“STUDY OF CHANGES IN COAGULATION PROFILE OF PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY USING CARBON DI OXIDE PNEUMOPERITONEUM’’

Dissertation submitted

To

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY, CHENNAI

With partial fulfillment of the regulations for the award of the degree of

M.S (General Surgery)

Branch-I

Government Kilpauk Medical College

Chennai- April -2016

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation titled " STUDY OF CHANGES IN COAGULATION PROFILE OF PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY USING CARBONDIOXIDE PNEUMOPERITONEUM'' is a bonafide and genuine research work carried out by me under the guidance of Prof. USHA DORAIRAJAN MS, FRCS, Department of General Surgery, Kilpauk Medical College, Chennai-10.

This dissertation is submitted to **THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY CHENNAI** in partial fulfillment of the degree of M.S. General Surgery examination to be held in **April 2016**.

Date:

Place: **DR. BHARATH . N**

CERTIFICATE

This is to certify that this dissertation is the bonafide work of

DR. BHARATH .N

On

"STUDY OF CHANGES IN COAGULATION PROFILE OF PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY USING CARBON DI OXIDE PNEUMOPERITONEUM''

During his course in M.S. General Surgery from JANUARY 2015 to September 2015 at Government Kilpauk Medical College, Chennai-10.

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This is to certify that the dissertation titled **"STUDY OF CHANGES IN COAGULATION PROFILE OF PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY USING CARBON DI OXIDE PNEUMOPERITONEUM''** is a bonafide research work done by **Dr.BHARATH.N** , post graduate in M.S. General Surgery, Kilpauk Medical College, Chennai-10 under my direct guidance and supervision in my satisfaction, in partial fulfillment of the requirements for the degree of **M.S. General Surgery**.

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INSTITUTIONAL ETHICAL COMMITTEE
GOVT.KILPAUK MEDICAL COLLEGE,
CHENNAI-10
Protocol ID No.15/01/2015 Dt. .01.2015
CERTIFICATE OF APPROVAL

The Institutional Ethical Committee of Govt. Kilpauk Medical College, Chennai reviewed and discussed the application for approval "Changes in coagulation profile of patients undergoing laproscopic cholecystectomy using CO2 Pheumoperitoneum". -For Project Work- submitted by Dr. N. Bharath, PG in General Surgery, KMC, Chennai-10.

The Proposal is APPROVED.

The Institutional Ethical Committee expects to be informed about the progress of the study any Adverse Drug Reaction Occurring in the Course of the study any change in the protocol and patient information /informed consent and asks to be provided a copy of the final report.

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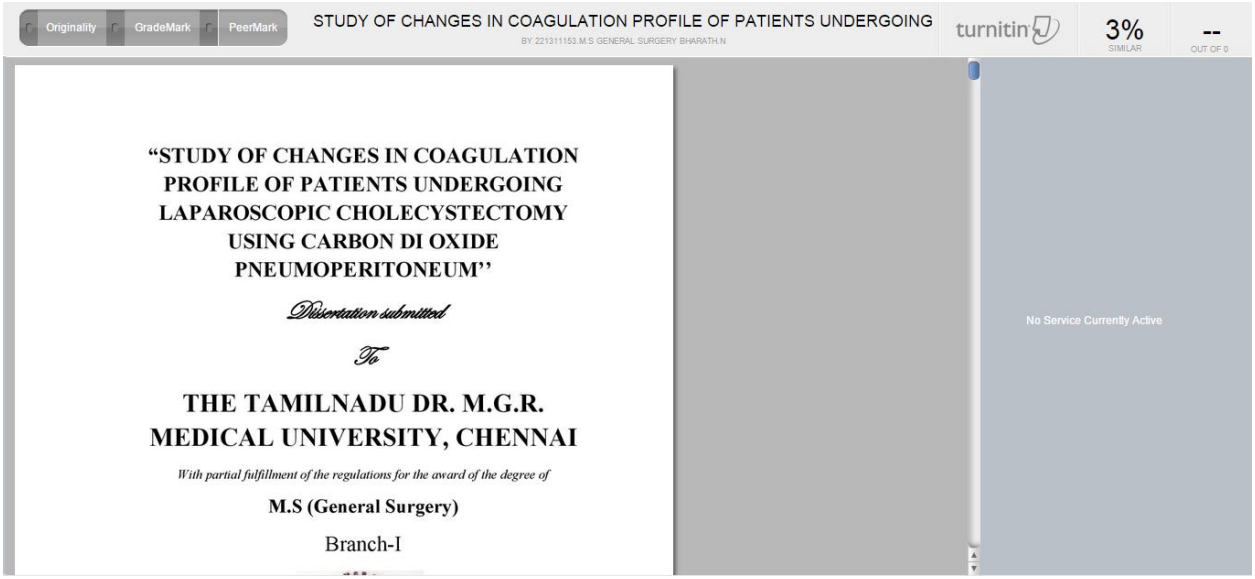
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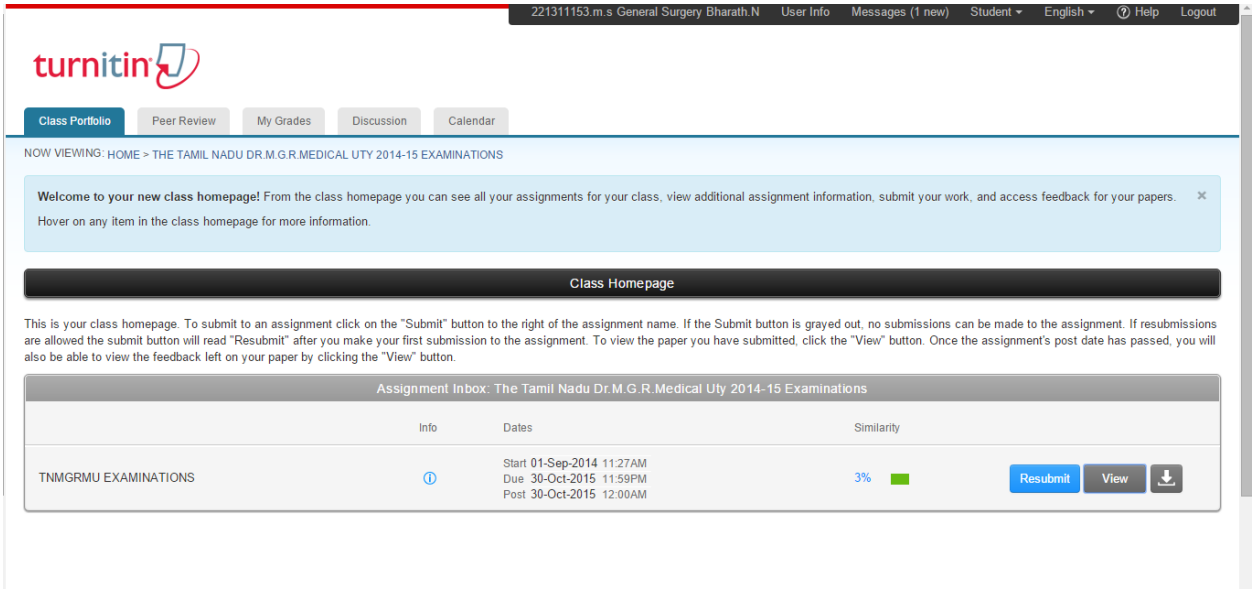
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ABSTRACT

Topic: Study of changes in coagulation profile of patients undergoing laparoscopic cholecystectomy using carbon dioxide pneumoperitoneum

Background: Laparoscopic cholecystectomy is a common surgical procedure and carbon dioxide pneumoperitoneum created for this purpose may alter the coagulation profile of these patients. This study aims to find the effects of carbon dioxide pneumoperitoneum on coagulation profile and assess if there is an increased risk of thrombosis.

Materials and methods: A clinical observational study was conducted with 50 patients who underwent laparoscopic cholecystectomy using carbon di oxide pneumoperitoneum. The prothrombin time and D-dimer values were calculated before and after surgery .using the paired t test data was analyzed.

Results: The study showed a decrease in the prothrombin time and increase in the D-dimer value post operatively. The mean of prothrombin time after surgery was 0.13 seconds lower than the preoperative value and D-dimer was found to be elevated three times the pre operative values. The p value calculated for both were highly significant.

Conclusion: Laparoscopic cholecystectomy using carbon dioxide pneumoperitoneum leads to hypercoagulable states. Hence stringent measures need to be taken to put the patient on prophylaxis for deep vein thrombosis to avoid dire consequences

Keywords: Laparoscopic cholecystectomy, Carbon dioxide Pneumoperitoneum, Coagulation Profile, Prothrombin time, D-Dimer, Hypercoagulation, DVT prophylaxis

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INTRODUCTION

Laparoscopy is one of the widely used tools for diagnostic and therapeutic purposes in recent times. Laparoscopy offers the advantage of better cosmesis, lesser post-operative pain, shorter hospital stay, early return to normal life and work. With advancements in technology and instrumentation, laparoscopy has entered into every array of surgical field.

A working cavity is one of the requisites for laparoscopy. This cavity is commonly created by positive pressure pneumoperitoneum using carbon di oxide. In 1924, Richard Zolliker of Switzerland first proposed the use of carbon di oxide for creation of pneumoperitoneum as it was noncombustible and hence electrocoagulation was possible during surgery.

Carbon di oxide pneumoperitoneum affects normal physiology. It is easily absorbed from the peritoneal cavity into circulation. It may affect the cardiovascular, respiratory and coagulation system, to name a few.

Laparoscopy has its complications due to increased intraabdominal pressure, carbon di oxide absorption from peritoneum during insufflation and reverse trendenlenberg position adopted during surgery.

The first laparoscopic cholecystectomy was performed in 1986 in Germany. Over the past 30 years there has been a gradual but drastic change in the methodology. The duration of surgery, complications have reduced over time. Laparoscopic cholecystectomy is now the gold standard procedure. And with over 5,00,000 procedures being done annually, laparoscopic cholecystectomy assumes a great significance in general surgical specialty.

Effects of carbon di oxide pneumoperitoneum need to be studied in detail with respect to individual systems. This study aims to study the effects of carbon di oxide pneumoperitoneum on the coagulation system of patients undergoing laparoscopic cholecystectomy , and make the surgeon aware of the detrimental effects , if any.

AIM OF THE STUDY

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

2. Assess if there is an increased risk of thrombosis post-operatively.

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

Reasons for conducting the study:

1. Laparoscopic cholecystectomy is becoming more commonly used due to wider availability of facilities.

2. No proper studies on effects of laparoscopic surgery using carbon di oxide pneumoperitoneum on coagulation system in India.

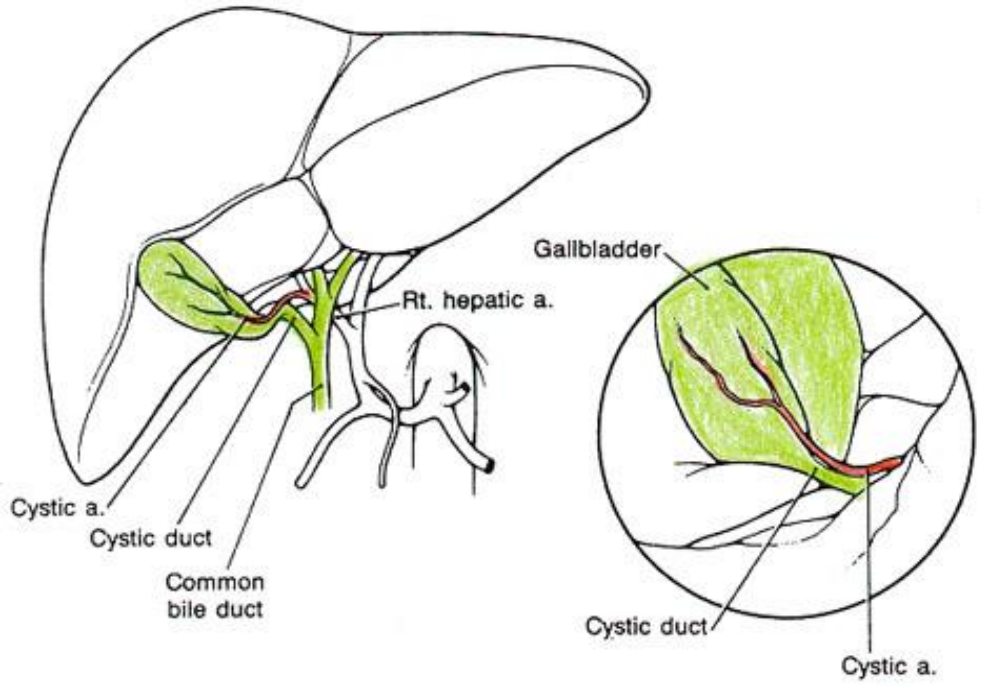
3. To assess if there is an increase in the associated morbidity and mortality due to thrombotic phenomena.

4. To assess if patients undergoing laparoscopic cholecystectomy surgeries are in need of prophylaxis against deep vein thrombosis.

