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Impact of CO2 Pneumoperitoneum on LFTS in Laparoscopic Cholecystectomy Surgery: A Prospective Surgery

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ABSTRACT

Background: Transient abnormalities in liver function tests (LFTs) following uncomplicated laparoscopic cholecystectomy (LC) have been attributed to CO_2 pneumoperitoneum–related hepatosplanchnic perfusion changes, yet the magnitude and time course of these alterations remain clinically relevant in routine standard-pressure practice. Objective: To quantify perioperative changes in ALT, AST, bilirubin, and ALP after uncomplicated LC performed under 14 mmHg CO_2 pneumoperitoneum and to assess whether longer CO_2 insufflation duration is associated with greater postoperative enzyme elevation. Methods: In this prospective observational study conducted at Sandeman Provincial Hospital, Quetta (January–July 2025), 100 adults (20–70 years) with uncomplicated gallstone disease and normal baseline LFTs underwent standardized LC with CO_2 pneumoperitoneum maintained at 14 mmHg. ALT, AST, bilirubin, and ALP were measured preoperatively and on postoperative day 2 and day 10. Paired t-tests compared postoperative values with baseline. Results: On postoperative day 2, ALT increased from 28.19±5.29 to 51.11±13.06 U/L ($p<0.001$), AST from 31.23±5.51 to 53.79±12.92 U/L ($p<0.001$), and bilirubin from 0.8229±0.1378 to 1.3840±0.2727 mg/dL ($p<0.001$), while ALP showed no clinically meaningful rise. Enzyme elevations were more pronounced with longer CO_2 insufflation duration and returned near baseline by day 10. Conclusion: Uncomplicated LC under standard-pressure CO_2 pneumoperitoneum is associated with reversible elevations in ALT, AST, and bilirubin that normalize by postoperative day 10, with greater changes observed after prolonged insufflation exposure.

Keywords

Laparoscopic cholecystectomy; liver function tests; CO_2 pneumoperitoneum; ALT; AST; bilirubin.

INTRODUCTION

Laparoscopic cholecystectomy (LC) has become the preferred operative approach for uncomplicated gallstone disease because it offers shorter hospital stay, reduced postoperative pain, faster recovery, and lower wound-related morbidity compared with open surgery (1). Its scope has further expanded with the incorporation of fluoroscopic intraoperative cholangiography and laparoscopic common bile duct exploration in patients with suspected choledocholithiasis, allowing minimally invasive management in selected cases (2,3). Despite these advantages, transient postoperative abnormalities in liver function tests (LFTs) following uncomplicated LC have been consistently reported, raising questions about their pathophysiology, magnitude, and clinical relevance, particularly in patients exposed to standard-pressure carbon dioxide (CO_2) pneumoperitoneum (4-7).

Physiologically, CO_2 pneumoperitoneum and elevated intra-abdominal pressure (IAP) can induce splanchnic circulatory alterations by compressing abdominal vasculature and reducing venous return, with downstream effects on portal venous flow and hepatic microcirculation (8-12). Experimental and clinical observations suggest that pneumoperitoneum can reduce hepatic and portal blood flow, and that this reduction becomes more pronounced at higher pressures, with portal venous flow reportedly decreasing substantially at IAP levels around 14 mmHg (13-15). These hemodynamic shifts may contribute to transient hepatocellular enzyme elevation through relative hepatosplanchnic hypoperfusion, ischemia-reperfusion effects, and oxidative stress responses (6,8,10,11). However, findings in the literature are not fully consistent, as some studies report no significant compromise of splanchnic circulation at moderate IAP ranges (11–13 mmHg), suggesting that the magnitude of hepatic impact may depend on additional factors such as insufflation duration, patient positioning, anesthetic protocol, and operative manipulation (12). Furthermore, postoperative enzyme elevation has been observed even in laparoscopic procedures anatomically distant from the liver, implying that systemic pneumoperitoneum-related mechanisms may contribute beyond direct hepatic handling alone (16).

