ISSN No:-2456-2165

A Study of Alteraton in Liver Function Tests Following Laparoscopic Cholecystectomy

[1] Dr. Kunal Malhotra, Resident doctor
[2] Dr. Amit Bhambri, Resident Doctor
[3] Dr. Subhash Sharma, Senior Resident
[4] Dr. Ashok Kaundal, Assoc. Prof.
[5] Dr. Anil Malhotra, Prof. & Head
Deptt. of Surgery, I.G. Medical college & Hospital, Shimla. (Himachal Pradesh)

Abstract:-

➢ ***Introduction***

Minimally invasive surgery, especially laparoscopic surgery, has changed the face of general surgery. Cholecystectomy is the commonest abdominal surgical procedure in Western world. & laparoscopic cholecystectomy (LC) is accepted as gold standard. LC is usually considered to be a safer procedure than open cholecystectomy (OC) in terms of metabolic, hormonal and immunological changes.

In the last decade, several studies have shown 'unexplained' changes in postoperative liver function tests (LFTs) in patients undergoing laparoscopic procedures. It has been observed that, following laparoscopic surgery, the level of certain serum liver enzymes rose markedly in most patients who had shown normal LFT preoperatively, & may be due to hepatocellular dysfunction secondary to one or combination of CO2 pneumoperitoneum, diathermy use on liver, manipulation of liver, hepatic artery branch injury and general anaesthesia. Due to all these observations, gasless laparoscopy has been proposed by some surgeons.

Nevertheless, some studies indicate that, if the patient's preoperative liver function was very poor, laparoscopic surgery might not be the optimal choice for treating certain abdominal diseases.

➢ ***Aims***

There have been few studies in tertiary care hospital to evaluate the potential harmful effects of laparoscopic surgery on hepatic function. This study was intended to assess the alteration and clinical significance of unexplained disturbances in liver enzymes following laparoscopic cholecystectomy. And to correlate the duration of laparoscopic surgery and the causes and clinical significance of unexplained disturbances in liver enzymes.

➢ ***Methods***

The study was conducted in Indira Gandhi Medical College, Shimla and comprised of 200 patients, of symptomatic cholelithiasis & in all patient laparoscopic cholecystectomy (LC)was done between 1st May 2012 to 30th April 2018.In all the patients, liver function tests were done pre -operatively and post operatively (within 24 hrs.). The obtained data was analysed for effect of laparoscopy cholecystectomy on liver function test.

➢ ***Results***

The elevation of liver enzymes was more with advancing age & were more common in females (87.5%). Liver enzymes were found elevated in immediate post-op. period (after 24 hrs.). However, we observed that the levels of S. ALP were decreased in 52% of patients after 24 hours of surgery. This rise in the liver enzyme level was seen more pronounced in patients who had prolonged CO2 insufflation time. The transient elevation of liver enzymes showed no apparent clinical implication in most patients who underwent laparoscopic surgery.

➢ ***Conclusion***

Transient mild abnormality in liver function tests is a usual finding after LC without clinical significance & without any consequences in healthy patients. But it can deteriorate the liver function in patients with severe liver disease, in which the low-pressure pneumoperitoneum or gasless laparoscopy can be an alternative.

Keywords:- *Laparoscopic Cholecystectomy (LC), C02 Pneumoperitoneum, Liver Function Tests (LFT).*

ISSN No:-2456-2165

I. INTRODUCTION

The credit of performing first ever cholecystectomy goes to Carl Langenbach1882.However,Muhe presented the first report of laparoscopic cholecystectomy at Germany in 1986.Reddick and Olsen described the technique of laparoscopic cholecystectomy (LC) which is commonly practiced today[1].

Routine LFTs includes S. bilirubin (total and direct), SGOT, SGPT, ALP, GGT, albumin, PT/INR.Although many medical and surgical conditions are associated with elevated of bilirubin and liver enzymes levels.Deranged liver enzymes and bilirubin have also been reportedfollowing LC.

The laparoscopic surgery is performed by the insufflation of carbon dioxide into the peritoneal cavity as it does not support combustion, after absorptionit is readily excreted via the lungs[2] and it is 20 times more soluble in serum than room air or oxygen. During most cases of the LC, a pneumoperitoneum of 12-14 mm Hg CO_2 is established[3].

