
“AN OBSERVATIONAL STUDY ON EFFECT OF
CARBON DIOXIDE PNEUMOPERITONEUM ON
LIVER FUNCTION TEST IN LAPAROSCOPIC
CHOLECYSTECTOMY”

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ENDORSEMENT

This is to certify that the dissertation entitled “**AN OBSERVATIONAL STUDY ON EFFECT OF CARBON DIOXIDE PNEUMOPERITONEUM ON LIVER FUNCTION TEST IN LAPAROSCOPIC CHOLECYSTECTOMY**” is a bonafide research work done by **REG NO. BH0112010**

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ABBREVIATIONS

CO ₂	:	Carbon dioxide
AST	:	Aspartate aminotransferase
ALT	:	Alanine aminotransferase
ALP	:	Alkaline phosphatase
CDP	:	Carbon dioxide pneumoperitoneum
TP	:	Total proteins
TB	:	Total Bilirubin
DB	:	Direct Bilirubin
S	:	Serum
SGOT	:	Serum Glutamate Oxaloacetic Transaminase
SGPT	:	Serum Glutamate Pyruvate Transaminase
Cm	:	Centimeter
M	:	meter
Min	:	minute
ml	:	milliliter
mmHg	:	millimeter mercury
Mg	:	milligram
Nm	:	nanometer
PP	:	pneumoperitoneum
PaCO ₂	:	Arterial pressure of carbon dioxide
O ₂	:	Oxygen
Kg	:	kilogram

H ₂ O	:	water
g	:	microgram
T	:	Students paired t test
IAP	:	Intraabdominal pressure
LC	:	Laparoscopic cholecystectomy
OC	:	Open cholecystectomy
U/L	:	Units per litre
mg/dL	:	milligram per deciliter
N	:	Number of cases
No	:	Number
ERCP	:	Endoscopic retrograde cholangio pancreatography
Yrs	:	years
Std	:	standard
SD	:	Standard deviation
SEM	:	Standard error of mean
Hrs	:	hours
Hs	:	highly significant
Vhs	:	very highly significant

ABSTRACT

Introduction:In 1985, Muhe performed the first laparoscopic cholecystectomy. For over 25 years, laparoscopic cholecystectomy has replaced open cholecystectomy in the management of benign gallbladder diseases and has become the gold standard for symptomatic cholelithiasis. In 1985, Muhe performed the first laparoscopic cholecystectomy.¹Further development of this technique was done by Mouret and Dubois.

The main advantages of laparoscopic cholecystectomy include the reduction of tissue trauma due to small skin incisions and reduction in adhesion formation, a reduction in patient morbidity, shortening in hospital stay, and early return to normal activity. The conversion rate and complications associated with LC depend on the experience of the surgeon and the degree of difficulty faced during surgery. Various centers have reported widely varying rates of conversion to open operation (range: 1.5% to 6%). The reported incidence of bile duct injury is between 0% to 1% in LC. Because of these distinct advantages, the procedure has gained worldwide popularity and has now become one of the most common operations performed in general surgical practice. LC is essentially a safe procedure with low morbidity and mortality rate.

It was noted that following a laparoscopic cholecystectomy (LC), liver function parameters were disturbed.⁴The introduction of carbon dioxide under pressure into the peritoneal cavity may cause changes in the splanchnic microcirculation, which may affect cardiac, pulmonary, liver and kidney physiology. Changes have also been found in intracranial pressure, blood acid-base control and the immune system.⁵

Aim of the study: To investigate the effect of laparoscopic cholecystectomy on liver function in humans and the possible mechanisms involved in such an effect.

Methods: Blood samples of 100 patients undergoing laparoscopic cholecystectomy preoperatively once and post operatively on day 1 were collected. These blood samples were tested for liver function- serum bilirubin (total and direct), serum alanine amino transferase (ALT), serum aspartate aminotransferase (AST) , serum alkaline phosphatase, total proteins and serum albumin. The pre op and post op levels of these liver function test values were compared.

Results: The level of serum AST, ALT, bilirubin (total) and ALP were increased significantly during the first 24 hrs. post operatively after laparoscopic cholecystectomy as compared to baseline values. The levels of serum albumin and total proteins were decreased during the first 24 hrs post operatively after laparoscopic cholecystectomy as compared to baseline values.

Conclusion: There may be a transient elevation of hepatic enzymes after laparoscopic cholecystectomy and the major causative factor seemed to be CO₂ pneumoperitoneum.

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INTRODUCTION

For over 25 years, laparoscopic cholecystectomy has replaced open cholecystectomy in the management of benign gallbladder diseases and has become the gold standard for symptomatic cholelithiasis. It has become the procedure of choice for most patients referred for elective cholecystectomy. In 1985, Muhe performed the first laparoscopic cholecystectomy.^{1,2} This technique was further developed by Mouret and Dubois.

The main advantage of laparoscopic cholecystectomy includes the reduction of tissue trauma due to small skin incisions and reduction in adhesion formation. The increasing interest in laparoscopy is mostly attributable to cumulative evidence suggesting a reduction in patient morbidity, shortening in hospital stay, and early return to normal activity.

The basic differences between open and laparoscopic cholecystectomy are in approach, degree of tissue damage and CO₂ pneumoperitoneum. Laparoscopy requires the establishment of pneumoperitoneum in order to provide adequate surgical exposure and maintain operative freedom. The laparoscopic cholecystectomy is performed by the insufflation of the gas in the peritoneal cavity. Carbon dioxide is the preferred gas for creation of pneumoperitoneum, because it is inexpensive, highly soluble, chemically stable, rapidly eliminated, physically inert, suppresses combustion and also creates good illumination. Carbon dioxide is a normal product of human metabolism and at physiological levels nontoxic.³ After absorption from the peritoneum, it is readily excreted via the lungs. Carbon dioxide is 20 times more soluble in serum than room air or oxygen and has been shown to be absorbed 32 times more quickly than room air when used for double-contrast barium enemas.

Laparoscopic cholecystectomy offers many advantages compared to open cholecystectomy. The conversion rate and complications associated with LC depend on the experience of the surgeon and the degree of difficulty faced during surgery. Various centers have reported widely varying rates of conversion to open operation (range: 1.5% to 6%). The reported incidence of bile duct injury is between 0% to 1% in LC. Because of these distinct advantages, the procedure has gained worldwide popularity and has now become one of the most common operations performed in general surgical practice. LC is essentially a safe procedure with low morbidity and mortality rate.

CO₂ pneumoperitoneum is an insufflation of carbon dioxide into the abdominal cavity in order to enable visualization of organs and easier manipulation of instruments during laparoscopic surgeries. Pressure that is being used is between 12 to 20 mmHg, but it is usually 14 mmHG, and it is higher than a pressure in the portal system, which is between 7 to 10 mmHG.⁷ CO₂ pneumoperitoneum and increased intraabdominal pressure can induce many pathophysiologic disturbances. The CO₂ pneumoperitoneum is associated with a number of local and systemic effects, such as alterations in hemodynamic and cardiovascular function as well as disturbances in the acid base balance. One of the major effects of CO₂ pneumoperitoneum is a reduction in portal venous and hepatic arterial blood flow.⁶

The pressure needed in abdomen, for the majority of operations, is 12-20mmHg, and to achieve that pressure, it is necessary to apply around 5 l of gas into the abdomen, depending on the thickness and muscular strength of the front abdominal wall. The effects of CO₂ pneumoperitoneum are divided into:

1. The physiological effects of CO₂ absorption and
2. Chemo dynamical effects from increased intraabdominal pressure

Although LC offered many advantages over laparotomy, concerns arose regarding the effects of pneumoperitoneum on the cardiovascular and respiratory system. One of the important hemodynamic changes is the transient reduction in hepatic blood flow caused by a pneumoperitoneum. The pressure of a created pneumoperitoneum and its duration was shown to influence the degree of hepatic ischemia by causing elevations in liver enzymes.⁸

Studies have shown that alterations of intraabdominal pressure in a short time period, leads to the undulation of portal blood flow which leads to repeated intervals of ischemia and reperfusion of the organs, release of free radicals, which damage hepatocytes, particularly Kupffer's and endothelial cells. Studies have shown that possible cause of the transient damage to liver function is diathermia and warmth in liver parenchyma.⁹

In a study in Jordan, Twenty-four (24) hours after surgery, there was a statistically significant change of all the eight parameters, except alkaline phosphatase in patients who underwent LC, whereas only 3 patients from the OC group, had changes of alanine aminotransferase and aspartate aminotransferase and 2 patients had raised levels of direct bilirubin, and there were no changes observed among those who had conventional hernia repair. It was found that 83% of the patients showed more than a 100% increase in at least one parameter, 43% showed an increase in two or more parameters, and 23% showed an increase in three or more parameters. It was also observed a significant drop of total proteins and albumin levels in all patients who had LC.¹⁰

In a study in china, In patients who underwent LC and LCR, the level of serum ALT and AST were increased significantly during the first 48 hours post operations in both LC and LCR patients. However, there was no significant change of

the serum liver enzymes detected in both patient who underwent OC and OCR. Hence, there was statistically significant difference in change of both ALT and AST levels between LC and OC patients and LCR and OCR patients respectively. The level of both enzymes returned to normal values in LC, OC and OCR patients by the 7th day post operatively except LCR patients whose enzymes remained at a higher level.¹¹

In a study in Italy, laparoscopic cholecystectomies were performed with a pneumoperitoneum and a gasless technique. All patients had postoperative changes in serologic hepatic tests. Slow return to normality occurred 48 or 72 hours after the operation. The increase in AST and ALT was statistically significant and was correlated to the level and duration of pneumoperitoneum. The serologic changes in the gasless group were significantly lower than in the laparoscopic cholecystectomy group with pneumoperitoneum at 14 mmHg. There was no statistically significant difference between the gasless group and the laparoscopic cholecystectomy group with pneumoperitoneum at 10 mmHg. There was no mortality and morbidity in the pneumoperitoneum group.¹²

New concerns have arisen regarding the effects of Carbon dioxide pneumoperitoneum on cardiovascular and respiratory systems, with the increasing use of laparoscopic surgery. An important hemodynamic change is the transient reduction in hepatic blood flow caused by carbon dioxide pneumoperitoneum. In 1994, Halevy et al. were the first to report that the pressure created by carbon dioxide pneumoperitoneum and its duration influence the degree of hepatic ischemia and can cause liver enzyme elevation.¹³

Though, the 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 CO₂ pneumoperitoneum and postoperative mesenteric ischemia reports following laparoscopic procedures have raised concern about local and systemic effects of increased intraabdominal pressure during laparoscopic procedures. This study aims to investigate the alterations in the serum levels of liver enzymes after LC performed under constant intraperitoneal pressure (14mmHg) at KLES Prabhakar Kore Hospital, Belgaum , Karnataka. India

AIMS AND OBJECTIVES OF THE STUDY

The aim of our study was to investigate:

1. The incidence of alterations in liver function following laparoscopic cholecystectomy in the Indian population
2. To study the significance of these alterations in patients and the safety of the procedure.