Clinically, several investigations have shown that serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), and bilirubin may rise after LC without evidence of bile duct injury, often returning toward baseline within days, and generally without clinically apparent hepatic dysfunction (17-19). Nevertheless, the degree of enzyme elevation appears variable, and evidence suggests that longer pneumoperitoneum duration and higher insufflation pressures may intensify biochemical changes (18,19). In many low-resource and high-volume public sector settings, including tertiary surgical units, standard-pressure pneumoperitoneum around 12–14 mmHg remains routine. However, there is limited local evidence quantifying postoperative LFT changes under standard pressure and exploring whether CO_2 insufflation duration is associated with greater biochemical disturbance in this context. Therefore, this prospective study was designed to quantify perioperative changes in ALT, AST, bilirubin, and alkaline phosphatase (ALP) before and after uncomplicated LC performed under 14 mmHg CO_2 pneumoperitoneum, and to evaluate whether longer CO_2 insufflation time is associated with greater postoperative enzyme elevation. We hypothesized that ALT, AST, and bilirubin would increase significantly within 48 hours after LC and normalize by postoperative day 10, with greater elevations observed in patients exposed to longer durations of CO_2 pneumoperitoneum.

MATERIALS AND METHODS

This prospective observational study was conducted in the Surgical Department, Sandeman Provincial Hospital/Bolan Medical College, Quetta, Pakistan, from 04 January 2025 to 04 July 2025. After approval from the institutional ethical committee and obtaining written informed consent from all participants, 100 patients undergoing elective laparoscopic cholecystectomy were enrolled according to predefined eligibility criteria. Adult patients aged 20–70 years with uncomplicated gallstone disease and normal preoperative liver function parameters were included, while patients were excluded if they had undergone endoscopic retrograde cholangiopancreatography and sphincterotomy within the preceding 10 days, required intraoperative cholangiography, experienced perioperative complications such as bile duct injury, biliary leak, obstruction, or infection, had known coexisting chronic liver disease (including hepatitis B, hepatitis C, or cirrhosis), or were classified as high-risk due to significant cardiopulmonary or renal comorbidities. Patients were also excluded if conversion to open surgery occurred or if postoperative complications that could influence liver enzymes developed, ensuring that biochemical changes could be interpreted within the context of uncomplicated LC (16–19).

All laparoscopic cholecystectomies were performed by the same consultant surgical team under standardized general anesthesia. Induction and maintenance followed a uniform protocol using propofol, succinylcholine, isoflurane, and vecuronium, selected because commonly used anesthetic agents can influence splanchnic circulation but are considered to have minimal clinically meaningful interference with hepatic enzyme measurements under standardized exposure (20-22). Pneumoperitoneum was established using CO_2 insufflation via Veress needle, and intra-abdominal pressure was maintained at 14 mmHg throughout all procedures. A standard four-trocar technique was performed with the patient positioned in slight reverse Trendelenburg. Monopolar diathermy was used for gallbladder bed dissection and hemostasis, the gallbladder was extracted, and a subhepatic drain was placed. The duration of CO_2 insufflation was recorded intraoperatively for each case and was later used to explore the relationship between pneumoperitoneum exposure time and postoperative enzyme elevation (23-27).

Postoperatively, all patients received uniform intravenous glucose and electrolyte infusions for 24 hours. Prophylactic antibiotic therapy consisted of ceftriaxone 1 g intravenously at induction, followed by additional doses at 12-hour intervals as per the institutional protocol, and postoperative analgesia was provided with intravenous nalbuphene 10 mg at 12-hour intervals as required. At 24 hours after surgery, all patients underwent an erect abdominal radiograph to evaluate residual subdiaphragmatic free gas as an indirect postoperative check of CO_2 absorption. Liver function testing included ALT, AST, total bilirubin, and ALP, measured at three standardized timepoints: preoperatively (baseline), on the second postoperative day before discharge, and on the tenth postoperative day at follow-up and stitch removal. All assays were performed in a single laboratory using the same instrumentation to reduce analytical variability. Only patients with baseline values within the laboratory reference range were included, using the following normal ranges: ALT 5–42 U/L; AST 5–42 U/L; total bilirubin 0.3–1.2 mg/dL; and ALP 80–306 U/L (28-32).

