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Study Of Changes In Coagulation Profile Of Patients Undergoing Laparoscopic Cholecystectomy Using Carbon Di Oxide Pneumoperitoneum

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A B S T R A C T

INTRODUCTION: Laparoscopic cholecystectomy has replaced open cholecystectomy and is now the gold standard procedure for gallbladder disease. Pneumoperitoneum plays a crucial role in the procedure and carbon dioxide is commonly chosen gas. 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 METHOD: This prospective and observational study includes 50 patients undergoing Laparoscopic cholecystectomy under General Anaesthesia. Patient's 3cc blood was drawn just before surgery and 6 hour after surgery to analyse PT and D-Dimer and then was compared.

RESULTS: In 34 patients Prothrombin Time decreased 6hour after surgery, while 1 patient experienced an increase and rest 15 patients maintained similar Prothrombin Time values. The mean difference between the two groups was 0.130, with a 95% confidence interval ranging from 0.031 to 0.229, the p-value was 0.0109. D-dimer values revealed an increase in all patients postoperatively. The mean D-dimer levels before and after surgery were 0.1834 mcg/ml and 0.3364 mcg/ml, respectively, with standard deviations of 0.0486 and 0.0395, respectively. During the 2weeks postoperative follow-up, none of the patients showed clinical signs of DVT.

CONCLUSION: The study reveals a notable increase in D-dimer levels and a significant decrease in prothrombin time, indicating activation of both the coagulation and fibrinolytic systems following laparoscopic cholecystectomy. Activation of the coagulation system can predispose to thromboembolism, particularly deep vein thrombosis. However, none of the 50 patients in our study experienced such complications. This suggests effective compensatory mechanisms in response to mild changes in the coagulation profile. Larger and more comprehensive studies are needed to further elucidate these changes in the coagulation system and to quantitatively assess the risk associated with laparoscopic cholecystectomy using carbon dioxide pneumoperitoneum.

Keywords: Laparoscopic cholecystectomy, D-dimer, Thromboembolism, Deep vein thrombosis (DVT).

INTRODUCTION

Laparoscopic surgery is a minimally invasive surgery that has revolutionized the field of general surgery, in recent years, laparoscopic techniques have become increasingly prevalent, providing numerous advantages for both patients and healthcare providers. The widespread adoption of these techniques is largely due to their superior outcomes, including reduced hospital stays, faster recovery times, and lower incidence of wound-related complications compared to conventional open surgical methods. Its ability to combine technical precision with patient-centred benefits makes it a cornerstone of contemporary medicine, promising continued

advancements and improvements in surgical techniques and patient experiences. With advancements in technology and surgical instruments, laparoscopy has become integral part across various surgical disciplines.
In laparoscopy, establishing a functional working space is essential. This space is typically achieved by creating positive pressure pneumoperitoneum, using carbon dioxide. Pneumoperitoneum plays a crucial role in enabling the procedure's success and ensuring patient safety. In 1924, Richard Zolliker from Switzerland proposed the use of carbon dioxide for creating pneumoperitoneum. Carbon dioxide was chosen because it is a physiological end product, non-combustible, economical, freely available and allows for the use of electrocoagulation.
Laparoscopic cholecystectomy is the procedure of choice for majority of gallbladder disease if feasible. It has replaced open cholecystectomy and is now the gold standard procedure. It is one of the most commonly performed general surgical procedure worldwide. The first laparoscopic cholecystectomy was performed by Prof. Erich Muhe of Boeblingen, Germany in 1986. Since then there has been continuous development in methodology. In 2022, approximately 3.3 million laparoscopic cholecystectomies were performed in India [(1)], hence laparoscopic cholecystectomy holds considerable importance within the field of general surgery.
The effects of carbon dioxide pneumoperitoneum on various organ systems require detailed investigation. This study aims to elucidate its impact specifically on the coagulation profile thus allowing surgeons to make informed decisions, adjust surgical techniques, and provide appropriate perioperative management to optimize patient outcomes.

AIMS AND OBJECTIVES

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

MATERIALS AND METHOD

The present study was a hospital-based observational study conducted in the Department of General Surgery at Gauhati Medical College and Hospital (GMCH), Guwahati, over a period of one year from 1st September 2022 to 31st August 2023, with a sample size of 50 cases. The study population included patients scheduled for elective laparoscopic cholecystectomy who met the predefined inclusion and exclusion criteria and provided informed consent. Inclusion criteria comprised patients of both sexes aged between 18 and 60 years, diagnosed with gallstones, chronic cholecystitis, or in the recovery phase of acute cholecystitis, with surgery duration ranging from 90 to 180 minutes. Only those who underwent laparoscopic cholecystectomy and consented to participate were included. Exclusion criteria included patients younger than 18 or older than 60 years, surgery exceeding three hours, conversion to open surgery, and those with associated hypertension, on anticoagulant therapy, known malignancies, bleeding or clotting disorders, deep venous thrombosis, or pregnancy. All 50 patients undergone Laparoscopic cholecystectomy under General Anaesthesia. Patient's 3cc blood was drawn just before surgery and 6 hour after surgery to analyse PT and D-Dimer and then was compared.

RESULTS AND ANALYSIS

Among the cohort of 50 patients who underwent surgery, 38 were female and 12 were male. The most prevalent age group among both genders was 41-50 years, with the 51-60 years age group following closely behind.

