a specialist needle known as a "Veress needle." In order to avoid puncturing the intestines, the needle is usually 12–15 cm long and has a blunt tip that is spring-loaded. It is necessary to elevate the anterior abdominal wall in order to generate counter pressure before inserting the needle into the abdominal cavity. A telescopic port is blindly inserted when gas is insufflated and the needle is passed into the peritoneal cavity. Additional ports can be created with the help of visual guides.

Two big advantages of the Veress method are how fast it is and how no specialised equipment is needed. The risk of harm to the bowel and other vascular structures underneath is higher.

With Hasson's open approach, you won't need that kind of needle. Furthermore, we meticulously monitor each phase. A 1–1.5 cm deep incision is made in the umbilicus to gain access to the rectus. To visually evaluate the entry to the peritoneal cavity, insert an umbilical port, and insufflate gas for pneumoperitoneum, it is necessary to open the rectus and peritoneum under magnification. A telescope is inserted under the patient's vision during the laparoscopic surgery. Additional ports are inserted beneath the patient's eyes.

There is less risk of damage to the gut or vascular tissues with the open approach because everything is done under careful watch. One disadvantage is that it takes longer than the Veress technique.

Major problems during laparoscopy most often occur during the insertion of the umbilical trocar. The presence of adhesions at the entrance site is the leading cause of these issues.

While Hasson's approach is used in 38% of situations, the Veress methodology is supposedly used in 62%. There are a few ways to get to the peritoneum, but general surgeons usually go with Hasson's technique because it's the safest.

The ideal range for pneumoperitoneum is twelve to fifteen millimetres of mercury. Applying greater forces at the point of entrance can reduce the likelihood of injury.

Carbon di oxide as the "Gas of choice"

Pneumoperitoneum is best created using carbon dioxide because of its high diffusion coefficient. Being a common end metabolic product, it is easily metabolised and passes the body without causing any problems. The fact that it dissolves easily in both blood and tissues and poses little danger of gas embolism are two advantages.

Patients experiencing long-term procedures or those with previous cardiac problems are at increased risk of carbon dioxide inducing cardiac arrhythmias, hypercarbia, tachycardia, and acidosis.

Carbon dioxide is ideal in every way: it is cheap, readily available, and produced. Because it is not combustible, medical personnel are not endangered in the event of a leak. Not only is it fragrance-free, but it also does not irritate the skin.

Because of its widespread use and the reasons mentioned above, carbon dioxide is currently considered the "gas of choice" for inducing pneumoperitoneum.

Laparoscopic instruments

The surgeon's knowledge of instrumentation and ability to "trouble shoot" certainly help to allay anxiety and contribute to optimal patient care.

Operating room setup

The operating room setup includes equipment which properly positions the patient. Operative laparoscopic and video equipment and well-coordinated assistant and nursing team are all required.

Anasthesiologist should be well versed with the potential problems and complications of laparoscopy.

Essential equipments

1. Optic Equipments
    - Laparoscope 5mm, 10mm – 100, 300
    - Computed chip video camera
    - Light source
    - Video monitors and video recorder
2. Abdomen Access Equipments
    - Veress needle
    - Hasson cannula
    - Gas cylinder (C02)
    - Trocar and cannulas
    - Insufflators

3. Laparoscopic Instruments

    - Atraumatic grasping forceps
    - Bipolar coagulation forceps
    - Dissecting forceps – Maryland
    - Scissors
    - Clip applicators
    - Staplers
    - Endo pouches (or) Sacs
    - Sutures and needles
    - Needle holder
    - Suction and irrigation system

Surgical procedure

Laser and electrocautery (monopolar or bipolar) are the two modalities utilised for hemostasis and coagulation. To prevent thermal damage, it is essential to have a clear view of the entire instrument tip at all times.

Among the several benefits of laparoscopic cholecystectomy is a significantly shorter hospital stay and lower overall cost. The same steps as an open cholecystectomy are taken to prepare the patient, induce anaesthesia, and sterilely drape them.

An orogastric tube is commonly used to decompress the stomach and assist in exposing the upper abdomen, while the use of a urinary catheter is context dependent.

The choice between an open or closed approach for accessing the peritoneal cavity and creating a pneumoperitoneum is up to the surgeon's expertise and personal preference. Making a little incision at the umbilicus, slicing through the abdominal wall fascia, immediately incising the peritoneum, and inserting a blunt trocar, called a Hasson cannula, are all steps in the open approach.

One alternative is the closed approach, which involves making an incision and then inserting a needle into the peritoneal cavity to insufflate the abdomen before trocars are placed. After a CO2 pneumoperitoneum has been set up, a quick exploration is carried out and three more 5-mm ports are inserted into the right midclavicular line, subxiphoid site, and right anterior axillary line.

The gallbladder fundus is lifted towards the right shoulder via the lateral port located at the anterior axillary line. The infundibulum and porta hepatis are exposed by this retract. To access the gallbladder infundibulum, the midclavicular trocar is inserted and withdrawn inferolaterally to expose the triangle of Calot. The cystic duct is disoriented from its almost parallel alignment with the common hepatic duct due to the lateral distraction of Hartmann's pouch.

To reach the gallbladder's base, the dissection must be performed along the infundibulum's anterior and posterior surfaces. Ultimately, the triangle of Calot will be cleared of all fibrofatty tissue by this dissection.

The infundibulum can be inferolaterally tractioned to reveal the cystic duct and cystic artery, two processes that enter the gallbladder. The overlaying lymph node, called Calot's node, is a helpful landmark for the cystic artery.

In order to reduce the possibility of unintentional iatrogenic bile duct injury, a crucial view of safety is maintained, which involves seeing the liver bed through the space above the cystic artery and through the cystic duct.

After enough tissue removal, clips are attached to the cystic duct and artery. When a cholangiography is carried out, the cystic duct is not transected but rather incised and snipped next to the gallbladder.

The next step is to insert a cholangiographic catheter into the cystic duct and biliary tree to take fluoroscopic pictures". This is done after the duct has been incised.

After a normal cholangiogram or in the absence of cholangiography, the cystic duct is transected after being twice clipped on the common duct side.

In addition to transsecting the previously severed artery, electrocautery is used to separate the gallbladder from the liver bed. Thorough hemostasis is required during this dissection since the gallbladder's veins drain straight into the liver bed via venules.

Having exposed the porta and triangle of Calot, the cystic duct and cystic artery clips are examined right before the fundic attachments are dissected, thanks to the superior traction of the fundus. After that, the gallbladder is removed from the body via the umbilical port. When dealing with acute cholecystitis or if the gallbladder was exposed during dissection, it is recommended to use a plastic bag for retrieval.

THE PHYSIOLOGIC EFFECTS OF PNEUMOPERITONEUM

We only have a partial understanding of the numerous repercussions of the pneumoperitoneum. Both the internal abdominal pressure and the chemical make-up of the gas, most commonly carbon dioxide, contribute to the side effects.

Particularly in individuals with low blood volume, the intra-abdominal veins collapse due to the intra-abdominal pressure of pneumoperitoneum, which reduces venous return. Cardiac output may fall as a result of reduced venous return. Myocardial oxygen demand rises as a result of a compensatory rise in heart rate. Laparoscopic procedures aren't always safe for high-risk cardiovascular patients, and they might not even be able to handle the demand. The elevated intra-abdominal pressure in healthy individuals with full intra-abdominal capacitance veins and an expanded volume may work as a pump to raise the pressure at the right atrial filling valve.

The increase in heart rate and systemic vascular resistance is caused by a separate process related to catecholamine release, which is induced by CO2 pneumoperitoneum. Impaired visceral blood flow and hypertension could result from this. An increase in both heart rate and mean arterial pressure following pneumoperitoneum induction is typical. Nevertheless, hypotension, end-organ hypoperfusion, and ST-segment alterations can result from the pressure on the heart in elderly, impaired patients.

Patients must be adequately hydrated before surgery in order to reduce the cardiovascular effects of pneumoperitoneum. One way to prevent vagal-mediated bradycardia is to gradually insufflate the belly, which reduces the vagal reaction to peritoneal stretching. In addition, the insufflation pressures should be reduced from the customary 15 to 12 mmHg or pneumoperitoneum should be evacuated while the anesthesiologist sorts out the cardiovascular changes if cardiovascular effects are noticed during insufflation or during pneumoperitoneum maintenance. One way to improve venous return is to remove patients from the steep reverse Trendelenburg posture. The effects of desufflation may not always wear off immediately.

Diaphragmatic excursion is decreased due to the restricted mobility of the diaphragm caused by the higher intra-abdominal pressures. The results show an increase in inspiratory pressure and a decrease in functional residual capacity and pulmonary compliance. In people who do not have cardiovascular problems, the physiologic dead space and shunt do not vary significantly. There was a 50% rise in peak airway pressure and an 81% increase in plateau airway pressure following pneumoperitoneum induction. During the time when intra-abdominal pressure was elevated, bronchopulmonary compliance fell 47%. The peak pressure stayed 36% higher and the plateau pressure 27% higher for 2 AND 6 hours following desufflation. At 86% of the value before insufflation, compliance stayed.

Because of the cardiovascular consequences of pneumoperitoneum and direct pressure on the renal veins, urine production is typically decreased during laparoscopic surgeries. Oliguria, which may persist for up to an hour following the pneumoperitoneum's release, is one of the primary effects of high intraabdominal pressure, which also triggers the pituitary gland to secrete antidiuretic hormone (ADH). Urine production is increased after aggressive fluid hydration during pneumoperitoneum. It is important to evaluate positional changes when anuria is reported, as they can impact urine collection with the Foley catheter.

CARBON DIOXIDE RELATED EFFECTS

HYPERCAPNIA

Pneumoperitoneum causes acidosis and hypercapnia, which are symptoms of carbon dioxide being absorbed from the peritoneal cavity. To account for these changes, the ventilated patient's respiratory rate or vital capacity must be increased. When respiratory rates are high, there is less time for gas mixing, which means more deadspace ventilation, and when tidal volumes are high, barotraumas are possible. It takes around 30 minutes after the pneumoperitoneum is introduced for PaCO2 to reach its first steady state. After this time, rising PaCO2 levels indicate that the body's buffers, of which bone makes up more than 90%, are depleted. The slipping of the port and the diffusion of carbon dioxide either extraperitoneally or subcutaneously might be the causes of sudden spikes. After the port is moved, the problem will go away on its own.