Continuous variables were summarized as mean ± standard deviation and categorical variables as frequencies and percentages. Within-patient comparisons of postoperative enzyme levels (postoperative day 2 and day 10) relative to baseline were analyzed using Student's paired t-test for each biochemical marker. Statistical analyses were performed using SPSS version 23.0, and two-sided p-values were interpreted with statistical significance set at <0.05.

RESULTS

A total of 100 patients underwent uncomplicated laparoscopic cholecystectomy during the study period. Female patients constituted 88% (n=88) of the cohort and males 12% (n=12). The age ranged from 21 to 70 years with a mean age of 52 years. No patient developed hemodynamic instability during the postoperative period, and there was no mortality.

Biochemical assessment demonstrated a statistically significant rise in serum ALT, AST, and total bilirubin on the second postoperative day compared with baseline, followed by a return to near-baseline values by postoperative day 10. Mean ALT increased from 28.19 ± 5.29 U/L preoperatively to 51.11 ± 13.06 U/L on postoperative day 2 ($p<0.001$), representing an absolute mean rise of 22.92 U/L. Mean AST increased from 31.23 ± 5.51 U/L preoperatively to 53.79 ± 12.92 U/L on postoperative day 2 ($p<0.001$), an absolute mean rise of 22.56 U/L.

Mean total bilirubin increased from 0.8229 ± 0.1378 mg/dL to 1.3840 ± 0.2727 mg/dL on postoperative day 2 ($p<0.001$), an absolute mean rise of 0.5611 mg/dL. By postoperative day 10, mean ALT (29.16 ± 5.40 U/L), AST (31.20 ± 5.75 U/L), and bilirubin (0.8280 ± 0.1370 mg/dL) returned to baseline-comparable levels (Table 2). In contrast, ALP showed no clinically meaningful rise; mean ALP decreased from 204.46 ± 43.67 U/L preoperatively to 184.51 ± 41.80 U/L on postoperative day 2 and returned to 203.42 ± 43.04 U/L on postoperative day 10, indicating no postoperative cholestatic pattern and no significant enzyme derangement in this parameter (Table 3).

When enzyme elevation patterns were examined by CO_2 insufflation duration categories, greater postoperative elevations were observed in patients exposed to longer pneumoperitoneum time. Among patients with CO_2 insufflation up to 40 minutes (15% of cohort), postoperative day-2 elevations were comparatively limited (ALT up to 45%, AST up to 40%, bilirubin up to 30%). In contrast, for insufflation up to 60 minutes (27% of cohort), enzyme elevations increased markedly (ALT up to 95%, AST up to 80%, bilirubin up to 70%), and for insufflation up to 70 minutes (20% of cohort), ALT and AST elevations reached up to 100% with bilirubin elevations up to 80%.

In the subgroup with CO_2 exposure above 70 minutes (5% of cohort), ALT elevation exceeded 110% and AST elevation exceeded 100%, with bilirubin elevation up to 100% on postoperative day 2 (Table 4). No residual subdiaphragmatic free gas was detected on postoperative imaging at 24 hours in any case, consistent with complete absorption of residual CO_2 within the observed period.

