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**Original Research Article**

# Changes in liver function tests in laparoscopic cholecystectomy versus open cholecystectomy in a tertiary care center

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## ABSTRACT

**Background**: Gallstone disease is a major health problem worldwide particularly in the adult population. The traditional open cholecystectomy (OC) has been replaced by laparoscopic cholecystectomy (LC), with LC becoming the gold standard for management of gall stone disease. Elevation in the levels of liver enzymes following LC is a major cause of concern. Hence the present study determines and compares the changes in liver function tests following Laparoscopic cholecystectomy with open cholecystectomy, as well the significance of these changes is studied.
**Methods**: A total of 100 patients with symptomatic cholelithiasis were selected in the study from October 2020 to October 2022. The cases were randomly divided into two groups, Group LC and Group OC. The blood samples were collected for Liver Function Tests (LFT)-Pre-operatively, Post-operative Day (POD)-1, POD-2 and POD-7 and enzyme alterations were studied.
**Results**: The study demonstrated increase in levels of Serum AST, ALT, ALP in LC group on POD-1 and POD-2 with $p<0.001$, while the levels returned to reference values on POD-7. In OC group the increase in levels of Serum AST, ALT, ALP were observed on POD-1 only with $p<0.05$ and the levels returned to normal values by POD-2 of majority of patients. The changes in LFT were higher in LC group compared to OC group (where the changes were slight).
**Conclusions:** Cholecystectomy especially laparoscopic, leads to transient significant hepatic enzyme alterations which can be attributed to CO2 pneumoperitoneum, surgical manipulations, diathermy and arterial injury. These derangements at times may be of concern to surgeons for its implication to the integrity of biliary tract.

**Keywords**: Liver Function Tests, Laparoscopic cholecystectomy, Tertiary center, Pneumoperitoneum

## INTRODUCTION

Gallstone disease is a major health problem worldwide particularly in the adult population. The traditional open cholecystectomy (OC) has been replaced by laparoscopic cholecystectomy (LC) with LC becoming the gold standard for management for gall stone disease. The major benefits of Laparoscopic cholecystectomy include: minimal tissue trauma, subsequent decreased incidence of intra-abdominal adhesions, less post-operative pain, decreased duration of hospital stay, early resumption to work, improved cosmesis and quality of life.[1] With so many benefits of LC there are some drawbacks as well. One such drawback is the alterations in the Liver Function Tests (LFT) which is a major cause of concern. The slight changes in liver function tests after OC has been studied widely, while in LC not much of studies have been done. Some studies attributed these changes to hepatocellular dysfunction secondary to one or combination of CO2 pneumoperitoneum, diathermy extruding liver, branch of

the hepatic artery injured and general anesthesia.[2] CO2 pneumoperitoneum is among the main factor for causing this rise in LFT post LC. The elevation however is usually transient, and the LFT return to normal levels without any intervention.[3,4] In some studies where preoperative liver function tests were evaluated as one of the possible predictive factors for the conversion of a laparoscopic procedure to open cholecystectomy; it was found that impaired LFT were not associated with an increased risk of conversion. Hence our study is aimed to determine and compare the changes in liver function tests before and after cholecystectomy (laparoscopic and open cholecystectomy) as well compare the changes in LC vs OC and to know the clinical significance of such changes.

### *Aims and objectives*

Aim and objectives of current study were; to perform a prospective observational study at a tertiary care centre in eastern India studying. To investigate the changes in liver function tests during post-operative periods (Day-1, Day-2 and Day-7) in both laparoscopic cholecystectomy and open cholecystectomy and to compare the results, and to determine the significance of these alterations in patients. The liver function tests included were; aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and serum bilirubin (S. Bilirubin).

## METHODS

The prospective study was conducted at the department of surgery, Patna medical College and Hospital after taking all the permissions from the institutional ethics committee of Patna medical college and hospital. The due permissions from the head of department of surgery was also obtained.

### *Study subjects and duration*

The patients admitted in the general surgery department from the surgical outdoor as well the surgery emergency for symptomatic cholelithiasis. The study took place from October 2020 to October 2022.

### *Sample size*

A total number of 100 patients diagnosed as cholelithiasis were included in the study. These cases were randomly divided into two groups (LC and OC) consisting of 50 cases each after signing well explained written consent to be the part of the study.

