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# EFFECT OF LAPAROSCOPIC CHOLECYSTECTOMY ON LIVER FUNCTION: A SINGLE INSTITUTION STUDY AT A DISTRICT LEVEL HOSPITAL.

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**ABSTRACT**

**Background:** The introduction of minimal access surgery for gallbladder surgery has revolutionized the treatment of gallstones. The present study has been undertaken to see the changes in liver function tests (LFTs) after laparoscopic/open cholecystectomy and to know the clinical significances of such disturbances

**Aims and objectives:** To compare and correlate change in LFT in patients who underwent LC to those who underwent OC.

**Material and Methods :** The present study was conducted in Jawaharlal Lal Nehru Memorial hospital Srinagar in the department of surgery. A total 1800 patients of cholelithiasis were included in this study from Dec 2014 to Dec 2017. Three blood samples were taken, pre-operatively; 24 hours after surgery;72 hours after surgery for comparison of the enzyme level alterations.

**Results:** In LC patients, there were rise in the levels of serum bilirubin, AST and ALT after 24 hrs of surgery from the preoperative value and then again fall was noted after 72 hrs of surgery.

**Conclusions:** An elevation of serum liver enzymes after laparoscopic cholecystectomy occurs due to transient decrease in splanchnic blood flow. These changes return to normal in 3-4 days after procedure and they have no clinical consequences in patients with normal hepatic function.

**KEYWORDS** : Laparoscopy; Liver function tests; Open cholecystectomy

## Introduction

One of the most common surgery performed is cholecystectomy due to gall stone disease. This can be achieved either through open approach or by means of minimal access surgery. Laparoscopic cholecystectomy (LC) has become the gold standard for managing gall stone disease. Moreover the facilities, training of minimally invasive surgery is so widespread that more and more patients are getting benefitted by the advantages offered by minimally invasive approach. In minimally invasive approach gas is insuffulated into the peritoneal cavity during procedure with resultant increase in intra-abdominal pressure. The adverse physical effects of intra abdominal hypertension have been recently reviewed in detail (1). The effect of intra-abdominal pressure on blood flow to the liver in patients undergoing laparoscopic cholecystectomy using a laser-Doppler technique has been studied. Both hepatic and gastric microcirculation fell significantly with a pneumoperitoneum of 12 mmHg, indicating splanchnic ischemia (2). There have been conflicting reports of any significant rise in liver function parameters following LC, few studies have shown the serum level of certain liver enzymes rise markedly in patients which were preoperatively normal implying hepatic hypo perfusion. (3-5)

The present study was conducted in Jawaharlal Lal Nehru Memorial hospital Srinagar in the department of surgery. This hospital has the distinction of only hospital run by department of health to have a minimal access unit. LC has been performed routinely in our hospital for last 12 years. On an average 15-20 LC are routinely performed each week in our hospital at present. Due to increased avenues for training in minimal access, open cholecystectomy (OC) has been near completely been replaced by LC in our hospital. The present study was conducted to compare any difference in the post operative changes in the liver function enzymes in patients undergoing OC or LC and the significance there of.

## Material and Methods

A total 1800 patients of cholelithiasis were included in this study from Dec 2014 to Dec 2017. OC was performed in 856 and LC in 944 patients in the study. Patients from 20 to 70 years of age were included in this study. Those cases diagnosed as pregnancy, common bile duct (CBD) stones, high levels of enzymes before operation, with biliary injury, positive serology for hepatitis B or C virus, those who had undergone ERCP or had cirrhosis on liver biopsy were excluded from the study. On admission, a detailed history of each patient was taken and a thorough general and local physical examination was done. The routine investigations including baseline LFTs, ultrasonography (USG) was performed in all cases. Cholecystectomy was performed under general anesthesia with intravenous anesthesia induction followed by continuous volatile anesthesia under mechanical ventilation. The study was approved by the institutional ethics committee.

LC was performed at 12-14 mmHg of pneumoperitoneum was created and maintained by intra peritoneal CO2 insufflation with an automatic insufflator. Patient head was elevated with a right side up tilt. Standard four ports were made; two 10 mm port-umbilical site, epigastrium region and two 5 mm port; right lateral, another in subcoastel region two fingers below midclavicular area. Pneumoperitoneum was created. Calot's triangle identified and clip was applied to the cystic duct and cystic artery. Anatomy was delineated in all cases with care taken not to injure the CBD. Gall bladder was removed from the liver bed with the help of diathermy. OC was performed using a right subcoastel incision and abdomen was opened in layers. Gall bladder recognized cystic duct and artery ligated separately. Gall bladder was removed from the liver bed with the help of the diathermy. Third generation antibiotic ceftriaxone + sulbactum were used for 2 days Paracetamol was used for analgesia on first day and SOS on subsequent days.