Table 1. Baseline Demographic Characteristics of the Study Cohort (n=100)

Variable	Value
Age (years), mean ± SD	52 ± (not reported)
Age (years), range	21–70
Sex (female), n (%)	88 (88%)
Sex (male), n (%)	12 (12%)
Mortality	0

Table 2. Changes in ALT, AST, and Total Bilirubin at Baseline, Postoperative Day 2, and Postoperative Day 10 (n=100)

Parameter	Timepoint	Mean	SD	Paired Comparison vs Baseline	p-value
ALT (U/L)	Preoperative	28.19	5.29	—	—
	Post-op Day 2	51.11	13.06	Increased	<0.001
	Post-op Day 10	29.16	5.40	Returned near baseline	Not reported
AST (U/L)	Preoperative	31.23	5.51	—	—
	Post-op Day 2	53.79	12.92	Increased	<0.001
	Post-op Day 10	31.20	5.75	Returned near baseline	Not reported
Total Bilirubin (mg/dL)	Preoperative	0.8229	0.1378	—	—
	Post-op Day 2	1.3840	0.2727	Increased	<0.001
	Post-op Day 10	0.8280	0.1370	Returned near baseline	Not reported

Table 3. Changes in Alkaline Phosphatase (ALP) at Baseline, Postoperative Day 2, and Postoperative Day 10 (n=100)

Timepoint	Mean ALP (U/L)	SD
Preoperative	204.46	43.67
Post-op Day 2	184.51	41.80
Post-op Day 10	203.42	43.04

Table 4. CO_2 Insufflation Duration and Observed Elevation Pattern in Hepatic Enzymes on Postoperative Day 2

Patients %	CO_2 insufflation Duration	ALT elevation	AST elevation	Bilirubin elevation
15%	Up to 40 minutes	Up to 45%	Up to 40%	Up to 30%
33%	Up to 50 minutes	Up to 70%	Up to 60%	Up to 45%
27%	Up to 60 minutes	Up to 95%	Up to 80%	Up to 70%
20%	Up to 70 minutes	100%	Up to 100%	Up to 80%
5%	Above 70 minutes	Above 110%	Above 100%	Up to 100%

DISCUSSION

Laparoscopic cholecystectomy performed under CO_2 pneumoperitoneum is widely recognized to induce complex hemodynamic and metabolic alterations, even in otherwise uncomplicated cases, due to the combined effects of increased intra-abdominal pressure, CO_2 absorption, and surgical positioning (34-39). In the present study, a statistically significant elevation in ALT, AST, and total bilirubin was observed on the second postoperative day compared with baseline, with normalization to near preoperative levels by postoperative day 10. These findings reinforce the consistent observation reported across multiple clinical series that transient postoperative derangements in hepatocellular enzymes and bilirubin may occur after routine LC even in the absence of bile duct injury or overt hepatic dysfunction (40-42).

The pathophysiological basis for these biochemical changes is most plausibly related to transient hepatosplanchnic hypoperfusion during pneumoperitoneum. Experimental and clinical studies have demonstrated that intra-abdominal pressures in the range commonly used during laparoscopic surgery may exceed portal venous pressure, contributing to reduced portal flow and altered hepatic microcirculation (5,8–11). In particular, portal venous flow reduction has been reported during abdominal insufflation, and hepatic perfusion compromise has been observed even at relatively modest pressure levels (8–10). Although some authors have suggested that moderate IAP ranges may not significantly compromise splanchnic circulation in all settings, heterogeneity in patient factors, anesthetic exposure, ventilation strategy, and operative duration may account for discrepant results (12). In older or physiologically vulnerable individuals, hepatic perfusion may be further influenced by perioperative anesthetic and circulatory changes, which can modify hepatic blood flow during surgical stress (41).

In addition to vascular compression and reduced venous return, CO_2 absorption may contribute indirectly to altered systemic physiology through hypercapnia and respiratory acidosis, which can increase systemic vascular resistance and alter regional perfusion patterns if not adequately compensated by ventilatory control (7). The combination of reduced splanchnic perfusion during insufflation and restoration during desufflation has been conceptualized as an ischemia-reperfusion sequence, with oxidative stress and free radical generation proposed as contributory mechanisms for transient cellular injury reflected biochemically by enzyme elevation (34–36). While the present study did not directly measure portal flow, oxidative markers, or microcirculatory parameters, the observed temporal pattern—early enzyme rise with subsequent normalization—supports the likelihood of a reversible physiological process rather than structural hepatic injury, consistent with prior clinical observations (16–19).

