"EFFECTS OF LAPAROSCOPIC PROCEDURES ON HEPATIC ENZYMES"

By

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DISSERTATION SUBMITTED TO
SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, KOLAR, KARNATAKA
IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF

DOCTOR OF SURGERY

IN

GENERAL SURGERY

Under the guidance of

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2018

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ACKNOWLEDGEMENT

First and foremost I am thankful to the **“Almighty God”** for all his blessings and giving me the strength both mentally and physically to complete this task.

I would like to express my deep gratitude and sincere thanks to my guide **Dr. P.N SREERAMULU,** Professor and Head, Department of General Surgery, for preparing me for this task, for his guidance, advice, suggestions and enduring patience saw me through the completion of this dissertation work, showing great care and attention to details and without his supervision and guidance this dissertation would have been impossible. He has been an invaluable source of encouragement and support not just for this thesis but throughout my entire course. His knowledge of practical skills has guided and inculcated in me a sense of confidence. With whole hearted gratitude, I wish to acknowledge my unrepayable debt to him.

I am highly indebted to all PG teachers **Dr. MOHAN KUMAR. K, Dr. BHASKARAN. A , Dr. KRISHNA PRASAD. K, Dr. SHASHIREKHA C.A** and **Dr. PRAKASH DAVE** Department of General Surgery, for their invaluable guidance and constant encouragement. Their knowledge has been highly inspirational. They all have been my source of motivation.

My heartful thanks to all my consultants Dr. Naveed Khan, Dr. Srinivasan. D, Dr. Asadulla Baig, Dr. Pavan B.K, Dr. Amal, Dr. Ravikaran, Dr. Vikranth, Dr. Padmalakshmi, Dr. Prakash for their practical tips, invaluable advice and constant encouragement. I am thankful for their, valuable guidance and helping me with my dissertation.

My heartful thanks to all my seniors, my colleagues, my friends, my Juniors and interns for their co-operation and help in carrying out this study.

I would like to express my deepest gratitude to my beloved parents and my siblings for their constant support and encouragement to complete this study.

I extend my heartfelt gratitude to all the patients for their participation and cooperation in this study.

I would also like to thank Department of Biochemistry and pathology for their co-operation and help.

I would also like to thank all the OT and Paramedical Staff especially **Mr Prakash** for his help and assistance.

My sincere thanks to **DR. MAHESH V** statistician for helping me with statistical analysis.

It gives me great pleasure in preparing this dissertation and I take this opportunity to thank everyone who have made this possible.

Dr. AMIT MITTAL

LIST OF ABBREVIATIONS

(in alphabetical order)

ALP	-	Alkaline phosphatase
ALT	-	Alanine aminotransferase
AST	-	Aspartate aminotransferase
cm	-	Centimeter
CO_2	-	Carbon dioxide
ERCP	-	Endoscopic retrograde cholangio pancreatography
H_2O	-	Water
hrs	-	Hours
Hs	-	highly significant
IAP	-	Intraabdominal pressure
kg	-	Kilogram
LAVH	-	Laparoscopic assisted vaginal hysterectomy
LC	-	Laparoscopic cholecystectomy
m	-	Meter
Mg	-	Milligram
µg	-	Microgram
mg/dL	-	milligram per deciliter
min	-	Minute
ml	-	Milliliter

mmHg	-	millimeter mercury
N	-	Number of cases
Nm	-	Nanometer
No	-	Number
O_2	-	Oxygen
$PaCO_2$	-	Arterial pressure of carbon dioxide
P	-	Probability
R	-	Correlation coefficient
S	-	Serum
SGOT	-	Serum Glutamate Oxaloacetic Transaminase
SGPT	-	Serum Glutamate Pyruvate Transaminase
STB	-	Serum Total Bilirubin
Std	-	Standard
T	-	Students paired t test
U/L	-	Units per litre
yrs	-	Years

ABSTRACT

INTRODUCTION: Laparoscopic surgeries have become the surgery of choice for many surgical procedure but its adverse effects on liver are often neglected.

AIM: To measure Liver enzymes, Serum bilirubin, CO_2 insufflation pressure and duration of procedure in patients undergoing laparoscopic procedures.

Correlate the liver enzymes and serum bilirubin with the duration of procedure, insufflation pressure and type of laparoscopic procedure.

METHODS: Blood sample were collected from 103 patients undergoing various types of laparoscopic procedures preoperatively once and on post-operative day 1 and day 3 and was tested for liver enzymes and serum total bilirubin. Various parameters were noted and data was analyzed.

RESULT: In all patients who underwent laparoscopic procedures, the level of serum bilirubin, serum AST, ALT, and alkaline phosphatase were increased significantly on 1st post-operative day. By the 3rd post-operative day, the level of AST, ALT, bilirubin and alkaline phosphatase returned to near pre-operative values.

With increase in duration of procedure there was more increase in AST, ALP, ALT values on 1st post-operative day. There was no significant correlation between duration of procedure and STB on 1st post-operative day.

There was no significant correlation noted between increased insufflation pressure and elevation in liver enzymes and Serum bilirubin.

CONCLUSION: We conclude that transient elevation of hepatic enzymes and serum bilirubin occurs after all laparoscopic procedures which does not have any clinical significance in patients with normal hepatic function. Duration of pneumoperitoneum correlated directly with elevation of liver enzymes and does not correlate with elevation of serum bilirubin and the duration of laparoscopic procedure should be kept to minimum

KEY WORDS: Laparoscopic procedures, Liver enzyme, Pneumoperitoneum

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INTRODUCTION

INTRODUCTION

The new era has seen several changes in the field of medicine. With newer technology and access to advanced services provided by different fields of medicine, the surgical skills have improved from older mind set of bigger incision, better surgeries to a less tissue damaging, cosmetically acceptable small incision or laparoscopic surgeries which have better patient acceptability. Laparoscopic surgeries have changed many general surgical procedures from performing standard open procedures to minimally invasive procedures which have better cosmoses, less tissue damage, thereby leading to better patient compliance.

Many diseases in the past were not managed surgically due to high chances of damaging surrounding structures but the present day scenario is different as these situations are managed easily with laparoscopic approach, like impalpable testes, gallbladder disease, Hirschsprung's disease and many more such procedures which have more complications if done via open surgical approach[1]. Any technique has its own pros and cons, which applies to laparoscopic surgeries also. The adverse effects of laparoscopic surgeries on patient’s body are often neglected.

The widely known adverse effect of laparoscopic surgeries is its effects on liver function. In the last few years, many studies have shown ‘unexplained’ changes in liver enzymes during postoperative period after laparoscopic procedures. The serum liver enzymes increases significantly in many patients who had a normal liver enzymes before the procedure[2,3,4].

Very few studies are available to justify the correlation between Laparoscopic Surgeries and liver enzyme elevation. The cause for elevated liver enzymes have remained unknown so far. The effect may be attributed to hepatocellular dysfunction due to either CO_2 pneumoperitoneum, diathermy extruding liver, injury to branch of the hepatic artery or general anesthesia[5]. This study was done to evaluate the changes in serum liver enzymes pre-operatively and post-operatively following laparoscopic procedure.

OBJECTIVES

AIMS AND OBJECTIVES

- To measure Liver enzymes, insufflation pressure, duration of procedure in patients undergoing laparoscopic procedures.

- To correlate the duration of procedure, insufflation pressure and type of laparoscopic procedure with elevation of liver enzymes.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

HISTORY OF LAPAROSCOPIC SURGERY

Ezekiel and Celsus[6] described the drainage of the abdomen of "bad humours" around 25 BC – AD 50 surgically by insertion of trocar. The first recorded endoscopy was by the use of reflected light to inspect the cervix which was performed by Albukasim who was an Arabian physician[7].

The concept of minimally invasive surgery can be traced back to 19th century. The data of using tube instruments date back during Mesopotamia civilization and ancient Greece.

The modern techniques of endoscopy were started in 1805 with Phillip Bozzini[8] an obstetrician from Frankfurt. He used wax candle as the light source for the mirror and examined the urethra and urinary bladder for stones and inspected the vagina.

In 1897 Nitze an Urologist from Berlin along with Rayne, an optician and a Viennese master invented the first ever cystoscope which had lenses, and a platinum conductor to create a lighting effect[9].

First successful attempt of “ventroscopy”, i.e., an intra-abdominal inspection using light beam of a candle, from frontal mirror to mirror reflector of tube, inserted through a culdotomy opening in 1901, by a gynecologist Dr. Fon Ott from Petrograd[10].

The first successful documented laparoscopy was done on dogs by George Kelling[11] in 1902.

In 1910, First successful thoracoscopy and laparoscopy on humans using a cystoscope was done by Hans Christian Jacobaeus[12]. He also introduced the word “Laparoscopy” into practice.

In 1947, Raoul Palmer[13] used CO2 gas for insufflating abdomen and also introduced the concept of controlling intra-abdominal pressure. He suggested that intra-abdominal pressure should not exceed 25 mm Hg and also suggested that speed of insufflation should not exceed 400-500 cc per minute[14].

Professor Kurt Semm[15] the German gynecologist and engineer, from the city of Kill has supervised and has put into practice the modern techniques of laparoscopy and automatic insufflators.

The use of telescope has seen a drastic increase since the invention of fiber optic light in 1952 and the lens system by British doctor Hopkins[16].

In 1977, De Kok performed appendicectomy using partial laparoscopic support[17]. Gallstones extraction using laparoscopy was done on animals by a group of doctors from Germany which was supervised by doctor Fremberg[7] in 1979.

In 1980’s an Englishmen, Patrick Steptoe[18] started performing laparoscopic sterilization in females in operation theatre.

The solid camera was first introduced in 1982 after which a new era of video laparoscopy began.

First laparoscopic appendicectomy was described by Semm[15] in 1983.

First laparoscopic cholecystectomy using Carbonic gas for insufflation and modified proctoscope for visualization was done by Doctor Mühe[19], the surgeon from Boeblingen in 1985.

In 1986, group of Japanese engineers made a matrix which allowed transferring of video signals to monitors which brought a revolution in endoscopic technology.

Warshow[20] in 1986, identified the stage of cancer pancreas using laparoscopy.

In France, Phillipe Mouret[21] did first video-laparoscopic cholecystectomy in 1987.

Minimally invasive surgeries were widely used in many surgical directions because of which many complex instruments and devices were invented. Laparoscopy became popular in mid 90's. In the present day 90% surgeries for cholelithiasis is done by laparoscopy.

In 1994, Robotic arm was used to hold Laparoscopic instruments and camera[22].

HISTORY OF LAPAROSCOPIC SURGERY IN INDIA[23]

Diagnostic laparoscopy was performed on a cirrhotic patient using Nitze-type telescope, a feeble filament light bulb and atmospheric air to create pneumoperitoneum with the help of a sigmoidoscope by Dr F.P. Antia, a physician at the KEM hospital, Mumbai.

Excellent clarity of vision was observed by using Storz laparoscope to perform a diagnostic laparoscopy by a famous Gynecologist Dr. N.D. Motashaw at KEM hospital in 1971.

In 1990, the first laparoscopic cholecystectomy in India was performed at the JJ Hospital Mumbai. Few months later Dr. Jyotsna Kulkarni in Pune performed laparoscopic cholecystectomy.

Dr. J.B. Agarwal and Dr. A. Dalvi held the first workshop on minimal access surgery (MAS) in KEM hospital, Mumbai.

The Indian Association of Gastrointestinal Endo-Surgeons was formed in Mumbai by a group of laparoscopic surgeons in 1993 with Dr. T. E. Udwadia as Founder President and Dr. JB Agarwal as Honorary secretary.

In 1992, Dr. M.G. Bhat started laparoscopic surgery in Karnataka

INTRODUCTION TO LAPAROSCOPY

The term laparoscopy is derived from the Greek word which literally means to see from the flank side. Laparoscopic surgery is also known as the "minimally invasive surgery", Band-Aid surgery or keyhole surgery. In the lay man's language, it is known as the "computer surgery".

In modern surgical era conventional operations are now done using ports into the body through small incisions with the aid of a camera so that the abdominal cavity can be visualized to diagnose a condition or to perform surgery.

