https://doi.org/10.46344/JBINO.2022.v11i04.16

# A CASE CONTROL STUDY OF SERUM LIPID PROFILE AND LIVER FUNCTION TEST IN PATIENT WITH CHOLELITHIASIS IN TERTIARY CARE CENTER

**Dr. Navin Kumar Sah., Dr. Suprita Gupta., Mr. Anup Shamsher Budhathoki., Mr. NirdhanYadav., Dr. Akash Raya & Dr. Sanjay Kumar Sah**

Lecturer, Department of Biochemistry, National Medical College, Birgunj, Nepal

Professor and Head, Department of Biochemistry, National Medical College, Birgunj, Nepal

Lecturer, Department of Biochemistry, National Medical College, Birgunj, Nepal

Lecturer, Department of Biochemistry, National Medical College, Birgunj, Nepal

Lecturer, Department of Surgery, National Medical College, Birgunj, Nepal

Lecturer, Department of Biochemistry, National Medical College, Birgunj, Nepal

**Email**: navinks15aug@gmail.com

## ABSTRACT

**Background:** Cholelithiasis is a chronic recurrent hepatobiliary disease that impairs metabolism of cholesterol, bilirubin and bile acids accounting for the formation of gallstones. **Objectives**: To evaluate the derangements of serum lipid profile and liver function test in gallstone cases. **Methodology:** A hospital based cross sectional study of 105 subjects of cholesterol gallstone (GS), carried out in the Department of Biochemistry from December 2019 to April 2020 at National Medical College & Teaching Hospital (NMCTH) Birgunj, Nepal. All the patients were worked up and assessed according to Liver function tests, and Serum lipid profile. **Results:** The serum levels of lipid profile parameters (TC, TG, LDL, VLDL) and the TC/HDL, LDL/HDL, and TG/HDL ratios were found to be significantly higher in the patients with cholelithiasis than in the healthy people chosen as the controls. In addition, significantly higher levels of TP, bilirubin, ALP, ALT, and AST were found in the cholelithiasis patients than in the controls. **Conclusion:** Higher levels of serum lipid profile and liver functions test were observed in the cholelithiasis patients suggests that these serum lipids increase the risk of formation of cholesterol stones in the biliary system, as well as increasing the atherogenic index of the cholelithiasis patients.

***Key words***: Cholelithiasis, Cholesterol Gallstone, Lipid profile, Liver function test

## INTRODUCTION

Cholelithiasis is a chronic recurrent hepatobiliary disease and it is one of the most prevalent gastrointestinal diseases, Reshetnyak (2012). The prevalence of gallstone disease varies from country to country and from place to place. The prevalence was observed ranging from 10% to 21.9% in Western Europe and North America, Getachew(2008),3% to 15%in Asians population, less than 5% in Africans and the incidence ranging from 10% to 20% of the world population. Pradhan (2009 a). Cholelithiasis is common in Nepal and most commonly involved age group (32.5%) is found to be 30-39 years with a predominance in female (M: F=1:3.2), Pradhan(2009 b).

The occurrence of gallstone (GS)disease is a well-established risk factor for gallbladder carcinoma. The incidence of gallbladder carcinoma is significantly high in Nepal comprising 2.63% out of all cholecystectomy specimens. Gallstone can cause variety of complications including cholecystitis, choledocholithiasis, gallstone ileus, acute gallstone pancreatitis, biliary obstruction, gallbladder empyema or perforation, Getachew(2008). The risk factors for developing of gallstone disease are gender, age, genes and race. Additional factors are obesity, rapid weight loss, glucose intolerance, insulin resistance, high dietary glycemic load, alcohol use, diabetes mellitus, hypertriglyceridemia, drugs and pregnancy. Some degree of four major groups of factors may be identified for the formation of cholesterol gallstones disease: those that contribute to (1) bile cholesterol supersaturation; (2) cholesterol precipitation and crystallization core formation; (3) those that cause impairment of basic gallbladder functions (contraction, absorption, secretion, etc); and (4) impairment of the enterohepatic circulation of bile acids, Reshetnyak (2012).

