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TO STUDY POST-OPERATIVE COAGULATION PROFILE AND DEEP VENOUS THROMBOSIS IN LOWER EXTREMITIES IN PATIENTS UNDERGOING ELECTIVE LAPAROSCOPIC CHOLECYSTECTOMY WITH CO_2 PNEUMOPERITONEUM

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ABSTRACT **Aim:** To analyse the post-operative coagulation profile and deep venous thrombosis in lower extremities in patients undergoing elective laparoscopic cholesystectomy with CO2 pneumoperitoneum. **Material and methodology:** The present descriptive observational study was conducted in the department of General Surgery, Teerthanker Mahaveer Medical College and Research Centre, Moradabad (U.P.) among 120 patients presenting to the hospital with trauma, during the study period. Mode of injury was noted. Time interval between the injury and admission in hospital was also recorded. After resuscitating the patients, all patients were subject to clinical & radiological examination and management. Then patients were scheduled for elective laparoscopic cholecystectomy for symptomatic gall stone disease. Pre-Op and Post-Op Coagulation profile (PT, INR, APTT, D-DIMER (6 hours before surgery and 24 hours after surgery)) and Colour doppler scan of lower extremities (7 day Post-Operatively) findings were noted. **Results:** Mean height, weight and BMI of study subjects was 158.30±4.83 cm, 64.80±10.72 kg and 24.79±6.15 respectively. There was significant improvement in mean prothrombin time, D-dimer, INR and APTT after the surgery when compared to pre surgery values with statistically significant difference. Surgical complications were present among only 5 (4.17%) subjects. Deep vein thrombosis was absent among all the study subjects. **Conclusion:** It was concluded that there was statistically significant decrease in values of PT, INR and APTT and increase in D-dimer levels when compared before and after surgery, so elective laparoscopic cholesystectomy with CO2 pneumoperitoneum can be considered as a potential predictor for coagulation.

KEYWORDS :

Introduction:

After the introduction of laparoscopic surgery, laparoscopic cholecystectomies (LCs) have been accepted as a gold-standard procedure for the symptomatic gall bladder stone.[1,2] Laparoscopic cholecystectomy is minimally invasive surgery to remove the gallbladder. It helps people when gallstones cause inflammation, pain or infection. The surgery involves a few small incisions, and most people go home the same day and soon return to normal activities. It provides tremendous advantages to patients, including smaller wounds, less postoperative discomfort and shorter hospital stay. The advantage of laparoscopic cholecystectomy over the open procedure seems to be related to the reduced surgical trauma.[2]

In order to achieve better visibility of the surgical field, the "CO2 pneumoperitoneum technique" is used. The pneumoperitoneum (PNP) is the crucial element in laparoscopic surgery. The surgeons performing laparoscopy should understand the basic physiologic changes occurring during PNP, recognize the clinical changes and make appropriate intraoperative adjustments to minimize the adverse changes. Controlled intra-abdominal pressure (IAP) within the abdominal cavity is tasked to facilitate smooth operation of the surgeon, raising the anterior abdominal wall up and suppressing the other abdominal organs and soft tissues of the back.[3,4] Pneumoperitoneum with CO_2 has been used in clinical practice, since the introduction of laparoscopic cholecystectomy in the late 1980s.

Carbon dioxide is the most suitable gas for insufflation into the abdominal cavity, because it meets several important criteria: not flammable and it is possible to use electrocoagulation, very soluble in blood and tissues, it is easily eliminated through the lungs, is nontoxic and it is inexpensive.[5,6] Approximately 15 years of experience and tens of thousands of cases have led to a strong knowledge base for advance laparoscopy. But our experience with and understanding of the effects of CO2 pneumoperitoneum are far from nascent.[7] Much has still to be learned however, concerning the pathophysiology and systemic complications of laparoscopic surgery.

It has long been known that a hypercoagulability state develops after surgery. The reported incidence of postoperative DVT in laparoscopic cholecystectomy varies considerably between 0 and 55%.[8] Most publications regarding laparoscopic cholecystectomy during the early 1990s were retrospective reports of personal or institutional experience with the operation. In most reports, data on complications were included, but whether complications were actively looked for or case-notes just checked retrospectively was not mentioned. The only firm conclusion from this variability in incidence is that further studies are needed. So, the present study was undertaken to evaluate the effect of laparoscopic cholesystectomy with CO_2pneumoperitoneum on post -operative coagulation profile and deep venous thrombosis in lower extremities.

Material and methodology: The present descriptive observational study was conducted in the department of General Surgery, Teerthanker Mahaveer Medical College and Research Centre, Moradabad (U.P.) among the patients presenting to the hospital with trauma, during the study period from the date of acceptance from CRC & IEC committees till 30th June, 2022. A total of 120 patients were included in the study.

