"Impact of Pneumoperitoneum at Various Pressure Levels on Liver Physiology and Function"

Mehboob Hussain Bhat[1], Sajad Ahmad Bhat[2*], Gh Hussain Mir[3], Arman Sadykov[4], Dar Mumtaz Ahmad[5], Gumarova Zhannat[6], Ruhi Charak[7]

Medical officer, Govt Medical College Anantnag, J&K, India
Professor, Department of Biochemistry, Nims University, Rajasthan Jaipur, India,
Consultant Surgeon, Department of Medical Health Education, J&K Srinagar, India.
Head & Consultant, Department of Intervention cardiology, Almaty Multi profile Clinical Hospital, Almaty Kazakhstan,
Consultant Interventional Cardiology, Almaty Multidisciplinary Clinical Hospital, Almaty, Kazakhstan,
Associate Professor, Department of medicinal and biological chemistry, West Kazakhstan Marat Ospanov Medical University, Aktobe Kazakhstan,
Assistant Professor, Department of Biochemistry, Nims University, Rajasthan, Jaipur, India.
Corresponding Author: Dr Sajad Ahmad Bhat,
Professor, Department of Biochemistry,NIMS University, Rajasthan Jaipur, India,
Email:drsajad191@gmail.com

ABSTRACT

For more than 25 years, laparoscopic cholecystectomy (LC) has superseded open cholecystectomy (OC) in the treatment of benign gallbladder illnesses and has become the gold standard for symptomatic cholelithiasis. It has grown in popularity around the world and is now one of the most common procedures performed in general surgery. Today, more than 90% of cholecystectomy procedures are performed laparoscopically1. Although LC had several advantages over laparotomy, new questions developed about the consequences of a pneumoperitoneum on the hemodynamic, circulatory, and respiratory systems2.One of the most significant hemodynamic alterations is the transitory reduction in hepatic blood flow caused by pneumoperitoneum. A two-year prospective study was conducted in the Postgraduate Department of General Surgery, Government Medical College, Srinagar. During this time, laparoscopic cholecystectomy was performed on 150 patients with symptomatic. Our research showed that following laparoscopic cholecystectomy, elevations in liver enzymes (bilirubin, AST, ALT, GGT, ALP, and LDH) might happen at both high and low pressures, with DOP lasting longer than 60 minutes. Changes may be related to a decrease in portal venous flow at high pneumoperitoneum pressures when examined in conjunction with data gathered from earlier.

Key Words: LC, OC, AST, ALT, LDH, laparoscopic, Pneumoperitoneum

Introduction:

For more than 25 years, laparoscopic cholecystectomy (LC) has superseded open cholecystectomy (OC) in the treatment of benign gallbladder illnesses and has become the gold standard for symptomatic cholelithiasis. It has grown in popularity around the world and is now one of the most common procedures performed in general surgery. Today, more than 90% of

cholecystectomy procedures are performed laparoscopically[1]. Although LC had several advantages over laparotomy, new questions developed about the consequences of a pneumoperitoneum on the hemodynamic, circulatory, and respiratory systems[2]. One of the most significant hemodynamic alterations is the transitory reduction in hepatic blood flow caused by pneumoperitoneum[3,4,5,6]. The pressure and duration of a generated pneumoperitoneum have been shown to alter the degree of hepatic ischemia by elevating liver enzymes[4,7,8]. The intra-abdominal pressure used in laparoscopic surgery is 15 mm Hg, which is higher than the typical portal blood pressure (7-10 mmHg). This pneumoperitoneum could so limit portal flow and impair liver function. Experimental studies have shown that hepatic perfusion decreases as intraabdominal pressure rises above 6 mm Hg[9]. Other variables have also been suggested, including traction on the liver and electrocautery. Halevy[10] was the first to study changes in LFT (liver function tests) following LC (laparoscopic cholecystectomy), and he found that postoperative enzyme levels increased by up to 70% with no detrimental clinical consequence. Several studies over the last decade have reported 'unexplained' variations in postoperative liver function tests (LFT) in individuals having laparoscopic procedures[1,9].

