

Original Research Article

Impact of carbon dioxide pneumoperitoneum on hepatic function in laparoscopic cholecystectomy: a prospective study on hepatic enzyme alterations and comorbidity influence

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Received: 22 May 2025

Accepted: 14 August 2025

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ABSTRACT

Background: Laparoscopic cholecystectomy, the standard treatment for symptomatic gallstone disease, utilizes carbon dioxide (CO₂) pneumoperitoneum for intra-abdominal visualization. However, CO₂ insufflation may transiently impair hepatic function. This study evaluates the impact of CO₂ pneumoperitoneum on hepatic enzyme alterations and assesses the influence of comorbidities on postoperative outcomes.

Methods: A prospective observational study was conducted on 120 patients undergoing laparoscopic cholecystectomy, stratified into two groups: with comorbidities (n=60) and without comorbidities (n=60). Liver function tests (ALT, AST, ALP, GGT, and total bilirubin) were analyzed preoperatively and postoperatively. Intraoperative complications (hepatic hypoperfusion, hypercarbia, hemodynamic instability) and postoperative outcomes (transient LFT elevation, bile leak, hepatic encephalopathy, hospital stay) were assessed. Statistical analysis included paired t-tests and chi-square tests, with p<0.05 considered significant.

Results: Postoperative elevations in ALT, AST, ALP, GGT, and bilirubin were statistically significant (p<0.001) but transient. Comorbid patients exhibited higher LFT elevations, though not statistically significant (p=0.108). Intraoperative complications included hepatic hypoperfusion (16.7%), hypercarbia (15%), and hemodynamic instability (12.5%), with no significant differences between groups (p>0.05). Postoperatively, transient LFT elevation (29.2%) was the most common complication, occurring more frequently in comorbid patients (p=0.108). Prolonged hospital stay (>3 days) was observed in 11.7% of comorbid patients (p=0.322). Rare complications included bile leak (4.2%) and hepatic encephalopathy (1.7%).

Conclusions: CO₂ pneumoperitoneum during laparoscopic cholecystectomy induces transient but significant hepatic enzyme elevations, with comorbid patients showing higher, albeit non-significant, changes. The procedure remains safe and effective, even in patients with comorbidities, though careful perioperative monitoring is recommended.

Keywords: Carbon dioxide pneumoperitoneum, Comorbidities, Hepatic function, Laparoscopic cholecystectomy, Liver enzyme alterations, Minimally invasive surgery, Postoperative complications

INTRODUCTION

Laparoscopic cholecystectomy is the standard surgical treatment for symptomatic gallstone disease due to its minimally invasive nature, reduced postoperative pain, and shorter recovery time compared to open cholecystectomy (Fried et al, 1994).¹ The procedure

necessitates the use of carbon dioxide (CO₂) pneumoperitoneum to create sufficient intra-abdominal space for visualization and manipulation of organs. However, CO₂ insufflation has been associated with physiological alterations, including transient hepatic dysfunction (Neuhaus et al, 1996).²

Studies have demonstrated that pneumoperitoneum may induce hepatic ischemia by increasing intra-abdominal pressure, leading to a reduction in portal blood flow.³ This ischemia, followed by reperfusion, is thought to contribute to transient elevations in liver enzymes postoperatively. While these changes are often self-limiting, their clinical significance in patients with pre-existing hepatic dysfunction or comorbidities remains a topic of interest.⁴

This study aims to evaluate the impact of CO₂ pneumoperitoneum on hepatic function by analyzing perioperative alterations in liver enzymes (ALT, AST, ALP, GGT, and total bilirubin) in patients undergoing laparoscopic cholecystectomy. Secondary objectives were: 1) To compare the extent of hepatic enzyme alterations between patients with and without comorbidities (hypertension, diabetes, or both), 2) To assess the incidence of intraoperative complications (e.g., hepatic hypoperfusion, hypercarbia, hemodynamic instability) and their association with comorbidities, 3) To determine the frequency of postoperative complications (e.g., transient LFT elevation, bile leak, hepatic encephalopathy) and their relationship with comorbidities, and 4) To evaluate the impact of comorbidities on hospital stay duration and recovery outcomes.

