"COMPARATIVE STUDY OF CHANGES IN COAGULATION PROFILE IN PATIENTS UNDERGOING LAPAROSCOPY CHOLECYSTECTOMY USING CARBONDIOXIDE- PNEUMOPERITONEUM BEFORE AND AFTER SURGERY."

BY

REG NO: BH0121010

Dissertation

Submitted to
KAHER, Belagavi, Karnataka,
In partial fulfilment of the requirements for the degree of

MASTER OF SURGERY (M.S.)

in

GENERAL SURGERY

DEPARTMENT OF GENERAL SURGERY
JAWAHARLAL NEHRU MEDICAL COLLEGE,
KAHER, BELAGAVI – 590010
KARNATAKA.

DECEMBER-2024 / JANUARY -2025

KLE ACADEMY OF HIGHER EDUCATION AND RESEARCH,

BELAGAVI, KARNATAKA.

Endorsement

This is to certify that the dissertation entitled **Comparative study of changes in coagulation profile in patients undergoing laparoscopy cholecystectomy using carbon dioxide pneumoperitoneum before and after surgery** is a bonafide research work done by **REG NO. BH0121010**

Dr. SHRISHAIL C. METGUD,MS

Professor & Head,

Department of General Surgery,

KAHER's J. N. Medical College,

Belagavi

Professor & HOD
Dept. of General Surgery
J.N. Medical College, BELAGAVI.

Date: 01/07/24

Place: Belagavi

Dr. N. S. MAHANTASHETTI,MD

Principal,

KAHER's J. N. Medical College,

Belagavi

PRINCIPAL
J.N. Medical College,
BELAGAVI- 590 010

KAHER BELAGAVI J.N. MEDICAL COLLEGE

Date: 1/07/24

Place: Belagavi

UNDERTAKING

I, **REG NO: BH0121010** here by declare that the information and the data mentioned in my dissertation entitled **"COMPARATIVE STUDY OF CHANGES IN COAGULATION PROFILE IN PATIENTS UNDERGOING LAPAROSCOPY CHOLECYSTECTOMY USING CARBONDIOXIDE-PNEUMOPERITONEUM BEFORE AND AFTER SURGERY."** belongs to me and is original. I am aware of the definition of Plagiarism as detailed below:

- An act or instance of using are closely imitating the language and thoughts of another author without authorization and the representation of that authors work as one's own, as by not crediting the original author.
- A piece of writing or other work reflecting such unauthorised use or imitation.
- The deliberate or reckless representation of another's words, thoughts, or ideas as one's own without attribution in connection with submission of academic work, whether graded or otherwise.

I hereby declare that the dissertation prepared by me is original-one and does not involve plagiarism anywhere. In case at a later stage, it is found that I have indulged in plagiarism, then, I am solely responsible for the same and the institution is at liberty to take any disciplinary action against me including cancellation of dissertation or any other penalties imposed by the university.

Date: 2/7/24

Place: Belagavi

REG NO: BH0121010

PLAGIARISM CLEARANCE

KLE ACADEMY OF HIGHER EDUCATION AND RESEARCH

JAWAHARLAL NEHRU MEDICAL COLLEGE

(A constituent unit of KLE Academy of Higher Education & Research Deemed-to-be-University)

(Recognized by National Medical Commission, New Delhi)

Accredited 'A+' Grade by NAAC (3rd Cycle) **Placed in Category 'A' by MoE (GoI)**

Nehru Nagar, Belagavi- 590 010, Karnataka, INDIA

0831 – 2471350 0831 – 2470759 www.jnmc.edu principal@jnmc.edu

Ref No: MDC/PG/ Date: 29-06-2024

"ACCEPTANCE LETTER"

The softcopy of thesis entitled: **"COMPARATIVE STUDY OF CHANGES IN COAGULATION PROFILE IN PATIENTS UNDERGOING LAPAROSCOPY CHOLECYSTECTOMY USING CARBON DIOXIDE PNEUMOPERIOTNEUM BEFORE AND AFTER SURGERY"** has been submitted for anti-plagiarism check through Turnitin software. The scan has been carried out and the scanned output reveals a match percentage of **01%** which is within the acceptable limits of **10%** as per the guidelines given by UGC.

Guide.

KAHER BELAGAVI J.N. MEDICAL COLLEGE

Dr. (Mrs.) N.S. Mahantashetti.
Chairperson-Antiplagiarism Committee &
Principal,
J. N. Medical College, Belagavi.

To,
Reg. No. BH0121010
Postgraduate Student,
2021-22 Batch,
Department of General Surgery
J. N. Medical College, Belagavi.

ETHICAL CLEARANCE

K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH
(Deemed – to- be- University)
Accredited 'A+' Grade by NAAC in (3rd Cycle) Placed in Category 'A' by MHRD (GoI)
JNMC INSTITUTIONAL ETHICS COMMITTEE
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)
Website: http//www.jnmc.edu
E-Mail : dome@jnmc.edu
Phone: (+ 91-(0)831 Office : 2472550
Principal: 2471701
Fax No. +91 (0)831 – 2470759

Ref No.MDC/JNMCIEC/ 09 **Date: 27/09/2022**

To,

REG NO: BH0121010
PG Student in General Surgery,
J. N. Medical College,
BELAGAVI.

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"COMPARATIVE STUDY OF CHANGES IN COAGULATION PROFILE IN PATIENTS UNDERGOING LAPAROSCOPY CHOLECYSTECTOMY USING CARBONDIOXIDE- PNEUMOPERITONEUM BEFORE AND AFTER SURGERY.",** is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee.

(Dr. Smita Sonoli)
Member Secretary
JNMC Institutional Ethics Committee
J.N.Medical College, Belagavi.

(Dr. Harsha Hegde)
Chairman,
JNMC Institutional Ethics Committee
J.N.Medical College, Belagavi

LIST OF ABBREVIATIONS.

JNMC	Jawaharlal Nehru Medical College
KAHER	KLE Academy of Higher Education and Research
KLE	Karnataka Lingayat Education
LC	Laparoscopic cholecystectomy
DVT	Deep Vein Thrombosis
INR	International Normalized Ratio
PT	Prothrombin Time
APTT	Activated Partial Thromboplastin Time
LMWH	Low Molecular Weight Heparin
CO2	Carbon di oxide

ABSTRACT

Background: Minimally invasive surgery has become the procedure of choice for many disorders, laparoscopic cholecystectomy being the most commonly performed operation. In order to achieve better visibility of the surgical field, the ‘‘CO2 pneumoperitoneum technique’’ is used. There are many advantages to LCs such as a shorter hospitalization time, minimal postoperative pain and an easy recovery. However, there are also a few systemic disadvantages due to increase in intra-abdominal pressure.

Aim-To determine the changes in coagulation profile of patients undergoing laparoscopic cholecystectomy using carbon di oxide pneumoperitoneum.

To determine if patients undergoing laparoscopic cholecystectomy have to be started on prophylaxis for deep vein thrombosis to prevent complications.

Materials & Methods- A total of 27 eligible patients were evaluated in in an observational study over a period of one year in tertiary care hospital Detailed history, clinical examination and basic routine investigations will be done for all the participants in the study. A total of 3 cc of blood will be drawn under strict aseptic precautions. One sample will be taken prior to surgery and the other sample 6 hours after onset of pneumoperitoneumSamples will be processed for prothrombin time and D-dimer in pateints undergoing laparoscopic cholecystectomy.

Results: Our study concludes that due to pneumoperitoneum as due to activation of coagulation cascade mechanism Preoperatively mean D-Dimer was 152.53 where as post operatively mean D-Dimer was 301.48 and preoperatively mean

PROTHROMBIN TIME/INR was d O.98 where as post operatively mean PROTHROMBIN TIME/INR was 1.04.

Conclusion: When pre- and post-operative data from the same group were compared, laparoscopy caused statistically significant changes in the coagulation parameters. The increase in these values indicates the tendency of the inflammatory process caused by either pneumoperitoneum or surgical stress, even though the small sample size makes it impossible to draw firm conclusions. Yes, one of the most discussed and still highly contentious topics is the thrombotic risk associated with laparoscopic surgery.furthur studies are required to find out about anticoagulation prophylaxis

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF GRAPHS

INTRODUCTION

[1]Cholelithiasis is the most common biliary pathology. Gallstones are present in 10 to 15% of the general population and asymptomatic in the majority (>80%).The prevalence of gallstone varies widely in different parts of the world. In India it is estimated to be around 4%.

Changing incidence in India is mainly attributed to westernization and availability of investigation that is ultrasound in both rural and urban areas and due to change in socioeconomic structure. Approximately 1-2% of asymptomatic patients will develop symptoms requiring cholecystectomy per year.

Cholelithiasis is rare in the first two decades. Incidence gradually increases after 21 years and reaches its peak in 5^{th} and 6^{th} decade. Women are more affected than men in the ratio of 4:1.[4] In 1992, The National Institute of Health (NIH) [58] consensus development conference stated that laparoscopic cholecystectomy "provides a safe and effective treatment for most patients with symptomatic gallstones."[5]

Laparoscopic cholecystectomy has become the gold standard in the treatment of gallbladder pathology and is replacing open cholecystectomy. The rate of conversion from laparoscopic cholecystectomy to open cholecystectomy is 5 to 10%.[6]

After almost 30 years of struggle for survival, laparoscopy proved not only its right for existence but is now considered, even by the most persistent sceptics, to be the 'gold standard' for several surgical procedures. The advantages of smaller skin scars, reduced trauma to the patient, lesser post-operative pain and shorter duration of hospital stay have made laparoscopy the procedure of choice for most surgical interventions.

However these advantages of laparoscopic surgeries come at a price. The pneumoperitoneum (PNP) required for laparoscopy results in pathophysiological changes.[7]Pneumoperitoneum is produced by administration of carbon dioxide (CO2) into the peritoneal cavity during laparoscopic procedures.[8,9]Both pneumoperitoneum and CO2 cause adverse cardiovascular effects.[10]Immediately after pneumoperitoneum plasma levels of norepinephrine, epinephrine and plasma rennin activity increase.[11]The renin-angiotensin-aldosterone system is also activated by increasing catecholamine levels. All these changes come together to contribute to elevated arterial pressure, increase systemic and pulmonary vascular resistance and reduced cardiac output.[12]Both mechanical and neurohumoral factors contribute to these hemodynamic changes.[13,14]

Hemodynamic stability during peri-operative period is of paramount importance as there are many patients who have a compromised cardiovascular status and are on medications. The anaesthesiologist‘s traditional approach to provide anaesthesia for laparoscopic procedures has been the emphasis on maintaining hemodynamic stability by avoiding hypertension, hypotension and tachycardia.

To prevent these adverse hemodynamic effects many interventions have been studied. They may be surgical interventions such as abdominal wall lift method (Laparotensors) providing gasless field for visualization, low intra-abdominal pressure techniques or use of Helium/Argon gas instead of CO2. Anesthetic interventions to prevent such hemodynamic changes could be the use of various modes of anaesthesia such as epidural or spinal or combined epidural and general anaesthesia techniques for the procedure; or the use of various pharmacological drugs such as opioids, esmolol, sodium nitroprusside, nitroglycerine and alpha-2 adrenergic agonists. But the search for the ideal agent to control this instability in hemodynamics

is still on.

