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ORIGINAL RESEARCH

To evaluate the alteration in liver function test in patients undergoing Laparoscopic Cholecystectomy

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Abstract

Introduction- Symptomatic gallstone disease can be responsible for a wide variety of symptoms. The annual complication rate is 1–3% for symptomatic gallstones, but only 0.1–0.3% in patients with asymptomatic stones .Elevation in values of liver enzymes such as AST and ALT after an uneventful lap cholecystectomy has become a well-known finding which was once considered as incidental in previous studies, transient hepatic malfunction was suspected.

Material and method- The present study was conducted in the Department of General Surgery at GMC & Rajindra Hospital Patiala. 50 patients of cholelithiasis were included in the study. Blood samples taken pre-operatively, after 24 hours of surgery, after 72 hours, POD 7 and POD 10 of surgery for comparison of the hepatic enzyme level alterations.

Results - On statistical analysis, No statistically significant difference was found in the mean values of serum bilirubin done at pre-op with POD 1(p=0.419), POD 3(p=0.717), POD 7 (p=1.00), and POD 10 (p=0.322). Mean values of Aspartate transaminase (AST) on correlating pre-op with POD 1 (p=0.000), and POD 3 (p=0.000). However, no statistically significant difference was found in the mean values pre-op and POD 7 (p=0.408) & pre-op and POD 10 (p=0.340). The mean values of Alanine transaminase (ALT) on correlating pre-op with POD 1 (p=0.000), and POD 3 (p=0.000). However, no statistically significant difference was found in the mean values pre-op and POD 7 (p=0.066), pre-op and POD 10 (p=0.537).

Conclusion- These changes return to normal in7 days after procedure and these changes are clinically insignificant but biochemically significant. So, laparoscopic surgeons may not be apprehensive about these elevations of AST/ALT levels of liver enzymes.

Introduction

Gallstone disease is the term used to refer to the presence of stones in the gallbladder or common bile duct and the symptoms or complications they cause[1]. Most people with gallstone disease have asymptomatic gallbladder stones, meaning the stones are confined to the gallbladder and they do not have any symptoms. Symptomatic gallstone disease can be responsible for a wide variety of symptoms[2]. The annual complication rate is 1–3% for symptomatic gallstones, but only 0.1–0.3% in patients with asymptomatic stones.[3] Transcutaneous sonography allows simultaneous assessment of the intrahepatic and extrahepatic bile ducts. Using these criteria, cholecystitis can be diagnosed clearly and

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reproducibly. Along with clinical examination, detailed patient's history, arouse suspicion of liver function tests should be determined for systematic diagnosis of gall stones.[4]
Some of the liver enzymes and end products of the metabolic pathway which are very sensitive for the abnormality occurred may be considered as biochemical marker of liver dysfunction. Commonly available tests include alanine transaminase (ALT) and aspartate directly or with some other organs.[5] transaminase (AST), alkaline phosphatase (ALP), gammaglutamyl transferase, serum bilirubin, prothrombin time, or international normalised ratio and serum albumin. They reflect different functions of the liver—that is, to excrete anions (bilirubin), hepatocellular integrity (transaminases), formation and the subsequent free flow of bile (bilirubin and ALP), and protein synthesis (albumin).[6] An isolated or conjugated alteration of biochemical markers of liver damage in patients can challenge the clinicians during the diagnosis of disease related to liver. Elevation in values of liver enzymes such as AST and ALT after an uneventful lap cholecystectomy has become a well-known finding which was once considered as incidental in previous studies, transient hepatic malfunction was suspected.[7] Although the clinical significance of these changes in enzyme levels has not been clarified. One of the important hemodynamic changes is the transient reduction in hepatic blood flow caused by a pneumoperitoneum.[8] The most recent experimental studies have been also conducted on the alterations in hepatic function during laparoscopic surgery and the effect of laparoscopy on liver enzyme. [9] More precisely the observation of hemodynamic & metabolic impairment related to CO2 pneumoperitoneum and postoperative. mesenteric ischemia reports following laparoscopic surgeries have raised concern about local & systemic effects of increased intra- abdominal pressure during laparoscopic surgeries. This study aims to investigate the changes in the Liver Function Test after Laparoscopic Surgerys performed under intraperitoneal pressure of 12mmHg.