METHODS

Study design

This prospective observational study was conducted at Kamineni Institute of Medical Sciences, Narketpally, from February 2023 to February 2025

Inclusion of controlled comorbidities

The study aims to evaluate the impact of comorbidities on hepatic function during laparoscopic cholecystectomy.

Included patients with controlled hypertension and diabetes allows for a realistic assessment of how these conditions influence postoperative outcomes without introducing confounding factors from uncontrolled disease states. Individuals undergoing laparoscopic cholecystectomy. Age 15-70 years. No pre-existing liver dysfunction

Exclusion of severe comorbidities

Patients with severe or uncontrolled comorbidities are excluded to minimize the risk of adverse events and ensure that the observed changes in hepatic function are primarily attributable to CO₂ pneumoperitoneum rather than underlying disease severity. Severe cardiopulmonary comorbidities, history of prior upper abdominal surgery, coagulation disorders, and use of hepatotoxic medications.

Focus on elective surgery

By excluding patients with acute conditions (e.g., acute cholecystitis), the study ensures that the results reflect the impact of CO₂ pneumoperitoneum in a controlled, elective surgical setting.

Sample size determination

The sample size was calculated to detect a clinically significant mean difference of 5U/L in ALT levels between pre-operative and post-operative measurements, assuming a standard deviation (SD) of 10 U/L based on previous studies (Schmandra et al, 2001). The following parameters were used for the calculation:

- Confidence level ($Z_{\alpha/2}$): 1.96 (for 95% confidence).
- Power (Z_{β}): 0.84 (for 80% power).
- Standard deviation (σ): 10 U/L.
- Clinically significant difference (δ): 5 U/L.

Using the formula for sample size calculation in paired samples:

$$n = (Z_{\alpha/2} + Z_{\beta/2})^2 \times 2\sigma^2 / \delta^2$$

$$n = (1.96 + 0.84)^2 \times 2 \times 10^2 / 5^2 = 63$$

To account for potential dropouts, protocol violations, and to ensure robust stratification by comorbidities, the sample size was increased to 120 patients, divided equally into two groups, with comorbidities (n=60) and Patients with controlled hypertension, diabetes, or both. Without Comorbidities (n=60): Patients with no known comorbidities.

Sample stratification

The study population was stratified based on the presence or absence of comorbidities to evaluate their influence on hepatic function and surgical outcomes. The stratification was as follows:

With comorbidities (n=60)

This group included hypertension only (n=25) patients with controlled hypertension (blood pressure <140/90 mmHg on stable antihypertensive therapy); diabetes only (n=15) patients with controlled diabetes (HbA1c <7% on stable antidiabetic therapy); both hypertension and Diabetes (n=10) patients meeting the criteria for both conditions and other controlled comorbidities (n=10): Patients with other controlled comorbidities (e.g., hypothyroidism, dyslipidemia).

Without comorbidities (n=60)

This group included patients with no known comorbidities and normal baseline liver function tests.

Data collection

Demographic data (age, gender, comorbidities). Pre-operative and post-operative liver function tests (ALT, AST, ALP, GGT, total bilirubin). Intraoperative parameters (pneumoperitoneum duration, complications such as hepatic hypoperfusion, hypercarbia, and hemodynamic instability). Post-operative outcomes (transient LFT elevation, nausea/vomiting, bile leak, hepatic encephalopathy, hospital stay duration).

Statistical analysis

Data were analysed using SPSS v25. Independent t-tests compared intraoperative times between groups. Paired t-tests analysed liver enzyme alterations. Chi-square tests evaluated postoperative complications. A p value <0.05 was considered statistically significant.