Prothrombin time is a measure of coagulation, which evaluate extrinsic pathway (factor VII) and common pathway protein factor (fibrinogen, prothrombin, Factor V and X). There was no statisticall significant perioperative decrease in PT (p value >0.05) that could indicate hypercoagulability. Activated partial prothrombin time is a direct measure of coagulation, which test theintrinsic pathway (factor XII, XI, IX, VIII)

Thrombin, an enzyme with weak proteolytic activity, acts to convert fibrinogen into fibrin fibers that enmesh platelets, blood cells, and plasma to finally form the clot. One of the primary down-regulators of the coagulation cascade is antithrombin

III, which exerts its down-regulatory effect through the inactivation of several activated factors, including factors X, IX, XII and thrombin. By inactivating the numbered factors, thrombin production is reduced. Antithrombin also binds with thrombin and thereby blocks thrombin's interaction with fibrinogen.

D-Dimer levels have been used as a marker of intravascular clot formation. D-Dimer is a cross-linked fibrin degradation product, which forms as a result of a breakdown of fibrin. D-Dimer levels are frequently increased after surgery or trauma and indicate the presence of an intravascular clot that has undergone lysis.

CO2 pneumoperitoneum enhances the activation of coagulation and fibrinolysis associatewith laparoscopic cholecystectomy. Patients with risk factors like old age, obesity or with expected long duration of laparoscopic surgery are likely to have significant activation of coagulation, making them a vulnerable risk group for development of postoperative deep vein thrombosis, warranting some form of thromboprophylaxis.[26]

OBJECTIVES

- To determine the changes in coagulation profile of patients undergoing laparoscopic cholecystectomy using carbon di oxide pneumoperitoneum.
- To assess if there is an increased risk of thrombosis post-operatively.
- To determine if patients undergoing laparoscopic cholecystectomy have to be started on prophylaxis for deep vein thrombosis to prevent complications

REVIEW OF LITERATURE

HISTORICAL ASPECTS

The Roman Celsus in his text, De Medicina (translated by W.G. Spencer in 1935), mentioned the liver and described its anatomic location in an accurate form: "The liver, which starts from the actual partition under the precordia on the right side, is concave within (that is on the inferior surface) and convex without; its projecting part rests lightly on the stomach and it is divided into four lobes. Outside its lower part, the gallbladder adheres to it."[15]

Vesalius found (that he had) a hemoperitoneum coming from an abscess which had eroded the portal vein. The gallbladder was yellow and contained 18 calculi. Very light, of a triangular shape with even edges and surfaces everywhere, green by color somewhat blackish. The spleen was very large."[15]

Morgagni published in 1769 an analysis of disease under the title Seats and Causes of Disease, among which are those of the liver and biliary tract.[15]

Vater (1684-1751) was the first to describe the papilla of the duodenum.[15]

Petit introduced the term biliary colic.

1878: Kocher performed a cholecystostomy in two stages.

1971 Glenn,. In the first stage, he packed the wound with gauze to the bottom of the gallbladder, and 8 days later he emptied the residual stones from the gallbladder.

1885: Tait performed first cholecystostomy for gallbladder lithiasis in one stage.

1882: Langenbuch performed first elective cholecystectomy

1882: Von Winiwarter developed Cholecystenterostomy.

1895: Kocher wrote an article on internal choledochoduodenostomy to remove supra-ampullary choledochal calculi.

1897: Kehr placed a rubber tube in the common bile duct through the cystic duct this was the first systematic use of biliary intubation.

1898: Thornton performed the first removal of a stone from the common bile duct.

1898: MacBurney published his experience with duodenostomy and papillotomy in patients with impacted periampullary calculi.

1898: Buxbaum observed biliary calculi on plain x-rays.

1912: Kehr developed T-tube.

1923: Bakes developed choledochoscopy.

1924: Graham developed oral cholecystography.

1932: Mirizzi developed Postoperative cholangiography.

1937: Mirizzi developed Intraoperative cholangiography.

1989: Dubois in Paris published the first series of laparoscopic cholecystectomies.[15]

HISTORY OF LAPAROSCOPY AND LAPAROSCOPIC CHOLECYSTECTOMY:

Laparoscopy (from the Greek, Laparo meaning the flank and Skopein meaning to examine), was first performed in 1901 by George killing of Dresden, Germany using room air filtered through sterile cotton for pneumoperitoneum and a wide cystoscope to view the abdominal cavity of dog. The use of carbon dioxide (co2) for pneumoperitoneum was first recommended by Richard Zollikofer of Switzerland in 1924.[16]

The primary mode of insufflation was the Veress needle which wasintroduced by Janos Veress of Hungary in 1938.[16]

In 1933, A German general surgeon, Feowers, was the first to report laparoscopic lysis of abdominal adhesions for the diagnosis of bowelobstructions.[16]

Kurt Semm incorporated new aspects of fiber optic and used automatic gasinsufflator which allowed precise controlled intra abdominal pressure.[17]

In 1983, Lukichev and colleagues described laparoscopic cholecystectomy for acute cholecystitis.[17]

In 1985, Muhe of Boblinger, Germany performed the first laparoscopic assisted cholecystectomy.[18]

In 1987, a French surgeon in Lyon, Phillipe Mouret, performed the first video-laparoscopic cholecystectomy.

ANATOMY

The extra-hepatic biliary tree consists of the right and left hepatic ducts, common hepatic duct, cystic duct and gallbladder and the common bile duct.

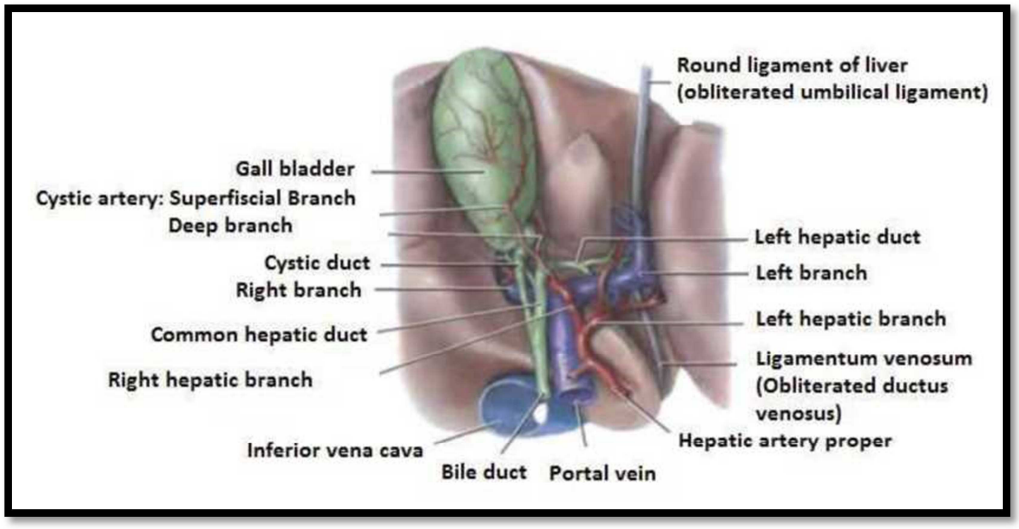


FIGURE1: Showing anatomy of gall bladder, inferior view

GALL BLADDER:

• The gall bladder is a flask-shaped, blind-ending diverticulum attached to the common bile duct by the cystic duct. It usually lies in a shallow fossa in the liver parenchyma covered by peritoneum continued from the liver surface. This attachment can vary widely.[19]

The gall bladder lies on a fibrous or cystic plate, which is part of the perihilar system of fibrous tissue. The cystic plate attaches directly on to the anterior surface of the right portal pedicle.

The hepatic parenchyma lies deep to the cystic plate,through which small bile ducts may penetrate to enter the gallbladder. Between the muscularis of the gallbladder and the cystic plate, a thin layer of areolar tissue thickens progressively from the top of the gallbladder downward.

• During dissection of the gallbladder from the liver, the posterior surface of the cystic artery and bile duct will be reached when the areolar tissue is left on the cystic plate. Should dissection be undertaken deep into the cystic plate, the surface to the right portal pedicle may be breached and result in injury to the right portal pedicle structures and the right hepatic duct.

NECK:

Neck lies at the medial end close to the porta hepatis, and almost always has a short peritoneal cover attached to the liver (MESENTERY); this mesentery usually contains the cystic artery.

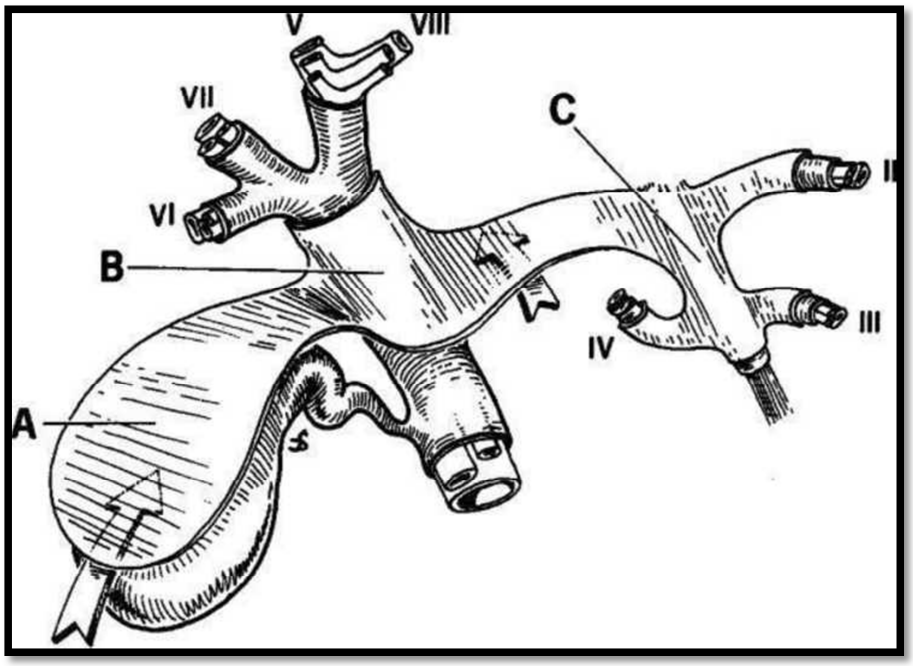


FIGURE 2: The anatomy of the plate system. cystic plate (A) above the gallbladder, the hilar plate (B) above the biliary confluence and at the base of the quadrate lobe, and the umbilical plate (C) above the umbilical portion of the portal vein.

BODY AND FUNDUS:

The body of the gall bladder normally lies in contact with the liversurface. It lies anterior to the 2nd part of the duodenum and the right end of the transverse colon. The fundus lies at the lateral end of the body and usually projects past the inferior border of the liver to a variable length. It often lies in contact with the anterior abdominal wall behind the 9th costal cartilage where the lateral edge of the right rectus abdominis crosses the costal margin. This is the location where enlargement of the gall bladder is best sought on clinical examination.

The fundus of gall bladder may be folded back upon the body of gall bladder: PHRYGIAN CAP.

EXTRAHEPATIC BILIARY TREE CYSTICDUCT

The cystic duct is about 3 to 4 cm in length, passes posteriorly to the left from the neck of gallbladder, and joins the common hepatic duct to form the common bile duct. It almost runs parallel to it and is adherent to common hepatic duct for a short distance before joining it.