Material and method

The present study was conducted in the Department of General Surgery at GMC & Rajindra Hospital Patiala. 50 patients of cholelithiasis were included in the study. Patients were subjected to the required preoperative investigations and were selected for elective surgical management. Patients between 15-90 years of age, normal liver function test, no history of any abdominal surgery and had given consent were include in the study. Patient with pregnancy, concomitant bile duct stones, high levels of liver enzymes before operation, hepatitis B or C virus, any collagen disorders, on hepatotoxic drugs, any pre-existing renal, pulmonary and cardiac complications , who had not given their consent were excluded from this study. Laparoscopic cholecystectomy was performed in all included patients. Blood samples taken pre-operatively, after 24 hours of surgery, after 72 hours, POD 7 and POD 10 of surgery for comparison of the hepatic enzyme level alterations.

Pre-Operative Investigations

CBC (Hb, TLC, DLC, Platelet Count), RBS / FBS, Renal Function Tests (Blood Urea, Serum Creatinine), Liver Function Tests (Total S. Bilirubin, ALT, AST, Alkaline Phosphatase), Triple H (HIV 1 &2, HBsAg, HCV), Serum Electrolytes (Na^+, K^+), ECG.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp Results on continuous measurements were presented as Mean ± SD (Min-Max) & categorical as Frequency (Percentage). Inferential statistics like paired t test was used to check difference between the groups. The significance of level adopted was 5%. A two tailed Probability value (p-value) < 0.05 was considered as statistically significant and p-value ≤ 0.01 considered as highly significant. P-value > 0.05 was considered as non-

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significant

Observation and Results

Table 1 - Mean value for Serum bilirubin at different intervals of observations in the study population

Observation Interval	N	Mean	Std. Deviation	Minimum	Maximum
PRE-OP	50	0.574	0.307	0.2	1.2
POD 1	50	0.548	0.280	0.2	1.2
POD 3	50	0.566	0.304	0.2	1.2
POD 7	50	0.574	0.311	0.2	1.2
POD 10	50	0.582	0.310	0.2	1.2

Table 2 – Correlation of serum bilirubin Pre-operatively with bilirubin levels at 1st, 3rd, 7th and 10th day.

Sr.no	Serum Bilirubin Values	Serum Bilirubin level		Correlation of serum bilirubin values between	P value	Sig
		Mean	Std. Deviation			
1	Pre-OP	0.574	0.3076	Pre-OP and POD 1	0.419	NS
2	POD 1	0.548	0.2808			
3	Pre-OP	0.574	0.3076	Pre-OP and POD 3	0.717	NS
4	POD 3	0.566	0.3041			
5	Pre-OP	0.574	0.3076	Pre-OP and POD 7	1.00	NS
6	POD 7	0.540	0.2850			
7	Pre-OP	0.574	0.3076	Pre-OP and POD 10	0.322	NS
8	POD 10	0.582	0.3108			

The results showed that the mean values of Serum Bilirubin at Pre- operative, Post-op day 1, Post-op Day 3, Post-op Day 7 and Post-op Day 10 were 0.57± 0.30, 0.54± 0.28, .56± 0.30, 0.57± 0.31 and 0.58± 0.31 respectively. **(Table 1).** On statistical analysis, No statistically significant difference was found in the mean values Pre-OP and Day 1(p=0.419), Pre-OP and Day 3(p=0.717), Pre-OP and Day 7 (p=1.00), Pre-OP and Day 10 (p=0.322). **(Table 2).**

Table 3 – Correlation of Aspartate transaminase (AST) Pre-operatively with AST levels at 1st, 3rd, 7th and 10th day.