Laparoscopic Cholecystectomy was performed in group LC patients and Open Cholecystectomy was done in group OC patients. Laparoscopic cholecystectomy was carried out using the standard four port technique and a pneumoperitoneum between 10-12 mmHg was maintained. Open cholecystectomy was performed with a right subcostal incision. A standardised institutional anaesthetic drug protocol was used for all patients in either group. Four blood samples were taken: pre-operatively; POD -1 (after 24 hours of surgery); POD-2 of surgery, POD-7 of surgery for comparison of the enzyme level alterations.

### *Inclusion criteria*

Inclusion criteria for current study were; patients between the age group of 18 to 70 years, patients with symptomatic gall stone disease and patients who gave the written consent to be the part of the study group.

### *Exclusion criteria*

Exclusion criteria for current study were; Patients below 18 years and above 70 years. Patients with abnormal liver function tests, patients with severe co-morbid conditions like cardio, respiratory and renal disease, immuno-compromised patients, patients with jaundice, chronic liver disease suspects, patients having bile duct pathology, patients who had undergone conversion to open surgery, patients who had undergone ERCP within one week before surgery and patients having haematological disorders.

### *Statistical method*

Data collected were calculated as mean±SD for both groups pre and postoperatively. For intergroup analysis of data, Student's independent t-test was employed. Intra-group analysis of data was carried by paired t-test. P values less than 0.05 was considered statistically significant.

## RESULTS

A total of 100 patients were included in our study out of which 12 percent were males and 88 percent were females (group LC having 10% males and 90% females; group OC having 14 % males and 86 % females) as shown in (Table 1).

**Table 1: Sex distribution of patients undergoing LC and OC.**

| Parameters | Group-LC | | Group-OC | | |
|---|---|---|---|---|---|
| **Sex** | **N** | **%** | **N** | **%** | **Total** |
| Male | 5 | 10 | 7 | 14 | 12 |
| Female | 45 | 90 | 43 | 86 | 88 |
| Total | 50 | 100 | 50 | 100 | 100 |

The maximum cholecystectomy was performed in the age group 41-50 years (those undergoing LC- 21 to 30 years and OC-41 to 50 years) as shown in (Table 2). To get the intragroup changes in LFT the post-operative enzyme levels were compared with pre-operative values by comparing standard means in the both groups as shown in (Table 3). At POD-1 in the Group LC, the changes in AST, ALT and ALP from preoperative levels was found to be statistically significant ($p<0.05$). In Group OC at POD-1, the change in AST, ALT and ALP was found to be

statistically significant (p<0.05) from the preoperative levels.

**Table 2: Age distribution of patients in group LC and group OC.**

| Parameters | Group-LC | | Group-OC | | |
|---|---|---|---|---|---|
| **Age groups (years)** | **N** | **%** | **N** | **%** | **Total** |
| 21-30 | 18 | 36 | 6 | 12 | 24 |
| 31-40 | 16 | 32 | 5 | 10 | 21 |
| 41-50 | 6 | 12 | 25 | 50 | 31 |
| 51-60 | 6 | 12 | 9 | 18 | 15 |
| 61-70 | 4 | 8 | 5 | 10 | 9 |

On POD-2 in Group LC, the change in AST, ALT and ALP was found to be (p<0.05) statistically significant from preoperative levels. No significant change (p>0.05) in AST, ALT and ALP and S. Bilirubin were found in Group OC when compared from preoperative levels.