REVIEW OF LITERATURE

HISTORICAL REVIEW

Laparoscopic surgery, also known as minimally invasive surgery (MIS) or 'keyhole' surgery, is a modern surgical technique for carrying out operations in the abdomen through cannulae (also known as ports) which are channels into the body through small incisions.⁴³

The earliest done laparoscopy reference dates back to biblical history (over two thousand years ago). At that time classical Galenic medical tradition was based on the concept of maintaining homeostasis by balanced production and excretion of bodily wastes. Imbalance led to disease states. Classical restoration to normal balance was by means of purgatives and cathartics. Alternatively, surgically draining the abdomen of "bad humours" by means of trocar insertion was in vogue as described by Ezekiel and Celsus (25 BC – AD 50).⁴⁴

In 1882, Carl Langebuch (1846-1901) of Germany performed the first cholecystectomy.⁴⁴ In 1985 (103 years later), Prof Dr Erich Mühe of Germany performed the first laparoscopic cholecystectomy (LC). He performed 94 such procedures before another surgeon, Phillippe Mouret of Lyon, France, performed his first laparoscopic cholecystectomy in 1987, followed by Francois Dubois of Paris, France, in 1988.

George Kelling, a surgeon from Dresden, Germany, documented the first laparoscopy performed on a live dog. And this was presented at the 73rd Congress of German Naturalists and Physicians in September 1901. He performed laparoscopy by creating pneumoperitoneum using filtered air and he used cystoscopy and trocar, thus establishing many of the basic principles of laparoscopy that are still in use. In 1910,

Hans Christian Jacobaeus, of Sweden, reported the first laparoscopic surgery in humans.

The introduction of the computer chip television camera was a key event in the development of laparoscopy, as the procedure could then be conducted while viewing a projected image of the abdominal contents, as well as providing a better view of the internal structures. This also allowed free movement of the surgeon's hands, making it easier to perform more complex procedures. Before the development of the camera, this approach was reserved only for diagnostic purposes and a few simple surgical procedures in gynecologic applications.

The 3 most important, basic instruments used in the first laparoscopic cholecystectomy were the laparoscope, the hemoclip, and the pistol grip scissors¹

The laparoscope had been used by gynecologists for many years for diagnostic purposes before the general surgeon. Mühe initiated laparoscopic cholecystectomy in 1985.¹

The other essential instruments used at that time were the hemoclip, namely the Weck-Reynolds pistol grip clip applier and the Weck-Reynolds pistol grip scissors, which were important for the ligation and cutting of the cystic duct and artery during laparoscopic cholecystectomy. Walker Reynolds, Jr's interest in hemoclips began in 1970 when these devices were used for hemostasis of blood vessels in conjunction with staple surgery.¹

To perform laparoscopic procedures the abdominal cavity is inflated with gas to create the pneumoperitoneum. Pneumoperitoneum distends and separates the abdominal wall from its contents. Visual clarity, space to perform diagnostic and therapeutic procedures and maintenance of a normal physiologic state is required for safe effective surgery. The use of carbon dioxide (CO₂) for creating a PP was

suggested by Richard Zollikofer from Switzerland. The absence of oxygen in the abdominal cavity cleared the way for the use of electrocoagulation.

A Veress needle is a spring-loaded needle used to create pneumoperitoneum for laparoscopic surgery. The Veress needle was in 1932 developed by the Hungarian János Veress surgeons with the goal of a safe puncture technique for creating a therapeutic pneumothorax (collapsed lung) in the treatment of pulmonary tuberculosis



PNEUMOPERITONEUM BY VERESS NEEDLE

Today laparoscopic cholecystectomy is one of the most commonly undertaken procedures in general surgery, with more than 500,000 cases performed annually. Laparoscopic cholecystectomy offers many advantages compared to open cholecystectomy. The conversion rate and complications associated with LC depend on the experience of the surgeon and the degree of difficulty faced during surgery. Different centers have reported widely varying rates of conversion to open operation (range: 1.5% to 6%). The reported incidence of bile duct injury is between 0% to 1% in LC. Because of these distinct advantages, the procedure has gained worldwide popularity and has now become one of the most common operations performed in

general surgical practice. LC is essentially a safe procedure with low morbidity and mortality rate.

EQUIPMENT AND INSTRUMENTATION

EQUIPMENT

1. Telescope
2. Video Camera
3. Light Sources
4. Insufflators
5. Video Monitors

Telescope

The standard laparoscope consists of a metal shaft 24 cm in length containing a series of quartz-rod lenses that carry the image through the length of the scope to the eyepiece. The telescope contains parallel optical fibers that transmit light into the abdomen from the light source via a cable attached to the side of the telescope. Telescopes offer either a straight-on view with the 0 degree or can be angled.

The 30-degree telescope provides a total field of view of 152 degrees compared with the 0-degree telescope, which only provides a field of view of 76 degrees.

The most commonly used telescope has a diameter of 10 mm and provides the greatest light and visual acuity. The next most commonly used telescope is the 5-mm laparoscope, which can be placed through one of the working ports for an alternative view. The camera is attached to the eyepiece of the laparoscope for processing.

Video Camera

A high-resolution video camera is attached to the eyepiece of the telescope and acquires the image for projection on the monitor. The video image is transmitted via a cable to a video unit, where it is processed into either an analog or a digital form. Analog is an electrical signal with a continuously varying wave or shift of intensity or frequency of voltage. Digital is a data signal with information represented by ones and zeros and is interpreted by a computer. These are the methods by which the picture is transmitted to the video monitor. The camera and cable are designed so that they can be sterilized in glutaraldehyde.

Light Sources

High-intensity light is created with bulbs of mercury, halogen vapor, or xenon. The bulbs are available in different wattages and should be chosen based on the type of procedure being performed. Because light is absorbed by blood, any procedure in which bleeding is encountered may require more light. The light is carried to the fiberoptic bundles of the laparoscope via a fiberoptic cable. A fibre optic light guide cable, which is 5mm thick and 225cm long, is desirable. Thick cable carries more light. Long cable is more convenient and less likely to be stretched and damaged. The cable should be handled with utmost care.

Insufflators

An insufflator delivers gas from a high-pressure cylinder to the patient at a high rate with low and accurately controlled pressure.

Video Monitors

High-resolution video monitors are used to display the image. Smaller monitors may be used if placed close to the operative field. Larger monitors provide little advantage outside of a display setting.



LAPAROSCOPIC CHOLECYSTECTOMY

Laparoscopic cholecystectomy has received nearly universal acceptance and is currently considered the criterion standard for the treatment of symptomatic cholelithiasis. Many centers have special “short-stay” units or “24-hour admissions” for postoperative observation following this procedure.¹⁴

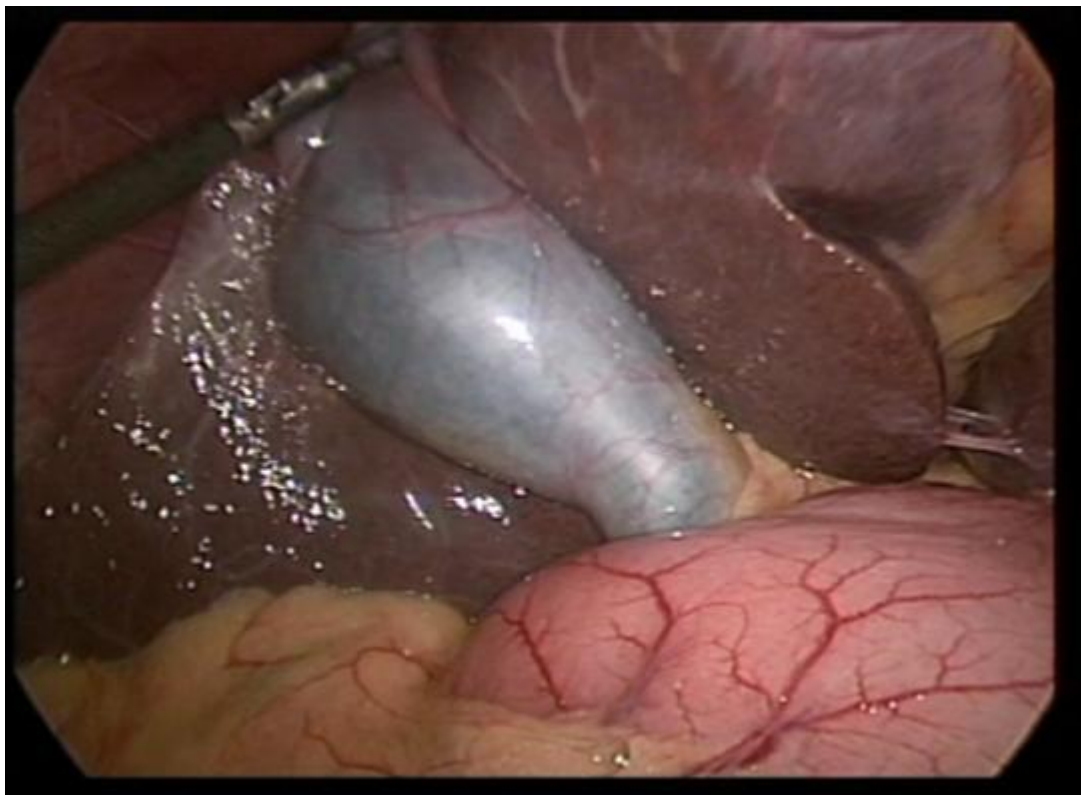
Conventional 4 port laparoscopic cholecystectomy is replaced by 3 ports and 2 ports and SILS (Single incision laproscopiccholecystectomy). A suture needle is used to fix the gall bladder to abdominal wall in the right hypochondrial region with 2 ports in 2 port laparoscopic cholecystectomy. These 3 and 2 port laparoscopic cholecystectomy have the advantages of less scar formation compared to conventional 4 port laparoscopic cholecystectomy. The laparoscopic surgeries have the advantages of reduction in number of emergency operations and decreased morbidity, fewer CBD exploration, shortened hospital stay, reduced total costs in expert hands and for cosmetic purposes.