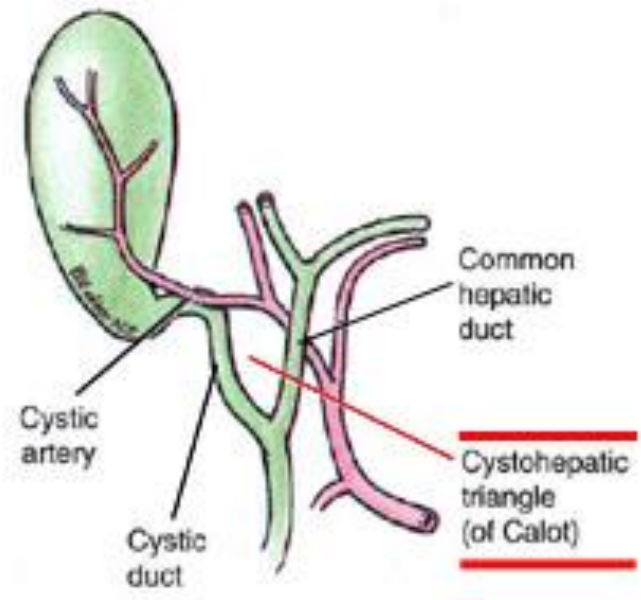
Anatomy of Gall bladder[1]:

The gall bladder is a pear or pyriform shaped organ that lies in close proximity to the liver(its inferior surface) . The gallbladder is divided anatomically into the fundus , body, infundibulum and the neck. The gallbladder opens into the cystic duct , through which bile enters and exits the gallbladder into the common bile duct.

The arterial supply of the gallbladder is by the cystic artery, which is a branch of the right hepatic artery. The venous drain is through the cystohepatic veins, These are multiple in number and are unnamed. Lymphatic drainage is mainly through the lymph node of Lund. Parasympathetic supply is through the right vagus and sympathetic through T7-9.



The Calot's triangle forms an important landmark for performing cholecystectomy, for it is here that both the cystic duct and cystic artery are ligated and cut. The Calot's triangle is formed medially by the common hepatic duct superiorly by the inferior liver surface and the cystic duct laterally and inferiorly.



The contents of the Calot's triangle are the cystic artery and the lymph node of Lund. The normal volume of gallbladder varies from 30-50ml. but in cases of obstruction the size may increase manifold. The gallbladder is usually not palpable. A palpable gall bladder could mean an obstructive pathology in the common bile duct or rarely the cystic duct itself.

CHOLECYSTECTOMY:

Cholecystectomy is the surgical removal of gall bladder. Indications[2] include symptomatic gall stones, gall bladder polyps greater than 1 cm, acute and chronic cholecystitis, acalculous cholecystitis, empyema gall bladder, mucocoele of gall bladder, typhoid carriers and gallstone pancreatitis.

Prophylactic cholecystectomy is done in diabetic patients, immunocompromised patients, patients undergoing organ transplant, congenital hemolytic anemia, patients undergoing bariatric surgery and porcelain gall bladder.

Absolute Contraindications of laparoscopic cholecystectomy include patients unfit for general anesthesia, patients with coagulation disorders, suspected gall bladder carcinomas as it might cause port site metastasis, and patients unwilling for laparoscopic procedure.

Relative contraindications are previous upper abdominal surgeries due to dense adhesions, liver cirrhosis as the liver is too brittle for retraction, portal hypertension as there may be multiple venous collaterals, patients with cardiac or respiratory complications and pregnancy.

Problems associated with cholecystectomy may range from difficult Calot's dissection, dense adhesions, perioperative bleeding from the pedicle or liver bed, anomalies of cystic duct and cystic artery may also pose a challenge.

Complications after cholecystectomy include infection and sub phrenic abscess, bleeding from the cystic artery and liver bed. The common bile duct or the hepatic duct may get injured inadvertently. A bile leak or a biliary fistula or a stricture formation are some rare but serious complication. Iatrogenic injury to colon , duodenum or mesentery may occur in presence of dense adhesions.

HISTORY OF LAPAROSCOPIC CHOLECYSTECTOMY[3,4]

1882- Carl Langbuch from Germany performs the first cholecystectomy.

1980- Semm performs first laparoscopic appendectomy.

1984- Erich Muhe designs the galloscope (laparoscope for cholecystectomy)

1985- Sept12 – Erich Muhe performs the first laparoscopic cholecystectomy.

Uses pistol grip scissors, pistol grip applier and hemoclips.

Uses Verres technique to create pneumoperitoneum.

1986- Muhe presents the case before the German Surgical society and is rejected by them.

1987- Lyon performs his first laparoscopic cholecystectomy in France.

1988- First laparoscopic cholecystectomy in USA.

1990- Perissat, Dubios, Cushieri acknowledged by SAGES for having performed Laparoscopic Cholecystectomy

1992- Muhe receives GSS anniversary award as acknowledgement for his contribution.

1997- Navarra et al performs the first single incision laparoscopic surgery.

1999- Muhe presents “THE FIRST LAPAROSCOPIC CHOLECYSTECTOMY” in TEXAS in STORZ conference ascertaining his place in history as the first person to have performed laparoscopic cholecystectomy .

LATEST ADVANCEMENTS IN CHOLECYSTECTOMY

There was a time when the surgical society believed that “Larger problems meant larger incisions.” With advancements in field of anesthesia, fiber optics, instrumentation, the focus has shifted towards minimally invasive surgery and less or no visible scars, is the order of the day.

Cosmesis has become an important objective. Minimal scars also mean lesser postoperative pain, lesser adhesions and minimal postoperative complications. This search has led to opening of new avenues in fields of single incision laparoscopy, natural orifice laparoscopic surgery, three dimensional laparoscopic surgery and robotic surgery.

Stal Pert in 1687, found gall stones in a patient who underwent laparotomy for peritonitis. Two centuries later, Langenbuch performed the first open cholecystectomy on a patient. The open technique remained the gold standard procedure for nearly a century. Till the other methods came and took over. Open cholecystectomy is still used in cases where there are dense adhesions, or when a common bile duct exploration is needed in addition to a cholecystectomy.

Minilap cholecystectomy was in vogue for a short duration. Ultrasound and other radiographic methods were used to localize the position of the gall bladder and Calot's triangle. A smaller incision, one third the size of the conventional one, is put right above the location of the gall bladder. The incision is deepened and with the use of retractors, dissection is carried out in the Calot's triangle. In case of difficulties the incision can be extended as required.

This technique is still used in places where laparoscopic techniques have not come into use. This technique can also be used in patients who are not fit for general anesthesia, and for some cases where there is a difficulty in laparoscopy and needs conversion to open surgery.

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

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

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

Once the news of laparoscopic cholecystectomy spread, surgeons in different parts of the world started attempting laparoscopic surgeries, and laparoscopic surgery overtook the open method and became the procedure of choice. Even after 30 years and in spite of many new techniques that have evolved, Laparoscopic cholecystectomy remains the gold standard procedure.

The four port method is the conventional and still widely used method. Researchers have tried to reduce the number of ports and also tried using smaller ports for better cosmesis.

The fourth trocar to retract the liver has been debated by many as to be an unnecessary addition in simple cases, and that cholecystectomy can be performed with no greater difficulty or increased operative time without the fourth trocar being placed.

The introduction of transabdominal sutures meant that the ports required to retract the liver lost their relevance. Sutures can be placed to on the gall bladder and anterior abdominal wall for retraction of the gall bladder during dissection at the Calot's triangle

This led to the two port cholecystectomy. As the number of suture placed varied from one to three, and it needed expertise the search for a better technique continued. This method also had the disadvantages that the level and retraction could not be changed during the surgery as per the surgeon's need.

To solve these issues SILS, or the single incision laparoscopic surgery came into the mainstream, it employed a special port called the R- port. The R-port is a specialized large umbilical trocar. It has provisions for the insertion of three 5mm instruments at slightly different angles at each other. This allowed for making only a single 2.5 cm incision in the umbilicus, created by open method, and hence left the patient with a single scar in the umbilicus.

SILS is thus an advanced minimally invasive surgical procedure. It also allows easy retrieval of the specimen through the large 2.5 cm incision. The only major disadvantage being that the R port is an extremely costly instrument and adds up to the surgical cost.

The presence of a 2.5 cm scar in the umbilicus was cosmetically unsightly for a few and hence came the concept of Natural Orifice Transluminal Endoscopic Surgery or (NOTES). The use of a natural orifice for laparoscopy is being tried for a variety of surgery, e.g.: thyroidectomy through trans-oral route.

Cholecystectomy has now been tried through many routes and many more are in the process of development. Some of these techniques are trans -gastric, trans-anal, trans-vaginal, trans-colonic routes. This requires the use of colonoscopes, vaginal platform instruments, staplers and flexible endoscopic instruments.

The problems associated with these techniques include higher set up cost, steep learning curve, perforating a normal organ for access into the peritoneal cavity, chances of introduction of infection into the peritoneum, soiling of the surgical field and finally closing of the perforation created for surgery.

NOTES is an area that is undergoing tremendous innovations, and might throw open a window for development of separate branch, given its wide range of applications.

Animal and human clinical experiments are being carried out in robotic surgeries. With the advent of robotics and robotics assisted techniques into the field of surgery, we live in a world where we wake up to a new and a brighter day each time.

LAPAROSCOPY:

Laparoscopy is the endoscopic visualization of peritoneal cavity. It usually assisted by pneumoperitoneum that helps to distend the peritoneal cavity and separate the abdominal wall from the contents.

This pneumoperitoneum helps in visual clarity of visualized abdominal organs. It provides the necessary space to perform diagnostic and therapeutic procedures. It reduces the chances of injury to the adjacent organs. It helps maintain normal physiological state which is required for safe effective surgery

PNEUMOPERITONEUM:

The gas chosen for pneumoperitoneum depends on many factors. Some of them are the type of anesthesia given, method of gas delivery, physiological compatibility, non-combustibility, minimal or no toxicity of the gas, ease of use, safety, cost, no harm on leakage of gas, easy excretion of gas through metabolism.

Some of the commonly employed gases are carbon di oxide, nitrous oxide, helium, oxygen, argon and air. Each of them have their own advantages and disadvantages and hence have different medical applications.

Creation of pneumoperitoneum:

Pneumoperitoneum is created by of the two methods. Closed techniques of Veress and the Open technique of Hasson's.

Veress method uses a specialized needle "Veress needle" for the creation of pneumoperitoneum. The needle is classically 12 to 15 cm long and has a blunt end which is spring loaded to protect the bowel. The needle is inserted into the abdominal cavity after the anterior abdominal wall is lifted up to apply counter pressure and once the needle is inside the peritoneal cavity, the gas is insufflated and telescope port is inserted blindly. Other ports are created under visual guidance.

Advantage of Veress method being that it is quicker and needs no other specific instrument. Disadvantage is that, there are more chances of injury to bowel, and vascular structures underneath.

Open method of Hasson's requires no such needle. And every step is done under vision. 1 to 1.5 cm Incision is made in the umbilicus and deepened to reach the rectus. Rectus and peritoneum are opened under vision and entry into peritoneal cavity is checked and umbilical port is inserted and gas for pneumoperitoneum is insufflated. A telescope is inserted under vision and laparoscopy is done. Other ports are also inserted under vision.

Advantage of open method is that there are no or minimal risks of injury to bowel or vascular structures as every step is done under vision. Disadvantage is that it takes a longer time when compared to the Veress method.

The major complication of laparoscopy occurs mainly at the time of insertion of the umbilical trocar. These complications may result mainly due to adhesions at site of entry.

It is reported that the Veress technique is used in 62% of cases and Hasson's method is used in 38 % of cases. But it is the Hasson's method which is used by majority of general surgeons as it is deemed to be the safer option for access into the peritoneum.

The optimal pressure for pneumoperitoneum is 12-15 millimeters of mercury. Higher pressures may be used during the first entry port to reduce chances of injury.

Carbon di oxide as the "Gas of choice" :

CO_2 is the most preferred gas for the creating pneumoperitoneum as it has a high diffusion co-efficient. It is also a normal end metabolic product; hence excess is easily tolerated and is rapidly cleared from the body. It offers the advantage that it is highly soluble in blood and tissues and carries the lowest risk of gas embolism.

But carbon dioxide has its disadvantages that it can cause arrhythmias, hypercarbia, tachycardia and acidosis in cardiac patients and in those undergoing long duration surgeries.

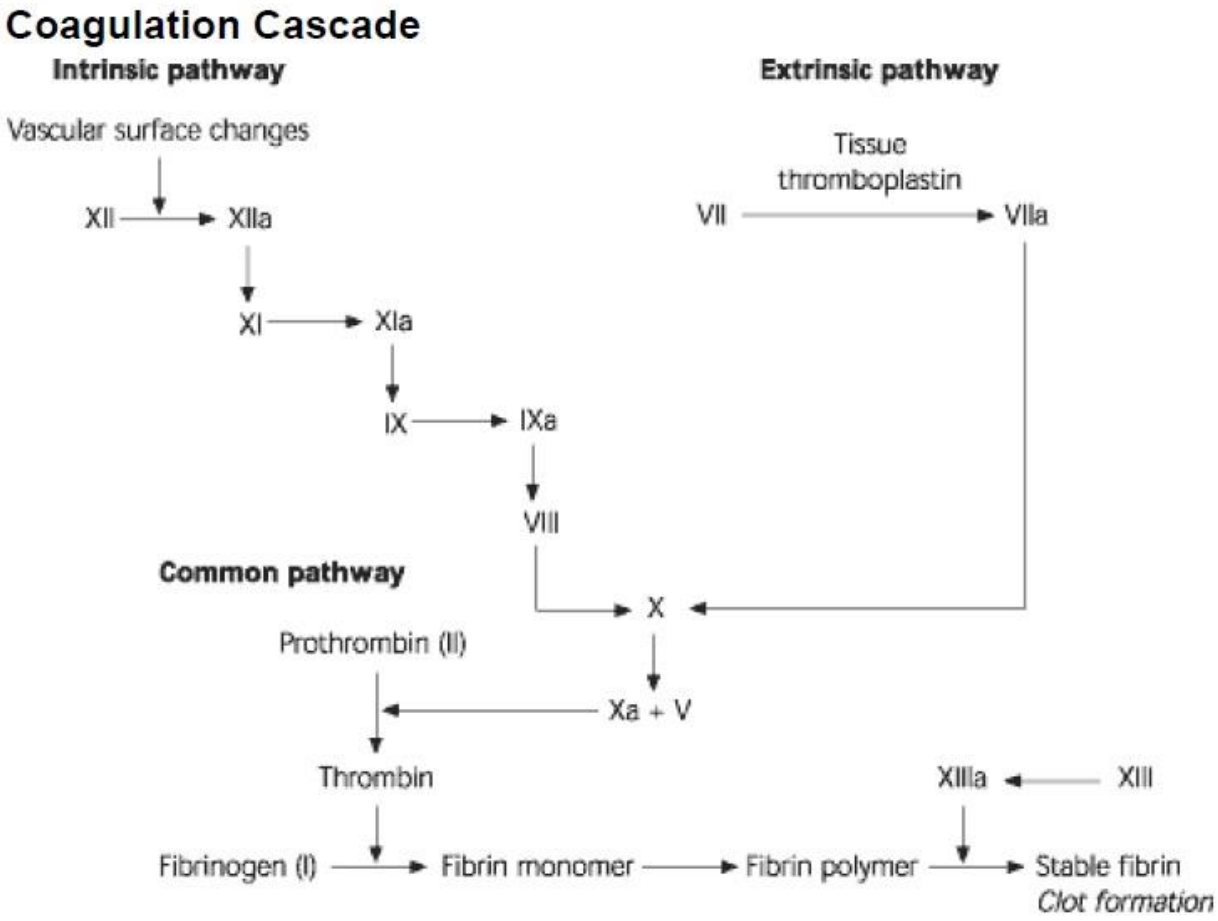
Carbon dioxide is easy to manufacture, easily available and cost effective. It is non-combustible and causes no harm to medical personnel in event of leakage. It is a non-irritant and has little to no smell.