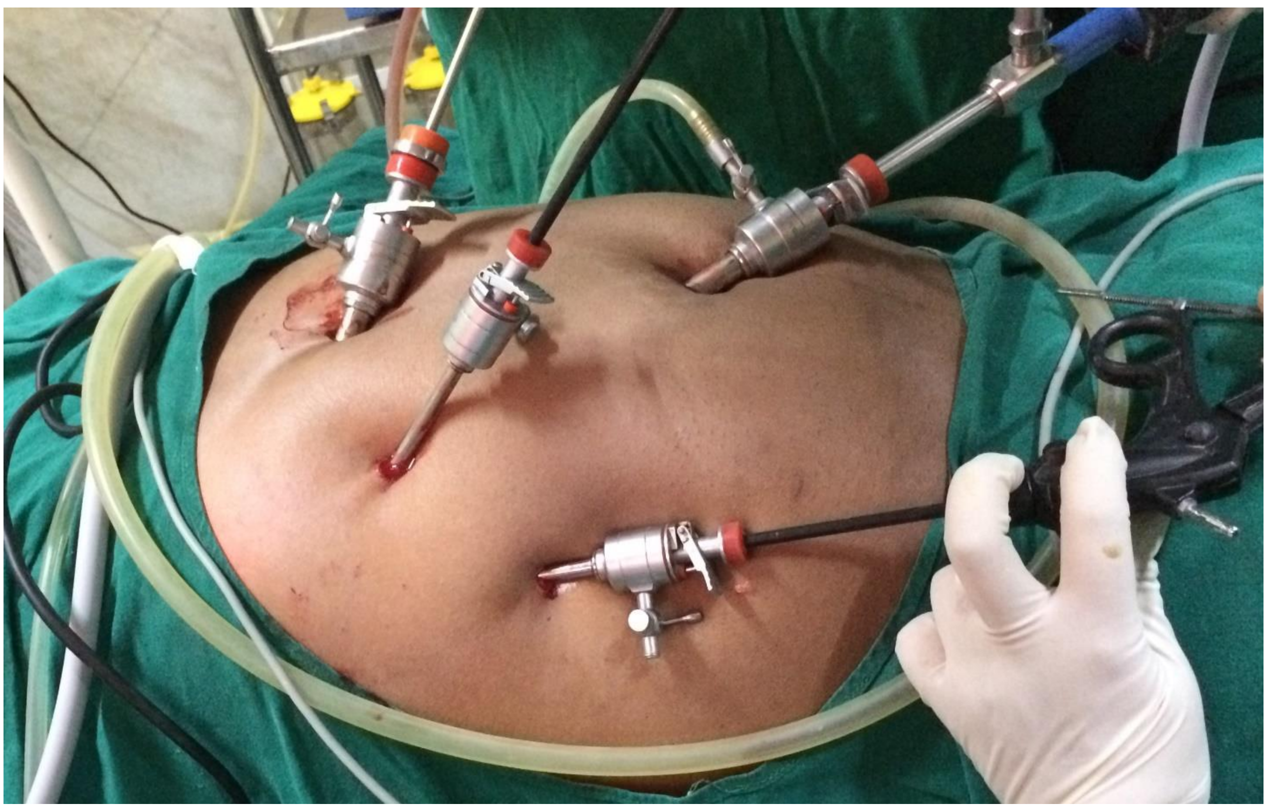


Figure 1: Laparoscopic cholecystectomy surgery with trocars in situ

AN OVERVIEW OF LAPAROSCOPIC SURGERY

Patient positioning

↓

Part preparation

↓

Equipment

↓

Site selection

↓

Port Placement and Characteristics

↓

Access or Placement of the First Port

↓

Creation of Pneumoperitoneum

↓

Placement of Secondary ports

↓

Completion of surgical procedure

↓

Hemostasis and then Fascial closure

↓

Suturing

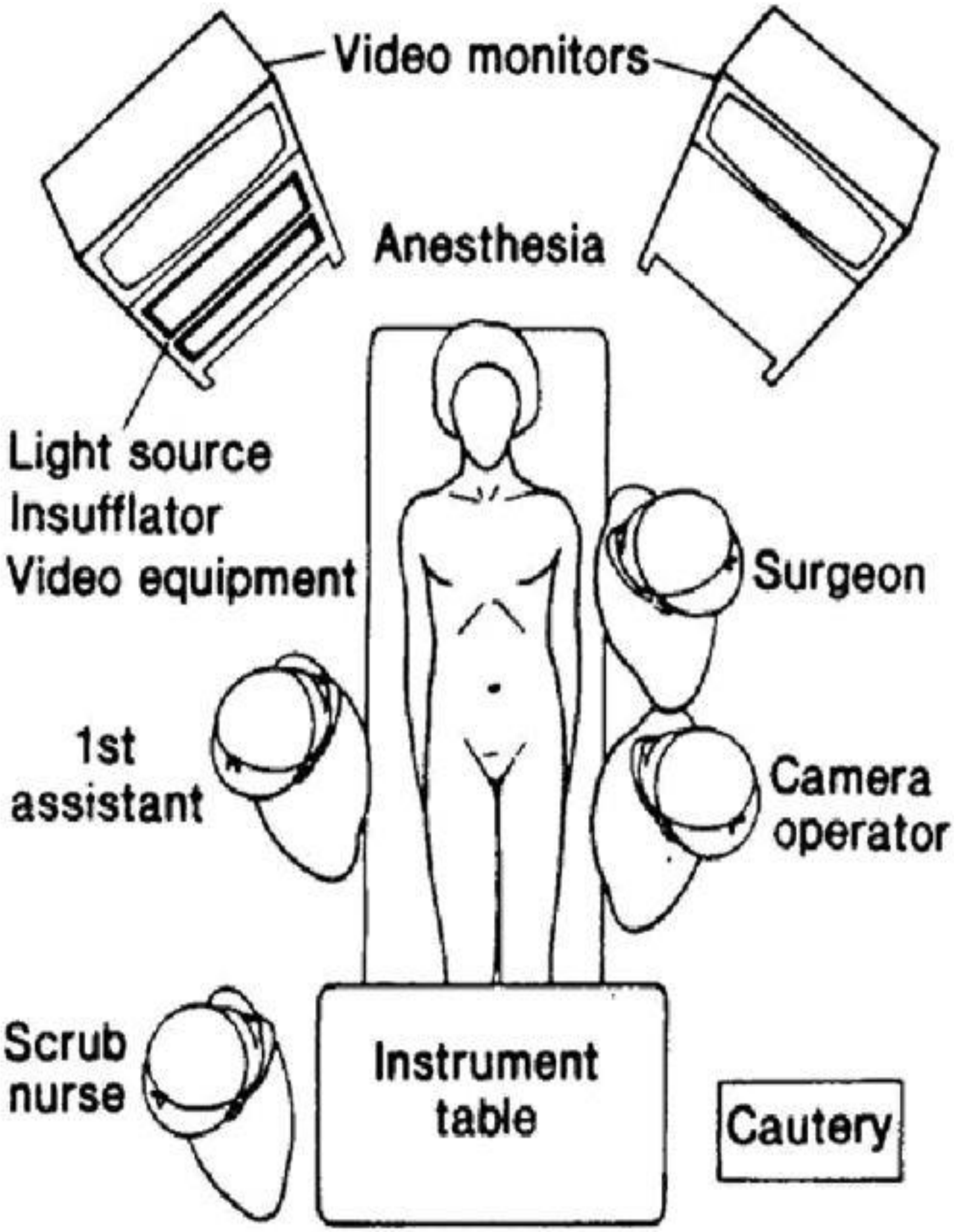


Figure 2: The Setup for Laparoscopic Cholecystectomy

Figure 3 : Laparoscopy Trolley

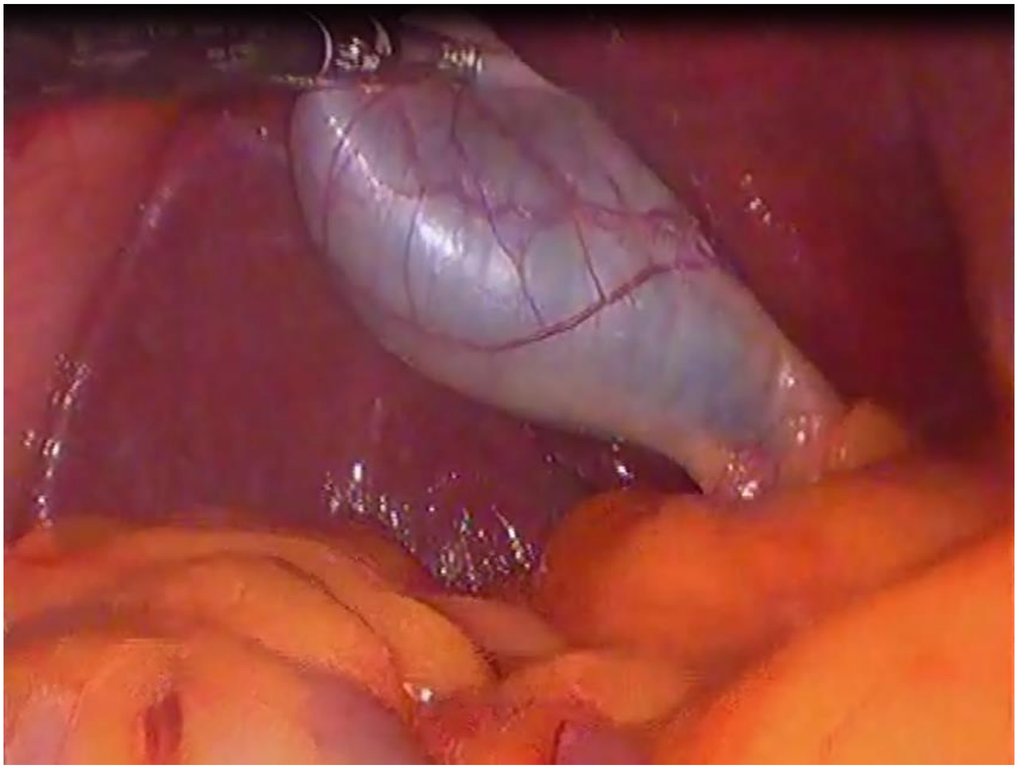


Figure 4: Laparoscopic cholecystectomy

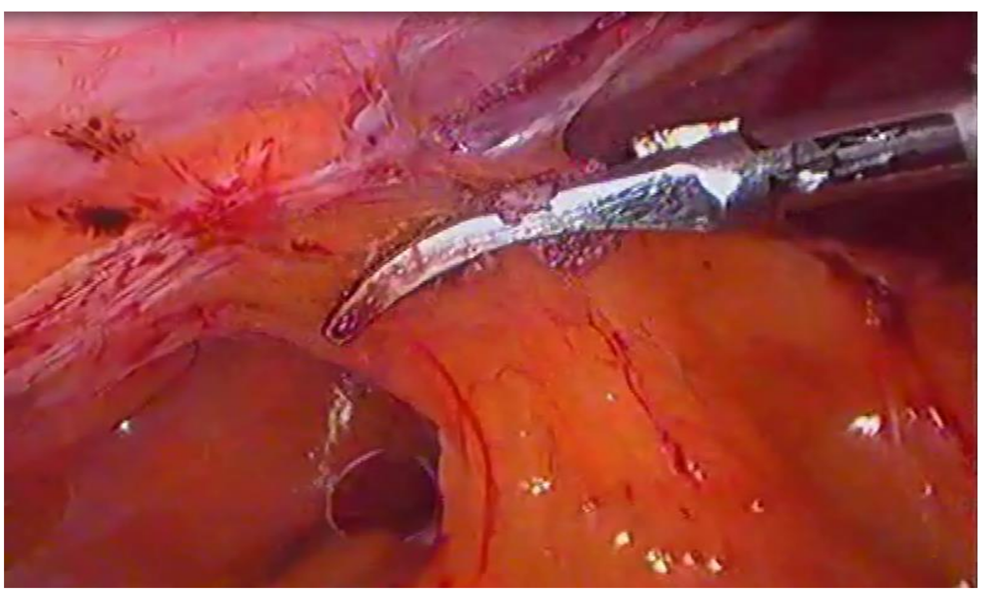


Figure 5 : Diagnostic Laparoscopy (Adhesiolysis)

Figure 6: Ongoing Laparoscopic appendicectomy

Figure 7: Laparoscopic Appendicectomy

EQUIPMENT AND INSTRUMENTATION[24]

The instruments used for laparoscopy are expensive. Hence it should be ensured that all instruments are compatible and fits into the cannulae and various cables will connect to one another.

VIDEO IMAGING SYSTEMS

This is the important technological advance in laparoscopic field. It allows surgeons to work together while watching a video monitor.

Components of this system:

1. Light source
2. Fibre optic light guide cable
3. Telescope
4. Video camera system
5. Video monitor
6. Video recorder

LIGHT SOURCE:

As laparoscopic procedures allow simultaneous vision via a television camera with recording of the operative procedure, it requires a Xenon light source or a 250-watt halogen lamp. A Storz light source with a self-adjusting light intensity can be used. Cold light is a misnomer. Modern light sources have thermal shield which helps in reducing the amount of heat transmitted through the cable, thereby minimizing the risk of burns internally.

FIBEROPTIC LIGHT GUIDE CABLE:

This is 5mm thick and 225cm long. Thick cable helps in carrying more light. As the length of the cable increases, it is less likely to be stretched and damaged. The cable should be handled gently. It should not be bent sharply along its length either during use or when stored.

TELESCOPES:

These are rigid instruments that employ Hopkins rod lens system of optics. This rod lens system consists of a series of quartz rod lenses, image reversal system, optical fibres for transmission of light, an objective lens and an eyepiece. Rigid laparoscope sizes range from 3mm to 10mm in diameter with a variety of viewing lenses. The advantages of 0 degree or end/forward viewing laparoscope are easier to use with least amount of image distortion and produce brighter images. Whereas advantages of angled scopes (30,40 degree) gives greater versatility to operator to look around the corners and over surface of solid structures. Flexible laparoscopes have been developed using fibre optic bundles for visualization. It provides greater flexibility in the viewing angle.

VIDEO CAMERA SYSTEM :

Consists of a “chip camera”, controller, a high-resolution video monitor and video tape recorder. The video cameras are used for video endoscopy. These cameras are available in 1.25 and 1.67 cm diameters. These are based on either a single chip design which can provide 450 lines of horizontal resolution or a triple chip design which provides over 700 lines of horizontal resolution, but is more expensive. The cameras which attach directly to the laparoscope are preferable to those which require additional coupling. Focusing should be easy to achieve. Automatic white balance and colour bars are essential features. The camera should be sterilisable

VIDEO MONITOR :

To visualise video image, it should ideally be recorded on a video tape. This helps the surgeon to assess his own technique. It provides an accurate, permanent documentation of the procedure.

INSTRUMENTS FOR EXPOSURE AND MANIPULATION

INSUFFLATOR

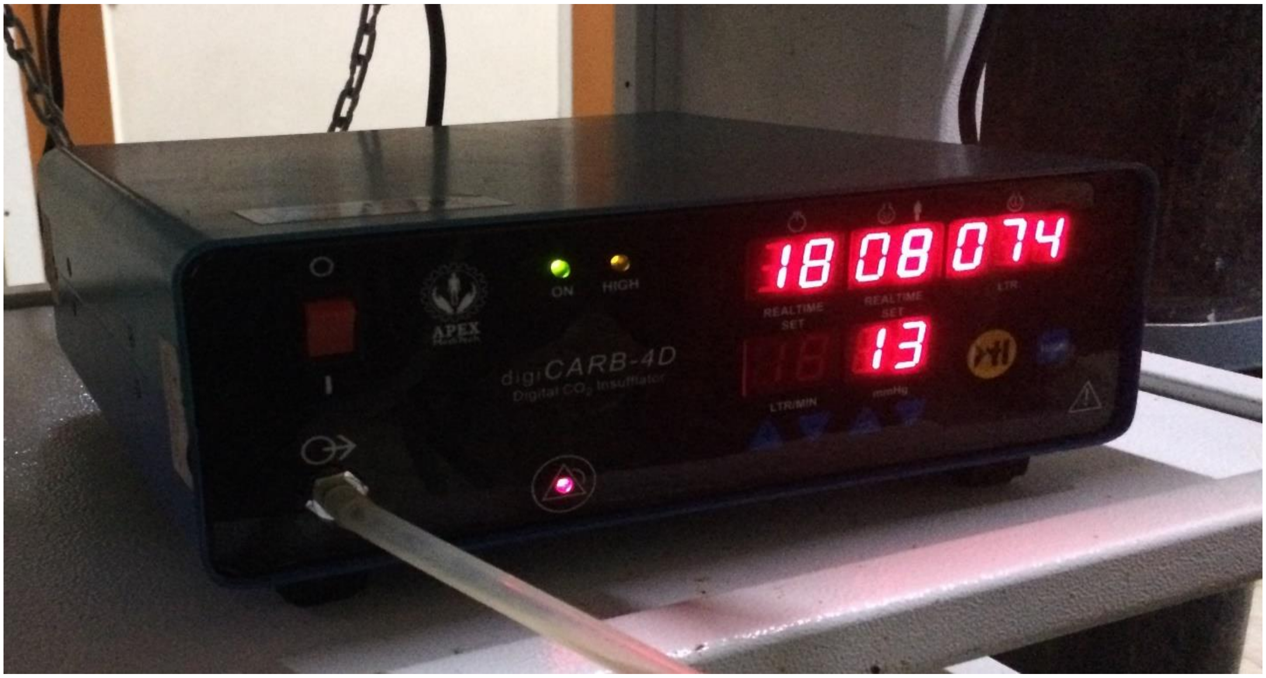


Figure 8: Insufflator

Laparoscopic procedures require uniform abdominal distension, which is always pre-set to safe limits of intra-abdominal pressure of 12-14mmHg. This should be maintained constantly. Electronically controlled insufflators are capable of delivering flow rates of at least 6 litres/min, preferably 8-10 litres/min. For creating pneumoperitoneum Carbon dioxide is considered the most suitable gas. It is easily available, non-combustible, cheap and soluble in plasma pressure of 12-14mmHg.