BILE DUCTS:

The larger biliary ducts have external fibrous and internal mucous layers. The former is fibrous connective tissue which contains variable amount of connective tissue which contain variable amount of longitudinal, oblique and circular smooth muscles. The epithelial covering is columnar and contains many tubuloalveolar mucous glands.

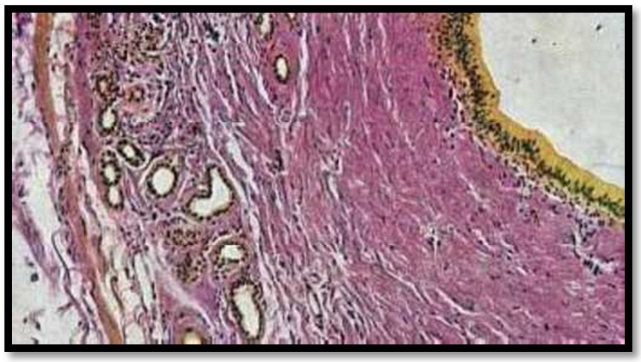


FIGURE 3: Microscopy of common bile duct Physiology

Bile is made up of bile salts, bile pigments and other substances dissolved in an alkaline medium. About 500 ml is secreted daily. The glucuronides of the bile pigments, bilirubin and biliverdin are responsible for golden yellow colour. Entire pool recycles twice per meal and 6 to 8 times per day.

Table 1: Composition of hepatic bile

Water	97.0%
Bile salts	0.7%
Bile pigments	0.2%
Cholesterol	0.06%
Inorganic salts	0.7%
Fatty acids	0.15%
Lecithin	0.1%
Fat	0.1%
Alkaline	

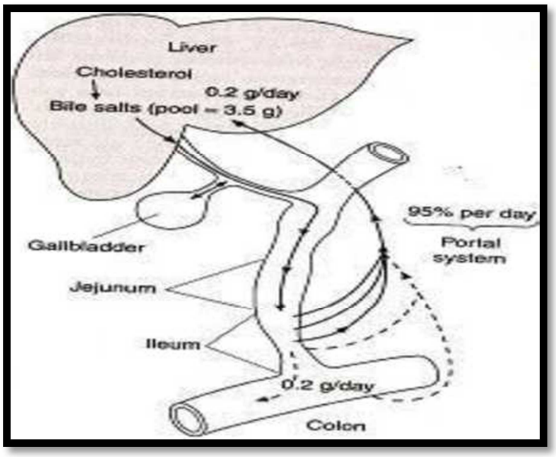


FIGURE 4: Showing enterohepatic circulation of bile salts.

BILIRUBIN METABOLISM AND EXCRETION

Most of the bilirubin in the body is formed by the breakdown of hemoglobin. it is bound to cytoplasmic proteins. It is conjugated to glucuronic acid by UDP-glucuronyl transferase, this diglucuronide is water soluble and is transported actively against concentration gradient into bile canaliculi.

A small amount of bilirubin glucuronide escapes into blood, where it is bound to albumin and excreted in urine.The intestinal mucosa is relatively impermeable to conjugated bilirubin but is permeable to unconjugated bilirubin and to urobilinogen. Small amounts of urobilinogen enters the general circulation through portal circulation and is excreted in urine.

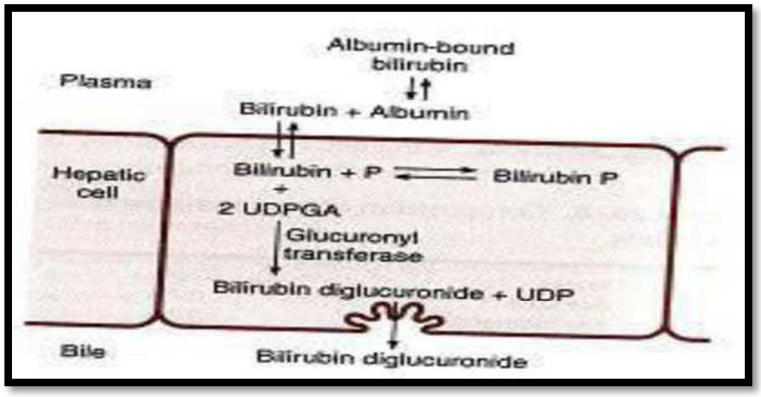


FIGURE 5: Metabolism of bilirubin in liver. p-intracellular binding protein, udpga-uridine diphosphate glucuronic acid, udp-uridine diphosphate.

REGULATION OF BILIARY SECRETION:

The tone of sphincter of Oddi decreases when food enters mouth. Fatty acids and amino acids in the duodenum release CCK, which cause gall bladder contraction. Substances that cause contraction of gallbladder are called cholagogues.

PATHOGENESIS:

In the west, about 80% are cholesterol stones, containing more than 50%ofcrystalline cholesterol monohydrate. The remainder are composed predominantly of bilirubin calcium salts and are designated pigment stones.

CHOLESTROL STONES

Cholesterol is rendered soluble in bile by aggregation with water soluble bile salts and water insoluble lecithin, both of which act as detergents. When cholesterol concentration, exceed the solubilizing capacity of bile (supersaturation).

Bile must be supersaturated with cholesterol: this appears to be a primary defect, mediated by abnormal regulation of hepatic mechanisms for delivering cholesterol to bile. The excess free cholesterolis toxic to gallbladder, penetrating the wall and exceeding the ability of the mucosa to detoxify it by esterification. Gallbladder hypo motility ensues. Muscular stasis appears to result both from intrinsic neuromuscular dysmotility and decreased response neuromuscular response to CCK.[21]

1. Gallbladder hypomotility promotes nucleation.[21]
2. Cholestrol nucleation in bile is accelerated: due to shift in balance between antinucleating and pronucleating proteins and presence of micro precipitates of inorganic or organic calcium salts.
3. Mucus hypersecretion in the GB traps the crystals, permitting their aggregation into stones.

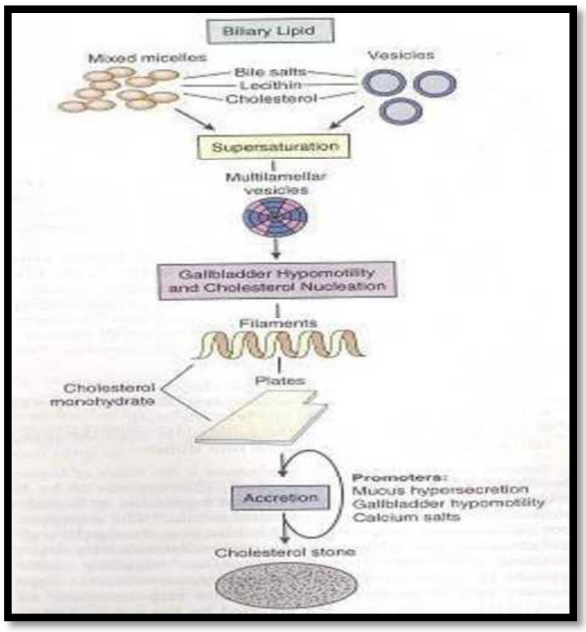


FIGURE 6: Schematic representation of four contributory factors for cholelithiasis: supersaturation, gallbladder hypomotility, crystal nucleation and accretion within the gallbladder mucous layer.[21]

TABLE 2: Superimposed conditions that exacerbate defective GB emptying and cholesterol stone formation

Prolonged fasting	Total parentral nutrition
Pregnancy	Spinal cord injury
Rapid weight loss	

PIGMENT STONES

Pigment stones are complex mixtures of abnormal insoluble calcium salts of unconjugated bilirubin along with inorganic calcium salts. Infection of biliary tract with E.coli or ascaris lumbricoids or by the liver flukes opisthorchis sinensis leads to release of microbial P-glucuronidase, whichhydrolyses bilirubin glucuronides to unconjugated bilirubin.[21]

MORPHOLOGY CHOLESTEROL STONES

Arises exclusively in GB and are composed of cholesterol ranging from 100 to 50%. Pure cholesterol stones are pale yellow, round to ovoid and have a fine granular, hard external surface which on transection reveals a glistening radiating crystalline palisade. With increasing proportions of calcium carbonate, phosphates and bilirubin, the stones exhibit discolouration and may be lamellated and gray white to black on transection.[21,22]

Most often multiple stones are present that range upto several centimeters in diameter. Surfaces of multiple stones may be rounded or faceted, owing to tight apposition. Stones composed largely of cholesterol are radiolucent; sufficient calcium carbonate is found in 10 to 20% of cholesterol stone to render them radiopaque.

PIGMENT STONES

Are classified as black and brown stones. Black pigment stones are found in sterile gallbladder bile, and brown in infected intrahepatic and extrahepatic ducts.

Mucin glycoproteins act as binding proteins in both cholesterol and pigment stones.

THE NATURAL HISTORY OF GALLSTONES

In 1992, it was estimated that 10% to 15% of the adult population in the United States had gallstones, about 1 million patients are newly diagnosedannually. Gallstones are the most common digestive disease.[23]

EPIDEMIOLOGY:

Gallstones are most common gastrointestinal illness with a prevalence of 11 to 36% in autopsy reports. Only first degree relatives of the patients with gallstones and obesity

(BMI >30 kg/m^2) have been identified as strong risk factors for the development of symptomatic gallstone disease.[24]

TABLE 3: Risk factors for gallstones

Obesity	First degree relatives
Rapid weight loss	Drugs: Ceftriaxone, postmenopausal estrogens, total parenteral nutrition
Childbearing	Ethnicity: Native American(Pima Indian) , Scandinavian
Multiparity	Ileal disease, resection or bypass
Female sex	Increasing age

COMPLICATIONS OF GALLSTONES[25]

1. Acute cholecystitis
2. Chronic calculus cholecystitis
3. Choledocholithiasis with or withoutcholangitis
4. Gallstone pancreatitis
5. Gallstone ileus
6. Gallbladdercarcinoma.

COMPLICATIONS DUE TO LAPAROSCOPIC CHOLECYSTECTOMY AND CHANGES IN COAGULATION PROFILE

Related to changes in coagulation profile ptinr and d dimer in laparoscopic cholecystectomy

Patients with risk factors like old age, obesity or with expected long duration of laparoscopic surgery are likely to have significant activation of coagulation, making them a vulnerable risk group for development of postoperative deep vein thrombosis, warranting some form of thromboprophylaxis.

Significant postoperative decrease in APTT and antithrombin III suggested activation of coagulation while decrease in D-dimer suggested activation of

Fibrinolysis.(26)

a) PNEUMOPERITONEUM RELATED COMPLICATIONS

Pneumoperitoneum related complications include carbon dioxide embolism, vasovagal reflex, cardiac arrhythmias and hypercapnia acidosis. Hypercapnia and acidosis are due to absorption of carbon dioxide from the peritoneal cavity. Sudden increases in Paco2 may be related to port slippage and extraperitoneal or subcutaneous diffusion of co2. It is managed by desufflating the abdomen for 10 to 15 min. If reinsufflation results in recurrent hypercapnia, then change the insufflations gas or convert to open. Carbon dioxide embolism is characterized by unexplained hypotension and hypoxia. Characteristic mill wheel murmur is detected on auscultation. This is produced due to the contraction of right ventricle against the blood gasinterface. There is an exponential decrease in end tidal co2 due to completeright ventricular outflow obstruction.[27]

It is managed by immediate evacuation of pneumoperitoneum and placement of the patient in left lateral decubitus, head down (Durant)position. This allows the co2 bubble to float to the apex of the right ventricle, where it is less likely to cause right ventricular outflow obstruction. Patient is hyperventilated with 100% oxygen.[28] cholecystitis and choledocholithiasis.

