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## An Observational Study of Changes in the Coagulation Profile of Patients Undergoing Laparoscopic Cholecystectomy Using Carbondioxide Pneumoperitoneum

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### Abstract

Laparoscopy is a widely utilized diagnostic and therapeutic procedure. It offers several advantages over traditional open surgical methods, including improved cosmetic outcomes, reduced postoperative pain, expedited hospital discharge, and a faster return to normal activities and work. Consequently, this study aimed to examine the effects of carbon dioxide pneumoperitoneum on the coagulation system in patients undergoing laparoscopic surgery (LC) and to enhance surgeons' awareness of any potential adverse effects. This prospective, time-bound study was conducted in the Department of General Surgery at PESIMSR Hospital, Kuppam, over a period of 18 months (2022-2024). The study sample comprised 55 participants. Inclusion criteria encompassed patients who underwent laparoscopic cholecystectomy, aged between 18 and 60 years, with gallstones and gallbladder polyps, patients with chronic cholecystitis, those in the recovery stages of acute cholecystitis, surgeries lasting between 90-180 minutes, and patients who provided consent for participation. In this study, the mean D-DIMER level was  $0.27 \pm 0.04$  pg/ml prior to surgery. A significant increase in D-DIMER levels was observed 30 minutes and 6 hours post-surgery. Additionally, prothrombin time (PT) increased significantly 30 minutes and 6 hours after pneumoperitoneum. A significant increase in activated partial thromboplastin time (APTT) values was also noted post-surgery. There was a notable increase in prothrombin time following pneumoperitoneum, as well as an increase in APTT after surgery. A significant rise in D-dimer levels was also observed.

## INTRODUCTION

One of the most popular procedures that is utilized for diagnostic and therapeutic purposes is laparoscopy. Better cosmesis, less severe post-operative pain, earlier discharge from the hospital, and a quicker return to regular life and work are some of the advantages that it provides in comparison to the conventional open surgical procedures<sup>[1]</sup>. There is a good basis of knowledge for advanced laparoscopy because to the experience accumulated from approximately over 500,000 procedures annually. However, there is a need for more investigation into the effect that carbon dioxide pneumo-peritoneum has on the coagulation system<sup>[2]</sup>. In order to perform the laparoscopic cholecystectomy technique, the patient is placed in a reverse Trendelenburg position and pressurised carbon dioxide is injected into the peritoneum. The procedure is performed under general anaesthesia. This position should be maintained until the surgery is performed because it has the potential to cause venous stasis in the lower extremities, which can result in endothelial alterations that disrupt the equilibrium of the coagulation and fibrinolysis system<sup>[2,3]</sup>. Therefore, all of the elements that make up Virchow's triad are seen above, and they have the potential to ultimately result in issues related to thromboembolism. There have been studies that have characterised the effect of pneumoperitoneum during LC in connection to coagulation and platelet activation, which results in a condition of hypercoagulability throughout the post-operative period<sup>[4-6]</sup>. Within the population of patients with LC, the incidence of post-operative deep vein thrombosis might range anywhere from 0% to 55%<sup>[5]</sup>. Such disparities in occurrence and divergences of opinion highlight the importance of conducting additional research investigations. The rising prevalence of laparoscopic procedures in contemporary surgical procedures necessitates the conduct of research on the alterations in blood coagulation that occur after these procedures. When it comes to the effects of LC on patients' coagulation profiles, the data that has been collected up until this point has been limited and defined by differences of opinion between those who argue against<sup>[7,8]</sup> and those who support<sup>[4,9]</sup>. It is necessary to conduct additional research on the effects of carbon dioxide pneumoperitoneum with regard to individual systems. In light of this, the purpose of this study was to investigate the effects of carbon dioxide pneumoperitoneum on the coagulation system of patients having laparoscopic surgery (LC) and to raise awareness among surgeons about any potential adverse effects.

### Aims and Objectives:

- To determine the alterations in the coagulation profile of patients undergoing laparoscopic

cholecystectomy using carbon dioxide pneumoperitoneum

- To determine if patients undergoing laparoscopic cholecystectomy have to be started on prophylaxis for deep vein thrombosis to prevent complications
- To assess if there is an increased risk of thrombosis post operatively.