Although LC offered many advantages over open cholecystectomy, new concerns arose regarding the effects of a pneumoperitoneum on the cardiovascular and respiratory system[4]. These changes are well tolerated even in older and more debilitated patients.[5,6]One of the important hemodynamic changes following LC is the transient reduction in hepatic blood flow caused by a pneumoperitoneum.[7]The pressure of pneumoperitoneum and its duration influences the degree of hepatic ischemia[8]. This results in elevations in liver enzymes alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma glutamyl transferase (GGT), bilirubin, and international normalized ratio (INR)[9]. Though, the LC is associated with transient elevation of liver enzymes, the disturbances after LC are self-limited and not associated with any morbidity in patients with a normal liver function[9,10].

II. MATERIAL AND METHODS

The study was conducted in the department of General Surgery, Indira Gandhi Medical College, Shimla. The study comprised of 200 patients, selected randomly of ultrasound proved symptomatic cholelithiasis & admitted for elective laparoscopic cholecystectomy (LC) between 1st May 2012 to 30thApril 2018. Written informed consent was taken from all the patients. All patients were evaluated by history, clinical examination, biochemical and sonological findings.

All the patients, liver function tests were done pre and postoperatively(within 24-48 hrs)byBeckman Coulter Au-680 auto-analyser in the Department of Biochemistry Indira Gandhi Medical College, Shimla. From each patient, 5 ml of blood samples were taken in a serum tube for biochemical analysisfor following liver function tests:Aspartate Aminotransferase (AST or SGPT), Alanine Aminotransferase (ALT or SGOT),Serum bilirubin (total and direct), Alkaline Phosphatase (S. ALP)&Serum Gamma Glutamyl Transferase (G.G.T)

These biochemical tests were once measured pre-operatively and then post-operatively after 24 hours.In all patients LC was performed.

INCLUSION CRITERIA: All ultrasonographically proved cases of symptomatic cholelithiasis of both sexes between 18 to 70 years of age, with normal LFT were admitted and taken up for elective laparoscopic cholecystectomy.

EXCLUSION CRITERIA:Patients with raised preoperative S. bilirubin (total and direct), ALP, SGOT, SGPT and GGT, with proven choledocholithiasis or dilated common bile duct, history of jaundice, uncontrolled diabetes mellitus, cholangitis , uncontrolled hypertension, pancreatitis, tuberculosis, acute cholecystitis, underlying bleeding diathesis, post ERCP, with chronic cardiac and renal diseases,, COPD, poor cardio-pulmonary reserve, portal hypertension,cirrhosis of liver , HbsAg positive patients, pregnancy, OCP users, previous upper gastrointestinal tract surgery, morbid obesity , gall bladder carcinoma and concomitant malignant diseases & having hepatotoxic medication. Those patients who had intraoperative complications or converted to open cholecystectomywere not included in the study.

All patients received general anaesthesia by same anaesthetic drugs (propofol, succinyl, isoflurane and vecuroniums) that are known either not to affect or has minimal effect on the enzymatic activity of the liver.

Laparoscopic cholecystectomy wasperformed with the instruments of the standard company (Stryker) available in the Department of General Surgery.Pneumoperitoneum was created using a Verres's needle through which $C0^2$ was insufflated into peritoneal cavity upto a pressure of 14 mm Hg at the rate of 3-4 litres/minute, by electronically controlled insufflators (Fig.1). The insufflator also had an adjustment, which controlled and maintained the maximum intra-abdominal pressure at a pre-set level of 14mmHg. Any inadvertent rise of intra-abdominal pressure triggered off a visual and audio alarm. To control haemorrhage, the mono-polar diathermy or harmonic scalpel was used in all patients& gall bladder was removed through umbilical port (Fig.2).

All data was expressed as the mean ± standard deviation. The data was analysed for finding the significance of effect of laparoscopy on hepatic function by using the students paired t test. The P value less than 0.005 was considered to be statistically significant.

Statistical analysis was performed with the Statistical Package for the Social Sciences (SPSS software).

