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Research Article

LIVER ENZYME ALTERATIONS AFTER LAPAROSCOPIC CHOLECYSTECTOMY IN A TERTIARY CARE CENTER

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ABSTRACT

Objective: Cholelithiasis is a prevalent global health concern, with laparoscopic cholecystectomy (LC) emerging as the preferred surgical intervention. While LC offers an advantage such as shorter hospital stays, it poses potential risks, including cardiovascular impediments because of hemodynamic and ventilatory changes. The current research study was done to assess the impact of LC on hematological parameters, comparing pre-operative and post-operative levels.

Methods: The study comprised 51 subjects undertaking LC, and preoperative and postoperative blood samples were analyzed for various hematological parameters. Parameters investigated included hemoglobin (Hb), mean corpuscular volume, mean corpuscular Hb, mean corpuscular Hb concentration, hematocrit, platelet count, mean platelet volume (MPV), and liver function tests such as alanine transaminase and alkaline phosphatase.

Results: Preliminary findings demonstrated significant alterations in hematological parameters post-LC. Changes in MPV, leukocytes, neutrophils, neutrophil–lymphocyte ratio, platelet–lymphocyte ratio, and coagulation factors were observed. Moreover, there was a notable proliferation in thromboembolic measures connected with pneumoperitoneum pressure and surgery duration.

Conclusion: LC induces substantial changes in hematological parameters, potentially contributing to postoperative complications. Understanding these alterations is crucial for implementing appropriate pre-, peri-, and post-operative measures to minimize morbidity, mortality, and overall health-care costs. Further investigations are required in interpreting the principal mechanisms and refine strategies for optimizing patient outcomes in LC.

Keywords: Laparoscopic cholecystectomy, Hemodynamic and ventilatory changes, Hematological parameters.

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INTRODUCTION

Cholelithiasis is a common disease worldwide, with prevalence rates of 10–15% in Western populations and 3–5% in African and Asian populations [1]. In India, women (n=38) have a higher prevalence of cholelithiasis than men (n=15). Northern Indians were more likely to have it than Southern Indians, with Maharashtra, especially those living in coastal areas, coming in second [2]. Laparoscopic cholecystectomy (LC) forms the preferred surgical procedure for removing symptomatic gallbladder disease and cholelithiasis, replacing open cholecystectomy since the 1990s [3].

Although LC offers shorter hospital stays and faster recoveries, it carries a threat of cardiovascular difficulties in susceptible individuals because of its effects on hemodynamics and ventilation. Augmented pneumoperitoneum pressure and hypercarbia during laparoscopic surgeries can lead to changes in hemodynamic parameters [4-6]. The elevated intra-abdominal pressure compresses abdominal blood vessels, including the inferior vena cava, aorta, splanchnic vessels, hepatic artery, portal veins, and renal vasculature. This can result in temporary ischemia in the liver cells, causing an increase in serum alanine aminotransferase (ALT) levels. Higher intra-abdominal pressure is also associated with more fluctuations in hemodynamics and abnormalities in LFTs [4,7-9].

Several researches have described modifications in hematological parameters through laparoscopic measures [10,11]. Substantial differences have been observed between pre and post-insufflation values of leukocytes, neutrophils, neutrophil–lymphocyte ratio, platelet–lymphocyte ratio, and mean platelet volume (MPV). An increase in MPV with higher intra-abdominal pressures can be a clinical indicator of intra-abdominal hypertension [10,11]. Another research documented the increased thromboembolic episodes associated with CO_2 insufflation, likely due to changes in coagulation factors and reduced fibrinolytic system activity. This rise in thromboembolic events was straightly linked to pneumoperitoneum pressure and duration of surgery [12].

Given the various changes in these variables described by several researches, it is important to clearly define the effects of LC on hematological parameters under different circumstances. This will help in implementing appropriate measures before, during, and after surgery to minimize complications, mortality, hospitalization, and overall costs for patients and health-care institutions. Hence, the primary aim was to compare hemoglobin (Hb), mean corpuscular volume (MCV), mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, hematocrit (Hct), platelets, MPV, and LFTs such as ALT and ALP before and after LC.

METHODS

A total of 51 patients comprising 26 male and 25 female subjects with an average age of 52 years (from 31 to 88 years) were admitted to Air Force Hospital of Tertiary Care Center in Kanpur, India, between the period of May 2022 and January 2023 for LC. Before the procedure, all patients had normal levels of serum transaminases. The laboratory tests were conducted using a single type of instrument in the same laboratory. The normal range for the hematological parameters was

aspartate aminotransferase (AST) 5–40 U/L, ALT 5–35 U/L, alkaline phosphatase (ALP) 46–150 U/L, and total bilirubin 0.3–1.2 mg/dL. Anesthesia protocol used was consistent for all patients, with drugs selected to minimize any impact on liver enzyme activity.

