Original Article

DOI: 10.7860/JCDR/2023/59653.18084

Alterations in Liver Enzymes in the Postoperative Period Following Laparoscopic and Open Cholecystectomy: A Prospective Study

Surgery Section

UPASANA CHOUDHURY[1], PARTHA SARATHI DUTTA[2]

(cc) BY-NC-ND

ABSTRACT

Introduction: Laparoscopic Cholecystectomy (LC) is one of the most common procedures that is being performed by a general surgeon, and is the treatment of choice for symptomatic gallstone disease. Any abnormalities in the postoperative period because of the procedure is a thing of concern for the operating surgeon.

Aim: To compare the changes in the levels of liver enzymes in the immediate and delayed postoperative period following LC and following Open Cholecystectomy (OC) with respect to the preoperative values.

Materials and Methods: This was prospective interventional study carried out in the General Surgery wards of Bankura Sammilani Medical College and Hospital, Bankura, West Bengal, India, from February 2020 to August 2021. A total of 43 patients who underwent LC and 43 patients who underwent OC were randomly selected from the surgical wards. Their levels of Alkaline Phosphatase (ALP), Aspartate Transaminase (AST), Alanine Transaminase (ALT) and total bilirubin were noted in the preoperative period, 24 hours after the surgery and seven days after the surgery. The changes in the levels of the above-mentioned parameters were analysed using paired t-test via International Business Machines Statistical Package for the Social Sciences II (IBM SPSS II) software version 25.0.

Results: The mean age of the study participants who underwent OC was 40.98±12.46 years while the mean age for those who underwent LC was 36.42±10.53 years. There was a significant increase in the levels of AST (27.02±7.272 IU/L to 53.70±19.902 IU/L), ALT (26.21±7.399 IU/L to 50.21±14.410 IU/L) and total bilirubin (0.601±0.173 mg/dL to 0.782±0.261 mg/dL) in the immediate postoperative period (24 hours after surgery) p-value <0.01 among the patients who underwent LC but returned to its baseline preoperative value within seven days of the surgery. No such significant change was noted in the levels of the liver enzymes (AST: 30.93±8.160 IU/L to 32.14±16.988 IU/L, ALT: 31.51±10.762 IU/L to 31.14±10.921 IU/L) among patients undergoing OC.

Conclusion: The transient increase in the liver enzymes (AST, ALT and total bilirubin) 24 hours after LC maybe related to the increased intra-abdominal pressure due to CO_2 pneumoperitoneum which decreases the venous return and thereby cardiac output, thus leading to tissue ischaemia. Absence of this effect leads to no significant change in the liver enzymes in the postoperative period following OC.

Keywords: Aspartate, Bilirubin, Pneumoperitoneum, Transaminases

INTRODUCTION

The LC is one of the most common procedures which is being performed by all general surgeons on a daily basis for gallstone disease. The worldwide prevalence of the gallstone disease varies widely, ranging from 5% in China, 10-22% in India to 9-21% among Europeans to as high as 64-73% among American Indians (based on ultrasonographic survey among females) [1]. The liver enzymes namely ALP, ALT, and AST and total bilirubin levels should theoretically remain unchanged in the postoperative following cholecystectomy. A rise in the above mentioned parameters following cholecystectomy is usually suggestive of injury to the biliary tree [1].

Despite being the gold standard procedure, laparoscopic surgery comes with its own set of complications pertaining to pneumoperitoneum. Pneumoperitoneum has been seen to cause air embolism, hypercarbia with acidosis, ventricular arrhythmia and a significant change in liver enzymes [2]. A significant change in the liver enzymes namely AST and ALT after LC without any bile duct injury in the intraoperative period may thus raise concern among the surgeons as well as the patients.

Similar study have been attempted in the past comparing the liver function parameters in the preoperative and postoperative period after laparoscopic surgery [3]. While, this study not only makes the similar comparison but also compares it with the alterations of the same parameters after open surgery. The aim of this study was to compare the changes in levels of ALP, AST, ALT and total bilirubin levels in the postoperative period after LC and after OC.

MATERIALS AND METHODS

This prospective interventional study was conducted in the surgical wards of Bankura Sammilani Medical College and Hospital, Bankura, West Bengal, India, between February 2020 and August 2021. All patients admitted in the General Surgery wards who were taken up for elective cholecystectomy. After getting approval from the Institutional Ethics Committee, data was collected using a predesigned questionnaire which included interview, clinical examination and laboratory investigation after obtaining appropriate consent from the patient.