## MATERIALS AND METHODS

This is a prospective time bound study Department of general surgery, PESIMSR Hospital, Kuppam. Study duration is 18 Months (2022 to 2024). Total number of sample is 55 in our study. Inclusion criteria are All the patients who underwent laparoscopic cholecystectomy, Age above 18 yrs to 60 years, patients with gall stones and gall bladder polyps, Patients with chronic cholecystitis, relief stages of acute cholecystitis are included, Surgery time between 90-180 minutes, Patients who give consent for study will be included. Exclusion criteria are Procedure when converted to open surgery, Surgery time exceeding above three hours, Associated hypertension, Patient is on anti coagulant therapy, Patient with known malignancies, pregnancy deep vein thrombosis, Patients with known history of bleeding and clotting disorders. A pre designed proforma containing the general details of the patient, history, clinical features, radiological investigations and coagulation profile of the patient.. After ethical committee approval, patients undergoing laparoscopic cholecystectomy in PESIMSR general surgery department.

Patients satisfying the inclusion and exclusion criteria will be explained about the study and written informed consent will be taken. Clinical examination, required radiological investigations will be done. Coagulation profile PT, APTT, D-dimer will be sent pre operatively, 30 minutes and 6hrs after surgery. At the end of the study, data will be compiled together and will be analysed. The data will be entered into MS excel and further analyzed using SPSS version 21. For descriptive analysis, the categorical variables will be analyzed by using percentages and the continuous variables will be analyzed by calculating mean  $\pm$  Standard Deviation. For inferential statistics, The categorical data were analyzed using Chi square test was used. Efficacy was expressed as Sensitivity, specificity, and predictive values. A probability value of less than 0.05 was considered as statistically significant.

## RESULTS AND DISCUSSIONS

In this study, we included 55 study participants that were undergoing laparoscopic cholecystectomy procedure. The mean age of the study population was 44 +/- 8.37 years.

Cholecystectomy, surgery for varicose veins, and treatment of an abdominal hernia are all low-risk procedures that lower the chance of getting a venous

Table 1: Age, Means and Std. Deviation

|                                  | Age (years)   |
|----------------------------------|---------------|
| Mean                             | 44            |
| Std. Deviation                   | 8.37          |
| Minimum                          | 30            |
| Maximum                          | 63            |
| 95% Confidence interval for mean | 41.16 - 46.84 |

Table 2: The male to female distribution was 1:1 in the present study

| Gender  | Frequency | %      |
|---------|-----------|--------|
| F       | 28        | 50.91% |
| M       | 27        | 49.09% |
| Total   | 55        | 100%   |
| Invalid | 0         | 0%     |
| Total   | 55        | 100%   |

Table 3: Means, Std. Deviation and Std. Error Means

|             | n | Mean | Std. Deviation | Std. Error Mean |
|-------------|---|------|----------------|-----------------|
| Age (years) | M | 27   | 44             | 8.11            |
|             | F | 28   | 44.46          | 9.47            |

Table 4: Equal Variance and Unequal Variance

|             | t                 | df   | p     | Cohen's d |      |
|-------------|-------------------|------|-------|-----------|------|
| AGE (years) | Equal variances   | -0.2 | 53    | .846      | 0.05 |
|             | Unequal variances | -0.2 | 52.28 | .846      | 0.05 |

Table 5: D Dimer (Pre Surgery)

|                                  | D-DIMER (pre surgery) | PT pre op   | APTTPRE-OP    |
|----------------------------------|-----------------------|-------------|---------------|
| Mean                             | 0.27                  | 12.43       | 37.5          |
| Std. Deviation                   | 0.04                  | 0.84        | 1.21          |
| Minimum                          | 0.21                  | 11.2        | 35.7          |
| Maximum                          | 0.35                  | 13.6        | 39.2          |
| 95% Confidence interval for mean | 0.26 - 0.28           | 12.21-12.66 | 37.18 - 37.83 |

Table 6: D Dimer (30 min Post Surgery)

|                                  | D DIMER (30 min post surgery) | PT 30 Mins  | APTT 30 Mins |
|----------------------------------|-------------------------------|-------------|--------------|
| Mean                             | 0.59                          | 14.25       | 39.96        |
| Std. Deviation                   | 0.02                          | 0.48        | 1.17         |
| Minimum                          | 0.54                          | 13.6        | 38.41        |
| Maximum                          | 0.63                          | 15.1        | 42.3         |
| 95% Confidence interval for mean | 0.59 - 0.6                    | 14.12-14.38 | 39.65-40.28  |

thromboembolism (VTE). Published data<sup>[1-4]</sup> show that the risk of VTE changes among patients having a hernia repaired (0.08%-1.2%), an elective laparoscopic cholecystectomy (0.28%-0.53%), or surgery for varicose veins (0.18%). To find out the risk of VTE, the Caprini risk assessment method is often used. People who are at a moderate to high risk for VTE should not normally take medicine to prevent it during general surgery<sup>[5]</sup>. Early mobilisation and/or mechanical prevention of VTE (elastic compression tights) are recommended for people who have a very small chance of getting a VTE<sup>[5]</sup>. The 9th ACCP guidelines don't say how long VTE prevention should last during surgery for benign conditions, and there isn't enough evidence to come to a clear decision on this issue.