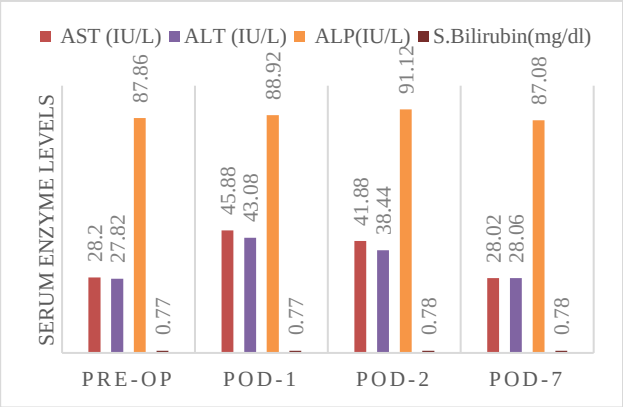


**Figure 1: Changes in LFT in Laparoscopic cholecystectomy.**

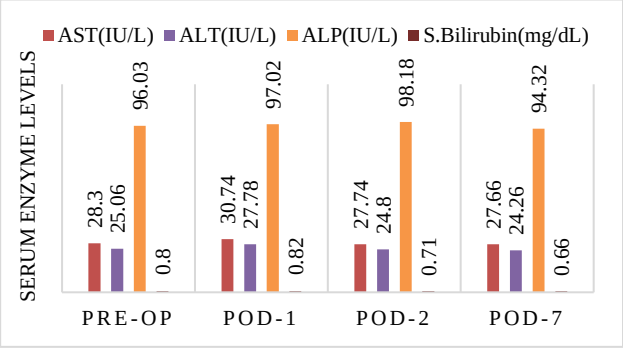


**Figure 2: Changes in LFT in open cholecystectomy.**

On POD-7, in Group LC and OC no significant change (p>0.05) in levels of AST, ALT, ALP and S. Bilirubin was found from pre-operative levels. The S. Bilirubin levels in Group LC and OC on POD- 1, 2 and 7 were not found significant (p>0.05) on comparing from preoperative values.

The intragroup changes in LFT indicated a much higher increase in the levels of hepatic enzymes (AST, ALT and ALP) in group-LC on POD-1 as compared to POD-2 from pre-operative (pre-op) levels which reverted to reference values by POD-7 as shown in (Figure 1). While in group-OC the changes in enzyme levels (AST, ALT and ALP) from the pre-operative values were slight, with majority of patients having LFT in normal range by POD-2 as depicted in (Figure 2). The intergroup changes in LFT i.e., LC vs. OC. Preoperatively the serum enzyme levels in Group LC and OC were almost similar (Table 4). At POD-1 and POD-2, the mean difference in the values of AST and ALT were statistically significant (p<0.05) between the two groups. The difference in ALP and S. Bilirubin was found to be statistically insignificant (p>0.05). On POD-7 the mean difference between Group LC and OC in AST, ALT, ALP and S. Bilirubin were insignificant.

## DISCUSSION

Out of 100 patients who were included in our study for cholecystectomy 12 % were males and 88 % were females. The results suggested that female gender were more predisposed to gallstone disease owing to the fact that estrogen increases biliary cholesterol secretion causing cholesterol supersaturation of bile.[5] In our study, the intragroup changes in LC group denoted increase in the levels of Serum AST, ALT and ALP on POD-1 from pre-operative values; which was much higher as compared to that on POD-2. The values returned to normal by POD-7. In OC group the levels of AST, ALT and ALP also slightly increased from pre-operative values on POD-1 with return to normal levels on POD-2 of majority of patients. The results we got were similar to the other studies including that done by Singal et al in 2015 where he found out that 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 (near to normal value) after 72 hrs of surgery. In 2019, *Bellad et al* conducted a study and found out that the level of serum AST, ALT, bilirubin (total) and ALP were increased significantly during the first 24 hrs postoperatively after laparoscopic cholecystectomy as compared to baseline values and the levels of serum albumin and total proteins were decreased, whereas in our study insignificant changes in S. bilirubin levels were found.[7]

The studies supporting the intergroup changes included that done by Hasukic et al where he found out that a higher number of patients had increased values of ALT (26/50 vs. 5/50) and AST (23/50 vs. 6/50) in LC compared to OC group at 24 hr. Although the difference was statistically significant (p<0.000 for ALT and p = 0.0004 for AST), the increased level decreased at 48 hr compared to 24 hr, whereas in our study the statistically significant (p<0.05) increase in values of both AST and ALT in LC compared to OC was found to be increased both at 24hr (POD-1) as well at 48hr (POD-2), while not on POD-7.

