

## Effect of Age of Patient and Duration of Laparoscopic Cholecystectomy on Liver Function Tests

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### Abstract

**Background:** Laparoscopic Cholecystectomy is one of the most commonly performed general surgical procedures and entails creation of pneumoperitoneum with pressures averaging 12 mmHg. It is known that creation of pneumoperitoneum artificially increases the intra-abdominal compartment pressure. Increased intraperitoneal pressure exerts several undesirable effects on visceral perfusion. The present study was conducted to observe the effects of Laparoscopic cholecystectomy, performed at pneumoperitoneal pressure of 12 mmHg, on liver function tests in Cholelithiasis patients depending on age and duration of surgery. All patients enrolled in the study had normal liver functions preoperatively.

**Aims and objectives:** To statistically compare preoperative levels of Serum Bilirubin, SGOT, SGPT and Serum Alkaline phosphatase with post operative levels of These parameters 24 and 72 hours after surgery in three groups of patients defined as young, elderly, and middle aged. LFT data of patients were also compared by grouping them into two categories defined by duration of surgery being less than or exceeding 1 hour.

**Materials and methods:** The present study was conducted at the Department of Surgery, of a zonal hospital in Pune, India. A total of 100 patients diagnosed with Cholelithiasis who underwent Laparoscopic cholecystectomy were studied from 26 Oct 2022 till 31 Oct 2023. The studied population consisted of patients from both genders, between 18 and 75 years of age. Patients were preoperatively grouped for comparison into three categories, vis. young (18-39 years), middle aged (40-59 years) and elderly (60-75 years). Post operatively patients were further grouped and compared based on whether their surgery took longer than 1 hour or less than an hour. All patients underwent LC at pneumoperitoneal pressure of 12 mmHg after recording normal LFT values preoperatively. LFT consisting of Serum Bilirubin, SGOT, SGPT and Serum Alkaline phosphatase was conducted on the day prior to LC and repeated 24 hours and 72 hours after Surgery. The results were statistically compared using ANOVA and post hoc analysis. The studied population had no evidence of

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obvious or suspected bile duct injury or bile spillage during surgery. Patients with preoperative diagnosis of choledocholithiasis / biliary strictures, serologically proven hepatitis and pregnant patients were excluded from the study.

**Results:** After 24 hours of the procedure elevation of the levels of all four tested parameters was observed to an extent of double their preoperative values. All Four parameters showed a declining trend at 72 hours post-surgery. Serum Bilirubin levels were significantly greater when the procedure took more than 1 hour. Post operative S Bil levels were greater among elderly patients than among young patients. SGOT levels were significantly greater among elderly patients than among middle aged patients on POD3. SGPT levels on POD 1 were higher among patients whose surgery took longer than 1 hour. Age and duration of surgery did not affect Serum ALP levels significantly.

**Conclusions:** Transient increase in Serum Bilirubin, SGOT, SGPT and Alkaline phosphatase is observed after uncomplicated laparoscopic cholecystectomy and may be attributed to CO<sub>2</sub> pneumoperitoneum, Surgical manipulation, and diathermy. Elderly patients more than 60 years of age were found to have significantly higher Serum Bilirubin values on POD 1 and POD 3 as compared to patients aged between 18 and 39 years, although these values were consistently within the normal physiological range. Serum Bilirubin values were significantly higher (though within normal range) among patients whose surgery took more than an hour as compared to those whose procedure took less than 1 hour. SGOT levels on POD 3 and SGPT levels on POD 1 were significantly higher among the elderly and among those patients whose surgery took longer than 1 hour, respectively. Serum alkaline phosphatase levels fell back within normal range by POD 3 in all patients enrolled in the study. The study indicates that patients aged more than 60 years appear to have significant subclinical derangements in LFT values after LC. The same is true for LC of more than 1 hour duration. The afore mentioned derangements do not translate to deterioration in clinical status.