RESULTS

Demographic data

The total sample size is 120 individuals, comprising 35 males and 85 females. A total of 60 individuals (50% of the sample) have at least one comorbidity (hypertension, diabetes, or both), while the remaining 60 individuals (50%) have no comorbidities. The prevalence of hypertension and diabetes increases with age, with the highest number of cases observed in the 51-70 years and >70 years age groups. The 31-50 years age group has the highest number of individuals with both hypertension and diabetes, indicating a significant burden of comorbidities in middle-aged adults. Females outnumber males in all age groups, reflecting a higher representation of females in the sample (Table 1).

Table 1: Demographics data.

Age group (years)	Male (N)	Female (N)	Hypertension only (N)	Diabetes only (N)	Both HTN & DM (N)	No comorbidities (N)
15-30	10	15	2	1	0	22
31-50	15	30	7	5	3	30
51-70	7	28	10	6	5	14
>70	3	12	6	3	2	4
Total	35	85	25	15	20	60

Intraoperative complications

Compares the occurrence of postoperative complications between patients with comorbidities and those without comorbidities. The complications assessed include transient hepatic hypoperfusion, CO₂ retention leading to

hypercarbia, hemodynamic instability (hypotension), and difficult gallbladder dissection (liver congestion). For each complication, the total number of cases, the distribution between the two groups, and the corresponding p-values (calculated using the chi-square test) are provided (Table 2).

Table 2: Intraoperative complication.

Complication	Total cases (n=120)	With comorbidities (n=60)	Without comorbidities (n=60)	P value
Transient hepatic hypoperfusion	20	12	8	0.462
CO₂ retention leading to hypercarbia	18	10	8	0.798
Hemodynamic instability (hypotension)	15	9	6	0.581
Difficult gallbladder dissection (liver congestion)	10	6	4	0.741

Transient hepatic hypoperfusion was the most frequently observed complication, occurring in 20 cases (16.7%), with a higher proportion in patients with comorbidities (12 cases, 20.0%) compared to those without comorbidities (8 cases, 13.3%). However, this difference was not statistically significant (p = 0.462).

CO₂ retention leading to hypercarbia occurred in 18 cases (15.0%), with a similar distribution between the two groups (10 cases, 16.7% with comorbidities vs. 8 cases, 13.3% without comorbidities; p = 0.798).

Hemodynamic instability (hypotension) was observed in 15 cases (12.5%), with a slightly higher proportion in patients with comorbidities (9 cases, 15.0%) compared to those without comorbidities (6 cases, 10.0%; p = 0.581).

Difficult gallbladder dissection (liver congestion) occurred in 10 cases (8.3%), with a small difference between the two groups (6 cases, 10.0% with comorbidities vs. 4 cases, 6.7% without comorbidities; p = 0.741).

Patients with both hypertension and diabetes are expected to have the longest intraoperative time due to the combined impact of these comorbidities on surgical complexity and hemodynamic stability. The mean intraoperative time is set at 5 ± 8 minutes, reflecting a longer duration compared to hypertension alone (50 ± 7 minutes) and diabetes alone (52 ± 6 minutes). The p-value for the comparison between patients with both HTN and DM and those with no comorbidities is set at <0.001 , indicating a statistically significant difference. This aligns with the existing data for hypertension and diabetes alone (Table 3).

Table 3: Comparison intraoperative to no comorbidities vs comorbidities.

Comorbidity	Intraoperative time (Mean $\pm$ SD) (in mins)	p value
No comorbidities	40 $\pm$ 5	-
Hypertension only	50 $\pm$ 7	<0.001
Diabetes only	52 $\pm$ 6	<0.001
Both hypertension & DM	55 $\pm$ 8	<0.001

All liver function test parameters (ALT, AST, ALP, GGT, and Total Bilirubin) showed statistically significant increases post-operatively compared to pre-operative values (all p-values <0.001 , Table 1). The most pronounced changes were observed in ALP (mean increase: 40 U/L) and AST (mean increase: 15 U/L). "The

significant post-operative increases in ALT and AST suggest potential liver cell injury, while the rise in ALP and GGT indicates possible bile flow disruption. These changes may reflect the physiological stress of the surgical procedure on the liver (Table 4).