Patients with pulmonary insufficiency, those undergoing lengthy surgeries, and the elderly are at increased risk of developing difficult-to-control hypercapnia and acidosis. Desufflation of the abdomen for ten to fifteen minutes is our reaction to this. If repeated episodes of hypercapnia occur after reinsufflation, we will either switch insufflation gases or switch to an open operation. Even after desufflation, acidosis may linger for a few more hours. Carbon monoxide embolism and capnothorax are two less common but potentially fatal consequences of pneumoperitoneum.

CARBON DIOXIDE EMBOLUS

Even though CO2 embolisms are extremely rare, newer studies employing more sensitive diagnostics have shown that small gas bubbles are frequently seen in the right side of the heart during laparoscopic surgeries. Unexplained drops in blood pressure and oxygen levels during surgery might be signs of a clinically significant CO2 embolism. Auscultation of the chest can reveal the presence of a distinctive millwheel murmur. Stroking the blood-gas contact causes the right ventricle to constrict, resulting in this.

The anesthesiologist typically observes a steep drop in end-tidal CO2, which is in line with the presence of a totally blocked right ventricle outflow. Prompt drainage of the pneumoperitoneum and positioning the patient in the left lateral decubitus posture with their head down (Durant) are the cornerstones of treatment. The CO2 bubble can then "float" to the top of the right ventricle, where it poses less of a threat of blocking the outflow route to the right ventricle.

Hyperventilating and administering 100% oxygen to the patient is crucial during this time. Also, a central venous line can be used to aspirate gas.

CAPNOTHORAX/PNEUMOTHORAX

Carbon dioxide can escape into the chest through a diaphragmatic defect or by tracking through fascial planes during esophageal hiatus dissection, both of which can lead to capnothorax. The most typical cause is the right side opening of the pleuroperitoneal ducts, however it can also occur on the left side. Pneumothorax can be caused by pleural rips during fundoplication or by the usual culprits, such as burst bullae.

A decrease in O_2 saturation (due to shunting caused by lung collapse), an increase in airway pressure, a decrease in pulmonary compliance, and a rise in carbon dioxide and end-tidal CO_2 are typical effects of carbon dioxide gas in the chest.

The treatment consists of reducing intra-abdominal pressure to an absolute minimum, correcting hypoxemia with ventilator adjustments, applying positive end-expiratory pressure (PEEP) if feasible, and desufflate the belly.

Since this typically goes away with anaesthetic control, thoracentesis is not recommended.

Typically, a red rubber catheter is inserted across the diaphragm (via the pleural defect) and a trocar site is brought out to remove the capnothorax right at the end of the treatment. Once the lung is inflated, the external end of the catheter is submerged in water and retrieved as soon as the bubbles stop. In the event that 2 L/min of O_2 flow does not reveal hypoxia, we refrain from taking chest radiographs in the recovery room following these procedures. To aid in the absorption of carbon dioxide from the pleural space, patients should be maintained on supplemental oxygen.

Although, various studies on laparoscopic cholecystectomy are available, the frequency and duration of postoperative pneumoperitoneum are not well established. Moreover, the observation of hemodynamic and metabolic impairment related to CO_2 pneumoperitoneum and postoperative mesenteric ischemia reports following laparoscopic procedures have raised concern about local and systemic effects of increased intra-abdominal pressure during laparoscopic procedure.

MATERIALS AND METHODS

Source of Data: [Dr Prabhakar Kore charitable hospital, Belagavi, Karnataka, 590010]

Study Design: Observational study

Study Period: Currently study will be carried out for 1 year from September 1st 2022 to 31st August 2023

F tests - ANOVA: Repeated measures, between factors

Analysis:	A priori: Compute required sample size		
Input:	Effect size f	=	0.5500000
	α err prob	=	0.05
	Power (1-β err prob)	=	0.95
	Number of groups	=	2
	Number of measurements	=	3
	Corr among rep measures	=	0.5
Output:	Noncentrality parameter λ	=	14.5200000
	Critical F	=	4.1708768
	Numerator df	=	1.0000000
	Denominator df	=	30.0000000
	Total sample size	=	32
	Actual power	=	0.9578225

Sampling technique: All patients admitted in Dr KLE PRABHAKAR KORE HOSPITAL undergoing laparoscopic cholecystectomy can be considered as study subjects for research

Inclusion Criteria:

1. Patients willing to participate
2. 18 to 60 years of age
3. Cholelithiasis patients undergoing laparoscopic cholecystectomy

Exclusion Criteria:

1. Chronic liver disease
2. Laparoscopic converted to open surgeries
3. Pregnancy
4. Frozen abdomen
5. Coagulopathy

STUDY PROTOCOL:-

Data collection procedure: Patients admitted for elective laparoscopic cholecystectomy will undergo routine pre-operative investigations including CBC, LFT, MR, and coagulation profile. Post-operatively, LFT will be conducted on the 1st, 2nd, and 7th day. A comparison of pre-operative and post-operative LFT results will be performed. Data was collected and stored in MS Excel. Statistical analysis have been conducted using R and MS Excel.

STATISTICAL ANALYSIS

The Raw data was collected and entered into MS Excel. Editing and preparation of data was performed for further analysis.

Descriptive statistics was performed by using the proportional or frequency distribution of the parameters. The frequency distribution for both qualitative data and categories of quantitative data was presented in form of tables along with graphical presentation of data.

Inferential Statistical Methods Used:

1. Paired t test was applied to determine the significance of mean difference between pre and different post duration values.

   The P Value < 0.05 will be considered as level of significance.

Microsoft Excel and R Studio (Open source analytical tool V 1.2.335) was used to collect the data, perform the basic calculation, statistical analysis and presentation of results.

RESULTS AND INTERPRETATION

Table 1: Distribution of Study Population on the basis of Age Group

Age Group	Frequency	Percent
20-30 Years	4	12.5
30-40 Years	6	18.75
40-50 Years	9	28.125
50-60 Years	4	12.5
60-70 Years	3	9.375
70-80 Years	6	18.75
Total	32	100

Table 1 show the cases according to Age Group, where maximum subjects were found in 40-50yrs i.e. 28.125% followed by 30-40yrs & 70-80yrs (18.75%), 20-30yrs & 50-60yrs (12.5%) and 60-70yrs (9.375%).

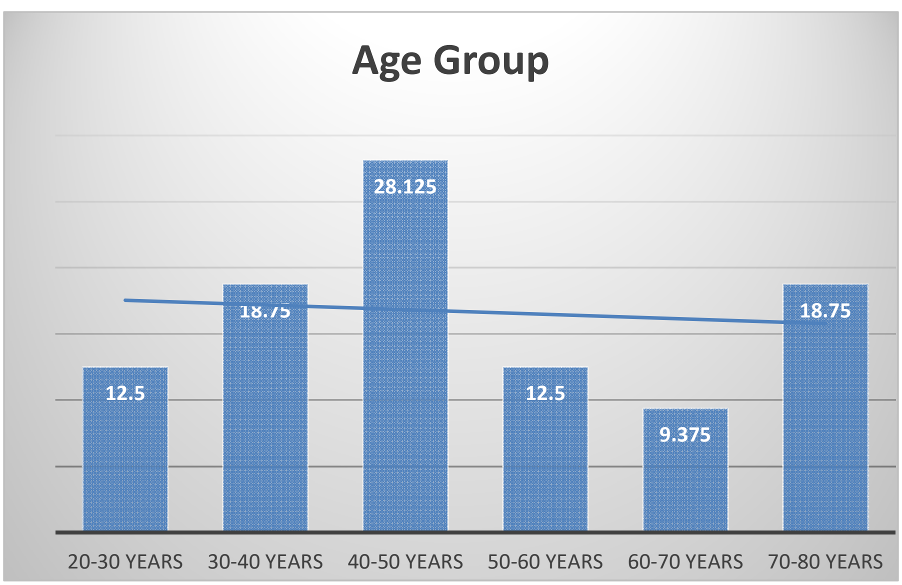


Table 2: Distribution of Study Population on the basis of Sex Group

SEX	Frequency	Percent
F	13	40.625
M	19	59.375
Total	32	100

Table 2 show the cases according to Sex Group, where a maximum number of subjects were Males i.e. 59.375% and Females were less in number approximately 40.625%.

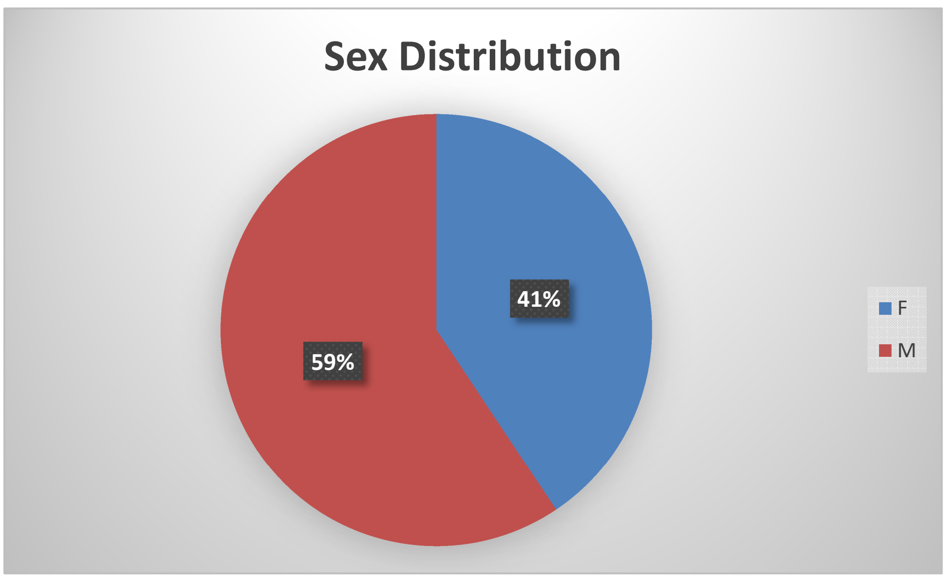


Table 3: Distribution of Study Population on the basis of Diagnosis

DIAGNOSIS	Frequency	Percent
CALCULOUS CHOLECYSTITIS	8	25
CHOLELITHIASIS	24	75
Total	32	100

Table 3 show the cases according to Diagnosis, where a maximum number of subjects were Cholelithiasis i.e. 75.0% and Calculous Cholecystitis were less in number approximately 25.0%.