Blood samples were taken from the superficial vein before the operation as a part of routine pre-operative preparation and 24 hours after the operation for comparison of the enzyme level alterations. Third blood sample was taken after 72 hours. Biochemical analyses for enzymes were done using the same analyzer. The accepted normal values are; for AST, 5-40 U/L (by IFCC kinetic method), for ALT, 5-35 U/L (by IFCC kinetic method), for serum bilirubin, 0.2-1 mg/dL (Jendrassik and Grof method), for ALP, 28-112 U/L (by IFCC kinetic method using P-nitrophenylphosphate). Enzyme levels were calculated as mean ± standard deviation (SD)

for both groups and for both preoperative and post operative values. Statistical analysis included chi-square test, paired t-test, ANOVA test was done. All the observations were recorded, procedure was explained to the patient and separate consent was taken.

**Observations**

The mean age of the patients in the LC and OC was 40.2 and 47.4 years respectively (Table 1). The mean gender preponderance of the male: female ratio in the LC and OC was 1:8.1 and 1:7.2 respectively. Both the groups were comparable in age, sex and duration of surgery. Use of post operative analgesia and hospital stay was significantly less in LC group ($p<0.05$). The most common clinical symptom was dyspepsia which was seen in all the cases of LC and in 82% of cases in OC. Pain right hypochondrium was present in 86% of cases in both LC and OC. Nausea and vomiting were observed in 78% of the cases in LC and 74% cases in OC. Previous history for admission was seen in similar number of patients in LC (62%) and OC (68%) groups. In both groups, the changes occurring in liver enzymes pre- and post-operative were noted.

In LC the duration of surgery was taken from the time of insertion of veress needle to the time of applying last stitch while in OC group it was taken from the time of skin incision to completion of skin suturing. The mean duration of surgery in LC group was 55.4 minutes and in OC group the mean duration of surgery was 66.8 minutes ( $P>0.05$)

There was rise in the mean value of serum bilirubin AST and ALT after 24 hrs of surgery from the preoperative value and then again fall (near to normal value) after 72 hrs of surgery except in the mean value of ALP (Table 2, Figure 1). The study showed no significant change in serum bilirubin from preoperative (0 hrs) value to postoperative value (24 hrs). In LC group the serum levels of AST and ALT showed significant rise after 24 hrs of surgery ($P=0.0001$) and non significant rise after 72 hrs of operation whereas ALP showed no significant rise in both after 24 and 72 hrs of surgery (Table 3).In OC group there were slight variations in the mean value of all the liver enzymes (which were within the normal range) but there were no significant rise in the mean value of them after 24 hrs of surgery (Figure 1). There was no significant difference in serum bilirubin, AST, ALT and ALP after 24 and 72 hrs of surgery from preoperative value as the $P>0.05$ in all the cases.(Table3)

In our study it was observed that the patient undergoing LC with minimum duration of surgery (40 min) has less variation in LFT (serum bilirubin, AST, ALT) than those where the duration of surgery was more (90 min). The overall rise in LFT parameters in OC group was quite low as compared to the LC group. The P value was significant when comparison was made between the mean values of AST and ALT after 24 hrs of surgery in LC and OC group.

**Discussion**

Cholecystectomy is one of the commonly performed surgical procedure and laparoscopic approach is considered to be the gold standard for this procedure. Usually pneumoperitoneum is sustained at a pressure of 12-14 mmHg in LC, which may result in variety of abnormal physiological changes involving the respiratory, cardiovascular, and hepatorenal systems. The increased intra abdominal pressure due to pneumoperitoneum causes decreased blood flow lead to adverse glomerular filtration and tubular functions which produce abnormal biochemical parameters (2,6). By keeping the low range of pressure 8-10 mmHg for pneumoperitoneum has been shown to decrease the adverse physiological changes without affecting the outcome of surgery, in present study pressure was kept at 12-14 mm Hg.