ISSN No:-2456-2165

Fig.1: Showing pneumoperitoneum by Verres's needle at constant pressure of 14mmHg.

Fig.2: Gall bladder removed from epigastric port after laparoscopic surgery.

III. RESULTS

In this study following observations were made out: youngest patient was of 18 years and eldest was of 70 years. Maximum patients were in the age group of 30 – 40 years (30%)& majorityof patientswere below 50 years of age (Fig.3). There was increase in level of alteration of liver enzymes with increasing age of the patients.

Majority of patients were females (80%). Alteration in LFTs after surgery was seen predominantly in female sex.

LIVER FUNCTION TESTS (Table 1.): The pre-op. and post-op. mean values of total bilirubin were 0.775 mg/dl and 1.42 mg/dL respectively. And mean value of total bilirubin was raised by 0.645 mg/dl postoperatively, withP<0.001*.This showed statistically highly significant rise in total S. bilirubin levels 24 hours after surgery. Postoperatively, total S. bilirubin was raised 176 patients ,16patients had drop in level whereas 8 patients had no change in level. The value of Pearson Correlation Coefficient was 0.19. Hence on increasing the duration of surgery (pneumoperitoneum) there was increase in level of total bilirubin in serum.

In post-operativeperiod, direct S. bilirubin levels were raised in 136 patients, 36 patients had drop in levels whereas 14 patients had no change in levels. The pre-op. and post-op. mean values of direct bilirubin were 0.309 mg/dl & 0.813 mg/dl and mean value of direct bilirubin was raised by 0.504 mg/dl postoperatively.While, on increasing the duration of surgery (pneumoperitoneum) there was mild or no increase in level of direct bilirubin in serum.

Postoperatively SGOT levels were raised in 192 patients &8 patients had drop in level.The pre-op. and post-op. mean values of values of SGOT were 34.908(IU/L) & 87.332 (IU/L) respectively and was raised by 52.424 IU/L postoperatively (P<0.001).Hence on increasing the duration of surgery (pneumoperitoneum) there was increase in level of SGOT in serum.

Postoperatively SGPT levels were raised in 192 patients, 4patients had drop in levels whereas 4 patients had no change in levels. Thepre-op. and post-op. mean values of SGPTwere 38.714 IU/L &85.192 IU/Lrespectively & raised by 46.478 IU/L postoperatively. Therewas statistically significant rise in SGPT levels 24 hours after surgery. And with increase in the duration of surgery (pneumoperitoneum), there was increase in level of SGPT in serum.

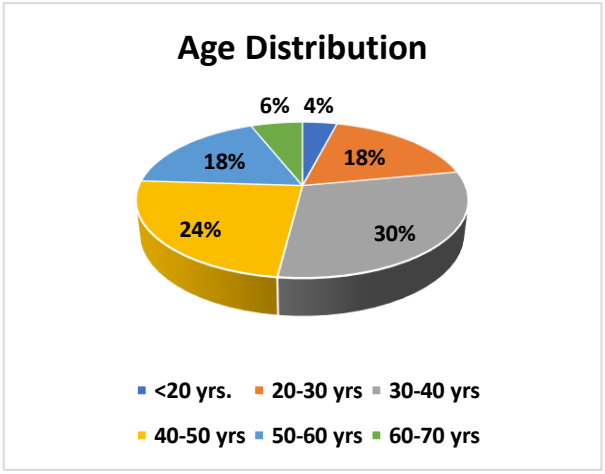

Fig 3: Showing age distribution.

In 88 patients ALP levels were raised while104 patients had drop in level of ALP & in 8 patients, there was no change in ALP levels postoperatively. Thepre-op. and post-op. mean values of ALP were 101.935IU/L & 94.38IU/L respectively &decreased by 7.55 IU/L postoperatively.Statistically there was no significant rise in ALP levels 24 hours after laparoscopic cholecystectomy.

In 196 patients GGT levels were raised & whilein 4 patients there was drop in level of GGT postoperatively.The pre-op. and post-op. mean values of GGT were 32.92IU/L & 59.12IU/L respectively and was raised by 26.2 IU/L postoperatively. It was observed that on increasing the duration of surgery (pneumoperitoneum) there was increase in level of GGT in serum.