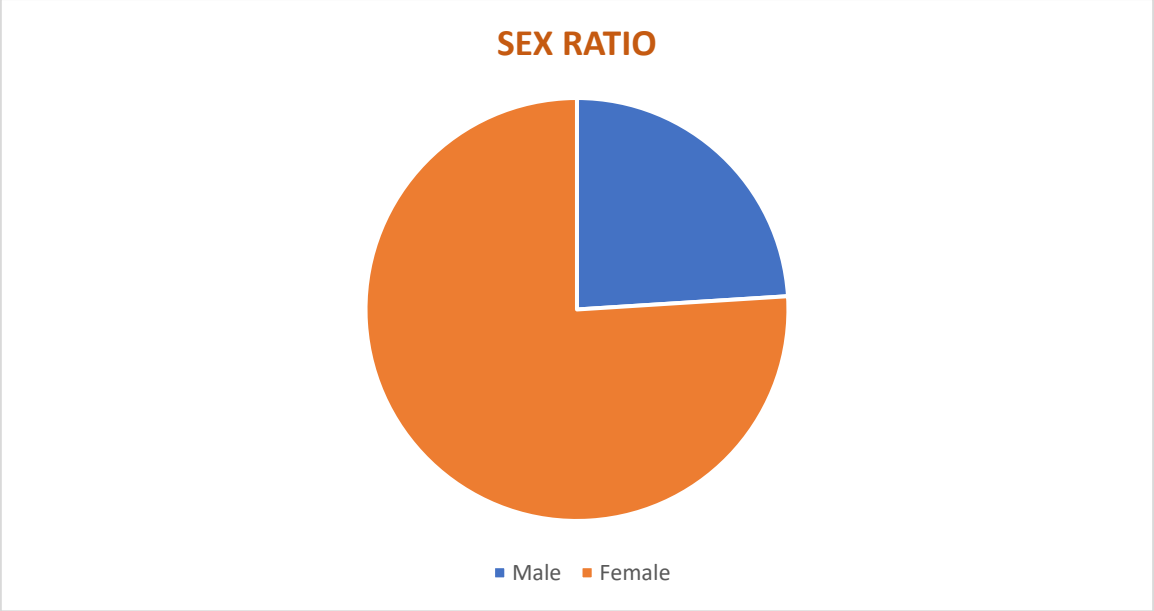

Figure 1: Sex Ratio of our study population.

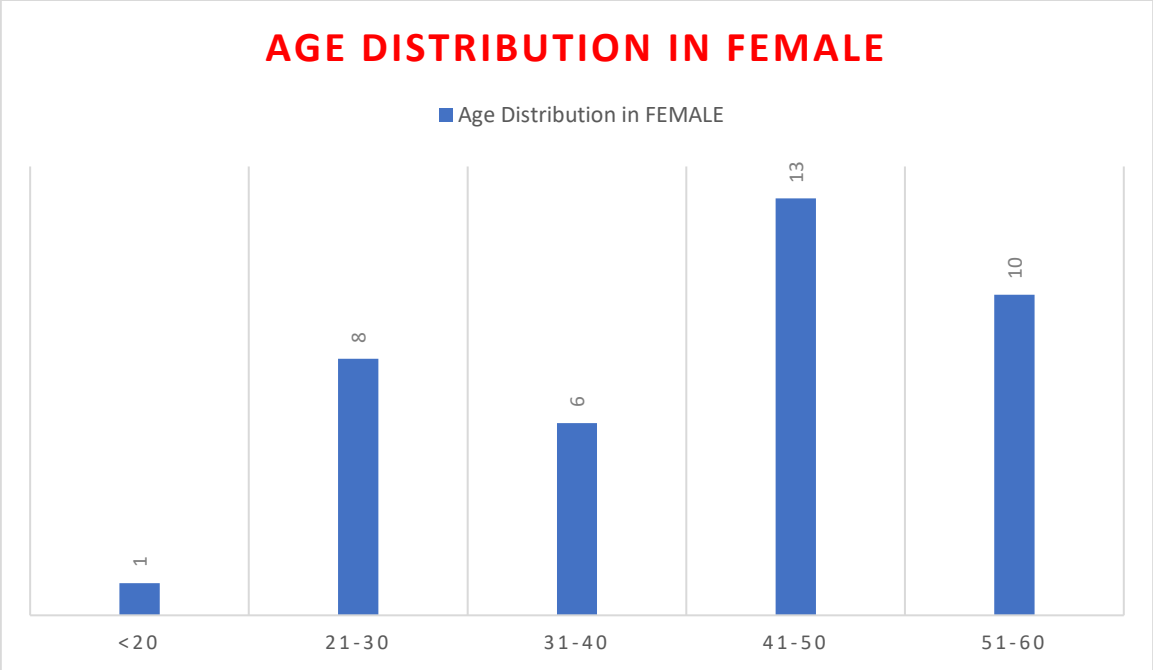

Figure 2 : Age distribution in female of our study population.

