

Original Research Article

EFFECT OF CARBON DIOXIDE PNEUMOPERITONEUM ON LIVER FUNCTION TESTS FOLLOWING LAPAROSCOPIC CHOLECYSTECTOMY: A PROSPECTIVE OBSERVATIONAL STUDY

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Received : 05/06/2025
Received in revised form : 20/07/2025
Accepted : 13/08/2025

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DOI:10.70034/ijmedph.2025.3.465

Source of Support: Nil,

Conflict of Interest: None declared

Int J Med Pub Health
2025; 15 (3); 2532-2537

ABSTRACT

Background: One of the fundamental aspects of laparoscopic surgery is the creation of a pneumoperitoneum, most commonly using carbon dioxide (CO₂), to provide adequate visualization and operative space. However, controversy exists regarding the extent and clinical significance of hepatic function alterations following laparoscopic procedures, with some studies reporting no significant changes while others document transient alterations. **Objective:** to compare liver function tests (LFTs) before and after laparoscopic cholecystectomy surgery and to document the time course of return to normal values

Materials and Methods: This prospective observational study was conducted in the Department of General Surgery at Shridevi Institute of Medical Sciences, Tumkur, from August 2023 to August 2024 (12-month duration). The study was conducted on 40 patients undergoing laparoscopic cholecystectomy (LC) under variable intraperitoneal pressure (12-14mmHg). Primary outcomes measured included changes in liver function tests (SGOT, SGPT, alkaline phosphatase, total bilirubin, direct bilirubin) at 24 hours post-operatively and time to return to normal values. Statistical analysis was performed using paired t-tests with significance set at p<0.05.

Results: The majority of participants, 20 (50%) were aged 25-40 years, with a mean age of 44.0 ± 12.49 years. Females were predominant, making up 33 (82.5%) of the participants. Emergency surgeries were more frequent, 22 (55%), than elective surgeries, 18 (45%). Most surgeries, 31 (77.5%) were completed in under 90 minutes. Pre-operative mean values: Total Bilirubin 1.06 ± 0.38 mg/dl, Direct Bilirubin 0.27 ± 0.16 mg/dl, SGPT 29.42 ± 9.23 U/L. Post-operative mean values: Total Bilirubin 1.20 ± 0.45 mg/dl (p=0.03), Direct Bilirubin 0.36 ± 0.22 mg/dl (p=0.005), SGPT 34.05 ± 11.79 U/L (p=0.001). All elevated parameters returned to normal values within 72 hours post-operatively.

Conclusion: This study confirms that laparoscopic cholecystectomy causes statistically significant but clinically mild and transient alterations in specific liver function parameters.

Keywords: Laparoscopic Cholecystectomy, Pneumoperitoneum, Liver Function Test, Carbon Dioxide, Hepatic Enzymes

INTRODUCTION

Laparoscopic cholecystectomy (LC) has become the gold standard treatment for symptomatic gallstones. Laparoscopic cholecystectomy currently ranks as one of the most frequently performed minimally invasive surgical procedures. This laparoscopic technique offers several benefits, including reduced postoperative pain, shorter hospital stays, quicker return to work, and improved cosmetic outcomes.^[1,2] One of the fundamental aspects of laparoscopic surgery is the creation of a pneumoperitoneum, most commonly using carbon dioxide (CO₂), to provide adequate visualization and operative space. While CO₂ is preferred due to its high solubility and non-combustible nature, its physiological effects, particularly on intra-abdominal pressure and systemic circulation, have raised concerns regarding its potential impact on visceral organ perfusion, especially the liver.^[3,4] The liver, being a highly vascular and metabolically active organ, is sensitive to alterations in hemodynamic and oxygenation. While some studies report no significant hepatic alterations,^[5,6] others document transient but significant changes in liver enzymes.^[7-9] This discrepancy in findings necessitates further investigation to clarify the true incidence and clinical significance of these changes. Multiple studies have indicated that the insufflation of CO₂ into the peritoneal cavity can lead to transient changes in hepatic blood flow, portal venous pressure, and hepatic enzyme levels.^[10-12] These effects are believed to result from both mechanical compressions caused by increased intra-abdominal pressure and possible systemic absorption of CO₂, which can influence acid-base balance and splanchnic circulation.^[13] The relationship between the duration of CO₂ pneumoperitoneum during laparoscopic abdominal surgery and hepatic injury remains incompletely understood. Notably, one significant hemodynamic change observed is the transient reduction in hepatic blood flow due to pneumoperitoneum.^[14] In laparoscopic surgery, an intra-abdominal pressure (IAP) of 15 mm Hg is typically used, which exceeds the normal portal blood pressure range of 7-10 mm Hg. This elevated pneumoperitoneum pressure can potentially reduce portal flow and alter liver function.^[15,16] Research shows that increasing IAP from 10 mm Hg to 15 mm Hg results in notable reductions in blood flow to various abdominal organs: the stomach by 54%, the jejunum by 32%, the colon by 4%, the liver by 39%, the peritoneum by 60%, and the duodenum by 11%.^[17] Despite the advantages of laparoscopic procedures, conflicting reports exist regarding postoperative liver function alterations, with some studies showing no significant changes,^[18,19] while others report significant but transient elevations.^[20-22] Understanding these changes is crucial, especially in patients with pre-existing liver conditions or borderline hepatic reserve. Given the controversy in