**Keywords:** Laparoscopic cholecystectomy; Liver function tests; Surgical procedure; Cholelithiasis.

## Introduction

Laparoscopic Cholecystectomy is one of the commonest surgical procedures for treating Symptomatic patients of Cholelithiasis [1]. A number of studies, the earliest being the one conducted by R Halevy, et al. in 1994, have observed rise in LFT values after LC [2]. The “squeeze” effect of pneumoperitoneum compounded by damage of liver cells by prolonged use of diathermy on the liver surface causes transient spillage of liver enzymes into the circulation [2]. Kinking and tenting of the Common bile duct occurring during surgery, leads to transiently raised liver enzyme levels [2]. The deleterious effects of CO<sub>2</sub> insufflation have been reviewed in

detail by a number of studies [3]. A 2013 study showed that hepatic microcirculation fell significantly during LC performed with a pneumoperitoneum of 12 mmHg [4]. Studies conducted in 2001 and 2012 showed that creation of pneumoperitoneum at 12 mmHg causes alteration in hepatic function since it exceeds the normal portal blood pressure of 7-10 mmHg [5,6]. Other studies have shown that Free radicals generated by inflation and deflation of pneumoperitoneum can damage Kupffer cells and endothelial cells of the hepatic sinusoids [7,8]. Elevated SGPT levels are known to persist longer than elevation in SGOT levels due to differences in their half-life in the circulation (about 47 hours for SGPT and 17 hours for total SGOT) [9]. A

prospective study done in 2009 found that 37.5% of studied subjects showed more than 100% increase in at least one parameter of liver function after LC [10]. The authors attributed Subclinical hepatic dysfunction after LC to the negative effects of pneumoperitoneum on hepatic blood flow [10]. A 2015 study by Singhal, et al., concluded that significant alterations occur in Liver enzyme levels due to surgical manipulation, diathermy, patient position, arterial injury, and CO<sub>2</sub> pneumoperitoneum [11]. Several studies have demonstrated that in 1.2% to 12.4% of cholecystectomies there occurs silent passage of small stones through the cystic duct down into the Common Bile Duct, resulting in deranged LFT values [12,13]. A 2010 study conducted by Bhoora Singh, et al., observed that CO<sub>2</sub> pneumoperitoneum activates the sympathetic nervous system [14]. A 2011 study by Ahmed, et al., reported that the rise in Serum alkaline phosphatase is minimal following LC and that mild to moderate elevation in levels of liver enzymes do not have any deleterious effects [15]. In light of the above-mentioned background, researchers decided to carry out an observational study at the institution, using standard statistical tools to study the manner in which each LFT parameter is affected by age of patients and duration of LC.

## Materials and methods

The present study was conducted at the Department of Surgery, of a Zonal Hospital in Pune, India. The studied sample was drawn randomly from patients of Cholelithiasis, seen at the Surgical Outpatient Department of the institution.

- Sample size: 100 patients.

- Intervention: All patients underwent LC between 26 Oct 2022 and 31 Oct 2023.
- Gender: Male and female patients were enrolled.
- Age: Patient ages ranged between 18 and 75 years.

Preoperative History-taking and physical examination was done for all cases. Complete blood count, Renal Function test, LFT and PT INR values and viral marker status were obtained for all patients. Ultrasound study of the abdomen was done prior to surgery. LFT consisting of Serum Bilirubin, SGOT, SGPT and Serum Alkaline phosphatase was conducted on the day prior to LC and repeated 24 hours and 72 hours after Surgery. The values were statistically compared.

## Inclusion criteria

- Normal base line liver function tests during Pre anesthesia checkup and on the day prior to surgery.
- Normal Gall bladder and Biliary anatomy on Abdominal ultrasonography.

## Exclusion criteria

- Pregnancy.
- Choledocholithiasis.
- Biliary Stricture.
- Serologically Proven Hepatitis.
- Evidence of obvious or suspected bile duct injury or bile spillage during the procedure.

Biochemical Analyzer used for all measurements taken during the study: Siemens Dimension EXL 200. Normal ranges

of test result values for this analyzer are given below: -

Serum Bilirubin (Total)=0.1-1.2 mg / dl

Serum SGOT=8-48 U / L

Serum SGPT=7-55 U / L

Serum Alkaline Phosphatase: 40-145 U/L

### Statistical analysis

Tests used: ANOVA with post hoc Tuckey HSD.