The study protocol for all procedures was approved by the Institutional Review Board for Ethical Clearance of Teerthanker Mahaveer Medical College and Research Centre, Moradabad (U.P.), and was performed in accordance with the Code of Ethics of the World Medical Association according to the Declaration of Helsinki of 1975, as revised in 2000. All patients/attendants were asked to sign a written consent form (in the language they best understand) for clinical examination, radiological examination & lab investigations prior to commencement of the study. Only those individuals, who volunteer to participate in the study, were included and the data was kept confidential. The participation in the study did not affect the quality of care they received.

Inclusion Criteria

1. All patients scheduled for elective laparoscopic cholecystectomy for symptomatic gall stone disease.
2. Patient more than 18yrs years of age.
3. Patients with ASA Grade 1 & ASA Grade 2.

Exclusion Criteria

1. Patients with acute cholecystitis, cholangitis, acute pancreatitis or other acute inflammation.
2. Patients with recent (6 months) surgery, recurrent or recent (<2 years) malignancy
3. Patients with current or recent (6 months) thromboembolic disease, hemato- logical disorder, renal, hepatic, rheumatic or vascular disease.
4. Patients with pre-existing coagulation disorder
5. Patients taking corticosteroids or other drugs that could affect their immunological responses
6. Patients with pregnancy or on anticoagulant treatment including aspirin or on oral contraceptives or danazol were also not included in the study.

Methodology

All the patients presenting to the hospital with trauma, not falling in exclusion criteria were evaluated. All demographic details including name, age and gender, and detailed medical history was recorded. Mode of injury was noted. Time interval between the injury and admission in hospital was also recorded. After resuscitating the patients, all patients were subject to clinical & radiological examination and management. Then patients were scheduled for elective laparoscopic cholecystectomy for symptomatic gall stone disease. Pre-Op and Post-Op Coagulation profile (PT, INR, APTT, D-DIMER (6 hours before surgery and 24 hours after surgery)) and Colour doppler scan of lower extremities (7 day Post-Operatively) findings were noted.

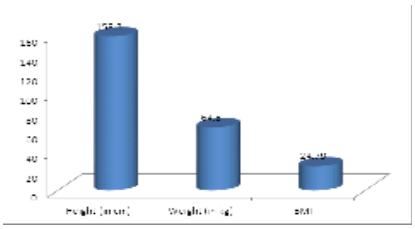
Statistical analysis: Data was analyzed using SPSS V24.0 package. Appropriate statistical techniques were used for the analysis of data. t test was used to compare the statistical difference between the groups.

Results: Of the 120 patients involved in surgery, maximum (n=76, 63.3%) were females and rest (n=44, 36.7%) were male subjects. Male to female ratio of study subjects was 1: 1.73. The mean age of the study subjects was 49.03±8.75. Of the total 120 subjects, maximum (n=53, 44.17%) were from age group 41-50 years, followed by 36 (30%) subjects from 51-60 years age group, 16 subjects (13.33%) were >60 years of age and remaining 15 subjects (12.5%) were aged between 30-40 years. (Table 1)

Table 1: Gender distribution among the study subjects

Gender	N	%
Male	44	36.7
Female	76	63.3
Age Group (in years)		
30-40	15	12.5
41-50	53	44.17
51-60	36	30.00
>60	16	13.33
Total	120	100
Mean±SD	49.03±8.75	

Hypertension was reported by 17 study subjects (14.2%) and diabetes mellitus was co-existing in 10 patients (8.3%). Mean height, weight and BMI of study subjects was 158.30±4.83 cm, 64.80±10.72 kg and 24.79±6.15 respectively. The body mass index of study subjects varied from 19.86 to 31.20. (graph 1)



Graph 1: Descriptive analysis of anthropometric parameters

Mean prothrombin time before and after surgery was 13.26±1.03 and 13.04±0.94. The difference in prothrombin time before and after surgery was statistically significant (p<0.01). Mean D-dimer levels before and after surgery was 132.15±20.29 and 349.78±68.56 respectively. The difference between mean D-dimer levels before and after surgery was statistically significant (p<0.01). Mean International normalized ratio (INR) before and after surgery was 0.99±0.023 and 0.97±0.018 respectively. The difference between mean International normalized ratio (INR) before and after surgery was statistically significant (p<0.01). Similar results were reported for APTT (Table 2).