The GS disease is a complex disease that may be caused by various environmental and genetic factors as well as their interactions. Polymorphisms at several candidate genes, such as cholecystokinin receptor A (CCK-AR), cholesterol 7-a hydroxylase (CYP7A1), adenosine triphosphate-binding cassette transporters (ABCG8), β3-adrenergic receptor (ADRB3) and MUC1 and MUC2 genes are found to be associated with GS disease, Chuang et al. (2012), mutation in the CYP7A1 gene results in a deficiency of the enzyme cholesterol 7-hydroxylase, which catalyzes the initial step in cholesterol catabolism and bile acid synthesis. Mutations in the MDR3 gene, which encodes the phospholipid export pump in the canalicular membrane of the hepatocyte, may cause defective phospholipid secretion into bile, resulting in cholesterol supersaturation of bile and formation of cholesterol gallstones in the gallbladder and in the bile ducts, Greenberger & Paumgartner (2008). An aberrant and enhanced expression of Mucin gene is concern to the lithogenic process, because of the mucus becomes more viscous and contribute in both the nuclear formation of stones and their enlargement in the biliary tract, Chuang et al. (2012).

The changes in bile composition are closely related to the disorders of lipid

metabolism in liver. Moreover, during the formation of cholesterol GS, different links in the disturbance of lipoprotein cholesterol metabolism and their effects in lactogenesis process still have many controversies. Some investigators reported that gallstone patients had hyperlipidemia, Channa et al., (2010). Abnormal liver function tests are most common in patients with gallstones. Increase in the level of Alkaline phosphatase (ALP) has emerged as the most reliable predictor of gallstones after ultrasonography and Bilirubin is also represented one of the indicators of gallstones but not as reliable as Alkaline phosphatase. The degree of hyperbilirubinemia reflects the degree of liver dysfunction affecting both nutrition and reticuloendothelial cells, Aslam et al.,(2013).

In order to establish effective diagnostic clinical strategies for the early detection and prognosis of gallstones in Nepal, this study was conducted to evaluate the derangements of serum lipid profile and liver function test in gallstone diseases in patients attending tertiary care hospital for treatment.

**METHODOLOGY**

A hospital- based cross sectional study, conducted from December 2019 to April 2020 in the Department of Biochemistry at National Medical College & Teaching Hospital (NMCTH), Birgunj, Nepal. A total of 105 diagnosed subjects of cholesterol GS cases were included in this study. The confirmation of the stone to be cholesterol stone was done by visual inspection after the surgery. For the purpose of comparison 105 normal subjects were selected as the control group. Ethical approval was taken from the Institutional Committee (IRC) of the NMCTH.

Inclusion criteria included all referred samples from diagnosed case of patients with cholelithiasis from the Department of Surgery, and exclusion criteria included known case of diabetic mellitus, patient with renal failure, nephrotic syndrome, pancreatitis and cardiac failure, and other cases of acute abdomen, viral hepatitis, cirrhosis, and chronic alcoholic and chronic smoker.

All the patients were worked up and assessed according to detailed history, complete clinical examination, Liver function tests, and Serum lipid profile. Study variables for lipid profile test included serum triglycerides, total Cholesterol, HDL, VLDL and LDL, as well as liver function test included ALP, Alanine transaminase (ALT), Aspartate transaminase (AST), albumin and bilirubin. Transabdominal ultrasonography (TAU) was used for the identification and diagnosis of cholelithiasis.

About 5 ml of venous blood in plain vial was collected aseptically from antecubital vein after 12 hours overnight fast and serum was separated by centrifugation (3000 rpm for 5 minutes). Clear serum was collected & kept in - $20^0$ C until the test was performed.

The measurement of all parameters was done in fully automated biochemistry

analyzer (Mindray BS-360E, Shenzhen, China) following IFCC recommended standard protocol.

Data was collected on pre-tested questionnaire proforma. Data was analyzed by using statistical software SPSS Version 17.0. Prevalence of gallstone disease was assessed and association of gall stones with derangement of lipid profile and liver function test was noted.

**RESULTS ANALYSIS**

A total of 105 diagnosed subjects of cholesterol GS cases were included in this study. The cases and controls were further categorized into normal and high, as well as low and normal groups.