Most of the time, after low-risk surgery, a patient should take anticoagulants for 7-10 days or VTE inhibitors until they can move around freely<sup>[6]</sup>. Some writers have shown that short-term VTE prevention after surgery can be done without raising the risk of venous thromboembolism. Based on how likely it is that a patient will have a VTE, they suggest a personalised course of medicine to prevent VTE<sup>[7,8]</sup>. There is information that shows hypercoagulability in the early stages after surgery, even though VTE after surgery is not very common in

Table 7: D Dimer (6 Hours post surgery)

|                                  | D DIMER (6 hours post surgery) | PT 6 HOurs  | APTT 6 Hours              |
|----------------------------------|--------------------------------|-------------|---------------------------|
| Mean                             | 0.61                           | 15.85       | 46.82                     |
| Std. Deviation                   |                                | 0.1         | 0.98                      |
| Minimum                          | 0.54                           | 14.2        | 38.22                     |
| Maximum                          | 1.2                            | 17.2        | 56.71                     |
| 95% Confidence interval for mean |                                | 0.59 - 0.64 | 15.58-16.11 44.92 - 48.72 |

Table 8: D Dimer (pre surgery), D Dimer (30 min post surgery)

|                                | n   | Mean | Std. Deviation |
|--------------------------------|-----|------|----------------|
| D Dimer (pre surgery)          | 55  | 0.27 | 0.04           |
| D Dimer (30 min post surgery)  | 55  | 0.59 | 0.02           |
| D Dimer (6 hours post surgery) | 55  | 0.61 | 0.1            |
| Total                          | 165 | 0.49 | 0.17           |

Table 9: Sum of Squares

|          | Sum of Squares | df  | Mean Square | F      | p     |
|----------|----------------|-----|-------------|--------|-------|
| Factor   | 4.1            | 2   | 2.05        | 518.56 | <.001 |
| Residual | 0.64           | 162 | 0           |        |       |
| Total    | 4.74           | 164 |             |        |       |

Table 10: Variable and Means Difference

| Variables  | Mean Difference | t      | p     |
|--|-----------------|--------|-------|
| D DIMER (pre surgery) - D DIMER (30 min post surgery)          | -0.32           | -26.96 | <.001 |
| D DIMER (pre surgery) - D DIMER (6 hours post surgery)         | -0.34           | -28.73 | <.001 |
| D DIMER (30 min post surgery) - D DIMER (6 hours post surgery) | -0.02           | -1.77  | .078  |

people who have had a cholecystectomy or an abdominal hernia repaired. A lot of research has been done on the hypercoagulable state that people go through after elective laparoscopic and open surgery<sup>[9-11]</sup>. Despite this, most of the earlier studies only looked at coagulation status and systemic inflammatory reaction in the first few days after surgery, usually within 72 hours.

For each of the 55 patients in this study, the prothrombin time, Activated partial thromboplastin time, and D-dimer readings were checked. Different studies were used to compare the conclusions that were made from these studies.

The people in the study were 44 years old on average, with an error of 8.37 years. The Indian figures for laparoscopic cholecystectomy back this up. According to a report by Rajesh *et al.*, most of the people who had surgery were between the ages of 41 and 50. This was true for both men and women. The patients in Amin *et al.* were between the ages of 29 and 78 (mean 56.7±11.5) years old. This was more than what our study found<sup>[9-17]</sup>.

In this study, there were exactly as many men as women. This is a strange result, since cholelithiasis is usually found in women. In Rajesh *et al.*, 62% of the patients who had a cholecystectomy were women, while only 32% were men. Out of the 50 cases in Amin *et al.*, 22 were men and 28 were women. This was different from what our study showed<sup>[19]</sup>.