For the above mentioned reasons Carbon di oxide is widely used and is at present the "GAS OF CHOICE" for creating pneumoperitoneum.

COAGULATION PATHWAY:

The coagulation of blood[5] depends on the balance between two groups, procoagulants and anticoagulants that is present in blood. In response to endothelial damage, prothrombin activators are formed and these cause conversion of

prothrombin into thrombin. Thrombin catalyzes the conversion of fibrinogen into fibrin, which results in a stable clot. The conversion of prothrombin to thrombin requires tissue factor or factor III, factor X-A, factor V and calcium.



PROTHROMBIN :

Prothrombin is a plasma protein formed by the liver. It is involved in the process of coagulation. It is Vitamin K dependent. On exposure to prothrombin activators, it is

converted into thrombin. Thrombin further helps in conversion of fibrinogen into fibrin and thus forms clots.

Prothrombin time is the indicator of concentration of prothrombin in blood. Upon collection, Blood is oxalated to prevent conversion of prothrombin to thrombin. large amounts of calcium ion and tissue factor is then mixed. This activates the extrinsic pathway for coagulation .The time required for coagulation is denoted as the prothrombin time.

Normal time is around 12 seconds.

D-dimer:

It is the product of degradation of crosslinked fibrin (XII Factor)[6]. It is an indicator of ongoing process of activation of hemostatic system. The reference value is less than 250 ng/ml or 0.5 ug/ml fibrinogen equivalent units.

D-dimer has various uses as it can be used in evaluation of thrombus formation, ruling out deep vein thrombosis, monitoring anticoagulant therapy, disseminated intravascular coagulation, and in snake venom poisoning. It is also a cost effective rapid tool to rule out pulmonary embolism in patients with low risk of the condition.

D-dimer levels can be increased in pregnancy, inflammation, malignancy, heart diseases, trauma, liver diseases and post-surgical treatment.

In an adult with a clinically low pretest probability (Well's score), there is a 99 % negative predictive value, when the d-dimer test is negative, in patients less than 80 years of age.

REVIEW OF LITREATURE

Sages { Society of American Gastro and Endoscopic Surgeons } [7]

recommendation:

"Prophylaxis has to be tailored for each patient based on their estimated risk. All laparoscopic procedures carry a risk of hypercoagulability. Short and less complicated or less complex procedures like laparoscopic appendectomy and laparoscopic cholecystectomy carry a low risk of venous thromboembolism."

"Patient positioning during surgery may alter the DVT risk. But the evidence is not significant enough to suggest that DVT prophylaxis should be changed based only on body position. The reverse trendenlenberg position and increased intraabdominal pressure may decrease the venous return and thus cause increased risk for deep vein thrombosis."

"Laparoscopic procedures that extend beyond one hour may need venous thromboembolism prophylaxis. Compression dressing, unfractionated heparin, low molecular weight heparin may be used to this effect."

SAGES recommends that the risk factors for deep vein thrombosis are duration of surgery greater than 1 hour, previous H/o venous thromboembolism, age more than 40, myocardial infarction in the past, features of congestive cardiac failure, immobilization, patients undergoing hormone replacement therapy, varicose veins, oral contraceptive use, diagnosed malignancy, multiparous women, history of chronic renal failure, known case of inflammatory bowel disease, severe infection and obesity

SAGES recommends that each of the factors are given one point. If the total of positive factors is 0 or 1 then the patient need not be given prophylaxis or the patient may be subjected to one method, either pneumatic compression dressings or Unfractionated Heparin(UH) or low molecular weight heparin(LMWH).

If the sum of the factors is 2 or greater than 2 then the patient has to be put on unfractionated heparin or low molecular heparin in addition to pneumatic compression dressing to prevent deep vein thrombosis.

The University of Michigan gives a table [8] and its own recommendations for deep vein prophylaxis. These recommendations are widely accepted across multiple specialties and also by anesthetists worldwide.

The table consists of a list of factors- high risk ones carrying 5 points medium risk factors carrying 3 and 2 points and a low risk factors carrying 1 point each. The sum of positive factors is derived and recommendations are given for each category.

Scores of zero carry a very low risk and need no further action.

Patients having score of 1 and 2 have a low risk and may need compression dressings.

Patients with scores of 3 and 4 have a moderate risk and need compression dressing or heparin.

Patients with scores of 5 and above carry a high risk of DVT and need both heparin and compression devices.

Factors carrying 5 points
Stroke within last 1 month
Multiple trauma within the past 1 month
Acute spinal cord injury within 1 month
Elective major lower extremity arthroplasty/Hip, pelvis or leg fracture

2 points	**3 points**
61-74 years of age	Age greater than 75 years
Central venous access	Family H/o thrombosis
Laparoscopic surgery duration(>45min)	H/o DVT / PE
Arthroscopic surgery	Positive Prothrombin 20210A
Major surgery (duration >45 minutes)	Positive Factor V Leiden
Malignancy	Positive Lupus anticoagulant
Immobilizing plaster cast <1 month	Heparin-induced thrombocytopenia (HIT)
Patient confined to bed >3 days	Elevated anticardiolipin antibodies

FACTORS CARRYING 1 POINT
Age between 41-60 years
Myocardial infarction
History of major surgery within the past 1 month
Minor surgery planned
H/o inflammatory bowel disease
Obesity (BMI greater than 25)
Patient currently at bed rest
Varicose veins
Congestive heart failure
Swollen legs : edema –thrombophlebitis
History of Sepsis in the past 1 month
Abnormal pulmonary function
Oral contraceptives treatment or hormone replacement therapy
History of unexplained stillborn infant in the past
Pregnancy or postpartum in the past 1 month
More than 3 Recurrent spontaneous abortion
Premature birth
Serious respiratory disease including pneumonia

Deep vein thrombosis prophylaxis can be given by one of the following methods.

Pneumatic compression devices are calf length pneumatic devices which increase lower extremity venous blood flow they also cause fibrinolysis. The advantage of pneumatic compression device is that they don't pose an increased risk of bleeding. Disadvantage is that once features of deep vein thrombosis set in the use of these devices may carry an increased risk.

Unfractionated heparin is given subcutaneously or through intravenous route. It is given in the dosage of 5000 international units 6^{th} hourly. The disadvantage of unfractionated heparin is that it has to be repeated multiple times a day. It also has an increased risk of bleeding. It can be stopped 6 hours before surgery and started six hours after surgery

Low molecular weight heparin is usually given in a twice daily dosing. It is administered through subcutaneous route. This delivers a lower dose and has lesser incidence of heparin induced thrombocytopenia.

A combination of the above is frequently used for Deep vein thrombosis prophylaxis.

STUDIES AND THEIR RESULTS

Alteration in the hemodynamics during laparoscopy depends on concomitant disease process, intraabdominal pressure during surgery, amount of carbon di oxide that gets absorbed during circulation, position of the patient during surgery, nature of the procedure, operative time and neuro-humeral response. The intravascular volume, preexisting cardiac status and anesthetic agent used also play a role.

The following studies look into the relation between Carbon dioxide pneumoperitoneum –reverse trendenlenberg position on the cardiovascular and coagulation system.

Baker .J et al [9]conducted a study on 60 patients and found that "Carbon di oxide pneumoperitoneum may cause blunting of inflammatory response due to acidosis at cellular level"

Kehlet [10] also mentioned that "There is not much difference in the coagulation system in laparoscopic and open procedure and changes could mainly be attributed to the position of patient in laparoscopic surgery (Reverse Trendenlenberg)."

Kehlet et al. [10] stated that "Carbon di oxide pneumoperitoneum may attribute to increased post-operative morbidity. Patients undergoing laparoscopic surgery with carbon di oxide had higher incidence of nausea, vomiting, shoulder pain and fatigue when compared to those undergoing gasless cholecystectomy."

Kehlet et al [10] stated "There is no major difference on endocrine and metabolic response between the groups undergoing laparoscopic and open procedure but there is a marked decrease in inflammatory response in the former."

Marshal et al[11] stated "Cardiac output ,central venous pressure, heart rate and mean arterial pressure (MAP) measurements remained the same before and after carbon di oxide insufflation during laparoscopic procedures."

But they also mentioned that "There was an increase in the partial pressure of carbon di oxide and decrease in the pH during creation of pneumoperitoneum."

In a study in 60 patients Chopra et al [12] found that "There was a highly significant increase in heart rate, end tidal carbon di oxide, systolic blood pressure, diastolic blood pressure and mean arterial pressure in the laparoscopic group. There were also changes in the SpO2, electrocardiogram of patients in the laparoscopic group."

Chopra et al mentioned that "These physiological changes need no major intervention at most times but they need continuous monitoring peroperatively and post operatively to pick complications if any arise."

Muller C M et al [13] conducted a study on 119 patients and told that "Carbon di oxide output increases upto 50 % in patients undergoing laparoscopic cholecystectomy."

Cunningham et al [14] in a study of 103 patients found that "Patients put in reverse trendenlenberg position had a 50% decline in cardiac index and a 50% fall in venous return." He also noted an increase in heart rate and mean arterial pressure.

Laparoscopic cholecystectomy was reported to have no effects on the coagulation system in various studies.

Dexter et al [15] studied 26 patients and he analyzed clotting factors. "Stress response, cytokine release and neuro-humeral response during surgery were stated as the major factors that caused thromboembolic phenomenon. Of the 26 patients studied, only Euglobin clot lysis time was found to be raised. All other clotting factors were found to be normal. He hence concluded that laparoscopic surgery does not increase the risk of thromboembolism."

Jens Fromholt [16] compared laparoscopic surgeries done using carbon di oxide with ones conducted without pneumoperitoneum and stated that "There was no difference in the prothrombin time and d-dimer in both the groups."

He hence concluded that "He could not decide if patients undergoing laparoscopic cholecystectomy were at a higher risk of thromboembolic complications when compared to patients undergoing gasless cholecystectomy"

Dabrowiecki et al [17] conducted a larger study on 100 patients. He took blood samples from upper limb (cubital vein) and lower limb (femoral vein) post operatively in patients undergoing laparoscopic procedures and revealed that "There was no change in the coagulation profile of the two samples and suggested that the venous stasis in lower limbs in these patients does not contribute to alterations in the hemostatic mechanisms."

Khairy et al[18] found that "The change in the thrombin time was not significant post-surgery. He indicated that the pneumoperitoneum thus did not alter the thrombin time in the patients and postoperative thrombosis did not correlate to the thrombin time."

Martinez Ramos et al[19] observed twenty patients on a long term basis. He took multiple samples: preoperatively, at the onset of pneumoperitoneum, at the end of surgery, 24 hours after surgery and 7th day post operatively. He saw there were no thromboembolic phenomena even after 16 months of follow up.

Rahr et al[20] found that "The coagulation profile did not change much and hence no major changes occurred in the coagulation system in patients who underwent laparoscopic procedures."

Joegruson T et al[21] studied the Partial thromboplastin time, Anti X-A, fibrinogen in patient undergoing laparoscopic cholecystectomy. Samples were taken 1 hour before surgery, 24 hours after surgery and 7th Post-operative day. He concluded that there were no significant changes in the values studied.

Natkaniec et al[22] postulated that laparoscopic surgery caused stasis of blood in the inferior vena cava and common iliac vein. He studied coagulation profile in 25 patients and told that there was no change in the coagulation profile of patients.

Multiple studies have been conducted to assess the risk of thrombosis post laparoscopic cholecystectomy. The following studies inferred that the risk of thromboembolism increased post surgery.

Trifeletti et al [23] noted that "In circumstances such as traumatic injuries and surgery in patients, the level of fibrin A peptide was elevated and a consequent increase in the level of blood fibrinogen occurred. This led to hyper coagulation."

Trifilleti et al [23] noticed that "There was a significant increase in the fibrinogen levels 8 hours after surgery. This, he noted, may be due to the decreased response against stress. This decreased response to stress may be due to pneumoperitoneum, anesthetic that act on liver, decreased blood flow through the portal vein, fluids infused during surgery."

He concluded that "The concentration of fibrinogen is the highest eight hours post-surgery. And this time period poses the greatest risk for further development of DVT."

Huang et al[24] discovered that "The postoperative alterations in the coagulation system is one of the main causes of deep vein thrombosis."

Hans et al[25] reported that "Activation of the coagulation system by laparoscopic procedure causes promotion of hypercoagulable state."