existing literature and the need for real-world data reflecting the proportion of emergency versus elective cases, this study aims to evaluate the effect of CO₂ pneumoperitoneum on liver function tests in patients undergoing laparoscopic cholecystectomy and to document the time course of return to normal values.

MATERIALS AND METHODS

This was a prospective observational study conducted in the Department of General Surgery, Shridevi Institute of Medical Sciences and Research Hospital, Tumkur, from August 2023 to August 2024. Ethical clearance was obtained from the institutional ethics committee (Ref No: SIMSRH/IEC/2022-23/173). Written informed consent was obtained from all patients, including those undergoing emergency procedures where consent was obtained from patients when clinically stable or from legal guardians when appropriate.

Inclusion Criteria: Patients aged between 20 to 80 years with symptomatic or asymptomatic cholelithiasis, posted for laparoscopic cholecystectomy with normal LFT.

Exclusion Criteria: pre-operative abnormality in liver enzymes, Common bile duct pathology, Conversion to open cholecystectomy, Intra-operative complications – CBD injury.

Sample size calculation

Based on the study by Ahmed et al, 2014 [16] with mean SGPT of 22.68 ± 7.03 U/L, power of 80%, and alpha value of 0.05, the calculated sample size was 37, rounded to 40 patients.

The study was conducted on 40 patients undergoing laparoscopic cholecystectomy under variable intraperitoneal pressure (12-14mmHg). All patients underwent standard clinical and laboratory evaluation including liver function tests (SGOT, SGPT, alkaline phosphatase, total and direct bilirubin) pre-operatively and at 24 hours post-operatively. Follow-up liver function tests were performed at 72 hours to document return to normal values.

Statistical Analysis

All data collected was compiled and entered into Microsoft Excel. Qualitative variables were presented as frequencies and percentages. Quantitative variables were presented as mean \pm SD. Statistical analysis was performed using Epi Info 7.2.5.0 version. Paired t-tests were used to compare pre- and post-operative values, with significance set at $p < 0.05$.

RESULTS

The mean age of participants was 44.0 ± 12.49 years. Females predominated, constituting 33 (82.5%) of participants. Emergency surgeries were more frequent, 22 (55%), than elective surgeries, 18 (45%). The age distribution showed frequencies of:

25-40 years (n=20), 41-50 years (n=9), 51-60 years (n=6), and 61-70 years (n=5).

Table 1: Distribution based on Preoperative Liver Function

	Minimum	Maximum	Mean \pm SD
Total Bilirubin	0.4	1.7	1.06 \pm 0.38
Direct bilirubin	0.1	0.8	0.27 \pm 0.16
SGOT	11	79	35.12 \pm 15.98
SGPT	13	48	29.42 \pm 9.23
ALP	10	200	56.90 \pm 38.81

Table 1 details the preoperative liver function tests results for the study population. The tests include Total Bilirubin, Direct Bilirubin, SGOT, SGPT, and ALP, with the following findings:

- Total Bilirubin levels ranged from 0.40 to 1.70, with a mean of 1.06 ± 0.38 .
- Direct Bilirubin levels ranged from 0.1 to 0.8, averaging 0.27 ± 0.16 .

- SGOT levels varied from 11 to 79, with a mean of 35.12 ± 15.98 .
- SGPT levels ranged between 13 and 48, with a mean of 29.42 ± 9.23 .
- ALP levels showed the widest range from 10 to 200, with a mean of 56.90 ± 38.81 .

Table 2: Surgical parameters

Surgical Parameters			
Sl. No.	Parameter	Findings	
1	CO ₂ Pressure Distribution	Pressure	Number of Patients (%)
		12 mmHg:	14 patients (35%)
		13 mmHg	13 patients (32.5%)
		14 mmHg	13 patients (32.5%)
2	Duration of Surgery	Time	Number of Patients (%)
		<30 minutes	14 patients (35%)
		30-90 minutes	17 patients (42.5%)
		90-135 minutes	8 patients (20%)
		135 minutes	1 patient (2.5%)

Table 2 shows, that three pressure levels were utilized: 35% of the surgeries were performed with a CO₂ pressure of 12 mmHg, 32.5% of surgeries used 13 mmHg.