Inclusion criteria: All patients in the age group of 18-60 years who were admitted for cholecystectomy were included in the study.

Exclusion criteria: Patients having deranged liver function tests since the preoperative period, cholelithiasis along with choledocholithiasis, stage I carcinoma of gallbladder and patients for whom laparoscopic technique was converted to open due to some unavoidable reason are excluded from the study.

Study Procedure

Simple randomisation technique has been used for selection of the sample. At the beginning of every week (Sunday), a day was randomly selected (by the roll of a dice and the corresponding day of the week was chosen according to the result), and on that day, the first patient who met all the above selection criteria, who underwent LC, and the first patient who underwent OC were included in the groups LC and OC, respectively. A total of 86 patients were selected and divided equally into two groups of 43; namely OC (those who underwent OC) and LC (those who underwent LC).

Measurement of the liver function test parameters in the preoperative period (24 hours before the surgery) and in the postoperative period, on day 1 (24 hours after the surgery) and on day 7. These parameters included serum ALP, AST, ALT, and serum total bilirubin levels.

The normal values for the above-mentioned parameters were taken as follows [2]:

- ALP: 40-129 IU/L
- AST (SGOT): 8-48 IU/L
- ALT (SGPT): 7-55 IU/L
- Total bilirubin: 0.1-1.2 mg/dL

All laboratory investigations were done from the biochemistry laboratory of the institution.

Operative standardisations: All the OC procedures were performed in supine position, while all the LC procedures were carried out in reverse Trendelenburg's position. All patients irrespective of the type of surgery received same preanaesthetic medications. All surgeries were done under general anaesthesia using propofol as the induction agent, and scoline for intubation. Sevoflurane and atracurium were used for the maintenance of the anaesthesia, and neostigmine was used during reversal. The average duration for OC (from skin incision to closure of the wound) was two hours, while that for LC (from insertion of trocar through the umbilical port to removal of gallbladder via the umbilical port) was 1.5 hours. The intra-abdominal pressure following pneumoperitoneum in LC was maintained at 12-15 mm of Hg.

STATISTICAL ANALYSIS

Analysis of the collected data was done using IBM SPSS-II software version 25.0. The means of the preoperative values of the different parameters of the liver function test were compared with the means of the postoperative (after 24 hours and after seven days) values of the same parameters. The means were compared using paired t-test. The p-value less than 0.05 were considered statistically significant.

RESULTS

The mean age of the patients who underwent OC was 40.98±12.46 years while the mean age was 36.42±10.53 years for those who underwent LC. The age and gender distribution of the two groups have been demonstrated in [Table/Fig-1].

Age group (in years)	Open Cholecystectomy (OC)		Laparoscopic Cholecystectomy (LC)	
	Male	Female	Male	Female
10-20	0	4	0	1
21-30	2	5	3	10
31-40	3	10	4	13
41-50	2	7	1	6
51-60	1	9	0	5
Total	8	35	8	35

[Table/Fig-1]: Shows the age and gender distribution among the two groups (OC and LC).

There was no mortality or morbidity. In [Table/Fig-2], among the patients who underwent OC, the ALP shows a significant decrease 24 hours after the surgery and remains so after seven days of the surgery while ALT, AST and total bilirubin, there was no significant change in the values of these parameters in the immediate as well as delayed postoperative period compared to the preoperative values.

In [Table/Fig-3], among the patients who underwent LC, ALP value did not show any significant change in the postoperative period, compared to its preoperative value while AST, ALT and total bilirubin shows a rising trend 24 hours after the surgery only to decline seven days after the surgery.