Sr.no	Aspartate transaminase (AST) Values	Aspartate transaminase (AST)		Correlation of Aspartatetransaminase (AST) values between	P value	Sig
		Mean	Std. Deviation			
1	Pre-OP	34.96	11.17	Pre-OP and POD 1	0.000	HS
2	POD 1	44.70	6.05			
3	Pre-OP	34.96	11.17	Pre-OP and POD 3	0.000	HS
4	POD 3	44.78	6.23			
5	Pre-OP	34.96	11.17	Pre-OP and POD 7	0.408	NS
6	POD 7	34.74	10.66			
7	Pre-OP	34.96	11.17	Pre-OP and POD 10	0.340	NS
8	POD 10	34.12	9.64			

On statistical analysis, A statistically highly significant difference was found in the mean values Pre-OP and Day 1(p=0.000), Pre-OP and Day 3(p=0.000). However, no statistically significant difference was found in the mean values Pre-OP and Day 7 (p=0.408), Pre-OP and Day 10 (p=0.340).(table 3)

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Table 4 – Correlation of Alkaline Phosphatase (ALP) Pre-operatively with ALP levels at 1st, 3rd, 7th and 10th day.

Sr.no	Alkaline Phosphatase (ALP) Values	Alkaline Phosphatase (ALP)		Correlation of Alkaline Phosphatase (ALP) values between	P Value	Sig
		Mean	Std. Deviation			
1	Pre-OP	79.76	17.220	Pre-OP andPOD 1	0.454	NS
2	POD 1	79.58	16.711			
3	Pre-OP	79.76	17.220	Pre-OP andPOD 3	0.637	NS
4	POD 3	78.80	14.439			
5	Pre-OP	79.76	17.220	Pre-OP andPOD 7	0.501	NS
6	POD 7	79.14	13.507			
7	Pre-OP	79.76	17.220	Pre-OP andPOD 10	0.130	NS
8	POD 10	78.54	13.784			

On statistical analysis, no statistically significant difference was found in the mean values Pre-OP and Day 1(p=0.454), Pre-OP and Day 3(p=0.637), Pre-OP and Day 7 (p=0.501), Pre-OP and Day 10 (p=0.130).(table 4)

Discussion

The present study was conducted to evaluate the alterations in the liver function tests following laparoscopic cholecystectomy. This study was conducted on 50 patients of cholelithiasis admitted in the department of General Surgery, Government Medical College and Rajindra Hospital, Patiala, Punjab. In all the patients who underwent laparoscopic cholecystectomy , blood samples for studying the enzyme levels were taken at different intervals such as Pre-operative, after 24 hours (Day 1), after 72 hours (Day 3), after 7 days and after 10 days of surgery. In our study the pre-operative mean values of Serum Bilirubin at Baseline, Post-op day 1, Post-op Day 3, Post-op Day 7 and Post-op Day 10 was 0.57± 0.30, 0.54± 0.28, 0.56± 0.30, 0.57± 0.31 and 0.58± 0.31 respectively. No statistically significant difference was found in the mean values of serum bilirubin on comparing the values at pre-op with and post-op Day 1, Day 3, Day 7, and Day 10. The results were similar to the study done by Kumari S et al[10], which showed that the total bilirubin and direct bilirubin had almost negligible increase within the first 24 hours following surgery and that too only in 2% of the patients. However, in studies conducted by Halevy A et al[11] and Tan M et al[12] noticed that there was significant increase in the level of serum bilirubin postoperatively on day 1 as compared to the pre-operative levels. In our study no significant transient change was observed in serum bilirubin at post-operative day 1, 3, 7 and 10.

In our study no statistically significant difference was found in the mean values of Alkaline Phosphatase (ALP) on comparing thevalues at pre-op with and post-op Day 1, Day 3, Day 7, and Day 10. However, Halevy et al[11] observed a rise of ALP in 53% patients but the values were all within normal limits. Saber et al[13] showed only 4% rise of ALP Laproscopic Cholecystectomy and no rise in ALP in Open Cholecystectomy .The raised alkaline phosphatase came to normal after 72 hrs. In our study, the mean value of ALP showed no significant change from preoperative values, which was within the normal limit.