Adverse effects of Pneumoperitoneum

Lindberg et al conducted a study to quantify the risk of thromboembolic complications after laparoscopic cholecystectomy by a survey of the literature. The authors reviewed 60 laparoscopic cholecystectomy series consisting of 153,832 patients. The average mortality was 0.08%. The average rate of fatal pulmonary embolism was 0.02% and total pulmonary embolism 0.06%. The average rate of reported deep vein thrombosis was 0.03%. The conclusions drawn were that laparoscopic cholecystectomy is a safe procedure, and the rate of clinically evident postoperative thromboembolic complications is probably lower than after conventional cholecystectomy. An underreporting of the lesser complications is likely. The risk is not negligible, though, and some authors have recommended thromboembolism prophylaxis, although further studies are necessary to find the optimal prophylaxis strategy.[29]

G Wazz et al carried out a research study to evaluate perioperative changes in the venous system and to determine the frequency of deep venous thrombosis associated with minimally invasive surgery. Sixty-one patients completed the investigations (coagulation profile and lower limb venous duplex scan) on admission and on the first postoperative day. The median duration of pneumoperitoneum was 45 minutes (range: 18-90 minutes). None of postoperative scans revealed thrombosis. No significant changes in the postoperative coagulation profile were identified. Perioperative scans

of the left femoral vein revealed an increase in cross-sectional area (P<0.05) and a decrease in peak blood velocity (P<0.05). **The authors concluded that** in low-risk patients for thromboembolism, laparoscopy with pneumoperitoneum at pressures below 12 mm Hg per se did not increase the prevalence of deep venous thrombosis. This implies that venous hemodynamic changes observed during pneumoperitoneum did not cause deleterious venous stasis. Still, caution needs to exercised with regard to the view that no special precautions to prevent deep venous thrombosis are warranted in patients undergoing laparoscopy.(30)

A study was carried out by Garg PK et al to determine the alteration in coagulation profile and incidence of DVT in laparoscopic cholecystectomy and they concluded that CO(2) pneumoperitoneum enhances the activation of coagulation and fibrinolysis associated with laparoscopic cholecystectomy. Patients with risk factors like old age, obesity or with expected long duration of laparoscopic surgery are likely to have significant activation of coagulation, making them a vulnerable risk group for development of postoperative deep vein thrombosis, warranting some form of thromboprophylaxis(26)

Dimitris et al conducted a study examine whether inherent patient-related risk factors (age, gender) modify the effect of laparoscopic cholecystectomy (LC) upon the coagulation and fibrinolysis cascades. This observational study included 119 low-risk for deep vein thrombosis (DVT) patients undergoing elective LC, without thromboprophylaxis. Pre-operatively and 24 h post-operatively the authors measured PT eINR, aPTT, FDP, d-dimer, and fibrinogen. Color Doppler scan of the lower extremity was performed the 1st post-operative day. Differences before and after surgery were analyzed with respect to risk factors. No clinically or ultrasound evident DVT was observed. INR (1.04 ±0.06 vs. 1.12 ± 0.11, p < 0.0001), d-dimer (0.38±0.36

vs. 0.9 ± 0.64, p < 0.0001), plasma fibrinogen (380.8 ±74.9 vs. 403.8 ± 78.8, p = 0.0001) and FDP positivity exhibited statistically significant increase after surgery. The levels of aPTT did not exhibit any significant change. Concerning d-dimer, older age was associated with higher pre-operative concentrations; older patients accordingly exhibited more intense increase in d-dimer and FDP positivity after surgery. Male sex was associated with higher PTeINR and aPTT before surgery, as well as with more pronounced increase in PT- INR postoperatively; similarly, older age was associated only with higher PT-INR before surgery. The authors concluded that despite no DVT, significant increase in PT-INR, d-dimer, FDP and fibrinogen appeared after LC. This may be attributed to surgical trauma and pneumoperitoneum effects on the portal vein flow. Elderly subjects and males seem particularly vulnerable, demonstrating more sizeable changes(26)

Previously we have reported that large increases in lung and chest wall elastances as well as lung resistance occur with abdominal insufflation of carbon dioxide during laparoscopic surgery. To examine whether these effects were reversible with abdominal deflation, we calculated lung and chest wall elastances and resistances from measurement of airway flow and pressure and esophageal pressure in 17 anesthetized/paralyzed patients undergoing laparoscopic surgery. Measurements were made immediately prior to abdominal insufflation and after deflation. Lung and chest wall elastances and resistances were not changed from baseline (P > 0.05), although total respiratory elastance remained slightly increased compared to baseline (P < 0.05). The change in total respiratory elastance did not correlate with abdominal insufflation time, surgical site, smoking history, or physical characteristics of the patients. There were no differences in frequency and tidal volume dependences of the elastances and resistances before and after abdominal insufflation (P > 0.5). We

conclude that residual changes in respiratory mechanics caused by carbon dioxide insufflation during laparoscopic surgery are minor, and that the reported compromise of respiratory function indicated by pulmonary function tests after laparoscopy does not appear to be due to changes in passive mechanical properties of the lungs or chest wall.(31)

The increased intra-abdominal pressure during pneumoperitoneum, together with the head-up tilt used in upper abdominal laparoscopies, would be expected to decrease venous return to the heart. The goal of our study was to determine whether laparoscopy impairs cardiac performance when preventive measures to improve venous return are taken, and to analyze the effects of positioning, anesthesia, and increased intra-abdominal pressure. With the passive head-up tilt in awake and anesthetized patients, the cardiac index (CI), stroke index (SI), central venous pressure (CVP), and pulmonary capillary wedge pressure (PCWP) decreased, and systemic vascular resistance increased. With the patient under anesthesia, SI decreased, but CI did not change significantly as a result of the compensatory increase in heart rate. Carbon dioxide (CO2) insufflation at the start of laparoscopy produced increases in CVP and PCWP as well as mean systemic and mean pulmonary arterial pressures without changes in CI or SI. Toward the end of the laparoscopy, CI decreased by 15%. The hemodynamic values returned to nearly prelaparoscopic levels after deflation of the gas, and CI was elevated during the recovery period, whereas systemic vascular resistance was decreased in comparison with the baseline .

We have measured cardiovascular changes associated with insufflation of carbon dioxide and the reverse Trendelenburg position during laparoscopic cholecystectomy, using transoesophageal echocardiography in 13 healthy patients. End-tidal carbon dioxide values increased after insufflation of carbon dioxide, with values significantly

($P < 0.05$) increased after lateral tilt positioning. Creation of a pneumoperitoneum was associated with increases ($P < 0.05$) in left ventricular end-systolic wall stress, concomitant with increases ($P < 0.01$) in peak airway pressure and systemic arterial pressure. In addition, left ventricular end-diastolic area decreased ($P < 0.05$) after reverse Trendelenburg positioning. Left ventricular ejection fraction was maintained throughout the study.(32)

In another study, cardiovascular changes associated with insufflation of carbon dioxide and reverse Trendelenburg (rT) position during laparoscopic cholecystectomy were measured using Transesophageal echocardiography in 13 ASA I and II patients. End tidal carbon dioxide was increased after insufflation of carbon dioxide with values significantly ($p<0.005$) increased after lateral positioning. Creation of pneumoperitoneum was associated with increases ($p<0.01$) in peak airway pressure and systemic arterial pressure. Left ventricular end diastolic area decreased ($p<0.05$) after reverse Trendelenburg positioning. Left ventricular ejection fraction was maintained throughout the study.[33]

To evaluate the haemodynamic and respiratory changes during laparoscopic cholecystectomy in elderly ASA III patients. This clinical descriptive study included 16 patients aged > 75 yr. Anaesthesia was induced with fentanyl and etomidate and maintained with N2O in O2 (50%), fentanyl and isoflurane as needed. Inspired minute volume was kept constant during anaesthesia. Cardiovascular monitoring included a radial artery catheter and a pulmonary artery catheter for measurement of CO, RVEF and SvO2, and calculation of right ventricular end diastolic volume indexed (RVEDVI). Haemodynamic variables, arterial and venous blood gas analyses were collected before and 10 min after anaesthetic induction, 15, 30 and 60 min after

insufflation (IAP = 12 mmHg) followed by a 10 degrees head-up tilt, and after exsufflation.

We conclude that gradual abdominal insufflation to 12 mmHg followed by a limited 10 degrees head-up tilt is associated with cardiovascular stability in elderly ASA III patients.(34)

Hemodynamics during laparoscopic cholecystectomy under general anesthesia (isoflurane in N2O/O2 (50%)) were investigated in 15 nonobese ASA Class I patients by using invasive hemodynamic monitoring including a flow-directed pulmonary artery catheter. During surgery, intraabdominal pressure was maintained automatically at 14 mm Hg by a CO2 insufflator, and minute ventilation was controlled and adjusted to avoid hypercapnia. Hemodynamics were measured before anesthesia, after the induction of anesthesia, after tilting into 10 degrees head-up position, 5 min, 15 min, and 30 min after peritoneal insufflation, and 30 min after exsufflation. Induction of anesthesia decreased significantly mean arterial pressure and cardiac index (CI). Tilting the patient to the head-up position reduced cardiac preload and caused further reduction of CI. Peritoneal insufflation resulted in a significant increase (+/- 35%) of mean arterial pressure, a significant reduction (+/- 20%) of CI, and a significant increase of systemic (+/- 65%) and pulmonary (+/- 90%) vascular resistances. The combined effect of anesthesia, head-up tilt, and peritoneal insufflation produced a 50% decrease in CI. Administration of increasing concentrations of isoflurane, via its vasodilatory activity, may have partially blunted these hemodynamic changes. These results demonstrate that laparoscopy for cholecystectomy in head-up position results in significant hemodynamic changes in healthy patients, particularly at the induction of pneumoperitoneum.(35)

In another study, 41 patients undergoing laparoscopic cholecystectomies were monitored using the SphygmoCor pulse wave analyzing system. Peripheral blood pressures (PBP), central aortic blood pressures (CBP), augmentation index (ALX@HR75) and subendocardial viability ratios were measured at rest (phase1), after anaesthetic induction (Phase 2), after peritoneal inflation (Phase 3) and after peritoneal deflation (Phase 4). Induction of anaesthesia resulted in a statistically significant reduction in both the peripheral blood pressure and central aortic pressures, accompanied by a decrease in augmentation pressure and augmentation index. Peripheral blood pressures did not change along with the peritoneal cavity insufflation, except for a moderate increase in systolic blood pressure. In contrast to this, an increase could be observed in central aortic pressure (106.77±18.78 vs. 118.05±19.85 mmHg, $P<0.01$) which was accompanied by increased augmentation pressure (18.97±10.80 vs. 31.55±12.01; $P<0.001$) and augmentation index (7.31±5.59 vs. 12.61±7.56, $P<0.001$), indicating a rise in peripheral arterial stiffness.[36]

COMPLICATIONS OF LAPAROSCOPIC CHOLECYSTECTOMY

A) HEMORRHAGE

i) TROCAR SITE BLEEDING

ii) HAEMORRHAGE DUE TO BLUNT DISSECTION OF ADHESIONS can be managed with electrocautery.

iii) SUDDEN AND PULSATILE BLEEDING IN CALOT'S TRIANGLE

iv) GALLBLADDER FOSSA BLEEDING

b) BILE DUCT INJURY

c) Bowel injury

. The jejunum, ileum and colon can be injured by veress needle and trocars while duodenum is likely to be injured during dissection.

d) Wound infection and incisional hernia

The risk of wound infection following laparoscopic cholecystectomy is less than 1% and the risk of incisional hernia is 0.5%.[23].

e) DIAPHRAGMATIC INJURY

f) PANCREATITIS.