Electronic insufflators continuously monitor: -

- Pressure at the tip of the Veress needle or trocar sheath during insufflation.
- The flow rate in litres/min.
- The volume of gas used at any given time after commencing the procedure.
- The intra-abdominal pressure.

It allows low-pressure insufflation at 1 litre /min and rapid insufflation at 6-10 litres/min. Hence compensating for major gas loss during the procedure. Delivering a high flow rate is a vital safety feature during critical stages of laparoscopic surgery specifically when bleeding is present.

Insufflator also helps in controlling and maintaining the maximum intra-abdominal pressure to a pre-set level of 12-14mmHg. Visual and audio alarms help to identify any inadvertent rise of intra-abdominal pressure. Insufflator has to be kept at least 1 meter away from the operation table as electrocautery is usually used. A second CO_2 cylinder should be kept as a standby.

PUNCTURE INSTRUMENTS

VERESS NEEDLE

It is used to create pneumoperitoneum. Spring loaded safety mechanism is used here whereby an obturator projects sharply beyond the sharp tip, thus avoiding injury to intra-abdominal structures. These needles are in different gauges and lengths.

TROCARS

Trocars are used for introduction of instruments, are available in 2 sizes- 11mm trocars for 10mm instruments and 5.5mm trocars for 5mm instruments. Trocars are made up of metal tube with a tapered end. The outer surface of these have a dull finish , minimizing the reflection of light in the abdomen. This also has a gate valve or trumpet valve which prevents gas escape. The outer end of the trocar has a gasket or 'washer', which grips any instrument passing through it to prevent gas leak.

TROCAR OBTURATOR

Trocar obturator is sharp pointed instrument. Hence it is safe to perforate the abdominal wall without indenting it deeply. These trocars have stopcocks within through which CO_2 can be insufflated. Disposable trocars are available which are more expensive. They have a retractable sheath on the trocar tip, which protects intraperitoneal structures from injury. Reusable ones are made of stainless steel. These are sterilized by keeping in Cidex solution or in formalin chamber.

SURGICAL INSTUMENTS

The instruments of laparoscopic surgery are modifications of standard open surgical instruments. These are 30 to 40cm in length with shaft diameter of 3 to 10mm. Working tips of these instruments are metal to allow use with electrocautery and to provide durability. Both reusable and disposable ones are available.

GRASPING AND DISSECTING INSTRUMENTS:

These instruments do not have any teeth or ratchet hence minimizes trauma during grasping. Two sizes of graspers are available - Small one for dissection and a larger one for grasping. These instruments can be dismantled and thoroughly cleaned. They are safer, longer lasting and economical. The hook is a unique laparoscopic instrument which comes in various shapes like L, J etc. with a short stubby tip or a long thin sharp tip.

INSTRUMENTS FOR RETRACTION:

The expandable retractor or the probes are used. Even the closed grasping forceps can be used for retraction.

INSTRUMENTS FOR OCCLUSION AND LIGATION:

CLIP APPLICATOR

Clip applicators are used to apply clip on structures to be occluded. Various reusable and disposable clip applicators are available. The reusable ones need to be withdrawn from the abdomen to be reloaded for each use. The disposable applicators are pre-loaded, hence all clips can be applied without withdrawing the instrument, and without the risk of their dropping into the peritoneal cavity. But these are not cost effective. Pre-made catgut endo-loop is needed to ligate vascular adhesions

INSTRUMENTS FOR DIVISION AND COAGULATION:

The hook scissors helps in division of the tissue from the underlying structures. For very delicate incisions and sharp dissections a very fine tipped micro-scissors are useful. Small insulated forceps helps in diathermy coagulation. A hook dissector, spatula dissector and fine point dissector helps in diathermy dissection. A ball-tipped insulated suction cannula can be used for coagulation of bleeding points.

ELECTRO-SURGICAL UNIT:-

Unipolar or bipolar electrocauteries can be used in these surgeries. Bipolar electrocautery is safer than unipolar as it requires careful application of the ground-plate to the patient, perfect cable settings, should also ensure that only the surgeon will operate the electrocautery.

INSTRUMENTS FOR IRRIGATION AND SUCTION:

Frequent flushing and suction of operative field is required as it provides a clear view which is needed for safe and clean laparoscopic surgery. This is done by instilling saline under pressure and also suck out the fluid. Irrigation and suction can be done simultaneously through a two-way 5mm cannula.

ENDOBAG:

These bags are used for removing excised tissues. These are made of thick plastic sheets. Condoms can be used alternatively, but they are thin and break easily.

WOUND CLOSURE INSTRUMENTS:

Forceps with teeth helps in wound closure . Vicryl suture material is used for suturing of sheath and subcutaneous tissue, and black silk material is used for skin closure.

INSTRUMENTS FOR LAPAROTOMY:

If for any reason open surgery is considered, laparotomy set to be always kept ready for immediate use.

COMMONLY PERFORMED SURGERIES BY LAPAROSCOPIC APPROACH

Some commonly performed operations include:

Cholecystectomy

Appendectomy.

Removal of patches of endometriosis

Adhesiolysis

Colectomy

Female sterilization

Treating ectopic pregnancy

Trans Abdominal Pre Peritoneal (TAPP) and Totally Extra Peritoneal (TEP) Hernia repair

Biopsy of various structures inside the abdomen

Diagnostic[25] – acute abdomen, infertility, liver disease and tumors, ascites, tumor staging, trauma

ADVANTAGES OF LAPAROSCOPY[26]

The main advantages of laparoscopic surgery versus open surgery

- Faster return to normal activities
- Economic effectiveness

In initial phase, the cost of laparoscopic surgery appears high but the cost associated with treatment of complications of open surgery and the work days lost due to disability, laparoscopic surgery seems relatively more beneficial.

Early postoperative advantages

- Reduced contamination of internal organs to external environment.
- Less pain
- Reduced post-operative pulmonary complications
- Shorter recovery time is observed than open (when the same surgery is done laparoscopically according various studies).
- Short hospital stay
- Reduced blood loss

Late postoperative advantages

- Cosmetically better
- Lesser wound complications
- Post-operative complications like obstruction, adhesions are relatively less when compared to open surgery
- Lesser chances of incisional hernia

DISADVANTAGES OF LAPAROSCOPY[26]

- The cost of laparoscopic equipment and instruments is high.
- Dysfunction of organs due to Carbon dioxide in the abdominal cavity.
- Requires more time to acquire skills
- Knowledge of conventional open procedure is important as some intraoperative complications are inevitable and needs conversion of laparoscopic surgery into open.
- Two dimensional orientation

- There is no tactile feedback of intraoperative organs in laparoscopy when compared to open procedures which is important to know local pathology.
- Bleeding is relatively harder to manage laparoscopically as field of vision gets obscured due to light absorption by extravasated blood and bleeding points retract within surrounding tissues.
- Intra operative iatrogenic complications are more likely to occur in difficult surgeries, surgeon should electively go for conversion to open surgery of such cases, without considering it as a failure for safety of the patient.
- One of the problem with minimal access approach is organ extraction.

PNEUMOPERITONEUM AND ITS PATHOPHYSIOLOGY[27]

The intra- or extra-peritoneal insufflation of carbon dioxide (CO2) through a Veress needle is the initial standard surgical technique.

12-15 mm Hg is the usual preset pressure which is sensed by electronic variable flow insufflator and when attained, it terminates the flow.

Desired number of trocars are then inserted and a video-laparoscope is introduced.

The observed physiological changes during laparoscopic surgeries can be due to

- PATIENT POSITION
- INTRODUCTION OF EXOGENOUS INSUFFLATING GAS, CO_2
- PNEUMOPERITONEUM AND INCREASED INTRA-ABDOMINAL PRESSURE

1. PATIENT POSITION

Alteration of patient position helps in displacement of viscera from surgical site during laparoscopic surgery.

The Trendelenburg position (15-20°) is used during insertion of trocar in upper abdomen surgeries while same position is used for longer periods in lower abdominal surgery. This position increases the right atrial pressure (RAP), venous return (VR), the cardiac output and central blood volume[28]. This leads to atelectasis by causing reduction in vital capacity(VC), lung compliance and functional residual capacity(FRC)[29].

Cephalad displacement of the diaphragm and carina can cause inadvertent right main stem bronchial intubation and hypoxemia. Nerve compression is possible in the head-down position. In prolonged laparoscopic procedures with Trendelenburg position brachial plexus injury has been reported. Increased intracranial and intraocular pressure has also been observed in Trendelenburg position by affecting the cerebral circulation[30].

The reverse Trendelenburg position (20°-30°) favours respiration and diaphragmatic function , but it can also lead to coronary insufficiency by decreasing Venous Return (VR), Pulmonary Capillary Wedge Pressure (PCWP), Right Atrial Pressure (RAP) and fall in the Mean Arterial blood Pressure (MAP) and Cardiac Output (CO) reflected by changes in the left ventricular end diastolic pressure. Pneumoperitoneum created during laparoscopic surgeries further worsens the condition by causing compression of inferior vena cava. Prolong steep head-up position causes venous stasis in the leg predisposing to deep vein thrombosis.[31,32]

2. INSUFFLATION OF EXOGENOUS GAS, CO_2

Adverse effects are seen after insufflation of an exogenous gas, produced by physiological changes as well as due to its pharmacological properties.

In the presence of methane (present in gut) or when electrocautery is used, room air and nitrous oxide can be inflammable, although these two were used to diagnose various gynaecological pathologies. CO_2 is the gas of choice for insufflation because of its easy availability, low cost, a high Ostwald's blood/gas partition coefficient (0.48), it is odourless, relatively inert, and non-combustible. Excretion is mainly via lungs after being buffered in blood by bicarbonates[33,34]. The incidence of gas embolism is rare (0.0016-0.013 per cent),due to high solubility. However it is a peritoneal irritant.

Rise in the end-tidal carbon dioxide (EtCO2) is mainly due to absorption of CO2 from peritoneal cavity leading to hypercarbia more after extraperitoneal insufflation than intraperitoneally. It results in a five-fold rise of arginine vasopressin (AVP) and stimulates the sympathetic nervous system[35]. 15-20 per cent increase in minute ventilation is required to maintain normal haemodynamics. Prolonged surgical time, with pulmonary pathology can result in diminished respiratory capacity for CO_2 excretion leading to hypercapnia and metabolic acidosis. Except in patients with cardiopulmonary compromise and associated ventilation perfusion mismatch, $PaCO_2$ usually correlates well with the $EtCO_2$. In such patients, direct estimation of PaCO2 may become necessary[36]. Incidence of arrythmias increases due to lowered threshold by acidosis[37]. When the $PaCO_2$ is increased by 30 per cent above the normal levels, haemodynamic alterations occurs. Tachycardia, increased systemic vascular resistance, systemic arterial pressure, central venous pressure and cardiac output are results of sympathetic stimulation due to mild hypercapnia. Coronary ischemia is caused as a result of the shortened pre-ejection period, the left ventricular ejection time and the diastolic filling phase of the coronary arteries. Thus patients with ischemic heart disease are at high risk if not managed properly.

Left ventricular function is reduced as a result of negative ionotropic effect on the heart exerted by severe hypercarbia.

In the post-operative period due to the slow mobilization of CO_2 from body stores into the serum for excretion, all these effects persists for long time when pneumoperitoneum is produced by nitrogen or helium gas these complications are less[34].

3. PNEUMOPERITONEUM AND INCREASED INTRA-ABDOMINAL PRESSURE

By insufflation of gases through Veress needle at the rate of 1-2 L/min, pneumoperitoneum is initiated. Overall pressure of the diaphragm at this point is about 50 kg in the Trendelenburg position at an IAP of 15mm Hg once pneumoperitoneum is achieved.

Increased IAP, temperature variations (hypothermia), CO2 absorption, and neuro hormonal stress response is produced as a result of pneumoperitoneum.

The introduction of several liters of gas into the abdominal cavity results in an increased intra-abdominal pressure. Cardiovascular changes associated with pneumoperitoneum depends on the interaction of factors including position of the patient, rate and amount of insufflation of CO_2.

INCREASED IAP INFLUENCES

The cardiovascular system

The respiratory system

The gastrointestinal system

Mesenteric circulation

Hepato-portal circulation

Renal function

Intracranial pressure (ICP) and intraocular pressure (IOP)

Cardiovascular System

12 mm Hg is standard pressure with minimum haemodynmic complications. Rise in IAP is the important cause for instability in laproscopic surgeries, due to excessive stretching of peritoneum, increase vagal tone causing bradycardia[38,39].

Cardiac output shows a biphasic change. Cardiac output is either increased or normal upto a pressure of 10mmHg. Additional increase in further (>15 mm Hg), the insufflated CO_2 compresses both the venous capacitance and the arterial resistance vessels. This produces a rise in the systemic vascular resistance (SVR), and the pulmonary vascular resistance (PVR) leading to an increased afterload. The mean arterial blood pressure rises and the cardiac output falls by 25-35 per cent. An IAP > 20 mm Hg reduces the renal and mesenteric blood flow markedly. Proportional opposing effects on the cardiovascular system is that it forces blood out of the abdominal organs and the inferior vena cava into the central venous reservoir, and at the same time it increases peripheral blood pooling in the lower extremities and thus tends to decrease central venous blood volume. High IAP augments venous return in patients with high right-sided pressures maintaining a patent inferior vena cava (IVC), whereas low right- sided pressures lead to a compressed IVC and a decrease in venous return[40].

The combined effect of anesthesia, head-up position and increased intra-abdominal pressure can reduce cardiac index (CI) by 50 per cent[31].

Respiratory System

The increased IAP causes cephalad displacement of diaphragm. Thus reducing the lung volumes, viz., tidal volume (TV), minute ventilation (MV) and functional respiratory capacity (FRC). Pulmonary compliance also reduces which causes increased airway pressure, and risk of barotrauma during intermittent positive pressure ventilation (IPPV)[31]. There is uneven distribution of the ventilation to non-dependent parts of the lungs which produces mismatch in ventilation and perfusion leading to hypoxia and hypercarbia[41].