### Grouping method

- Young: 18-39 years
- Middle Aged: 40-59 years
- Elderly: 60-75 years
- Duration Of Surgery: Less Than 1 Hour  
Duration of Surgery: More Than 1 Hour

### Sub groups

- Young and surgery took >1 hour
- Young and surgery took <1 hour
- Middle aged and surgery took >1 hour
- Middle aged and surgery took <1 hour
- Elderly and surgery took >1 hour
- Elderly and surgery took <1 hour

### Follow-up

All patients enrolled were planned for follow-up visit to the institution on 10th post operative day for suture removal, detailed history taking, physical and Biochemical examination if indicated. Subsequent visits would be three monthly for a period of one year.

### Observations and analysis

The mean age of subjects in the study was 49 years. 73 female and 27 male patients were

included in the study. In the patient group whose surgery took longer than 1 hour the mean duration of surgery was 85.5 minutes. Mean duration of surgery was 51 minutes in the group of patients whose procedure took less than an hour. Preoperative LFT values were similar among all groups and statistical difference in sample means was insignificant. Mean pre op, POD<sub>1</sub> and POD<sub>3</sub>-LFT values are summarized in Table 1 and Table 2.

Researchers conducted ANOVA and post hoc analysis of the LFT values obtained for the patients enrolled in the study. Level of significance was kept at 0.05.

Firstly, researchers compared the sample means of the following two groups

1. Duration of surgery >1 hour: 49 patients
2. Duration of Surgery <1 hour: 51 patients

Researchers found that patients whose surgery took longer than 1 hour had significantly higher S Bilirubin levels on POD<sub>1</sub> and POD<sub>3</sub>, than patients whose surgery took less than an hour. Researchers also observed significantly higher levels of SGPT on POD<sub>1</sub> in patients whose surgery took longer than 1 hour. Positive findings from this comparison are summarized in table 3.

Next, researchers compared the following three groups

1. Young (18-39 years of age): 34 patients
2. Middle aged (40-59 years of age): 34 patients
3. Elderly (60-75 years of age): 32 patients.

| S. No. | Measured Variable | Unit   | Young (Mean value) | Middle aged (Mean value) | Elderly (Mean value) | Duration >60 min (Mean value) | Duration <60 min (Mean value) |
|--------|-------------------|--------|--------------------|--------------------------|----------------------|-------------------------------|-------------------------------|
| 1      | Pre op S Bil      | mg /dl | 0.467              | 0.49                     | 0.488                | 0.494                         | 0.478                         |
| 2      | Pre op SGOT       | IU/ml  | 29.71              | 29.71                    | 29.844               | 29.796                        | 29.706                        |
| 3      | Pre op SGPT       | IU/ml  | 36.47              | 36.41                    | 36.375               | 36.39                         | 36.45                         |
| 4      | Pre op ALP        | IU/ml  | 73.4               | 73.4                     | 73.78                | 74.1                          | 72.9                          |
| 5      | POD 1 S Bil       | mg /dl | 0.8                | 0.8                      | 0.9                  | 0.87                          | 0.8                           |
| 6      | POD 1 SGOT        | IU/ml  | 65.6               | 66                       | 75.4                 | 72.2                          | 66                            |
| 7      | POD 1 SGPT        | IU/ml  | 80                 | 82                       | 81.7                 | 86.8                          | 76                            |
| 8      | POD 1 ALP         | IU/ml  | 124                | 124                      | 128                  | 127                           | 124                           |
| 9      | POD 3 S Bil       | mg /dl | 0.59               | 0.6                      | 0.678                | 0.67                          | 0.59                          |
| 10     | POD 3 SGOT        | IU/ml  | 43.32              | 42.6                     | 49.88                | 47.27                         | 43.2                          |
| 11     | POD 3 SGPT        | IU/ml  | 62.79              | 62                       | 63.281               | 62.82                         | 62.55                         |
| 12     | POD 3 ALP         | IU/ml  | 94.2               | 94                       | 97.9                 | 95                            | 95.7                          |