Table 2: Comparison of PT, D-dimer, INR and APTT before and after surgery

PT	Mean	SD	t test	p value
Before Surgery	13.26	1.03	5.74	<0.01*
After Surgery	13.04	0.94		
D-dimer				
Before Surgery	132.15	20.29	39.48	<0.01*
After Surgery	349.78	68.56		
INR				
Before Surgery	0.99	0.023	7.40	<0.01*
After Surgery	0.97	0.018		
APTT				
Before Surgery	23.26	1.04	19.92	<0.01*
After Surgery	22.63	0.87		

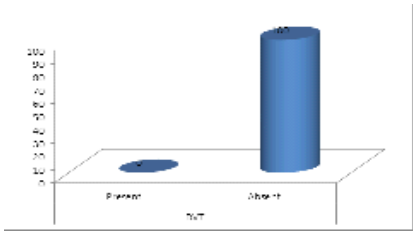
*: statistically significant

Surgical complications were present among only 5 (4.17%) subjects and remaining 115 subjects (95.83%) had no such complications. (Table 3)

Table 3: Surgical complications among the study subjects

Surgical complications	N	%
Present	5	4.17
Absent	115	95.83

Deep vein thrombosis was absent among all study subjects (n=120, 100%). (graph 2)



Graph 2: Deep vein thrombosis among the study subjects

Discussion: Laparoscopic cholecystectomies (LCs) is a well-accepted procedure for the symptomatic gall bladder stone and to achieve better visibility of the surgical field, the "CO_2 pneumoperitoneum technique" is used. There are many advantages to LCs such as a shorter hospitalization time, minimal postoperative pain and an easy recovery. However, there are also a few systemic disadvantages due to increases in intra-abdominal pressure. Insufflation of CO_2 into the abdominal cavity results in elevation of the diaphragm and the risk of regurgitation, a decrease in lung volume and compliance, increment in airway resistance and an increase in the ventilation perfusion ratio. In the cardiovascular system, intra-abdominal pressure causes an increase in systemic venous resistance (SVR) and mean arterial pressure (MAP) and a decrease in venous return and cardiac output due to pressure on the inferior vena cava. There are three major risk factors for deep vein thrombosis (DVT) during LCs: surgical trauma, pressure on the inferior vena cava and venous stasis on the lower extremities due to the anti-Trendelenburg position.

In present study maximum (n=76, 63.3%) involved subjects were females and rest (n=44, 36.7%) of the subjects were males. Male to female ratio of study subjects was 1: 1.73. These findings were almost similar to result of Stein PD et al., (2014) [48] who found in their research that 70% of the study subjects were females. According to findings of Garg PK et al[9] there were six male patients (12%) and 44 female patients (88%) in the study. Amin B et al[10] found in their study that out of the 50 patients, 22 were male and 28 were female.

In present study, the mean age of the study subjects was 49.03±8.75. Of the total 120 subjects, maximum (n=53, 44.17%) were from age group 41-50 years, followed by 30% subjects from 51-60 years age group, 13.33% subjects were >60 years of age and remaining 12.5% subjects were aged between 30-40 years. The age of the patients varies from 28 to 65 years. According to study done by Stein PD et al[11] mean age of study participants was 52±20 years. Amin B et al[10] found in their study that the age of the patients ranged from 29 to 78 years and mean age being 56.7±11.5 years.

Mean height, weight and BMI of study subjects was 158.30±4.83 cm, 64.80±10.72 kg and 24.79±6.15 respectively. Height of study subjects ranged between 150-168 cm, weight ranged from 40-94 kg. The body mass index of study subjects varied from 19.86 to 31.20. Garg PK et al[9] found in their research that The body mass index of patients varied from 21 to 29.6 kg/m^2. The mean body mass index was 24.09±1.99.

Donmez T et al[12] found that in two study groups according to the pneumoperitoneum pressure during Laparoscopic cholecystectomies (LC) mean weight was 78±13kg and 76±11kg. Mean height in both group was 165± 6 cm and mean BMI was 28.1±4.1 kg/cm^2 and 27.8±4.5 kg/cm^2.

In present study, difference in prothrombin time before and after surgery was statistically significant (p<0.01). Mean D-dimer levels before and after surgery was 132.15±20.29 and 349.78±68.56 respectively. Mean International normalized ratio (INR) before and after surgery was 0.99±0.023 and 0.97±0.018 respectively. The difference between mean D-dimer and International normalized ratio (INR) before and after surgery was statistically significant (p<0.01). Similar results were reported for APTT. This shows that values of parameters of blood coagulation when compared before pneumoperitoneum and after surgery; value of PT, INR and APTT were reduced whereas there was increase in D-dimer levels from 132.15 to 349.78. All these values were statistically significant. This suggest that pneumoperitoneum for LC increase the risk of venous thrombosis. Activated partialprothrombin time is a direct measure of coagulation, which tests the intrinsic pathway (factor XII, XI, IX, VIII) and common pathway protein factors (fibrinogen, prothrombin, Factor V and X). The present study shows statistically significant decrease in APTT, which suggests activated coagulation. D-Dimer levels have been used as a marker of intravascular clot formation. D-Dimer is a cross-linked fibrin degradation product, which forms as a result of a breakdown of fibrin. D-Dimer levels are frequently increased after surgery or trauma and indicate the presence of an intravascular clot that has undergone lysis. In present study a statistically significant increase in D-dimer levels suggests formation of intravascular clot.