As there is upward displacement of the diaphragm and carina due to raised IAP and Trendelenburg position it may result in right main stem bronchial intubation since the endotracheal tube remains fixed at its proximal end, which predisposing to hypoxaemia[32].

Gastrointestinal System

There is a risk of gastric acid aspiration due to high intra-gastric pressure during laparoscopic procedures as a result of increased IAP but the reflux is prevented by raised barrier pressure of lower oesophageal sphincter which exceeds far more than intra-gastric pressure[42].

Mesenteric Circulation

Decreased mesenteric circulation is mainly due to reverse trendelenburg position, mechanical compression of abdominal organs, hypercapnia induced sympathetic tone, release of vasopressin. Raised IAP causes collapse of capillaries and small veins leading to multi-organ dysfunction[43]

Hepatoportal circulation

IAP (> 20 mm Hg) can lead to prograde flow with increased resistance thereby adversely affecting the abdominal vasculature. Marked fall in hepatic and splanchnic circulation is observed in pneumoperitoneum due to release of various hormones (catecholamine, angiotensin, and vasopressin). There is an overall reduction of blood supply to all the organs except the adrenal glands.

Marked decrease blood supply is seen mostly in portal system of about 60 per cent causing liver dysfunction with increase of IAP of >20mmHg and this might persist postoperatively[44].

Renal Function

Renal haemodynamics are alterated by affecting cardiac output and also renal blood flow. Increase in sympathetic activity, elevation of plasma ADH and raised plasma renin-angiotensin activity due to mechanical obstruction of renal venous system due to raised IAP leads to increase in the renal vascular resistance leading to a fall in the filtration pressure and urine output[45].

Intracranial pressure (ICP) and Intraocular pressure(IOP)

Increase in ICP and IOP is due to compression of inferior vena cava and increase in lumbar spinal pressure thereby reducing the drainage from lumbar plexus with increase in IAP[40]. Hypercapnia causes vasodilatation in the central nervous system which also contributes to increase in ICP[46].

COMPLICATIONS DURING LAPAROSCOPY[26]

Laparoscopic procedures are associated with various complications which are potentially life threatening when compared to complications associated with conventional open approach. Surgeon should be well versed about these complications its management in order to improve patient care and safety to and decrease patient morbidity and mortality.

The incidence of laparoscopic complications is 1.1-5.2% in minor procedures and 2.5-6% in major ones.

Classification of laparoscopic complications:

The complications due to laparoscopic surgeries can be classified into two types

1. Based on the timing of complication

   Intraoperative complications

   Postoperative complications

2. Based on the type of complication

   Generally related to all laparoscopic procedures

   Specific to the type and site of surgery

BASED ON THE TIMING OF COMPLICATION

1. During Introduction Of Pneumoperitoneum

Cardiovascular: Arrhythmias, Vasovagal shock, Brady-arrhythmias, Tachy-arrhythmias, Hypotension, Cardiac Arrest, Hypertension

Respiratory: Hypercarbia, Gas Embolism

2. Insertion Of Trocars

Extravasation of Gas

- Subcutaneous Emphysema

The most common respiratory complication that occurs during laparoscopic procedures is Subcutaneous emphysema is caused by extra peritoneal insufflation of CO2 and is recognized by an increase in end-tidal CO_2 more than 25%. Subcutaneous emphysema can often be palpated.

- Pneumothorax
- Pneumomediastinum

Injury to organs: Stomach, Liver, spleen, Urinary Bladder

Injury to vessels

5 in 10,000 and 3 in 1,000 is estimated number of overall risk of trocar injury to intraabdominal structures which mostly associated with primary trocar insertion. According to Chandler and colleagues[36], the most commonly injured organ is the small bowel (25.4%), followed by the iliac artery (18.5%), colon (12.2%), iliac vein (8.9%), mesenteric vessels (7.3%), and aorta (6.4%).

3. Positioning Of Patient

Nerve Injuries

Endobronchial Intubation

Thermal Injuries

BASED ON THE TYPE OF COMPLICATION:

- **RELATED TO ALL LAPAROSCOPIC PROCEDURES**

1. Complications of access
2. Physiologic complications of the pneumoperitoneum

- **SPECIFIC TO THE TYPE AND SITE OF SURGERY.**

- **COMPLICATIONS OF THE OPERATIVE PROCEDURE.**

LIVER FUNCTION TESTS

Many tests have been used to diagnose liver pathology yet there is no specific test to find out exact lesion or pathology. Liver function test may be normal even in the presence of liver disease.

NORMAL BILE PIGMENT METABOLISM

Bilirubin is a tetrapyrrole that is transported, conjugated, stored and excreted by the liver cells. It is derived mainly from the red cells destroyed by the reticuloendothelial system at the end of natural life span and some from myoglobin breakdown, non-hemoglobin heme- containing proteins in the liver. The degradation of hemoglobin during erythrocyte maturation in the bone marrow, and the intra-medullary destruction also contributes to bilirubin formation. When the red blood cells are destroyed, the heme ring is opened and transformed into biliverdin, which is reduced to form bilirubin. The bilirubin combines with albumin to form a stable complex that is transported to the hepatic parenchymal cell. This complex is a lipid soluble pigment. The bilirubin-albumin complex is poorly soluble in water and is not excreted in urine.

The complex is transported via the portal vein or hepatic artery into the sinusoides of liver. The albumin is removed and the bilirubin is conjugated with the glucuronic acid to form di-glucuronide, which is water soluble and excreted as bile. This substance gives an immediate diazo reaction and is, therefore termed ‘direct reacting’ in the Van den Bergh test. It is readily excreted into the urine. Kidney and small intestine are the other sites for conjugation when there is liver pathology.

The conjugated bilirubin is excreted via the bile into the intestine is acted upon by bacteria to the formation of two compounds – the colorless urobilinogen, which is later converted to stercobilin that gives brown color of feces, and urobilin.

The normal daily fecal excretion varies between 40 and 300mg. A reduction in enteric bacteria is also responsible for the reduced pigment excretion. Some urobilinogen is reabsorbed by the portal system and is re-excreted by the liver and kidney

Measurements of serum bilirubin are helpful in differentiating jaundice resulting from hepatocellular disease and obstructive jaundice. Degree of jaundice and serial documentations of serum bilirubin will provides information about the excretion of bilirubin and underlying pathology.

SERUM ENZYMES

A large number of enzymes present in the liver are also found in the plasma in low volumes. The activity of these enzymes in the plasma is known by the rate of release from cells and the rate of clearance from plasma. Destruction of parenchymal cells of liver will release these enzymes into circulation which are in high concentration. Transaminases and dehydrogenases are the routinely measured enzymes in clinical laboratories.

In intra-hepatic or extra-hepatic pathology alkaline phosphatase, 5'-nucleotidase and leucine aminopeptidase are increased in patients with cholestasis. Increase in serum alkaline phosphatase activity is seen after accidental bile duct ligation which is due to release of enzyme that are newly synthesized in the liver.

Elevated alkaline phosphatase helps in early deduction of cholestasis or hepatic infiltration by tumor or granuloma in absence of jaundice.

Studies relating to liver function changes following laparoscopic surgeries

Tan M, Xu FF, et.al[5] in their study concluded that transient elevation of hepatic transaminases occurred after laparoscopic surgery. The major causative factor seemed to be the CO_2 pneumoperitoneum[48]. In most of the patients, the transient elevation of serum liver enzymes due to the negative effects of the pneumoperitoneum on the hepatic blood flow showed no apparent clinical implications but the study showed care should be taken before deciding to perform LC in patients with hepatic insufficiency.

However, if preoperative liver function was very poor, laparoscopic surgery may not be the best choice for the treatment of patients with certain abdominal diseases.

Similarly in their study Morino M, Giraudo G, et.al[49] concluded that the duration and level of intraabdominal pressure are responsible for changes of hepatic function during laparoscopic procedures.

Schilling MK, et.al[50] in their study concluded that laparoscopic procedures with a CO2 pneumoperitoneum should be performed at a pressure of 10 mm Hg or lower to avoid splanchnic microcirculatory disturbances.

Schmandra TC, Kim ZG, et.al[51] in their study concluded that elevated intraabdominal pressure generated by the pneumoperitoneum results in a reduction of portal venous flow. This effect is significantly stronger during carbon dioxide insufflation. Portal flow reduction may compromise hepatic function and cell-mediated immune response during laparoscopic surgery.

Also, Volz J, Koster S, et.al[52] in their study concluded that the morphological integrity of the peritoneum is temporarily disturbed by CO_2 pneumoperitoneum. Because Low Pressure Laparoscopic Cholecystectomy(LPLC) minimizes adverse hemodynamic effects on hepatic function, a low-pressure pneumoperitoneum should be considered for patients with compromised liver function, particularly those undergoing prolonged laparoscopic surgery.

METHODOLOGY

MATERIALS AND METHODS

This prospective study was conducted to evaluate the effect of laparoscopic procedures on liver function. The patients included in the study were selected by purposive sampling method from those who underwent laparoscopic procedures in R L Jalappa Hospital & Research Centre, Tamaka, Kolar. The study was conducted from December 2015 to June 2017.

All the patients studied were selected using Purposive sampling method for laparoscopic procedures after they underwent routine history taking, physical examination and investigations to exclude pre-existing liver diseases. Various laparoscopic procedures were performed on 103 patients and they constituted the study population.

Sample Size:

Sample size was estimated by using the proportion of subjects with increased AST in laparoscopic subjects was 58.2 % from the study by Singal R, Singal RP, Sandhu K, Singh B, Bhatia G, Khatri A[4] did a study on Evaluation and comparison of postoperative levels of serum bilirubin, serum transaminases and alkaline phosphatase in laparoscopic cholecystectomy versus open cholecystectomy using the formula:

$$\text{Sample size} = \frac{Z_{1-\alpha/2}{}^{2}\, p(1-p)}{d^{2}}$$

Here

$Z_{1-\alpha/2}$ = Is standard normal variate (at 5% type 1 error ($P<0.05$) it is 1.96 and at 1% type 1 error ($P<0.01$) it is 2.58). As in majority of studies P values are considered significant below 0.05 hence 1.96 is used in formula.
p = Expected proportion in population based on previous studies or pilot studies.
d = Absolute error or precision – Has to be decided by researcher.

P = 58.2% or 0.0.582

q = 41.8% or 0.418

d = 10% or 0.10

Using the above values at 95% Confidence level a sample size of 94 subjects undergoing laparoscopy will be included in the study.

Considering 10% Nonresponse a sample size of 94 + 9.4 ≈ 103 subjects will be included in the study.

Inclusion criteria:

- Patients undergoing laparoscopic procedures in the Department of General Surgery, R.L Jalappa Hospital, Tamaka, Kolar

Exclusion criteria:

- Patients with coexisting liver disease
- Patient on long term use of hepatotoxic drugs.
- Patients that develop complications such as bile duct injury, obstruction, infection, leakage and high grade fever during surgery and in the post-operative period

In all the patients selected for the study, the levels of Aspartate Aminotransferase (AST or SGPT, normal range 5-40 U/L), Alanine Aminotransferase (ALT or SGOT, normal range 5-35 U/L), Serum bilirubin (normal range 0.2-0.3 mg/dL) and Serum Alkaline Phosphatase (normal range100-290 U/L) were measured pre-operatively once and then post-operatively on Day 1 and Day 3.

Serum bilirubin was measured by Diazo reagent, AST was measured by Pyruvate oxidase/peroxidase method, ALT was measured by Multipoint enzymatic method and ALP was measured by P-Nitrophenyl phosphate as substrate. All the above parameters were analyzed using vitros 5.1FS dry chemistry analyser in clinical biochemistry section of R.L.J.H and RC.

During the surgery intraabdominal pressure (IAP), CO_2 insufflation pressure, duration of procedure (pneumoperitoneum) was recorded in each procedure. Perioperative antibiotics were administered in all patients

Statistical analysis:

Data was entered into Microsoft Excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and Proportions. Continuous data was represented as mean and SD. **Paired t test** is the test of significance for paired data such as before and after surgery for quantitative data. **ANOVA (Analysis of Variance)** was the test of significance to identify the mean difference between more than two groups for quantitative data. **Graphical representation of data:** MS Excel and MS word was used to obtain various types of graphs such as bar diagram, Pie diagram and Scatter plots.

Pearson correlation was done to find the correlation between two quantitative variables and qualitative variables respectively.

Correlation coefficient (r)	Interpretation
0 - 0.3	**Positive Weak correlation**
0.3-0.6	**Positive Moderate correlation**
0.6-1.0	**Positive Strong correlation**
0 to (-0.3)	**Negative Weak correlation**
(-0.3) to (-0.6)	**Negative Moderate Correlation**
(-0.6) to – (1)	**Negative Strong Correlation**

P value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Statistical software: MS Excel**,** SPSS version 22 **(**IBM SPSS Statistics, Somers NY, USA) was used to analyze data.

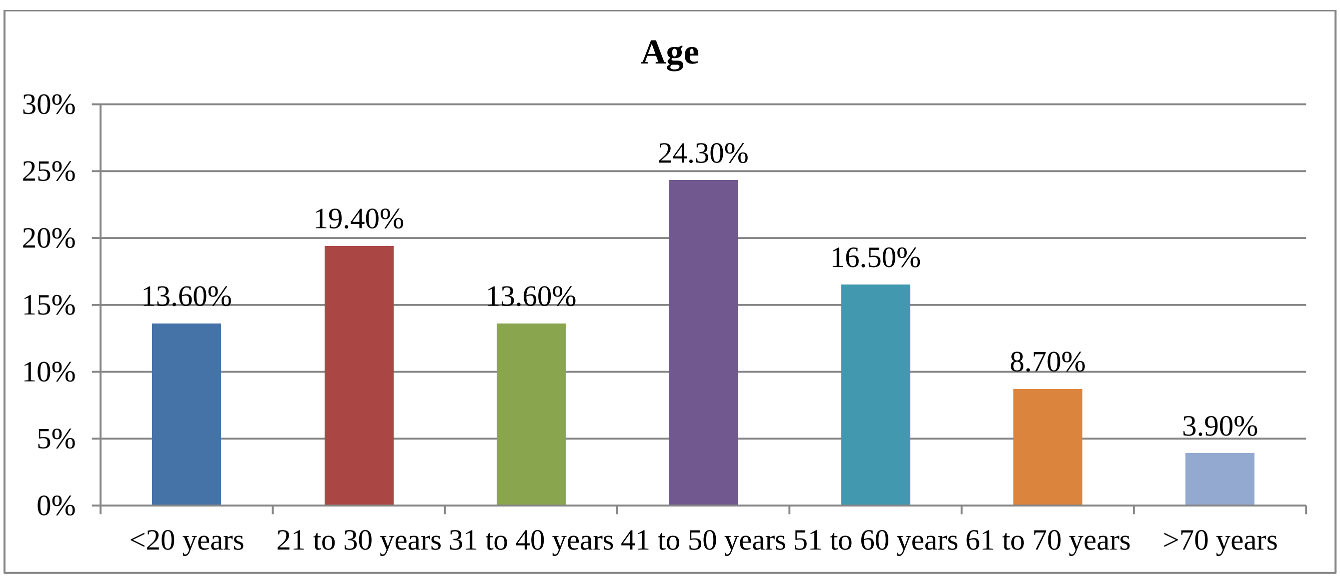
RESULTS

RESULTS:

Mean age of subjects was 41.81 ± 17.47 years. Majority of subjects were in the age group 41 to 50 years (24.3%), 19.4% were in the age group 21 to 30 years.