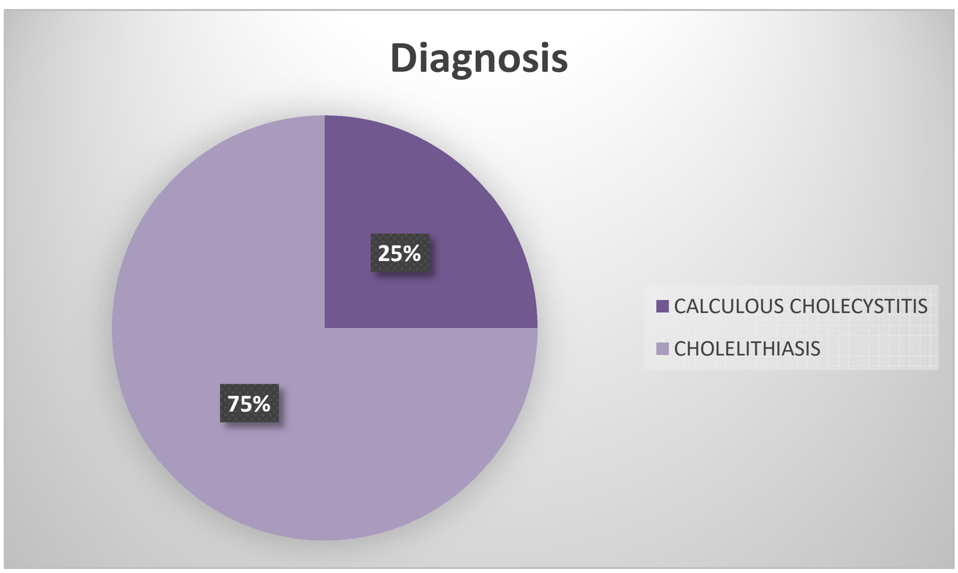


Table 4: Comparison of Mean Total Bilirubin between Pre and Post Durations

Pre-post Pair	N	Mean TB	Std. Deviation	Paired T Test	P Value	Result
PRE-OP	32	0.820	0.998	1.923	0.064	Non-sig
POD 1	32	0.717	0.775			
PRE-OP	32	0.820	0.998	1.716	0.096	Non-sig
POD 2	32	0.682	0.611			
PRE-OP	32	0.820	0.998	1.511	0.141	Non-sig
POD 7	32	0.622	0.390			

The above table shows the Pre-post comparison of Mean TB value between two different durations.

Paired t test for comparing the mean difference between two different durations was applied, which shows that there was no significant difference in the mean TB value for all the pre-post durations.

In the case of Pre-POD 1 the mean value 0.717 at Post operative Day 1 was non-significantly lower than the mean value 0.820 at pre duration.

In the case of Pre-POD 2 the mean value 0.682 at Post operative Day 2 was non-significantly lower than the mean value 0.820 at pre duration.

In the case of Pre-POD 7 the mean value 0.622 at Post operative Day 7 was non-significantly lower than the mean value 0.820 at pre duration.

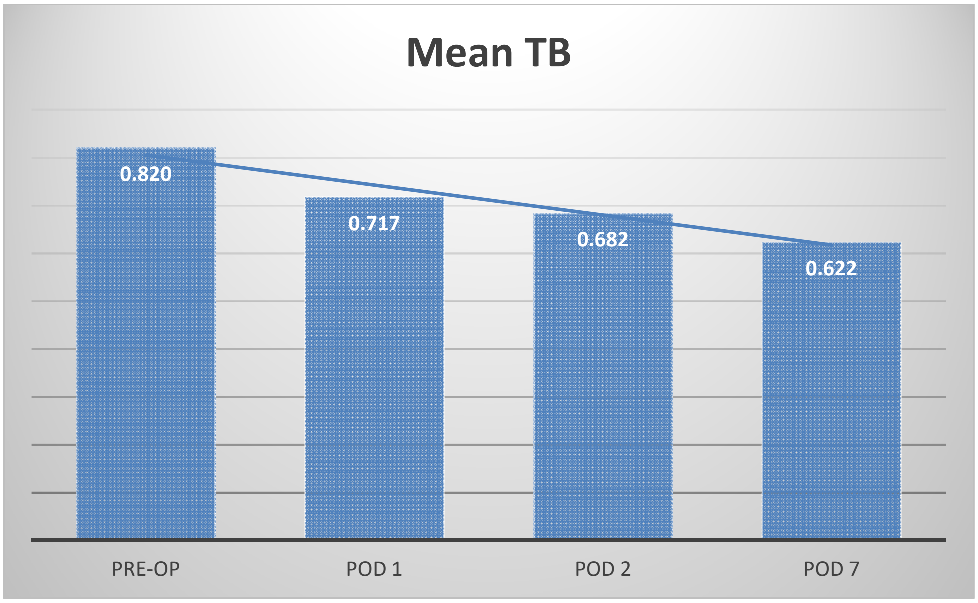


Table 5: Comparison of Mean DIRECT BILIRUBIN Between Pre and Post Durations

Pre-post Pair	N	Mean DB	Std. Deviation	Paired T Test	P Value	Result
PRE-OP	32	0.463	0.683	0.914	0.368	Non-sig
POD 1	32	0.420	0.490			
PRE-OP	32	0.463	0.683	1.253	0.220	Non-sig
POD 2	32	0.393	0.440			
PRE-OP	32	0.463	0.683	0.623	0.538	Non-sig
POD 7	32	0.407	0.311			

The above table shows the Pre-post comparison of Mean DB value between two different durations.

Paired t test for comparing the mean difference between two different durations was applied, which shows that there was no significant difference in the mean DB value for all the pre-post durations.

In the case of Pre-POD 1 the mean value 0.420 at Post operative Day 1 was non-significantly lower than the mean value 0.463 at pre duration.

In the case of Pre-POD 2 the mean value 0.393 at Post operative Day 2 was non-significantly lower than the mean value 0.463 at pre duration.

In the case of Pre-POD 7 the mean value 0.407 at Post operative Day 7 was non-significantly lower than the mean value 0.463 at pre duration.

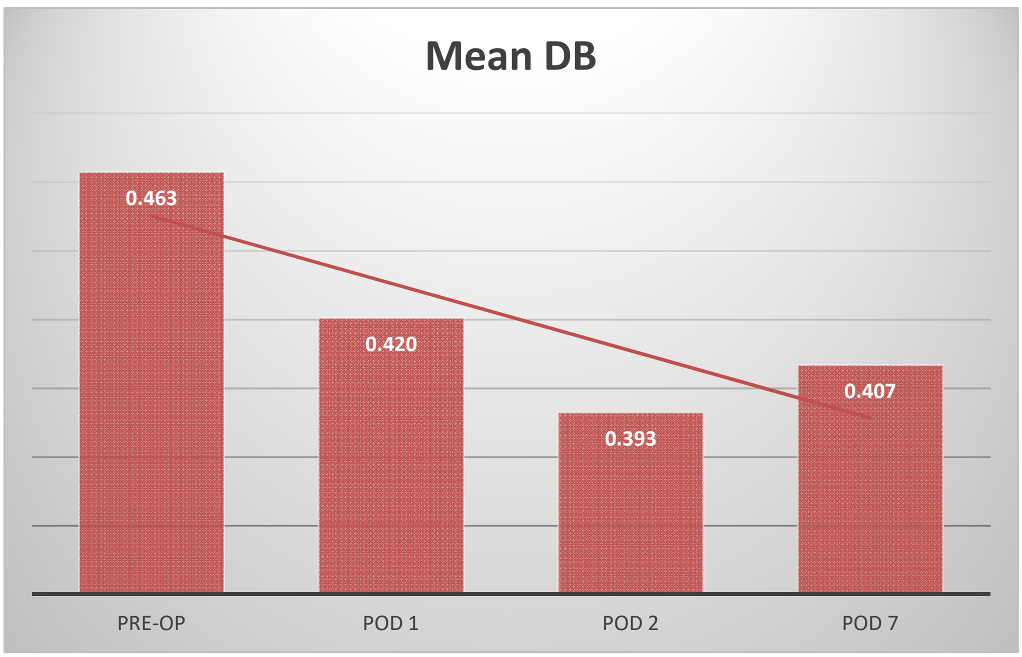


Table 6: Comparison of Mean Indirect Bilirubin Between Pre and Post Durations

Pre-post Pair	N	Mean IDB	Std. Deviation	Paired T Test	P Value	Result
PRE-OP	32	0.416	0.355	1.390	0.175	Non-sig
POD 1	32	0.385	0.323			
PRE-OP	32	0.416	0.355	1.110	0.275	Non-sig
POD 2	32	0.373	0.218			
PRE-OP	32	0.416	0.355	1.076	0.290	Non-sig
POD 7	32	0.353	0.210			

The above table shows the Pre-post comparison of Mean IDB value between two different durations.

Paired t test for comparing the mean difference between two different durations was applied, which shows that there was no significant difference in the mean IDB value for all the pre-post durations.

In the case of Pre-POD 1 the mean value 0.385 at Post operative Day 1 was non-significantly lower than the mean value 0.416 at pre duration.

In the case of Pre-POD 2 the mean value 0.373 at Post operative Day 2 was non-significantly lower than the mean value 0.416 at pre duration.

In the case of Pre-POD 7 the mean value 0.353 at Post operative Day 7 was non-significantly lower than the mean value 0.416 at pre duration.