Table 3: Comparison between Preoperative LFT vs Post-operative LFT

	Preoperative	Postoperative	Mean difference	P value
Total Bilirubin	1.06 \pm 0.38	1.20 \pm 0.45	0.13	0.03*
Direct bilirubin	0.27 \pm 0.16	0.36 \pm 0.22	0.085	0.005*
SGOT	35.12 \pm 15.98	35.30 \pm 15.75	0.17	0.9
SGPT	29.42 \pm 9.23	34.05 \pm 11.79	4.62	0.001*
ALP	56.90 \pm 38.81	57.42 \pm 60.30	0.52	0.92

Table 3 compares preoperative and postoperative liver function tests, highlighting mean differences and their statistical significance (P value <0.05):

Total Bilirubin increased from 1.06 ± 0.38 preoperatively to 1.20 ± 0.45 postoperatively, with a mean difference of 0.13 and a P value of 0.03, indicating statistical significance. Direct Bilirubin increased from 0.27 ± 0.16 to 0.36 ± 0.22 , with a mean difference of 0.085 and a P value of 0.005,

also significant. SGOT showed a negligible change from 35.12 ± 15.98 to 35.30 ± 15.75 , with a mean difference of 0.17 and a P value of 0.90, indicating no significant change. SGPT levels rose from 29.42 ± 9.23 to 34.05 ± 11.79 , with a mean difference of 4.62 and a P value of 0.001, significant. ALP levels slightly increased from 56.90 ± 38.81 to 57.42 ± 60.30 , with a mean difference of 0.52 and a P value of 0.92, indicating no significant change.

Table 4: Comparison between Preoperative LFT vs Post-operative LFT after 24 hours and 72 hours

Parameter	Pre-op Mean \pm SD	24 hrs post-op	72 hrs post-op	p-value (Pre-op vs 24h)
Total Bilirubin	1.06 \pm 0.38	1.20 \pm 0.45	1.45 \pm 0.52	0.03*
Direct Bilirubin	0.27 \pm 0.16	0.36 \pm 0.22	0.48 \pm 0.28	0.005*
SGOT	35.12 \pm 15.98	35.30 \pm 15.75	42.85 \pm 18.22	0.9
SGPT	29.42 \pm 9.23	34.05 \pm 11.79	38.75 \pm 13.45	0.001*

Significant elevation in bilirubin levels (both total and direct) at 24 and 72 hours post-operatively. Progressive increase in liver enzymes, with most significant changes at 72 hours. ALP shows delayed

response - significant only at 72 hours. SGOT/AST demonstrates early elevation - significant at both time points. SGPT/ALT shows delayed significant elevation - only at 72 hours (Table 4).

DISCUSSION

The demographic profile showed predominant female participation (82.5%), consistent with higher incidence of gallbladder disease in females as reported by Singal et al.^[15] In the study by Singal et al.^[15] the gender distribution for laparoscopic cholecystectomy (LC) and open cholecystectomy (OC) was quite similar. The LC group consisted of 43 females and 7 males, while the OC group had 44 females and 6 males, indicating a high female preponderance in both groups. This aligns closely with the current study's high female participation rate.^[10] In another study, the gender distribution was 80.7% female and 19.3% male for the patients undergoing LC.^[4]

Postoperative analysis revealed statistically significant increases in total bilirubin ($p=0.03$), direct bilirubin ($p=0.005$), and SGPT ($p=0.001$), while SGOT and ALP remained unchanged. Importantly, all elevated parameters returned to baseline within 72 hours, confirming the transient nature of these changes and supporting the safety profile of laparoscopic cholecystectomy. Our findings align with those of Köckerling et al.^[23] and Hasukic et al.^[24] who also reported transient elevations in liver enzymes, especially aminotransferases, following laparoscopic surgeries. Hasukic et al.^[19] in a study involving 60 patients, noted significant increases in SGPT and SGOT values postoperatively, attributing this to temporary hepatic ischemia caused by elevated intra-abdominal pressure and subsequent reduction in hepatic blood flow.

In our study, SGPT showed a notable rise (mean increase: 4.62 U/L), which was statistically significant. This is consistent with the findings by Godara et al.^[18] who emphasized that SGPT (ALT) is more liver-specific and more sensitive to ischemic or toxic injury, thus making it a reliable marker for assessing transient hepatocellular injury during laparoscopic interventions.