THE PROCEDURE OF LAPAROSCOPIC CHOLECYSTECTOMY

- a) After induction of general anesthesia an oral-gastric tube is placed to decompress the stomach and a Foley catheter is used to drain the bladder of urine.
- b) A small incision is made near the umbilicus and a needle (Veress) is inserted blindly into the peritoneal cavity.
- c) Carbon dioxide is introduced in the peritoneal cavity through the Veress needle which is now insufflated to 14mm mercury pressure.
- d) A trocar/port is placed into the now insufflated peritoneum and a laparoscope is introduced into the peritoneum which allows the inside of the peritoneum to be projected onto video screens on either side of the operating table.
- e) Three additional trocar ports are now placed in the right upper quadrant under direct vision, two are 5mm in diameter and one is 10mm in diameter. It is

through these ports that laparoscopic instruments, i.e., graspers, dissectors, scissors, etc. are introduced to separate the gallbladder from the liver bed and the biliary tree. This is accomplished in the following fashion:

- 1) The end of the gallbladder is grasped and pushed up toward the diaphragm. This places the cystic duct and cystic artery on stretch and permits the necessary separation of these structures prior to ligating them. Unfortunately when the end of the gall bladder is placed on stretch it can tent up the common bile duct to which it is attached.



- 2) To avoid this tenting up of the common bile duct and to gain better exposure of the cystic duct, common duct, cystic artery area (Triangle of Calot), a second grasping instrument is now used to grasp the proximal portion of the gall bladder (Hartmann's pouch) and retract it inferior laterally. This now opens up the cystic duct-common duct junction and allows for safe identification and dissection of this area.



- 3) Once the cystic duct, common bile duct and cystic artery have been clearly identified and dissected free of each other and other fibrous and fatty tissue, it is now safe to ligate and divide the cystic duct and the cystic artery. This is done by inserting a clipping instrument through the 10mm port and placing two clips proximally and distally then cutting between the clips. With this accomplished the gall bladder is then separated from the liver by dividing the peritoneum between the liver and the gall bladder using electrocautery. The electrocautery can be attached to any number of dissecting instruments designed for this purpose. Sharp dissection with electrocautery or laser light is very effective in both separating the gall bladder from the liver bed and stopping any bleeding which may be encountered during this part of the operation.



4)Once the gall bladder has been safely separated from the cystic duct, cystic artery and liver bed,the gall bladder is grasped and pulled out through 10mmport.

2 PORTS, LAPAROSCOPIC CHOLECYSTECTOMY PROCEDURE:

Two-port laparoscopic cholecystectomy has been reported to be safe and feasible. However, whether it offers any additional advantages remains controversial. There is a randomized trial that compared the clinical outcomes of two-port laparoscopic cholecystectomy versus conventional four-port laparoscopic cholecystectomy. One hundred and twenty consecutive patients who underwent elective laparoscopic cholecystectomy were randomized to receive either the two-port or the four-port technique. All patients were blinded to the type of operation they underwent. Four surgical tapes were applied to standard four-port sites in both groups at the end of the operation. All dressings were kept intact until the first follow-up 1 week after surgery. Postoperative pain at the four sites was assessed on the first day after surgery using a 10-cm unscaled visual analog scale (VAS). Other outcome measures included analgesia requirements, length and difficulty of the operation, postoperative stay, and patient satisfaction score on surgery and scars.

Overall pain score, analgesia requirements, hospital stay, and patient satisfaction score on surgery and scars were similar between the two groups. Two-port laparoscopic cholecystectomy resulted in less individual port-site pain and similar clinical outcomes but fewer surgical scars compared to four-port laparoscopic cholecystectomy.^{14,15}

SINGLE INCISION LAPAROSCOPIC CHOLECYSTECTOMY

A 1cm umbilical skin incision should be made and carried down to the peritoneum. The Gelports double wound retractor was inserted through the incision which stretches the fascial diameter to 1.5cms. A 5 or 10 mm trocar was inserted through the gelport centrally and the gelport with trocar was latched on to the wound

retractor ring. Pneumoperitoneum is established and 10mm 30° scopewas inserted. Two 5mm operating ports were inserted in 2 and 8 o clock positions with videoscope port as the center.¹⁶

PNEUMOPERITONEUM

Laparoscopy refers to endoscopic visualization of the peritoneal cavity usually assisted by a pneumoperitoneum that distends and separates the abdominal wall from its contents. For a safe effective surgery space to perform diagnostic, therapeutic procedures and Visual clarity and maintenance of a normal physiologic state is required. To perform laparoscopic procedures the abdominal cavity is inflated with gas to create the pneumoperitoneum.

Factors that determine the most appropriate gas for pneumoperitoneum are type of anaesthesia, non-combustibility, physiologic compatibility, toxicity, delivery method, ease of use, safety, and cost. Gases used for pneumoperitoneum include carbon dioxide (CO₂), air, oxygen, nitrous oxide (N₂O), argon, helium and mixtures of these gases.

CO₂ gas insufflation is preferred because it has

- a high diffusion coefficient ,isa normal metabolic end product rapidly cleared from the body.
- CO₂ is highly soluble in blood and tissues and does not support combustion.
- The risk of gas embolism is lowest with CO₂

Pneumoperitoneum is usually initiated by use of a needle (Veress or Tuohy) or trocar device to transverse the abdominal wall and distend the peritoneal cavity.¹⁷

Pneumoperitoneum with CO₂ has been used in clinical practice since the introduction of laparoscopic cholecystectomy in the late 1980s.

The physiologic effects of pneumoperitoneum include

1) Systemic absorption of CO₂ and

2) Hemodynamic and physiologic alteration in a variety of organs due to the increased intraabdominal pressure.

Other methods for creation of a working space include abdominal wall retraction, which may be performed either without gas insufflation or with low-pressure insufflation (5-7mmHg).

CREATION OF PNEUMOPERITONEUM

- Closed method: veress or tuohy needle
- Open method : Hasson method

CO₂ is instilled at a rate of 1litre/min. Initial pressure of 10mmHg or higher may indicate placement of needle in the pre-peritoneal or other closed space. A low flow rate of CO₂ should be used initially to avoid gas embolism or vagal stimulation from sudden stretching of the peritoneum. Upon insufflating approximately 1 litre of CO₂ increased tympani in all four quadrants is confirmed and the flow rate may be increased.

Hypercarbia and eventual systemic acidosis can occur by the CO₂ absorption across the peritoneal surface and into the systemic circulation. The increased intra abdominal pressure during pneumoperitoneum results in hemodynamic alteration and changes in femoral venous flow and renal, hepatic, and cardio respiratory function.^{18,19}

EFFECTS OF CARBON DIOXIDE ABSORPTION DURING PNEUMOPERITONEUM

Absorption of CO₂ across the peritoneum is eliminated through the lungs because of its high aqueous solubility and diffusibility. Pneumoperitoneum may result in systemic absorption of CO₂ and alteration of acid-base balance. CO₂ absorption can result in hypercapnia and acidosis if intraoperative ventilation is impaired.⁴⁵

Acidosis associated with hypercapnia has a depressive effect on myocardial contractility, whereas hypercapnia can stimulate the autonomic nervous system leading to tachycardia and increased myocardial contractility. Hypercapnia can cause cardiac arrhythmias, vasoconstriction of the pulmonary vessels, and a mixed response in cardiac function. Close intraoperative monitoring of end-tidal CO₂ (ETCO₂) or arterial partial pressure of CO₂ (PaCO₂) is therefore essential to prevent hypercapnia.

During pneumoperitoneum, the minute ventilation is increased to bring about the ventilatory changes. These appropriate ventilatory changes should be performed to eliminate the increased CO₂ load and prevent systemic acidosis.

An indirect method to quantify the amount of CO₂ absorbed during laparoscopy is by the total volume of exhaled CO₂ (VCO₂) during pneumoperitoneum. Elimination of the increased CO₂ load is primarily through the lungs

EFFECTS OF INCREASED INTRAABDOMINAL PRESSURE DURING PNEUMOPERITONEUM

To provide adequate visualization and exposure of the operative field the intra-abdominal pressure during laparoscopy is set at 15~14 mm Hg. Pneumoperitoneum is created in a state of acutely elevated intra-abdominal pressure. The normal intra-abdominal pressure of non-obese individuals is 5 mm Hg or less.²²

DURATION AND FREQUENCY OF PNEUMOPERITONEUM

The duration of pneumoperitoneum was directly related to the volume of air seen on the initial chest radiograph in the first 24 hours. In 1961, Bevan reported that 77% of his patients had pneumoperitoneum after a variety of abdominal operations. He found that after laparotomy pneumoperitoneum generally resolved by 10 days but could last significantly longer. Keiser and Lemmertz²¹ found that 50% of their patients had pneumoperitoneum after open cholecystectomy and that the pneumoperitoneum lasted for 4.9 days on an average.