Parameters	Preoperative Mean±SD	Early postoperative (after 24 hours) Mean±SD	p-value	Delayed postoperative (after 7 days) Mean±SD	p-value
ALP (IU/L)	91.67±20.312	85.35±16.064	**0.013**	84.93±19.410	**<0.001**
ALT (IU/L)	31.51±10.762	31.14±10.921	0.751	29.77±9.227	0.164
AST (IU/L)	30.93±8.160	32.14±16.988	0.624	31.49±10.446	0.690
Total bilirubin (mg/dL)	0.677±0.224	0.602±0.283	0.161	0.579±0.202	0.054

[Table/Fig-2]: Preoperative mean values, early postoperative (after 24 hours) mean values and delayed postoperative (after seven days) mean values of ALP, ALT, AST and total bilirubin of the patients who underwent Open Cholecystectomy (OC).
*Paired t-test has been used to compare the values and a p-value in bold font indicates statistically significant values

Parameters	Preoperative Mean±SD	Early postoperative (after 24 hours) Mean±SD	p-value	Delayed postoperative (after 7 days) Mean±SD	p-value
ALP (IU/L)	87.00±18.896	85.74±16.451	0.302	86.28±18.300	0.086
ALT (IU/L)	26.21±7.399	50.21±14.410	**<0.001**	25.88±5.889	0.595
AST (IU/L)	27.02±7.272	53.70±19.902	**<0.001**	26.95±6.008	0.887
Total bilirubin (mg/dL)	0.601±0.173	0.782±0.261	**<0.001**	0.519±0.156	**0.004**

[Table/Fig-3]: Shows the preoperative mean values, early postoperative (after 24 hours) mean values and delayed postoperative (after seven days) mean values of ALP, ALT, AST and total bilirubin of the patients who underwent Laparoscopic Cholecystectomy (LC).
*Paired t-test has been used to compare the values and a p-value in bold font indicates statistically significant values

DISCUSSION

The mean values of AST and ALT of the present study are similar to studies conducted by Tan M et al., in 2001-2002 among 286 patient who had underwent LC, and that of Ibrahim AM et al., who had conducted the study among 60 patients who had underwent various laparoscopic procedures both of these studies compared the means of AST and ALT levels in the preoperative period with those on the postoperative days 1 and 7 [Table/Fig-4] [4,5].

The significant change in AST, ALT and total bilirubin levels following LC is transient. Not noticing such a change among the patients who underwent OC, the first factor to be considered is CO_2 pneumoperitoneum. Halevy A et al., in 1994 were the first, who studied 67 patients who had underwent LC, to demonstrate the significant increase in AST and ALT after the surgery, and had postulated certain explanations for the same, the first one being increased intra-abdominal pressure following pneumoperitoneum [6]. In the year 2002, Nguyen NT et al., found that there was an increase in the level of transaminases, no change in the levels of Gamma-glutamyl Transferase (GGT) and decrease in the levels of ALP in the postoperative period after 24 hours among a group of 18 patients who underwent laparoscopic gastric bypass surgery compared to another group of 18 patients who underwent open gastric bypass [7]. The rise in the levels of transaminases was two to three-fold compared to their preoperative levels. And this change was attributed to the increased intra-abdominal pressure due to pneumoperitoneum. The increased intra-abdominal pressure created by the insufflation of CO_2 may have an ischaemic effect on the liver. This ischaemia of the liver tissue is caused by the reduction in the stroke volume. In 1999, Dexter SP et al., studied the hemodynamic changes in the body during LC with high pressure versus low pressure CO_2 pneumoperitoneum among 20 patients [8]. According to the study, the net venous outflow is a result of two opposing pressures- the mean systemic pressure which empties the veins, thereby increasing the venecaval outflow to the heart resulting in increase in the stroke volume as well as

Author and year of the study	AST (IU/L)			ALT (IU/L)		
	Preoperative	Postoperative day 1	Postoperative day 7	Preoperative	Postoperative day 1	Postoperative day 7
Tan M et al., 2003 [4]	28.4±20.2	41.5±24.7	29.1±18.7	23.3±11.6	38.8±15.2	25.1±14.3
Ibrahim AM et al., 2017 [5]	24.53±4.83	40.88±12.32	27.1±5.98	18.9±4.55	31.83±9.83	21.6±5.48
Present study	27.02±7.272	53.70±19.902	26.95±6.008	26.21±7.399	50.21±14.410	25.88±5.889