The cholelithiasis patients and control subjects of varying ages were included in this study. A major proportion of the participating patients (41%) were between 30-40 years in age group (35.10 ± 3.47). Similarly, a major proportion of the control subjects (30.5%) belonged to the 30-40 years age group. The mean of the age distribution of the control groups was (41.15 ± 13.36) years. The participating patients were overwhelmingly female (81%) than in males (19.0 %) (M: F = 1: 4.25). The control group also consisted of a considerably higher number of females (67.6%) than males (32.4%).

Statistically, there were mean serum levels of TC, TG, LDL, and VLDL significant ($p<0.05$) differences in the patients than in the control group as shown in table 1. The mean value of the HDL levels in the case group was lower than that in the control group, the difference was statistically significant ($p<0.05$) as shown in table 2. Categorical comparison of serum lipid parameters show statistically higher levels of the TC (21.9%) in the case group compared to 6.7% in the control group (Table 1). Similarly, the TG, LDL, and VLDL values in the case group were found to be 53.33%, 15.2% and 45.7%, respectively, compared to 12.4%, 4.76%, and 4.8% in the control group. The differences in these parameters between the case and control groups were statistically significant ($p<0.05$). As Table 2 shows, the serum level of HDL (63.80%) was lower in the case group than in the control group, and this difference was observed to be statistically significant ($p<0.05$).

The TC/HDL ratio of the case group was found to be statistically different ($p<0.05$) than that of the control group (Table 3). Similarly, the differences between the LDL/HDL and TG/HDL ratios of the case and control groups were also statistically significant ($p<0.05$).

A considerable difference in mean serum levels of total protein (TP), Albumin (ALB), Total Bilirubin (TB), Direct Bilirubin (DB), Indirect Bilirubin (IB), Alkaline Phosphatase (ALP), ALT and AST ($p<0.05$) was observed between the case and control groups. The categorical comparison of serum LFT parameters higher levels of TP (9.5%) and TB (7.6%) were found in the case group than in the control group (Table 4). Similarly, higher levels of DB and IB were seen in the case group (10.5% and 11.4% respectively, compared to 1%in the control group). ALP (17.1%) and ALT (16.2%) of the case group were also higher than those of the control group. These differences were statistically significant ($p<0.05$).

Additionally, the difference in the proportion of AST in the case group (8.6%) was statistically insignificant (p>0.05) than that in the control group (1.9%). It is evident from the data in Table 5 that the serum level of ALB was lower in only 1.9% of case group than in the control group. The difference was statistically insignificant (p>0.05).

**Table 1: Categorical comparison of serum lipid parameters between cases and controls**

| Variable | Group | | | | Chi Square value | p value |
|---|---|---|---|---|---|---|
| | Case (N=105) | | Control (N=105) | | | |
| | Normal(%) | High(%) | Normal(%) | High(%) | | |
| TC (mg/dL) | 82(78.1) | 23(21.9) | 98(93.3) | 7(6.7) | 9.96 | 0.003 |
| TG (mg/dL) | 49(46.7) | 56(53.3) | 92(87.6) | 13(12.4) | 41.49 | 0.000 |
| LDL (mg/dL) | 89(84.8) | 16(15.2) | 100(95.2) | 5(4.8) | 6.40 | 0.02 |
| VLDL (mg/dL) | 57(54.3) | 48(45.7) | 100(95.2) | 5(4.8) | 40.49 | 0.000 |

**Table 2: Categorical comparison of serum HDL between cases and controls**

| Variable | Group | | | | Chi Square value | p value |
|---|---|---|---|---|---|---|
| | Case (N=105) | | Control (N=105) | | | |
| | Normal(%) | Low(%) | Normal(%) | Low(%) | | |
| HDLc (mg/dL) | 38(36.2) | 67(63.8) | 89(84.8) | 16(15.2) | 51.82 | 0.000 |