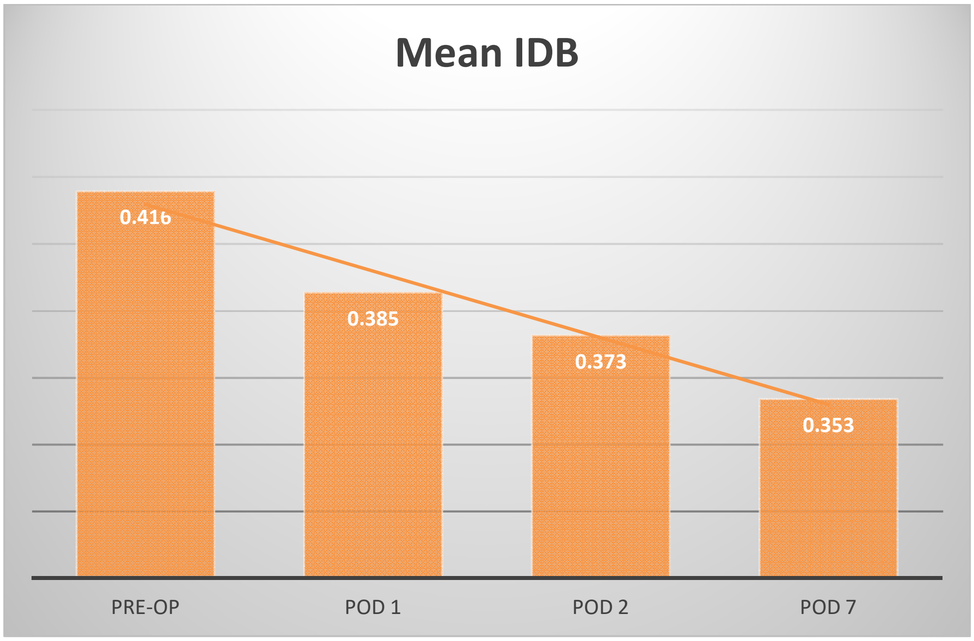


Table 7: Comparison of Mean Total Protiens Between Pre and Post Durations

Pre-post Pair	N	Mean TP	Std. Deviation	Paired T Test	P Value	Result
PRE-OP	32	6.727	1.507	1.034	0.309	Non-sig
POD 1	32	6.372	1.553			
PRE-OP	32	6.727	1.507	1.065	0.295	Non-sig
POD 2	32	6.469	1.080			
PRE-OP	32	6.727	1.507	1.887	0.069	Non-sig
POD 7	32	6.209	1.198			

The above table shows the Pre-post comparison of Mean TP value between two different durations.

Paired t test for comparing the mean difference between two different durations was applied, which shows that there was no significant difference in the mean TP value for all the pre-post durations.

In the case of Pre-POD 1 the mean value 6.372 at Post operative Day 1 was non-significantly lower than the mean value 6.727 at pre duration.

In the case of Pre-POD 2 the mean value 6.469 at Post operative Day 2 was non-significantly lower than the mean value 6.727 at pre duration.

In the case of Pre-POD 7 the mean value 6.209 at Post operative Day 7 was non-significantly lower than the mean value 6.727 at pre duration.

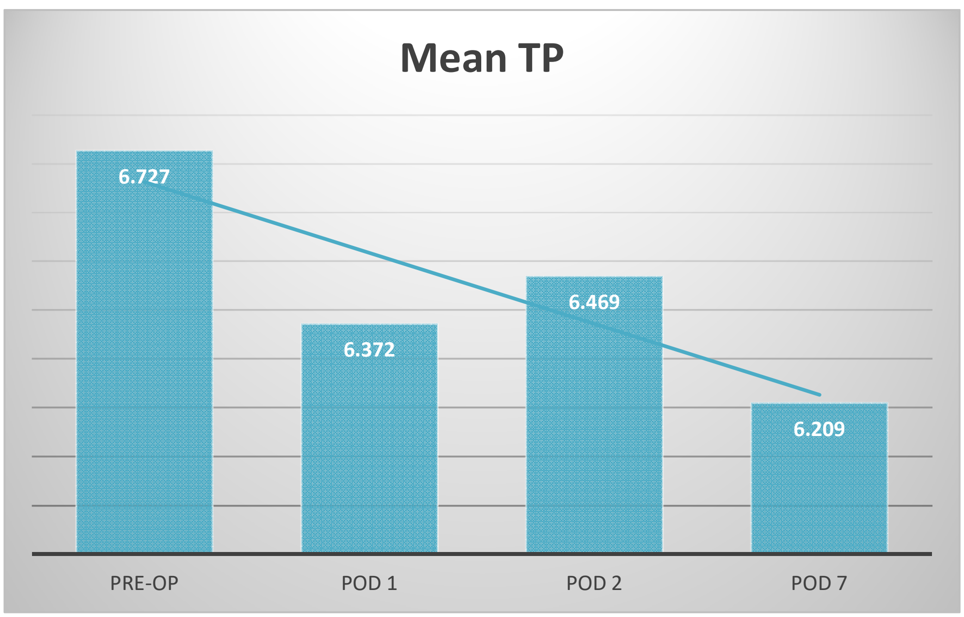


Table 8: Comparison of Mean ALBUMIN Between Pre and Post Durations

Pre-post Pair	N	Mean AB	Std. Deviation	Paired T Test	P Value	Result
PRE-OP	32	3.828	0.752	5.267	0.000	Sig
POD 1	32	3.547	0.720			
PRE-OP	32	3.828	0.752	6.513	0.000	Sig
POD 2	32	3.397	0.704			
PRE-OP	32	3.828	0.752	6.968	0.000	Sig
POD 7	32	3.203	0.622			

The above table shows the Pre-post comparison of Mean AB value between two different durations.

Paired t test for comparing the mean difference between two different durations was applied, which shows that there was significant difference in the mean AB value for all the pre-post durations.

In the case of Pre-POD 1 the mean value 3.547 at Post operative Day 1 was significantly lower than the mean value 3.828 at pre duration.

In the case of Pre-POD 2 the mean value 3.397 at Post operative Day 2 was significantly lower than the mean value 3.828 at pre duration.

In the case of Pre-POD 7 the mean value 3.203 at Post operative Day 7 was significantly lower than the mean value 3.828 at pre duration.

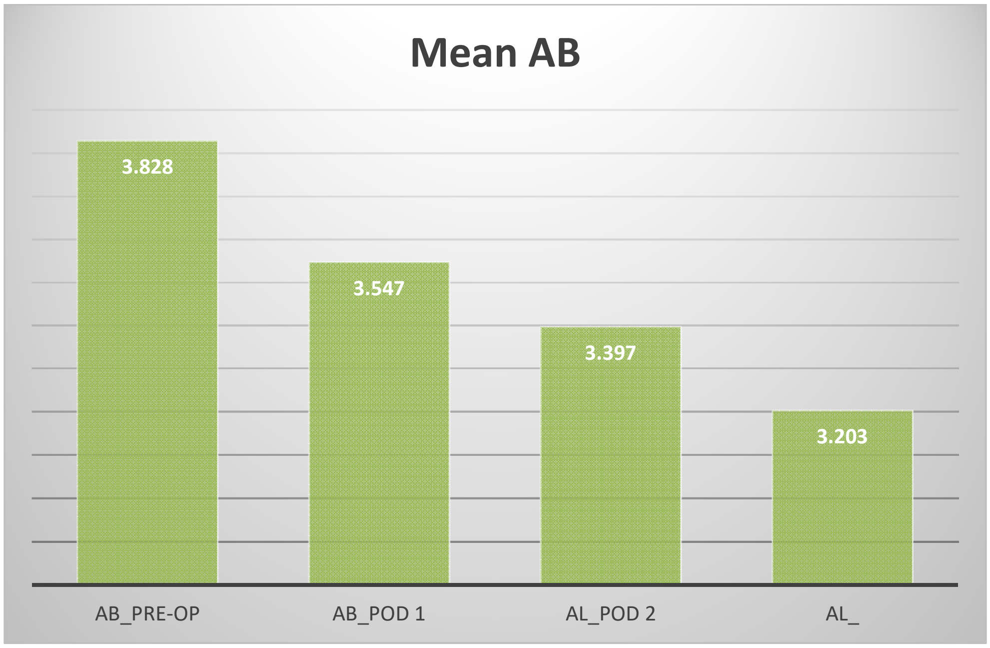


Table 9: Comparison of Mean GLOBULIN Between Pre and Post Durations

Pre-post Pair	N	Mean GL	Std. Deviation	Paired T Test	P Value	Result
PRE-OP	32	2.934	0.589	3.122	0.004	Sig
POD 1	32	2.740	0.678			
PRE-OP	32	2.934	0.589	3.651	0.001	Sig
POD 2	32	2.679	0.685			
PRE-OP	32	2.934	0.589	2.741	0.010	Sig
POD 7	32	2.708	0.673			

The above table shows the Pre-post comparison of Mean GL value between two different durations.

Paired t test for comparing the mean difference between two different durations was applied, which shows that there was significant difference in the mean GL value for all the pre-post durations.

In the case of Pre-POD 1 the mean value 2.740 at Post operative Day 1 was significantly lower than the mean value 2.934 at pre duration.

In the case of Pre-POD 2 the mean value 2.679 at Post operative Day 2 was significantly lower than the mean value 2.934 at pre duration.

In the case of Pre-POD 7 the mean value 2.708 at Post operative Day 7 was significantly lower than the mean value 2.934 at pre duration.

