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Liver enzyme alterations after laparoscopic cholecystectomy (LC) – a study

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Abstract

The purpose of this study was to evaluate the effect of adoption of laparoscopic approach for cholecystectomy on liver function tests. This was a retrospective analysis of the data of 242 patients who had undergone laparoscopic cholecystectomy (LC). Liver function tests were not ordered after LC in routine surgical practice unless there was some specific reason in the post-operative period to initiate them. In only 14 (5.8%) patients , liver function tests had been advised and only 2 (0.8%) patients had shown a self-resolving rise in the level of enzymes. The study concurs with the results of other studies that a rise in liver enzymes after LC is transient and carries no clinical implications in patients with normal pre-operative liver functions.

Keywords: Laparoscopic cholecystectomy, Liver enzymes, Intraperitoneal pressure, Pneumoperitoneum

1. Introduction

Laparoscopic approach is the gold standard for cholecystectomy in present era and open approach is adopted only for those specific indications when laparoscopic approach may not be feasible[1].

The advantages of laparoscopic approach include: reduction in patient morbidity, shortening of post-operative hospital stay, and early return to normal activity. Laparoscopic cholecystectomy (LC) like all other laparoscopic procedures involves creation of pneumoperitoneum with carbon dioxide gas for creation of space for surgical manipulation. However, deleterious effects of laparoscopic approach on the cardiovascular and respiratory system resulting in several pathophysiological changes in the patients have been reported in the literature[2-4].

In recent years, many studies have disclosed transient elevation of liver enzymes after LC, even in patients without iatrogenic bile duct injury and various reasons have been postulated for the phenomenon[5,6].

It was against this background that the author audited the verified logbook data to study the trends in liver function tests after LC.

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2. Materials and Methods

The data of patients recorded in the verified log-books, who had undergone elective LC from January 2002 to December 2021 were analyzed retrospectively, using data extraction form designed specifically for the purpose. Only those cases were included, in which in which, the author had participated at the various levels of management. The data collected included demographics, pre-operative and post-operative blood tests, operation and pneumoperitoneum times, and intraoperative complications, if any. The data were recorded and analyzed in Microsoft Excel-2016 software and SPSS Statistics 28 (trial version) and the data were expressed as means and numbers (with percentages). For the analyzes, the significance level was set at $P < 0.05$.

The exclusion criteria included the patients who had documented history, physical examination findings or investigations suggestive of pre-operative impairment of liver functions, immunocompromise, significant systemic disorders, biliary obstruction, acute cholecystitis, and else conversion to open surgery. The cases with deficient records were also excluded from the study.

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3. Results

There were 242 patients (112 males and 130 females) and symptomatic cholelithiasis was indication of LC in 238 and symptomatic/large polyps were indication in four cases. The mean pressure of carbon dioxide used in the study was 14 mm of Hg with standard deviation of 0.61 mm of Hg. The mean operation time was 72 min (range: 51–103 min; SD 18) and mean pneumoperitoneum time was 49 minutes (range: 37–76 min; SD 14). Out of the 242 cases, 228 (94.2%) had no record of any liver function tests in the post-operative phase and only 14 (5.8%) had records of post-operative liver functions within 1st week of the post-operative phase. Two hundred and forty cases had been discharged by 2nd day of operation. In only 2 (0.8%) cases, there had been transient rise in liver enzymes delaying the discharge from hospital.

In the first case (32-year-old female), the procedure had lasted 102 min and pneumoperitoneum time was 74 min. On the 1st post-operative day, the patient had vomited multiple times and complained of pain (8/10 on Visual Analog Pain Scale) in the right upper quadrant of abdomen. Blood investigations had revealed rise in liver enzyme levels that deteriorated over the subsequent 24 h as shown in Table 1.

Magnetic resonance cholangiopancreatography had been advised in view of raised enzymes particularly GGT and the study had revealed post-cholecystectomy status with normal biliary tree as shown in Figure 1.

The patient had improved symptomatically and liver enzymes had normalized by 5th post-operative day.