Although there were significant alterations in the liver enzymes of the study group patients and no adverse events / complications / mortality was observed. A weak positive co-relation between CO_2 insufflations time and the cases with elevated liver enzymes level was observed. Almost double the pre-op values were raised postoperatively in case of serum bilirubin (T), serum bilirubin (D), S.G.O.T, S.G.P.T and G.G.T. However, serum levels of A.L.P were found to be decreased after 24 hrs after surgery.

Liver function test	Pre-op. Value (Mean)	Post-op. Value (Mean)
Total Bilirubin	0.775(mg/dl)	1.42(mg/dl)
Direct Bilirubin	0.309(mg/dl)	0.813(mg/dl)
S.G.O. T	34.908(IU/L)	87.332(IU/L)
S.G.P. T	38.714(IU/L)	85.192(IU/L)
Alkaline Phosphatase	101.935(IU/L)	94.38(IU/L)
G.G. T	32.92(IU/L)	59.12(IU/L)

Table 1: Showing changes in LFT after surgery.

IV. DISCUSSION

Laparoscopic cholecystectomy is gold standard now a days. Andis mostly attributable to evidence suggesting a reduction in morbidity, short hospital stay and early return to normal activity by the patient[11].

However, many studies have disclosed unexplained changes in post-operative liver function after laparoscopic procedures[12,&] CO_2 pneumoperitoneum might be one of the main reasons for the change of serum liver enzymes, as this is the main difference between laparoscopic surgeries & open surgeries. A change in liver function tests of up to 70% has been reported with no adverse clinical outcome,which may bedue to increased pneumoperitoneum pressure, which causes hepatic dysfunction[4]. Studies have confirmedthat pneumoperitoneum leads toincreased intra-abdominal pressure, hypercarbiawith acidosis which leads to decreasein cardiac output and stroke volume.And same principle also explains decrease in gastrointestinal and hepatic perfusion[13].

The increased intra-abdominal pressure also leads to a mechanical impairment of the venous blood return leading to an increase in venous pressure of the lower extremity while decreasing the cardiac preload. Depending on the extent of these mechanisms,there may be a decrease in cardiac output and hypotension without an increase in the heart rate.

Studies have shown a decrease in splanchnic macro and microcirculation depending on the amount of intra-abdominal pressure leadingto an elevation of various hepatic enzymes, reflecting hepatocytic damage, an impaired function of the Kupffer cells[14].

In present study,the patients were between 18years to 70 years of agewhile 78% were below 50 years.It was observed that the alteration in liver enzymes was directly related to increase in the age of the patients.

Similarly, Nasir Zaheer Ahmad et al[15] reported that alteration in liver enzymes after surgery wasmore withadvancing age of the patients. However, Al-Jaberi TM et al[16]reported that there was no relation of age with alteration of liver function tests after laparoscopic cholecystectomy.

In our study, 80% patients were femalewith sexratio of4:1.

Among females, LFTs were deranged in 87.5% of cases whereas, derangement occurred in 60% of malegroup. There was significantly more alteration in liver function tests in females as compared to males& this finding is consistent with other studies[13,16] which showed changes in liver function parameters were more common in female patients.

The mean level of S. bilirubin (T) preoperatively was 0.77 ± 0.41 mg/dl. & was 1.42 ± 0.77 mg/dlpostoperatively. Similarly, the mean value of S. bilirubin (D) preoperatively was 0.30 ± 0.21 mg/dl& mean level was 0.81 ± 0.89 mg/dl post operatively thus, there was significant rise in the total and direct levels of S. bilirubin levels within 24-48 hrs after surgery.These findings are similar to study conducted by Morino M et al[9] that there was significant increase in S. bilirubin levels in 24 to 48 hours after surgery withslow return to normality after 48 or 72 hrs.Halevy A et al[17] also observed this & suggested that increased intraperitoneal pressure, squeezing the liver by cranial retraction of gallbladder during LC, cauterization of the liver bed for haemostasis, slippage of micro calculi in common bile duct, manipulation of external bile ducts and effects of general anaesthesia as possible causes of elevation of certain liver enzymes.