**Table 3: Intra-group change in serum levels (from pre-operative values) of study population (paired 't' test).**

| Parameters | Group-LC | | | | Group-OC | | | |
|---|---|---|---|---|---|---|---|---|
| | Mean | SD | T value | P value | Mean | SD | T value | P value |
| **POD-1** | | | | | | | | |
| AST (IU/l) | 45.88 | 12.42 | 15.18 | 0.0001$^{S}$ | 30.74 | 5.62 | 11.01 | 0.0001$^{S}$ |
| ALT (IU/l) | 43.08 | 9.61 | 16.36 | 0.0001$^{S}$ | 27.78 | 6.38 | 10.71 | 0.0001$^{S}$ |
| ALP (IU/l) | 88.92 | 26.28 | 7.00 | 0.0001$^{S}$ | 97.02 | 15.43 | 2.51 | 0.01$^{S}$ |
| S. Bilirubin (mg/dl) | 0.77 | 0.19 | 0.44 | 0.65$^{NS}$ | 0.82 | 0.15 | 1.9 | 0.05$^{NS}$ |
| **POD-2** | | | | | | | | |
| AST (IU/l) | 41.88 | 11.99 | 12.45 | 0.0001$^{S}$ | 27.74 | 5.28 | 1.55 | 0.13$^{NS}$ |
| ALT (IU/l) | 38.44 | 8.28 | 15.24 | 0.0001$^{S}$ | 24.80 | 5.93 | 1.05 | 0.30$^{NS}$ |
| ALP (IU/l) | 91.12 | 26.83 | 7.35 | 0.0001$^{S}$ | 98.18 | 14.77 | 0.14 | 0.88$^{NS}$ |
| S. Bilirubin (mg/dl) | 0.78 | 0.18 | 1.09 | 0.27$^{NS}$ | 0.71 | 0.17 | 2.2 | 0.1$^{NS}$ |
| **POD-7** | | | | | | | | |
| AST (IU/l) | 28.02 | 8.23 | 0.28 | 0.7803$^{NS}$ | 27.66 | 6.10 | 1.53 | 0.13$^{NS}$ |
| ALT (IU/l) | 28.06 | 6.32 | 0.45 | 0.65$^{NS}$ | 24.26 | 5.93 | 1.44 | 0.155$^{NS}$ |
| ALP (IU/l) | 87.08 | 25.37 | 3.59 | 0.06$^{NS}$ | 94.32 | 15.17 | 1.69 | 0.09$^{NS}$ |
| S. Bilirubin (mg/dl) | 0.78 | 0.19 | 1.69 | 0.09$^{NS}$ | 0.66 | 0.21 | 2.4 | 0.08$^{NS}$ |

*S= significant, *NS= Non-Significant, * t = t value , *p= p value , *SD = Standard Deviation

**Table 4: Pre-operative as well post-operative comparison of serum enzyme levels of Group-LC vs Group-OC (intergroup change).**

| Parameters | Group-LC | | Group-OC | | | |
|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | T value | P value |
| **Pre operative** | | | | | | |
| AST (IU/l) | 28.2 | 8.91 | 28.3 | 5.88 | 0.06 | 0.9$^{NS}$ |
| ALT (IU/l) | 27.82 | 7.56 | 25.06 | 6.51 | -1.9 | 0.06$^{NS}$ |
| ALP (IU/l) | 87.86 | 27.03 | 96.03 | 15.23 | 1.8 | 0.06$^{NS}$ |
| S. Bilirubin (mg/dl) | 0.77 | 0.19 | 0.80 | 0.16 | 0.8 | 0.3$^{NS}$ |
| **POD-1** | | | | | | |
| AST (IU/l) | 45.88 | 12.42 | 30.74 | 5.62 | -7.85 | 0.001$^{S}$ |
| ALT (IU/l) | 43.08 | 9.61 | 27.78 | 6.38 | -9.34 | 0.001$^{S}$ |
| ALP (IU/l) | 88.92 | 26.28 | 97.02 | 15.43 | 1.8 | 0.06$^{NS}$ |
| S. Bilirubin (mg/dl) | 0.77 | 0.19 | 0.82 | 0.15 | 1.46 | 0.14$^{NS}$ |
| **POD-2** | | | | | | |
| AST (IU/l) | 41.88 | 11.99 | 27.74 | 5.28 | -7.63 | 0.001$^{S}$ |
| ALT (IU/l) | 38.44 | 8.28 | 24.80 | 5.93 | -9.47 | 0.001$^{S}$ |
| ALP (IU/l) | 91.12 | 26.83 | 98.18 | 14.77 | 1.6 | 0.11$^{NS}$ |
| S. Bilirubin (mg/dl) | 0.78 | 0.18 | 0.71 | 0.17 | -1.99 | 0.07$^{NS}$ |
| **POD-7** | | | | | | |
| AST (IU/l) | 28.02 | 8.23 | 27.66 | 6.10 | -0.24 | 0.80$^{NS}$ |
| ALT (IU/l) | 28.06 | 6.32 | 24.26 | 5.93 | -2.1 | 0.09$^{NS}$ |
| ALP (IU/l) | 87.08 | 25.37 | 94.32 | 15.17 | 1.7 | 0.08$^{NS}$ |
| S. Bilirubin (mg/dl) | 0.78 | 0.19 | 0.66 | 0.21 | -0.44 | 0.65$^{NS}$ |