[Table/Fig-4]: Shows mean values of liver enzymes in the preoperative period and in the postoperative period following Laparoscopic Cholecystectomy (LC) in various studies [4,5].
AST: Aspartate transaminase; ALT: Alanine transaminase

the cardiac output, and venous resistance which decreases the outflow of the veins. It has been seen that the dominant pressure at an intra-abdominal pressure of 15 mm of Hg is the venous resistance, thereby resulting in the decrease in the cardiac output (even below the pre-insufflation baseline). Thus, blood supply to liver is also compromised leading to tissue ischaemia and rise in blood levels of AST and ALT. At low pressure (7 mm of Hg) CO_2 pneumoperitoneum, the dominant pressure is the mean systemic pressure thereby an increase in the cardiac output is noted. In our study, we have created pneumoperitoneum with an intra-abdominal pressure of 12-15 mm of Hg, thereby making it one of the possible reasons for the rise of liver enzymes. In 2005, Hasuki S et al., in 2014, Singal R et al., also noted these changes in liver enzymes in their studies [9,10]. They further noted that an intra-abdominal pressure of 12-14 mm of Hg of CO_2 caused more increase in the levels of serum transaminases than a pressure of 7-8 mm of Hg of CO_2, the latter being almost equal to portal venous pressure. Also, damage to the liver by the free radicals generated at the end of a laparoscopic procedure, as a result of ischaemia-reperfusion phenomenon was a possible factor for this change.

Another mechanism as suggested by Halevy A et al., in their study in 1994 is the "squeeze" effect on the liver which causes it to release the enzymes, as stated by other similar studies due to the prolonged traction of the gallbladder [6]. The prolonged traction of the gallbladder towards cephalad direction, causes the gallbladder to impinge on the liver bed and also indirectly putting pressure on the inferior vena cava, thereby decreasing the preload and hence the cardiac output. However, this traction is also applied in the OC where, along with the traction to the gall bladder, the edge of the liver is also elevated and retracted to expose the gallbladder fossa. This manoeuvre, to some extent relieves the pressure from the inferior vena cava thereby not decreasing the cardiac output. This may explain the absence of rise in the liver enzymes following OC.

The third mechanism which may cause injury to the liver as mentioned by Halevy A et al., is the prolonged use of diathermy, which generates heat that may damage the liver tissue [6]. The diathermy is used to dissect the gallbladder out from the liver bed. However, diathermy is used in open as well as in LC, hence, cannot explain the rise in liver enzymes exclusively in the postoperative period of LC.

Tan M et al., (2001-2002) in their study, pointed out the role of general anaesthesia in causing transient liver dysfunction [4]. However, both the groups LC and OC had been anaesthetised using the same drugs. Scapa E et al., (1998) explored the effect of general anaesthesia on the hepatic sinusoidal cells, 24 hours after the surgery in 20 patients after orthopaedic surgery, only to find a mild decrease in albumin level as the significant change [11]. Guven HE and Oral S (2003-2005) conducted a study among 267 patients who underwent LC and 54 patients who underwent OC, comparing the levels of ALP, AST, ALT, Lactate Dehydrogenase (LDH) and GGT levels in the postoperative period (after 24 hours) with their preoperative levels in both the groups [12]. They observed that there was significant rise in the levels of the AST, ALT, LDH and GGT 24 hours after the surgery among the patients who underwent LC, but no such elevation was noted among those who underwent OC. They ruled out the role of anaesthetic agents in contribution to the alteration in the hepatic enzymes as same drugs were used in both the group of patients.

Aberrant anatomy of the duct, cystic artery and right hepatic artery is not uncommon [13,14]. Inadvertent clipping of the right hepatic artery while clipping the cystic duct or cystic artery, will lead to increase in the liver enzymes in the postoperative period. But this rise in the ALT and AST shall be massive and it will continue to increase over time. The rise in the enzymes in this study was transient. So, as serious as a complication of clipping right hepatic artery may not be a suitable mechanism to explain this rise.

Limitation(s)

The limitation of the present study was limited sample size only among patients of the surgical ward of one hospital. It fails to explore whether the rise in the liver enzymes following LC is an exclusive feature for cholecystectomy or whether such changes are noted in other laparoscopic procedures.

CONCLUSION(S)

Thus, there was a significant but transient rise in the levels of ALT, AST and total bilirubin levels while the levels of ALP did not show a significant change in the first 24 hours following LC, which was not seen in the case of OC. The most likely mechanism which brings about this change is raised intra-abdominal pressure due to CO_2 pneumoperitoneum which leads to decreased blood supply to the liver, thereby causing ischaemic damage to the tissues, resulting in the liberation of the liver enzymes into the blood. If the liver function test was normal in the preoperative period, the operating laparoscopic surgeon need not worry.