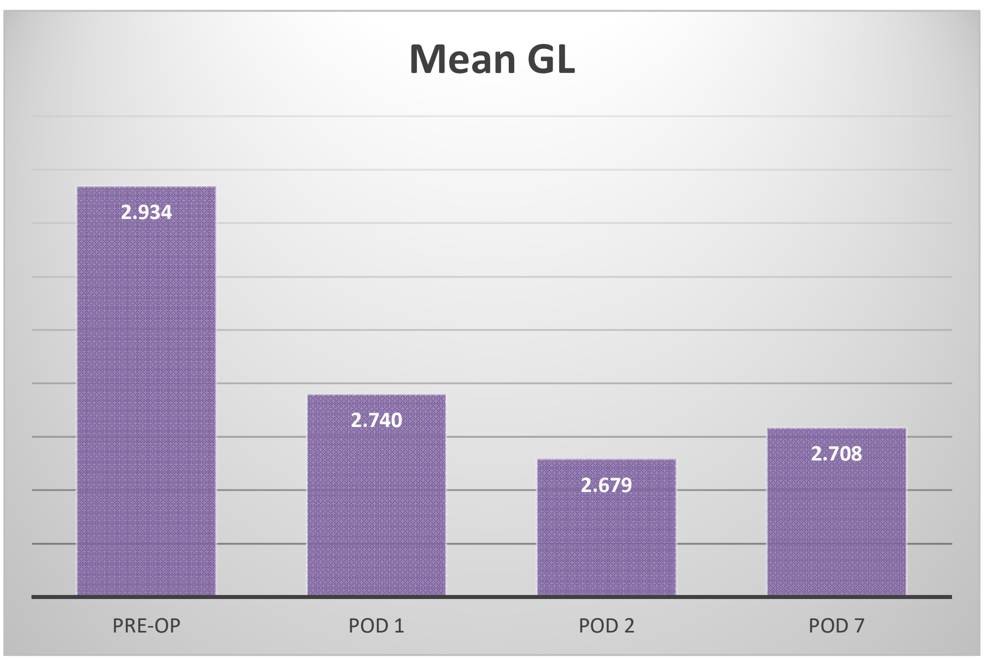


Table 10: Comparison of Mean ALBUMIN GLOBULIN RATIO Between Pre and Post Durations

Pre-post Pair	N	Mean AGR	Std. Deviation	Paired T Test	P Value	Result
PRE-OP	32	1.313	0.445	2.025	0.052	Non-sig
POD 1	32	1.227	0.372			
PRE-OP	32	1.313	0.445	2.663	0.012	Sig
POD 2	32	1.151	0.255			
PRE-OP	32	1.313	0.445	3.292	0.002	Sig
POD 7	32	1.107	0.271			

The above table shows the Pre-post comparison of Mean AGR value between two different durations.

Paired t test for comparing the mean difference between two different durations was applied, which shows that there was significant & non-significant difference in the mean AGR value for all the pre-post durations.

In the case of Pre-POD 1 the mean value 1.227 at Post operative Day 1 was non-significantly lower than the mean value 1.313 at pre duration.

In the case of Pre-POD 2 the mean value 1.151 at Post operative Day 2 was significantly lower than the mean value 1.313 at pre duration.

In the case of Pre-POD 7 the mean value 1.107 at Post operative Day 7 was significantly lower than the mean value 1.313 at pre duration.

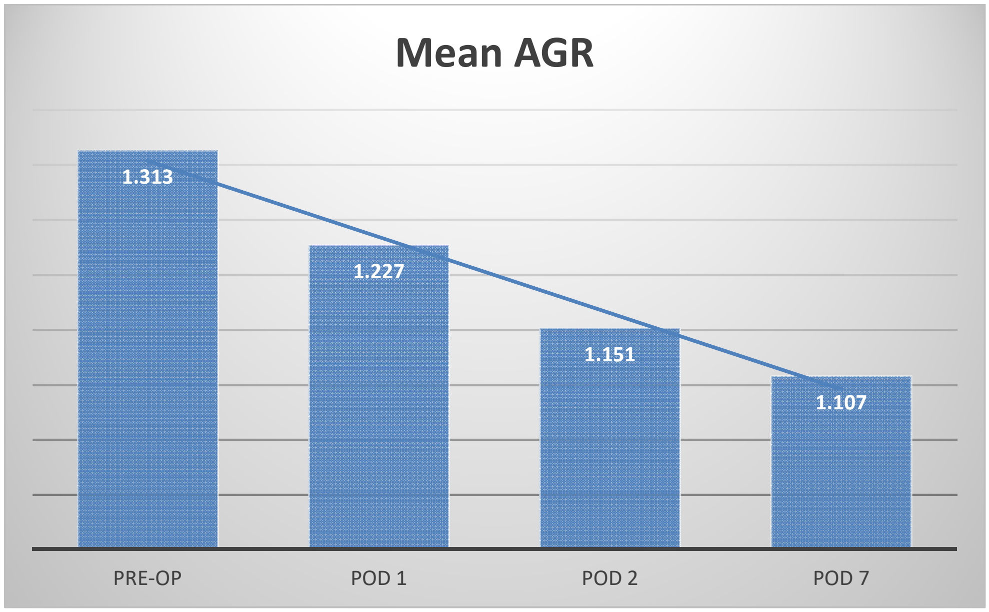


Table 11: Comparison of Mean ALT Between Pre and Post Durations

Pre-post Pair	N	Mean ALT	Std. Deviation	Paired T Test	P Value	Result
PRE-OP	32	24.219	18.316	-0.030	0.976	Non-sig
POD 1	32	24.281	16.336			
PRE-OP	32	24.219	18.316	1.214	0.234	Non-sig
POD 2	32	22.031	11.096			
PRE-OP	32	24.219	18.316	-0.202	0.841	Non-sig
POD 7	32	25.063	17.852			

The above table shows the Pre-post comparison of Mean ALT value between two different durations.

Paired t test for comparing the mean difference between two different durations was applied, which shows that there was no significant difference in the mean ALT value for all the pre-post durations.

In the case of Pre-POD 1 the mean value 24.281 at Post operative Day 1 was non-significantly higher than the mean value 24.219 at pre duration.

In the case of Pre-POD 2 the mean value 22.031 at Post operative Day 2 was non-significantly lower than the mean value 24.219 at pre duration.

In the case of Pre-POD 7 the mean value 25.063 at Post operative Day 7 was non-significantly higher than the mean value 24.219 at pre duration.

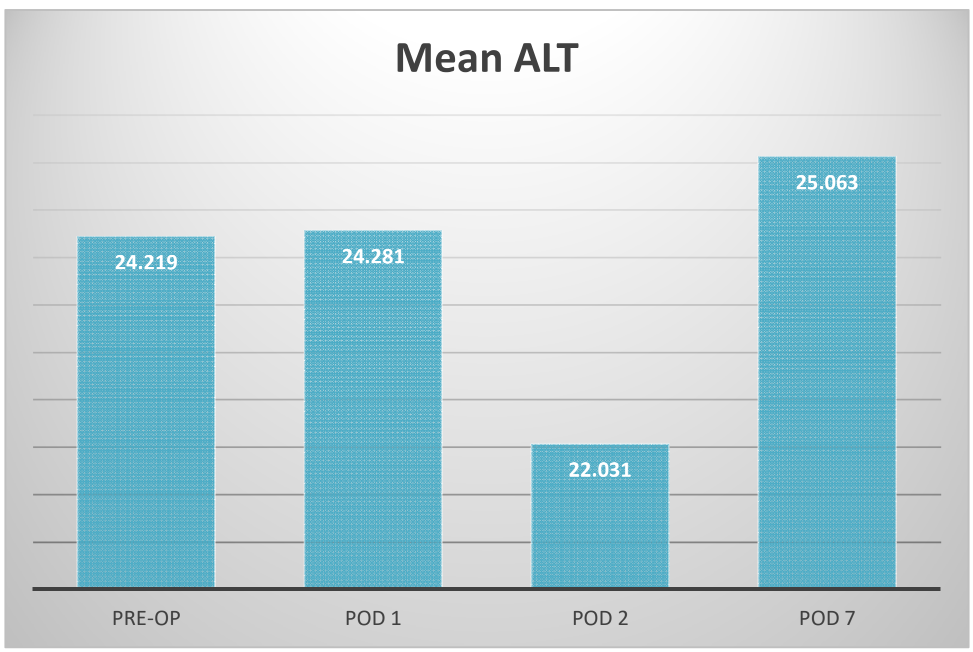


Table 12: Comparison of Mean AST Between Pre and Post Durations

Pre-post Pair	N	Mean AST	Std. Deviation	Paired T Test	P Value	Result
PRE-OP	32	25.313	12.249	-0.604	0.550	Non-sig
POD 1	32	26.813	14.781			
PRE-OP	32	25.313	12.249	0.813	0.423	Non-sig
POD 2	32	23.609	9.528			
PRE-OP	32	25.313	12.249	-0.628	0.534	Non-sig
POD 7	32	27.281	14.333			

The above table shows the Pre-post comparison of Mean AST value between two different durations.

Paired t test for comparing the mean difference between two different durations was applied, which shows that there was no significant difference in the mean AST value for all the pre-post durations.

In the case of Pre-POD 1 the mean value 26.813 at Post operative Day 1 was non-significantly higher than the mean value 25.313 at pre duration.

In the case of Pre-POD 2 the mean value 23.609 at Post operative Day 2 was non-significantly lower than the mean value 25.313 at pre duration.

In the case of Pre-POD 7 the mean value 27.281 at Post operative Day 7 was non-significantly higher than the mean value 25.313 at pre duration.