Table 1: Age distribution

		Count	%
Age	<20 years	14	13.6%
	21 to 30 years	20	19.4%
	31 to 40 years	14	13.6%
	41 to 50 years	25	24.3%
	51 to 60 years	17	16.5%
	61 to 70 years	9	8.7%
	>70 years	4	3.9%

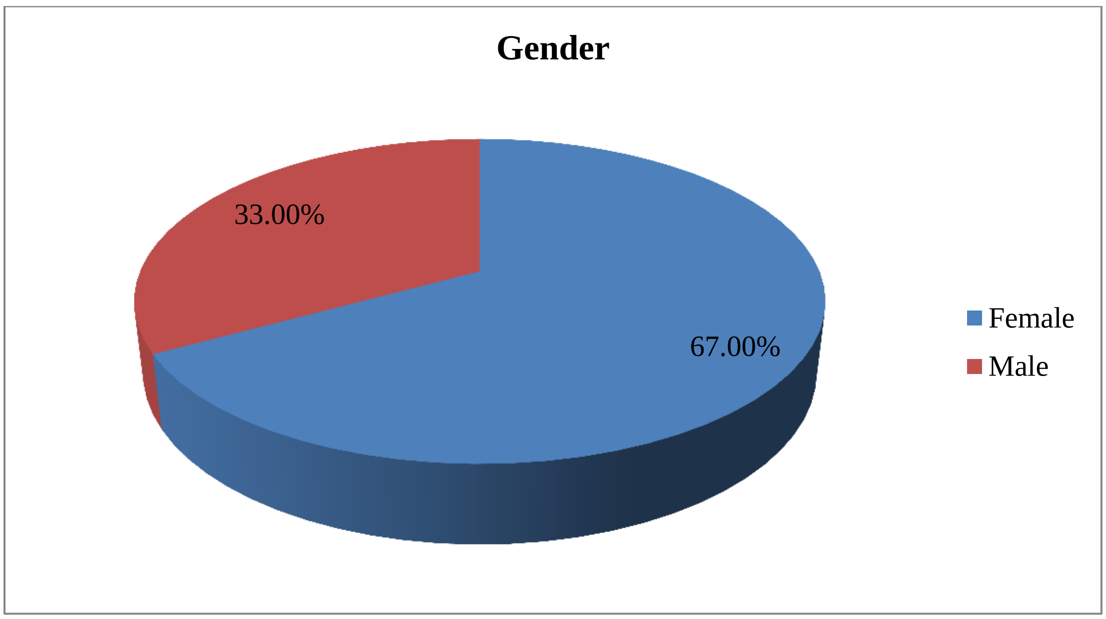


Graph 1: Bar diagram showing Age distribution of subjects

Table 2: Gender distribution

		Count	%
Gender	Female	69	67.0%
	Male	34	33.0%

In the study 67% were females and 33% were males.

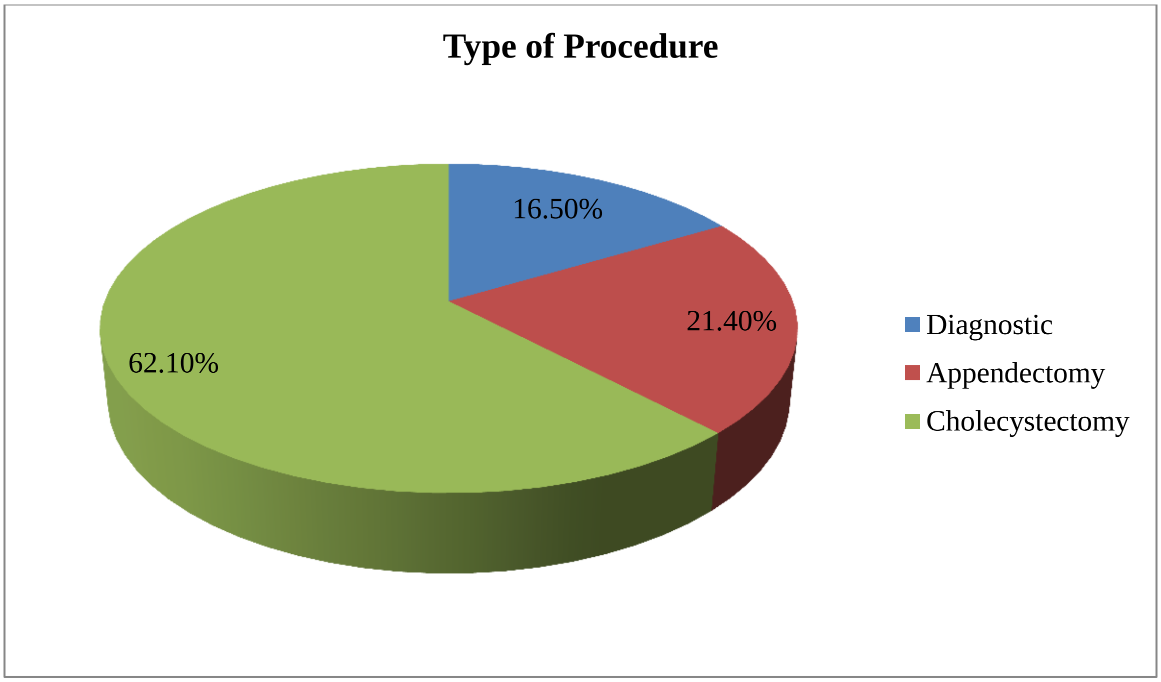


Graph 2: Pie diagram showing Gender distribution of subjects

In our study 16.5% patients underwent diagnostic laparoscopic procedure, 21.4% underwent laparoscopic appendectomy and 62.1% underwent laparoscopic cholecystectomy.

Table 3: Type of Procedure distribution of subjects

		Count	%
Type of Procedure	Diagnostic Laparoscopy	17	16.5%
	Laparoscopic Appendectomy	22	21.4%
	Laparoscopic Cholecystectomy	64	62.1%



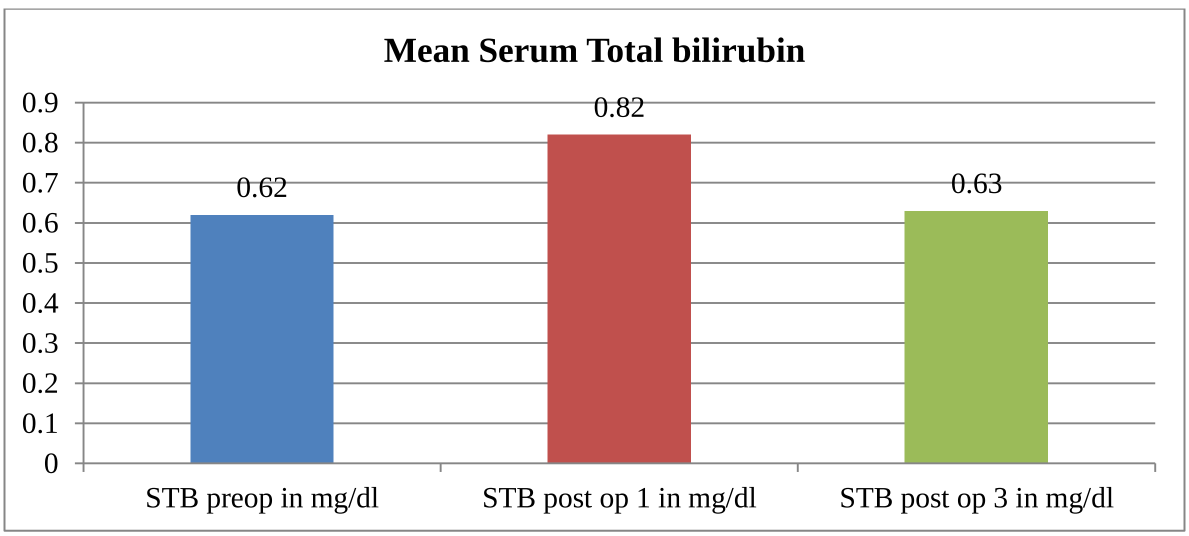
Graph 3: Pie diagram showing Type of Procedure distribution of subjects

Table 4: Comparison of Mean Serum Total bilirubin at different time interval

	Mean	SD	P value
STB preop in mg/dl	0.62	0.31	
STB post op 1 in mg/dl	0.82	0.36	<0.001*
STB post op 3 in mg/dl	0.63	0.27	0.417

*Paired t test

In our study pre-operative mean STB was 0.62 ± 0.31 mg/dl, which increased to 0.82 ± 0.36 mg/dl on 1st post-operative day and again reduced to 0.63 ± 0.27 mg/dl on 3rd post-operative day. There was significant increase in mean STB between Pre-operative and 1st Post-Operative day (P value <0.001). No significant difference was noted between pre-operative and 3rd post-operative day (P value = 0.417).



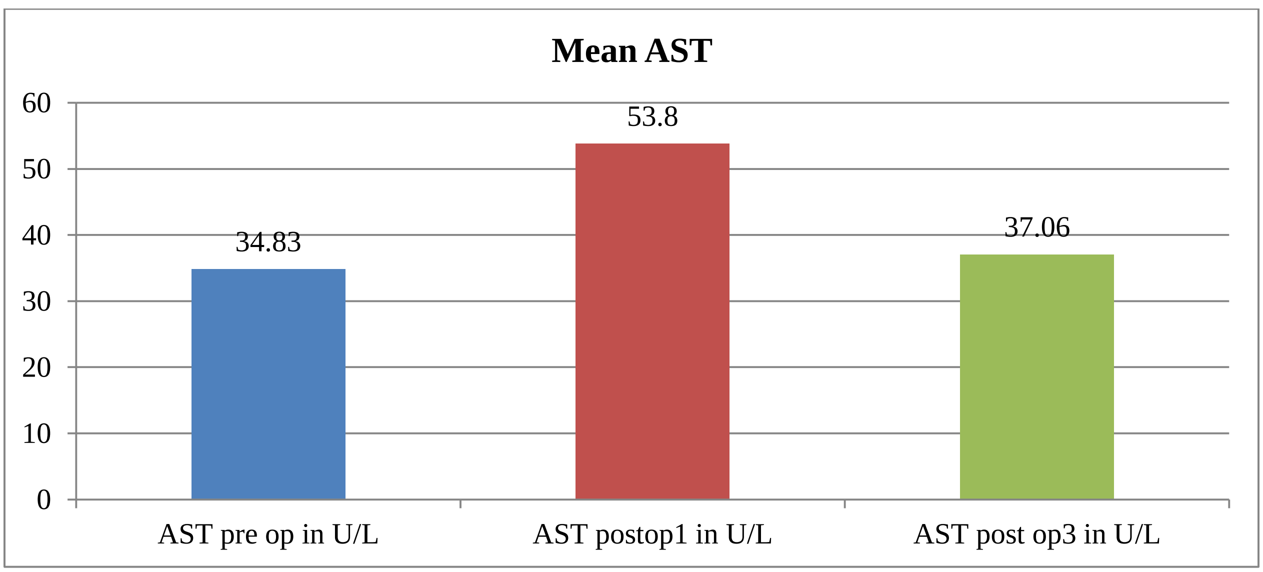
Graph 4: Comparison of Mean Serum Total bilirubin at different time interval

Table 5: Comparison of Mean AST at Different Time Interval

	Mean	SD	P value
AST pre op in U/L	34.83	24.80	
AST postop1 in U/L	53.80	28.96	<0.001*
AST post op3 in U/L	37.06	22.08	0.008*

*Paired t test

In our study preoperative mean AST was 34.83 ± 24.80 U/L which increased to 53.8 ± 28.96 U/L on 1st post-operative day and again reduced near to pre-operative value of 37.06 ± 22.08 U/L on 3rd post-operative day. There was significant increase in mean AST values between Pre-operative and 1st Post-operative day (P value <0.001).



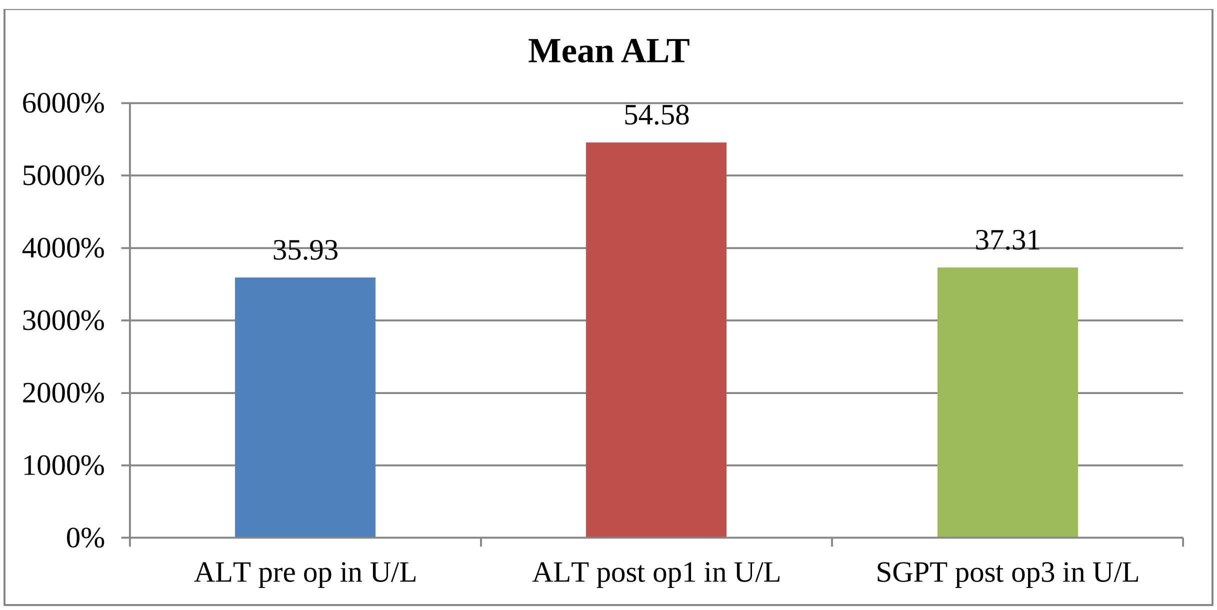
Graph 5: Comparison of Mean AST at Different Time Interval

Table 6: Comparison of Mean ALT at Different Time Interval

	Mean	SD	P value
ALT pre op in U/L	35.93	26.51	
ALT post op1 in U/L	54.58	29.28	<0.001*
ALT post op3 in U/L	37.31	23.55	0.044*

*Paired t test

In our study preoperative mean ALT was 35.93 ± 26.51 U/L which increased to 54.58 ± 29.28 U/L on 1st post-operative day and again reduced near to pre-operative value of 37.31 ± 23.55U/L on 3rd post-operative day. There was significant increase in mean ALT values between Pre-operative and 1st Post-Operative day (P value <0.001).