Although laparoscopic cholecystectomy is related with transitory rise of liver enzymes, abnormalities following the procedure are self-limiting and not associated with any morbidity in patients with normal liver function tests[4,6,11,12]

In laparoscopic cholecystectomy, the working space is generated by insufflating carbon dioxide into the peritoneal cavity at a typical pressure of 12-14 mmHg[13,14]. Despite the numerous clinical advantages of laparoscopic surgery, the unfavourable effects of CO2 pneumoperitoneum are cardiac, renal, splanchnic, and hepato-portal ischemia effects[11,15,16,17]. Jakimowicz et al. found a 53% decrease in portal flow and an increase in intraperitoneal pressure of up to 14mmHg[18]. Laparoscopic cholecystectomy under low pressure pneumoperitoneum (7-10mmHg) has also been shown to be possible[19,20,21]. Pneumoperitoneum is the conventional pre-requisite for laparoscopic surgery, but gas-less laparo-lift procedures have been used to minimise the negative effects of capnopneumoperitoneum. However, the exposure during surgery in laparo-lift instances is compromised[22].

Material & Methods:

A two-year prospective study was conducted in the Postgraduate Department of General Surgery, Government Medical College, Srinagar. During this time, laparoscopic cholecystectomy was performed on 150 patients with symptomatic cholelithiasis. The exclusion criteria were established to rule out any other known cause of liver function disturbances, including conversion to open cholecystectomy, acute inflammation or any other complication of gallstone disease, recent endoscopic retrograde cholangiopancreaticography (ERCP) and endoscopic sphincterotomy, choledocholithiasis, co-existing liver disease, any intra or postoperative complication, and incomplete data. The patient was in a little reverse Trendelenburg posture during the laparoscopic cholecystectomy, which was conducted under general anaesthesia using the 4-trocar technique. All patients were given similar anaesthetic medications.

Monopolar diathermy was utilised to treat hemostasis and gallbladder separation from the liver bed. Six liver function parameters were measured preoperatively at 1 hour, 24 hours, 1 week, and 3 weeks after surgery: bilirubin (direct and indirect), aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), γ-glutamyl-transpeptidase (γ-GT), and lactate dehydrogenase.

Inclusion Criteria: Patients of any age group undergoing laparoscopic procedures at Medical College Hospital Srinagar with preoperative Liver Function tests within normal norms.

Exclusion criteria include pre-operative abnormalities in liver enzymes and suspected or proven chronic liver disease. Common bile duct pathology. Conversion to open cholecystectomy. Haematological disorders. Patients who had undergone endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic sphincterotomy, as well as those with a history of using hepatotoxic medications, were at risk for CBD injury during surgery.

Results: Preoperative serum levels of different enzymes in study patients is shown in table 1

Table 2 and Figure 2 illustrate the relationship between pressure and postoperative levels of serum bilirubin. At high intra-abdominal pressure, postoperative bilirubin values are higher than preoperative values, and they return to preoperative levels after one week. At low pressure,

bilirubin levels do not increase levels and at moderate intra-abdominal pressure (12mm Hg) return to preoperative levels occurs after 24 hrs.

Preoperative serum levels of different enzymes in study patients are shown in table 1& Fig 1

Table 1: Comparison based on Pre-operative Serum Bilirubin, AST, ALT, GGT, ALP and LDH among various groups

Preop Parameter	IAP 15	IAP 12	IAP 10	
Serum Bilirubin	0.583	0.552	0.584	0.771
AST	31.52	25.52	28.24	0.102
ALT	30.28	24.24	27.20	0.085
GGT	57.48	50.26	52.16	0.115
ALP	85.74	90.60	78.46	0.125
LDH	196.86	209.30	212.88	0.271