MATERIAL AND METHODS

Source of the data: Study was conducted in patients undergoing laparoscopy cholecystectomy using carbondioxide-pneumoperitoneum before and after surgery in the Department of General Surgery, K.L.E.S Dr PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE, BELAGAVI

Study design: An observational study

Study period: The study was conducted from1st January 2023 to 31st December 2023

Sample Size: A total of 27 patients

SAMPLING DESIGN: Observational study.

SAMPLE SIZE:

The formula used for sample size calculation is,

$$n = \frac{\sigma_d^2 \left(Z_{\alpha/2} + Z_\beta \right)^2}{(\mu_1 - \mu_2)^2}$$

$$\sigma_d^2 = 2 \times (1 - \rho)\, \sigma^2$$

$$d = \frac{|\mu_1 - \mu_2|}{\sigma_d}$$

where μ_1 is the mean of the pre-test, μ_2 is the mean of the post-test, for 95% confidence level, $Z_{\alpha/2}$ values are 1.96 and for 85% power Z_β value is 1.0364.

Assuming the effect size of PT between timepoints (before and after surgery) to be 0.6, at 95% confidence level and 85% power, minimum sample size required is 27 subjects. As sample size increases, accuracy of result also increases.

INCLUSION CRITERIA

All patients operated for cholecystectomy laparoscopically will be included in the study.

Patient of both sexes

Age from 18 years to 60 years.

Patients with gall stones or gallbladder polyps.

Patients with chronic cholecystitis, relief stages of acute cholecystitis will be included.

Surgery time assuming between 90- 180 minutes.

Patients who give consent for study will be included.

Exclusion Criteria

Patients below age of 18 and above the age of 60.

Surgery time exceeding three hours.

Procedures converted to open surgery.

Associated hypertension.

Patients on anticoagulant therapy.

Patients with known malignancies.

Patients with known history of bleeding and clotting disorders.

Deep venous thrombosis.

Pregnancy.

Data collection

After obtaining institutional ethical committee clearance and written informed consent, detailed history, clinical examination and basic routine investigations was done for all the participants in the study. A total of 3 cc of blood was drawn under strict aseptic precautions. One sample was taken prior to surgery and the other sample 6 hours after onset of pneumoperitoneum. Samples were processed for prothrombin time and D-dimer Duplex scan was done to look for deep vein thrombosis. Each patient undergone uncomplicated LC under general anesthesia. A standard operative and anesthesia protocol was followed by all surgeons; the experience of the operating surgeon, as demonstrated by the past number of LCs performed, was recorded. With the patient in the trendelenburg position a versss needle through a small incision under the umbilicus will be used to insufflate with CO2 until pneumoperitoneum of 12 mmHg was achieved. The patient was then placed to anti-trendelenburg position with a left tilt throughout the operation. Standard American school positioning of the surgical team and four ports was used. Intraoperative cholangiogram was not performed. Patients were allowed to have free fluids by mouth, and ambulation was encouraged in the evening of surgery. Patient discharged after routinely, 24 -48 h after the operation.

STATISTICAL ANALYSIS PLAN:

Data was analyzed using statistical software IBM SPSS version 26 and Microsoft Excel 2021. Categorical variables were represented by frequencies and percentages. Continuous variables were represented by Mean ± SD / Median (Min, Max) form. Paired t test/Wilcoxon test was used to compare means/distributions of variables over time. P-value <0.05 indicated statistical significance.

OBSERVATIONS AND RESULTS

Table 4: Age distribution

Age (in years)	No of cases	Percentage (%)
≤ 30	1	3.70
31 – 40	8	29.63
41 – 50	7	25.93
51 – 60	10	37.04
61 – 70	1	3.70
Total	27	100

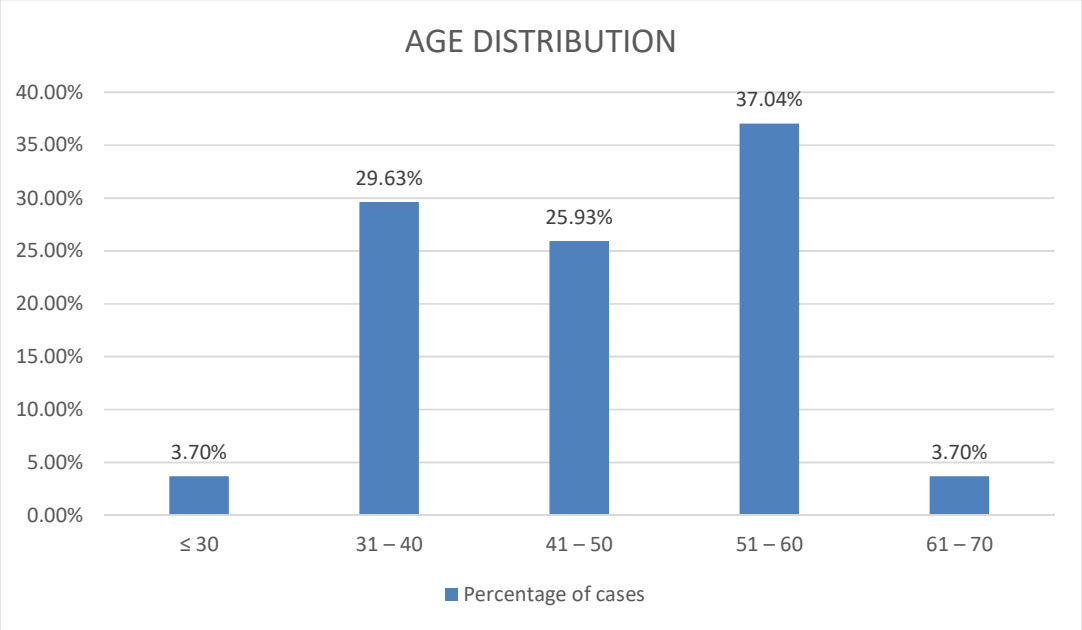


Table 5: Gender distribution

Gender	No of cases	Percentage (%)
Male	11	40.74
Female	16	59.26
Total	27	100

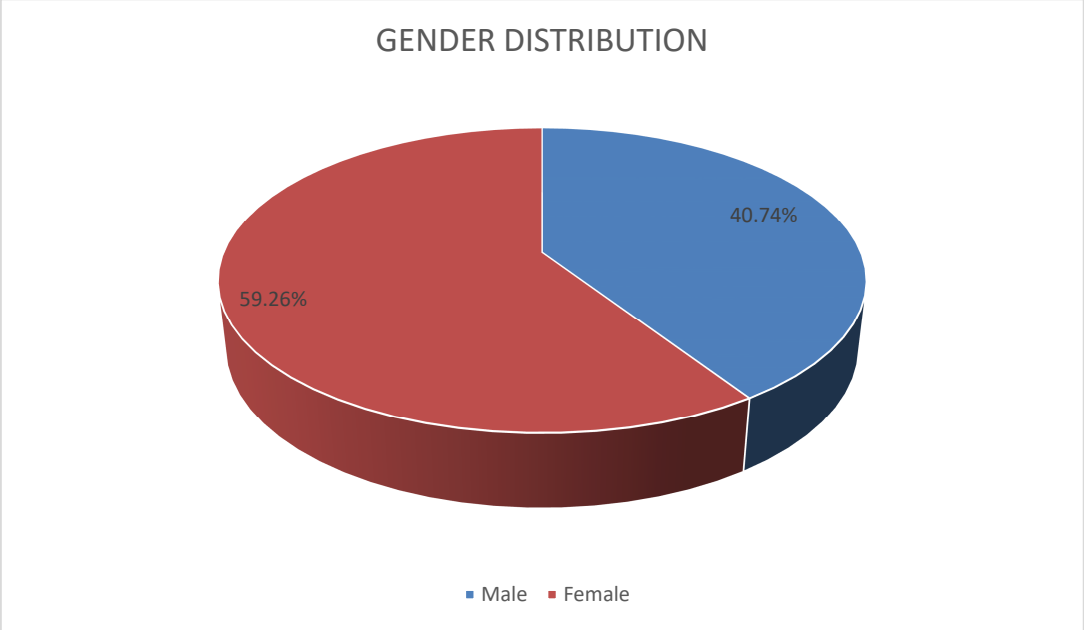


Table 6: Chief Complaints

Chief Complaints	No of cases	Percentage (%)
Pain in abdomen	18	66.67
Colicky abdominal pain	9	33.33
Total	27	100.00

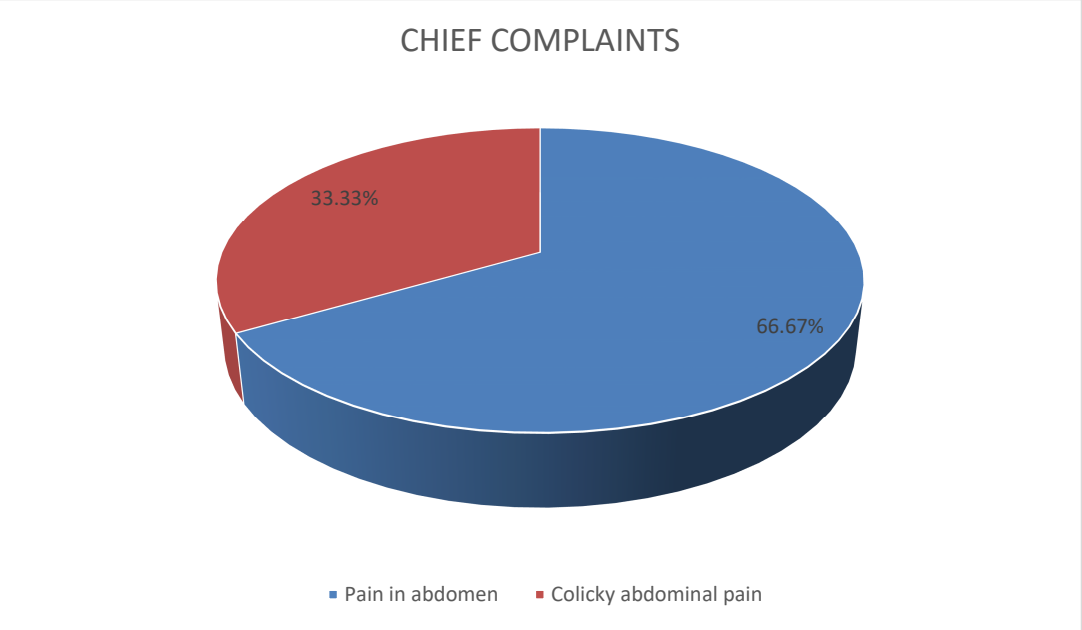


Table 7: Duration of surgery

Duration of Surgery (in mins)	No of cases	Percentage (%)
≤ 90	9	33.33
91 – 110	11	40.74
111 – 130	4	14.81
131 – 150	1	3.70
> 150	2	7.41
Total	27	100