Tan et al. (7) found statistically significant increased levels of hepatic transaminases during the first 48 hours post operation in patients undergoing LC compared to patients having open procedures. Similar effect was seen to be present in patients undergoing colon resection in their study. The degree of change in ALT following the operations was greater in LC patients than that in OC patients ($P<0.05$, D1; $P<0.01$, D2). The change of AST due to the operations was also greater in LC patients than that in OC patients ($P<0.05$, D1; $P<0.01$, D2). They concluded that laparoscopic surgery may not be optimal for patients with pre-existing liver impairment. Carboperitoneum is the most common cause for transient elevation of hepatic transaminase after laparoscopic surgery.(7) Omari and Bani-Hani (8) investigated the serum levels of eight parameters of liver function both before and 24 hrs after surgery in 142 consecutive patients who underwent LC, 23 patients who underwent OC and in 25 patients who underwent a conventional hernia repair. The intra abdominal pressure was maintained at 12 mmHg of carbon dioxide. They found that 83% of the patients showed more than 100% increase in atleast one parameter, 43% showed an increase in 2 or more parameters and 23% showed an increased in 3 or more parameters. Another prospective study was done to investigate the effect of abdominal perfusion pressure on LFTs after LC with intra abdominal pressure of 12 mmHg. They reported that 37.5% showed more than 100% increase in at least one parameter of liver function.(9) Negative effects of pneumoperitoneum on hepatic blood flow was most probable reason for subclinical hepatic dysfunction after LC (9). Ahmad noted very little or no change in the postoperative value of ALP when CO2 pressure was kept 12-15 mmHg. It is evident that the level of alteration is different for each enzyme and that most of the cases fall into the group that shows up to a 50% increase in the LFTs. This change can be labelled as mild elevation and is considered negligible by many. Increased bilirubin levels were seen in a fraction of patients; ALP was not found to increase to such a high level in our study. Mild to moderate elevation in LFTs may not be associated with any deleterious effect and in the absence of clinical indications, routine postoperative or preoperative LFT is unnecessary (10). Marakis et al. (11) reported the mean duration of surgery in LC was 55 min (range, 40-70 min). In our study, the mean duration of surgery in LC group and OC group was comparable at 55.4 minutes and 66.8 minutes respectively, which was non-significant ($P>0.005$) . In LC group we found that lesser operative time was associated with less elevation of liver enzymes.

In our study,exclusion criteria to eliminate known causes of liver function disturbances (CBD pathology and chronic liver diseases) was adopted. This was done in order to attribute any disturbances in liver function to the laparoscopic procedure itself. In present study the rise in AST and ALT were seen in >90% of the LC patients and the doubling in AST and ALT were seen in 18% and 22% patients respectively whereas 68% and 65% patients respectively showed rise of 50-100% after 24 hrs of surgery. The mean rise in mean values of enzymes in our study was similar to the studies of Guven et al. (12) and Sakorafas et al. (13) and Singal et al (14)(Table 4). In our study, the mean value of ALP did not show any change and was within normal limits. Mohamed et al. (15) in his study observed elevation in the levels of serum ALT and AST within 24-48 hours following operations in laparoscopic maneuver for undescended testicle (LMUDT patients compared with those in open maneuver for undescended testis (OMUDT) patients. The degree of change in ALT following LMUDT was greater than OMUDT and this difference was statistically significant ($P<0.05$). On the seventh day following the operations, both enzymes returned to normal value in LMUDT, and OMUDT patients. In his study, other liver function indices such as bilirubin, ALP, lactic dehydrogenase (LDH), total protein (TP) and gamma glutamyltransferase (GOT) also showed derangements. (15). These changes appear transient as the raised liver enzymes and bilirubin levels returned to their prospective values or within normal limits after a gap of 72 hours. However they may still cause worry to the surgeon regarding the integrity of the biliary tree. In our study ALP has remained normal and thus will be important in drawing a conclusion and persistent elevation of this parameter may be suggestive of breach in integrity of biliary tree before resorting to further intervention.

Our study has shown that there is disturbance of LFT following LC which is not related to the age, sex in relation to laparoscopy and

that pneumoperitoneum is the only variable not present in OC group. An intra-abdominal pressure of 12-14 mmHg of CO2 is higher than normal portal blood pressure of 7-10 mmHg, and is therefore capable of reducing portal blood flow and of causing alteration of the hepatic function. There is a possibility of free radical generation at the end of laparoscopic procedure due to ischemia-reperfusion phenomenon and may lead to transient hepatic parenchymal injury. One other possibility is thermal injury to hepatic parenchyma due to cautery use.

## Conclusions

Carboperitoneum, surgical manipulations, diathermy, patient position and arterial injury are probably the contributory factors for liver enzymes changes. Prolonged duration of Pneumoperitoneum results in increased levels of liver enzymes. These changes are transient and return to normal in 3-4 days after procedure and they have no clinical consequences in patients with normal hepatic function but they may still cause worry to the surgeon regarding the integrity of biliary tree. The low-pressure pneumoperitoneum could be a reasonable alternative.