The frequency and duration of pneumoperitoneum after traditional laparotomy have been well documented.

A study by Lemay et al.⁴⁶ 10 patients were evaluated in whom laparoscopy (insufflation with carbon dioxide) was performed for tubal ligation. All of these patients had postoperative pneumoperitoneum that was resorbed in the majority at day 3. Two patients had residual intraperitoneal gas as late as 9 days after surgery.

A study by Bryant et al.⁴⁷ 52% of the patients having post-laparotomy free air after biliary tract procedures and with the free air persisting for 2-11 days postoperatively.

In study by Millitz, the frequency of pneumoperitoneum after laparoscopic cholecystectomy was 46%. The pneumoperitoneum was graded as trace in 74% of

these patients and mild (<1 cm) in the remaining 26%. Author found all but one patient showed resorption of the pneumoperitoneum in the first week after surgery, with the remaining case resolving in the second week after surgery.

Pneumoperitoneum was seen less frequently in obese patients in a study and, when present, was often less extensive and resorbed faster than in average-weight and thin individuals. Only 33% of obese patients had pneumoperitoneum postoperatively; in comparison, 62% of patients who were thin or of average weight had this condition. These findings were previously noted for patients after conventional laparotomy^{22,23}. It has been proposed that in asthenic patients, more air is trapped beneath the lower part of the rib cage (partial roof of the peritoneal cavity) when the abdominal muscles are relaxed and the peritoneum is pulled up to close the incision.

CARDIAC FUNCTIONS AND HEMODYNAMIC CHANGES

Mean arterial pressure and heart rate has been shown to be altered by Abdominal insufflation with CO₂. Heart rate and mean arterial blood pressure is commonly increased during laparoscopy.^{48,49} There are various studies on hemodynamic effects of pneumoperitoneum on cardiac function. Several investigators have demonstrated a reduction in cardiac output during pneumoperitoneum^{50,51} whereas others^{52,53} have reported minimal change in cardiac function. A 30% reduction in cardiac index in patients who underwent laparoscopic cholecystectomy has been reported by Westerband et al.⁵⁰

Many factors influence cardiac function including preload, afterload, cardiac contractility, heart rate, and myocardial compliance. The preload is reduced by Hypovolemia and hence reduces cardiac output. Therefore, a euvolemic preoperative volume status is very important to minimize any cardiac depression associated with pneumoperitoneum. Measurement of filling pressures is the most accurate method for

estimation of intravascular volume; however, cardiac filling pressure can be falsely elevated during pneumoperitoneum. The increased intraabdominal pressure during pneumoperitoneum causes cephalad shift of the diaphragm and increases the pleural pressure that is transmitted to the cardiac chambers.

McLaughlin et al ²⁴ also demonstrated that cardiac index decreased by 30% within 30 minutes of initiation of pneumoperitoneum. In a comparative study of cholecystectomy performed by the abdominal wall lifting method versus laparoscopy, Ninomiya et al²⁵ reported that cardiac output was depressed during pneumoperitoneum but not during the abdominal wall lifting technique and suggested that the increased intraabdominal pressure during pneumoperitoneum is the main factor responsible for alteration of cardiac function.

Factors specific to laparoscopy that can affect intraoperative cardiac function include increased intra-abdominal pressure, reverse Trendelenburg positioning, and hypercarbia. Hypercarbia is normally avoided during laparoscopy because of appropriate ventilatory adjustments. In most clinical studies, a moderate rise in PaCO₂ levels (<45 mm Hg) should not contribute to cardiac impairment. In addition, reverse Trendelenburg positioning is not a major factor in alteration of hemodynamic status²⁶. The increased intra-abdominal pressure is the main factor that may account for cardiac depression. The mechanisms for reduction in cardiac output after abdominal insufflation include an increase in afterload and a decrease in preload by impeding venous return. Declan Fleming et al²⁷ reported that the afterload, as measured by systemic vascular resistance, increased by 25% of baseline after abdominal insufflation and decreased with desufflation.

RENAL FUNCTION

The increased intra-abdominal pressure during laparoscopy has been shown to alter renal function. A reduction in intraoperative urine output has been well documented during laparoscopic operations.^(28,29) In a trial comparing laparoscopic adrenalectomy with gasless laparoscopic adrenalectomy, Nishio et al²⁸ demonstrated that urine output decreased significantly with abdominal insufflation and improved upon desufflation. In a swine model, McDougall et al³⁰ demonstrated that the degree of intraoperative oliguria is dependent on the level of increased intra-abdominal pressure; higher intra-abdominal pressures resulted in a greater degree of oliguria. The mechanism for oliguria is related to the acute increased intra-abdominal pressure. In a study of critically ill patients, Kron et al³¹ reported that an acute increase in the intra-abdominal pressure to greater than 25mmHg resulted in acute renal insufficiency and abdominal decompression caused immediate improvement in renal function.

There are several mechanisms for diminished urine output during laparoscopy. Pneumoperitoneum has a direct pressure effect on the renal cortical blood flow. In a swine model, Chiu et al³² reported that superficial renal cortical perfusion decreased by 60% with abdominal insufflation and returned to baseline level after desufflation. Pneumoperitoneum also has a direct pressure effect on the renal vasculature, resulting in reduced renal blood flow. In a swine study, Are et al³³ demonstrated that renal blood flow decreased by 36% below baseline as measured by radioactive microspheres. In addition, intraoperative releases of certain hormones such as anti-diuretic hormone (ADH), plasma rennin activity, and serum aldosterone may diminish urine output. ADH facilitates water reabsorption in the distal tubules and concentrates the urine. Ortega et al³⁴ reported a precipitous rise in ADH concentrations during laparoscopic cholecystectomy, which was not observed during open cholecystectomy.

VENOUS STASIS

The true incidence of deep venous thrombosis after laparoscopic compared with open operation is unknown; however, some of the factors relating to Virchow's triad (endothelial injury, hypercoagulability, and venous stasis) are altered during laparoscopy. The main factor that is adversely affected during laparoscopy is venous stasis. The increased intra-abdominal pressure and reverse Trendelenburg position during laparoscopy have been shown to reduce femoral venous flow.

The increased intra-abdominal pressure during laparoscopy has a direct compressive effect on the inferior vena cava and iliac veins and decreases lower extremity venous flow. By the force of gravity during reverse Trendelenburg position, the abdominal viscera can also produce a compressive effect on the iliac veins resulting in a decrease in femoral venous flow.

In a study of laparoscopic cholecystectomy, Millard et al ³⁵ reported that a combination of pneumoperitoneum and 30° reverse Trendelenburg position decreased peak systolic velocity of the common femoral vein by 42%. Similarly, Idoet al³⁶ reported that abdominal insufflation reduced femoral vein velocity and the addition of reverse Trendelenburg has an additive effect by further reducing femoral vein velocity.

HEPATIC FUNCTION

Various studies observed the effects of pneumoperitoneum on intraoperative portal venous flow and postoperative changes in liver enzymes. In animal and human studies, the increased intra-abdominal pressure at 15 mm Hg has been shown to reduce portal venous flow ³⁷

In a clinical study of laparoscopic cholecystectomy, Jakimowics et al²⁰ reported a 53% reduction in portal blood flow with abdominal insufflation to 14 mm Hg. A reduction in portal venous blood flow during pneumoperitoneum may lead to hepatic hypoperfusion and acute hepatocyte injury. Portal hypoperfusion can lead to transient elevation of liver enzymes. Halevy et al³⁸ reported transient increases in the level of hepatic transaminases (ALT and AST) after laparoscopic cholecystectomy, which returned to baseline by 72 hours postoperatively.

LIVER ENZYME ALTERATIONS AFTER LAPAROSCOPIC CHOLECYSTECTOMY

Elevation of liver enzymes such as AST and ALT after non-complicated laparoscopic cholecystectomy has become a well-known finding which was once considered as incidental. In previous studies, transient hepatic malfunction was suspected. Although the clinical importance of these enzyme elevations has not been clarified.

The normal portal venous pressure is between 7-10mmHg and about half of the hepatic blood flow comes from the portal venous system, 14mmHg of pneumoperitoneum created with CO₂ is stated to be the major cause of transient hepatic ischemia during LC.

Halevy³⁸ et al suggested increased intra-peritoneal pressure, squeezing the liver by cranial retraction of gallbladder during LC, cauterization of the liver bed for hemostasis, manipulation of external bile ducts and effects of general anaesthesia as possible causes of elevation of certain liver enzymes. However, liver retraction for better exposure, manipulation of biliary tract for detecting possible common duct stones, electrocauterization of the liver bed were routinely performed in OC as well.

Güven⁸ investigated the alterations in AST, ALT, GGT, LDH and ALP levels before and 24 hours after the operations in LC patients and compared this change with the OC patients who were anesthetized with the same protocol. AST, ALT, GGT and LDH levels were elevated significantly 24 hours after LC. In LC patients, postoperative mean values of AST, ALT and LDH exceeded the upper limits of normal ranges. However, postoperative enzyme levels were within the normal ranges in patients who underwent OC. When compared with the OC patients the rise in AST, ALT, GGT and LDH levels were still significant for the LC group. In addition to AST and ALT, GGT and LDH were also influenced after LC. LDH elevations might be due to high intraperitoneal pressure making similar effects on intestines by reducing the mesenteric venous flow causing passive venous congestion.

Morino et al investigated the duration of pneumoperitoneum at constant pressure and found that when the duration of operation exceeds 60 minutes, elevations in AST and ALT levels become more significant.³⁹ Studies comparing the enzyme changes between LC and non-cholecystectomy laparoscopic operations were also conducted to examine effects of a pneumoperitoneum on these changes more accurately, excluding the other possible factors such as liver tissue damage and biliary tract manipulations that might interfere with results.