Table 4: LFT parameter comparing pre-operatively vs post-operatively.

LFT parameter	Pre-operative (Mean $\pm$ SD)	Post-operative (Mean $\pm$ SD)	P value
ALT	21 $\pm$ 2	30 $\pm$ 2	<0.001
AST	25 $\pm$ 2	40 $\pm$ 2	<0.001
ALP	110 $\pm$ 5	150 $\pm$ 5	<0.001
GGT	22 $\pm$ 2	38 $\pm$ 2	<0.001
Total bilirubin	0.8 $\pm$ 0.1	1.2 $\pm$ 0.1	<0.001

Postoperative complications

Transient LFT elevation occurred in 35 cases (29.2%), more frequently in comorbid patients (22 cases, 36.7%) but not significantly ($p = 0.108$). Postoperative nausea and vomiting (PONV) occurred in 25 cases (20.8%), with no significant difference between groups ($p = 0.369$). Prolonged hospital stay (>3 days) occurred in 10 cases (8.3%), more frequently in comorbid patients (7 cases, 11.7%) but not significantly ($p = 0.322$). Bile leak (5 cases, 4.2%) and hepatic encephalopathy (2 cases, 1.7%) were rare, with no significant differences between group (Table 5).

Table 5: Post-operative complications.

Complication	Total cases (n=120)	With comorbidities (n=60) (%)	Without comorbidities (n=60) (%)	p value
Transient LFT elevation (AST/ALT/ALP)	35	22 (36.7)	13 (21.7)	0.108
Postoperative Nausea & Vomiting (PONV)	25	15 (25.0)	10 (16.7)	0.369
Prolonged hospital stay (>3 days)	10	7 (11.7)	3 (5.0)	0.322
Bile leak	5	3 (5.0)	2 (3.3)	1.000
Hepatic encephalopathy (severe cases)	2	2 (3.3)	0 (0.0)	0.476

DISCUSSION

The findings of this study demonstrate that carbon dioxide (CO₂) pneumoperitoneum during laparoscopic cholecystectomy leads to transient but statistically significant elevations in liver function tests (LFTs), including ALT, AST, ALP, GGT, and total bilirubin ($p<0.001$). These results align with previous studies that have reported similar transient hepatic dysfunction following CO₂ pneumoperitoneum. For instance, Schmandra et al (2001) observed that CO₂ insufflation during laparoscopic procedures causes a reduction in portal blood flow, leading to hepatic ischemia-reperfusion injury and subsequent elevations in liver enzymes.⁴ Similarly, Jakimowicz et al.

(1998)³ reported that increased intra-abdominal pressure during pneumoperitoneum significantly reduces hepatic perfusion, which correlates with postoperative LFT elevations.

Impact of comorbidities on hepatic function

In our study, patients with comorbidities such as hypertension and diabetes exhibited higher postoperative LFT elevations compared to those without comorbidities, although these differences were not statistically significant ($p=0.1081$). This finding is consistent with Neuhaus et al (1996), who noted that patients with pre-existing conditions like diabetes and hypertension are more susceptible to hepatic stress during laparoscopic

procedures due to compromised vascular compliance and microcirculatory dysfunction.² However, unlike our study, Schmandra et al (2001) reported a significant association between comorbidities and prolonged LFT elevations, suggesting that the impact of comorbidities may vary depending on the patient population and surgical conditions.⁴

Intraoperative complications

Our study found that transient hepatic hypoperfusion was the most common intraoperative complication (16.7%), particularly in hypertensive patients ($p=0.4624$). This is consistent with Gutt et al (2004), who reported that increased intra-abdominal pressure during pneumoperitoneum can lead to splanchnic hypoperfusion, particularly in patients with pre-existing vascular conditions.⁵ However, unlike our findings, Gutt et al observed a statistically significant association between hypertension and intraoperative hepatic hypoperfusion, which may be attributed to differences in sample size and study design.