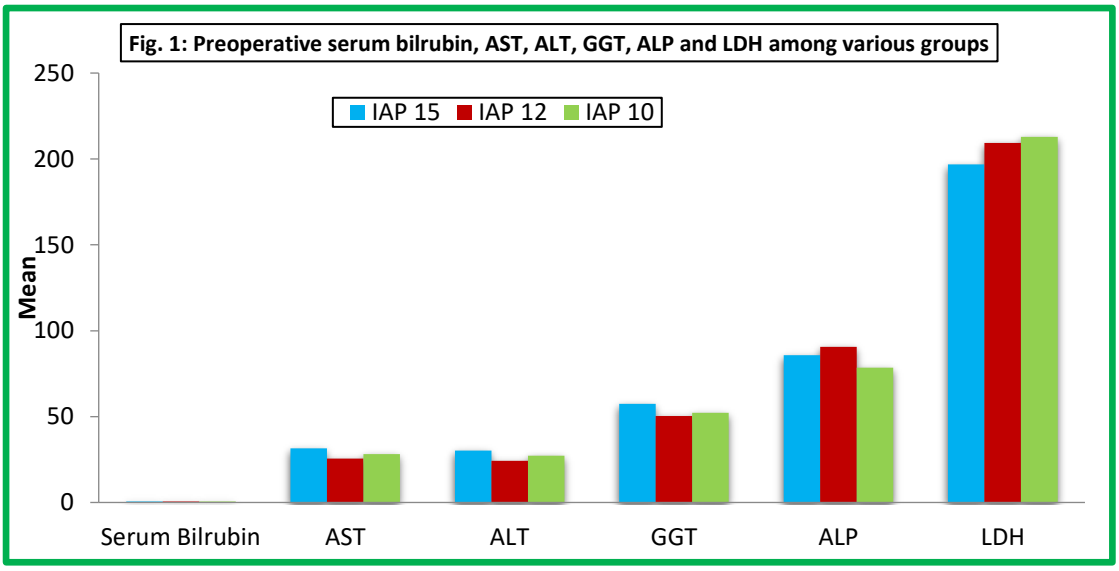
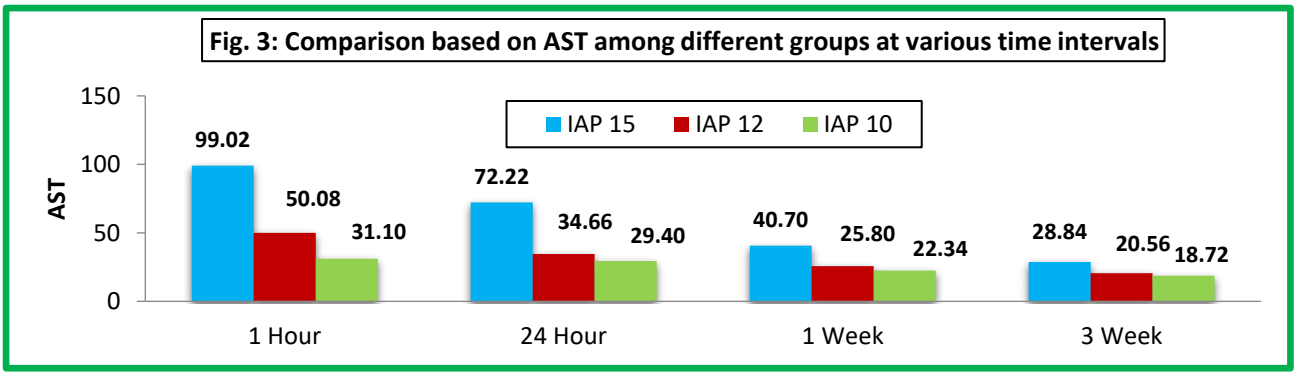