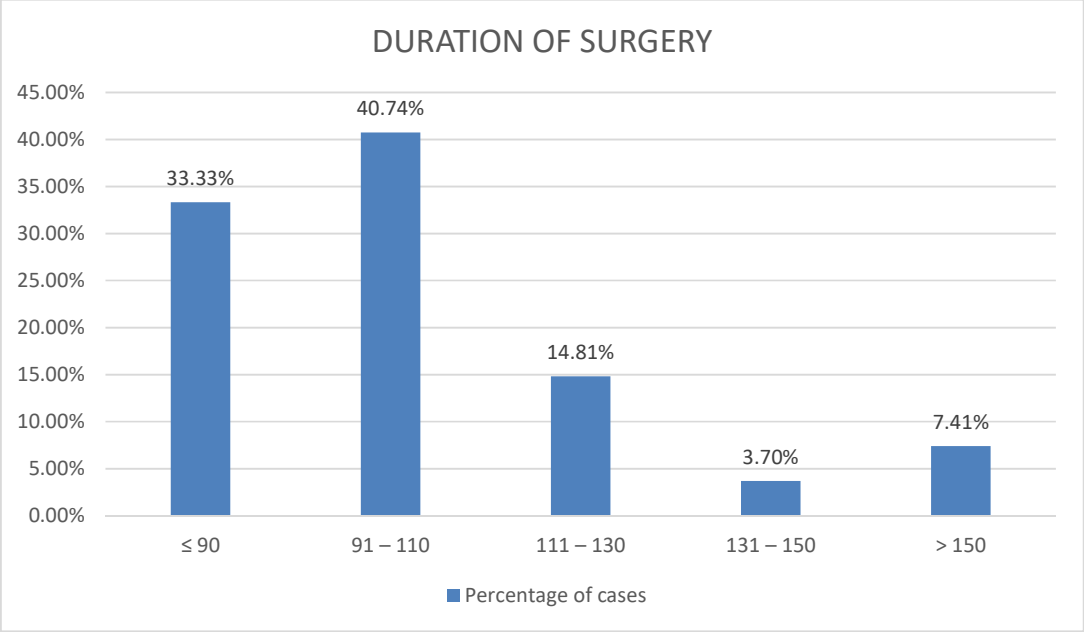


Table 8.Prothrombin/ International normalised ratio

Paired Samples Statistics					
		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Preop	.9778	27	.07454	.01435
	Postop	1.0407	27	.07765	.01494

Paired Samples Correlations				
		N	Correlation	Sig.
Pair 1	Preop & Postop	27	.709	.000

Paired Samples Test									
		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	Preop - Postop	-.06296	.05810	.01118	-.08595	-.03998	-5.631	26	.000

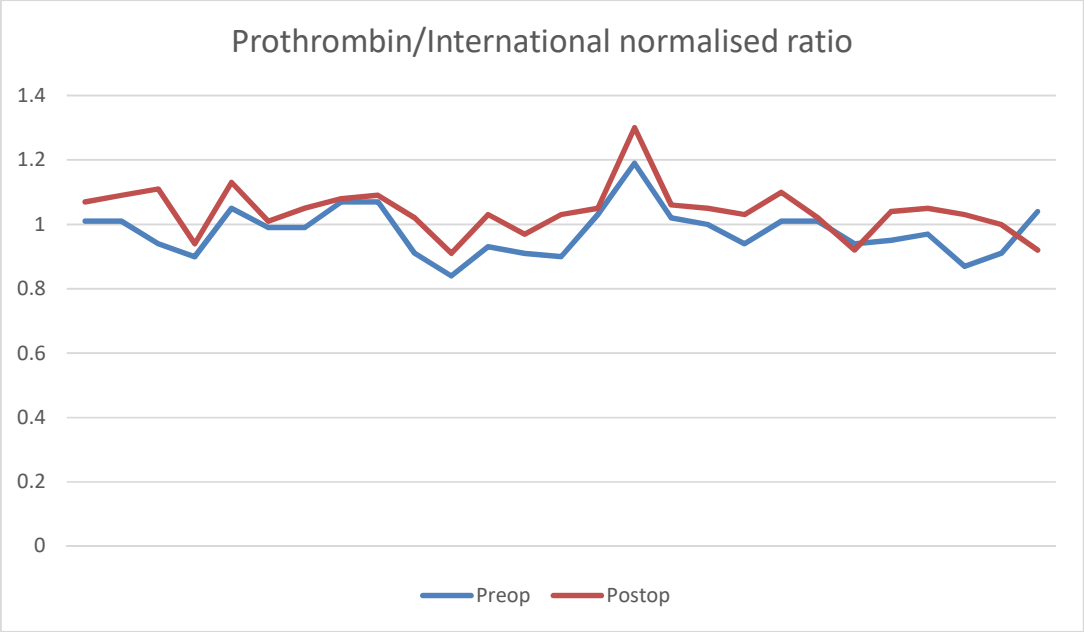
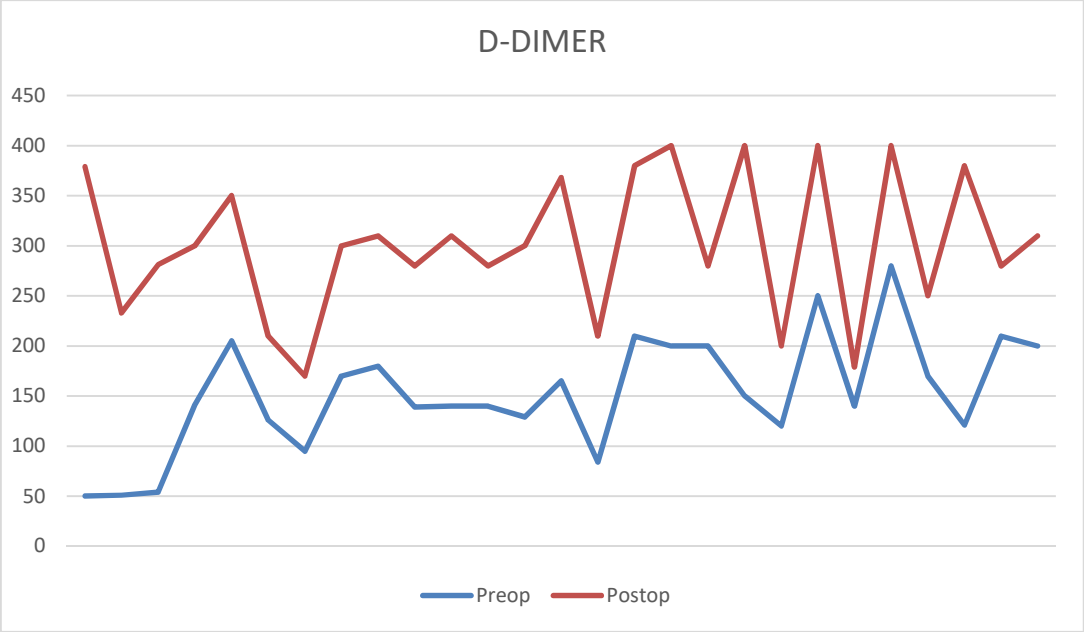

Prothrombin/International normalised ratio
1.4
1.2
1
0.8
0.6
0.4
0.2
0
Preop
Postop

Table 9: D-dimer

Paired Samples Statistics					
		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Preop	152.5926	27	57.52141	11.07000
	Postop	301.4815	27	71.54792	13.76940

Paired Samples Correlations				
		N	Correlation	Sig.
Pair 1	Preop & Postop	27	.487	.010

Paired Samples Test									
		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	Preop - Postop	-148.88889	66.49369	12.79672	-175.19291	-122.58486	-11.635	26	.000


D-DIMER
450
400
350
300
250
200
150
100
50
0
Preop
Postop

DISCUSSION

A fundamental step of the laparoscopic surgery is represented by the insufflation of a gas (carbon dioxide, CO2) inside the peritoneal cavity to allow the distention of the abdominal wall, which creates enough space for maneuver. The pneumoperitoneum induces multiple alterations to the physiological processes due to the increase in intra-abdominal pressure and to the direct effects of CO2 at the systemic level because of its absorption. Many of the effects of pneumoperitoneum on cardiovascular, respiratory and metabolic systems have been discussed in Literature.[2–5] Laparoscopic cholecystectomy represents the gold standard for the treatment of symptomatic gallbladder stones. There is no pressure standard for inducing pneumoperitoneum. The effects of gas and the pathophysiological changes induced by CO2 have prompted surgeons to try to use low pressure to avoid the onset of some complications such as venous thromboembolism. The usual pressure range of the pneumoperitoneum is between 12 and 14 mmHg. However, international guidelines do not recommend operating at lower pressure value with the purpose of avoiding the potentially negative effects of pneumoperitoneum on heart and lungs, because either there is no clear evidence of safety or low pressure could reduce the formation of a safe working chamber.[6, 7]. There are many studies in the Literature concerning the effects of laparoscopy on coagulation alterations and on the lower thromboembolic risk than open surgery. Thrombotic risks during laparoscopic surgery are mostly pneumoperitoneum related. The increase in intraabdominal pressure during pneumoperitoneum causes mechanical compression on the inferior vena cava with a reduction in venous return; moreover, the reverse Trendelenburg can induce blood stagnation in the lower limbs.[5] In addition, other Authors have recorded a state of hypercoagulability after the discharge of the patient from the hospital.[8] For this

reason, some Authors recommended a thromboembolic prophylaxis for patients undergoing laparoscopy.[9, 10]

Age distribution

In the present study age ranged from 30 years to 70 years with the mean age of 47.08 years. Most of the cases were observed having age from 51 to 60 years of age followed by 29.63% cases were observed having age from 31 to 40 years of age, 25.93% cases were observed having age from 41 to 50 years of age, 3.70% each cases were observed having age less than or equal to 30 years and having age from 61 to 70 years of age respectively.

In study done by Eva I et al[42], the patients' age ranged between 15 and 85 years, with an average age of 51 years.

In study done by Sunamak O te al[43], mean age was 46.6±14.5 years and BMI was 28.1±4.0% which is in concordance with our study

In study done by Amin B et al[44], age of the patients ranged from 29 to 78 (mean 56.7±115) years which is similar to our study.

Gender distribution

In the present study Female cases were higher than male cases with the M:F ratio of 0.69:1. 59.26% were female cases and 40.74% were male cases.

In study done by Eva I et al[42], 26 patients (60.5%) were female and 17 (39.5%) were male which is similar to our study

In study done by Sunamak O te al[43], 20 (80%) of the patients were female and 5 (20%) were male.

In study done by Amin B et al[44], 22 were male and 28 were female which is in concordance with our study.

Chief complaints

In the present study most of the cases i.e. 66.67% cases were observed having pain in abdomen where 33.33% cases were observed with Colicky abdominal pain complaints.

Duration of surgery

In the present study 40.71% cases were observed having duration of surgery form 91 to 110 mins followed by 33.33% cases having duration of surgery less than or equal to 90 mins, 14.81% cases were observed having surgery time from 111 to 130 mins and 7.41% cases were observed having duration of surgery more than 150 minutes where 3.70% cases were observed having duration of surgery from 131 to 150 minutes.108.15 mins mean duration of surgery was observed.