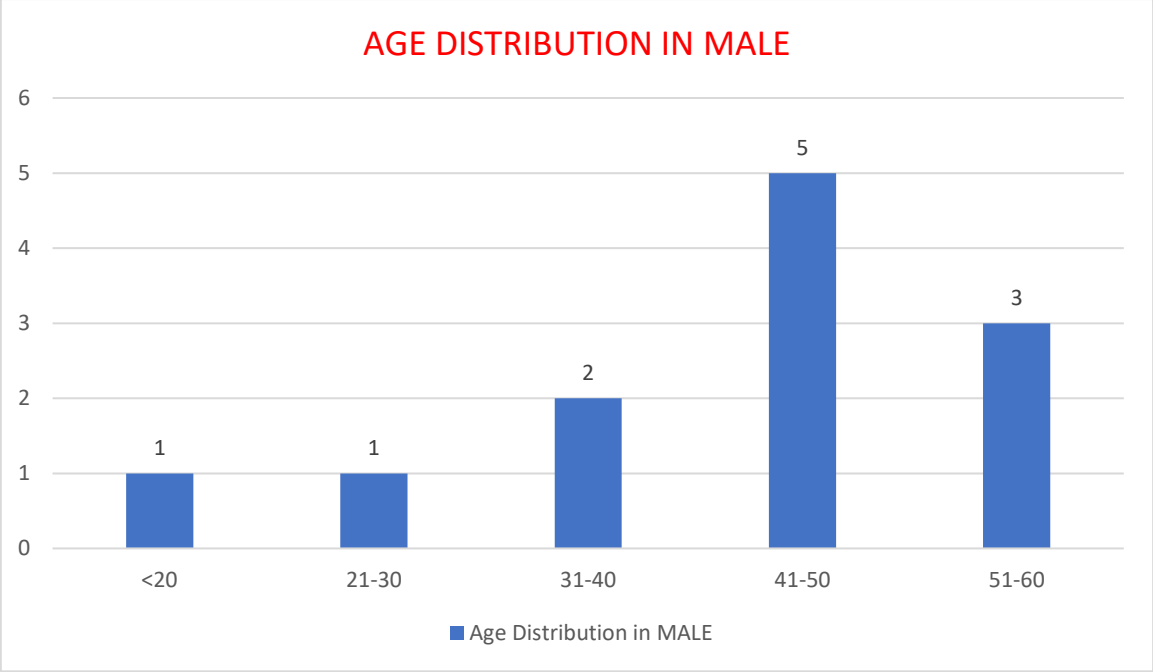

Figure 3 : Age distribution in male of our study population.

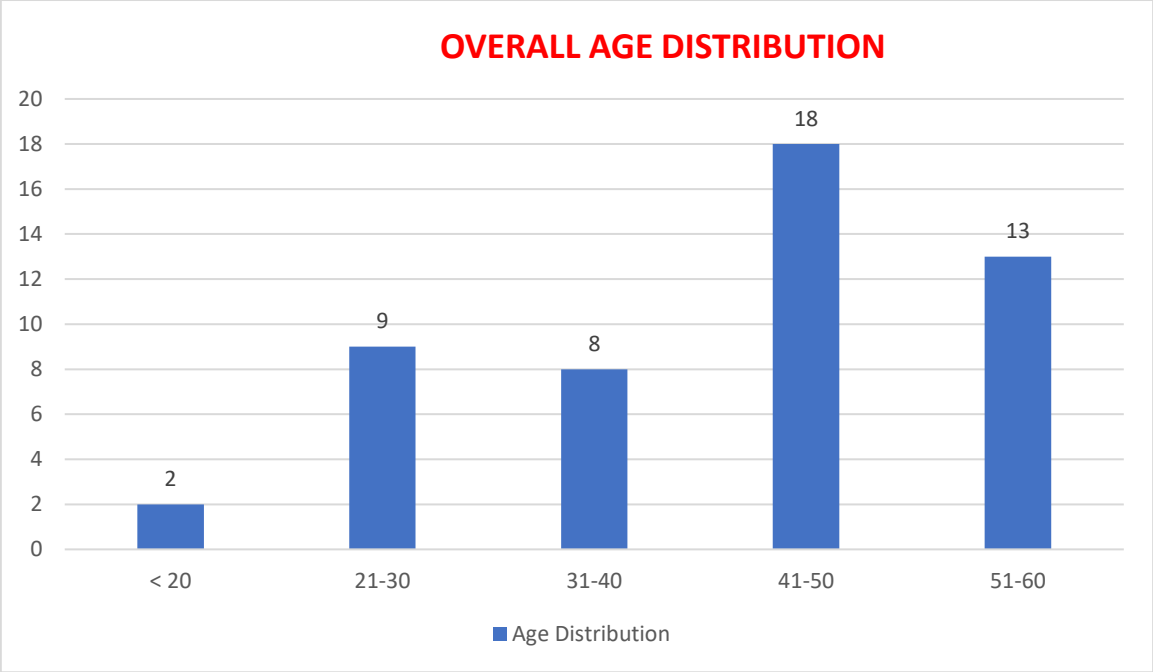

Figure 4 : Overall age distribution of our study population.

Surgical durations ranged from 43 minutes to 2 hours 30 minutes, with most surgeries lasting between 1 to 2 hours. Prolonged surgical times were typically due to factors such as dense adhesions in Calot's triangle, intrahepatic gallbladder location, and large gallbladder stones.

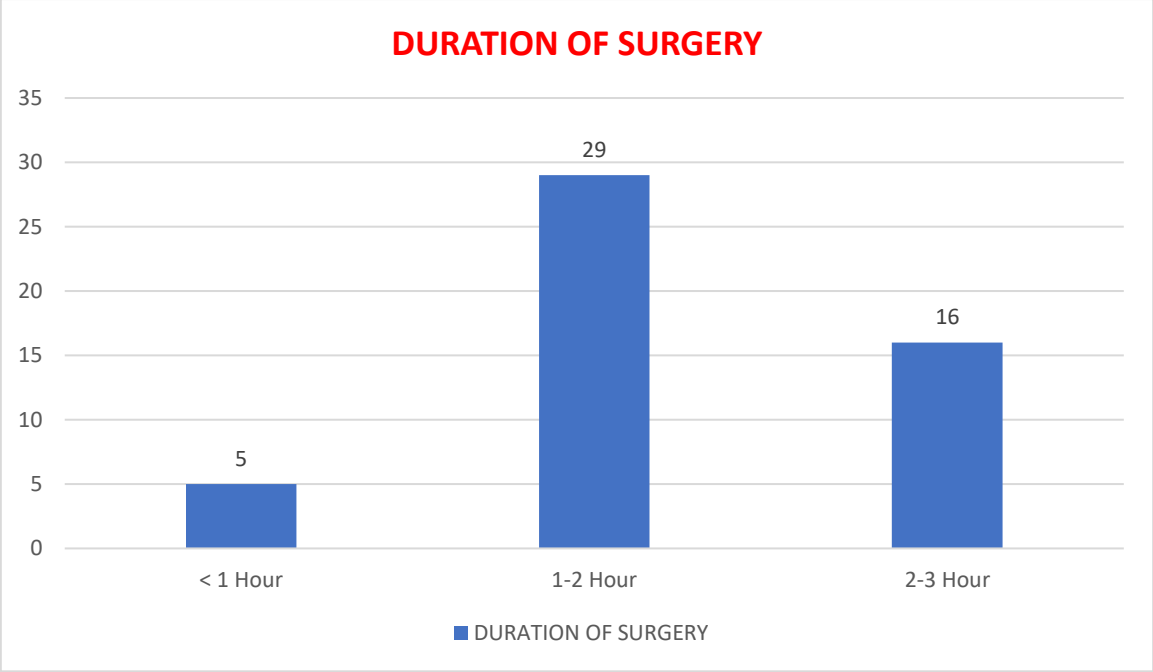

Figure 5: Duration of Surgery among our study population.