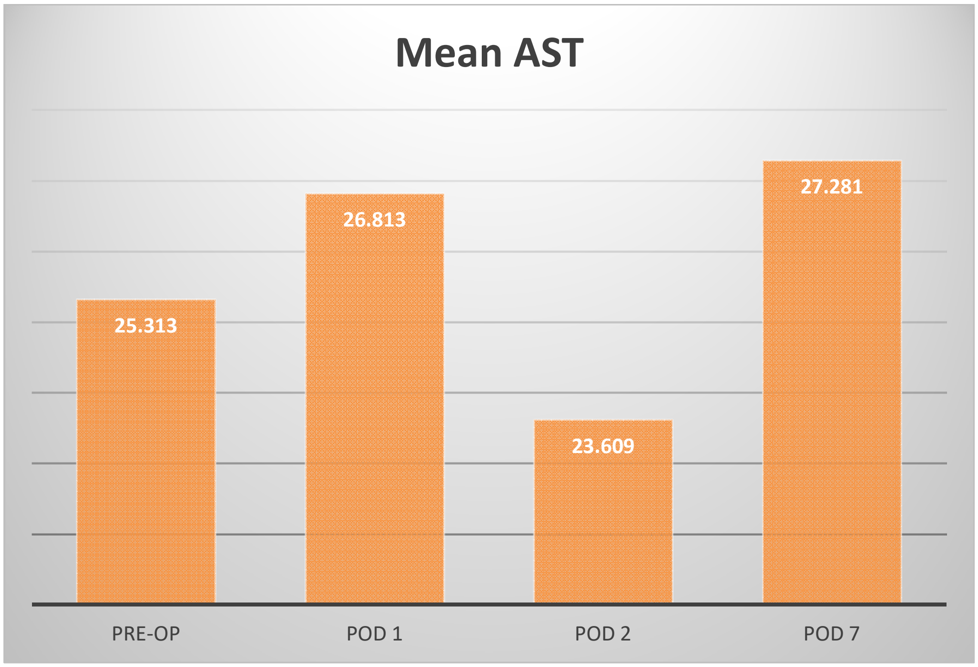


Table 13: Comparison of Mean ALP Between Pre and Post Durations

Pre-post Pair	N	Mean ALP	Std. Deviation	Paired T Test	P Value	Result
PRE-OP	32	120.094	70.573	1.284	0.209	Non-sig
POD 1	32	111.375	53.935			
PRE-OP	32	120.094	70.573	1.970	0.058	Non-sig
POD 2	32	104.906	42.743			
PRE-OP	32	120.094	70.573	2.678	0.012	Sig
POD 7	32	94.656	32.332			

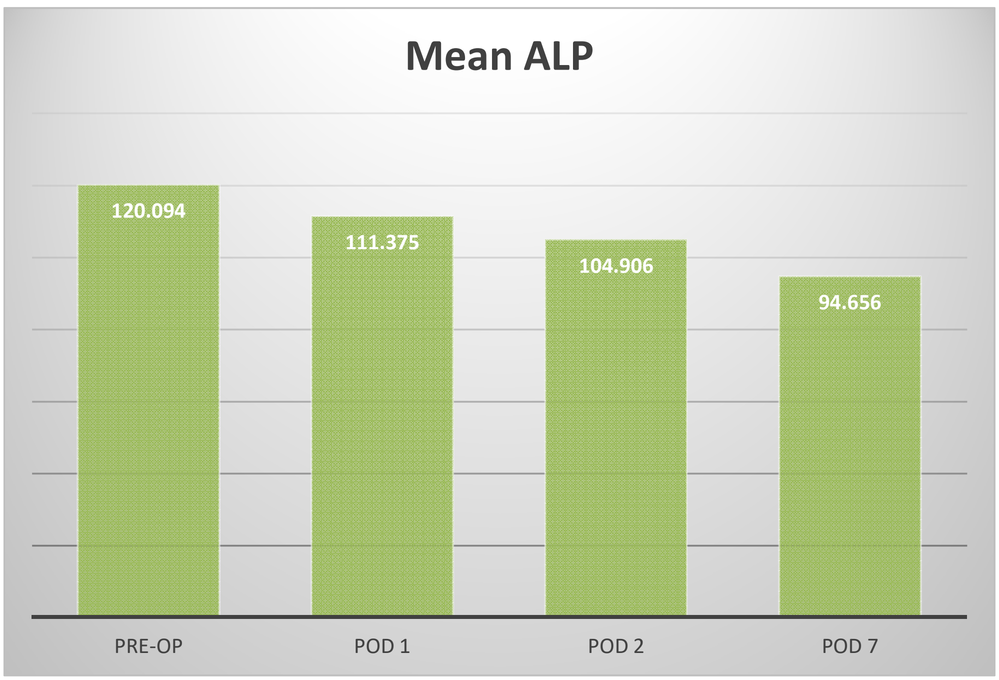
The above table shows the Pre-post comparison of Mean ALP value between two different durations.

Paired t test for comparing the mean difference between two different durations was applied, which shows that there was non-significant & significant difference in the mean ALP value for all the pre-post durations.

In the case of Pre-POD 1 the mean value 111.375 at Post operative Day 1 was non-significantly lower than the mean value 120.094 at pre duration.

In the case of Pre-POD 2 the mean value 104.906 at Post operative Day 2 was non-significantly lower than the mean value 120.094 at pre duration.

In the case of Pre-POD 7 the mean value 94.656 at Post operative Day 7 was significantly lower than the mean value 120.094 at pre duration.



DISCUSSION

- The study population is divided into six age groups, with the largest group being 40-50 years old. This age group makes up 28.125% of the total population. The other age groups include 30-40 years, 70-80 years, 20-30 years, 50-60 years, 60-70 years, and 70-80 years. The total number of subjects is 32. The age distribution is relatively even, with a peak in the 40-50 years age group. Understanding this distribution is crucial for research, as it can significantly influence outcomes and variables. Comparative analysis could reveal trends or patterns. However, additional demographic factors like gender or socio-economic status could provide further insights.
- Table 2 presents the study population distribution based on sex groups, with males accounting for 59.375% of the total population and females accounting for 40.625%. The total number of subjects is 32. The sex ratio indicates a higher proportion of males (59.375%) compared to females (40.625%). Understanding the sex distribution is crucial for analyzing gender-related implications and considering potential biases. Comparing this distribution with the age distribution could provide insights into demographic factors intersecting in the study population.
- Table 3 shows the study population's distribution based on different diagnoses. It reveals that Cholelithiasis is the most prevalent diagnosis, accounting for 75.0% of the total population. The total number of subjects is 32. The table highlights the clinical relevance of understanding the distribution of diagnoses, implications for research, and the need to analyze how age, sex, or other demographic factors correlate with these diagnoses.

- Table 4 compares mean total bilirubin (TB) levels between pre-operative and post-operative periods. The results show no significant difference in TB levels between the two periods. However, there is a consistent trend of lower TB levels in the post-operative periods compared to the pre-operative baseline. This trend is observed across all three post-operative time points. Monitoring TB levels is crucial post-operatively, as the slight decrease in TB levels could indicate that the surgical procedure or recovery process might impact liver function or bilirubin metabolism. The study's findings suggest that while there may be some changes post-operatively, these changes are not large enough to reach statistical significance with the given sample size. Future studies with larger sample sizes or different patient populations could potentially detect smaller, clinically relevant changes.
- Table 5 compares mean direct bilirubin (DB) values between pre-operative (PRE-OP) and post-operative days (POD 1, POD 2, and POD 7). The data shows no statistically significant differences in DB levels between the pre-operative period and each post-operative period. The trend of lower DB levels in the post-operative periods compared to the pre-operative baseline is consistent across all three post-operative time points, mirroring the observations for total bilirubin (TB) levels. The slight decrease in DB levels may reflect the normal course of recovery following surgery, with no indication of significant impairment of liver function. The study's findings suggest that the surgical procedure did not result in significant changes in DB levels as measured in the immediate post-operative period, indicating that the surgery did not adversely affect liver function.

- The table 6 compares mean indirect bilirubin (IDB) values between pre-operative and post-operative days (POD 1, POD 2, and POD 7). The data shows slight decreases in IDB values at POD 1, POD 2, and POD 7 compared to pre-operative levels, but these changes are not statistically significant. The paired t-tests did not find sufficient evidence to reject the null hypothesis that there is no difference in mean IDB values between pre-operative and post-operative time points. This suggests that the surgical procedure or recovery process did not lead to a significant change in IDB levels measured. In conclusion, there is no evidence to suggest a meaningful difference in IDB levels between pre-operative and post-operative durations based on the paired t-tests conducted.
- The table 7 compares mean total proteins (TP) values between pre-operative and post-operative days (POD 1, POD 2, and POD 7). The data shows no statistically significant difference in TP values between pre-operative and post-operative times. The mean TP value at POD 1 (6.372) is lower than the mean at PRE-OP (6.727), but not statistically significant. The mean TP value at POD 2 (6.469) is lower than the mean at PRE-OP (6.727), but not statistically significant. The mean TP value at POD 7 (6.209) is lower than the mean at PRE-OP (6.727), but not statistically significant. The clinical implications suggest that the surgical procedure or recovery process did not lead to a significant change in TP levels measured over time. Overall, TP levels remain relatively stable throughout these time points.
- The table 8 compares mean ALBUMIN (AB) values between pre-operative and post-operative days (POD 1, POD 2, and POD 7). The results show a significant decrease in AB values at POD 1, POD 2, and POD 7 compared to

pre-operative levels, indicating that the surgical procedure or post-operative recovery process has a measurable impact on ALBUMIN levels. This decrease may indicate physiological stress, altered nutritional intake, or other factors related to the surgical intervention. The low P values (all < 0.05) suggest strong evidence to reject the null hypothesis that there is no difference in mean AB values. The table suggests that Albumin levels are notably affected during the post-operative period, which should be considered in clinical assessment and management of patients undergoing these procedures.

- The table 9 compares mean GLOBULIN (GL) values between pre-operative and post-operative days (POD 1, POD 2, and POD 7). The results show a significant decrease in GL values at POD 1, POD 2, and POD 7 compared to the pre-operative baseline. This suggests a systemic response post-operatively that affects GLOBULIN synthesis or metabolism, potentially affecting immune status or inflammatory response. This finding could be clinically relevant in monitoring patients for post-operative complications or recovery. The low P values (all < 0.05) suggest strong evidence to reject the null hypothesis that there is no difference in mean GL values. The findings highlight the impact of surgery on Globulin levels and suggest potential implications for clinical management and monitoring of patients undergoing surgical procedures.
- The table 10 compares mean Albumin Globulin Ratio (AGR) values between pre-operative and post-operative days (POD 1, POD 2, and POD 7). The results show a significant decrease in AGR values at POD 2 and POD 7 compared to the pre-operative baseline, suggesting alterations in the balance of albumin and globulin post-operatively. This decrease can indicate changes

in protein synthesis, metabolism, or distribution, potentially influenced by factors such as inflammation, stress response, or changes in liver function. The table highlights the impact of surgical intervention on AGR and suggests potential implications for monitoring and managing patients post-operatively, particularly in assessing nutritional and liver function status. The findings suggest potential implications for monitoring and managing patients post-operatively.