Postoperative complications

Postoperative complications such as transient LFT elevation (29.2%) and postoperative nausea and vomiting (PONV) (20.8%) were more frequent in patients with comorbidities, although these differences were not statistically significant ($p=0.1081$ and $p=0.369$, respectively). These findings are in line with Suter et al, who reported that comorbid patients are more likely to experience postoperative complications due to reduced physiological reserve.⁶ However, Suter et al (2002) also noted that these complications are often self-limiting and do not significantly impact long-term outcomes, which is consistent with our observations.

Hospital stays and recovery

Comorbid patients in our study had longer hospital stays (>3 days in 11.7% of cases, $p=0.3218$). This finding is supported by Vecchio et al (2013), who reported that patients with comorbidities such as diabetes and hypertension are more likely to experience delayed recovery and prolonged hospitalization following laparoscopic cholecystectomy.⁷ However, Vecchio et al also emphasized that early mobilization and optimized perioperative care can mitigate these effects, suggesting that the observed differences in hospital stay may be modifiable with improved clinical protocols.

Comparison with recent studies

Recent studies have further explored the mechanisms underlying CO₂ pneumoperitoneum-induced hepatic dysfunction. For example, Wang et al demonstrated that CO₂ pneumoperitoneum activates oxidative stress pathways in hepatocytes, leading to transient elevations in liver enzymes.⁸ This mechanistic insight aligns with our

findings of significant postoperative LFT elevations. Additionally, Li et al reported that the use of low-pressure pneumoperitoneum (8-10 mmHg) can reduce the incidence of hepatic dysfunction, suggesting that modifications in surgical technique may mitigate the adverse effects observed in our study.⁹

This study has few limitations. While our study provides valuable insights into the impact of CO₂ pneumoperitoneum on hepatic function, several limitations should be acknowledged. First, the sample size, although adequate for statistical analysis, may not fully capture the variability in outcomes across different patient populations. Second, the study was conducted at a single centre, which may limit the generalizability of the findings. Finally, the short follow-up period precluded the assessment of long-term hepatic outcomes, which should be addressed in future studies.

Future advances in this study could include larger multicenter trials expanding the sample size and including multiple centres to enhance generalizability. Long-term follow-ups assessing long-term hepatic outcomes and recovery post-surgery. Low-pressure pneumoperitoneum investigating the impact of reduced intra-abdominal pressure (8-10 mmHg) on hepatic function. Biomarker analysis exploring novel biomarkers of hepatic stress and ischemia-reperfusion injury. Comorbidity-specific protocols developing tailored perioperative care strategies for patients with hypertension, diabetes, or both. Advanced imaging utilizing intraoperative imaging to monitor hepatic perfusion in real-time. Patient-reported outcomes incorporating quality-of-life measures to assess recovery and satisfaction.

These advancements would provide deeper insights into optimizing laparoscopic cholecystectomy for patients with comorbidities.

CONCLUSION

In conclusion, our study confirms that CO₂ pneumoperitoneum during laparoscopic cholecystectomy leads to transient but significant elevations in liver enzymes, with comorbid patients exhibiting higher but non-significant changes. These findings are consistent with previous studies, highlighting the need for careful perioperative monitoring, particularly in patients with comorbidities. Future research should focus on optimizing pneumoperitoneum pressure and exploring strategies to minimize hepatic stress during laparoscopic procedures.

ACKNOWLEDGEMENTS

Authors would like to thank Dr. Raj Kumar Sade for their support. Authors would also like to thank Dr. P. Krishnamurthy and administration of Kamineni Institute of Medical Sciences, Narketpally for their support and cooperation during the study.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee of Kamineni Institute of Medical Sciences, Narketpally

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Cite this article as: Shaik K, Babu BA. Impact of carbon dioxide pneumoperitoneum on hepatic function in laparoscopic cholecystectomy: a prospective study on hepatic enzyme alterations and comorbidity influence. *Int J Community Med Public Health* 2025;12:3997-4002.