There were no significant perioperative complications observed. Two patients developed port-site infections, which were successfully managed with intravenous antibiotics and regular antiseptic dressings. Most patients were discharged within 3 days post-surgery. 1 patient developed post cholecystectomy syndrome and was managed conservatively.

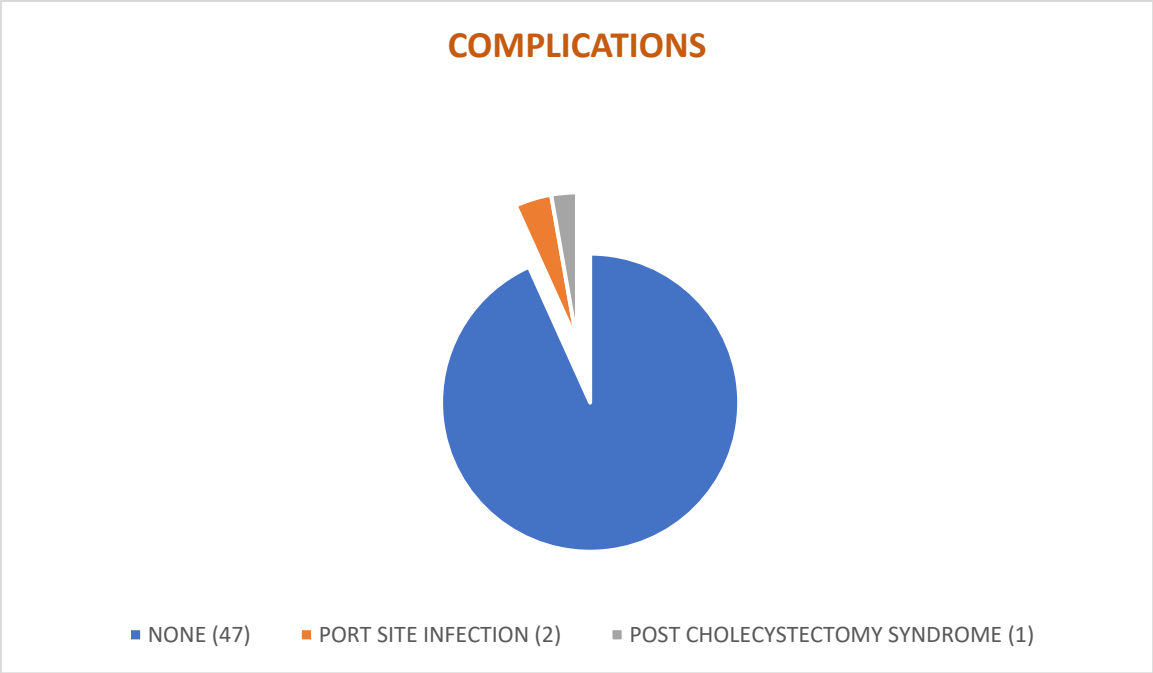

Figure 6: Complications among our study population.

The preoperative prothrombin time for the cohort of 50 patients ranged from 11.6 seconds to 14.1 seconds, with a mean value of 13.112 seconds. The standard deviation and standard error of the mean were calculated as 0.6419 and 0.0907, respectively.

Six hours following surgery, the prothrombin time for the same group of 50 patients ranged from 11 seconds to 14.1 seconds, with a mean of 12.814 seconds. The standard deviation and standard error of the mean were determined to be 0.6636 and 0.0938, respectively. The p-value was 0.0109.

Notably, not all patients exhibited a change in prothrombin time from preoperative to postoperative stages. Specifically, 15 patients maintained consistent prothrombin time values, while 34 patients showed a decrease in postoperative prothrombin time. Only one patient experienced an increase in postoperative prothrombin time.