**Table 1:** Mean values by age and duration of surgery considered separately.

| S. No. | Measured Variable | Unit   | Elderly <1 hour (Mean value) | Elderly >1 hour (Mean value) | Middle aged <1 hour (Mean value) | Middle aged >1 hour (Mean value) | Young <1 hour (Mean value) | Young >1 hour (Mean value) |
|--------|-------------------|--------|------------------------------|------------------------------|----------------------------------|----------------------------------|----------------------------|----------------------------|
| 1      | Pre op S Bil      | mg /dl | 0.47                         | 0.5                          | 0.5                              | 0.49                             | 0.46                       | 0.49                       |
| 2      | Pre op SGOT       | IU/ml  | 29.81                        | 29.87                        | 29.75                            | 29.67                            | 29.58                      | 29.87                      |
| 3      | Pre op SGPT       | IU/ml  | 36.31                        | 36.44                        | 36.5                             | 36.33                            | 36.53                      | 36.4                       |
| 4      | Pre op ALP        | IU/ml  | 73.19                        | 74.38                        | 72.63                            | 74                               | 72.89                      | 73.93                      |
| 5      | POD 1 S Bil       | mg /dl | 0.79                         | 1                            | 0.8                              | 0.81                             | 0.79                       | 0.81                       |
| 6      | POD 1 SGOT        | IU/ml  | 66                           | 84.81                        | 66.13                            | 66.61                            | 65.89                      | 65.33                      |
| 7      | POD 1 SGPT        | IU/ml  | 76                           | 87.38                        | 76.63                            | 86.89                            | 75.37                      | 85.93                      |
| 8      | POD 1 ALP         | IU/ml  | 124.19                       | 132.31                       | 122.94                           | 125.06                           | 123.79                     | 124.87                     |
| 9      | POD 3 S Bil       | mg /dl | 0.6                          | 0.76                         | 0.593                            | 0.64                             | 0.59                       | 0.6                        |
| 10     | POD 3 SGOT        | IU/ml  | 43.31                        | 56.44                        | 42.69                            | 42.61                            | 43.53                      | 43.07                      |
| 11     | POD 3 SGPT        | IU/ml  | 63                           | 63.56                        | 61.19                            | 62.72                            | 63.32                      | 62.13                      |
| 12     | POD 3 ALP         | IU/ml  | 95.94                        | 99.88                        | 95.44                            | 92.89                            | 95.63                      | 92.47                      |

**Table 2:** Mean values by age and duration of surgery considered together.

| S. No. | ANOVA Comparison Variables                 | ANOVA f statistic | p value | Result             | Tuckey HSD | p value  | Result   |
|--------|--|-------------------|---------|--------------------|------------|----------|--|
| 1      | Serum Bilirubin POD 1 (>1 hour vs <1 hour) | 5.9271            | 0.0167  | Significant        | 3.443      | 0.016718 | Significantly higher values for surgery time >1 hour |
| 2      | Serum Bilirubin POD 3 (>1 hour vs <1 hour) | 7.5712            | 0.0071  | Highly Significant | 3.8913     | 0.007065 | Significantly higher values for surgery time >1 hour |
| 3      | SGPT POD 1 (>1 hour vs <1 hour)            | 12.6201           | 0.0006  | Highly Significant | 5.024      | 0.001005 | Significantly higher values for surgery time >1 hour |

**Table 3:** Statistically significant results of ANOVA and post hoc test for comparing the sample means of two groups, vis. Duration of surgery more than 1 hour vs less than 1 hour.

| S. No. | ANOVA Comparison Variables                              | ANOVA f statistic | p value | Result      | Tuckey HSD | p value | Result   |
|--------|---|-------------------|---------|-------------|------------|---------|--|
| 1      | Serum Bilirubin POD 1 (Young vs Middle aged vs Elderly) | 3.7035            | 0.028   | Significant | 3.4        | 0.047   | Significantly higher values among Elderly as compared to Young       |
| 2      | Serum Bilirubin POD 3 (Young vs Middle aged vs Elderly) | 3.6304            | 0.0302  | Significant | 3.706      | 0.027   | Significantly higher values among Elderly as compared to Young       |
| 3      | SGOT POD 3 (Young vs Middle aged vs Elderly)            | 4.102             | 0.02    | Significant | 3.68       | 0.03    | Significantly higher values among Elderly as compared to middle aged |

**Table 4:** Statistically significant results of ANOVA and post hoc test for comparing the sample means of three groups, vis. Elderly vs Middle aged vs Young.