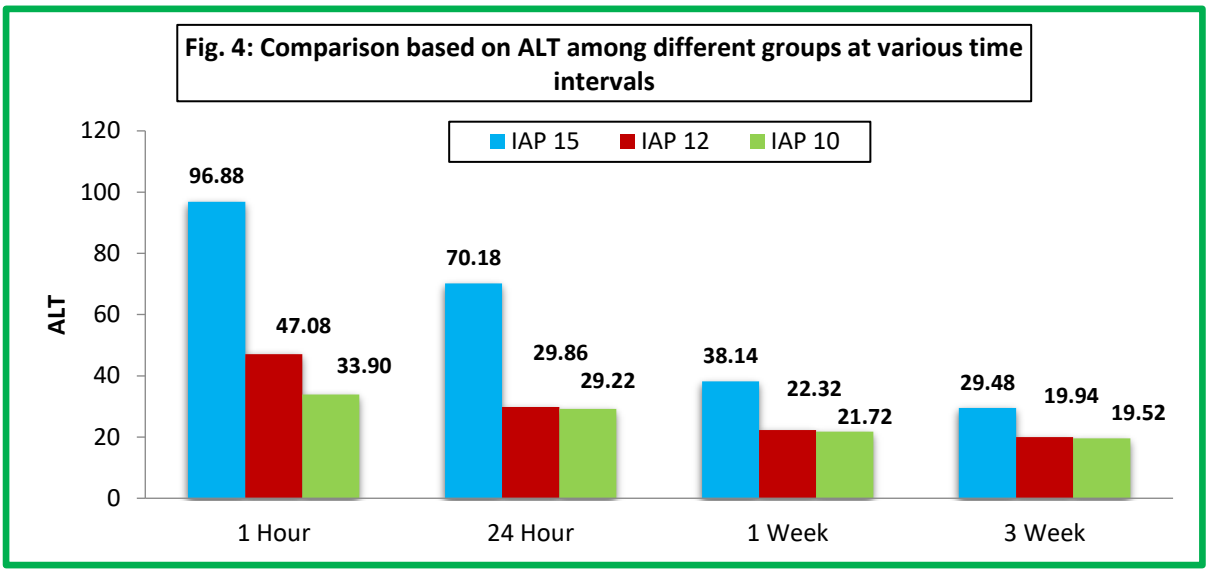
Table 2 and Figure 2 illustrate the relationship between pressure and postoperative levels of serum bilirubin.

Table 2: Comparison based on serum bilirubin among different groups at various time intervals				
	IAP 15	**IAP 12**	**IAP 10**	
1 Hour	1.38	1.21	0.63	<0.001*
24 Hour	1.01	0.62	0.51	<0.001*
1 Week	0.63	0.45	0.40	<0.001*
3 Week	0.52	0.37	0.31	<0.001*