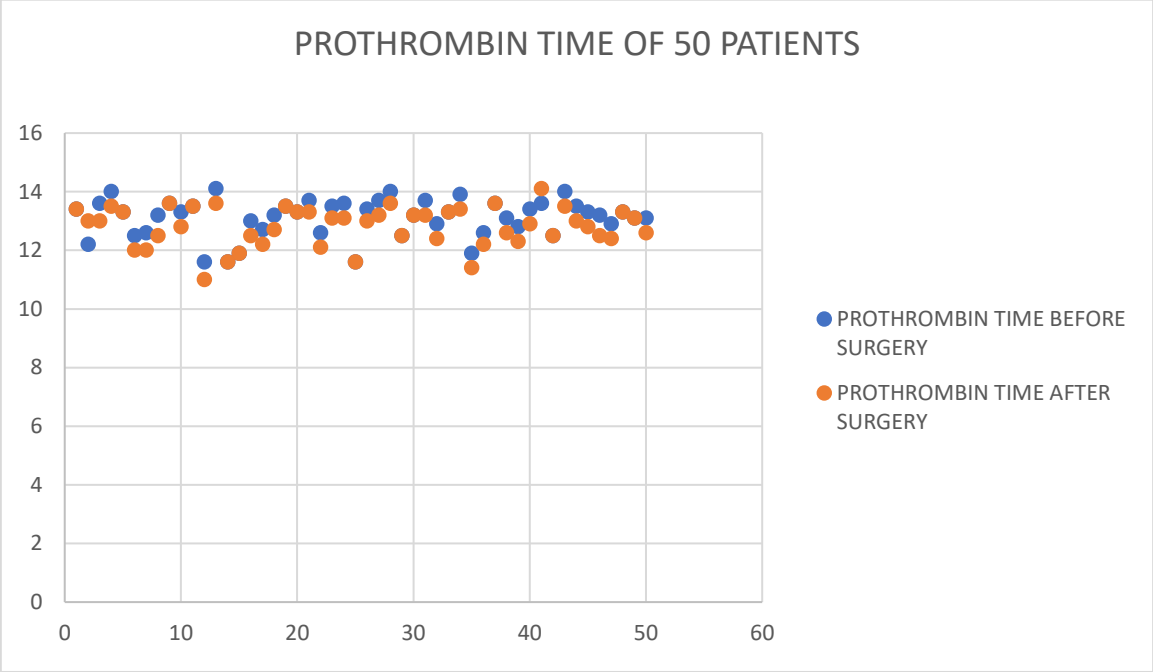

Figure 7: Prothrombin time Of 50 Patients in our study.

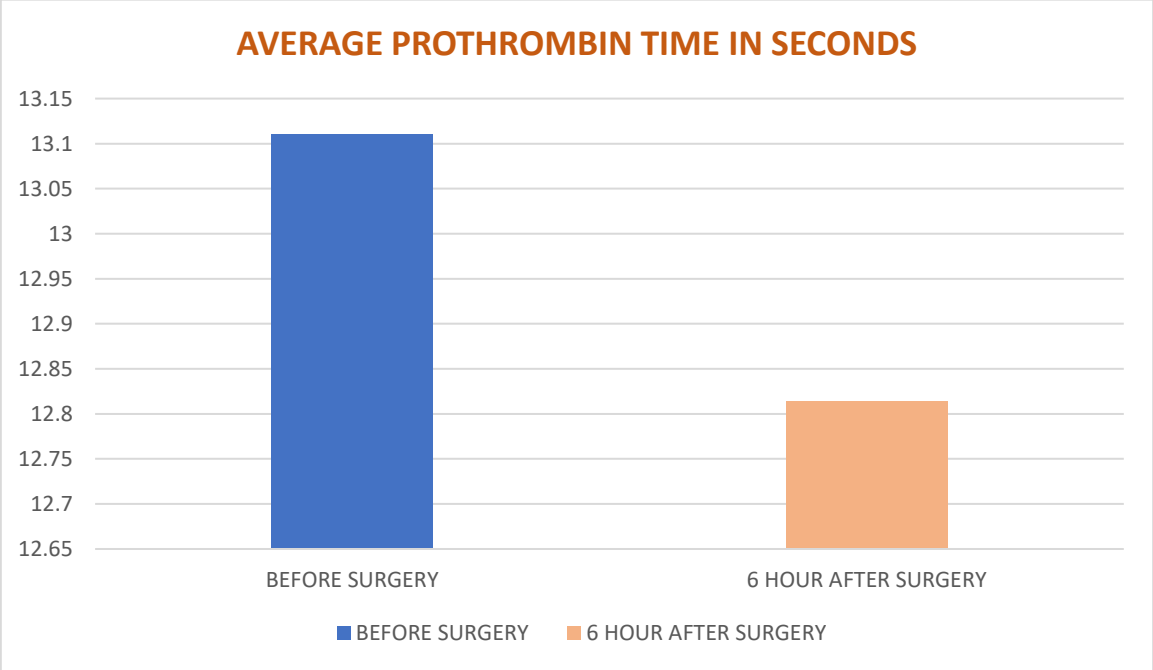

Figure 8: Average prothrombin time in seconds in our study.

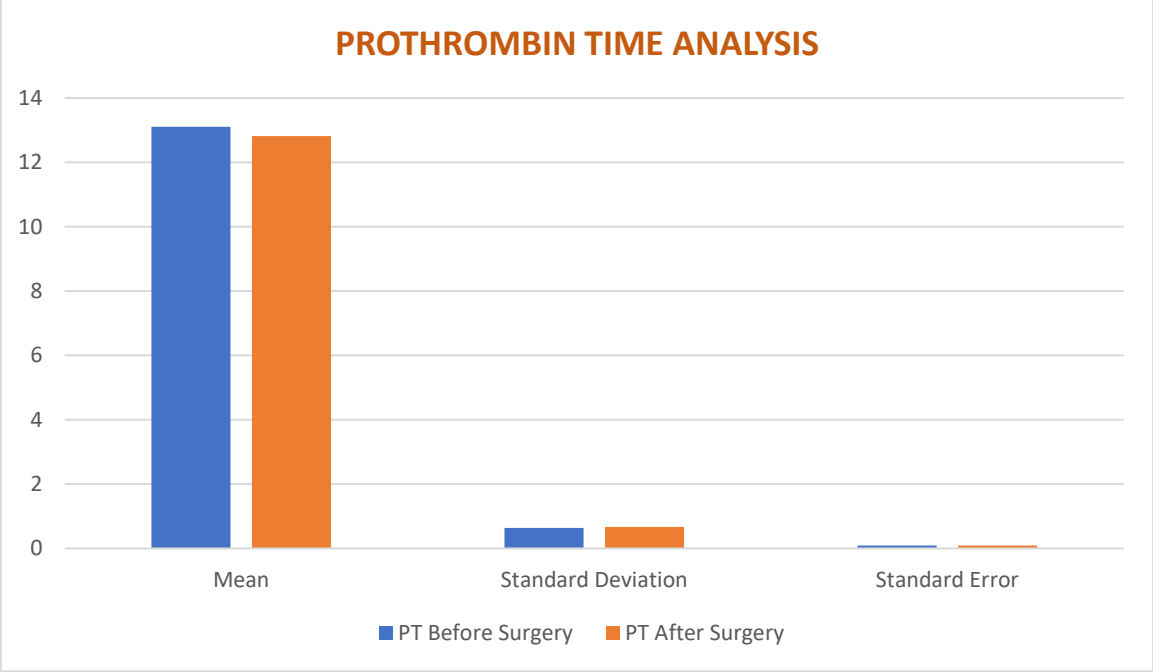

Figure 9: Prothrombin time analysis before and after surgery in our study.