Researchers found that Elderly patients had significantly higher S Bilirubin levels on POD 1 and 3 as compared with young patients. Elderly patients had higher SGOT levels on POD 3 as compared with Middle aged patients. Positive findings are summarized in table 4.

Finally, researchers compared the following six Sub groups:

1. Young and surgery took >1 hour: 15 patients
2. Young and surgery took <1 hour: 19 patients

3. Middle aged and surgery took >1 hour: 18 patients
4. Middle aged and surgery took <1 hour: 16 patients
5. Elderly and surgery took >1 hour: 16 patients
6. Elderly and surgery took <1 hour: 16 patients

Researchers found that Elderly patients whose surgery took >1 hour had significantly higher S Bilirubin levels on POD 1 and 3 than all other subgroups except among middle aged on POD 3, if their surgery took >1 hour. SGOT levels were significantly higher among

the elderly whose surgery took >1 hour than all other subgroups. ANOVA analysis found significant intergroup variance in levels of SGPT levels on POD 1, but Post hoc analysis

results were insignificant (p value >0.05) for inter group difference. Positive findings are summarized in Table 5.

| S. No. | ANOVA Comparison Variables | ANOVA f statistic | p value | Result             | Tuckey HSD p value | Result  |
|--------|----------------------------|-------------------|---------|--------------------|--------------------|---|
| 1      | Serum Bilirubin POD 1      | 4.7624            | 0.0006  | Highly Significant | <0.05              | Significantly higher values among Elderly whose surgery took >1 hour as compared to all other groups  |
| 2      | Serum Bilirubin POD 3      | 4.4254            | 0.0012  | Highly Significant | <0.05              | Significantly higher values among Elderly whose surgery took >1 hour as compared to all other groups ***except Middle aged patients whose surgery lasted >1 hour (p = 0.07) |
| 3      | SGOT POD 1                 | 2.936             | 0.0166  | Significant        | <0.05              | Significantly higher values among Elderly whose surgery took >1 hour as compared to all other groups  |
| 4      | SGOT POD 3                 | 4.1656            | 0.0018  | Highly Significant | <0.05              | Significantly higher values among Elderly whose surgery took >1 hour as compared to all other groups  |
| 5      | SGPT POD 1                 | 2.4495            | 0.0392  | Significant        | >0.05              | Tuckey HSD p values were however insignificant for intergroup difference  |

**Table 5:** Statistically significant results of ANOVA and post hoc test for Subgroup comparison of 6 groups (Elderly with surgery time >1 hour, Elderly with surgery time <1 hour, Middle aged with surgery time >1 hour, Middle aged with surgery time <1 hour, Young with surgery time >1 hour, Young with surgery time <1 hour).

Levels of Serum ALP did not show significant inter group/subgroup variance. Researchers observed two-fold or more increases in all LFT parameter values as compared to base line levels. The increase in level of SGOT, SGPT and ALP was beyond normal physiological range in all studied patients on POD 1. Serum Bilirubin stayed consistently within normal physiological range on POD 1

and POD 3 even though Levels observed postoperatively were significantly more than preoperative values.

SGOT levels of 72% patients had returned within normal range by POD 3. SGPT levels remained elevated beyond normal range in 64% patients on POD 3. 99% patients had ALP values within normal range on POD 3.

## Discussion

In a 2002 study, Tareq M Al-Jaberi, et al., found that changes in liver function parameters after laparoscopic cholecystectomy are common, carrying no clinical sequelae. They are more common in female patients and are not related to age, duration of surgery, or the acuteness of gallbladder inflammation. Assessment of direct bilirubin and alkaline phosphatase is sufficient for the routine evaluation of these patients postoperatively [16]. Researchers however, in the study, observed that Serum Bilirubin levels and SGOT levels were significantly higher among Elderly patients aged >60 years, especially so when the Surgical procedure had taken more than 1 hour. Middle aged patients aged 40-59 years, whose surgery took >1 hour also showed elevated levels of Serum Bilirubin, comparable to Elderly patients whose surgery took >1 hour.