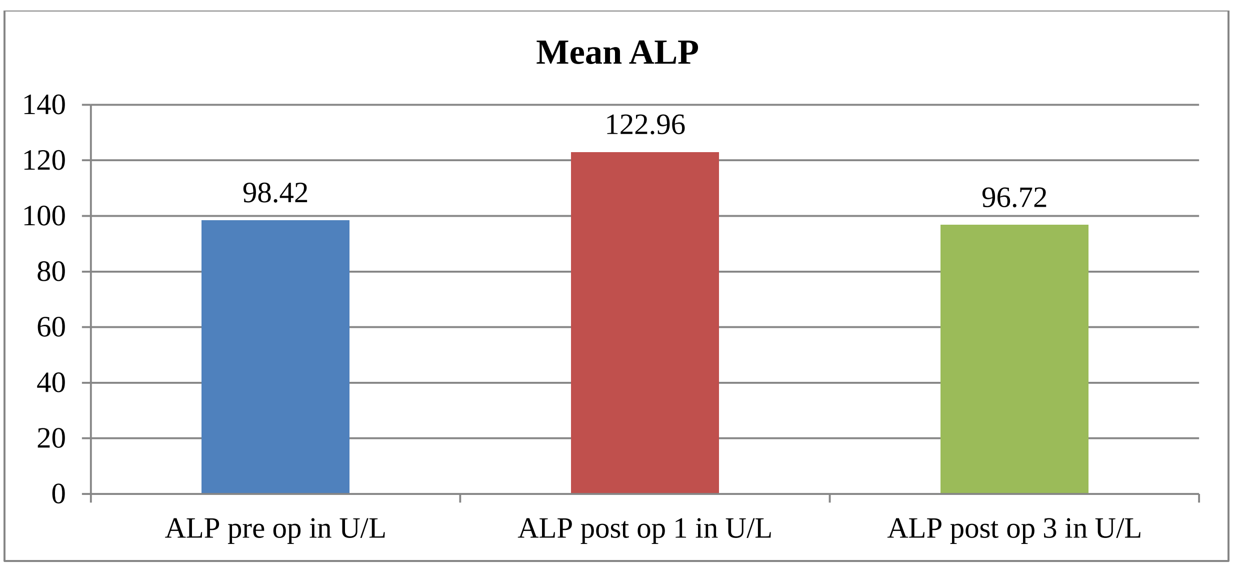
Graph 6: Comparison of Mean ALT at Different Time Interval

Table 7: Comparison of Mean Serum Alkaline Phosphatase at Different Time interval

	Mean	SD	P value
ALP pre op in U/L	98.42	51.64	
ALP post op 1 in U/L	122.96	46.67	<0.001*
ALP post op 3 in U/L	96.72	36.05	0.481

*Paired t test

In our study preoperative mean ALP was 98.42 ± 51.64 U/L which increased to 122.96 ± 46.67 U/L on 1st post-operative day and again reduced near to pre-operative value of 96.72 ± 36.05 U/L on 3rd post-operative day. There was significant increase in mean ALP values between Pre-operative and 1st Post-Operative day (P value <0.001).

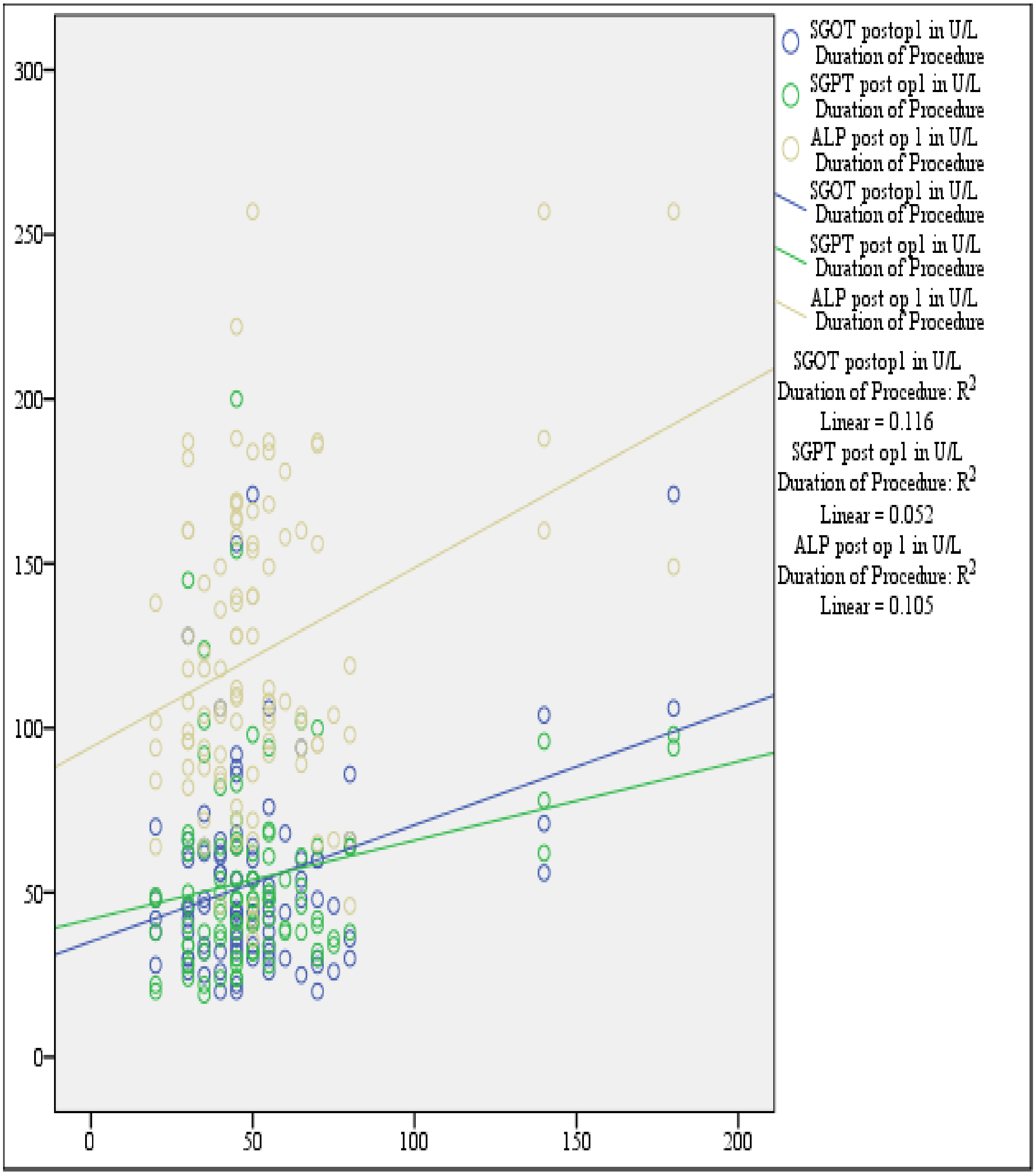


Graph 7: Comparison of Mean Serum Alkaline Phosphatase at Different Time interval

Table 8: Correlation between Duration of Procedure and Liver enzymes at 1 day post operative period

Correlations						
		Duration of Procedure	STB post op 1 in mg/dl	AST postop1 in U/L	ALT post op1 in U/L	ALP post op 1 in U/L
Duration of Procedure	Pearson Correlation	1	0.008	0.340**	0.227*	0.325**
	P value		0.939	<0.001*	0.021*	0.001*
	N	103	103	103	103	103
**. Correlation is significant at the 0.01 level (2-tailed).						

In the study there was significant positive correlation between Duration of procedure and Post-operative day 1 values of AST, ALT and ALP i.e. with increase in duration of procedure, there was more increase in Post-operative day 1 AST, ALT and ALP and vice versa. There was no significant correlation between Duration of procedure and mean STB on post-operative day 1.



Graph 8: Scatter plot showing Correlation between Duration of Procedure and AST, ALT and ALP at 1 day post operative period

Scatter plots were constructed by using duration of procedure in X axis and Liver enzymes in Y axis.

Table 9: Correlation between Inflation Pressure and Liver enzymes on post-operative day 1 period

Correlations						
		Inflation Pressure	STB post op 1 in mg/dl	AST postop1 in U/L	ALT post op1 in U/L	ALP post op 1 in U/L
Inflation Pressure	Pearson Correlation	1	-0.078	0.124	0.118	0.051
	P value		0.436	0.210	0.235	0.607
	N	103	103	103	103	103
**. Correlation is significant at the 0.01 level (2-tailed).						

In the study there was no significant correlation between Inflation pressure and Post-operative values of STB, AST, ALT and ALP on day 1.

Table 10: Comparison of Type of procedure with Liver enzymes at different intervals of follow up

	Type of Procedure						P value*
	Diagnostic		Appendectomy		Cholecystectomy		
	Mean	SD	Mean	SD	Mean	SD	
STB preop in mg/dl	0.53	0.22	0.62	0.28	0.64	0.34	0.430
STB post op 1 in mg/dl	0.79	0.31	0.76	0.34	0.85	0.38	0.609
STB post op 3 in mg/dl	0.56	0.23	0.62	0.24	0.65	0.29	0.413
AST pre op in U/L	41.41	33.48	38.45	31.75	31.84	18.70	0.276
AST postop1 in U/L	66.65	37.45	56.05	31.91	49.61	24.45	0.089
AST post op3 in U/L	42.35	29.60	37.95	25.79	35.34	18.28	0.501
ALT pre op in U/L	45.29	40.56	39.91	33.51	32.08	17.36	0.137
ALT post op1 in U/L	67.18	40.77	57.91	37.68	50.09	20.63	0.084
ALT post op3 in U/L	42.41	32.88	40.82	32.87	34.75	15.66	0.364
ALP preop in U/L	95.71	39.75	113.91	85.39	93.81	37.14	0.284
ALP post op 1 in U/L	127.12	51.47	132.82	51.92	118.47	43.54	0.430
ALP post op 3 in U/L	96.47	34.79	104.86	45.01	93.98	33.02	0.479

*ANOVA test

In the study there was no significant difference in mean Serum liver enzymes among different types of procedures.

Table 11: Percentage Change in Liver Enzymes on Day 1 and Day 3 Compared to Pre Op Values

	Mean	SD	Median
STB Percentage change on day 1	21.87%	31.19	23.0%
AST Percentage change on day 1	34.91%	22.71	39.1%
ALT Percentage change on day 1	34.65%	18.36	38.0%
ALP Percentage change on day 1	19.85%	19.16	21.6%

In our study all the liver enzymes and serum total bilirubin has increased from preoperative values.

Mean value of Serum Total Bilirubin has increased upto 21.87% on 1st post operative day .

Mean value of AST has increased upto 34.91% on 1st post-operative day

Mean value of ALT has increased upto 34.65% on 1st post-operative day

Mean value of ALP has increased upto 19.85% on 1st post-operative day

DISCUSSION

DISCUSSION

Laparoscopic procedures have gained popularity in recent days because of newer technologies like endoscopic optics, video cameras and endoscopic instrumentation, to add on to this many other advantages are incision is small, less postoperative pain, less postoperative discomfort, hospital stay is shortened, patients are ambulated early and can return to their routine activities early.[53]

Laparoscopic surgeries are also accompanied by unexplained significant physiological changes which are specifically unique to these procedures. There are unexplained changes in postoperative liver function reflected in serum liver enzymes in patients who have undergone laparoscopic procedures which is hypothetically attributed to CO_2 pneumoperitoneum. This study was undertaken to assess the change in liver enzymes and serum bilirubin after laparoscopic surgeries and if it has any clinical significance.

In the 103 patients who constituted our study population, 34 were male patients and 69 were females. Majority of subjects were in the age group 41 to 50 years (24.3%), Second common age group being 21 to 30 years (19.4%).

Patients who had undergone various types of laparoscopic procedures were included in the study. In our study group of 103 patients, 17(16.5%) patients underwent Diagnostic Laparoscopy, 22 (21.4%) patients underwent Laparoscopic Appendectomy and 64(62.1%) had undergone Laparoscopic Cholecystectomy. In all patients, the levels of serum bilirubin, serum AST, serum ALT and serum Alkaline phosphatase were checked preoperatively once and post operatively on day 1 and day 3.

Serum Total bilirubin (STB)

This is correlated with the study conducted by Hiremath S[54] who studied Effects of Carbon Dioxide Pneumoperitoneum on Liver Function Tests Following Laparoscopic Cholecystectomy and showed that mean value of pre-operative STB was 0.510 ± 0.286 mg/dl, which significant increase after 24 hrs of surgery to 0.684 ± 0.239 mg/dl (P = 0.000).

Nahvi IA, Nahvi IA, Habib M, Deewani SS[55] have evaluated the changes in the liver function tests and their clinical significance after uneventful laparoscopic cholecystectomy at different intra-abdominal pressures. They measured liver enzymes preoperatively, 24 hours post-operatively and on 7th postoperative day. Their study population was divided into 2 groups. Group A patients underwent Low Pressure Laparoscopic Cholecystectomy (LPLC) that is pneumoperitoneum maintained at 8mm of Hg and group B patients were subjected to High Pressure Laparoscopic Cholecystectomy (HPLC) in which pneumoperitoneum was maintained at 14 mm of Hg. In HPLC group mean value of pre-operative STB was 0.75 ± 0.10 mg/dl, which increased to 0.79 ± 0.09 mg/dl on post-operative day one and returned to near pre-operative values of 0.73±0.08 mg/dl on post-operative day 7. Whereas no significant change was noted in LPLC group.