The initial D-dimer levels of the cohort comprising 50 patients ranged from 0.07 to 0.27 mcg/ml, with an average value of 0.1834 mcg/ml. The standard deviation calculated was 0.0486, and the standard error of the mean was determined to be 0.0068.

Following six hours after surgery, all the patients showed a postoperative increase on D-Dimer value. The D-dimer values of 50 patients 6 hour after surgery ranged from 0.25 to 0.43 mcg/ml, showing a mean value of 0.3364 mcg/ml. The standard deviation for this measurement was 0.0395, with a standard error of the mean calculated as 0.0055. The analysis yielded a p-value of 0.001.

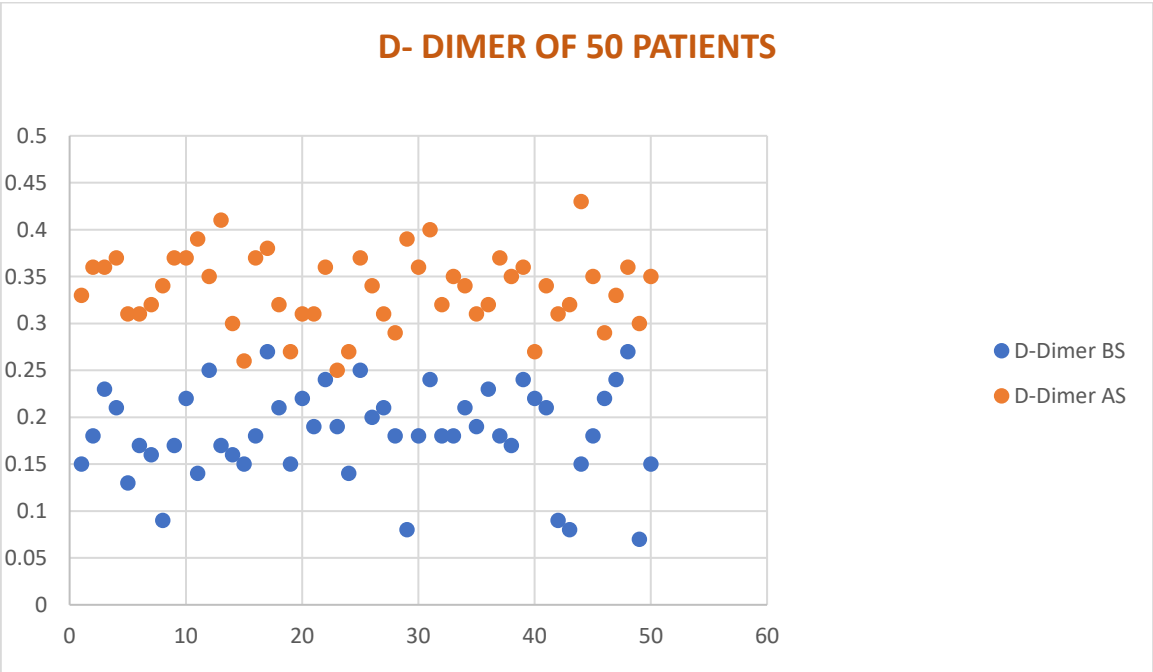

Figure 10 : D-dimer of 50 patients in our study.