Garg et al [26] reported that "Carbon dioxide pneumoperitoneum enhanced coagulation system and fibrinolytic system activation and hence a state of hypercoagulation occurred in these patients."

Amin et al[27] studied the coagulation profile of patients undergoing laparoscopic cholecystectomy. He inferred that "While the prothrombin time was elevated the activated partial thromboplastin time remained the same. This they said may lead to hypercoagulable states even within 6 hours post-surgery."

On the contrary some studies found that hypocoagulable states were common after laparoscopic surgery

Schietroma et al[28] studied the cytokine levels in patients undergoing laparoscopic and open procedure and found that " Hypercoagulation was seen almost after every surgery. This was attributed by him to the increased cytokine level. Since laparoscopic surgery causes lesser tissue damage, it releases lesser cytokines hence causes lesser hypercoagulability when compared to open surgery."

Schietroma et al further stated that "Prothrombin fragment, fibrinogen, plasminogen, D-dimer, soluble fibrin and Protein C, all were raised in open surgery compared to laparoscopy". He concluded that only mild hypercoagulability resulted after laparoscopic cholecystectomy and further studies are required to confirm the findings.

Lauro et al[29] observed 36 patients. He divided them into two groups laparoscopic and open, half of each group was put on deep venous thrombosis prophylaxis and other half was not given prophylaxis. He said that laparoscopy is associated with increased resistance to venous return from both the lower limbs and the resultant stasis could promote thromboembolic phenomenon.

He observed that fibrinogen and D-dimer were significantly higher in the open group while prothrombin time and partial thromboplastin time were unaffected. Perioperatively coagulative fibrinolytic changes were lower in laparoscopy when they were compared to the counterparts in the opposite group. And hence concluded that laparoscopy may indeed be advantageous with respect to coagulation system.

Yan MJ et al[30] found in his studies that "The levels of fibrinogen decreased after surgery. Thus patients are in a hypocoagulable state."

The timing of highest risk for thrombosis were reported at various time intervals following laparoscopic cholecystectomy

Custendil et al[31] reported "Higher incidence of thrombosis on the first post operative day following surgery."

Lord RV et al[32] reported "Higher incidence of thrombosis on the third post operative day following pneumoperitoneum."

Amin Buhe et al[33] suggested that "The first 8 hours following surgery carry the highest risk of thrombosis, this is because the patient is immobilized in bed , is in a state of fasting, discontinued on anticoagulation therapy, patient was on pneumoperitoneum."

He postulated that "The patients are at high risk within 8 hours after surgery for development of thrombosis, and 8 hours post-operation is the pivotal period of venous thrombosis".

The incidence of thrombosis too varied from 0.02% to as high as 55% depending on the technique used for diagnosing thrombosis

Milic DJ et al[34] in their study on 100 patients have stated that "Only one patient, a 73 year old female had evidence of deep vein thrombosis post operatively, and even this patient was observed and conservatively managed."

Millikan et al[35] did a metaanalysis of close to 77000 cases in 4000 hospitals , and reported just 3 fatalities due to deep vein thrombosis after surgery for laparoscopic cholecystectomy.

Patel et al[36] in a study of 20 patients reported that 11 patients developed signs of venous thrombosis radiographically, with none of the eleven being suspected clinically. The incidence of thrombosis was as high as 55%.

Milic et al[37] found an incidence of 6.9% and 16.07% in the laparoscopic group (4 out of 58) and open group (9 out of 56) . None of the 114 patients were given deep vein thrombosis prophylaxis.

Lindberg et al[38] reported a frequency of 2% in a study done on 50 patients after laparascopy. All the patients had been on prophylaxis and diagnosis was done using bilateral phlebography in the second week following surgery.

Blake et al[39] in a study conducted over 4 years on 587 patients , found signs of Deep vein thrombosis in none of the patients over a four week follow up. Eighteen patients in the study were on some form of prophylaxis.

He thus questioned the purpose of routine DVT prophylaxis in these patients as the was no risk benefit ratio and it added up to the medical costs incurred by the patient

Wazz et al[40] reported "In a study of 61 patients, none of them on prophylaxis, no incidence of postoperative thrombi on duplex scanning after unspecified laparoscopic procedures."

Mohammed Ali et al[41] stated that in over 100 cases of laparoscopic cholecystectomies followed up with duplex scan, physical examination ,only one case of partial thrombosis was seen (by duplex). None were on DVT prophylaxis. He hence conferred laparoscopic cholecystectomy a low risk procedure.

Schaepkens et al[42] reported 5 cases in whom DVT manifestations were picked up in duplex scan ,four in the group not receiving prophylaxis and one in the group receiving prophylaxis , in a study of 238 cases . He put the incidence at 2.10%. with no

significant difference in incidence between the groups receiving and not receiving prophylaxis.

Lindberg et al[43] reviewed 60 case series of laparoscopic cholecystectomy, with a total of 1,53,832 patients. He gave an incidence of 0.02% for fatal pulmonary embolism and 0.03% for deep vein thrombosis. He concluded that laparoscopic procedure was much safer than conventional procedure with respect to thromboembolic phenomenon.

Alatri et al[44] reported two cases of deep vein thrombosis, one in a case of laparoscopic hernia repair and another in a case of laparoscopic cholecystectomy. And reported that venous thromboembolism prophylaxis be given in patients even if the procedure is relatively noninvasive and laparoscopic.

Mayol et al[45] have reported "Two cases of pulmonary embolism after laparoscopic cholecystectomy and suggest a specific prophylaxis for prevention, as the risk of pulmonary embolism must not be underestimated."

Stein et al[46] put the incidence of Pulmonary embolism at 0.15%, Deep vein thrombosis at 0.40%, and Venous thromboembolism at 0.53%. This was after a review of patients who underwent laparoscopic cholecystectomy between 1998 till 2009.

He reports the fatalities to be 780 cases (0.02%) of the total 4,107,430 cholecystectomies. Fatalities increased with age.

Morris DL et al[47] have reported in a study of over 438 patients three cases had thromboembolic manifestations, one deep vein thrombosis, one fatal pulmonary embolism and a non-fatal pulmonary embolism.

He stated that post surgery there was increased fibrinolytic changes in plasma and this caused hypocoagulability of blood post-surgery and thus laparoscopic surgery decreased the risk of thromboembolism in these patients.

Studies were done to assess the risk benefit ratio of uncontrollable bleeding in patients receiving thromboprophylaxis

Persson et al[48] studied the incidence of uncontrollable peroperative bleeding in patients undergoing laparoscopic cholecystectomy who were put on prophylaxis. There

were 400 patients who had uncontrollable peroperative bleeding and 296 patients with postoperative bleeding. The odds ratio was 1.35 when compared to those who did not receive prophylaxis.

He mentioned that while the incidence of uncontrollable bleeding after prophylaxis increased, the incidence of thromboembolic phenomenon did not decrease in the patients receiving prophylaxis.

In a study conducted by Bradbury et al[49], he distributed questionnaires to 800 surgeons who performed laparoscopic cholecystectomy, 417 responded. He found that 74% recommended prophylaxis to all their patients and 20 % prescribed prophylaxis selectively. Surgeons performing lesser than 10 procedure per annum were more concerned about bleeding manifestations and hence used prophylaxis selectively.

Filtenborg et al[50] used the questionnaire method to assess the use of thomboprophylaxis by Danish surgeons performing laparoscopic cholecystectomy. He found that 93% of the institutions had a written protocol.

He observed that 37% surgeons used prophylaxis for all their patients and 7% used it selectively on their patients. 74 % used compression devices to counter this problem and 20% of surgeons reported to have faced thromboembolic complications following laparoscopic surgery.

Haas S et al[51] concluded after his study that "Shorter and less complicated laparoscopic procedures don't need Deep vein thrombosis prophylaxis."

Lord RV et al[52] divided 100 patients into two groups, half underwent minilap cholecystectomy and other half underwent Lap cholecystectomy. Both groups were put on prophylaxis for deep vein thrombosis prophylaxis, he mentioned that "if prophylaxis was given for DVT, there was no risk for thromboembolic phenomenon in both group of patients undergoing cholecystectomy."

Amin Buhe et al[53] studied the effects of laparoscopic cholecystectomy on coagulation profile he inferred that "Pneumoperitoneum for laparoscopic cholecystectomy may cause post-operative hypercoagulation. In patients and

hence may face increased risk for development of thrombosis and embolism postoperatively."

He further stated that “Patients may have the increase in risk even within 8 hours after the operation, which requires specific attention to prevent thrombosis. Thrombotic disorders being a severe complication, if not found and managed at the right time may progress into pulmonary thrombosis threatening the patients’ lives.”

MATERIALS AND METHODS:

This study will be a **CLINICAL OBSERVATIONAL** of 50 patients done at General Surgical department of Kilpauk Govt. Medical College Hospital between January 2015 to September 2015.

SIZE OF THE STUDY:

50 patients undergoing laparoscopic cholecystectomy.

STUDY METHODOLOGY

Patients who get admitted to Department of General Surgery, Government Kilpauk medical college hospital and who were diagnosed to have a gall bladder pathology and underwent laparoscopic cholecystectomy were included in the study. All who satisfied the inclusion criteria were retained in the study group and those who did not were excluded from the study. Consent was obtained from the patient regarding inclusion in study. History and clinical examination was done. Patient`s age sex, symptoms and their duration of surgery were recorded.

METHOD OF COLLECTION OF DATA:

- 50 eligible patients are chosen.
- Clinical assessment done at time of inclusion in the study.
- Detailed history and examination done.
- Basic routine investigations will be done for all patients
- 3 cc of blood will be drawn under strict aseptic precautions
- One sample prior to surgery
- One sample 6 hours after onset of pneumoperitoneum
- Samples will be processed for prothrombin time and D-dimer
- Duplex scan will be done to look for deep vein thrombosis
- Consent will be obtained for inclusion under study and for surgery

METHOD OF SURGERY :

- Procedure will be done under general anesthesia.
- Surgery will be done with standard laparoscopic equipment for all patients using carbon di oxide pneumoperitoneum
- The pressure of pneumoperitoneum will be maintained at 13 mmHg +/- 1 mmHg

SURGICAL STEPS:

- Patients will be put in classical supine position with table given a 30 degrees head up position and 15 degrees right up position to allow better visualization of gall bladder and Calot's triangle as it allows the colon and duodenum to fall away from the liver edge.
- Surgeon stands on the left of the patient with monitor placed near the right shoulder.
- A nasogastric tube and Foleys catheter are inserted to deflate the distended stomach and empty the urinary bladder.
- Pneumoperitoneum is created by open Hasson's method. A 1 to 1.5 cm incision is made in the umbilicus. Dissection is carried out and rectus sheath and peritoneum are opened in layers.
- After confirming entry into the peritoneal cavity, a 10 mm port is inserted and carbon dioxide is insufflated to a pressure between 12-14 mm Hg at a flow rate of around 3 to 3.5 liters per minute.
- A 0 degree 10 mm telescope is attached to light source and endo camera and inserted through the 10 mm port.
- Laparotomy is done to exclude injury to structures during port insertion, to exclude other suspected or associated pathologies and assess the feasibility of laparoscopic procedure.

- Rest of the ports are inserted under vision. A 10 mm working port is created in the epigastrium to the right of falciform ligament. Two 5mm port one each in the midclavicular line and another in the anterior axillary line are created to retract the gallbladder and to visualize the Calot's triangle.
- The cystic pedicle is exposed and dissection is carried out to create a window all around the cystic duct. Three clips are applied and cystic duct cut in between. Cystic artery is then isolated and clips applied and cut.
- The gall bladder is then removed from the liver bed by dissection in the loose fibrous layer which separates the gallbladder from the fascia covering the bed of the liver.
- The gall bladder is then delivered through the epigastric or the umbilical port.
- Hemostasis is ascertained and ports are removed under vision and pneumoperitoneum is released.
- Wound is closed in layers and patients are given analgesics for pain relief.
- Specimen is sent for histopathological examination and stones if present are sent for biochemical analysis

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 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.

Reasons for inclusion / exclusion:

- Age <18 left out because of problems with consent.
- Age >60 excluded because of abnormal coagulation profile in elderly.
- Patients with acute cholecystitis excluded because acute inflammation alters coagulation profile.
- Associated hypertension, malignancies, use of oral contraceptives excluded since these alter coagulation mechanisms.
- Surgery time greater than 3 hours excluded as they are known to produce thrombosis.
- Associated deep vein thrombosis and patients with bleeding disorders have an altered profile; hence are excluded.
- Pregnancy is excluded because of altered profile and ethical issues.

INVESTIGATIONS:

- Complete hemogram
- Urine routine
- Blood sugar
- Blood urea
- Serum creatinine
- Serum electrolytes
- USG abdomen

SPECIFIC INVESTIGATION

- Coagulation profile : Prothrombin Time

  D - dimer

- Duplex scan if indicated .