In a study comparing hepatic enzyme alterations in LC, gasless LC and LC under low pressure (below 10mmHg) pneumoperitoneum, Giraud et al found significant enzyme level rises after LC that are not seen after gasless or low pressure LC, underlining the absolute effect of intraperitoneal pressure on hepatic perfusion by means of enzyme level changes

Hasukic et al⁶³, in their randomized study comparing the effects of low and high pressure pneumoperitoneum on liver functions, stated that AST and ALT

elevations were significantly higher in patients operated under high pressure (14mmHg) pneumoperitoneum than those under low pressure (7mmHg).

The same significant enzyme level elevations were also observed in laparoscopic colectomy patients suggesting that a pneumoperitoneum plays the key role in transient hepatic ischemia causing enzyme elevations.^{39,40} Preoperative and postoperative levels of AST, ALT, GGT, ALP, LDH, prothrombin time and bilirubin have been investigated in various studies to determine the physiological basis of hepatic malfunction.^{10,58,61} However significant elevations after LC compared with OC have been defined for only AST and ALT levels. Time controlled studies have shown that these enzyme elevations last for about 3 days postoperatively and the significance between LC and OC values fade away after 2 days.

COMPARISON OF LC AND OC

Tan⁴⁰ tested the liver function of patients who underwent LC or OC. Author suggested that transient postoperative hypertransaminases in LC patients might be attributed to the following possible factors. The first factor of consideration was CO₂pneumoperitoneum. A second possible mechanism for alterations of serum liver enzymes after LC is the "squeeze" pressure effect on the liver. The traction of the gallbladder may free these enzymes into the blood stream. The third possibility may be the local effect of prolonged use of diathermy to the liver surface and spread of heat to liver parenchyma. In addition, transient liver dysfunction occurs in patients after some general anesthesia Another possible mechanism of alterations of serum liver enzymes that had been considered was the inadvertent clipping of the right branch of the hepatic artery or any other aberrant arterial branch supplying blood to the liver.

According to Halevy³⁸, the mechanism for alter enzymatic changes is unclear.

However, he postulate several possible explanations for this:

1. Increased intra-abdominal pressure should be proved by further studies in patients in whom pneumoperitoneum is created for purposes other than LC.
2. The "squeeze" pressure effect on the liver by the traction of the gallbladder may free these enzymes into the blood stream. But this should be studied using an animal model to determine the response.
3. Prolonged use of diathermy to the liver surface and spread of heat to the liver parenchyma. Some surgeons use diathermy to excise the gallbladder while performing open cholecystectomy.
4. Pulling on the gallbladder creates a transient kink in the extrahepatic ducts, which could induce an increase in the endoluminal pressure and a subsequent increase in enzyme levels.
5. Another issue is the passage of a small stone.
6. Inadvertent clipping of the right branch of the hepatic artery, or any other aberrant arterial branch supplying blood to the liver.
7. The combination of more than one cause.

MATERIALS AND METHODS

This prospective study was conducted to evaluate the effect of laparoscopic procedures on liver function. This study was carried out at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre

STUDY DESIGN:

This was a prospective study on Indian population. The study was carried out in 100 patients of cholelithiasis who underwent laparoscopic cholecystectomy in **KLES DR. PRABHAKAR KORE HOSPITAL, BELGAUM.**

STUDY PERIOD AND DURATION:

The present study was carried out for a period of one year from January 2013 to December 2013

Source of data:

Patients scheduled for elective cholecystectomy were included in the study.

Sample size:

The study sample was comprised of 100 patients of cholelithiasis who underwent elective laparoscopic cholecystectomy.

Sampling procedure:

Applying thumb rule, 100 cases of cholelithiasis who underwent elective laparoscopic cholecystectomy were taken up for study.

Ethical clearance:

The ethical clearance was obtained from institutional ethics committee, Jawaharlal Nehru Medical College, Belgaum prior to commencement.

Informed consent:

Those patients who fulfilled selection criteria were explained about the nature of study and a written informed consent was obtained prior to the enrolment.

STUDY METHODS:

The study was conducted with following objectives.

Objective:

1. To study the incidence of alteration in liver function following laparoscopic cholecystectomy in the Indian population.
2. To study the significance of these alterations in patients and the safety of the Procedure.

All the patients studied were selected for laparoscopic procedures after they underwent routine history taking, physical examination and investigations to exclude pre-existing liver diseases or generalized debility.

Inclusion Criteria:

- All patients undergoing laparoscopic cholecystectomy at our hospital
- The patients who have given written consent to be part of the study group
- The patients who were willing to comply with study protocol
- All the patients selected for the study had normal values of serum liver enzymes prior to the operations.

Exclusion Criteria:

- Any patient with pre-operative abnormality in liver enzymes
- Suspected or coexisting chronic liver diseases
- Common bile duct pathology
- Conversion to open cholecystectomy
- Hematological Disorders
- Intra – Operative Complication – bile duct injury
- Obstruction, infection, leakage and high grade fever in the post-operative period.

- Cases who had undergone endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic sphincterotomy within one week before the surgery.
- Incomplete data.

STUDY PROCEDURES

All patients with cholelithiasis undergoing laparoscopic cholecystectomy were invited to participate in the study and written informed consent was taken. All patients underwent a standard clinical and laboratory evaluation that includes briefly information about age, sex, address and routine investigation including ultra sound abdomen, which are done pre operatively.

Pre-operative investigations include liver function tests ALT, AST, alkaline phosphatase, and bilirubin(total), total proteins, serum albumin.

The subject satisfying inclusion and exclusion criteria were enrolled in the study. All such patients underwent LC.

The liver function tests were further done 24 hrs later and in some patients liver function test were repeated to monitor liver function. Along with, adverse events were noted in all the patients. The patients who developed intra-abdominal complications were excluded from the study.

STATISTICAL ANALYSIS:

- Demographic data were presented in mean and SD.
- All liver function tests parameter (ALT, AST, alkaline phosphatase, total proteins ,serum albumin, and bilirubin (total) was presented in mean and SD.
- Paired t test was applied to all liver function tests parameter to measure the significant change in liver function.

Appropriate statistical analysis was applied for comparing the incidences of adverse events and other complications. Additional exploratory (parametric as well as non-parametric) analysis of the data was performed as deemed essential by using appropriate statistical tests.

RESULTS

We studied 100 patients who underwent laparoscopic cholecystectomy from January 2013 to December 2013. 54 patients were females and 46 were males. The mean age was 48 years.

We observed significant increase in Bilirubin (total), AST, ALT, ALP and total proteins, serum albumin after performing laparoscopic cholecystectomy as compared to baseline values.

Bilirubin (total) pre operative was 0.66 ± 0.18 mg/dl , increased 24 hours after surgery to 1.18 ± 0.29 mg/dl (p value <0.0001)

SGOT and SGPT (AST and ALT respectively) were found to be significantly elevated from 24.5 ± 8.76 U/l to 40.9 ± 10.34 U/l (p value <0.0001) and from 30.9 ± 7.63 U/l to 53.5 ± 17.13 U/l (p value <0.0001) respectively.

Alkaline phosphatase showed elevation from pre operative values of 112.5 ± 38.11 U/l to 154.3 ± 39.15 U/l after 24 hours (p value <0.0001).

Total proteins showed a decrease from preoperative values of 6.85 ± 0.55 g/dl to 5.96 ± 0.49 g/dl after 24 hours (p value <0.0001).

Serum albumin showed a decrease from preoperative values 4.04 ± 0.39 g/dl to 3.19 ± 0.38 g/dl after 24 hours (p value <0.0001).

Paired t test applied. P value is significant if <0.05 , highly significant if <0.001

TABLE-1**Mean Age**

Parameter	Mean±SD
Age	47.8±10.80

TABLE-2

Sex distribution

Sex	Frequency	Percent
Female	54	54%
Male	46	46%
Total	100	100

GRAPH- 1

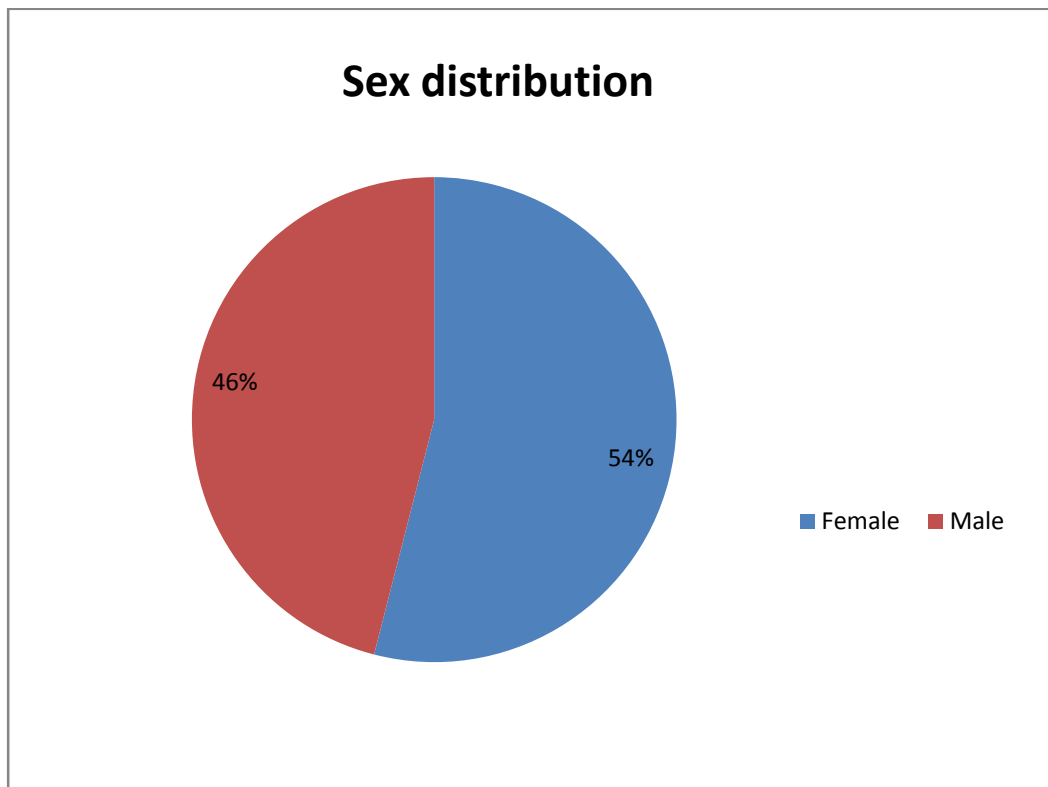


TABLE-3

SERUM TOTAL BILIRUBIN LEVELS PAIRED SAMPLES STATISTICS

Serum Total bilirubin	N	Mean (mg/dl)	SD	Mean Diff.	t	P
Pre op	100	0.66	0.18	-0.51	-18.086	<0.0001
Post op	100	1.18	0.29			