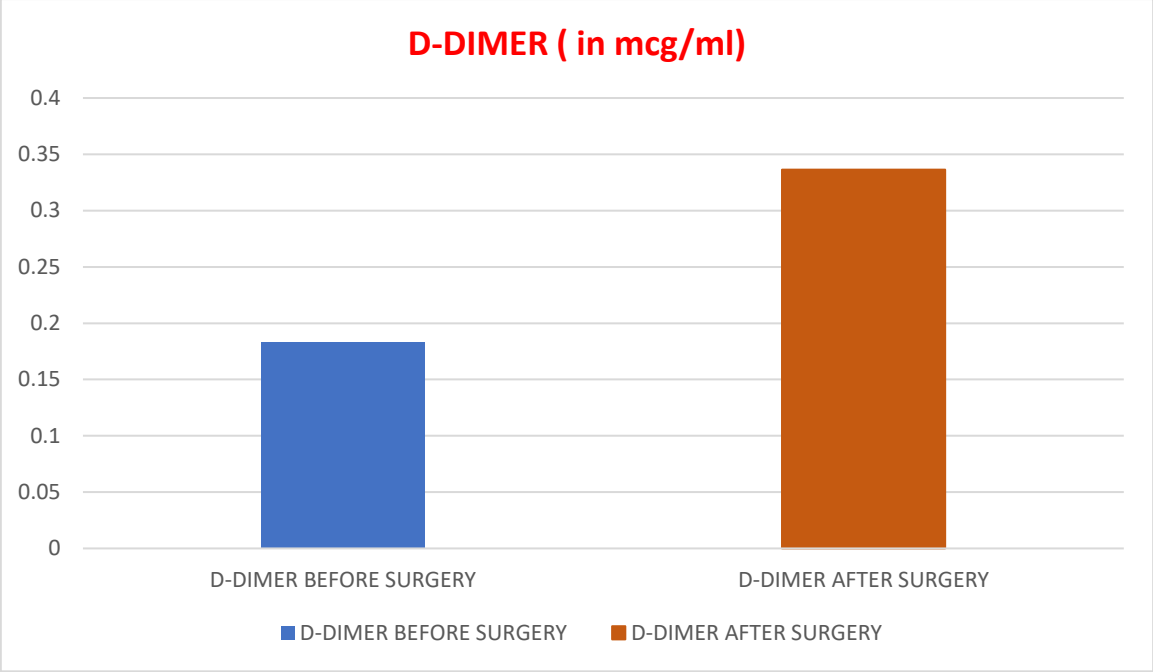

Figure 11: D-dimer (in mcg/ml) before and after surgery in our study

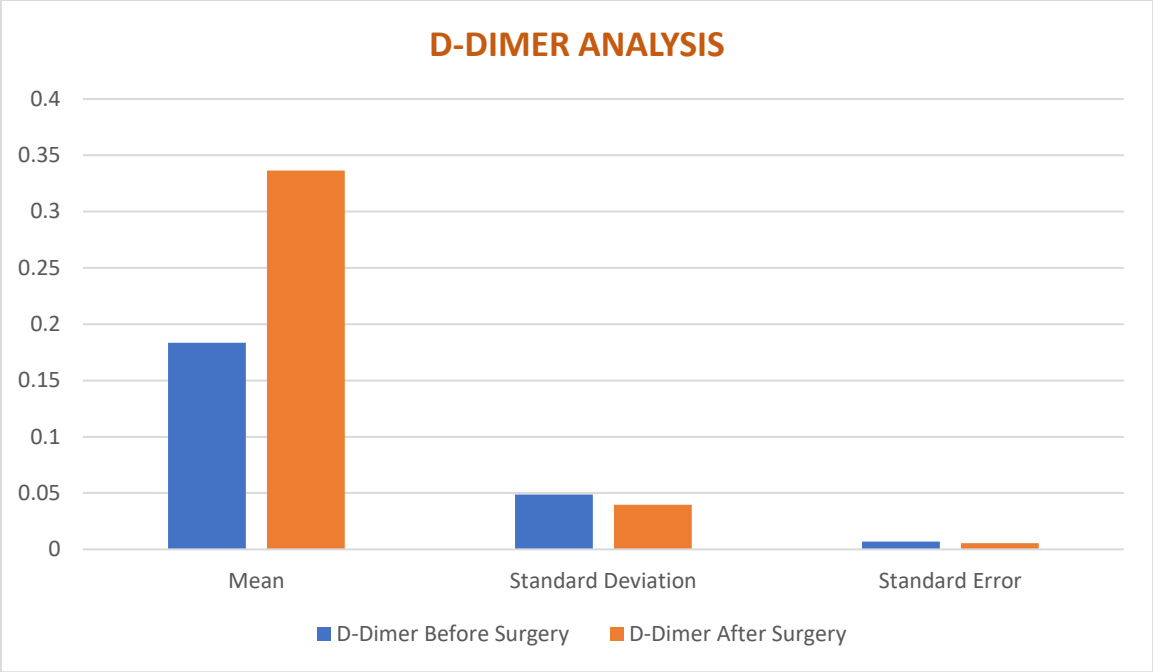

Figure 12: D-dimer analysis before and after surgery in our study

Table 1 : Prothrombin time analysis of 50 patients in our study.

PROTHROMBIN TIME of 50 PATIENTS		
	BEFORE SURGERY	6 HOURS AFTER SURGERY
MEAN	13.112	12.814
STANDARD DEVIATION	0.6419	0.6636
STANDARD ERROR	0.0907	0.098

Table 2 : D-dimer analysis before and after surgery in our study.

D-DIMER of 50 PATIENTS		
	BEFORE SURGERY	6 HOURS AFTER SURGERY
MEAN	0.1834	0.3364
STANDARD DEVIATION	0.0486	0.0395
STANDARD ERROR	0.0068	0.0055

DISCUSSION

Laparoscopic cholecystectomy is a commonly performed surgical procedure on a global scale. In 2022, an estimated 3.3 million laparoscopic cholecystectomies were performed in India.

Although generally safe, laparoscopic cholecystectomy carries risks such as bleeding, infection, bile duct injury, deep vein thrombosis, and pulmonary embolism. This study specifically investigates the impact of carbon dioxide pneumoperitoneum on patient's coagulation profiles.

The present study involved 50 patients undergoing laparoscopic cholecystectomy at Gauhati Medical College and Hospital over a 12-month period from 1st September, 2022 to 31st August, 2023. The analysis centred on examining the pre- and post-operative measurements of prothrombin time and D-dimer in these patients, and interference from them is derived and compared with other studies.

In our study there was a higher prevalence of female patients undergoing cholecystectomy, comprising 76% of the cases, while male patients accounted for 24%. This aligns with global trends and is consistent with the demographic distribution seen in India. Similar findings have been reported in studies by Kim et al [(2)], Jagannath P et al [(3)], and Arpita Bansal et al [(4)].

The majority of patients undergoing cholecystectomy fell within the 41-50 years age group for both sexes, followed by the 51-60 years age group. This demographic pattern is in accordance with findings from the study by Patel et al [(5)] .

In our study duration of surgery varied widely, ranging from 42 minutes to 2 hours 30 minutes, highlighting the unpredictable nature of cholecystectomy surgery. Analysis of patient' s prothrombin time revealed that results were not uniform in all the patients. While a significant number of patients exhibited stable prothrombin time values before and after surgery, the majority showed a decrease in postoperative prothrombin time. Only one patient demonstrated an increase in postoperative prothrombin time.

In our study the average preoperative prothrombin time was 13.112 seconds, whereas postoperatively, it averaged 12.814 seconds. The corresponding standard deviations were 0.6419 and 0.663, respectively. The small standard deviations indicate the precision of the mean values and suggest that similar results would be expected in a larger sample size. Upon charting these values, a statistically significant decrease in mean prothrombin time values was observed postoperatively, indicating a relative hypercoagulable state of blood during this period.