PROFORMA

1. **Patient name**
2. **IP No:**
3. **Department:**
4. **Hospital:**
5. **Age:**
6. **Sex:**
7. **Occupation**
8. **Chief complaints:**
9. **Past history:**
10. **Body mass index:**
11. **General examination.**
12. **Vitals**

a. Pulse rate:

b. Blood pressure:

c. Temperature:

13.Local examination:

a. Inspection

b. Palpation:

c. Percussion:

d. Auscultation:

14.Abdominal examination

15.Cardiovascular and respiratory system examination

16.Diagnosis:

Duration of surgery :

Table :

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

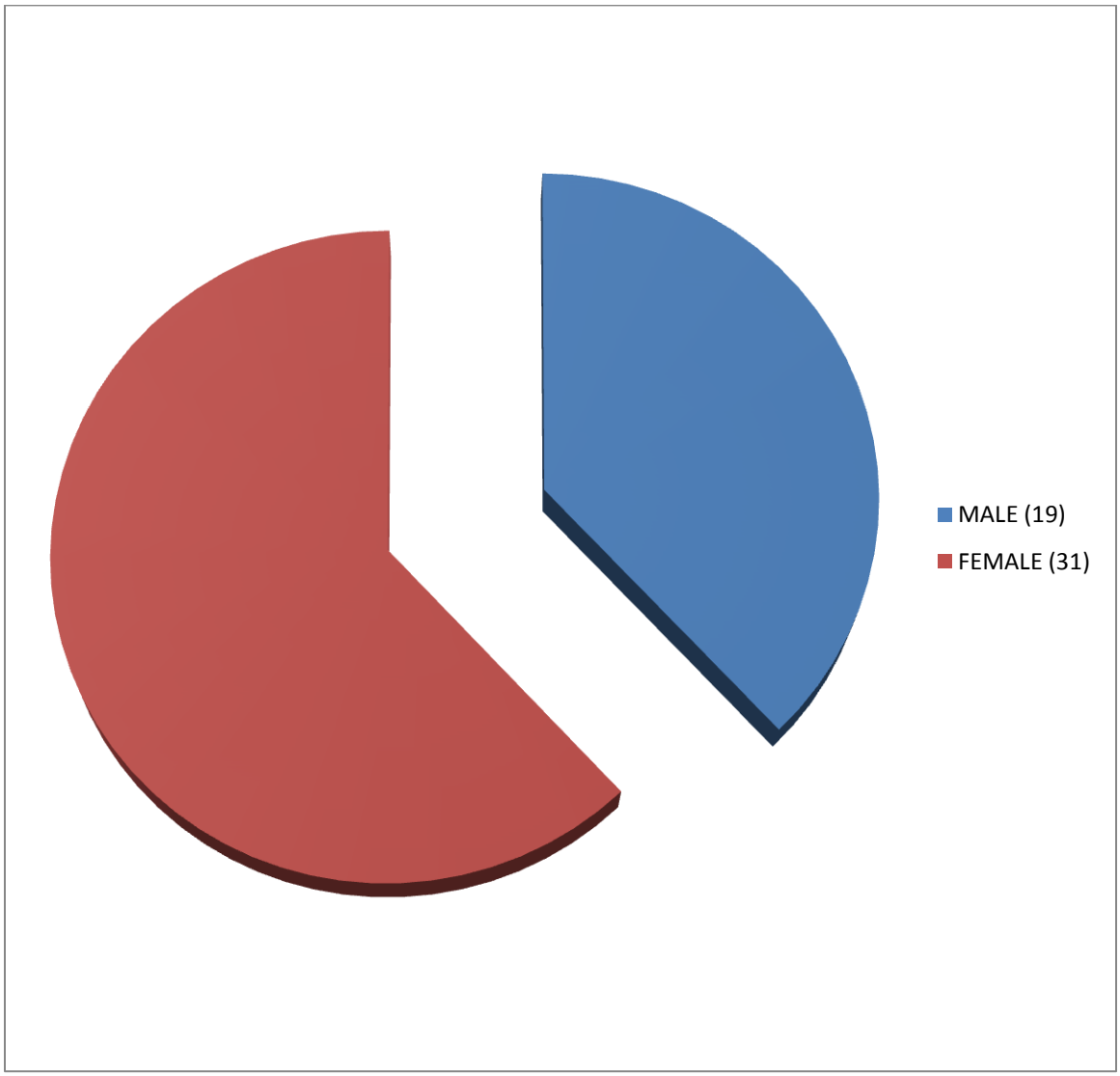
Data analysis :

Data collection was done. The prothrombin time and D-dimer values before and after the surgery were collected for all the 50 patients and were entered into the Microsoft excel sheet. The values were used for analysis.

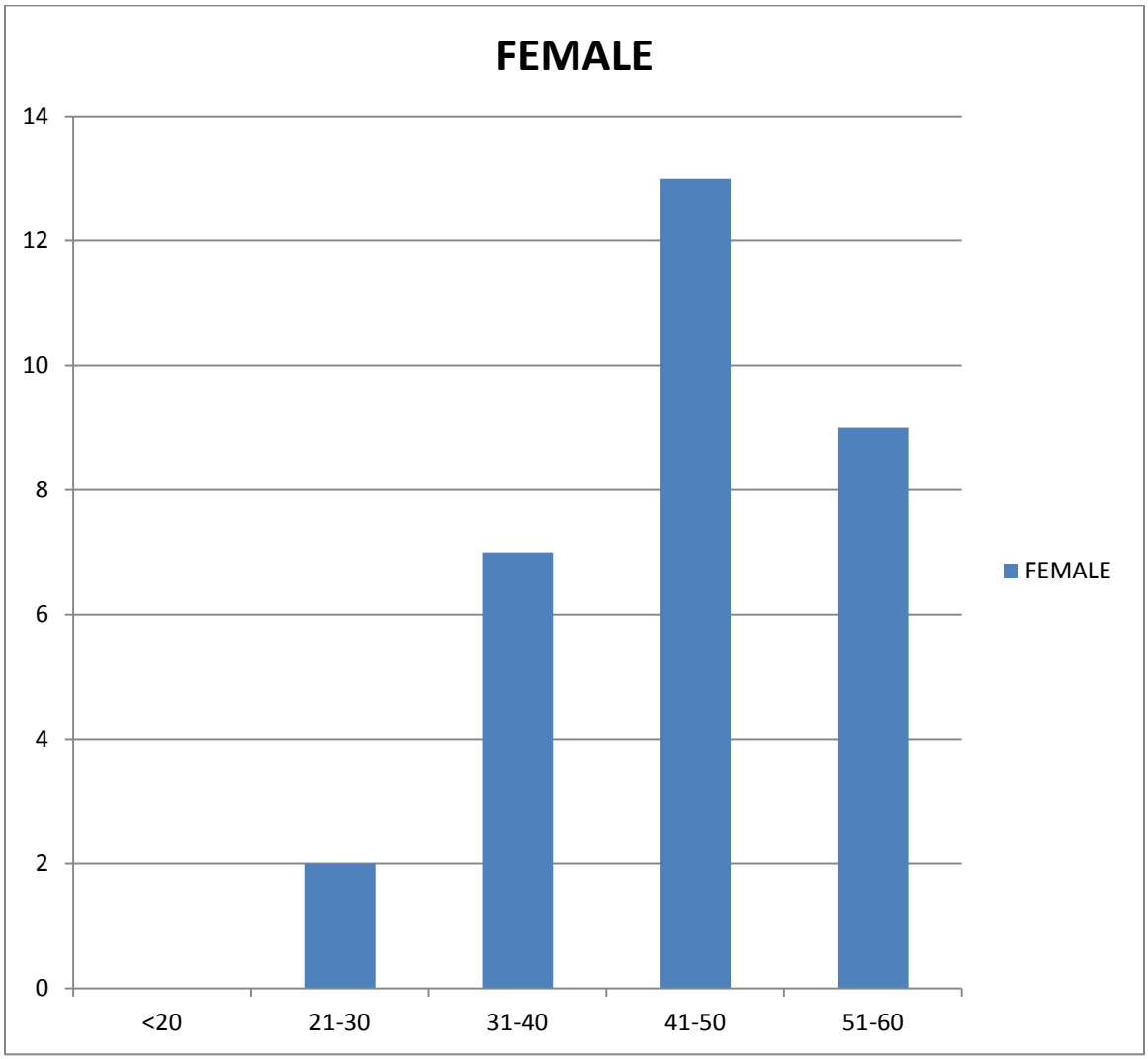
The Paired student T –test was used to analyze the values collected before and after the surgery . The software tools used for the purpose were downloaded from the internet . The values obtained were confirmed using another similar software to check the validity.

The mean of the two groups , the standard deviation, standard error of mean and the P-value were calculated. The results were again converted into pie charts, bar diagrams and scatter map for the sake of easy understanding , and are presented as follows.