GRAPH- 2

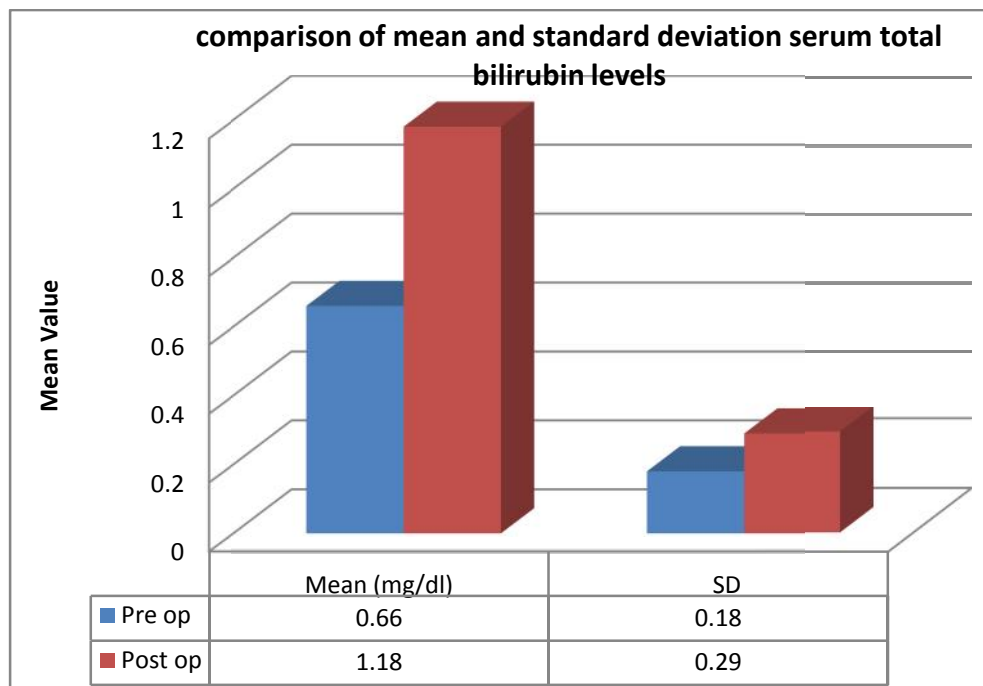


TABLE-4

SERUM ALP LEVELS PAIRED SAMPLES STATISTICS:

Alkaline phosphatase	N	Mean (U/ l)	SD	Mean Diff.	t	P
Pre op	100	112.50	38.11	-41.8	-11.787	<0.0001
Post op	100	154.3	39.15			

GRAPHS- 3

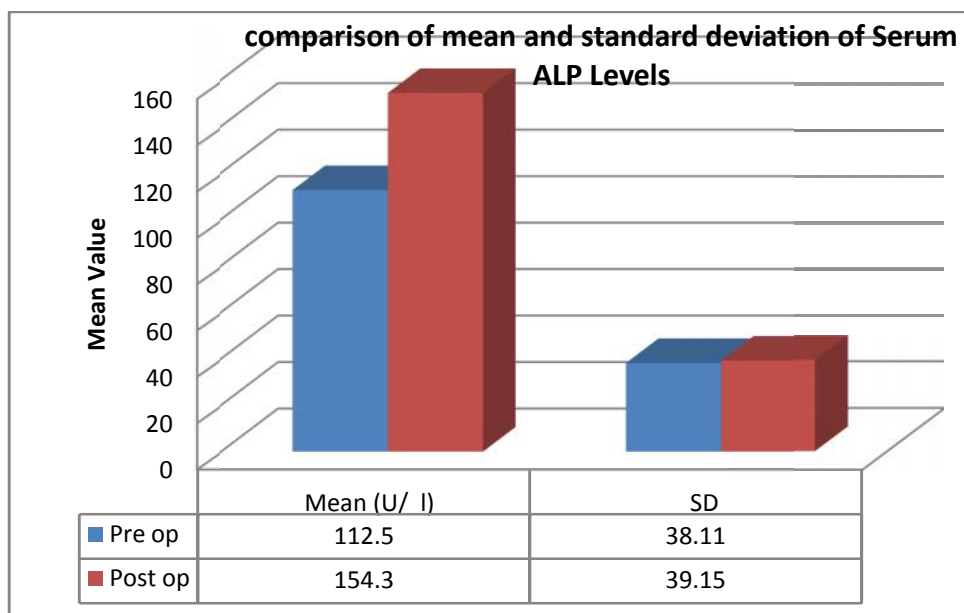


TABLE-5
SERUM AST LEVELS PAIRED SAMPLES STATISTICS

SERUM AST	N	Mean (u/l)	SD	Mean Diff.	t	P
Pre op	100	24.58	8.76	-16.4	-14.110	<0.0001
Post op	100	40.9	10.34			

GRAPHS- 4

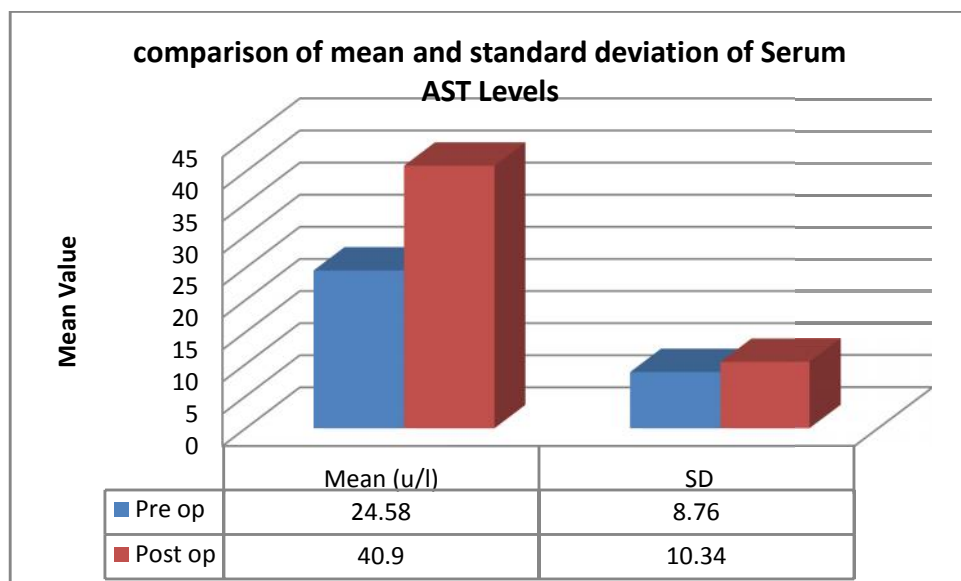


TABLE-6

SERUM ALT LEVELS PAIRED SAMPLES STATISTICS:

Serum ALT	N	Mean (u/l)	SD	Mean Diff.	t	P
Pre op	100	30.9	7.63	-22.6	-12.96	<0.0001
Post op	100	53.5	17.13			

GRAPH 5

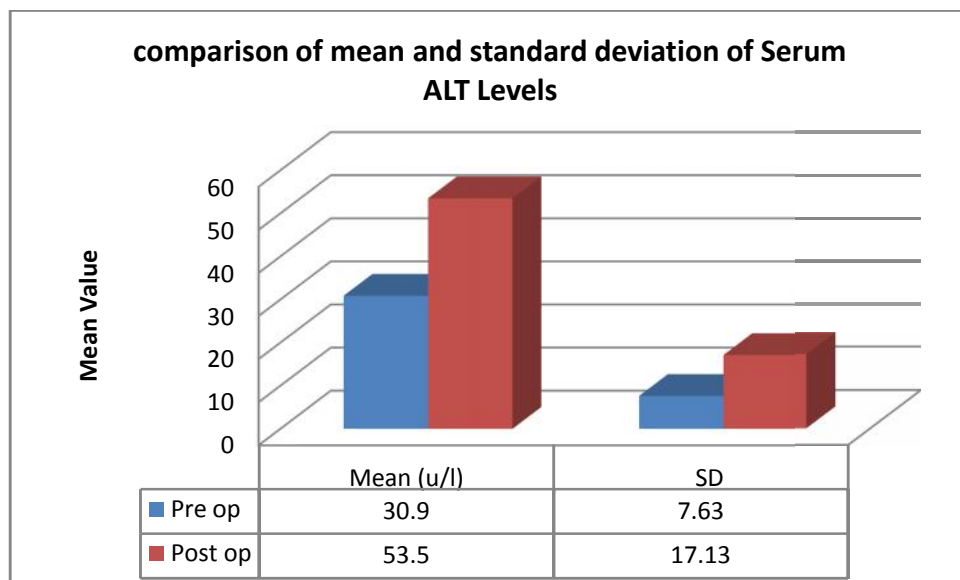


TABLE-7

TOTAL PROTEINS LEVELS PAIRED SAMPLES STATISTICS

Total proteins	N	Mean (g/dl)	SD	Mean Diff.	t	P
Pre op	100	6.85	0.55	-0.88	-17.030	<0.0001
Post op	100	5.96	0.49			