Our result also correlated with study done by Marakis G, Pavlidis T, Ballas K, Rafailidis S, Psarras K, Symeonidis N et al[3]. On Alterations In Liver Function Tests following Laparoscopic Cholecystectomy in which the mean STB was 0.64 ± 0.24 mg/ml preoperatively and was 0.95 ± 0.58 mg/ml 24 hours post-operatively there was increase of up to 48.4% which was statistically significant.

A study done by Rao PR, Kongara S, Snigdha Y, Kalyan KA[56] on Study of Alterations in Liver Function Tests Following Laparoscopic Surgeries showed that Serum bilirubin was 0.72 ± 0.156 mg/dl preoperatively which significantly increased to 1.14± 0.321mg/dl on post-operative day 1 and came down to 0.79 ± 0.155 mg/dl on post-operative day 3.

Singal R, Singal RP, Sandhu K, Singh B, Bhatia G, Khatri A[4] did a study on Evaluation and comparison of postoperative levels of serum bilirubin, serum transaminases and alkaline phosphatase in laparoscopic cholecystectomy versus open cholecystectomy showed that pre-operative mean STB was 0.53±0.1mg/dl which increased to 1.93±0.7mg/dl 24hrs after surgery and returned to near pre-operatively values of 0.54±0.1mg/dl after 72 hrs of surgery in laparoscopic surgeries but there was no significant difference in serum bilirubin preoperatively and postoperatively in open cholecystectomy patients.

Serum AST/ SGOT

In our study preoperative mean AST was 34.83 ± 24.80 U/L which increased to 53.8 ± 28.96 U/L on 1st post-operative day and again reduced near to pre-operative value of 37.06 ± 22.08 U/L on 3rd post-operative day. There was significant increase in mean AST values between Pre-operative and 1st Post-Operative day (P value <0.001).

Correlating this with study done by Hameed F, Ahmed B, Khan AA, Dab RH[2] on Impact of Pneumoperitoneum on Hepatic Functions after Laparoscopic Cholecystectomy (LC) showed that mean AST pre operatively was 31.23 ±5.51U/L which increased to 53.79 ±12.92 U/L on 2nd postoperative day and returned to 31.20± 5.75 U/L on 10th post-operative day. There was statistically significant increase in the levels of mean serum AST on 2nd post-operative day and by 10th post-operative day the values returned pre-operative levels.

A study done by Arora B[57] on Liver enzymes Alterations after Laparoscopic Cholecystectomy correlated with our study showing that mean AST value pre operatively was 28.2± 6.4 U/L and 24 hrs after surgery it was 36.6± 4.6 U/L showing a statistically significant increase in the AST values from pre operatively to 24 hrs postoperatively.

Hiremath S[54] who studied Effects of Carbon Dioxide Pneumoperitoneum on Liver Function Tests following Laparoscopic Cholecystectomy showed mean AST was found to be significantly elevated from 22.68 ± 7.031 U/L to 32.74 ± 7.731 U/L (P=0.000) 24 hrs postoperatively.

Nahvi IA, Nahvi IA, Habib M, Deewani SS[55] has evaluated the changes in the liver function tests and their clinical significance after uneventful laparoscopic cholecystectomy at different intra-abdominal pressures. They showed that mean AST increased from a preoperative value of 33.70±8.04 U/L to 80.38±19.94 U/L on post-operative day 1, the values returned to pre-operative values of 34.20±6.24 U/L on day 7 in HPLC group whereas no statistically significant change was noted in LPLC group.

Changes in the level of serum liver enzymes after laparoscopic surgery was the study done by Tan M, Xu FF, Peng JS, Li DM, Chen LH, Lv BJ[5] et al showed that mean AST increased after laparoscopic cholecystectomy from 28.4± 20.2 to 41.5 ±24.7 U/L on post op day 1 (P<0.05) and in laparoscopic colorectal cancer resection surgeries from pre-operative mean value of 27.3± 16.1 to 40.7±27.3 U/L on postop day 1 (P<0.05), Both of which were statistically significant. No statistical difference was noted in open cholecystectomy and open colorectal cancer resection surgeries patients.

Serum ALT/ SGPT

In our study preoperative mean ALT was 35.93 ± 26.51 U/L which increased to 54.58 ± 29.28 U/L on 1st post-operative day and again reduced near to pre-operative value of 37.31 ± 23.55U/L on 3rd post-operative day. There was significant increase in mean ALT values between Pre-operative and 1st Post-Operative day (P value <0.001).

Correlating this with the study done by Hameed F, Ahmed B, Khan AA, Dab RH[2] on Impact of Pneumoperitoneum on Hepatic Functions after Laparoscopic Cholecystectomy (LC) showed that ALT pre operatively was 28.19± 5.29 U/L, 2^{nd} day postoperatively was 51.11± 13.06 U/L and on 10^{th} post op day 29.16 ±5.40 U/L there was statistically significant increase in the levels of serum ALT was noted in samples of 2nd post-operative day and on 10^{th} post op day the values returned preoperative levels.

A study done by Arora B[57] on Liver enzymes alterations after Laparoscopic Cholecystectomy correlated with our study showing that mean ALT value pre operatively was 29.1 ± 8.6U/L and 24 hrs after surgery it was 37.9 ± 3.4U/L showing a statistically significant increase in the ALT values between pre-operative period and 24 hrs postoperatively.

Hiremath S[54] who studied Effects of Carbon Dioxide Pneumoperitoneum on Liver Function Tests Following Laparoscopic Cholecystectomy showed that ALT was found to be significantly elevated from 33.61 ± 10.40 U/L to 56.10 ± 15.08 U/L (P=0.000) 24 hrs postoperatively.

Changes in the level of serum liver enzymes after laparoscopic surgery was the study done by Tan M, Xu FF, Peng JS, Li DM, Chen LH, Lv BJ[5] et al showed that mean value of ALT increased after laparoscopic cholecystectomy from pre-operative value of 23.3±11.6 U/L to 38.8±15.2 U/L on post op day 1($P<0.05$) and it was 25.1±14.3U/L on postoperative day 7. In open cholecystectomy the ALT values were 21.8±16.7U/L on preoperative day, 28.2±13.7U/L on post op day 1, 27.3±18.3U/L on post op day 2 and 24.2±11.1U/L on day 7. There was statistically significant increase in ALT levels postoperatively in patients underwent laparoscopic surgeries but no significant changes preoperative and postoperative ALT values in open cholecystectomy group.

Our result also correlated with study done by Marakis G, Pavlidis T, Ballas K, Rafailidis S, Psarras K, Symeonidis N et al[3]. Alterations In Liver Function Tests Following Laparoscopic Cholecystectomy in which preoperative ALT was 31.88 ± 74.77 U/L was increased up to 93.28% postoperatively 61.62 ± 54.87 U/L after 24 hours of surgery. This was statistically significant ($p=0.001$).

Rao PR, Kongara S, Snigdha Y, Kalyan KA[56] did a study of Alterations in Liver Function Tests Following Laparoscopic Surgery and showed that mean value of preoperative ALT was 23.10 ± 6.125U/L which increased on post day 1 to a mean value of 39.37± 12.524 U/L and on postop day 3 mean ALT value was 26.82± 7.205 U/L. Mean values of ALT increased significantly ($p < 0.001$) by post-operative day 1 and they came down to near pre-op values by post-op day 3.

Ibrahim AMS, Boppana VB , Palani M[58] did a study on Evaluation of the Effects of Laparoscopic Surgeries on Hepatic Enzymes showed that mean SGPT pre-operatively was 18.9± 4.55 U/L which increased to 31.83 ±9.8259 U/L on post-operative day 1 and again reduced to 21.6±5.484 U/L on post-operative day 3. They concluded that when correlated to pre-op values, SGPT levels increased significantly on post-op day 1 (p= 0.0001). This value reverted back to near pre-op level by day 7.

Serum ALP

In our study preoperative mean ALP was 98.42 ± 51.64 U/L which increased to 122.96 ± 46.67 U/L on 1st post-operative day and again reduced near to pre-operative value of 96.72 ± 36.05 U/L on 3rd post-operative day. There was significant increase in mean ALP values between Pre-operative and 1st Post-Operative day (P value <0.001).

Our results are Correlated with the study done by Rao PR, Kongara S, Snigdha Y, Kalyan KA[56] on Alterations in Liver Function Tests Following Laparoscopic Surgery and showed that mean value of ALP in preoperative period was 101.03± 21.279 U/L, its value was 135.517± 31.472 U/L on post-operative day 1 and on postoperative day 3 it was 107.583± 22.865 U/L , showing that mean values of ALT increased significantly ($p < 0.001$) by post-operative day 1 and it came down to near pre-op values by post-operative day 3.

A study was done by Hameed F, Ahmed B, Khan AA, Dab RH[2] on Impact of Pneumoperitoneum on Hepatic Functions after Laparoscopic Cholecystectomy showed that mean ALP pre-operatively was 204.46 ±43.67 U/L, on 2nd day postoperatively was 84.51 ±41.80 U/L and on 10th post-operative day it was 203.42± 43.04 U/L which was not significant.

A study done by Arora B[57] on Liver enzymes Alterations after Laparoscopic Cholecystectomy showed that ALP value pre op was 86.7± 1.2 U/L and 24 hrs after surgery it was 87.5 ± 1.4 U/L (P value=0.051). There was no significant difference in the preoperative and postoperative values.

Hiremath S[54] did a study on Effects of Carbon Dioxide Pneumoperitoneum on Liver Function Tests Following Laparoscopic Cholecystectomy in which Alkaline phosphatase did not show any elevation, pre-operative values were 72.62 ± 14.36 U/L, and 24 hrs postoperatively was 71.81 ± 12.60 U/L (P = 0.350). No significant difference between preoperative and postoperative values which was different from our study.

Singal R, Singal RP, Sandhu K, Singh B, Bhatia G, Khatri A[4] did a study on Evaluation and comparison of postoperative levels of serum bilirubin, serum transaminases and alkaline phosphatase in laparoscopic cholecystectomy versus open cholecystectomy showed that mean value of ALP pre-operatively was 64.4±13.9 U/L, after 24 hrs was 63.3±14 U/L and after 72 hrs it was 67.4±21.6 U/L in patients underwent laparoscopic surgery. The mean value of ALP, showed slight fall after 24 hrs of surgery and then slight rise after 72 hrs of surgery which was within the normal limit but there was no significant difference was noted in ALP, preoperatively and postoperatively in open cholecystectomy patients.

Duration of pneumoperitoneum

In our study a positive correlation was noted between the duration of pneumoperitoneum and increased in Serum bilirubin and Liver enzymes which is similar to other study conducted by Hameed F, Ahmed B, Khan AA, Dab RH[2] on Impact of Pneumoperitoneum on Hepatic Functions after Laparoscopic Cholecystectomy (LC).

Pneumoperitoneum pressure

Intra-abdominal pressure in all the patients of our study was maintained between 12-14mmHg which was higher than normal portal venous pressure of 7-10mmHg. Thus the elevation in Serum bilirubin and liver enzymes can be attributed to relative ischemia of liver, as major blood to liver is supplied by portal vein. Pneumoperitoneum at 15 mmHg causes decrease blood flow to all abdominal organs, by 40-54% to stomach, by 44% to colon, by 39% to liver, by 32% to jejunum and by 60% to peritoneum[50].

Study conducted by Nahvi IA, Nahvi IA, Habib M, Deewani SS[55] has evaluated the changes in the liver function tests and their clinical significance after uneventful laparoscopic cholecystectomy at different intra-abdominal pressures. They have observed that laparoscopy cholecystectomy done at low pressure of 8mmHg does not produce elevation in liver enzymes.

Study conducted by Giraudo G, Brachet Contul R, Caccetta M, Morino M concluded that laparoscopic surgery without creating pneumoperitoneum does not produce much alterations in hepatic function[59].

SUMMARY

SUMMARY

This study was intended to correlate the Duration of procedure, Insufflation pressure and Type of laparoscopic procedure with elevation of serum bilirubin and liver enzymes.

We have found that Serum bilirubin and the liver enzymes (serum AST, ALT and Alkaline phosphatase levels) were found to be significantly elevated on 1st post-operative day irrespective of type of laparoscopic procedure.

These changes were found to be transient as the levels of all the above parameters came to near pre-operative value by post-operative day 3.

Patients with prolonged duration of pneumoperitoneum showed more elevation in the liver enzymes.

Elevation of serum bilirubin does not correlate with prolonged duration of pneumoperitoneum.

On post-operative day 1 maximum raise was found in mean values of AST and ALT i.e 34.91% and 34.65% respectively followed by serum total bilirubin which increased by 21.87% and least increase was noted in the mean values of ALP that increased by 19.85 %

No clinical significance was found to be associated with such elevation.

CONCLUSION

CONCLUSION

From our study we hereby conclude that

1. All laparoscopic procedures cause a transient elevation of serum bilirubin and liver enzymes.
2. Elevation in the liver enzymes correlated directly with the duration of pneumoperitoneum.
3. Elevation in the serum bilirubin but doesn't correlates with the duration of pneumoperitoneum.
4. These elevation does not have clinical significance in patients with normal hepatic function.

Thus duration of laparoscopic procedure should be kept to minimum and undue prolongation should be avoided. Decision to convert the operation to open surgery from a laparoscopic surgery should be prompt.

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ANNEXURES

ANNEXURE-I

INFORMED CONSENT FORM

I, Mr/Mrs………………………………………….. have been explained in a language I can understand, that I will be included in a study which is EFFECTS OF LAPAROSCOPIC PROCEDURES ON HEPATIC ENZYMES.

I have been explained that my clinical finding, investigations, periodic details will be assessed and documented for the study purpose.

I have been made to understand that I will not incur any added expenditure other than investigations, materials and cost for the laparoscopic procedure.

I have also been made to understand that this study will require a periodic liver function test [pre operatively, post operatively on day 1 and day 3].

I have been explained that my participation in this study is entirely voluntary and I can withdraw from the study anytime and this will not affect my relation with my doctor or the treatment for my ailment.

I have understood that all my details found during the study are kept confidential and while publishing or sharing of the findings, my details will be masked.

I, in my sound mind give full consent to be added in the part of this study.

Patients signature/ thumb impression:

1st Witness signature : 2nd witness signature :

DATE: TIME: PLACE:

ANNEXURE-II

PATIENT INFORMATION SHEET

Study title: "EFFECT OF LAPAROSCOPIC PROCEDURES ON HEPATIC ENZYMES"

Study location: R L Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Tamaka, Kolar.

Details-

Patients undergoing laparoscopic procedures in department of General Surgery, RL Jalappa Hospital will be included in the study. Patients with coexisting liver disease / long term use of hepatotoxic drugs. Patients that develop complications such as bile duct injury, obstruction, infection, leakage and high grade fever during surgery and in the post-operative period will be excluded from the study.