In a 2014 study, Vincenzo Neri, et al., concluded that the level of (serum) SGOT and SGPT increase significantly during 24-48 hours after LC ( $p < 0.0001$ ). The increase in (total and direct) bilirubin was not found to be statistically significant [17]. On the contrary ALP, GGT was significantly decreased ( $p < 0.001$ ). Three days after surgery LFTs returned to normal level in the patients with previous normal level of tests. The length of intervention did not show correlation with changes in LFTs (PCC 0.2) [17]. Researchers observed in the study that Serum Bilirubin levels on POD 1 and 3 on POD 1 were significantly higher among patients aged 60-75 years (although consistently within normal range in all

patients), especially when the surgery took >1 hour. SGOT levels on POD 1 and 3 showed a similar trend. SGPT levels were significantly higher among the elderly on POD 1.

In a 2019 study by Bellad, et al., observed that there was greater increase in liver function test values when the surgeries were prolonged for more than 80 minutes. However, the rise in LFTs was not found to be significant [80]. The study obtained similar results, but researchers also found statistically significant elevation in LFT values in the Elderly, when surgery was prolonged beyond 60 minutes.

A 2017 study by Abhishek Sharma, et al., concluded that prolonged duration of surgery and high intraabdominal pressure in laparoscopy change the liver enzyme values postoperatively but it is transitory. The changes in liver enzyme levels were less, if duration of surgery was up to 30-60 min, even under higher pneumoperitoneal pressures, greater than 12 mmHg [19]. Researchers found similar changes in LFT values in the study.

All the patients who underwent LC in the study, had an uneventful post op recovery, except for minor surgical site infections (Grade 1 or 2 with the Southampton scoring system). None showed any evidence of clinical deterioration. All patients were discharged on the third post operative day after surgery. Minor Surgical site infections were treated with short courses of oral antibiotics and resolved well in all affected patients.

From the results of the study, researchers draw the following conclusions



1. Serum Bilirubin and Liver enzyme levels increase by at least two folds after Laparoscopic Cholecystectomy. By the third post op day these values tend to start settling down to near normal levels. SGPT values tend to stay elevated longer than Serum Bilirubin, SGOT and ALP levels, attributable to the longer half-life of SGPT in blood.
2. Patients above 60 years of age and those whose surgery takes longer than 60 minutes have significantly higher postoperative LFT levels after LC than those below 60 years of age.
3. Individual Test parameter values are affected in the following manner:
  - a. Serum Bilirubin: Significantly higher levels are found among patients aged >60 years and among those whose surgery takes >1 hour, on first and third postoperative days after LC.
  - b. SGOT: Significantly higher levels are found among patients aged >60 years. Studied in isolation with age as a single input variable SGOT levels are not significantly different for different age groups. However, when age is studied with duration of surgery as a second input variable, SGOT levels are seen to be significantly elevated in patients aged >60 years whose surgery takes >1 hour.
  - c. SGPT: Significantly higher levels on post operative day 1, are found among patients whose surgery takes longer than 1 hour.
  - d. ALP: Levels are not affected by age of patient or duration of surgery.
4. The rise in LFT levels seen after uncomplicated LC are subclinical in nature and do not correlate with or prognosticate deterioration in the clinical condition of patients.

### Conclusion

Serum Bilirubin and Liver enzyme levels increase by at least two folds after Laparoscopic Cholecystectomy. By the third post op day these values tend to start settling down to near normal levels. Serum Bilirubin levels and SGOT levels are significantly higher among Elderly patients aged >60 years, especially so when the Surgical procedure has taken more than 1 hour. Middle aged patients aged 40-59 years, with surgery time >1 hour also show elevated levels of Serum Bilirubin, comparable to Elderly patients after surgery lasting >1 hour. Laparoscopic Cholecystectomy taking >1 hour significantly elevates SGPT levels on first post operative day. ALP levels after LC are not significantly affected by age or duration of surgery. Changes in LFT observed after LC are sub clinical in nature and do not translate to deterioration in the clinical condition of patients.

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