Subjects were excepted from the study, including those with raised liver enzyme levels 24 h before surgery, acute cholecystitis, gallbladder polyps, those undergoing cholecystectomy for acute biliary pancreatitis, individuals who had undertaken endoscopic retrograde cholangiopancreatography and sphincterotomy in 2 weeks before the laparoscopic operation, and patients who experienced difficulties after the procedure like bile duct injury or cholangitis.

The surgeries were achieved by the same surgical team under general anesthesia, maintaining intra-abdominal pressure at 12 mmHg of CO_2. Dissection of the gallbladder from the liver was done by monopolar diathermy. Intraoperative cholangiography was avoided to prevent iatrogenic liver enzyme alterations. Postoperatively, all patients received Ringer's lactate infusions and were administered antibiotics for only three doses (cefotaxime 1 g IV). To evaluate liver function, serum levels of bilirubin, ALT, AST, and ALP were measured 24 h before the operation and 24 h postoperatively.

Statistical analysis

Categorical variables were presented as n (% of cases), while continuous variables were reported as mean and standard deviation with a 95% confidence interval for the mean difference. Paired t-tests were used for comparing means of continuous variables. The normality assumption was tested before applying t-tests. Statistical significance was considered as $p<0.05$.

RESULTS

Various biochemical serum levels of pre and post-LC are shown in Table 1. Serum bilirubin level was found to be 0.41±0.24 and 0.67±0.48 pre-operative and post-operative subjects, respectively. The mean difference between pre and post-operative subjects along with 95% CI of mean difference was found to be −0.26 (−0.38–−0.13). Serum bilirubin level is significantly higher when compared to mean pre-operative serum bilirubin level ($p<0.05$). The pre-operative and post-operative serum AST level was found to be 32.14±13.72 and 50.57±25.05, respectively, with the mean difference (pre–post) along with 95% CI of mean difference was found to be –18.43 (−25.95–−10.91). The mean post-operative serum AST level is significantly higher compared to mean pre-operative serum AST level ($p<0.05$).

The pre-operative and post-operative serum ALT level was found to be 35.88±20.66 and 48.04±27.54, respectively, with the mean difference (pre–post) along with 95% CI of mean difference was −12.16 (−20.81–−3.50). The mean post-operative serum ALT level is significantly higher compared to mean pre-operative serum ALT level ($p<0.05$). The mean pre-operative and post-operative serum ALP level was found to be 106.31±45.74 and 99.72±41.85, respectively, with the mean difference (pre-post) along with 95% CI of mean difference was 6.59 (0.46–12.71). The mean post-operative serum ALP level was significantly lower when compared to mean pre-operative serum ALP levels ($p<0.05$). The mean pre-operative and post-operative serum AST/ALT ratio was 0.99±0.37 and 1.10±0.35, respectively. The mean difference (pre-post) along with 95% CI of mean difference was −0.11 (−0.24–0.024). The mean post-operative serum AST/ALT ratio has not shown any significant difference when compared to mean pre-operative serum AST/ALT ratio ($p>0.05$).

Liver function tests pre and post-operative LC are shown in Table 2. Distribution of post-operative incidence of abnormal serum bilirubin levels was found to be increased and it is significantly higher compared to pre-operative levels of serum bilirubin ($p<0.05$). The post-operative incidence of abnormal serum AST levels was found to be increased which is significantly higher compared to pre-operative levels of serum AST ($p<0.05$). Distribution of post-operative incidence of abnormal Sr. ALT levels was found to be increased and it is significantly higher compared to pre-operative levels of serum ALT ($p<0.05$). Distribution of post-operative incidence of abnormal serum ALP levels did not differ significantly when compared to pre-operative levels of serum ALP levels ($p>0.05$). Distribution of post-operative incidence of abnormal levels of serum AST/serum ALT ratio did not differ significantly compared to pre-operative levels of serum AST/serum ALT ratio ($p>0.05$).

DISCUSSION

Nowadays, laparoscopy is a common procedure in modern surgery. To continue benefiting society, its positive and negative consequences must be closely watched. Our research has yielded some intriguing findings that will contribute to a more comprehensive understanding of the consequences of this procedure. Significant variations were observed in the concentrations of some research factors. This implies

Table 1: Biochemical characteristics of serum levels pre and post-laparoscopic cholecystectomy

Parameters	Pre (n=51)		Post (n=51)		Difference (Pre-Post)		p-value
	Mean	SD	Mean	SD	Mean	95% CI	
Sr. Bilirubin	0.41	0.24	0.67	0.48	−0.26	−0.38–−0.13	0.001***
Sr. AST	32.14	13.72	50.57	25.05	−18.43	−25.95–−10.91	0.001***
Sr. ALT	35.88	20.66	48.04	27.54	−12.16	−20.81–−3.50	0.001***
Sr. ALP	106.31	45.74	99.72	41.85	6.59	0.46–12.71	0.036*
Sr. AST/ALT	0.99	0.37	1.10	0.35	−0.11	−0.24–0.024	0.106^{NS}

p-value <0.05 is significant. *p-value <0.05, ***p-value <0.001, NS: Non-significant