This finding is consistent with studies by Catheline et al [(6)], Schaepkens et al [(7)], D J Milic et al [(8)] , R Lord et al [(9)] and F. Lindberg et al [(10)] which have also reported postoperative hypercoagulability following laparoscopic cholecystectomy.

Table 3 : Comparisons of incidence of DVT in different studies.

Studies	Number of Patients	Patient developed DVT	Percentage
Our Study	50	0	0

Catheline et al [6]	2384	8	0.33 %
Schaepkens et al [7]	238	10	4.2 %
D J Milic et al [8]	58	4	6.89 %
R Lord et al [9]	41	1	2.4 %
F. Lindberg et al [10]	153,832		0.03%

In our study analysis of D-dimer values revealed an increase in D-Dimer value in all the patients postoperatively. The mean D-dimer levels before and after surgery were 0.1834 mcg/ml and 0.3364 mcg/ml, respectively, with standard deviations of 0.0486 and 0.0395, respectively. The small standard deviations indicate the precision of the mean values and suggest that similar findings would be expected in a larger sample size.

After charting, these changes were found to be statistically significant, indicating a high risk of thrombosis and activation of the fibrinolytic system postoperatively. Increased postoperative D-dimer levels have also been reported in other studies like, Okuda et al [11] , Schietroma et al [12] , Eva Intagliata et al [13] , and Lippi G et al [14] .

The findings of our study contradicts those of other studies such as Larsen JF et al [15] , Dexter et al [16] , and Jens Fromholt [17] , which have reported no change in coagulation profiles postoperatively.

In our study none of the patients received thromboprophylaxis, and none showed evidence of deep vein thrombosis. However, laboratory parameters indicate a subclinical hypercoagulable state.

It's important to note that D-dimer is not specific to deep vein thrombosis or pulmonary embolism; increased D-dimer levels postoperatively may reflect surgical trauma. The extent to which surgery contributes to the change in D-dimer levels has not been fully studied.

Increased intra-abdominal pressure can influence the coagulation profile by reducing venous return, leading to venous pooling and stasis in the lower limbs and pelvis. Venous stasis is a critical component of Virchow's triad, which can initiate the coagulation cascade.

During laparoscopic surgeries, intra-abdominal pressure is typically maintained between 12-14 mmHg. While these procedures last only a few hours, patients with chronic liver disease and ascites may experience much higher intra-abdominal pressures, up to 80 mmHg, over days to weeks. Despite this, these patients do not commonly exhibit thromboembolic risks. This paradox could be attributed to reduced production of coagulation factors in chronic liver disease patients, combined with gradual adaptation of homeostatic mechanisms to elevated intra-abdominal pressures.

Therefore, the observed changes in coagulation profile cannot be solely attributed to increased intra-abdominal pressure.

None of the patients in our study received prophylactic treatment because none exhibited additional risk factors necessitating such intervention.

Regarding patient positioning, all individuals were placed in reverse Trendelenburg position with a 30-degree upward tilt to the right. However, not all patients demonstrated consistent changes in their coagulation profiles. To comprehensively evaluate the impact of positioning, future studies should compare laparoscopic procedures utilizing Trendelenburg positioning versus reverse Trendelenburg positioning.

Our study reveals evidence of both coagulation activation and fibrinolysis following laparoscopic cholecystectomy, as evidenced by the postoperative decrease in Prothrombin Time and increase in D-dimer levels. While a mild postoperative hypercoagulable state was observed, the activation of fibrinolysis could potentially counterbalance the increased coagulation activity. The elevated D-dimer levels observed in our study suggest that this mechanism may contribute to the low incidence of thrombosis observed in our patient cohort.

Our analysis indicates that the occurrence of deep vein thrombosis in patients undergoing laparoscopic cholecystectomy is influenced by multiple factors, and carbon dioxide pneumoperitoneum alone does not appear to be the sole contributing factor. However, the use of carbon dioxide pneumoperitoneum during these surgeries

does impact patients' coagulation profiles, indicating a potential necessity for prophylactic measures against thrombosis in individuals at high risk. Recommendations from organizations such as SAGES [110] and ACCP [111] also underscore the importance of prophylactic measures in these settings.

CONCLUSION

From the prospective study on 50 patients undergoing Laparoscopic cholecystectomy over a period of 12 months, the following conclusions can be drawn:

1) Cholelithiasis is more common amongst middle aged patients. The prevalence is more in females than males.
2) Laparoscopic Cholecystectomy is a fairly safe surgery, without any major complications. The duration of surgery may vary from patient to patient.
3) The study reveals a notable increase in D-dimer levels and a significant decrease in prothrombin time, indicating activation of both the coagulation and fibrinolytic systems following laparoscopic cholecystectomy.
4) Activation of the coagulation system can predispose to thromboembolism, particularly deep vein thrombosis (DVT). However, none of the 50 patients in our study experienced such complications. This suggests effective compensatory mechanisms in response to mild changes in the coagulation profile.
5) Patients with risk factors such as advanced age, obesity, or a prolonged anticipated duration of laparoscopic surgery are at an increased risk of significant coagulation system activation. Consequently, these individuals are at high risk for developing postoperative deep vein thrombosis, warranting the implementation of thromboprophylaxis.
6) More extensive and detailed studies are required to better understand these changes in the coagulation system and to quantitatively evaluate the associated risks of laparoscopic cholecystectomy using carbon dioxide pneumoperitoneum.

LIMITATIONS: Limitations of the study are as follows:

1) The study enrolled a sample size of 50 patients only, which may have influenced the findings. A larger cohort might have produced varied results.
2) The study exclusively investigated patients undergoing laparoscopic cholecystectomy.
3) Patients undergoing laparoscopic procedures for conditions other than cholecystectomy, where carbon dioxide pneumoperitoneum is used, may exhibit specific changes in their coagulation profiles.
4) Blood samples were obtained 6 hours after pneumoperitoneum initiation. Collecting samples at different time points could potentially result in different conclusions.

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