**Table 1: Comparison of patients of LC and OC**

| Parameter | LC (956) | OC (844) | Value of difference (p value) |
|---|---|---|---|
| Age (Mean±SD) | 40.2±10.6 | 47.4±11.2 | P>0.005 |
| Sex (Male:Female) | 1:8.1 | 1:7.2 | P>0.005 |
| Duration of surgery | 55.4±14.2 min | 66.8±8.6 min | P>0.005 |

**Table 2 Changes in LFT in LC and OC (Mean distribution of LFT parameters)**

| Parameter | 24 hrs before surgery | | 24 hrs after surgery | | 72 hrs after surgery | |
|---|---|---|---|---|---|---|
| | LC | OC | LC | OC | LC | OC |
| Serum Bilirubin (mg/dL) | 0.58±0.1 | 0.55±0.1 | 0.93±0.3 | 0.76±0.2 | 0.61±0.1 | 0.52±0.1 |
| AST (IU/L) | 32.2±7.2 | 30.8±6.4 | 74.6±11.4 | 32.1±6.8 | 33.0±7.6 | 31.6±6.6 |
| ALT (IU/L) | 31.6±6.9 | 30.4±6.2 | 73.4±11.1 | 30.8±7.2 | 31.8±6.6 | 30.6±6.2 |
| ALP (IU/L) | 67.6±14.8 | 66.7±14.2 | 66.4±15.0 | 68.1±15.6 | 67.8±16.8 | 67.4±15.4 |

LFT, liver function test; LC, laparoscopic cholecystectomy; OC, open cholecystectomy; AST, aspartate transaminase; ALT, alanine transaminase; ALP, alkaline phosphatase.

**Table 3 Statistical analysis of liver enzymes in LC and OC patients**

| Parameter | P Value | |
|---|---|---|
| | LC | OC |
| Serum bilirubin 0-24 hrs | 0.098$^{NS}$ | 0.254$^{NS}$ |
| Serum bilirubin 0-72 hrs | 0.284$^{NS}$ | 0.834$^{NS}$ |
| AST 0-24 | 0.0001$^{Sig}$ | 0.846$^{NS}$ |
| AST 0-72 | 0.124$^{NS}$ | 0.246$^{NS}$ |
| ALT 0-24 | 0.0001$^{Sig}$ | 0.148$^{NS}$ |
| ALT 0-72 | 0.076$^{NS}$ | 0.125$^{NS}$ |
| ALP 0-24 | 0.388$^{NS}$ | 0.083$^{NS}$ |
| ALP 0-72 | 0.186$^{NS}$ | 0.544$^{NS}$ |

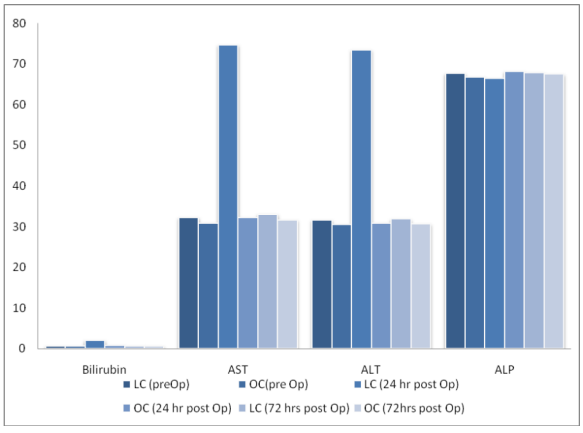
Sig, significant; NS, non significant; LC, laparoscopic cholecystectomy; OC, open cholecystectomy; AST, aspartate transaminase; ALT, alanine transaminase; ALP, alkaline phosphatase.

**Table 4 : Mean values of postoperative enzymes changes after LC in various studies**

| Author (reference no.) | Enzymes | Pre op mean value (IU/L) | Post op mean value (IU/L) |
|---|---|---|---|
| Sakorafas et al (13) | AST | 22.3±12.1 | 87.1±24.2 |
| | ALT | 21.6±13.4 | 82.8±19.1 |
| Marakis et al (11) | AST | 24.36±24.01 | 55.07±40.39 |
| | ALT | 31.88±74.77 | 61.62±54.87 |
| Guven et al (12) | AST | 22.76±6.44 | 61.72±28.13 |
| | ALT | 21.55±8.92 | 60.30±32.17 |
| Singal et al(14) | AST | 27.0±8.1 | 72.9±13.1 |
| | ALT | 26.0±8.9 | 72.4±12.9 |
| Our study | AST | 32.2±7.2 | 74.6±11.4 |
| | ALT | 31.6±6.9 | 73.4±11.1 |

LC, laparoscopic cholecystectomy; OC, open cholecystectomy; AST, aspartate transaminase; ALT, alanine transaminase

**Figure 1: Changes in LFT in LC and OC patients at 24 hrs and 72 hrs after surgery**

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