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Table 4: Mean values of postoperative enzymes changes after LC invarious studies

Authors	Enzyme	preoperative mean value (IU/L)	POD 1 mean value (IU/L)	POD 3 mean value (IU/L)	POD 7 mean value (IU/L)	POD 10 mean value(IU/L)
Tan M et al(2003)[12]	AST	28.4□20.2	41.5□24.7	44.2□14.5*	29.1□18.7	Not Analysed
	ALT	23.3□11.6	38.8□15.2	48.7□20.8*	25.1□14.3	
Sakorafaset al, (2005)[9]	AST	22.3□12.1	87.1 ± 24.2	103.5 ± 21.6	40.3±8.9	21.3±12.4
	ALT	21.6□13.4	82.8□19.1	99.3±19.5	45.6±13.4	23.2±11.3
Marakis etal (2006)[14]	AST	24.36□24.01	55.07□40.39	Not Analysed	Not Analysed	Not Analysed
	ALT	31.88□74.77	61.62□54.87			
Hameedet al(2009)[15]	AST	31.23□51	53.79□12.92	Not Analysed	Not Analysed	31.20□5.75
	ALT	28.19□5.29	51.11□13.06			29.16□5.40
Reddy P et al(2020)[16]	AST	34.83□24.80	53.80□28.96	37.06□22.08	Not Analysed	Not Analysed
	ALT	35.93□29.28	54.58□29.28	37.06□22.08		
Our study	AST	34.96□11.17	44.70□6.05	44.78±6.23	34.74±10.66	34.58± 9.67
	ALT	31.08□12.34	51.90□10.02	49.62□8.81	30.72□11.87	31.20□12.05

*Done at POD2

The present study showed that a statistically highly significant difference was found in the mean values of Aspartate transaminase (AST) on comparing pre-op values on POD 1(p=0.000) and POD 3(p=0.000). No statistically significant difference was found on comparing the mean values pre-op with POD 7(p=0.408) and POD 10(p=0.340). A statistically highly significant difference was found in the mean values of Alanine transaminase (ALT) on comparing pre-op values with POD 1(p=0.000) and POD 3(p=0.000). But no statistically significant difference was found on comparing the mean values pre-op with POD 7(p=0.66) and POD 10(p=0.537). The results of our study were comparable with a study conducted by Sakorafas et al[32] in 72 consecutive patients who underwent laparoscopic cholecystectomy who assessed serum liver enzymes were measured before operations and at 1,3,7, and 10 days post operation. It showed that alterations in hepatic function occur after laparoscopic cholecystectomy and appear to be clinically insignificant but were statistically significant. They found the increase in AST and ALT was statistically significant and Similarly, a study conducted by Tan M et al[22], collected blood samples from 286 patients who underwent laparoscopic cholecystectomy (LC), in which the level of serum ALT and AST increased significantly during the first 48 hours post surgery. On 7th post-op, the level of both enzymes returned to normal values. The results of enzyme levels in our study at POD 1 were also similar to a study conducted by Reddy et al[36] in which the preoperative mean AST was 34.83±24.80 IU/L which increased to 53.8±28.96 U/l on 1st postoperative day and again reduced near to pre- operative value of 37.06±22.08 IU/L on 3rd post-operative day. There was significant increase in mean AST values between Pre-operative and 1st Post- operative day (p <0.001). In this study preoperative mean ALT was 35.93±26.51 IU/L which increased to 54.58±29.28 IU/L on 1stpostoperative day and again reduced near to pre- operative value of 37.06±22.08 IU/L on 3rd post-operative day. There was significant increase in mean ALT values. Comparing it to our study the values of AST and ALT were also high during the 1st post-op day. However, they did not analyzed the liver enzymes at 7th and 10th day like our study

Conclusion

In conclusion, we showed that transient elevation of AST and ALT occurs after Laproscopic Cholecystectomy till 3rd day post-op. These changes return to normal in 7 days after

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procedure and these changes are clinically insignificant but biochemically significant. So, laparoscopic surgeons should not be apprehensive about these elevations of AST/ALT levels of liver enzymes.

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