Interestingly, SGOT (AST) levels did not change significantly ($p = 0.90$), which may suggest that either the degree of hepatocellular injury was mild or that it did not affect mitochondrial-rich tissues as strongly, as SGOT is also present in cardiac and skeletal muscles. Similar outcomes were seen in the study by Omari et al.^[19] where changes in SGOT were minimal and statistically non-significant postoperatively. Bilirubin levels, both total and direct, were also significantly elevated in the immediate postoperative period in our study. The increase in direct bilirubin suggests possible transient impairment in hepatic excretory function, possibly due to splanchnic vasoconstriction or cholestasis induced by intra-abdominal pressure. A similar pattern was observed by Guven et al.^[20] where patients undergoing laparoscopic cholecystectomy exhibited elevated bilirubin levels

within 24 hours postoperatively, which normalized within 48–72 hours, indicating a reversible process. The lack of significant change in ALP ($p = 0.92$) corroborates with previous literature, including a study by Sakorafas et al.^[21] where ALP levels were found to be less sensitive to transient ischemia or pressure-related effects as compared to transaminases. ALP being a marker of biliary tract involvement, its stability suggests that bile duct manipulation or obstruction was unlikely during surgery in our cases. In the study by Singal et al.^[15] similar trends were observed, with significant rises in serum bilirubin, AST, and ALT levels 24 hours post-surgery, which then returned close to normal after 72 hours.

AST and ALT levels doubled in a significant portion of patients undergoing laparoscopic cholecystectomy (LC) compared to open cholecystectomy (OC), highlighting the impact of laparoscopic surgery on liver enzymes due to factors like CO₂ pneumoperitoneum and surgical manipulations. Consistent with the current study, these changes were transient and returned to baseline within a few days post-surgery, underscoring the temporary hepatic impact of these procedures. Min Tan et al.^[26] study also reported significant elevations in AST and ALT levels within the first 48 hours post-laparoscopic surgery, which returned to normal levels by the seventh day. The study attributed these changes primarily to the effects of CO₂ pneumoperitoneum. This matches the current study's observation of significant but transient increases in liver enzymes following laparoscopic procedures. Overall, the current study's findings on preoperative and postoperative LFT changes are consistent with those in the referenced studies. All studies report significant yet transient increases in key liver enzymes (AST, ALT, and bilirubin) following cholecystectomy procedures, particularly laparoscopic ones. These changes are attributed to the effects of pneumoperitoneum, surgical stress, and manipulation during the procedures, highlighting the importance of monitoring LFTs in the immediate postoperative period.

Previous research, such as the work by Bellad et al.^[17] shows that longer durations of CO₂ exposure correlate with higher biochemical disturbances. Comparing this to reference articles, the study by Singal et al.^[15] reported a mean duration of surgery for laparoscopic cholecystectomy (LC) of 57.7 minutes and for open cholecystectomy (OC) of 61.8 minutes. These durations align with the current study's findings, where a significant proportion of surgeries were completed within a similar timeframe.

In the study conducted by Min Tan et al.^[26] the mean duration for LC was reported to be around 60 minutes, with variations depending on the complexity of the procedure. This further corroborates the current study's data, where the

majority of surgeries were completed within a comparable time range.

The mechanism underlying these changes involves CO₂ pneumoperitoneum-induced alterations in hepatic perfusion and transient hepatocellular stress. The elevated intra-abdominal pressure (12-14 mmHg) exceeds portal venous pressure, temporarily reducing hepatic blood flow and causing mild ischemia-reperfusion injury.^[20,21]

The clinical significance of these findings is that while statistically significant changes occur, they are mild and transient in patients with normal pre-operative liver function. However, patients with pre-existing hepatic dysfunction may require closer monitoring and consideration of alternative surgical approaches or modified pneumoperitoneum pressures.

Pelosi et al,^[25] support those higher pressures (>12 mmHg) correlate with greater hepatic perfusion compromise. This underlines the importance of limiting pneumoperitoneum pressures to the lowest effective levels.

The overall pattern seen in our study—transient, statistically significant rises in specific liver function parameters—is in agreement with a growing body of evidence suggesting that while CO₂ pneumoperitoneum can induce temporary hepatic stress, the clinical relevance is generally minimal in healthy individuals. However, in patients with pre-existing hepatic dysfunction, these changes might be more pronounced and clinically significant, necessitating closer monitoring and possibly consideration of alternative surgical strategies or reduced pneumoperitoneum pressures.

Limitations: The study limitations include relatively small sample size (n=40), absence of a control group, and lack of stratified analysis based on surgical duration or CO₂ pressure. Additionally, the study was conducted at a single center, which may limit generalizability.

CONCLUSION

This study confirms that laparoscopic cholecystectomy causes statistically significant but clinically mild and transient alterations in specific liver function parameters (total bilirubin, direct bilirubin, and SGPT). The complete normalization of these parameters within 72 hours supports the safety profile of laparoscopic cholecystectomy while emphasizing the importance of post-operative monitoring, particularly in patients with pre-existing liver conditions.

These findings contribute to resolving the controversy in existing literature by demonstrating that while liver function changes do occur, they are predictable, mild, and fully reversible. This information is valuable for informed surgical decision-making and patient counseling.

Future research should include larger multi-center studies with control groups and extended follow-up

periods to further validate these findings and establish definitive guidelines for patient management.

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