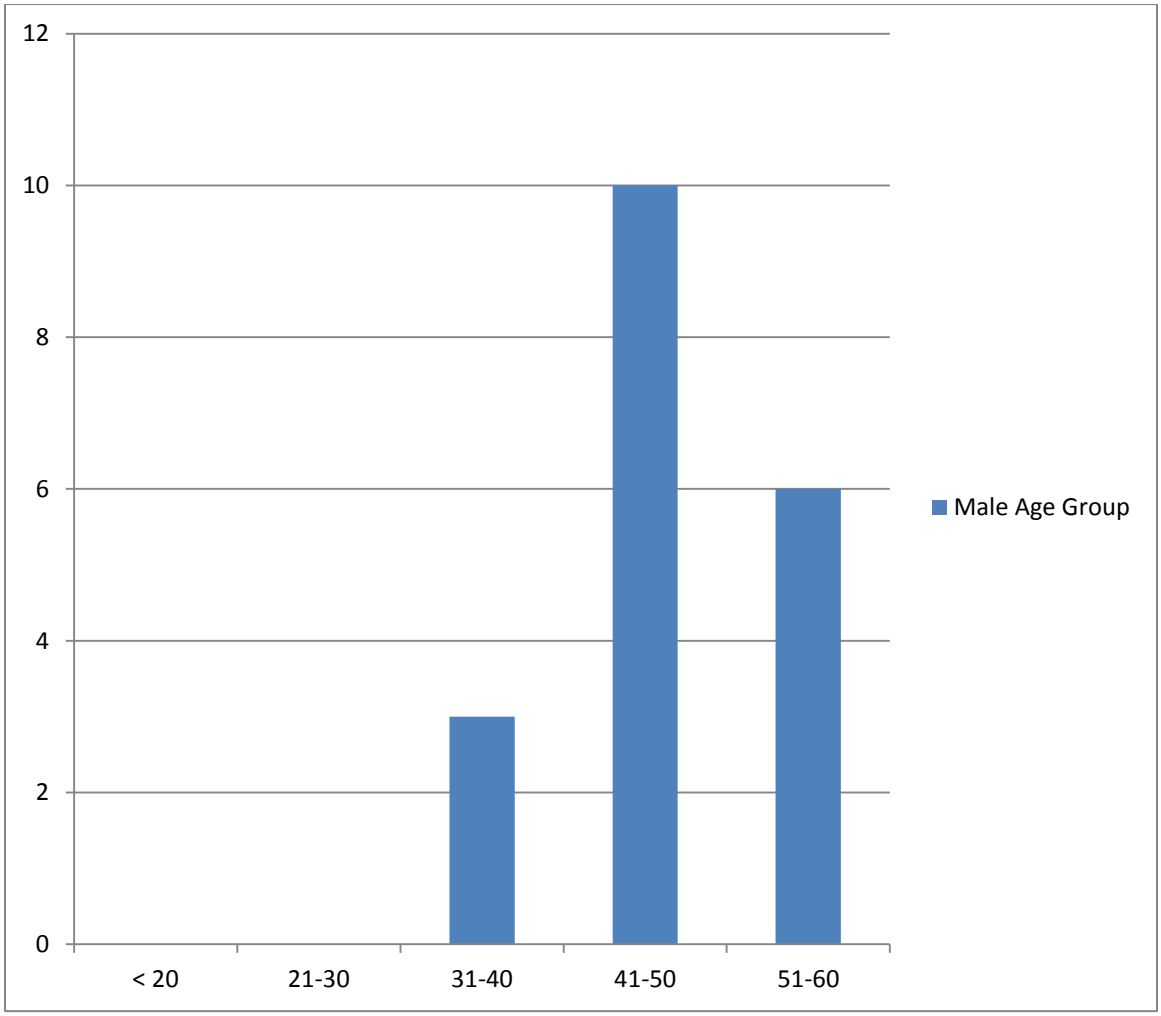
SEX RATIO



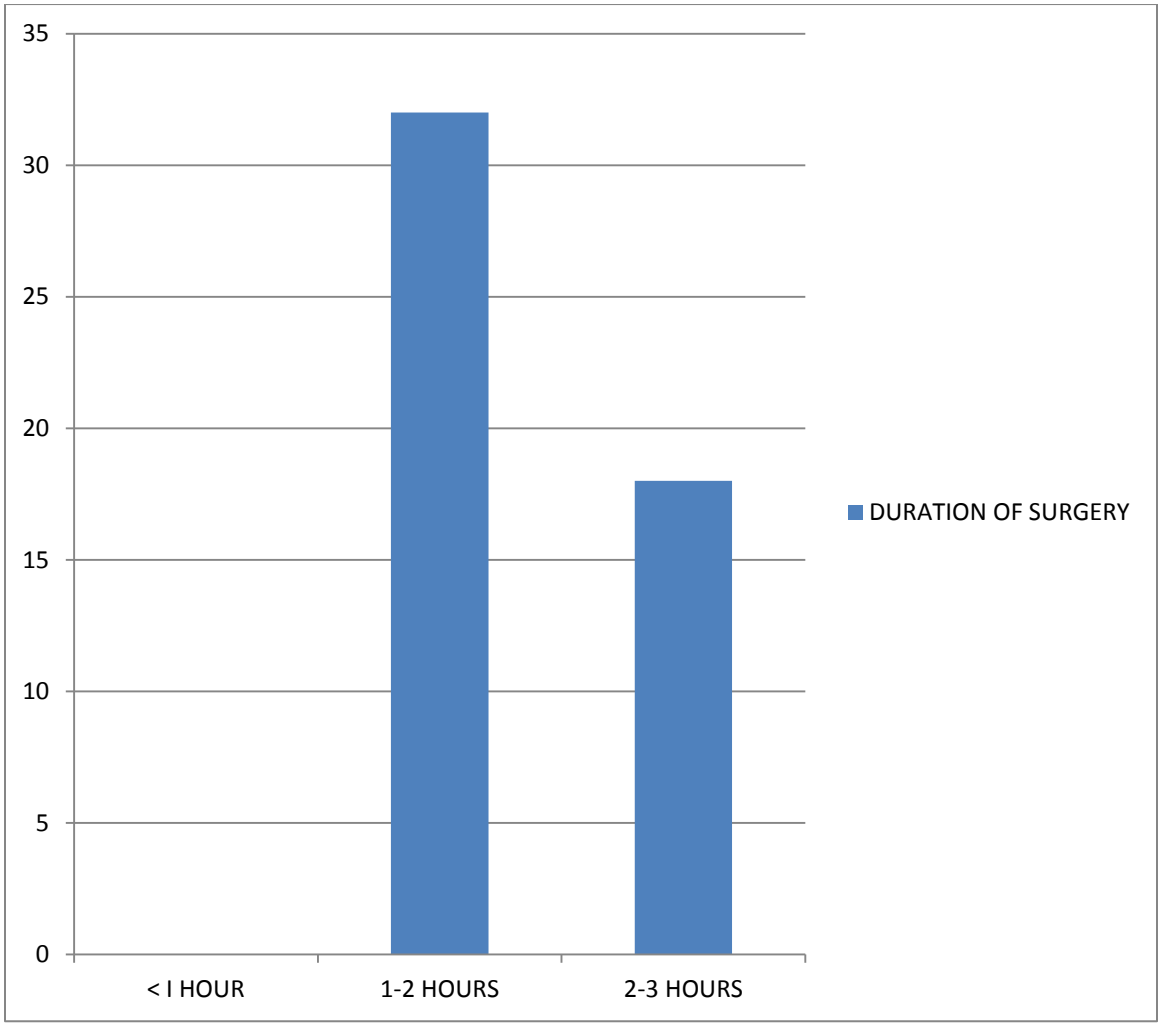
AGE DISTRIBUTION IN FEMALES



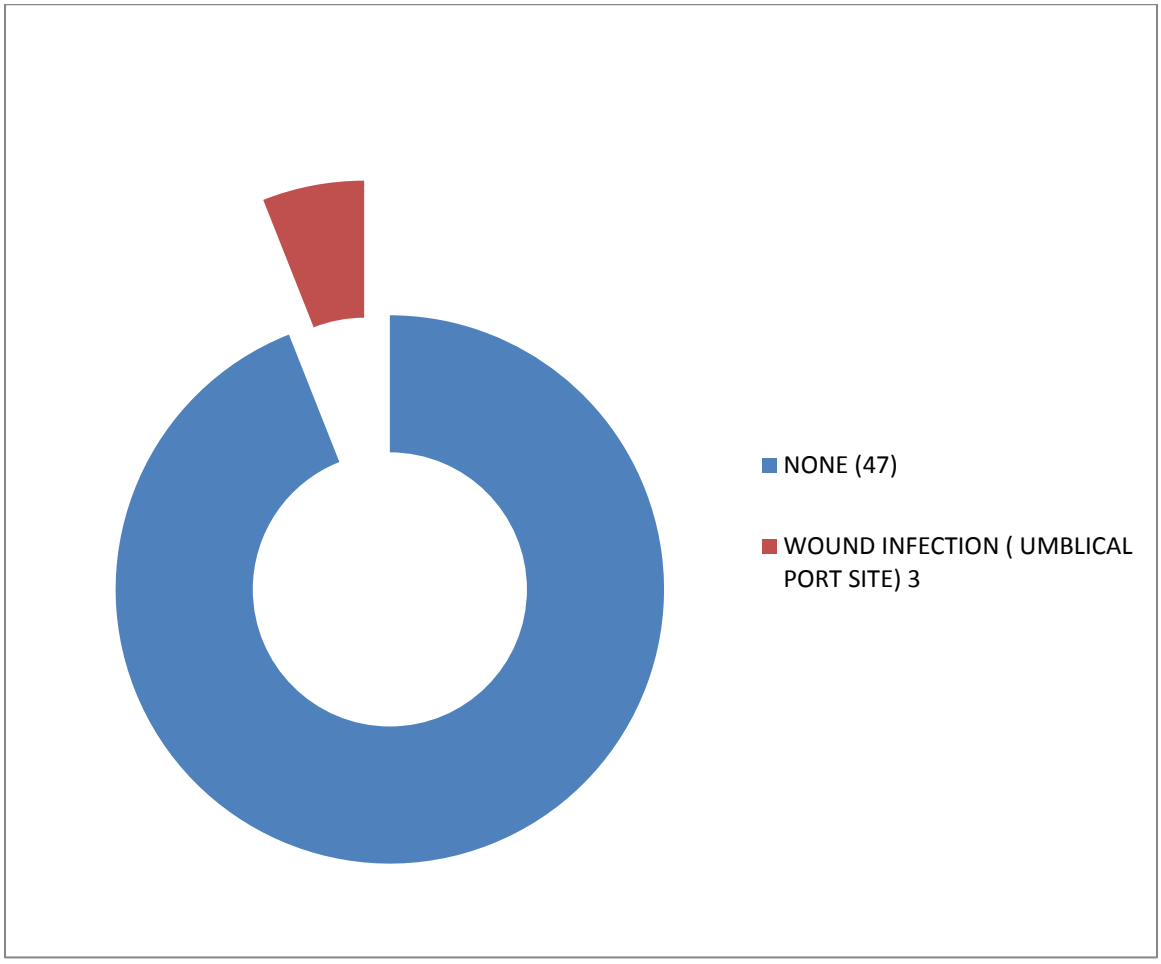
AGE DISTRIBUTION IN MALES



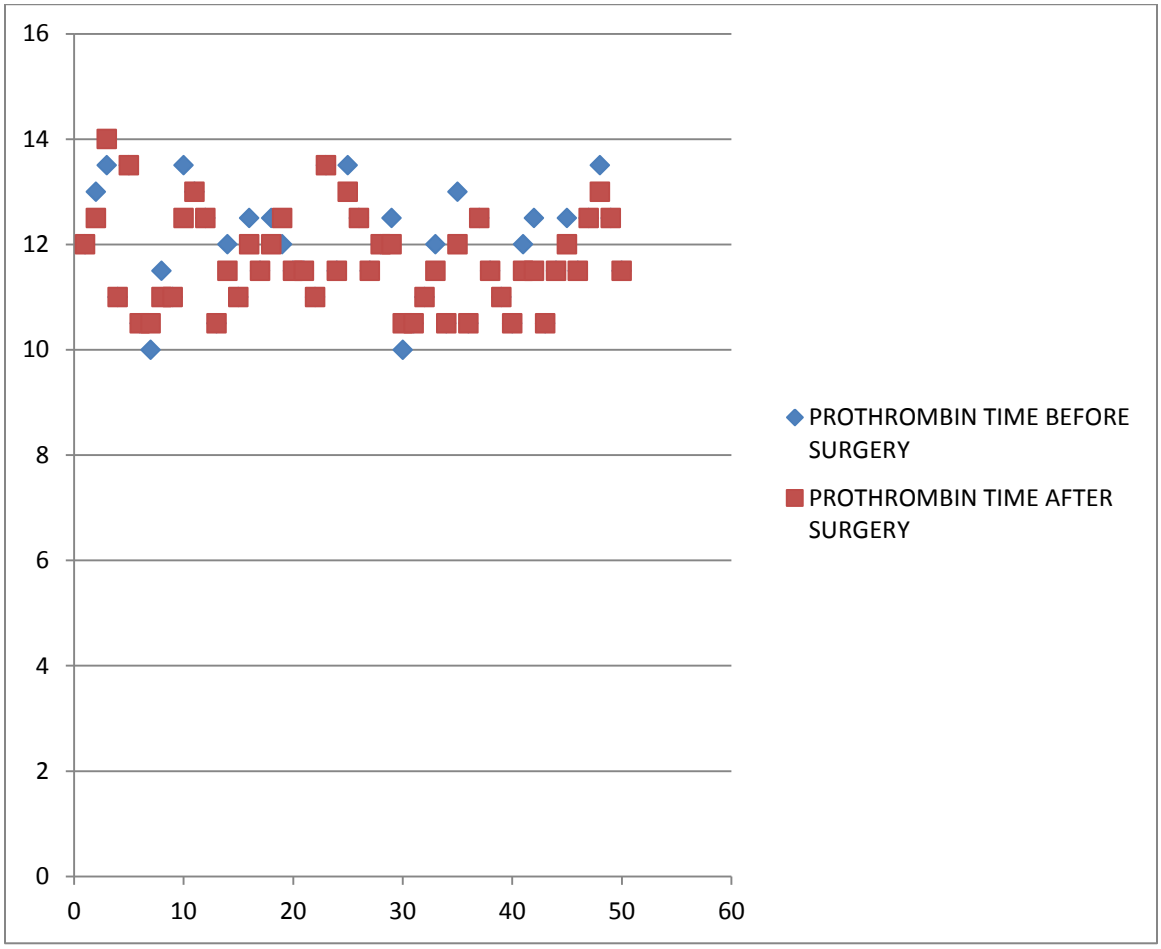
DURATION OF SURGERY



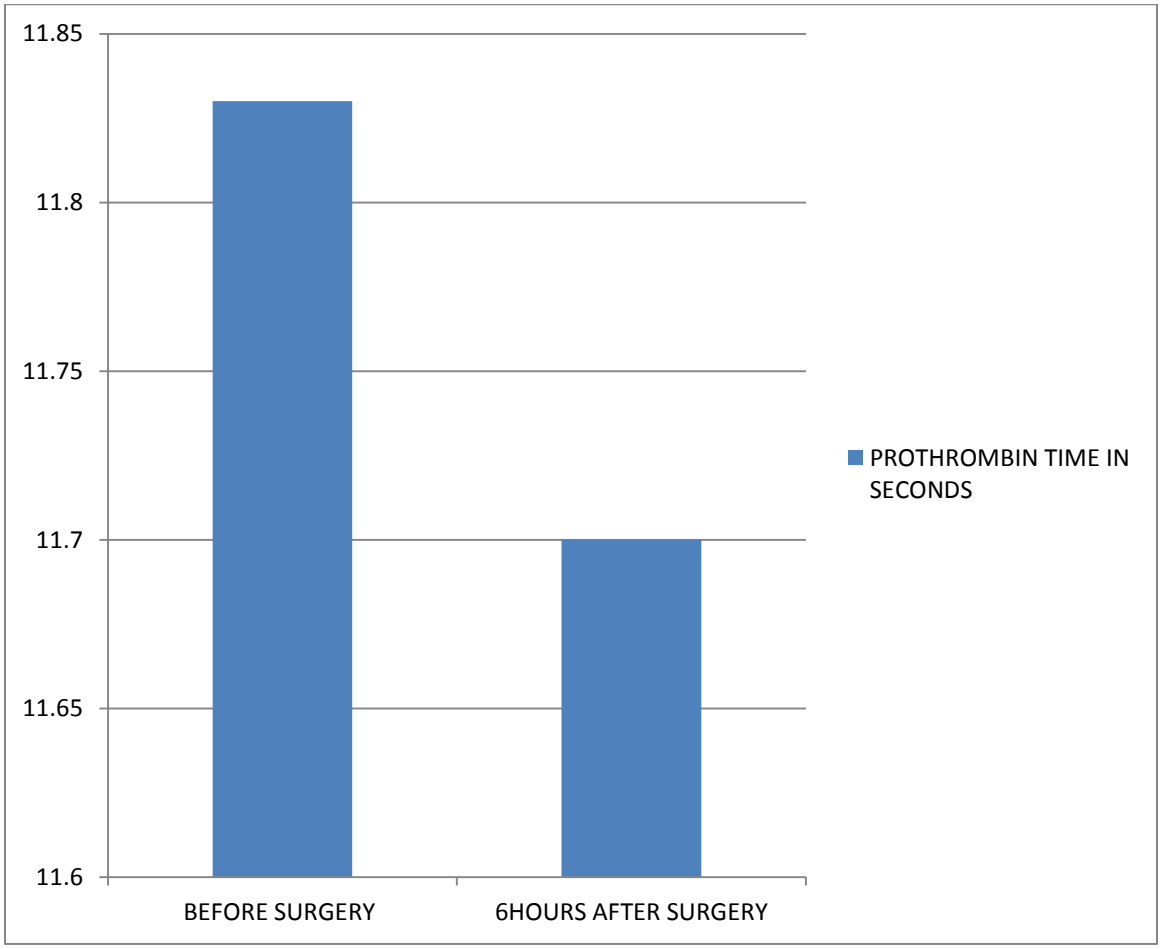
COMPLICATIONS



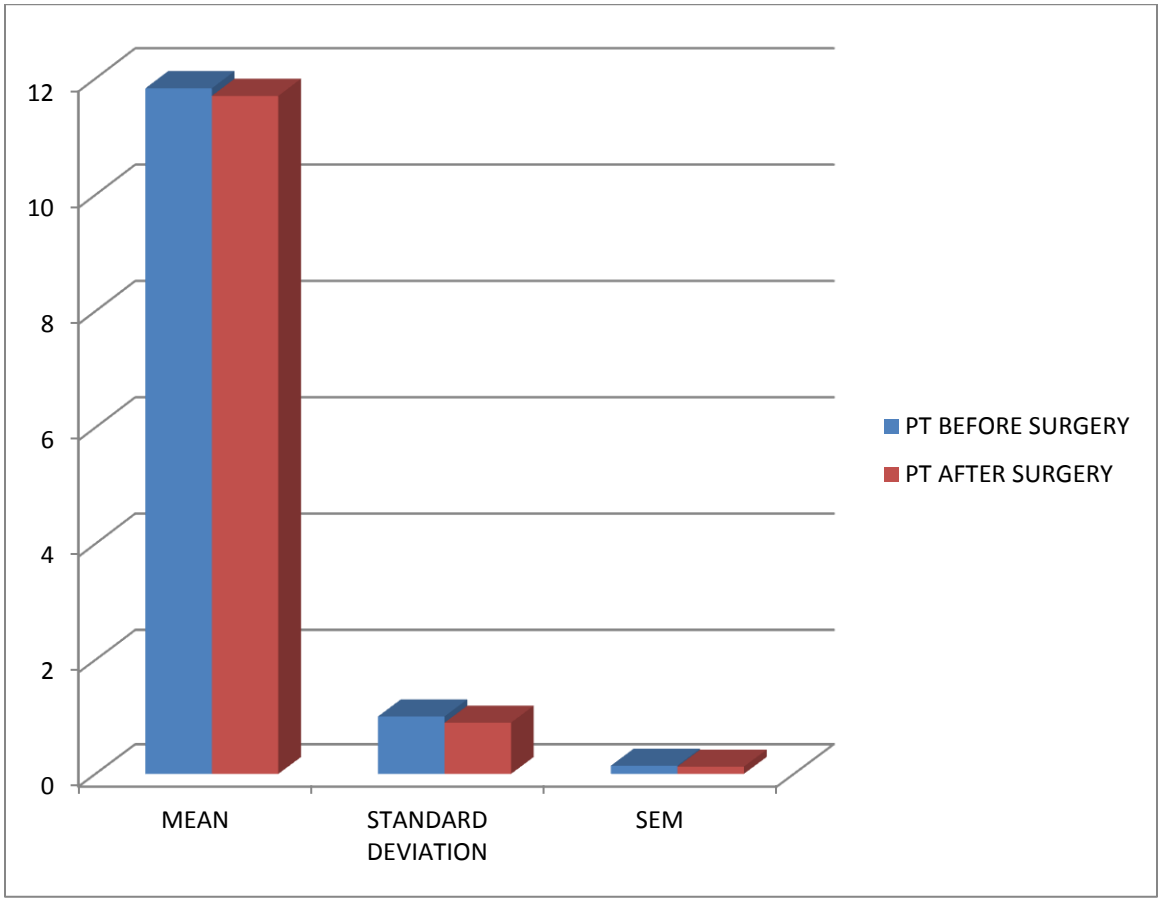
PROTHROMBIN TIME OF 50 PATIENTS



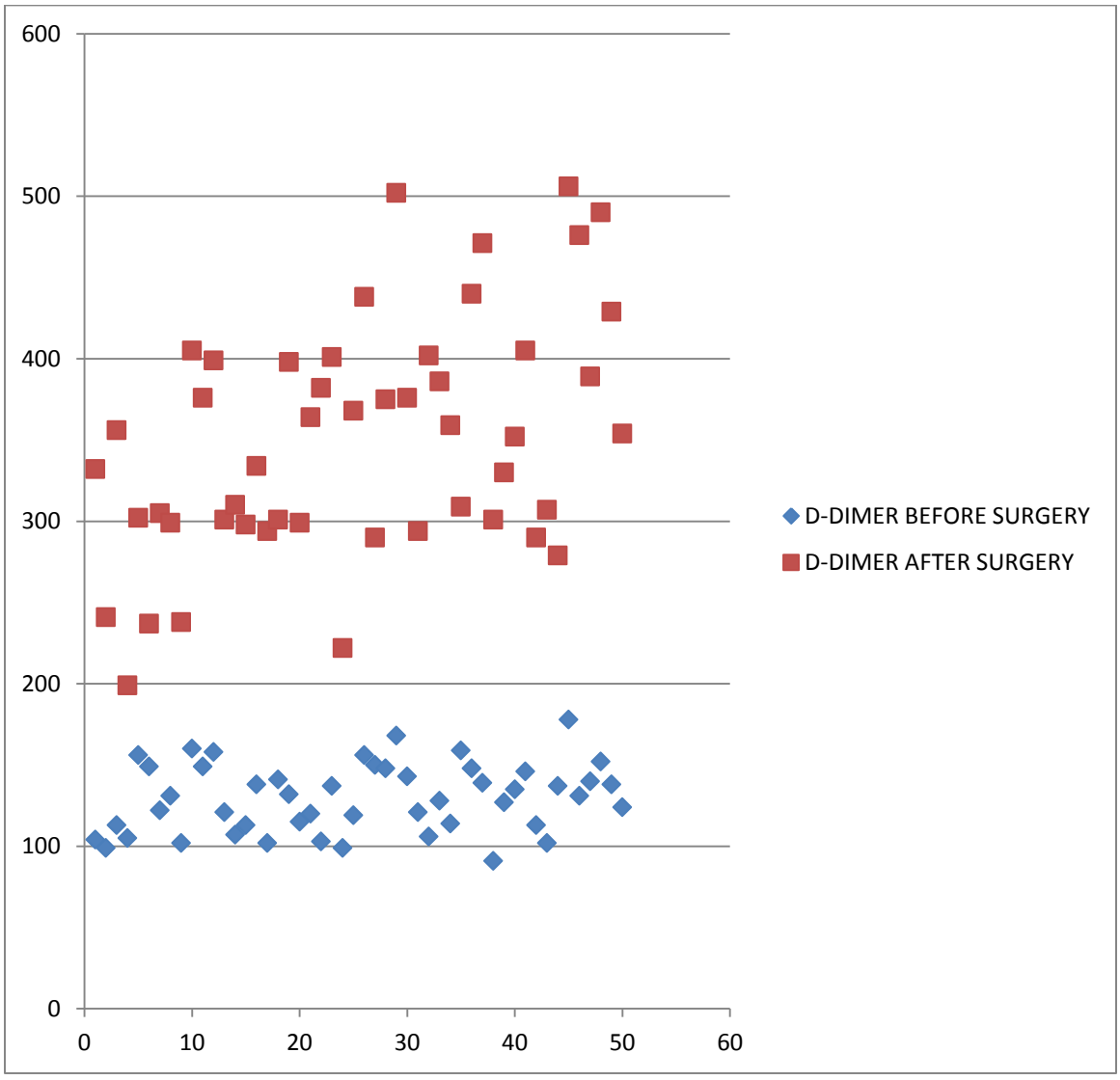
PROTHROMBIN TIME IN SECONDS



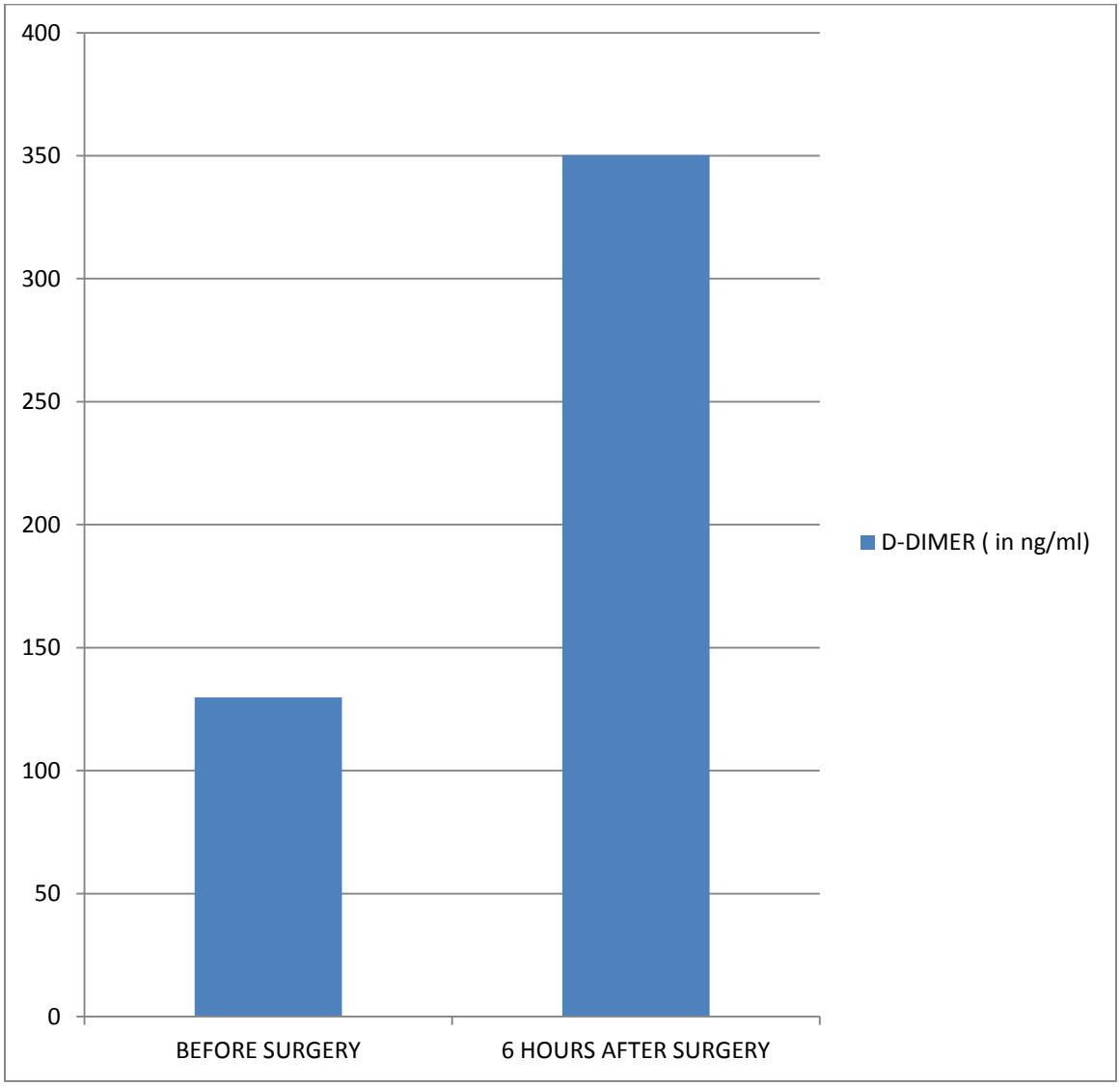
PROTHROMBIN TIME ANALYSIS