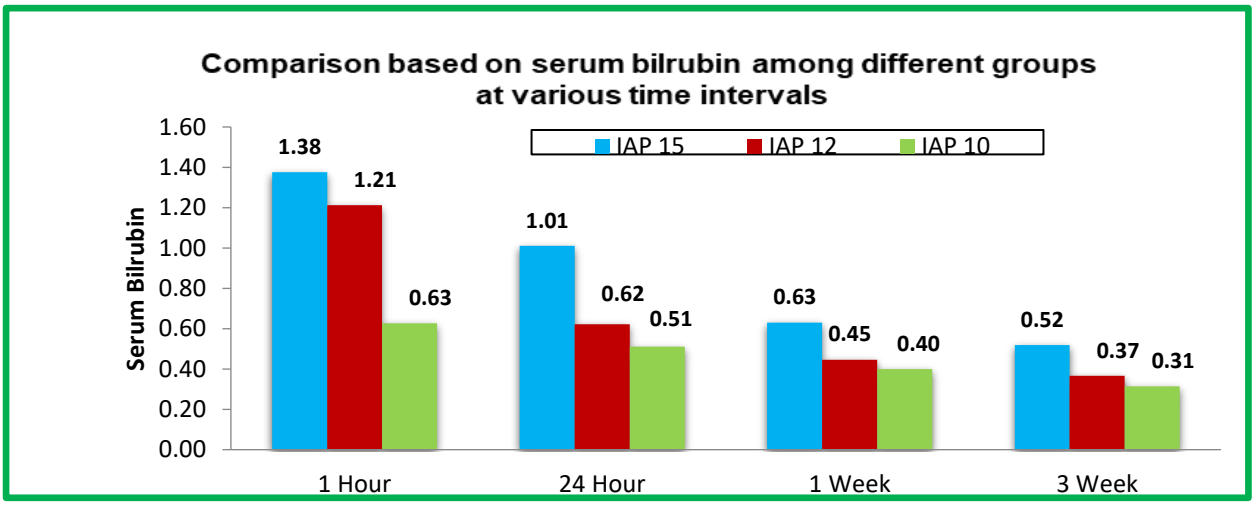
Fig. 3 & Fig. 4 show the effect on postoperative levels of serum AST and ALT, respectively. At 10 mm of Hg pressure, there is no rise in AST or ALT levels; however, at 12 and 15 mm of Hg pressure, there is a notable increase in both enzyme levels, which return to preoperative values after 24 hours and one week, respectively.

Fig. 3 & Fig. 4 show the effect on postoperative levels of serum AST and ALT





Effect on postoperative GGT and ALP levels is shown in table 7, fig 7 and table 8, fig. 8 respectively which shows that levels of the enzymes are significantly higher at higher pressures and return to preoperative levels is after one week as compared to laparoscopic cholecystectomies done at lower pressures where rise is not too much and also return to preoperative levels occurs after 24 hrs.