GRAPH 6

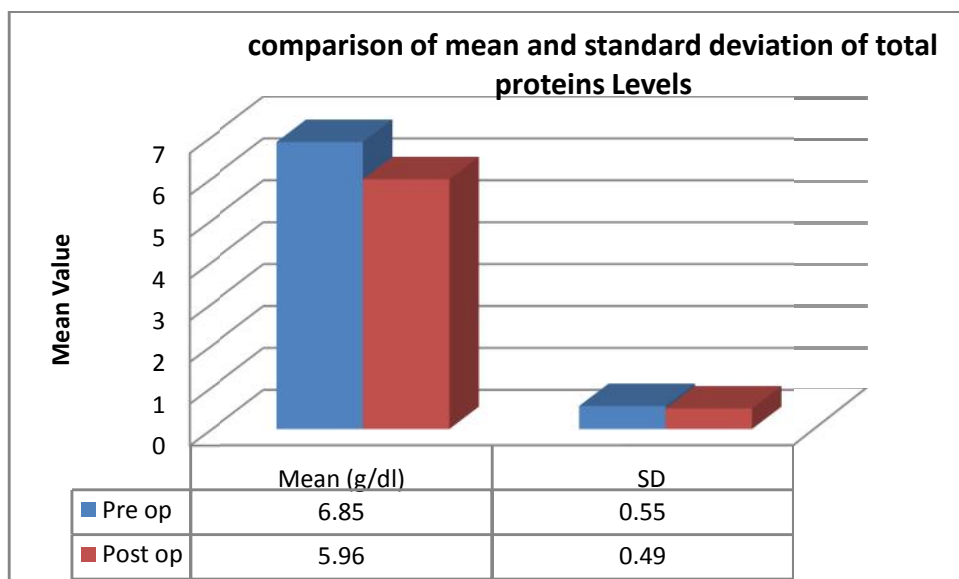
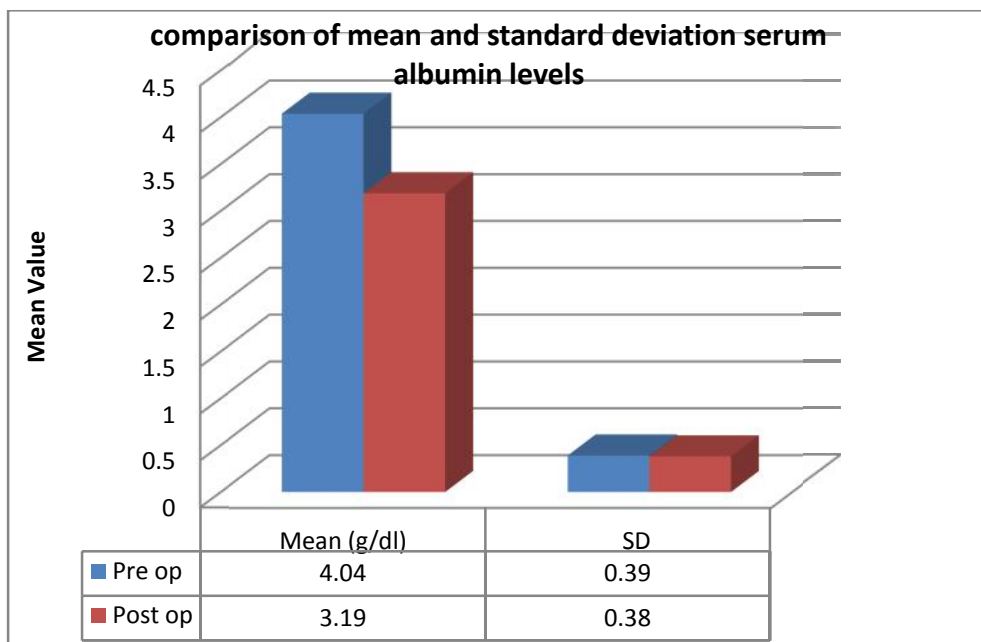


TABLE-5

SERUM ALBUMIN LEVELS PAIRED SAMPLES STATISTICS:

Serum albumin	N	Mean (g/dl)	SD	Mean Diff.	t	P
Pre op	100	4.04	0.39	-0.85	-18.030	<0.0001
Post op	100	3.19	0.38			

GRAPH 7



DISCUSSION

The introduction of laparoscopic surgery has changed dramatically the management of gallstone disease establishing the laparoscopic cholecystectomy as the method of choice for treating uncomplicated cholelithiasis. For over 25 years, laparoscopic cholecystectomy (LC) has replaced open cholecystectomy (OC) in the management of benign gallbladder diseases and has become the gold standard for symptomatic cholelithiasis. As it gained worldwide popularity, it has become one of the most common operations performed in general surgical practice.

Although LC offered many advantages over laparotomy, new concerns arose regarding the effects of a pneumoperitoneum on the cardiovascular and respiratory system.⁴¹ Laparoscopic cholecystectomy has been accepted as an alternative to laparotomy, but there is still controversy regarding the effects of pneumoperitoneum on splanchnic and hepatic perfusion.⁴²

However, the application of carbon dioxide pneumoperitoneum in high-risk patients may induce undesirable consequences in critically ill patients with cardiovascular, respiratory or renal insufficiency due to either hypercapnia or increased intraabdominal pressure.⁴⁵

The use of diathermy which may induce thermal damage to hepatic parenchyma, or the use of anaesthetic medications some of which might influence visceral blood flow have been addressed for these enzymatic changes. However, their effect is debatable, since both factors are used in the same manner in laparoscopic as well as in open cholecystectomy.

The occurring pathophysiological changes may be due to both carbon dioxide insufflation and increased intraabdominal pressure. Carbon dioxide, has high solubility in the blood and may cause hypercapnia with respiratory acidosis resulting

in increased heart rate, arterial pressure and systemic peripheral resistances.¹¹ The increased intraabdominal pressure on the other hand, affects the cardiovascular system by compressing inferior vena cava and pericardium, and thus decreasing directly the venous blood return to the right atrium and the cardiac output. The usual level of intraabdominal pressure (12-14 mm Hg) is higher than that of portal vein system (7-10 mm Hg); consequently, it may lead to reduction of portal blood flow and abnormalities in liver.^{56,57}

Disturbances in liver enzymes after laparoscopic cholecystectomy were first studied by Halevy et al³⁸ in 1994. The possible explanations included

1. Increased intraabdominal pressure
2. Squeeze pressure effect on the liver,
3. Excessive use of diathermy, pulling on the gallbladder, or
4. Passage of microcalculi into the bile duct..

More work was performed to evaluate the causes of this alteration after laparoscopic procedures, and it was found that low pneumoperitoneum pressure was associated with fewer adverse effects on liver function. The pneumoperitoneum pressure used for laparoscopic cholecystectomy is higher than the pressure in the portal venous system. This pressure impedes portal circulation and reduces portal flow up to 50%, which may cause depression of the hepatic reticular endothelial system. This observation explains why the change in liver function tests is related to the duration and pressure used for the pneumoperitoneum.

Though the exact mechanism for changes in liver enzyme is not known, following several mechanisms are cited to explain the condition.

1. The "squeeze" pressure effect on the liver by the traction of the gallbladder may free these enzymes into the blood stream. But this should be studied using an animal model to determine the response.
2. Prolonged use of diathermy to the liver surface and spread of heat to the liver parenchyma. Some surgeons use diathermy to excise the gallbladder while performing open cholecystectomy.
3. Pulling on the gallbladder creates a transient kink in the extrahepatic ducts, which could induce an increase in the endoluminal pressure and a subsequent increase in enzyme levels.
4. Another issue is the passage of a small stone.
5. Inadvertent clipping of the right branch of the hepatic artery, or any other aberrant arterial branch supplying blood to the liver.
6. The combination of more than one cause.

According to Tan et al¹¹, The level of serum ALT and AST increased significantly during the first 48 hours post operations in both LC and LCR patients. However, no significant change of the serum liver enzymes was detected in both OC and OCR patients. As a result, there was statistically significant difference in change of both ALT and AST levels between

LC and OC patients and LCR and OCR patients, respectively. By the 7th day post operation, the level of both enzymes returned to normal values in LC, OC and OCR patients except LCR patients whose enzymes remained at a higher level.

According to H. Baris Eryilmaz et al.⁵⁴, the results show that 14mmHg pressure pneumoperitoneum decreased the blood flow to the liver and increased postoperative 1st-hour serum AST and ALT levels. 10mmHg pressure pneumoperitoneum is superior to 14mmHg pressure pneumoperitoneum in laparoscopic cholecystectomy.

Jakimowicz et al showed that 14mmHg of intra-peritoneal pressure reduced the portal blood flow by 53% using the Doppler technique⁽⁶⁴⁾.

Hasukic et al, in their randomized study comparing the effects of low and high pressure pneumoperitoneum on liver functions, stated that AST and ALT elevations were significantly higher in patients operated under high pressure (14mmHg) pneumoperitoneum than those under low pressure (7mmHg)⁶³

In our study of 100 subjects of mean age of 47years, we observed significant increase in Bilirubin (total), Bilirubin, AST,ALT, ALP and decrease of serum albumin and total proteins after performing laparoscopic cholecystectomy as compared to baseline values. The finding of our study is in the line with the reported literature. However, the clinical importance of these enzyme elevations has not been clarified.

MedhatMoustafa et al,⁵⁵ showed that Disturbances of liver functiontests following laparoscopic cholecystectomy had been previously reported although their etiology still remained uncertain. Electrocautery, general anaesthesia, and the vasoconstrictive effect of CO₂ also cause reduced visceral blood flow may also have a role. In this study, it was found that all liver function tests which include AST,ALT, GGT, alkaline phosphatase, and bilirubin showed a transient rise in their values and in majority of cases these values went back to normal level in 48 to 72 hours following surgery.