In our study, the mean value of S.G.O.T preoperatively was 34.9 ± 18.2 (IU/L) .Whereas post operatively mean level was 87.3 ± 74.7 (IU/L). Thus, it was found that there was a significant rise ($P<0.001$) in the serum S.G.O.T levels in the immediate post-operative period (24-48 hrs).Similarly, the mean value of S.G.P.T preoperatively was 38.7 ± 35.8 (IU/L), whereas post operatively mean level was 85.19 ± 45.10 (IU/L). Thus, it was observed that there was a significant rise ($P<0.001$) in the serum S.G.P.T levels

ISSN No:-2456-2165

occurred within 24-48 hrs.Similar results were seen in other studies[15]which showed raised levels of SGPT and SGOT 24 hours after the procedure.

However, the mean value of serum A.L.P preoperatively was 101.9 ± 47.5 (IU/L). Whereas postoperative mean level was 94.38 ± 45.72 (IU/L). Thus, there was no significant rise (P=0.363) in the S.A.L.P levels. Similar results were seen inother studies[18] that all the liver enzymes namely SGOT, SGPT, GGT were raised postoperatively except ALP.

Similarly the mean value of S. G.G.T preoperatively was 32.92 ± 41.6 (IU/L).Whereas postoperative mean level was 59.12 ± 63.5 (IU/L). Thus, there was a significant rise (P<0.001) in the S. G.G.T levels in the immediate post-operative period.

Other studies [15] also reported significant increase in level of all the enzymes including GGT and suggested APP (abdominal perfusion pressure) as a determinant of interaction with mean arterial pressure (MAP) and IAP and causing elevation in liver enzymes, including GGT after 48 hours of surgery.

On the contrary, OdebergS et al[19] reported intra-abdominal pressures ranging between 11 - 13mm Hg are not associated with compromised splanchnic circulation and hence increased liver enzymes following laparoscopic cholecystectomy. All otherthe studies reported increase in level of S. bilirubin, SGOT, SGPT and GGT postoperatively. Whereas S. ALP levels fell in all of the studies except in study conducted by H. Erhan Guven et al[20]where it rose marginally. Therefore, above results equates our results with most of other studies conducted all over the world, however this finding of drop in ALP levels requires further evaluation.

We found that there was a positive correlation between duration of surgery and elevation of liver enzymes mainly S. bilirubin, SGOT, SGPT, GGT. However, there was negative correlation between duration of surgery and S. ALP levels, which needs further evaluation.

Our findings are consistent with other studies [21] whichdemonstrated that the frequency of change in liver function tests was directly proportional to the duration of pneumoperitoneum. Morino M et al[9] concluded that the duration and level of intra-abdominal pressure are responsible for changes of hepatic function during laparoscopic procedures.The increase of AST and ALT was statistically significant and correlated both to the level of pneumoperitoneum created (10 mmHg versus 14 mmHg) and the duration of pneumoperitoneum. Although no symptom appears in patients with normal hepatic function, they proposed that patients with severe hepatic failure should probably not be subjected to prolonged laparoscopic procedures.

Contrary to this, some studies [13]reported that the changes in liver function test after laparoscopic cholecystectomy are not related to the duration of surgery&duration of pneumoperitoneum time.

The most important factor of consideration is CO_2 pneumoperitoneum[12]. All the patients in our study were subjected to CO_2 pneumoperitoneum (14 mmHg) with varying time interval which showed significant increase in S. bilirubin, SGOT, SGPT, GGT, except ALP wherein level decreased with increase in duration of pneumoperitoneum. This finding is consistent with other similar studies[21,22,23]. The intra-abdominal pressure of 14mmHg used in our study was higher than the normal portal blood pressure of 7-10mmHg, this significantly higher pressure exerted by creation of pneumoperitoneum might be responsible for reduced portal blood flow, thereby causing sublethal ischemia of hepatocytes leading to liberation of hepatic enzymes into the circulation.

Thus, it is reasonable to speculate that reported differences in liver function tests could be caused by carbon dioxide pneumoperitoneum. The occurring pathophysiological changes may be due to both carbon dioxide insufflation and increased intra-abdominal pressure[12].