Asghar et al in his study found out that there was increase in AST, ALT, bilirubin and LDH, while no remarkable change in serum ALP was observed in the LC group in comparison to the OC group 24 hr after surgery, whereas in our study no remarkable changes on comparing the LC with OC group was found in both ALP and S. Bilirubin throughout the study. *Tan et al* in 2003, found out that the level of serum ALT and AST increased significantly during the first 48 hr post operations in both LC and LCR (laparoscopic colorectal cancer resection) patients. However, no significant change of the serum liver enzymes was detected in both OC and OCR (open colorectal cancer resection) patients. As a result, there was statistically significant difference in change of both ALT and AST levels between LC and OC patients and LCR and OCR patients, respectively. By the 7th day post operation, the level of both enzymes returned to normal values in LC,

OC and OCR patients. All the above studies also concluded that the change was transient in enzyme levels after laparoscopic or open cholecystectomy and major causative factor would be the CO2 pneumoperitoneum. The cause of changes in liver function tests were investigated in various studies in which the findings revealed that the main concern was the intraperitoneal pressure created during LC due to pneumoperioneum creation which was higher than the pressure in the portal venous system which in turn blocked portal circulation and reduced portal flow up to 50% and resulted in depression in the functions of hepatic reticular endothelial system[10]. Some studies proved that the variations in liver function tests were directly proportional to the duration and pressure used for pneumoperitoneum.[11] This suggested that LC is not the choice of treatment in patients with severe liver diseases or liver cirrhosis because it can det In our study the intra-abdominal pressure was kept between 12-14 mmHg and since CO2 pneumoperitoneum was used so this might be one of the reason contributing to the findings.

In our study, almost all the patients had changes in serum levels of liver enzymes post cholecystectomy. The other mechanism might be anaesthesia induced hepatic hypoperfusion.[13,14] But in the present study the same anaesthesia protocols were used in both the LC and OC patients, therefore this would have unlikely led to the enzyme changes we observed. Other possible causes of these alterations might be liver tractions, electro cauterization and manipulation of duct.

The limitations of this study include the small sample size of the subjects which was due to factors such as choice of patients to defer acute immediate surgery to a more planned one and refusal of consent. The study duration includes the period when first wave of COVID-19 was at its peak and there was a total lockdown. This affected the accessibility of patients to come to tertiary care centre. During the pandemic the surgeries were being done only in those case where it was utmost necessary. Another limitation is the fact that Patna medical college and hospital is a post graduate training institute and therefore in many cases laparoscopic cholecystectomy was being assisted by post graduate residents which might have led to slightly elevated surgery time. This increase in duration of surgery is turn a causative factor for alteration in LFT after cholecystectomy.[11]

## CONCLUSION

To conclude, our study shows that cholecystectomy, either Laparoscopic or Open cholecystectomy leads to transient and significant changes in hepatic enzyme levels (AST, ALT and ALP). LC causes more alterations compared to OC. The changes in liver function tests after surgery are self-limiting with no associated morbidities in any patient with normal LFT and these alterations return to reference values within 7 days of operation. The possible causes of these alterations might be liver tractions, electro cauterization or manipulation of duct. The additional major positive factor in the Laparoscopic cholecystectomy group seems to be CO2 pneumoperitoneum (pressure as well as the duration). Nevertheless, these results indicate that, if the patient's preoperative liver function is very poor (due to some liver pathology or other pathologies) then laparoscopic procedure may not be the optimal choice or if done then one should be very cautious.

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