In study done by Eva I et al[42], the average operating time was 96 minutes. prothrombin time/international normalized ratio **& D – Dimer**

In the present study preoperatively mean PROTHROMBIN TIME/INR was d O.98 where as post operatively mean PROTHROMBIN TIME/INR was 1.04 .Statistically significant difference was observed in PROTHROMBIN TIME/INR postoperatively. (p=<0.0001***) Preoperatively mean D-Dimer was 152.53 where as post operatively mean D-Dimer was 301.48. At post operatively significant increase in D-Dimer was observed.(p=<0.0001***).

In study done by Eva I et al[42], at post op significant increased was observed in D-Dimer levels in group A a statistically significant decrease in anti-thrombin III levels was detected in group B, and a statistically significant difference in PT ratio in patients belonging to group B was observed .

wherer as in our study ***) Preoperatively mean D-Dimer was 152.53 where as post operatively mean D-Dimer was 301.48 and preoperatively mean PROTHROMBIN TIME/INR was d O.98 where as post operatively mean PROTHROMBIN TIME/INR was 1.04

In study done by Sunamak O te al[43], , Prothrombin time, Thrombin Time, Activated partial thromboplastin time , INR, and D-dimer and fibrinogen levels significantly increased after the surgery in both of the groups. D-dimer level was significantly higher in 14-mmHg group at post24. We found a significant increase in Prothrombin 24 h after the surgery compared to preoperative value in the 10 mmHg group ($p = 0.048$) and the 14 mmHg group ($p < 0.001$). We observed a significant increase in Activated partial thromboplastin time 24 h after the surgery compared to preoperative value in the 10 mmHg group ($p < 0.001$). In the 14 mmHg group there was a significant increase in Activated partial thromboplastin 1 h ($p < 0.001$) and 24 h ($p < 0.001$) after the surgery compared to preoperative value. There were significant decreases in Thrombin time 1 h and 24 h after the surgery in both of groups compared to preoperative values ($p < 0.001$). INR significantly increased in the 14 mmHg group 24 h after the surgery ($p < 0.001$). D-dimer and fibrinogen significantly increased in both of groups 1 h and 24 h after the surgery ($p < 0.001$). Post 24 value of D-dimer was significantly higher in the 14 mmHg group compared to the 10 mmHg group. We didn't observe any significant difference between the groups on pre, post1 and post24 values of Prothrombin, activated partial throboplastin , Thrombin time , INR and

fibrinojen. wherer as in our study ***) Preoperatively mean D-Dimer was 152.53 where as post operatively mean D-Dimer was 301.48 and preoperatively mean PROTHROMBIN TIME/INR was O.98 where as post operatively mean PROTHROMBIN TIME/INR was 1.04.

In study done by Amin B et al[44] the pneumoperitoneum for laparoscopic cholecycstectomy lead to postoperative hypercoagulation in the patients, and thereby may increase the risks for development of postoperative thrombosis; Patients are at the risks for occurrence of thrombosis within 8 hours after the operation, to which attention should be paid in favor of preventing thrombosis. The Thrombin time values obtained at 0 and 8 hours post-operation were not significantly different as compared to the pre-pneumoperitoneum values ($P > 0.05$). (7) The D dimer values gradually increased after operation; as compared to pre-pneumoperitoneum values, D dimer at 0 and 8 hours after operation increased by 210.8 ng/ml and 525.9 ng/ml respectively ($P < 0.05$) and D dimer at 8 hours after operation increased by 315.1 ng/ml as compared to 0 hour post-operation ($P < 0.05$).

SUMMARY AND CONCLUSION

.When pre- and post-operative data from the same group were compared, laparoscopy caused statistically significant changes in the coagulation parameters. The increase in these values indicates the tendency of the inflammatory process caused by either pneumoperitoneum or surgical stress, even though the small sample size makes it impossible to draw firm conclusions. Yes, one of the most discussed and still highly contentious topics is the thrombotic risk associated with laparoscopic surgery.furthur studies are required to find out about anticoagulation prophylaxis.

In our recent study by Anna maria blak**e** discussed the risk of deep venous thrombosis during laparoscopic cholecystectomy and the need for routine deep venous thrombosis (DVT) prophylaxis. In an average of 4 weeks follow-up, 31 complications and 4 deaths were reported. These complications included wound infection (16), postoperative bleeding (3), persistent pain (3), pneumonia (3), retained CBD stones (2), asthma (1), papillary stenosis (1), ileus (1), and intra-operative bowel injury (1). None of the 587 patients in this study had symptoms of DVT or pulmonary embolism. espite the fact that DVT in this patient population is rare, many reports suggest the use of routine DVT prophylaxis with sequential compression devices (SCDs) or low-molecular-weight heparin (LMWH). Because no clinically detectable evidence was found of DVT in our study group despite the lack of any perioperative DVT prophylaxis, we question whether routine DVT prophylaxis is indicated or cost effective for routine laparoscopic cholecystectomy. A large prospective trial addressing this question is needed.(46)

BIBLIOGRAPHY

1) Rao KS, Meghavathu GN, Rao GS, Prasad HRT. Clinical Study of Gallstone Disease and Treatment Options. Journal of Evolution of Medical and Dental Sciences. 2015;4(79):13841-8.

2) IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 16, Issue 12 Ver. VII (Dec. 2017), PP 0104

3) Kevin C. The Gall bladder and bile ducts. In: Williams NS, Bulstrode CJK, O'Connell P.R. eds. Bailey and Love's Short Practice of Surgery. 26th ed. Boca Raton, FL: CRC Press; 2013: 1097- 1117.

4) Thompson Jr JE, Bennion RS, Doty JE, et al Predictive factors for bactibilia in acute cholecystitis. Arch Surg 1990;125:261-264

5) National Institutes of Health Consensus Development Conference Statement September 14-16, 1992

6) Predicting the conversion of laparoscopic to open cholecystectomy: an experience in a tertiary care hospital of central IndiaAshish Pratap Singh, Priyank Sharma, Sajith Babu S.M.*, A. P. S.Gaharwar

7) Joris J. Anesthetic management of laparoscopy. Miller RD (ed). miller's anesthesia,4thed. new york: Churchill Livingstone; 1994.pp.2011-29.

8) Hodgson C, McClelland R, Newton J. Some effects of the peritoneal insufflation of carbon dioxide at laparoscopy. Anaesthesia. 1970;25(3):382-90.

9) Blobner M, Felber AR, Gögler S, Weigl EM, Esselborn SJ. Carbon dioxide uptake from pneumoperitoneum during laparoscopic cholecystectomy. Anesthesiology. 1992 Sep 1;77(3A):A37.

10) Richardson JD, Trinkle JK. Hemodynamic and respiratory alterations with increased intra-abdominal pressure. Journal of surgical research. 1976 May 1;20(5):401-4.

11) Mann C, Boccara G, Pouzeratte Y, Eliet J, Serradeil-Le Gal C, Vergnes C, Bichet DG, Guillon G, Fabre JM, Colson P. The relationship among carbon dioxide pneumoperitoneum, vasopressin release, and hemodynamic changes. Anesthesia & Analgesia. 1999 Aug 1;89(2):278-83.

12) Lenz R, Thomas T, Wilkins D. Cardiovascular changes during laparoscopy. Survey of Anesthesiology. 1976;20(6):549-50.

13) Wahba R, Beique F, Kleiman S. Cardiopulmonary Function and Laparoscopic Choleoystectomy. Survey of Anesthesiology. 1995;39(5):323.

14) Joris J, Noirot D, Legrand M, Jacquet N, Lamy M. Hemodynamic Changes During Laparoscopic Cholecystectomy. Anesthesia & Analgesia. 1993;76(5):1067-71.

15) F.R.C.S. (Eng.). In three volumes (Loeb Classical Library). 6; x 44 in. Vol. I (1935). Pp.,499 + xiv. Vol. I1 (1938). Pp. 292 + lxviii. Vol. I11 (1938). Pp. 293-649 + VI. London : William Heinemann Ltd. Each volume, cloth, 10s. ; leather, 12s. 6d

16) Underwood, Robert. "The Laparoscopic Revolution", Laparoscopic Surgery Principles and Procedures Second Edition Revised and Expanded, 2004.

17) Soper, N.J.. "Laparoscopic cholecystectomy", Current Problems in Surgery, 199109

18) Litynski GS. Kurt Semm-the Magician from Kiel. In: Litynski GS, ed. Highlights in the History of Laparoscopy . Frankfurt, Germany: Barbara Bernert Verlag; 1996:131144.

19) Hassan, Ashfaq, Showqat Zargar, Aijaz Malik, and Pervez Shah. "Surgical significance of variations in anatomy in the biliary region", International Journal of Research in Medical Sciences, 2013

20) The Liver and Biliary Apparatus (gallbladder and Ducts) Review of MEDICAL EMBRYOLOGY Book by BEN PANSKY, PhD, M.D.

21) World J Hepatol 2012 February 27; 4(2): 18-34 ISSN 1948-5182 (online) © 2012 Baishideng

22) F.R.C.S. (Eng.). In three volumes (Loeb Classical Library). 6; x 44 in. Vol. I (1935). Pp.,499 + xiv. Vol. I1 (1938). Pp. 292 + lxviii. Vol. I11 (1938). Pp. 293-649 + VI. London : William Heinemann Ltd. Each volume, cloth, 10s. ; leather, 12s. 6d.

23) The Management of Gallstone Disease A Practical and Evidence-Based Approach Editors: Cox, Michael R., Eslick, Guy D., Padbury, Robert (Eds.)

24) Stinton LM, Shaffer EA. Epidemiology of gallbladder disease: cholelithiasis and cancer. Gut and liver. 2012 Apr;6(2):172.\

25) Takeyama, H.. "Expectant Management Is Safe for Cholelithiasis After Heart Transplant", Journal of Heart and Lung Transplantation, 200605

26) Garg PK, Teckchandani N, Hadke NS, Chander J, Nigam S, Puri SK. Alteration in coagulation profile and incidence of DVT in laparoscopic cholecystectomy. Int J Surg. 2009 Apr;7(2):130-5

27) https://www.ncbi.nlm.nih.gov/pubmed/1534210 [The effects of the carbon dioxide pneumoperitoneum in laparoscopic cholecystectomy on postoperative spontaneous respiration]. Tolksdorf W[1], Strang CM, SchippersE, Simon HB, truong s

28) "COLON", The American Journal of Gastroenterology, 9/2007

29) Lindberg F, Bergqvist D, Rasmussen I. Incidence of thromboembolic complications after laparoscopic cholecystectomy: review of the literature. Surg Laparosc Endosc. 1997 Aug;7(4):324-31.\

30) Wazz G, Branicki F, Taji H, Chishty I. Influence of pneumoperitoneum on the deep venous system during laparoscopy. JSLS. 2000 Oct-Dec;4(4):291

31) Fahy BG, Barnas GM, Nagle SE, Flowers JL, Njoku MJ, Agarwal M. Changes in lung and chest wall properties with abdominal insufflation of carbon dioxide are immediately reversible. Anesthesia & Analgesia. 1996 Mar 1;82(3):501-5.