Table 2: Characteristics of liver function tests pre and post-laparoscopic cholecystectomy

Parameters	Pre-operative				Post-operative				p-value
	Normal		Abnormal		Normal		Abnormal		
	n	%	n	%	N	%	n	%	
Sr. Bilirubin	50	98.0	1	2.0	45	88.2	6	11.8	0.025*
Sr. AST	46	90.2	5	9.8	29	56.9	22	43.1	0.001***
Sr. ALT	45	88.2	6	11.8	39	76.5	12	23.5	0.034*
Sr. ALP	48	94.1	3	5.9	46	90.2	5	9.8	0.317^{NS}
Sr. AST/Sr. ALT	30	58.8	21	41.2	21	41.2	30	58.8	0.072^{NS}

p-value <0.05 is significant. *p-value <0.05, ***p-value <0.001, NS: Non-significant

that even if laparoscopy seems harmless, the patient still needs to be given the right care and take precautions to ensure their well-being.

The average age of the subjects in our study was 42, and 85.2% were women. Similar numbers have been observed in a number of studies examining the disease's prevalence or pertaining to cholelithiasis surgery [13]. In addition, a Taiwanese study [14] discovered that females had a greater frequency of cholelithiasis. This makes sense because feminine gender has been related to an augmented threat of gallstone formation in multiple studies [15].

The chief objective of the current study was to describe blood alterations carried on by LC. First, we discovered that the levels of Hct and Hb had significantly decreased. Lindberg *et al*. provided confirmation of these findings [16]. The dilutional effect of I/V fluids used through the surgery provides an easy explanation for this. Furthermore, it makes sense why the MCV increased. Intraoperative fluids are given to prevent shock during the procedure and to prevent dehydration thereafter. As a result of laparoscopic surgeries, continuous administration with minimum bleeding causes blood dilution and a decrease in plasma osmolality. This ultimately causes a change in the amount of water inside the cells, which could raise the MCV.

Leukocytes were another variable that showed increasing amounts after surgery. The study carried out in Turkey by Bitkin *et al*. [11] provides evidence for this. This is because immunological pathways will be triggered by the trauma that occurs during surgery, and this will unavoidably result in an increase in leukocyte counts.

An important indicator of elevated intra-abdominal pressure is the MPV [11]. Therefore, it makes sense that our results, which were comparable to those published by Bitkin *et al.* [11], likewise revealed a considerable rise in MPV following the treatment. A further study carried out in Turkey by Celep *et al*. [10] supports this rise.

Nonetheless, Marakis *et al*. research discovered that the patients' MPV had dropped [17]. Several investigations have indicated enhanced thrombolytic response and coagulation action in these subjects, which is the reason for this [16,18]. This causes the platelets to become depleted, which is consistent with the findings of Marakis *et al*. who too observed a notable drop in the platelet counts. On the other hand, our study's platelet count showed no discernible variation [17].

Crema *et al*. observations revealed that no discernible variation in platelet counts [19] supports these findings. Studies indicate that only greater volume platelets are mobilized initially under stressful settings, like surgical procedures, account for our data, which demonstrate no substantial alteration in platelet counts however a proliferation in MPV. After at least 1 to 2 days, there is a rise in the total quantity of circulating cells [20,21].

ALT was the last research variable to exhibit a statistically significant increase throughout the process. Similar noteworthy findings are reported in a number of investigations [7,22,23]. After 3 to 10 days, the enzyme levels revert to normal, indicating that these changes are just temporary [24]. Eight mmHg is the typical intra-abdominal pressure. Alternatively, the pneumoperitoneum formed during laparoscopy imposes an increased pressure of roughly 14 mmHg. Numerous investigations have shown that pneumoperitoneum-induced hepatic hypoperfusion occurs. For example, a study by Jakimowicz *et al*. established that laparoscopic insufflation decreases portal venous flow [25]. ALT levels rise as a result of hepatic damage caused by this. However, ALP levels did not alter considerably, which is consistent with findings from other research like the one that.

CONCLUSIONS

Hematological parameter and liver enzyme values were significantly altered. To prevent more problems and morbidity, care must be taken to prevent these parameters from declining to risky levels. This study can also be used as a starting point for future research into how these parameters vary during the procedure depending on a variety of controllable factors and how best to minimize these variations.

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CONTRIBUTION OF AUTHORS

Dr. Amar Varshney involved in collection of articles, performing the study, statistical analysis manuscript writing, and final editing of manuscript. Dr. Vipin Kawatra involved in the review of literature, manuscript writing. Dr. K P Mishra and Dr. Surjeet K Dwivedi involved in final editing and proofreading of the manuscript.

CONFLICT OF INTEREST

Nil.

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