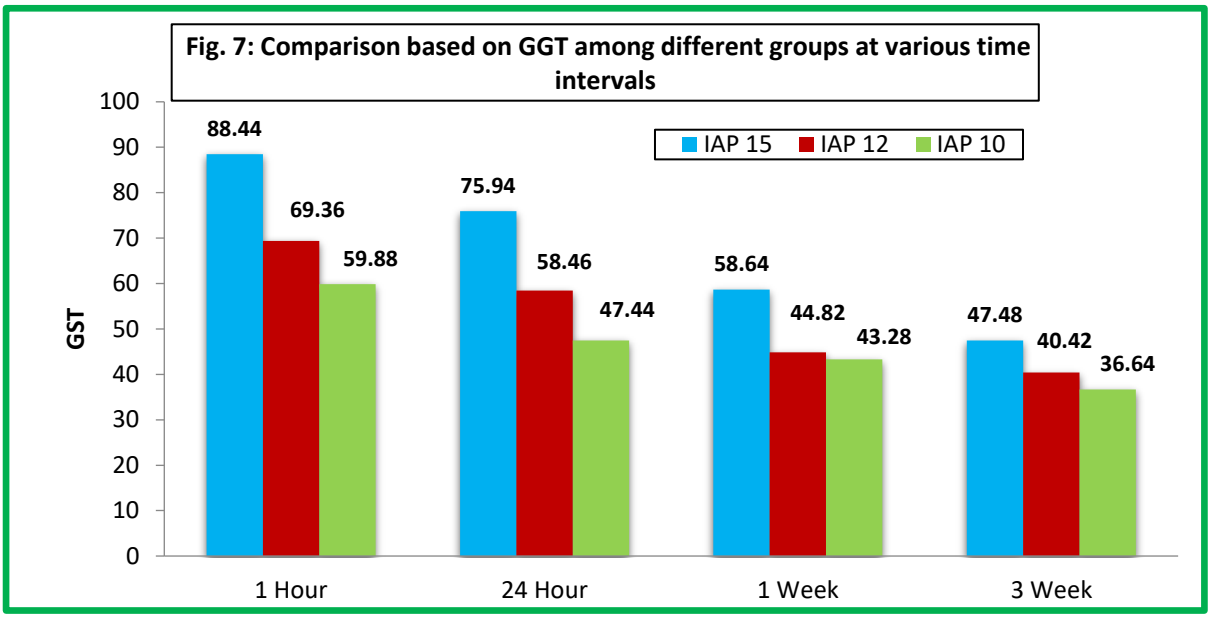


Fig. 7: Comparison based on GGT among different groups at various time intervals
GST
100
90
80
70
60
50
40
30
20
10
0
IAP 15
IAP 12
IAP 10
88.44
69.36
59.88
75.94
58.46
47.44
58.64
44.82
43.28
47.48
40.42
36.64
1 Hour
24 Hour
1 Week
3 Week

Discussion:

Elevation of liver enzymes following a simple laparoscopic cholecystectomy, once thought to be coincidental, has recently become a well-known occurrence. While there is uncertainty regarding the clinical significance of these enzyme increases, it was thought to be a temporary hepatic dysfunction. Numerous investigations have shown that patients undergoing laparoscopic cholecystectomy experience unanticipated alterations in liver function after surgery, and CO2 pneumoperitoneum may be a major contributing factor. Thus, the purpose of this study is to evaluate if there are any inexplicable changes in liver enzymes after laparoscopic cholecystectomy at various abdominal pressures.

Following laparoscopic cholecystectomy, increased intra-abdominal pressure and its impact on portal venous flow are most likely the main causes of elevated liver enzymes. Reduced portal blood flow results from the 15 mm of Hg of CO2 being used, which is higher than the typical portal pressure of 7-10 mm of Hg. We performed a 4-port laparoscopic cholecystectomy on 150 patients; 50 of them had an intra-abdominal pressure of 15 mm Hg, 50 at 12 mm Hg, and the remaining 50 at 10 mm Hg. Between the three groups, there was no discernible variation in the operative characteristics such as the length of symptoms or the duration of pneumoperitoneum.

Thirteen male and thirty-seven female patients underwent surgery at an intra-abdominal pressure of 15 mm Hg. The patients ranged in age from 22 to 70 years, with the majority of cases (39%) falling into the 30- to 40-year-old age range. Prior to surgery, the average blood bilirubin level was 0.583+0.246. Levels on day one and one hour after surgery were 1.01+0.46 and 1.38+0.54, respectively. Day 1's mean was higher than expected and in line with research by Mahendra Bendre et al[23], which found that day 1's post-operative mean was 1.10+0.32 and the pre-operative mean was 0.70+0.14 day 7 levels.
The AST mean values on day 1 after surgery were 72.22+28.03 and 31.52+15.13, respectively. These values were similar to the study conducted by *Rikki Singal et a*l[24], which found that the preoperative mean was 27+16.1 and the postoperative mean was 72.9+15.1.

Preoperatively, the mean ALT value was 30.28+15.61, and postoperatively, on day 1, it was 70.18+24.63. These values were similar to those found in a study by *Bryant L*R[12], which found pre-operative values of 33.61+12.23 and post-operative values of 67.10+20.8 on day 1. Prior to surgery, the average level of ALP was 85.74+25.75; following surgery, it was 106.6+18.18 on day 1 and 87.82+23.49 on day 7. The values were similar to those in a study by Joris J et al[13]., whose post-operative mean on day 1 and day 7 was 78.47+44.51 and the pre-operative mean was 79.4+30.91.

At 10 mm of Hg: Six male patients and forty-four female patients underwent surgery at this pressure. The serum bilirubin mean before surgery was 0.584+0.244. Day 1 and Day 7 post-operative means were, respectively, 0.51+0.19 and 0.40+0.17. In the study by Joris J et al[13]., the post-operative means on day 1 and day 7 were, respectively, 0.879+.27 and 0.391+0.16. Our study's findings are consistent with those of *Joris J et al*.'s[13] investigation.