32) Hirvonen EA, Poikolainen EO, Pääkkönen ME, Nuutinen LS. The adverse hemodynamic effects of anesthesia, head-up tilt, and carbon dioxide pneumoperitoneum during laparoscopic cholecystectomy. Surgical endoscopy. 2000 Mar 1;14(3):272-7

33) Cunningham AJ, Turner J, Rosenbaum S, Rafferty T. Transoesophageal echocardiographic assessment of haemodynamic function during laparoscopic cholecystectomy. BJA: British Journal of Anaesthesia. 1993 Jun 1;70(6):621-5

34) Dhoste K, Lacoste L, Karayan J, Lehuede MS, Thomas D, Fusciardi J. Haemodynamic and ventilatory changes during laparoscopic cholecystectomy in elderly ASA III patients. Canadian journal of anaesthesia. 1996 Aug 1;43(8):783-8.

35) Mann C, Boccara G, Pouzeratte Y, Eliet J, Serradeil-Le Gal C, Vergnes C, Bichet DG, Guillon G, Fabre JM, Colson P. The relationship among carbondioxide pneumoperitoneum, vasopressin release, and hemodynamic changes. Anesthesia & Analgesia. 1999 Aug 1;89(2):278-83.

36) Sárkány P, Lengyel S, Nemes R, Orosz L, Páll D, Molnár C, Fülesdi B. Non-invasive pulse wave analysis for monitoring the cardiovascular effects of CO 2 pneumoperitoneum during laparoscopic cholecystectomy-a prospective case-series study. BMC anesthesiology. 2014 Dec;14(1):98.

37) https://www.ncbi.nlm.nih.gov/pubmed/1534210 [The effects of the carbon dioxide pneumoperitoneum in laparoscopic cholecystectomy on postoperative spontaneous respiration]. Tolksdorf W[1], Strang CM, SchippersE, Simon HB, Truong S.

38) "COLON", The American Journal of Gastroenterology, 9/2007

39) J Minim Access Surg. 2012 Jul-Sep; 8(3): 85-89 Veress needle insertion through left lower intercostal space for creating pneumoperitoneum: Experience with 75 cases Sunil Kumar

40) Mushtaq Chalkoo, Shahnawaz Ahangar, Ab Hamid, Asim Laharwal, Umar Younus, Faud Sadiq, Sikender Iqbal. "Chapter 2 Laparoscopic Management of Difficult Cholecystectomy", InTech, 2012.

41) Sárkány P, Lengyel S, Nemes R, Orosz L, Páll D, Molnár C, Fülesdi B. Non-invasive pulse wave analysis for monitoring the cardiovascular effects of CO 2 pneumoperitoneum during laparoscopic cholecystectomy-a prospective case-series study. BMC anesthesiology. 2014 Dec;14(1):98.

42) Eva I, Rosario V, Cesare S, Clarissa V, Federica LP, Rosaria CR, Emma C, Veronica V. Hemocoagulative Modifications after Laparoscopic Surgery at Different Pneumoperitoneum Pressure Settings. International Journal of Surgery Protocols. 2022 Jan 1;26(1):41-8.

43) Sunamak O, DONMEZ T, Mihrapoglu S, Demiryas S, Erdem VM, Ferahman S. DOES LAPAROSCOPIC CHOLECYSTECTOMY AT LOW-PRESSURED PNEUMOPERITONEUM HAVE ADVANTAGOUS EFFECT ON COAGULATION PARAMETERS TO DECREASE VENOUS THROMBOEMBOLI RISK?. PONTE International Journal of Science and Research. 2016 Jun 16;72(6).

44) Amin B, Zhang C, Yan W, Sun Z, Zhang Y, Du D, Gong K. Effects of pneumoperitoneum of laparoscopic cholecystectomy on the coagulation system of patients: a prospective observational study. Chinese Medical Journal. 2014 Jul 20;127(14):2599-604.

45) Blake AM, Toker SI, Dunn E. Deep venous thrombosis prophylaxis is not indicated for laparoscopic cholecystectomy. JSLS. 2001 Jul Sep;5(3):2159

ANNEXURE-I - CONSENT FORM FORMAT

KAHER'S JNMC, BELAGAVI

INFORMED CONSENT FORM

"Comparative study of changes in coagulation profile in patients undergoing laparoscopy cholecystectomy using carbondioxide- pneumoperitoneum before and after surgery"

Name of student/Principal investigator:

Name of Guide/Co Investigator:

Objective: To determine the changes in coagulation profile of patients undergoing laparoscopic cholecystectomy using carbon di oxide pneumoperitoneum.

To assess if there is an increased risk of thrombosis post-operatively.

To determine if patients undergoing laparoscopic cholecystectomy have to be started on prophylaxis for deep vein thrombosis to prevent complications

Introduction: Minimally invasive surgery has become the procedure of choice for many disorders, laparoscopic cholecystectomy being the most commonly performed operation. In order to achieve better visibility of the surgical field, the ''CO2 pneumoperitoneum technique'' is used. There are many advantages to LCs such as a shorter hospitalization time, minimal postoperative pain and an easy recovery. However, there are also a few systemic disadvantages due to increase in intra-abdominal pressure.

Explanation of procedure: A total of 27 eligible patients were chosen. Detailed history, clinical examination and basic routine investigations will be done for all the

participants in the study. A total of 3 cc of blood will be drawn under strict aseptic precautions. One sample will be taken prior to surgery and the other sample 6 hours after onset of pneumoperitoneumSamples will be processed for prothrombin time and D-dimer.

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 not have nor get the 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 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 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 FORM FORMAT

KAHER'S JNMC, BELAGAVI

"Comparative study of changes in coagulation profile in patients undergoing laparoscopy cholecystectomy using carbondioxide- pneumoperitoneum before and after surgery"

Name of student/Principal investigator:

Name of Guide/Co Investigator:

Study Centre:

Patient Name:

Patients Age:

Identification Number:

Patient may check these (√) boxes

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected

I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to

this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study

I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well- being or any unexpected or unusual symptoms. I hereby consent to participate in this study

I hereby give permission to undergo complete clinical examination and necessary investigations.

Signature of Investigator Signature/thumb impression

Study Investigator's Name: Patient's Name and Address

INFORMATION SHEET

We are conducting a study on "Comparative study of changes in coagulation profile in patients undergoing laparoscopy cholecystectomy using carbondioxide pneumoperitoneum before and after surgery" and for that your clinical details may be valuable to us. We are selecting certain patients and if you are found eligible, we may be using your clinical details in such a way so as to not affect your final report or management. The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared. Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled. The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Once you are considered eligible for the study, your consent will be taken, the entire surgical procedure along with its indications will be explained to you. After the surgical procedure is done, you will be under constant monitoring by the doctor at ward rounds and once we find you suitable to be discharged, you will be discharged and then followed up. D-dimer and prothrombin level will be recorded before and after the surgery. If any complications are encountered, you will be asked to report us immediately.

Signature of investigator Signature of participant

Date:

CONSENT STATEMENT

I am making a voluntary decision to participate in the study "COMPARATIVE STUDY OF CHANGES IN COAGULATION PROFILE IN PATIENTS UNDERGOING LAPAROSCOPY CHOLECYSTECTOMY USING CARBONDIOXIDE- PNEUMOPERITONEUM BEFORE AND AFTER SURGERY". 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 participant:

Signature or left thumb impression of the participant:

Name of the witness:

Signature or left thumb impression of the witness:

Name of the investigator:

Signature of the investigator:

ANNEXURE II - CASE PROFORMA

Patient name

IP No:

Department:

Hospital:

Age:

Sex:

Occupation

Chief complaints:

Past history:

Body mass index:

General examination.

Vitals

a. Pulse rate:
b. Blood pressure:
c. Temperature:

Local examination:

Inspection

Palpation:

Percussion:

Auscultation:

Abdominal examination

Cardiovascular and respiratory system examination

Diagnosis:

Duration of surgery:

Table:

	Before surgery	6 hours after the surgery
Prothrombin time		
D-dimer		

CALCULATION OF PROTHROMBIN TIME

	Before surgery	After surgery
Mean		
Standard deviation		
Standard error of mean		

CALCULATION OF D-DIMER

	Before surgery	After surgery
Mean		
Standard deviation		
Standard error of mean		

master chart thesis comparative studies in coagulation profile using d dimer and ptinr in laparoscopi cholecystectomy to look for deep venous thrombosis

sr no	ip no	Age/Sex	chief complaints	comorbidities	Bmi	diagnosis	duration of surgery	preop		postop
							90 min	ptinr	d dimer	ptinr
1	10048887	32 m	pain in abdomen	nil	20	cholelithiasis		1.01	50	1.07
							95 min			
2	10049958	48 f	colicky abdominal pain	nil	19	cholelithiais		1.01	51	1.09
							90 min			
3	1004731	60 m	abdominal pain	nil	22	cholelithiasis		0.94	54	1.11
							110 min			
4	10049447	42 m	colicky abdominal pain	nil	19.5	cholelithaisis		0.9	141	0.94
							115 min			
5	1200008	58 m	pain in abdomen	nil	22	cholelithiasis		1.05	205	1.13
							120 min			
6	1198457	47 m	abdominal pain	nil	19.5	cholelithiasis		0.99	126	1.01
							125 min			
7	1193646	57 m	abdominal pain	nil	21	cholelithiasis		0.99	95	1.05
							110 min			
8	10040462	70 m	colicky abdomonal pain	nil	23	cholelithiasis		1.07	170	1.08
							100 min			
9	1188622	40 f	abdominal pain	nil	22	cholelithasis		1.07	180	1.09
							90 min			
10	100009776	38 m	abdominal pain. nil		21	cholelithiasis		0.91	139	1.02
							80 min			
11	10010253	40 m	colicky abdominal pain. nil		22	cholelithiasis		0.84	140	0.91
							100 min			
12	10009487	31 f	abdominal pain	nil	21	cholelithiasis		0.93	140	1.03
							90 min			
13		54 f	colicky abdominal pain. nil		20	cholelithiasis		0.91	129	0.97
							100 min			
14	1203847	33 f	abdominal pain	nil	19	cholelithiasis		0.9	165	1.03
							110 min			
15		50 m	abdominal pain	nil	21	cholelithiasis		1.03	84	1.05
							90 min			
16	1196448	30 f	colicky abdominal pain. nil		20	cholelithiasis		1.19	210	1.3
							150 min			
17	10044829	57 f	abdominal pain	nil	24	cholelithiasis		1.02	200	1.06
							110 min			
18	1135694	45 f	colicky abdominal pain nil		21	cholelithiasis		1	200	1.05
							100 min			
19	1196735	33 f	abdominal pain	nil	20	cholelithiasis		0.94	150	1.03
							90 min			
20		34 f	abdominal pain	nil	21	cholelithiasis		1.01	120	1.1
							170 min			
21	1201128	59 f	abdominal pain	nil	20	cholelithiasis		1.01	250	1.02
							90 min			
22	1192985	49 f	colicky abdominal pain. nil		22	cholelithiasis		0.94	140	0.92
							175 min			
23	1194877	55 f	abdominal pain	nil	23	cholelithiasis		0.95	280	1.04
							120 min			
24	1190576	53 f	abdominal pain	nil	21	cholelithiasis		0.97	170	1.05
							110 min			
25		60 f	abdominal pain	nil	20	cholelithiasis		0.87	121	1.03
							90 min			
26		60 m	colicky abdomonal pain. nil		20	cholelithiasis		0.91	210	1
							100 min			
27	1187280	45 f	abdominal pain	nil	21	cholelithiasis		1.04	200	0.92

ic
d d dimer
379
233
281
300
350
210
170
300
310
280
310
280
300
368
210
380
400
280
400
200
400
179
400
250
380
280
310