The observed decreases in APTT indicate an activated coagulation. The increase in D-dimer indicates that both coagulation and fibrinolysis are activated, since it is the end product of the degradation of fibrin, which has to have been formed by coagulation in the first phase. Increased coagulation activity is commonly seen after surgery and can be considered part of the normal response to surgical trauma. It is therefore difficult to know what is caused by the pneumoperitoneum and what is caused by the surgical procedure itself.

These results were in accordance to result of study done by Amin B et al[10] where venous blood specimens were taken from each patient before and at the end of pneumoperitoneum (i.e., 0 hour after surgery) and at 8 hours after surgery for determination of prothrombin time (PT), activated partial thromboplastin time (APTT), fibrinogen (Fib), thrombin time (TT), and D-dimer (DD). The PT values slightly increased ($P > 0.05$) at the end of pneumoperitoneum and decreased by 0.5 seconds at 8 hours after surgery; APTT at 0 and 8 hours decreased by 1.4 seconds ($P > 0.05$) and 3.7 seconds ($P < 0.05$) respectively as compared to pre-pneumoperitoneum values; FIB determined at 0 hour post-operation increased by 0.1 g/L as compared to pre-pneumoperitoneum values ($P > 0.05$); however, the FIB values at 8 hours after operation increased by 1.2 g/L as compared to the pre-pneumoperitoneum values ($P < 0.05$), and increased by 1.1 g/L as compared to 0 hour post-operation ($P < 0.05$); TT values obtained at 0 and 8 hours post-operation were not significantly different as compared to the pre-pneumoperitoneum values ($P > 0.05$); and the DD values gradually increased after operation; as compared to pre-pneumoperitoneum values, DD at 0 and 8 hours after operation increased by 210.8 ng/ml and 525.9 ng/ml respectively ($P < 0.05$) and DD at 8 hours after operation increased by 315.1 ng/ml as compared to 0 hour post-operation ($P < 0.05$).

Garg PK et al[9] found in their research that PT did not show any significant operative variation both at 6 and 24 h postoperatively compared to the preoperative value. APTT, D-dimer and Anti Thrombin III showed statistically significant variation both at 6 and 24 h postoperatively. In study done by Donmez T et al[12] they found a significant increase in PT 24 h after the surgery compared to preoperative value in the 10 mmHg group ($p=0.048$) and the 14 mmHg group ($p < 0.001$). They observed a significant increase in APTT 24 h after the surgery compared to preoperative value in the 10 mmHg group ($p < 0.001$). In the 14 mmHg group there was a significant increase in APTT 1 h ($p < 0.001$) and 24 h ($p < 0.001$) after the surgery compared to preoperative value. There were significant decreases in TT 1 h and 24 h after the surgery in both of groups compared to preoperative values ($p < 0.001$). INR significantly increased in the 14 mmHg group 24 h after the surgery ($p < 0.001$). D-dimer and fibrinogen significantly increased in both of groups 1 h and 24 h after the surgery ($p < 0.001$).

In present study surgical complications were present among only 5 (4.17%) subjects and remaining 115 subjects (95.83%) had no such complications. Colour doppler scan of lower extremities (7 Day Post-Op) to look for any evidence of deep vein thrombosis. None of the patients showed evidence of deep vein thrombosis on Colour doppler imaging. These findings were in accordance to result of Garg PK et al[9] who also found no case of deep vein thrombosis after surgery in their study subjects.

Limitations: There are certain restrictions on the current investigation. First, this was a study that had trouble matching cases of open cholecystectomy with LCs alone. Therefore, a control design will strengthen the study's validity and improve the generalisation of findings, however open cholecystectomy cases are challenging to recruit because the majority of patients prefer LCs. Second, more thorough results about the postoperative risks of thrombosis would have been acquired if additional time points (such as 16 and 24 hours after surgery) had been planned for postoperative observations on coagulation parameters. Therefore, larger, randomised, controlled clinical investigations are required to define the extent and character of postoperative venous thrombosis risks following LC.

Conclusion: Although laparoscopic cholecystectomy appears to be less traumatic to the patients than open surgery, decreased venous return from lower extremities and hypercoagulability occurring in patients undergoing elective laparoscopic cholecystectomy with CO_2 pneumoperitoneum makes it a potent risk factor for deep venous thrombosis. From present study it was concluded that there was statistically significant decrease in values of PT, INR and APTT and increase in D-dimer levels when compared before and after surgery, so can be considered as a potential predictor for coagulation.

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