Various studies investigated determined the physiological basis of hepatic malfunction.^{58,59,60} However significant elevations after LC compared with OC have been defined for only AST and ALT levels. Studies have shown that these enzyme elevations last for about 3 days postoperatively and the significance between LC and OC values fade away after 2 days.^{61,62}

In our study, all the patients were discharged within four days after surgery. No patients developed any complication or significant disability or adverse event. These signify that the changes in the liver enzymes are transient and recovered without any sequelae.

To conclude, our present study demonstrated that bilirubin (total), AST, ALT, ALP elevations and decrease in total protein and serum albumin could occur after LC. When analyzed together with the data collected from previous studies, these changes may be attributed to the reduction of portal venous flow under high pressures of a pneumoperitoneum.

There has been no proof to state that these enzyme changes are reflecting a true hepatic or other organ ischemia in otherwise healthy patients since all patients recovered without any sequelae within 5 days. However, surgeons should be cautious before planning to perform LC in patients with known hepatic insufficiency. LC performed under a low pressure pneumoperitoneum or gasless LC using abdominal wall retractors might be feasible in these patient populations.

CONCLUSION

Laparoscopic cholecystectomy has replaced open cholecystectomy in the management of benign gallbladder diseases and has become the gold standard for symptomatic cholelithiasis. It is also the procedure of choice for most patients referred for elective cholecystectomy. It offers many advantages over open cholecystectomy. Transient reduction in hepatic blood flow, which is caused by pneumoperitoneum. These changes may be attributed to the reduction of portal venous flow under high pressures of a pneumoperitoneum. These result in elevation in liver enzymes bilirubin (total), AST, ALT, ALP and decrease in levels of total proteins and serum albumin. However, clinically it is not found to have any significant effect. However, surgeons should be cautious before planning to perform LC in patients with known hepatic insufficiency.

SUMMARY

The laparoscopic cholecystectomy, a minimal-access approach surgery, offers many advantages that include a markedly reduction in hospital stay and decreased cost. Laparoscopic cholecystectomy has replaced open cholecystectomy (OC) in the management of benign gallbladder diseases and has become the gold standard for symptomatic cholelithiasis.

Although LC offered many advantages over laparotomy, new concerns arose regarding the effects of a pneumoperitoneum on the cardiovascular and respiratory system. These changes are well tolerated even in older and more debilitated patients, and except for a slight increase in the incidence of cardiac arrhythmias, no other significant cardiovascular complications occur.

One of the important hemodynamic changes is the transient reduction in hepatic blood flow caused by a pneumoperitoneum. The pressure of a created pneumoperitoneum and its duration was shown to influence the degree of hepatic ischemia. This results in elevations in liver enzymes ALT, AST, alkaline phosphatase, bilirubin, and reduction in total proteins and serum albumin. Though, the LC is associated with transient elevation of liver enzymes, the disturbances after LC are self-limited and not associated with any morbidity in patients with a normal liver function.

We observed significant increase in Bilirubin (total),AST,ALT,ALP after performing laparoscopic cholecystectomy as compared to baseline values.

Though the exact mechanism for changes in liver enzymes is not known, following several mechanisms are cited to explain the condition.

The "squeeze" pressure effect on the liver by the traction of the gallbladder may free these enzymes into the blood stream.

Prolonged use of diathermy to the liver surface and spread of heat to the liver parenchyma. Some surgeons use diathermy to excise the gallbladder while performing open cholecystectomy.

Pulling on the gallbladder creates a transient kink in the extrahepatic ducts, which could induce an increase in the endoluminal pressure and a subsequent increase in enzyme levels.

Passage of a small stone.

Inadvertent clipping of the right branch of the hepatic artery, or any other aberrant arterial branch supplying blood to the liver. The combination of more than one cause.

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- Transumbilicalgelport access technique for performing single incision laparoscopic surgery (sils) Journal of gastroenterology surgery, january 2009, volume 13, [issue 1](#), pp 159-162

17. douglas e.jakimowott, md, [contributors](#) | [main](#) | [chapter 25. Laparoscopic hysterectomy](#) »Pneumoperitoneum: production, management, effects and consequences
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INFORMED CONSENT

Title of Research Study: An Observational study of effect of carbon dioxide pneumoperitoneum on liver function test in laparoscopic cholecystectomy

Principal Investigator:-

Co-investigator:-

Associate Professor

Post Graduate Student,

Department Of General Surgery,

Department Of General Surgery,

J.N.Medical College, Belgaum.

J.N.Medical College, Belgaum.

You are requested to participate in a study, that is, an attempt to find out the effect of carbon dioxide pneumoperitoneum on liver function test in laparoscopic cholecystectomy.

The laparoscopic surgery is performed by the insufflation of gas into the peritoneal cavity. During most of the surgery, a pneumoperitoneum of 12 to 14 mmhg carbon dioxide is established. One of the important hemodynamic changes is the transient reduction in hepatic blood flow caused by a pneumoperitoneum. This results in elevation of liver enzymes. Though the LC is associated with transient elevation of liver enzymes, the disturbances after LC are self-limited and not associated with any morbidity in patients with normal liver function.

In an effort to know the effect of carbon dioxide pneumoperitoneum on liver function test in laparoscopic cholecystectomy, this observational study is carried out.

This study will be conducted by _____, Post Graduate in Department of Surgery, under the direct supervision and guidance of _____ Associate Professor, Department of Surgery, J. N. Medical College, Belgaum.

You need to be eligible, meeting all the selection criteria to participate in this study. You should be willing to provide information about yourself. 60 subjects will be enrolled in this study in whom liver function test is done before and 24hrs after laparoscopic cholecystectomy.

If you agree to participate in this study, liver function test will be done 24hrs before and after laparoscopic cholecystectomy..

Taking part in the study will not affect the cost of treatment i.e. it will be similar to the cost of standard procedure. In the event that you become injured as a result of taking part in this study, treatment will be offered to you or you will be given information about where to receive medical care: but you/your insurance company will be responsible for the costs. However, no reimbursement, compensation or free medical care will be given.

Every effort will be made to protect the confidentiality of the information you provide. This means that the researchers will not let anyone, not a part of the study, see the information you provide. Only _____ and _____ will have access to the information collected. Results of this study may be published but your name will not be revealed.

Taking part in this study is voluntary; you may choose not to enroll in this study. Your decision will not change the present or future health care services offered to you at KLES Dr. Prabhakar kore Hospital, Belgaum. The alternative that you have is to undergo the traditional procedure that is carried out in KLES Hospital.

If you have any queries about the study, you may contact (_____); (Mobile _____). If you need any further information regarding your rights as a study participant, you may also contact _____ , Chairman of Institutional Ethics Committee, JNMC, Belgaum

CONSENT FOR PARTICIPATION IN RESEARCH STUDY

Mr/Mrs/Miss. _____

_____ we are requesting you to enroll yourself in study titled–“**AN OBSERVATIONAL STUDY ON EFFECT OF CARBON DIOXIDE PNEUMOPERITONEUM ON LIVER FUNCTION TESTS IN LAPAROSCOPIC CHOLECYSTECTOMY**”

Conducted by _____ Post Graduate in M.S. General surgery under the guidance of _____, Associate Professor, Department of General Surgery, J.N. 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 you will be asked some questions regarding your present complaint and you are supposed to answer to the best of your knowledge.

Your participation in research is voluntary. Your decision whether or not to participate in the study will not affect your relationship with J.N.MedicalCollege. If you decide to participate you are free to withdraw at any time. The purpose of research is

–“**AN OBSERVATIONAL STUDY ON EFFECT OF CARBON DIOXIDE PNEUMOPERITONEUM ON LIVER FUNCTION TESTS IN LAPAROSCOPIC CHOLECYSTECTOMY**”

Procedure Involved:

If you agree to enroll yourself in my study, you will be interviewed regarding your present, past and family history, then you will be clinically examined in detail

and investigated accordingly. Your Liver Function Test will be done 24hours before and 24hours after laparoscopic cholecystectomy .

Voluntary Participation/Withdrawal:

Taking part in the study 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 hospital.

Alternatives:

Even if you decline the participation in the study, you will get the routine line of management.

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.

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 you will remain confidential.

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.

Compensation:

In the event of injury related to the study, treatment will be made available through KLES Hospital & MRC, Belgaum. There is no compensation or payment for such medical treatment by law. If you are injured you may contact

at Department of General Surgery, KLES Hospital& MRC or by Ph.

No:

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 _____, Department of General Surgery, KLES Hospital and MRC, Ph. No. _____ or phone number: _____ or _____ Associate 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 _____ Prof. & Head of Pathology as Chairman of J. N. Medical College Institutional Ethical Committee of Human Subjects Research, Phone No. _____ at J. N. Medical College, Belgaum

Consent for participation in research trial

I, _____ 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 form 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 : _____

**“AN OBSERVATIONAL STUDY ON EFFECT OF CARBON DIOXIDE
PNEUMOPERITONEUM ON LIVER FUNCTION TESTS IN
LAPAROSCOPIC CHOLECYSTECTOMY”**

Family History :

GENERAL PHYSICAL EXAMINATION:

Built and Nourishment:

Weight:

Pallor / Icterus / Cyanosis / Clubbing / Edema / Lymphadenopathy

Vital Signs : PR: /min; BP: mmHg; RR: /min; Temp:

SYSTEMIC EXAMINATION:

Per Abdomen examination:

Respiratory System:

Central Nervous System:

Cardio-Vascular System:

ONS:	24 hours before surgery	24hours after surgery
Total bilirubin		
Direct bilirubin		
SGOT		
SGPT		
Alkaline phosphatase		
Total proteins		
Serum albumin		