- The table 11 compares mean ALT values between pre-operative and post-operative days (POD 1, POD 2, and POD 7). The results show no statistically significant difference in mean ALT values between the two time periods. The mean ALT values at POD 1 (24.281) are slightly higher than the mean at PRE-OP (24.219), but not statistically significant. The mean ALT values at POD 2 (22.031) are lower than the mean at PRE-OP (24.219), but not statistically significant. The mean ALT values at POD 7 (25.063) are slightly higher than the mean at PRE-OP (24.219), but not statistically significant. This stability in ALT levels post-operatively indicates that the surgical procedure did not cause acute liver damage or significant stress on liver function. In conclusion, the table indicates no significant changes in ALT levels, which is generally reassuring in assessing liver health and function post-operatively.
- The table 12 compares the mean AST values before and after a surgical procedure. The data shows no significant difference in AST values between pre-operative and post-operative days. The mean AST values at POD 1 (26.813) and POD 2 (23.609) were slightly higher than the mean at PRE-OP (25.313), but not statistically significant. The mean AST values at POD 7 (27.281) were slightly higher than the mean at PRE-OP (25.313). The paired t-

tests did not find a statistically significant difference in mean AST values between pre-operative and post-operative time points. This suggests that the surgical intervention did not lead to significant acute changes in AST levels, suggesting no significant damage to liver cells or other tissues releasing AST into the bloodstream. In conclusion, the table indicates no significant changes in AST levels post-operatively, indicating that the surgical procedures did not result in significant changes.

- The table compares the mean ALP (Alkaline Phosphatase) values between pre-operative and post-operative days. The results show a significant decrease in mean ALP values at post-operative day 7 compared to the pre-operative baseline. This suggests that the surgical intervention may have influenced ALP levels by this time point. However, there were no significant differences at pre-operative and post-operative time points. The significant decrease in mean ALP values at post-operative day 7 suggests that the surgical procedure may have affected liver function or bone metabolism. Changes in ALP levels can reflect alterations in liver function due to surgical stress or recovery, as well as changes in bone metabolism possibly influenced by anesthesia or immobilization post-surgery. The table highlights the potential impact of surgical intervention on ALP levels, which should be considered in clinical assessment and management of patients undergoing these procedures, particularly in monitoring liver and bone health post-operatively.

LIMITATIONS:

1. This was a single centre-based study.

2. LESS SAMPLE SIZE DUE TO HIGH FOLLOW UP RATE

CONCLUSION

- The study found no significant changes in total bilirubin and direct bilirubin levels between pre- and post-operative periods, suggesting stable liver function.
- However, significant decreases in albumin and globulin levels suggest physiological stress or nutritional intake may influence these markers, potentially influencing immune and inflammatory responses.
- Changes in alkaline phosphatase levels suggest possible effects on liver function or bone metabolism.

SUMMARY

- The study examines the impact of surgical procedures on various biochemical markers before and after the procedure.
- Results show no significant difference in total bilirubin (TB) levels between pre-operative and post-operative periods, suggesting a normal course of recovery without significant impairment of liver function.
- There were no significant changes in direct bilirubin (DB) levels between pre-operative and post-operative periods.
- Indirect bilirubin (IDB) levels remained stable throughout the observed time points.
- AB values decreased significantly at all post-operative time points compared to pre-operative levels, suggesting physiological stress or altered nutritional intake.
- GL values decreased significantly at all post-operative time points, suggesting systemic response post-surgery affects GL synthesis or metabolism, potentially impacting immune status or inflammatory response.
- Surgical intervention may influence ALP levels, reflecting changes in liver function or bone metabolism post-surgery. These findings contribute to understanding the impact of surgery on liver function, protein metabolism, and overall physiological responses.

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ANNEXURE-I

KAHERs JNMCBELAGAVI

<u>INFORMED CONSENT FORM</u>

" OBSERVATIONAL STUDY OF EFFECT OF CO2 PNEUMOPERITONEUM ON LIVER FUNCTION FOLLOWING LAPAROSCOPIC CHOLECYSTECTOMY"

Name of Student/Principal Investigator:

Name of Guide/Co Investigators:

Objective:

Introduction:

Explanation of procedure:

Withdrawal from participation in the study: Participation in this study is voluntary. You will be free to decide whether to participate in this study or continue participation once enrolled. In case you decide to withdraw your participation, you are free to do so. However, please convey the decision to the principal investigator.

Possible benefits from participating in the study: You will/will not have nor get any benefits by participating in this study. The data gathered will help the population at large.

Possible risks from participating in the study: There are no risks involved in participating in this study.

Privacy and confidentiality: The information collected from you will be coded, to prevent any person from identifying you. Your identity will never be revealed. The data collected from you will be kept confidential and only processed or aggregated data will be used for publication.

Financial incentives: You will not receive any payment for participating in this study.

Authorization for publication of aggregated data: Results obtained after processing of the aggregated data will be published for scientific purposes and or presented to scientific groups.However, your identity will never be revealed.

Questions: In case of any questions with regard to this study, you are free to contact: "Nameof student/PI, mobile number, email ID" If you have any question or complaints with regard to your right as study participant you may contact Dr Harsha Hegde, Chairperson, Ethical committee of JNMC, 0831-2473777 Extension 4052.

Legal rights: By signing this consent form, we are not waving any of your legal rights.

CONSENT STATEMENT

I am making a voluntary decision to participate in the study **"OBSERVATIONAL STUDY OF EFFECT OF CO2 PNEUMOPERITONEUM ON LIVER FUNCTION FOLLOWING LAPAROSCOPIC CHOLECYSTECTOMY".** My signature below indicates that I have decided to participate and I have read the information provided above or the information provided above has been read to me in the language that I understand best. I was given the opportunity to ask questions and that they have been answered to my satisfaction.

Name of the participant:

Signature/left thumb impression of participant:

Name of the Witness:

Signature/left thumb impression of Witness:

Name of the investigator:

Signature of the investigator:

ANNEXURE-II

PROFORMA

TITLE:- OBSERVATIONAL STUDY OF EFFECT OF CO2 PNEUMOPERITONEUM ON LIVER FUNCTION FOLLOWING LAPROSCOPIC CHOLECYSTECTOMY

NAME:-

	PRE-OP	POD-1	POD-2	POD-7
TOTAL BILIRUBIN				
DIRECT BILIRUBIN				
INDIRECT BILIRUBIN				
TOTAL PROTEIN				
ALBUMIN				
GLOBULIN				
A/G: RATIO				
ALT(SGPT)				
AST(SGOT)				
ALP				