Acknowledgement

Authors were grateful to Dr. Soumik Ghosh for the technical help that he has provided for this research. Also, this research would have been incomplete without the inputs from my friend, Pritwish Mitra.

REFERENCES

[1] Shaffer EA. Gallstone disease: Epidemiology of gallbladder stone disease. Best Pract Res Clin Gastroenterol. 2006;20(6):981-96. Doi: 10.1016/j.bpg.2006.05.004. PMID: 17127183.
[2] Maingot's Abdominal Operations. Michael J. Zinner, Stanley W. Ashley, O. Joe Hines. 13th edition. Pp.1156.
[3] Ambole AS, Kulkarni G, Biradar JM, Patil S. Assessment of LFTs in patients undergoing Cholecystectomy. J Adv Med Dent Scie Res. 2017;5(11):122-24.
[4] Tan M, Xu FF, Peng JS, Li DM, Chen LH, Lv BJ, et al. Changes in the level of serum liver enzymes after laparoscopic surgery. World journal of Gastroenterology. 2003;9(2):364-67.
[5] Ibrahim AM, Bopanna VB, Palani M. Evaluation of the effects of laparoscopic surgeries on hepatic enzymes. IOSR Journal of Dental and Medical Sciences. 2017;16(8):22-28.
[6] Halevy A, Gold-Deutch R, Negri M, Lin G, Shlamkovich N, Evans S, et al. Are liver enzymes and bilirubin levels significant after laparoscopic cholecystectomyin the absence of bile duct injury? Ann Surg. 1994;219(4):362-64.
[7] Nguyen NT, Braley S, Fleming NW, Lambourne L, Rivers R, Wolfe BM. Comparison of postoperative hepatic functions after laparoscopic and open gastric bypass. The American Journal of Surgery. 2003;186(1):40-44.
[8] Dexter SP, Vucevic M, Gibson J, McMahon MJ. Hemodynamic consequences of high- and low-pressure capnoperitoneum during laparoscopic cholecystectomy. Surg Endosc. 1999;13:376-81.
[9] Hasuki S. CO_2-pneumoperitoneum in laparoscopic surgery: Pathophysiological effects and clinical significance. World Journal of Laparoscopic Surgery. 2014;7(1):33-40.
[10] Singal R, Singal RP, Sandhu K, Singh B, Bhatia G, Khatri A, et al. Evaluation and comparison of postoperative levels of serum bilirubin, serum transaminases and alkaline phosphatase in laparoscopic cholecystectomy versus open cholecystectomy. J Gastrointest Oncol. 2015;6(5):479-86.

[11] Scapa E, Pinhasov I, Eshchar J. Does general anaesthesia affect sinusoidal liver cells as measured by beta-N-acetyl hexosaminidase serum activity level? Hepatogastroenteerology. 1998;45(23):1813-15.
[12] Guven HE, Oral S. Liver enzyme alterations after laparoscopic cholecystectomy. J Gastrointestinal Liver Dis. 2007;16(4):391-94.
[13] Dancygier H. Anomalies of the Gallbladder and the cystic duct. In: Clinical Hepatology. Springer, Berlin, Heidelberg. (2010).
[14] Andall RG, Matusz P, du Plessis M, Ward R, Tubbs RS, Loukas M, et al. The clinical anatomy of cystic artery variations: A review of over 9800 cases. Surg Radiol Anat. 2016;38:529-39.

PARTICULARS OF CONTRIBUTORS:
1. Senior Resident, Department of General Surgery, Bankura Sammilani Medical College, Bankura, West Bengal, India.
2. Associate Professor, Department of General Surgery, Bankura Sammilani Medical College, Bankura, West Bengal, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Upasana Choudhury,
BID Villa, Opposite Durga Mandir, Throght The Lane Beside Cure Hospital, Lokpur, Bankura-722102, West Bengal, India.
E-mail: upasanachoudhury743@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Aug 23, 2022
- Manual Googling: Dec 21, 2022
- iThenticate Software: Jan 31, 2023 (3%)

ETYMOLOGY: Author Origin

EMENDATIONS: 7

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Aug 14, 2022**
Date of Peer Review: **Nov 11, 2022**
Date of Acceptance: **Feb 01, 2023**
Date of Publishing: **Jun 01, 2023**