Patients in this study will have to undergo routine preoperative investigations like CBC, Blood grouping and typing, BT, CT, RFT, Serum Electrolytes, HIV, HBSAg, Random blood sugar, ECG, Chest X-ray PA View.Usg abdomen and pelvis,ALT, AST, ALP, Sr total bilirubin, Serum direct bilirubin pre-operatively and post-operatively on Day 1 and 3.

Please read the following information and discuss with your family members. You can ask any question regarding the study. If you agree to participate in the study we will collect information (as per proforma) from you or a person responsible for you or both. Relevant history will be taken. This information collected will be used only for dissertation and publication.

All information collected from you will be kept confidential and will not be disclosed to any outsider. Your identity will not be revealed. This study has been reviewed by the Institutional Ethics Committee and you are free to contact the member of the Institutional Ethics Committee. There is no compulsion to agree to this study. The care you will get will not change if you don't wish to participate. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study.

For further information contact

Dr. Amit mittal (Post graduate)

Mobile No:- 7760848977

Department of General Surgery

SDUMC , Kolar

ANNEXURE-III

PROFORMA

Name: H.No:

Age/Sex:

Diagnosis:

Laparoscopic Procedure:

Time Began: Time Ended:

Duration of Pneumoperitoneum:

Intra-op. liver/bile duct injury:

Pre-existing liver disease/Other diseases:

Pre-op.:

AST – S. Alkaline Phosphatase –

ALT – Serum total Bilirubin –

Post-op. Day 1:

AST – S. Alkaline Phosphatase –

ALT – Serum total Bilirubin –

Post-op. Day 3:

AST – S.Alkaline Phosphatase –

ALT – Serum total Bilirubin –

ANNEXURE-IV

KEY TO MASTER CHART

- H.No:- Hospital ID of the patient
- DOP:- Duration of pneumo peritoneum
- CO_2 IP :- Carbon dioxide Insufflation pressure
- NOP:- Name of procedure
- STB1 :- Serum total bilirubin pre operatively
- STB2 :- Serum total bilirubin on post-operative Day 1
- STB3 :- Serum total bilirubin on post-operative Day 3
- AST1 :- Aspartate transaminase pre operatively
- AST2 :- Aspartate transaminase on post-operative Day 1
- AST3 :- Aspartate transaminase on post-operative Day 3
- ALT1 :- Alanine transaminase pre operatively
- ALT2 :- Alanine transaminase on post-operative Day 1
- ALT3 :- Alanine transaminase on post-operative Day 3
- ALP1:- Alkaline phosphatase pre operatively
- ALP2:- Alkaline phosphatase on post-operative Day 1
- ALP3:- Alkaline phosphatase on post-operative Day 3
- LC:- Laparoscopic Cholecystectomy
- LA:- Laparoscopic Appendectomy
- DL:- Diagnostic Laparoscopy

MASTER CHART

Sl.No	H.No	Age in yrs	Sex	DOP in min	CO2 IP mmhg	N O P	STB1 in mg/dl	STB2 in mg/dl	STB3 in mg/dl	AST1 in U/L	AST2 in U/L	AST3 in U/L	ALT1 in U/L	ALT2 in U/L	ALT3 in U/L	ALP1 in U/L	ALP2 in U/L	ALP3 in U/L
1	260182	75	F	45	14	LC	0.4	0.61	0.62	29	54	45	31	41	42	88	72	60
2	104380	28	F	40	12	LC	0.24	0.42	0.43	29	56	43	27	38	40	119	104	100
3	208908	34	M	30	14	LC	1.2	0.54	0.56	42	30	34	62	50	48	217	187	174
4	270575	42	F	40	12	LC	0.5	0.62	0.54	15	20	18	34	44	40	38	46	42
5	272704	23	F	140	12	LA	1	0.72	0.73	107	71	40	70	78	47	459	257	233
6	305257	40	M	35	14	LC	0.25	0.23	0.32	35	25	35	24	19	30	76	64	70
7	477953	20	F	35	14	LC	0.54	0.73	0.44	23	46	28	99	124	95	121	144	120
8	99685	23	F	40	12	DL	0.81	1.4	0.9	45	62	40	53	82	48	67	92	65
9	190418	65	M	35	14	LC	0.24	0.73	0.5	26	64	24	29	63	32	92	123	94
10	214130	50	F	30	14	LC	0.7	1.5	0.8	28	60	32	33	66	38	98	160	100
11	231471	32	F	50	14	LC	1.43	1.8	1.2	20	42	26	22	48	24	92	140	100
12	277317	45	F	60	14	LC	0.56	0.98	0.52	29	68	30	30	54	37	116	158	117
13	289625	55	F	40	14	LC	0.73	1.04	0.82	24	66	30	33	54	38	123	136	122
14	318776	56	M	50	12	LC	0.47	0.96	0.52	15	30	18	21	40	28	140	156	148
15	323915	34	F	45	14	DL	0.45	0.86	0.52	31	68	34	36	72	35	100	169	106
16	293408	70	F	50	12	LC	0.67	0.94	0.7	30	54	38	23	46	22	51	66	58
17	238989	65	M	45	14	LC	0.87	0.95	0.62	20	42	28	21	38	25	119	158	126
18	384622	60	F	40	12	LC	0.67	0.96	0.65	28	61	29	22	50	24	68	118	76
19	394011	76	M	140	14	LC	0.48	0.86	0.49	29	56	32	34	62	38	98	188	100
20	314152	36	M	50	14	LC	0.34	0.45	0.42	34	42	38	22	32	29	122	184	132
21	395862	42	F	60	14	LC	0.62	0.92	0.66	22	44	26	23	38	26	116	178	115
22	389301	50	F	45	14	DL	0.58	0.84	0.62	26	54	30	38	64	36	101	188	106
23	181104	40	M	20	14	DL	0.37	0.86	0.42	22	48	26	14	20	16	50	84	58
24	240834	57	F	30	14	LC	1.21	1.64	1.3	20	38	26	25	40	28	51	96	55
25	240852	95	M	30	14	LC	0.7	0.9	0.8	27	45	28	33	68	36	80	99	92
26	226940	14	M	20	12	DL	0.27	0.64	0.32	27	42	30	23	48	26	80	102	86
27	258241	65	M	35	14	LC	0.36	0.72	0.4	22	48	26	22	32	23	56	94	66
28	286939	47	F	40	14	LC	0.79	1.04	0.8	80	106	76	55	64	62	115	149	112
29	295168	32	F	45	14	LC	0.66	0.94	0.68	31	38	35	29	54	32	141	169	140
30	298245	26	M	30	14	DL	0.26	0.36	0.32	16	30	17	17	24	22	69	82	74
31	303535	45	M	45	14	LC	1.16	1.18	1.14	16	20	17	22	41	20	89	102	90
32	334897	40	F	30	14	LA	0.2	0.34	0.28	18	26	20	21	28	26	116	118	104

33	341081	42	F	35	14	LA	0.55	0.64	0.62	24	32	28	35	38	35	107	118	112
34	380864	55	F	40	14	LC	0.8	1.4	1	27	32	28	22	36	32	96	106	100
35	397543	19	M	20	12	LA	0.57	0.66	0.61	21	28	32	32	38	32	143	138	142
36	360950	45	M	35	14	LC	0.75	0.86	0.76	69	74	72	87	92	88	84	104	94
37	420519	23	F	45	12	LC	0.56	0.84	0.66	22	34	32	17	24	22	95	112	104
38	428654	70	M	45	12	LC	0.77	1	0.82	18	22	17	21	30	26	51	65	54
39	440339	24	F	30	14	LC	1.7	2	1.6	57	66	62	27	34	32	72	88	82
40	193806	24	F	40	14	LC	0.6	0.8	0.4	17	26	24	18	24	22	72	84	78
41	198052	24	F	35	12	LA	0.57	0.66	0.64	22	34	32	14	22	16	81	88	84
42	194319	28	F	45	14	LC	0.73	0.88	0.77	85	92	86	55	66	62	115	110	104
43	194004	60	M	45	14	LC	0.33	0.44	0.38	28	36	32	18	24	22	68	76	72
44	219338	28	F	50	14	LC	0.46	0.74	0.64	24	34	36	28	32	24	28	36	31
45	217267	47	M	30	14	DL	0.27	0.32	0.28	133	128	122	175	145	146	200	182	178
46	222904	20	M	50	14	LC	0.4	0.61	0.62	29	54	45	31	41	42	88	72	60
47	218964	42	F	60	14	LC	0.24	0.27	0.22	29	30	28	27	39	28	119	108	102
48	69675	45	F	55	12	LC	1.2	0.54	0.51	42	30	28	62	50	48	217	187	180
49	230348	50	F	50	14	LA	0.5	0.72	0.48	15	42	18	34	62	30	38	42	38
50	224637	65	F	55	14	LC	0.3	0.8	0.5	17	26	18	32	61	31	69	108	64
51	236865	54	M	180	14	DL	0.7	0.92	0.73	107	171	104	70	98	45	159	257	150
52	256742	26	M	55	14	LC	0.25	0.83	0.32	35	45	35	24	69	30	76	104	70
53	258295	45	F	45	14	DL	0.74	1.03	0.44	23	86	28	99	154	95	121	164	120
54	259319	70	F	35	12	DL	0.81	1.4	0.9	45	62	40	53	102	48	67	72	65
55	261334	29	F	45	14	LC	0.24	0.73	0.3	26	64	24	29	83	32	93	163	88
56	288336	56	F	65	12	LA	0.7	1.5	0.8	28	60	32	33	46	28	98	160	100
57	272000	64	F	45	12	LC	1.43	1.8	1.2	20	42	26	22	48	24	92	140	100
58	293204	50	M	70	14	LC	0.56	0.96	0.52	29	60	28	30	64	35	116	186	108
59	298922	60	M	30	14	LA	0.6	1.5	0.8	28	62	30	34	46	28	98	160	100
60	296463	58	F	50	14	LC	0.43	0.8	0.3	20	42	26	22	48	24	92	140	104
61	179799	18	M	45	12	LA	0.56	0.98	0.52	29	88	30	30	64	37	118	168	117
62	309716	19	F	50	12	LA	0.73	0.94	0.82	24	46	26	33	54	38	122	166	132
63	315437	40	M	70	14	LC	0.47	0.56	0.52	16	20	18	21	30	28	140	156	148
64	315354	43	F	55	14	LC	0.45	0.56	0.52	31	38	34	36	42	35	104	108	106
65	321397	37	F	65	14	LC	0.7	0.9	0.8	27	25	28	33	38	36	84	89	92
66	313794	15	F	55	14	LA	0.27	0.34	0.32	27	32	30	23	28	26	80	92	86
67	324337	23	M	70	12	LA	0.36	0.42	0.4	22	28	26	22	32	28	56	65	66
68	325884	60	M	80	14	LA	0.79	0.84	0.8	80	86	76	55	64	62	115	119	118
69	207080	53	M	75	14	LC	0.67	0.74	0.7	32	46	38	23	36	32	51	66	58

70	310480	45	M	45	12	LC	0.87	0.95	0.92	20	32	28	21	28	25	119	128	126
71	333478	47	F	80	14	LC	0.47	0.56	0.52	24	36	32	29	38	35	56	66	62
72	338992	26	F	30	14	LA	0.48	0.56	0.52	29	46	32	34	62	38	98	108	106
73	344252	60	F	50	12	LC	0.34	0.45	0.42	34	60	38	22	42	29	122	154	130
74	345151	78	F	45	14	LC	0.62	0.72	0.66	22	44	32	23	48	26	116	138	115
75	349024	27	F	50	14	DL	0.58	0.64	0.62	28	44	36	38	54	36	102	128	106
76	351759	35	F	20	14	DL	0.37	0.46	0.42	22	38	24	14	22	16	50	64	52
77	179944	31	M	55	14	LA	1.21	1.34	1.3	20	42	26	27	50	28	52	96	55
78	301025	65	F	65	14	LC	0.4	0.61	0.42	29	54	29	31	61	32	88	102	86
79	374474	25	F	55	14	LA	0.24	0.42	0.24	29	76	30	27	48	28	119	184	100
80	382562	13	F	70	12	LA	1.2	0.54	0.56	42	60	44	62	100	68	117	187	114
81	229592	45	F	80	14	LC	0.5	0.82	0.54	15	30	18	34	64	40	38	46	42
82	366554	45	M	50	14	LC	1	0.72	0.93	107	171	110	70	98	47	159	257	163
83	404956	45	F	20	14	DL	0.25	0.63	0.22	35	70	35	24	49	28	76	94	70
84	407511	45	F	55	14	LC	0.57	0.66	0.61	22	48	28	32	68	32	143	168	142
85	417934	50	F	65	14	LC	0.75	0.86	0.76	69	94	72	87	102	88	84	104	84
86	420970	45	F	55	14	DL	0.56	0.84	0.66	22	34	24	17	34	20	95	112	94
87	430321	18	F	70	12	LA	0.77	1	0.82	18	30	17	21	40	26	51	95	54
88	431350	55	F	80	14	LC	1.6	2	1.6	57	66	62	27	64	30	72	98	82
89	431876	20	M	75	12	LA	0.6	0.8	0.7	18	26	20	18	34	22	72	104	78
90	424743	36	M	45	12	LC	0.58	0.65	0.64	22	44	22	14	30	16	81	128	84
91	454457	20	F	140	14	LC	0.73	0.88	0.77	85	104	86	55	96	58	115	160	104
92	454378	30	F	30	14	LC	0.33	0.44	0.38	28	46	30	18	34	20	68	96	72
93	454290	60	F	50	14	LC	0.46	0.74	0.48	24	44	26	28	32	24	28	46	30
94	452665	11	F	45	14	LA	0.27	0.32	0.28	133	156	130	175	200	176	200	222	198
95	404940	60	F	50	14	LC	0.67	0.74	0.7	30	64	38	23	46	24	51	86	51
96	469908	16	F	30	14	DL	0.87	0.95	0.87	20	42	28	22	28	25	119	128	126
97	444916	55	M	45	14	LC	0.71	0.92	0.73	27	45	28	33	48	36	80	109	92
98	462689	39	F	55	14	LC	0.27	0.34	0.32	27	52	30	23	48	26	80	102	86
99	464635	49	F	65	14	DL	0.36	0.42	0.4	22	48	26	22	52	24	56	94	66
100	470884	21	F	55	12	LA	0.79	0.84	0.8	80	106	78	55	94	55	115	149	112
101	470467	20	F	70	14	LC	0.36	0.42	0.4	22	48	26	22	42	24	56	95	56
102	477415	26	F	180	14	DL	0.79	0.84	0.8	80	106	76	55	94	55	115	149	118
103	480163	30	F	40	14	LA	0.67	0.74	0.7	32	56	38	23	46	24	51	86	58