The average AST values prior to surgery were 28.24+13.17. Postoperative levels were 29.40+9.47 on day 1 and 22.34+8.13 on day 7. The postoperative values on day 1 and day 7 were 32.87+11.53 and 26.33+9.82, respectively, according to a study by Joris J et al The findings are consistent with our research. On day one, the mean ALT values were 27.20+14.57, and on day seven, the mean values were 21.72+10.97 and 29.22+9.99, respectively. Post-operative values in the *Joris J et al*[13] study was 40.56+11.22 on day 1 and 30.27+15.11 on day 7, respectively, and the outcomes were similar.

The average ALP levels prior to surgery were 78.46+34.60. Day 1 and Day 7 post-operative ALP levels were 81.02+22.72 and 68.26+20.05, respectively. The post-operative mean values on days 1 and 7 were 83.03+48.23 and 76.60+54.60, respectively, according to a study by Joshi MR et al. These values are similar to those found in our study.
The mean GGT levels were 52.16+17.61 prior to surgery, and they were 47.44+13.64 and 43.28+12.52 on day 1 and day 7 following surgery, respectively. The levels of GGT do not rise after surgery. S. Hasukic et al[16]. report that in both HPLC and LPLC, GGT levels did not alter from basline. Serum LDH levels were 212.88+55.98 on average before surgery, 217.80+76.77 on day 1, and 194.50+55.09 on day 7.S. Hasukic et al[16]. state that serum LDH levels are still present.

Conclusion:

Our research showed that following laparoscopic cholecystectomy, elevations in liver enzymes (bilirubin, AST, ALT, GGT, ALP, and LDH) might happen at both high and low pressures, with DOP lasting longer than 60 minutes. Changes may be related to a decrease in portal venous flow at high pneumoperitoneum pressures when examined in conjunction with data gathered from earlier research. After one week, enzyme levels return to pre-operative levels. Surgeons should exercise caution when intending to conduct LC in patients with known hepatic insufficiency, even if there is no evidence to suggest that these enzyme alterations in otherwise healthy individuals are indicative of a real hepatic ischemia. For certain patient populations, low pressure pneumoperitoneum LC or gasless LC with abdominal wall retractors may be practical.

Acknowledgement

I would like to share my gratitude to all the co-authors for their timely contribution.

Conflict of interest

No conflict of interest.

Ethical approval

Ethical approval were provided by Institutional Ethical Committee of Postgraduate Department of General Surgery, Government Medical College, Srinagar, India

References:

1. Gurusamy KS, Davidson BR. Surgical treatment of gallstones. Gastroenterology Clin North Amer 2010; 39: 229-44.
2. Odeberg-Wernerman S. Laparoscopic surgery - effects on Circulatory and respiratory physiology: an overview. Eur J SurgSuppl 2000; 585: 4-11.
3. Saber AA, Laraja RD, Nalbandian HI, Pablos-Mendez A, Hanna K. Changes in liver function tests after laparoscopic Cholecystectomy: not so rare, not always ominous. Am Surg 2000; 66: 699-702.
4. Morino M, Giraudo G, Festa V. Alterations in hepatic function during laparoscopic surgery. An experimental clinical study. SurgEndosc 1998; 12: 968-972.
5. Sakorafas G, Anagnostopoulos G, Stafyla V, et al. Elevation of serum liver enzymes after laparoscopic cholecystectomy. N Z Med J 2005; 118: U1317.
6. Hasukic S, Kosuta D, Muminhodzic K. Comparison of postoperative hepatic function between laparoscopic and open cholecystectomy. Med PrincPract 2005; 14: 147-150.
7. Hasukic S. Postoperative changes in liver function tests: randomized comparison of low and high-pressure laparoscopic cholecystectomy. SurgEndosc 2005; 19: 1451-1455.
8. Giraudo G, BrachetContul R, Caccetta M, Morino M. Gasless laparoscopy could avoid alterations in hepatic function. SurgEndosc 2001; 15: 741-746.
9. Tauro LF, Sheetal CM, Aithala PSM, Shetty SR, D"Souza CS, Rao BSS, Shenoy DH, Rao K. Evaluation of effects of laparoscopic surgery on hepatic function. Journal of Clinical Diagnosis and Research 2008; 2(6): 1155-62.
10. Halevy A, Gold-Deutch R, Negri M, et al. Are elevated liver enzymes and bilirubin levels significant after laparoscopic cholecystectomy in the absence of bile duct injury? Ann Surg 1994; 219: 362-364.
11. Omari A, Bani-Hani KE. Effect of carbon dioxide pneumoperitoneumon liver function following laparoscopic cholecystectomy. JLaparoendoscAdvSurg Tech A. 2007 Aug; 17(4): 419-24.