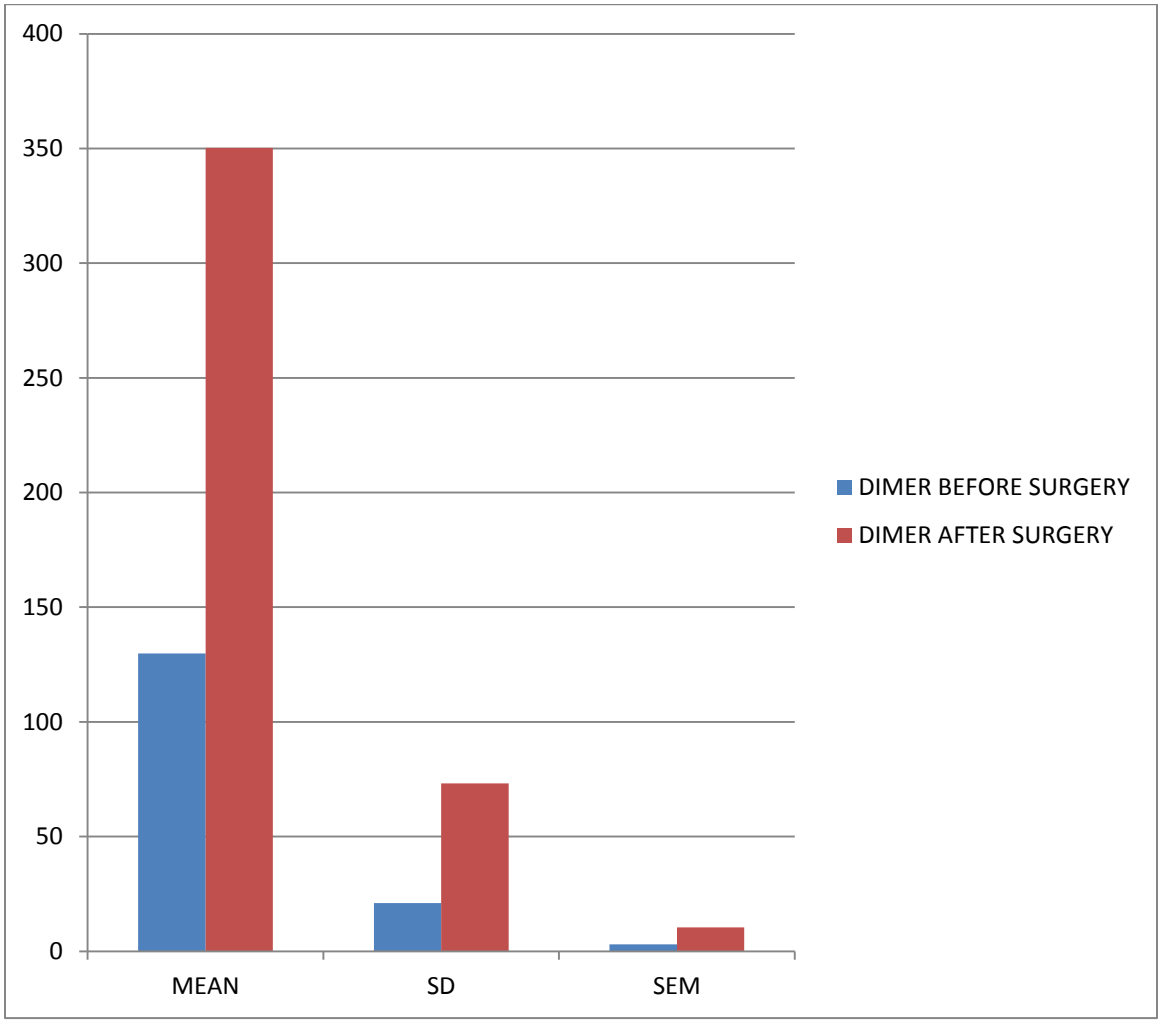
D-DIMER OF 50 PATIENTS



D-DIMER (in ng/ml)



D-DIMER ANALYSIS



PROTHROMBIN TIME		
	BEFORE SURGERY	AFTER SURGERY
MEAN	11.83	11.7
STANDARD DEVIATION	1.008	0.898
STANDARD ERROR OF MEAN	0.143	0.127

D DIMER		
	BEFORE SURGERY	AFTER SURGERY
MEAN	129.78	350.22
STANDARD DEVIATION	21.01	73,21
STANDARD ERROR OF MEAN	2.97	10.35

Results:

Of the 50 patients operated , 31 were female and 19 were male patients. The most common age group was 41-50 years among both female and male groups. Followed by the age group of 51-60.