An important finding in this study is the apparent relationship between longer duration of CO_2 insufflation and greater postoperative enzyme elevation. Earlier work has suggested that elevated intra-abdominal pressure is a key driver of biochemical changes, and that the magnitude of derangement may vary with pneumoperitoneum exposure and operative duration (18,19). The descriptive trend in the present cohort demonstrates that patients exposed to longer insufflation times had higher observed elevations in ALT, AST, and bilirubin on postoperative day 2. Although the current analysis did not compute a formal correlation coefficient or regression estimate, the gradient pattern aligns with prior evidence suggesting that longer pneumoperitoneum exposure may exacerbate hepatosplanchnic hypoperfusion and metabolic stress responses (9,18,19). This time-dependent effect also supports the rationale for exploring low-pressure techniques or alternative strategies in selected patients, particularly those with limited cardiopulmonary reserve or borderline hepatic function, as previously suggested in the context of gasless laparoscopy and pressure-minimization approaches (20).

Notably, ALP did not show clinically meaningful postoperative elevation in this study. This is consistent with the expectation that pneumoperitoneum-related changes predominantly reflect transient hepatocellular enzyme leakage and bilirubin fluctuation rather than a cholestatic pattern, particularly when bile duct injury and obstruction are excluded (16,17). Similarly, other investigators have reported that postoperative enzyme elevations after LC are commonly not accompanied by clinically significant biliary complications, and may occur without ominous implications when duct injury is not present (16–18). The absence of residual free subdiaphragmatic gas on postoperative imaging at 24

hours further supports the expected rapid absorption of CO_2, although biochemical alterations may persist beyond gas absorption due to transient perfusion-related or oxidative processes (21-26).

The strengths of this study include its prospective design, standardized operative technique under a uniform pneumoperitoneum pressure, consistent anesthetic protocol, and repeated measurement of key LFT parameters at clinically relevant timepoints. However, several limitations should be recognized. First, the study lacked a control comparator group (e.g., open cholecystectomy, low-pressure pneumoperitoneum, or gasless laparoscopy), limiting causal inference regarding the independent effect of pressure level. Second, objective hemodynamic or perfusion measures such as portal venous flow assessment were not performed, and oxidative stress markers were not measured, restricting mechanistic interpretation (8–11,34–36). Third, the analysis of insufflation duration was descriptive rather than inferential; future studies should model enzyme changes as continuous outcomes using correlation or multivariable regression, including operative duration and patient covariates as potential confounders (18,19). Finally, although strict exclusion criteria strengthened internal validity by reducing alternative causes of enzyme elevation, the findings may not be generalizable to higher-risk patients, complicated gallstone disease, or cases requiring intraoperative cholangiography.

Overall, the present findings support the conclusion that temporary postoperative derangements in ALT, AST, and bilirubin are common after uncomplicated LC under standard-pressure pneumoperitoneum and tend to normalize within 10 days, with greater elevations observed following longer CO_2 exposure. These biochemical changes appear clinically benign in carefully selected uncomplicated cases, but their magnitude and time-dependence warrant consideration when interpreting early postoperative LFT abnormalities and when selecting pneumoperitoneum strategies for vulnerable patient groups (13–20).

CONCLUSION

This prospective study demonstrates that uncomplicated laparoscopic cholecystectomy performed under CO_2 pneumoperitoneum at 14 mmHg is associated with a statistically significant but transient rise in ALT, AST, and total bilirubin by postoperative day 2, with return to near baseline values by postoperative day 10, while ALP remains largely unchanged. The magnitude of postoperative enzyme elevation appears greater among patients exposed to longer durations of CO_2 insufflation, supporting the view that pneumoperitoneum-related hepatosplanchnic effects are the primary contributors to these reversible biochemical alterations, which were not accompanied by clinically apparent hepatic dysfunction in this cohort.

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