12. Bryant LR, Wiot JF, Kloecker RJ. A study of the factors affecting the incidence and duration of postoperative pneumoperitoneum. SurgGynecolObstet 1963; 117:145-50.
13. Joris J, Cigarini I, Legrand M, Jacquet N, De Groote D, Franchimont P et al. Metabolic and respiratory changes after cholecystectomy performed via laparotomy or laparoscopy. Br J Anaesthesia 1992 Oct; 69(4):341-5.
14. Berggren U, Gordh T, Grama D, Haglund U, Rastad J, Arvidsson D et al. Laparoscopic versus open cholecystectomy: Hospitalization, sick leave, analgesia and trauma responses. Br J Surg 1994 Sept; 81(9):1362-5.
15. Junghans, T, Bohm B, Grundel K, Schwenk W, Muller JM. Does pneumoperitoneum with different gases, body position and intraperitoneal pressures influence renal and hepatic blood fl ow? Surgery 1997 Feb; 121(2): 206-11.
16. Hasukic S, Mesic D, Dizdarevic E, Keser D, Hadziselimovic S, Bazardzanovic M. Pulmonary function after laparoscopic and open cholecystectomy. SurgEndosc 2002 Jan; 16(1): 163-5,
17. Westerband A, Van De Water J, Amzallag M, Lebowitz PW, Nwasokwa ON, Chardavoyne R. et al. Cardiovascular changes during laparoscopic cholecystectomy. SurgGynaecolObstet 1992 Dec;175(6):535-8.
18. Jakimowicz J, Stultiens G, Smulders F. Laparoscopic insufflations of the abdomen reduces portal venous flow. SurgEndosc 1998; 12: 129-132.
19. Davides D, Birbas K, Vezakis A, McMahon MJ. Routine low-pressure pneumoperitoneum during laparoscopic cholecystectomy. Surg Endosc1999 Sep:13(9): 887-9.
20. Wallace DH, Serpell MG, Baxter JN, O'dwyer PJ. Randomized trial of different insufflation pressures for laparoscopic cholecystectomy. Br J Surg 1997 Apr; 84(4):455-8.
21. Kar M, Kar JK, Debnath B. Experience of laparoscopic cholecystectomy under spinal anesthesia with low- pressure pneumoperitoneum-prospective study of 300 cases. Saudi J Gastroenterol 2011May-Jun; 17(3): 203-7.
22. Vezakis A, Davides D, Gibson JS, Moore MR, Shah H, Larvin M et al. Randomized comparison between low-pressure laparoscopic cholecystectomy and gasless laparoscopic cholecystectomy. SurgEndosc 1999 Sep;13(9):890-3.
23. Dr. Mahendra Bendre, Dr. Shahaji Chavan, Dr. Nilesh Sinha, Dr. Nishith Reddy; Study of effect of pneumoperitoneum on liver function following laparoscopic cholecystectomy; Journal of Medical Science and Clinical Research; Vol- 5, Issue-04 April 2017.
24. Singal R, Singal R P, 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 GastrointestOncol 2015; 6(5): 479-486