The duration of the surgery ranged from 1hour 25 minutes to 2 hours 50 minutes. The reasons for prolonged surgical time were dense adhesions in the Calot's triangle and gall bladder adherent to the liver bed.

There were no major peroperative complications. There was wound infection at the umbilical site in 3 patients which settled with conservative treatment with a course of antibiotics.

There were no major postoperative complications in the operated patients during hospital stay and during the follow up period. The mean hospital stay was 4 days.

The prothrombin time of the patients before surgery ranged from 10 to 13.5 seconds, with the mean at 11.83 seconds. The standard deviation was 1.008 and standard error of mean was 0.143.

The prothrombin time of patients 6 hours after surgery ranged from 10.5 seconds to 14 seconds . The mean of prothrombin time after surgery was 11.7 seconds. The standard deviation was 0.898 and the standard error of mean being 0.127.

Not all patients had a change in prothrombin time before and after surgery. While some had elevated prothrombin time, some had decreased prothrombin time and few showed no change at all.

The difference in the mean between the two groups was 0.130. The confidence interval at 95% was between 0.031 to 0.229. The p- value was 0.0109 (<0.05) . Hence the value was statistically extremely significant.

The values for D-dimer were analyzed . The D-dimer value before surgery for the 50 patients ranged from 99 to 178 , with the mean at 129.78. The standard deviation was 21.01 and standard error of mean was at 2.97.

The D-dimer values after surgery varied between 199 and 506. The mean was calculated to be 350.22 with the standard deviation at 73.21 and standard error of mean at 10.35.

The D-dimer of all the patients showed a drastic increase post surgery. The difference in mean of the two groups was 220.44 and the confidence interval of 95 % lay between 240 to 200.83. The p-value of the D-dimer analysis was at 0.001was meant it was extremely significant statistically.

On follow up none of the patients developed signs of deep vein thrombosis clinically when they turned up for follow up to 2 weeks post surgery.

Discussion:

The values of prothrombin time and D-dimer of the 50 patients were analyzed. The inferences derived from them were compared with other similar studies.

There was a higher incidence of female patients undergoing cholecystectomy 62%, compared to male 32%. This matches the global rates and rates in India which also shows a higher female predisposition towards gall bladder pathologies.

The majority of the patients who underwent surgery were in the age group of 41-50 years in both the sexes. The second highest was seen in the age group of 51-60 years. These two groups constituted 76% of the cases. Showing that the disease incidence increased after the age of 40 years.

The duration of surgery varied between 1 hour 25 minutes to 2 hours 50 minutes. This shows the unpredictability of the duration of the surgery the longest taking twice the time for the shortest procedure.

The prothrombin times of patients when analyzed showed that the results were not uniform for all patients . while some showed an elevation in prothrombin time indicating hypocoagulability , there were a few who had decreased prothrombin time after surgery showing hypercoagulability.

The prothrombin time was not altered in most of the patients 62% (31 out of 50). This gave the appearance that there was not much difference in the coagulation profile with respect to prothrombin time.

The mean of the prothrombin time before surgery was 11.83 and the one after surgery was 11.7. The standard error of mean was 0.143 and 0.127. This small value showed the accuracy of the mean and that a similar mean would have been obtained with a study with a larger sample.

These values when charted showed that the decrease in the mean was statistically significant. Hence the prothrombin time can be considered to decrease , and there is hypercoagulability of blood.

The study goes in line with other studies by Hans et al [25], Garg et al[26] and Schietroma et al[28] who also support the fact that there is a state of hypercoagulabilty.

When the D-dimer values are analyzed, all the patients are seen to have an increase in the d-dimer values. With many showing a two fold increase in the d-dimer values before and after surgery.

The mean of the D-dimer before and after surgery where calculated to be 129.78 and 350.22 and the standard error of mean was 2.97 and 10.35. The difference in the mean was 220.44 .This increase clearly indicates the undergoing fibrinolytic process.

Statistically too the values were found to be extremely significant with a p value of 0.001. thus this increase in d-dimer suggests the high risk of thrombosis leading to activation of fibrinolytic systems.

The high values of D- dimer post surgery were also seen in many studies like the study by Amin buhe[33] et al where post operative d-dimer values have been shown to get elevated by close to 5 times the pre operative values.

The findings of the study though contradicts the studies by Rahr et al [20] ,Yan MJ[30] et al , Martinez et al[19]. who report hypocoagulabilty of blood post operatively or no change in coagulation profile.

The change in the coagulation profile can be attributed to be due to surgery and is not specific to laparoscopy with carbon di oxide pneumoperitoneum as other studies by Jens Fromholt [16]and Schietroma et al[28] have shown similar rise in values after open surgery and gasless laparoscopic surgeries too.

D-dimer is not specific for pulmonary thrombosis or deep vein thrombosis. The changes or increase can be brought out by surgery in itself. The quantum of change brought by surgery has not been studied though. Values greater than 250 ng/ml are indicative of fibrinolytic activity.

These changes in coagulation factors cannot be attributed to the position of patient alone. All the patients being put on reverse trendenlenberg position with a 30 degree tilt with a right up tilt given. Not all patients showed a similar change in coagulation profile.

The effect of position can only be studies if studies are done comparing laparoscopic procedures that adopt a trendenlenberg position to procedures that employ reverse trendenlenberg position.

The effect of increased abdominal pressure may have a role to play in the alteration of coagulation profile. Increase in intraabdominal pressure is associated with decreased venous return, venous pooling in lower limbs and pelvis and this stasis in the lower half of the body could contribute significantly to the observed changes.

Stasis of blood is a component of Virchow's triad[5] and could trigger the coagulation pathway. Intra abdominal pressures of 12-14 mmHg are maintained for a period of few hours during laparoscopic surgery. In patients suffering from chronic liver disease with ascites , abdominal pressures ranging from 15 mmHg to as high as 80 mmHg have been recorded[6]. These pressure are present for periods ranging from weeks to months. But these patients are not at increased risk for thrombotic phenomenon. This can also be due to decreased production of coagulation factors by the diseased liver and steady increase

in pressure allowing time for homeostatic mechanism. Hence increased intraabdominal pressure cannot be held solely responsible for the alteration in profile of coagulation.

While Custendil et al[31] and Lord RV[32,52] in their studies found increased incidence of thrombosis on the first and third days following surgery , no such observations were made during the study.

None of the patients in the study were put on prophylaxis of any form because there were no added risk factors that indicated their need. .

On the contrary to many studies that reported the incidence of thrombosis postoperatively, there were no cases who developed signs of thrombosis though the patients showed increased coagulation profile. This was probably due to the small size of the population under study. The incidence of post operative thrombosis was placed at 0.02 % (1 in 5,000) in the larger studies done elsewhere.

The analysis of these factors, show that causation of deep vein thrombosis is multifactorial, and only carbon di oxide pneumoperitoneum cannot be held responsible in patients undergoing laparoscopic cholecystectomy. But Laparoscopic cholecystectomy using carbon di oxide pneumoperitoneum does play a role in altering the coagulation profile of patients, and hence may need the use of prophylactic measures for thrombosis in high risk individuals.

Conclusion :

The study was done with the objective to find if there was a change in the coagulation profile in laparoscopic cholecystectomy using carbon dioxide pneumoperitoneum and if there is an increased risk of thrombosis.

The study shows a marked increase in the d-dimer values and a significant decrease in the prothrombin time. This goes to prove that there is activation of both coagulation and fibrinolytic systems post laparoscopic cholecystectomy.

This activation of coagulation system could spell a disaster if the patients were to face a thromboembolic phenomenon post cholecystectomy. But none of the 50 patients operated by us had any thromboembolic problems postoperatively. This could mean that the body has effective counter mechanisms to deal with this change in coagulation profile.

When assessed if there is a need for prophylaxis against thrombosis, the study shows change in the coagulation profile resulting in a hypercoagulable state.

Hence it is better that for patients undergoing laparoscopic cholecystectomy stringent measures are taken and patients are put on some form of stringent deep vein thrombosis prophylaxis, preferably Low molecular weight Heparin.

The surgeon is hence left with a daunting task of looking into the cost- risk-benefit ratio for individual patients with respect to deep vein thrombosis prophylaxis. The presence of even a single risk factor should necessitate the surgeon to start the patient on prophylaxis to avoid dire consequences.

Finally larger and detailed studies are required to throw more light on these changes in the coagulation system and quantitatively determine the risk associated for laparoscopic cholecystectomy using carbon di oxide pneumoperitoneum.

Limitations:

1) The study was conducted on a small size of 50 patients. A study with a larger sample size could have yielded different results.

2) The study was conducted only for patients undergoing cholecystectomies laparoscopically.

3) Patients treated for other diseases using carbon dioxide pneumoperitoneum laparoscopically could have changes in their coagulation profile

4) In the study blood sample was taken 6 hours after the onset of pneumoperitoneum. Samples taken at a different time period could have produced different results.

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சுய ஒப்புதல் படிவம்

ஆய்வு செய்யப்படும் தலைப்பு: இரத்த உறைதலில் கார்பன்டை ஆக்ஸைடு மூலம் லேப்ராஸ்போபிக் பித்தப்பை அகற்ற அறுவைச் சிகிச்சையினால் ஏற்படும் மாற்றம் பற்றிய ஆய்வு.

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1) இரத்த உறைதலில் கார்பன்டை ஆக்ஸைடு மூலம் லேப்ராஸ்போபிக் பித்தப்பை அகற்ற அறுவைச் சிகிச்சையினால் ஏற்படும் மாற்றம் பற்றிய ஆய்வின் விவரங்கள் எனக்கு தெளிவாக விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும் அதற்கான விளக்கங்களை பெறவும், வாய்ப்பு அளிக்கப்பட்டுள்ளது என அறிந்து கொண்டேன். ( )

2) நான் இந்த ஆய்வில் தன்னிச்சையாக தான் பங்கேற்கிறேன். எந்த காரணத்தினாலோ, நான் இந்த ஆய்வில் இருந்து வில ஆசைப்பட்டால் எந்த பிரச்சனையும் இன்றி விலகலாம் என்றும் அறிந்து கொண்டேன். ( )

3) இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்த மேலும் ஆய்வு மேற்கொள்ளும்பொழுதோ இந்த ஆய்வில் பங்கு பெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவை இல்லை என அறிந்தேன். ( )

4) இந்த ஆய்வில் பங்கு கொள்ள நான் சுய நினைவோடும் முழு சம்மதத்தோடும் ஒப்புதல் அளிக்கிறேன். ( )

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விலாசம் :

ஆய்வாளரின் பெயர் :

ஆய்வாளரின் கையொப்பம் :

தேதி :

இடம் :

S.NO	IP number	Age	Sex	PT BS	PT AS	D-dimer BS	D-dimer AS
1	149146	45	M	12	12	104	332
2	245	41	M	13	12.5	99	241
3	641	39	F	13.5	14	113	356
4	1025	49	F	11	11	105	199
5	975	58	F	13.5	13.5	156	302
6	1189	57	M	10.5	10.5	149	237
7	1472	39	F	10	10.5	122	305
8	1384	48	M	11.5	11	131	299
9	1764	27	F	11	11	102	238
10	1735	60	M	13.5	12.5	160	405
11	1994	55	F	13	13	149	376
12	1838	48	F	12.5	12.5	158	399
13	1807	31	F	10.5	10.5	121	301
14	2086	39	M	12	11.5	107	310
15	2279	40	F	11	11	113	298
16	2680	52	F	12.5	12	138	334
17	2877	32	M	11.5	11.5	102	294
18	2991	57	F	12.5	12	141	301
19	2673	50	F	12	12.5	132	398
20	3095	46	M	11.5	11.5	115	299
21	3041	49	M	11.5	11.5	120	364
22	3562	52	M	11	11	103	382
23	3992	60	F	13.5	13.5	137	401
24	4773	37	F	11.5	11.5	99	222
25	4710	53	F	13.5	13	119	368
26	5002	58	F	12.5	12.5	156	438
27	5348	43	F	11.5	11.5	150	290
28	5791	46	M	12	12	148	375
29	5899	59	F	12.5	12	168	502
30	6302	39	F	10	10.5	143	376

31	6074	42	F	10.5	10.5	121	294
32	6288	44	F	11	11	106	402
33	6341	50	M	12	11.5	128	386
34	6657	30	F	10.5	10.5	114	359
35	6890	42	F	13	12	159	309
36	7074	45	M	10.5	10.5	148	440
37	7302	53	M	12.5	12.5	139	471
38	7763	38	F	11.5	11.5	91	301
39	7509	41	F	11	11	127	330
40	7850	46	F	10.5	10.5	135	352
41	8153	55	M	12	11.5	146	405
42	8924	41	F	12.5	11.5	113	290
43	8577	38	M	10.5	10.5	102	307
44	9116	43	F	11.5	11.5	137	279
45	9884	60	F	12.5	12	178	506
46	9417	44	M	11.5	11.5	131	476
47	9710	47	F	12.5	12.5	140	389
48	10079	42	F	13.5	13	152	490
49	10654	59	M	12.5	12.5	138	429
50	11376	46	M	11.5	11.5	124	354