During laparoscopic procedure, the sudden alteration of intra-abdominal pressure could cause the undulation of portal blood flow. This undulation and “re-perfusion of organs” and blood flow may cause “ischemia and re-perfusion injury to tissues and organs,especially the Kupfer and endothelial cells of hepatic sinusoids by generation of free-radicals. Thus, might result in elevation of liver enzymes after laparoscopic surgery[9].

Another possible mechanism for alterations of serum liver enzymes is the “squeeze pressure” effect on the liver. By traction of the gall bladder by fourth port leading to folding of liver may release the liver enzymes into the blood circulation[12]. In our study, all the patients were subjected to traction on the fundus of the gall bladder and squeeze pressure theory could be a contributing factor for raised liver function test.Prolonged use of diathermy to the liver surface in laparoscopic cholecystectomy and the spread of heat to liver parenchyma[12] may cause damage to hepatic tissue and this hypothesis is supported by some studies[24].

Transient liver dysfunction has been reported in patients after use of certain general anaesthetic drugs[15]. However, no hepatotoxic anaesthetic drugs were used in our study. Hence general anaesthesia as a cause is debatable.

Another possible mechanism considered was the inadvertent clipping of the right branch of the hepatic artery or any other aberrant arterial branch supplying blood to the liver[13]. Moreover, the fact that increase in liver enzyme values has been reported to occur after laparoscopic colectomyalso, suggests that arterial injury is not a possible mechanism for the elevation of liver enzymes after laparoscopic cholecystectomy.

No complication or mortality in patients was seen in this study and in subsequent follow ups.The alterations in hepatic enzymes of our study are comparable with the observations given in literature. But, in order to ensure accurate conclusions, a strict exclusion criterion was set in this study by excluding the patients with known liver function test abnormality, conditions which could affect hepatic enzymes per-operatively i.e. conversion to open cholecystectomy or any other post-operative complications. It is concluded that transient elevation of hepatic enzymes occurs after uneventful LC without any apparent clinical implications. These transient alterations return to normal levels within 10 days after operation on patients follow up[12]. Major causative factor seems to be the CO_2 pneumoperitoneum and increased intra-abdominal pressure.In patients with poor preoperative liver functions, laparoscopic surgery might not be the optimal choice for treating certain abdominal diseases[9]. Recent studies done by Giraudo G et al[25] suggested that gasless laparoscopy can avoid causing alterations in hepatic function. So, this could be tried as an alternative in patients with poor liver function. In contrast to this suggestion, a recent study of laparoscopic cholecystectomy in cirrhotic patients has confirmed that the procedure can be safely carried out in patients with Child Classes A and B cirrhosis of the liver with no significant increase in complications[15].

V. CONCLUSION

Transient elevation of liver enzymes and bilirubin are usual finding after an uneventful LC without any significant clinical consequences. The major causative factor seemed to be raised intra-abdominal pressure due to CO_2 pneumoperitoneum, longer duration of surgery,diathermy use &surgical manipulation of liverduring laparoscopic surgery. Despite the fact that it has not any consequences in otherwise healthy patients, it could deteriorate the liver function in patients with severe liver disease who undergo long lasting pneumoperitoneum. In such cases the low-pressure pneumoperitoneum or gasless laparoscopy by abdominal wall lifting could be reasonable alternatives.