Table 1. Perioperative liver enzyme test results in Case 1

Enzyme/ Unit	Normal values	Pre-operative	Post-operative 1	Post-operative 2	Post-operative 5
Total Bil/ mg/dl	0.2–1.2	0.4	1.1	1.7	0.9
AST/U/L	0.0–37.0	14.3	214.7	403.1	47
ALT/U/L	0.0–65.0	13.7	574.1	767.1	66
GGT/U/L	5.0–85	16.1	412	1058.7	15
ALP/U/L	50–260	64.4	226	258	234

Bil: Bilirubin, AST: Aspartate-aminotransferase, ALT: Alanine-aminotransferase, GGT: Gamma-glutamyltransferase, ALP: Alkaline phosphatase

In the second case (47-year-old male), the elective procedure had lasted 98 min and pneumoperitoneum time was 72 min. On the 2nd post-operative day, the patient had complained of pain (7/10 on Visual Analog Pain Scale) in the right upper quadrant of abdomen. Liver function tests had revealed raised liver enzyme levels that normalized over the subsequent 3 days as shown in Table 2, with the alleviation in symptoms.

The two patients had been periodically followed up for 12 months. They did not develop any further complications and had remained symptom free.

4. Discussion

The phenomenon of transient derangement of hepatic enzymes after laparoscopic procedures, in the absence of bile duct injury, has been reported in the literature and multiple causes have been proposed. Halevy *et al.* were the first to report this phenomenon when in 1994, they suggested increased intra-peritoneal pressure, squeezing of the liver by cranial retraction of the Gallbladder, electrocoagulation of the liver bed for hemostasis, manipulation of external biliary ducts, and the effects of general anesthesia to be the possible factors that lead to a rise in the level of liver enzymes[7]. Guven and Oral, however, argued that only the increased intra-peritoneal pressure due to pneumoperitoneum can be the possible causative agent for liver enzyme alterations as the rest of the factors mentioned by Halevy *et al.* also exist in open cholecystectomy (OC) without any documented increase

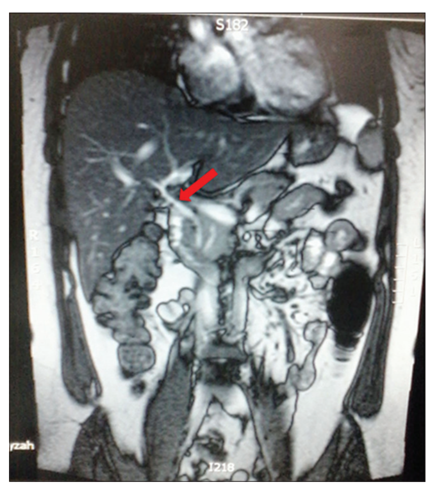

Figure 1. Magnetic resonance cholangiopancreatography showing post-cholecystectomy status and normal biliary tree (red arrow).

Table 2. Perioperative liver enzyme test results in Case 2

Enzyme/Unit of measurement	Normal values	Pre-operative day 1	Pre-operative day 2	Pre-operative day 5
Total Bil/mg/dl	0.2–1.2	0.6	2.1	1.2
AST/U/L	0.0–37.0	17.8	213.2	40
ALT/U/L	0.0–65.0	21.7	167.4	64.3
GGT/U/L	5.0–85	11.1	188.5	86.7
ALP)/U/L	50–260	67.6	303	254

Bil: Bilirubin, AST: Aspartate-aminotransferase, ALT: Alanine-aminotransferase, GGT: Gamma-glutamyltransferase, ALP: Alkaline phosphatase

in levels of hepatic enzymes[8]. Hasukic *et al.*[9] evaluated the effects of pneumoperitoneum on liver functions during LC and OC in a prospective study by enrolling 100 patients and subjecting half of the patients to each surgical operation (LC-50 and OC-50). The groups were otherwise similar in age, sex, weight, and height. Total bilirubin, alkaline phosphatase

(ALP), GGT, and LDH levels remained unchanged from the baseline in both the groups but a higher number of patients after LC showed increased values of alanine-aminotransferase (ALT) (26/50 vs. 5/50) and aspartate-aminotransferase (AST) (23/50 vs. 6/50). The difference was statistically significant ($P < 0.000$ for ALT and $P = 0.0004$ for AST), but the enzyme levels returned to normal limits by 48 h in all the patients. The results of the study indicated that LC is associated with transient rise in the levels of ALT and AST. The authors stressed that the liver function disturbances encountered after LC are self-limiting and not associated with any sort of morbidity if liver is otherwise healthy.