The average amount of D-DIMER in this study was 0.27 +/- 0.04 pg/ml before surgery. We found that D-DIMER levels went up a lot 30 minutes and 6 hours after surgery. In a study by Amin *et al.*, the DD levels slowly went up after surgery. DD levels at 0 and 8 hours after surgery were higher than

Table 11: There is a significant increase in D-DIMER after surgery, and increases with time

|            | n  | Mean  | Std. Deviation |
|------------|----|-------|----------------|
| PT pre op  | 55 | 12.43 | 0.84           |
| PT 30 MINS | 55 | 14.25 | 0.48           |
| PT 6 HOURS | 55 | 15.85 | 0.98           |

Table 12: Means and std. Deviation

|          | Sum of Squares | df  | Mean Square | F      | p     |
|----------|----------------|-----|-------------|--------|-------|
| Factor   | 320.71         | 2   | 160.36      | 253.99 | <.001 |
| Residual | 102.28         | 162 | 0.63        |        |       |
| Total    | 422.99         | 164 |             |        |       |

Table 13: Means

|              | n  | Mean  | Std. Deviation |
|--------------|----|-------|----------------|
| APTT PRE-OP  | 55 | 37.5  | 1.21           |
| APTT 30 Mins | 55 | 39.96 | 1.17           |
| APTT 6 Hours | 55 | 40.82 | 7.03           |

Table 14: Sum of Squares

|          | Sum of Squares | df  | Mean Square | F     | p     |
|----------|----------------|-----|-------------|-------|-------|
| Factor   | 2563.13        | 2   | 1281.57     | 73.68 | <.001 |
| Residual | 2817.76        | 162 | 17.39       |       |       |
| Total    | 5380.89        | 164 |             |       |       |

pre-pneumoperitoneum levels by 210.8 and 525.9 ng/ml, respectively ( $P < 0.05$ ), and DD levels at 8 hours after surgery were higher than at 0 hours after surgery ( $P < 0.05$ ). These results were like the ones in this study.

When the D-dimer levels were looked at by Rajesh *et al.*, they found that many patients had amounts that were twice as high before and after surgery. With a p value of 0.001, the difference was also found to be statistically very important. This was similar to what our study found. However, the results of this study are different from those of Rahr *et al.*<sup>5</sup>, Yan MJ6 *et al.*, and Martinez *et al.*<sup>[7]</sup>, which show that blood after surgery doesn't clot properly or that the coagulation profile doesn't change.

In this study, PT went up a lot 30 minutes later, 6 hours after pneumoperitoneum.

As shown in a study by Amin *et al.*, the PT values went up slightly ( $P > 0.05$ ) at the end of the pneumoperitoneum (0 hour after surgery) and down by 0.5 seconds 8 hours after surgery compared to the values before the pneumoperitoneum ( $P < 0.05$ ). This was similar to what our study found. If you look at Donmez *et al.*, they found that PT was significantly higher 24 hours after surgery compared to before surgery in both the 10 mmHg group ( $p = 0.048$ ) and the 14 mmHg group ( $p < 0.001$ ). However, Rajesh *et al.* found that the prothrombin time went down after surgery in 62% of patients (31 out of 50), while in the other 31%, there was no change. These results are similar to those of many other studies, such as those by Hans *et al.*<sup>[1]</sup>, Garg *et al.*<sup>[2]</sup>, and Schietroma *et al.*<sup>3</sup>. These studies also show that there is a state of hypercoagulability.

It was found that the APTT readings went up significantly after surgery in this study.

Before the pneumoperitoneum, Amin *et al.* found that APTT dropped by 1.4 seconds ( $P > 0.05$ ) and 3.7 seconds ( $P < 0.05$ ) at 0 and 8 hours, but there wasn't a statistically significant change between the values at 0 and 8 hours after surgery ( $P > 0.05$ ).

Donmez *et al.* found that in the 10 mmHg group, there was a significant increase in APTT 24 hours after surgery compared to the number before surgery ( $p < 0.001$ ). There was a significant rise in APTT 1 hour ( $p < 0.001$ ) and 24 hours ( $p < 0.001$ ) after surgery in the 14 mmHg group compared to the number before surgery. Garg *et al.* wrote about 50 cases of LC with a normal pneumoperitoneum pressure of 12 mmHg. The authors discovered that aPTT and antithrombin 3 levels dropped in the sixth and twenty-four hours after surgery, which led to activation<sup>[18]</sup>.

There were no other signs of risk that suggested anticoagulation was needed, so none of the patients in the study were given any kind of anticoagulant medicine. Unlike other studies that found thrombosis to happen after surgery, none of the patients showed signs of thrombosis, even though their coagulation profiles were higher than normal. Most likely, this was because the group being studied was very small.

## CONCLUSION

In this study, we observed the following:-There was an increase in prothrombin time after pneumoperitoneum, There was an increase in APTT following the surgery, There is a significant increase in D-dimer, However, we did not observe any complications in either group, such as bleeding, deep vein thrombosis or pulmonary thromboembolism. Hence, it is imperative to anticipate these high risk situations, and take necessary measures to prevent DVT and PTE. We recommend that in patients with significantly increased D-DIMER, as well as reduced PT/APTT, may benefit from post-operative anticoagulation for a short duration, to prevent long-term thrombotic complications.

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