REFERENCES

[1]. Graham EA, Cole WH, Copher GH. Diseases of gall bladder and bile ducts. Philadelphia. Lea and Febiger. 1928; 12:142-4.
[2]. Hasulic S, Kosuta D, Muminhodzic K. Comparison of postoperative hepatic function between laparoscopic and open cholecystectomy. Med Princ Pract. 2005; 14(3): 147-50.
[3]. Ibraheim O.A. Lactate and acid base changes during laparoscopic cholecystectomy Middle East J Anesthesiol, 2006; 18(4): 757-68.
[4]. Schwenk W, Haase O, and Junghans T. Perspectives in sequential pneumatic compression of the lower extremities for laparoscopic surgery. Acta Chir Belg. 2002; 102(2): 83-91.
[5]. Odeberg-Wernerman. Laparoscopic surgery-Effects on circulatory and respiratory physiology: an overview. Eur J Surg Suppl. 2000; (585): 4-11.
[6]. Gutt C.N. Circulatory and respiratory omplications of carbon dioxide insufflation. Dig Surg, 2004; 21(2): 95-105.
[7]. Saber A.A. Changes in liver function tests after laparoscopic cholecystectomy: not so rare, not always ominous. Am Surg. 2000; 66(7): 699-702.
[8]. Sakorafas G, Anagnostopoulos G, Stafyla V. Elevaion of serum liver enzymes after laparoscopic cholecystectomy. NZ Med J, 2005; 118(1210):U1317.
[9]. Morino M, G. Giraudo and Festa. V. Alterations in hepatic function during laparoscopic surgery. An experimental clinical study. Surg Endosc. 1998;12(7): 968-72.
[10]. Hasukic S. Postoperative changes in liver function tests: randomized comparison of low- and high-pressure laparoscopic cholecystectomy. Surg Endosc. 2005; 19.
[11]. Soper NJ, Stockmann PT, Dunnegan DL. Laparoscopic cholecystectomy: the new "Gold Standard". Arch Surg 1992; 127: 917-923.
[12]. Tan M, Xu FF. "Changes in the level of serum liver enzymes after laparoscopic surgery." World J Gastroenterol 2003 15; 9(l; 2): 364-367
[13]. Tareq M, Jaberi AL, Mostafa F. Tolba. Liver Function Disturbances Following Laparoscopic Cholecystectomy: Incidence and Significance. Journal of Laparoendoscopic& Advanced Surgical Techniques. December 2002, 12(6): 407- 10.
[14]. Gutt CN, Kim ZG, Schemmer P. Impact of laparoscopic and inventional surgery on Kupffer cells, tumor-associated CD44 expression, and intrahepatic tumor spread. Arch Surg 2002; 137: 1408-1412.
[15]. Zaheer Ahmad N. Routine Testing of Liver Function Before and After Elective Laparoscopic Cholecystectomy: Is It Necessary? JSLS. 2011;15(1): 65–69.
[16]. Al-Jaberi TM, Tolba MF, Dwaba M. Liver function disturbances following laparoscopic cholecystectomy: incidence and significance. J Laparoendosc Adv Surg Tech A 2002; 12: 407-410.
[17]. Halevy A, Gold-Deutch R, Negri M. Are elevated liver enzymes and bilirubin levels significant after laparoscopic cholecystectomy in the absence of bile duct injury. Ann Surg 1994; 219: 362-364.
[18]. Omari A, Bani-Hani KE. Effect of carbon dioxide pneumoperitoneum on liver function following laparoscopic cholecystectomy. J Laparoendosc Adv Surg Tech A. 2007 Aug; 17(4): 419-24.
[19]. Odeberg S, Ljungqvist O, Sollevi A. Pneumoperitoneum for laparoscopic cholecystectomy is not associated with compromised splanchnic circulation. Eur J Surg 1998; 164: 843-848.
[20]. Guven HE, Oral S. Liver enzyme alterations after laparoscopic cholecystectomy. J Gastrointestin Liver Dis. 2007; 16: 391-4.

[21]. Schilling MK, Redaelli C, Krahenbuhl L. Splanchnic microcirculatory changes during CO_2 laparoscopy. J Am Coll Surg 1997; 184: 378-82.
[22]. Schmandra TC, Kim ZG, Gutt CN. Effect of insufflation gas and intra-abdominal pressure on portal venous flow during pneumoperitoneum. Surg Endosc 2001; 15: 405-8.
[23]. Hameed F, Ahmed B, Khan A. Impact of Pneumoperitoneum on Hepatic Functions after Laparoscopic Cholecystectomy (LC). A.P.M.C July-December 2009; 3: 100-106.
[24]. Raut V, Bhat N, Kinsella J. Bipolar scissors versus cold dissection tonsillectomy: a prospective, randomized, multi-unit study. Laryngoscope 2001; 111: 2178-2182.
[25]. Giraudo G, BrachetContul R, Caccetta M. Gasless laparoscopy could avoid alterations in hepatic function. Surg Endosc 2001; 15: 741-746.