Tan *et al.*[10], Sakorafas *et al.*[11], Saber *et al.*,[12] and Koirala *et al.*[13] also in their respective studies attributed the rise in hepatic enzymes to the increase in the intra-peritoneal pressure and found the phenomenon to be transient as these enzymes return to the normal value within 7 days. These studies concluded that the hepatic enzyme changes are expected to be clinically silent in patients with normal pre-operative liver functions. Hasukic[14] compared the effects of low- and high-pressure pneumoperitoneum on liver functions and found that AST and ALT elevations were significantly higher in patients operated under high pressure (14 mmHg) pneumoperitoneum than those under low pressure (7 mmHg). Gupta *et al.*[15] also conducted a similar study with similar conclusions and suggested that low-pressure LC should be considered in all patients undergoing LC, especially those patients with compromised liver functions.

Giraudo *et al.*[16] conducted a study to compare hepatic enzyme alterations in conventional LC, gasless LC, and LC under low pressure (below 10 mmHg) pneumoperitoneum and found a significant rise in enzyme levels only after LC thereby proving the negative relationship of the raised intra-peritoneal pressure with hepatic perfusion.

Maleknia and Ebrahimi[17] in a study published in 2020 demonstrated a transient increase in liver function tests and bilirubin after LC. They enrolled 128 cases and found no significant difference in the serum levels of ALP on 1st and 2nd post-operative days ($P > 0.05$) but there was a statistically significant increase in the levels of total bilirubin, AST, and ALT ($P < 0.05$). However, the difference between the levels on 1st and 2nd post-operative days was significant only for total bilirubin. Compared to baseline levels, LDH had a significant increase after 2nd post-operative day ($P = 0.001$); but not after the 1st post-operative day ($P > 0.05$).

Morino *et al.*[18] investigated the effect of the duration of pneumoperitoneum at constant pressure and found that the elevations in AST and ALT levels become more significant when the duration of operation exceeds 60 min. Sharma *et al.*[5] also concluded, on the basis on their prospective study, that the magnitude of pressure of pneumoperitoneum has no significant any adverse effects on hepatic enzyme levels postoperatively but it is the time up to which pneumoperitoneum is retained cavity that is the cause of transient adverse effects.

The studies have proven that the transient elevation of serum liver enzymes does not have any apparent clinical implications and this explains the absence of post-operative liver function tests in 228 (94.2%) cases. However, if pre-operative liver functions are deranged, then care needs to be exercised and low-pressure/gasless laparoscopic surgery/open surgical interventions are preferred over conventional laparoscopic techniques[2-5,7]. A similar recommendation has been made by El-leathy *et al.* for pediatric patients[19].

The weaknesses of this study are that the source of data is the verified individual log-book and the number of patients is low. However, the results do concur with the findings of larger-magnitude institutional studies from other centers of the world.

5. Conclusion

The rise in hepatic enzymes after LC is transient and carries no clinical implications in patients with normal pre-operative liver functions. The liver enzyme changes are related to the duration of pneumoperitoneum and the magnitude of pressure. The liver enzyme alterations *per se* do not warrant assessment of post-operative liver function tests.

6. Informed Consent

The author expresses gratitude to the patients for allowing the usage of data and images for academic purposes including publication in a medical journal. The two patients, whose data have been cited in Figure 1 and Tables 1 and 2, were contacted and duly explained the purpose of the study and thereby the informed consent was sought.

7. Conflict of Interest

None.

8. Funding

None.

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