ANNEXURE-III MASTER CHART

				TOTAL BILIRUBIN				DIRECT BILIRUBIN				INDIRECT BILIRUBIN				TOTAL PROTIEN				ALBUMIN				GLOBULIN				A/G RATIO				ALT (SGPT)				AST (SGOT)				ALP			
S. NO	AGE/SEX	IP NUMBER	DIAGNOSIS	PRE-OP	POD 1	POD 2	POD 7	PRE-OP	POD 1	POD 2	POD 7	PRE-OP	POD 1	POD 2	POD 7	PRE-OP	POD 1	POD 2	POD 7	PRE-OP	POD 1	POD 2	POD 7	PRE-OP	POD 1	POD 2	POD 7	PRE- OP	POD 1	POD 2	POD 7	PRE-OP	POD 1	POD 2	POD 7	PRE-OP	POD 1	POD 2	POD 7	PRE-OP	POD 1	POD 2	POD 7
1	48/M	10017142	CHOLELITHIASIS	0.45	0.41	0.38	0.4	0.23	0.2	0.21	0.24	0.22	0.2	0.18	0.11	7.3	6.2	6.4	7.3	4	3.8	3.6	3.5	3.3	3.1	3.5	3.1	1.2	1.1	1.1	1.2	35	28	26	30	24	25	26	22	84	78	76	90
2	42/F	10022294	CHOLELITHIASIS	0.68	0.52	0.58	0.6	0.51	0.48	0.4	0.5	0.17	0.15	0.18	0.11	7	7.2	7.5	7	3.7	3.5	3	2.9	3.3	3	2.9	2.5	1.1	1	1.2	1.1	13	15	18	25	12	11	12.5	20	177	87	92	90
3	43/M	10023091	CHOLELITHIASIS	0.54	0.54	0.56	0.8	0.23	0.45	0.5	0.6	0.31	0.14	0.19	0.12	7.2	7.3	7.5	6.9	4.8	4	3.8	3	2.4	2	2.6	3	2	1.9	1.1	2	60	58	55	45	48	45	40	59	99	100	112	126
4	29/F	10025054	CHOLELITHIASIS	0.62	0.5	0.75	0.66	0.16	0.13	0.15	0.11	0.46	0.5	0.59	0.6	7	6.9	6	5.9	4.2	4	3.7	3.5	2.8	2.9	3.5	3.2	1.5	1.6	1.9	0.9	12	15	18	112	15	52	56	88	112	115	126	135
5	35/M	10026371	CHOLELITHIASIS	1.02	0.98	0.92	0.7	0.47	0.32	0.36	0.2	0.55	0.33	0.34	0.36	7.8	7.6	7.4	7	4.7	4.5	4.6	4.7	3.1	2.9	2.4	2.6	1.5	1.6	1.2	1.1	28	26	22	23	38	34	36	30	90	88	83	80
6	34/F	10029851	CHOLELITHIASIS	0.36	0.33	0.32	0.28	0.16	0.14	0.11	0.16	0.2	0.1	0.3	0.6	8.2	8.2	7.8	7.7	4.2	4.1	3.8	3.7	4	3.8	3.8	3.6	1	1.2	1.2	1	27	26	22	28	24	22	26	30	127	90	84	88
7	70/M	10030074	CHOLELITHIASIS	1.42	1.28	1.26	1.22	0.86	0.76	0.72	0.66	0.56	0.49	0.46	0.55	6.1	7	6.2	6.9	2.8	2.8	2.6	2.2	3.3	2.9	2.5	3.2	0.8	1	0.9	0.6	30	28	26	30	28	26	25	22	189	172	153	114
8	40/F	10031471	CALCULOUS CHOLECYSTITIS	0.21	0.19	0.18	0.19	0.14	0.9	0.8	1.2	0.07	0.07	0.06	0.09	8.3	0.1	6.8	5.6	4.5	4.4	4.3	3.5	3.8	2.4	2.8	2.8	1.2	1.1	0.9	0.8	28	28	26	22	31	28	24	29	209	196	112	103
9	38/F	10034410	CALCULOUS CHOLECYSTITIS	0.48	0.42	0.38	0.4	0.2	0.1	0.1	0.2	0.28	0.33	0.34	0.36	8.1	7.8	7.6	7.7	4.3	3.2	3.6	3.6	3.8	3.8	3.5	3.2	1.1	0.6	0.8	0.8	24	22	26	30	28	26	25	22	98	87	85	60
10	39/F	1160458	CALCULOUS CHOLECYSTITIS	0.62	0.55	1	0.84	0.31	0.28	0.37	0.3	0.31	0.27	0.63	0.54	7.8	7.8	7.2	7.6	4	3.9	3.7	4	3.8	3.9	3.5	3.6	1.1	1.1	1	1.1	19	17	18	18	20	19	21	20	112	103	88	100
11	43/M	1156748	CHOLELITHIASIS	1.37	1.38	1.13	1.17	0.46	0.48	0.38	0.32	0.91	0.9	0.74	0.85	7.5	7.1	7	6.4	5.5	5.2	4.6	4.1	2	1.9	2.4	2.3	2.8	2.73	1.91	1.8	18	20	20	22	23	22	20	19	86	84	80	71
12	70/F	1154709	CHOLELITHIASIS	0.31	0.63	0.66	0.7	0.04	0.2	0.34	0.4	0.27	0.43	0.3	0.37	7.6	7	6.3	7	4.4	4	3	3.2	3.2	3	3.3	3.4	1.4	1.3	0.9	0.94	19	70	19	20	30	82	28	20	67	61	158	130
13	46/M	1156383	CHOLELITHIASIS	5.86	4.65	3.68	1.81	4	2.87	2.62	1.57	1.86	1.78	1.06	0.24	7.5	7	6.7	6.9	4.8	3.9	3.6	3.9	2.7	3.1	3.1	3	1.8	1.3	1.2	1.3	108	79	62	33	58	34	24	26	387	323	279	205
14	67/M	1156308	CALCULOUS CHOLECYSTITIS	1.64	0.95	0.77	1.62	0.68	0.47	0.52	0.8	0.96	0.48	0.25	0.82	4.8	4.8	4.6	6.4	2.4	2.3	2.1	3.3	2.4	2.5	2.5	3.1	1	0.9	0.8	1.1	10	9	10	10	10	10	11	16	12	169	111	125
15	70/M	1156105	CHOLELITHIASIS	1.19	0.76	0.83	0.86	0.59	0.4	0.27	0.4	0.6	0.36	0.56	0.46	7.2	7.3	8	7.6	4.5	4.4	4.8	3.4	2.7	2.9	2.3	2.2	1.7	1.5	1.5	0.8	33	19	11	20	23	19	14	22	98	75	105	107
16	72/F	1154631	CHOLELITHIASIS	0.15	0.2	0.2	0.4	0.12	0.1	0.2	0.23	0.03	0.1	0.2	0.25	5.4	3.6	3.2	3	2.8	1.7	1.8	1.9	2.6	1.9	2	2	1.1	0.9	0.9	0.95	15	12	18	24	1	10	20	20	79	56	60	40
17	56/F	1157440	CHOLELITHIASIS	0.25	0.41	0.47	0.53	0.1	0.1	0.13	0.18	0.15	0.31	0.34	0.36	7.7	6.9	7.4	7.6	4.5	3.9	4.2	3.9	3.2	3	3.2	3.7	1.4	1.3	1.3	1.05	12	35	32	40	14	44	25	21	112	96	107	92
18	62/M	1101041	CHOLELITHIASIS	0.58	0.56	0.56	0.54	0.28	0.26	0.25	0.31	0.3	0.3	0.29	0.25	6.8	7.2	7.12	5.5	3.7	3.4	3.3	3.2	3.1	3.18	2.9	3.1	1.2	1.1	1.1	1.05	31	29	25	24	49	46	38	36	98	95	92	80
19	25/F	5113246	CHOLELITHIASIS	0.91	0.89	0.86	0.8	0.2	0.2	0.2	0.18	0.7	0.72	0.7	0.74	6.9	6.6	6.8	4.3	3.1	3	2.7	2.2	3.2	3.89	3.5	2.5	1.1	1.1	1.1	1.02	15	14	16	19	21	20	16	11	300	220	186	152
20	78/M	110326	CHOLELITHIASIS	0.69	0.66	0.64	0.45	0.46	0.44	0.41	0.62	0.24	0.22	0.22	0.15	5.5	5.2	5.1	4.3	2.9	2.7	2.6	2.5	2.4	2.22	2.1	2.6	1.1	1.1	1.2	1.06	17	15	12	11	18	16	11	22	122	118	115	98
21	48/M	1125595	CHOLELITHIASIS	0.5	0.3	0.22	0.2	0.23	0.21	0.21	0.25	0.27	0.25	0.26	0.26	7.2	6.5	6.3	5.5	4	3.9	3.5	3.3	4	3.8	3.5	3.6	1.3	1.2	1.1	1.05	12	11	13	11	14	11	12	22	86	86	82	75
22	45/M	1135046	CHOLELITHIASIS	0.4	0.32	0.31	0.28	0.2	0.2	0.2	0.15	0.29	0.28	0.19	0.17	7.2	6.1	6.2	5.4	3.8	3.7	3.6	3.3	3.2	3.1	3	3.5	1.3	1.2	1.2	1.2	28	25	25	24	23	23	22	36	64	94	52	53
23	20/M	6701496	CALCULOUS CHOLECYSTITIS	1.3	0.82	0.84	0.65	0.53	0.54	0.53	0.49	0.77	0.76	0.74	0.56	5.5	4.6	4.6	4.3	3.4	3.2	3.2	3.5	2.1	1.7	1.5	1.9	1.6	1.1	1.1	1.3	13	12	15	14	45	28	24	15	98	87	82	70
24	51/M	1184864	CALCULOUS CHOLECYSTITIS	1.1	0.84	0.65	0.84	0.4	0.32	0.32	0.45	0.7	0.68	0.55	0.39	6.4	6.2	6.2	6.8	3.4	3.1	3.2	3.2	2.2	1.8	1.5	1.8	1.1	1.3	1.2	1.3	13	11	12	11	31	28	26	11	79	73	72	66
25	32/F	1142710	CALCULOUS CHOLECYSTITIS	0.4	0.32	0.32	0.25	0.2	0.22	0.32	0.44	0.2	0.15	0.3	0.44	6.1	5.6	5.8	5.1	4.3	4.1	3.6	3.5	2.2	1.8	1.6	1.56	2.4	1.5	1.4	1.2	22	24	19	18	13	22	23	35	160	145	133	112
26	62/M	1142524	CALCULOUS CHOLECYSTITIS	0.5	0.45	0.45	0.44	0.2	0.35	0.34	0.19	0.3	0.39	0.37	0.2	6.4	6.2	5.9	5.4	3.4	3.2	3.1	2.5	1.8	1.6	1.2	1.11	1.2	1.1	1.2	1.4	22	25	22	23	28	25	22	32	91	87	85	76
27	27/M	1142541	CHOLELITHIASIS	0.2	0.9	0.78	0.64	0.1	0.11	0.1	0.44	0.1	0.22	0.25	0.24	0.36	6.9	6.8	6.6	3.9	3.8	3.4	2.9	3.4	3.2	3.1	2.7	1.2	1.2	1.1	1.03	23	22	26	19	25	22	22	26	114	110	96	88
28	76/M	1142117	CHOLELITHIASIS	0.39	0.32	0.31	0.3	0.18	0.19	0.17	0.14	0.21	0.25	0.26	0.27	6.5	6.1	6.5	6.7	3.6	3.2	3	2.6	2.6	2.3	2.2	1.8	1.3	1.1	1.1	1.02	15	14	14	14	25	26	25	24	72	70	72	66
29	53/M	1141772	CHOLELITHIASIS	0.6	0.54	0.53	0.25	0.56	0.44	0.41	0.35	0.4	0.32	0.27	0.22	6.3	6.1	5.9	5.5	3.3	3.1	3.1	2.8	2.6	2.5	2.2	1.9	1.1	1.2	1.1	1.2	9	8	12	11	19	11	11	22	87	85	82	77
30	48/F	1141998	CHOLELITHIASIS	0.47	0.41	0.42	0.36	0.74	0.68	0.45	0.39	0.5	0.39	0.37	0.28	8.6	8.3	8.2	7.4	3.5	3.4	3.3	2.9	2.8	2.2	2.2	2.3	0.7	0.9	1.2	1.01	14	13	16	19	14	12	15	29	131	121	119	108
31	50/F	1141283	CHOLELITHIASIS	0.4	0.34	0.32	0.28	0.86	0.55	0.26	0.36	0.2	0.27	0.26	0.2	7.8	7.1	6.6	6.5	4	3.8	4	3.5	3	2.58	2.63	3.1	1	1.2	1.1	1.2	25	22	25	26	26	25	22	30	101	99	92	77
32	35/M	1151128	CHOLELITHIASIS	0.62	0.56	0.55	0.45	0.41	0.36	0.22	0.18	0.21	0.19	0.17	0.15	5.2	5.4	5.4	4.9	2.1	2.3	2.3	2.3	2.9	2.8	2.8	2.7	0.71	0.82	0.82	0.85	25	25	24	26	32	34	33	36	102	94	86	75