*p<0.05 significant

**Table 3: Comparison of serum mean levels of TC/HDL ratio, LDL/HDL ratio and TG/HDL ratio between cases and controls**

| Ratio | Group | | p value |
|---|---|---|---|
| | Case (N=105) Mean ± SD | Control (N=105) Mean ± SD | |
| TC/HDL | 4.85 ± 1.28 | 3.54 ± 0.69 | 0.000 |
| LDLc/HDL | 2.84 ± 1.08 | 1.96 ± 0.63 | 0.000 |
| TG/HDL | 5.03 ± 2.65 | 2.89 ± 0.69 | 0.000 |

*p<0.05 significant

**Table 4: Categorical comparison of serum LFT parameters between cases and controls**

| Variable | Group | | | | Chi Square value | p value |
|---|---|---|---|---|---|---|
| | Case (N=105) | | Control (N=105) | | | |
| | Normal(%) | High(%) | Normal(%) | High(%) | | |
| TP (g/dL) | 95(90.5) | 9(9.5) | 105 | 0 | 9.40 | 0.003 |
| TB (mg/dL) | 97(92.4) | 8(7.6) | 105 | 0 | 8.31 | 0.007 |
| DB (mg/dL) | 94(89.5) | 11(10.5) | 104(99) | 1(1) | 8.83 | 0.001 |
| IB (mg/dL) | 93(88.6) | 12(11.4) | 104(99) | 1(1) | 7.95 | 0.005 |

| | | | | | | |
|---|---|---|---|---|---|---|
| ALP (IU/L) | 87(82.9) | 18(17.1) | 103(98.1) | 2(1.9) | 14.15 | 0.000 |
| ALT (IU/L) | 88(83.8) | 17(16.2) | 102(97.1) | 3(2.9) | 10.83 | 0.002 |
| AST (IU/L) | 96(91.4) | 9(8.6) | 103(98.1) | 2(1.9) | 4.70 | 0.06 |

*p<0.05 significant

**Table 5: Categorical comparison of serum albumin between cases and controls**

| Variable | Group | | | | Chi Square value | p value |
|---|---|---|---|---|---|---|
| | Case (N=105) | | Control (N=105) | | | |
| | Normal (%) | Low (%) | Normal (%) | Low (%) | | |
| ALB (g/dL) | 103(98.1) | 2(1.9) | 105 | 0 | 2.019 | 0.5 |

*p<0.05 significant

## DISCUSSION

Cholelithiasis is one of the most common gastrointestinal diseases and it is also a burden of health problem for the developing country like Nepal. Pradhan(2009). This study included a total of 105 diagnosed subjects of cholesterol gallstones cases. The age of the patients in the case group ranged from 20 to 70 years (Mean ± SD = 42.32 ± 13.64). For the purpose of comparison 105 normal subjects served as a control group with matching sex and age distributions. In the present study, the mean of the age distribution of the control groups was (41.15 ± 13.36). GS was observed predominantly in the female patients with a M: F = 1:4.25 ratio. The findings of other studies reported that females are more likely to develop GS, Channa et al.,(2005) and predominant (32.5%) involved in the patients between 30-39 years of age (M: F=1:3.2).[4]It is also known that the prevalence of GS increases with increasing age, Getachew (2008).

The data generated during this study revealed that mean serum level of TC, TG, LDL, HDL and VLDL were significantly different (p<0.05) in the patients than in the controls. Similarly, categorical comparison analysis using the cutoff values (Table 1) indicated the levels of TC, TG, LDL and VLDL were significantly higher in the cases than in the controls (p<0.05). However, the HDL level was significantly lower in the cases (p<0.01) than in the controls (Table 2). This study is in agreement with others finding in which reported that a significant positive correlation between GS disease and increased levels of serum cholesterol, TG and LDL, and a decreased level of HDL, Al-Atrakchey et al. (2014), Atamanalp et al., (2013), Devaki et al., (2011). The study found that the means of the TC/HDL, LDL/HDL, and TG/HDL ratios in the case group were significantly different (p<0.05) than the corresponding to control group (Table 3). This shows that the cholelithiasis patients have higher atherogenic index. This is consistent with the findings suggested that gallstones are more likely to

have additional risk factors for heart disease because of high atherogenic index, Kumar D & Nagaraj, (2014).

Some of GS patients may have associated with metabolic syndrome, Al-Atrakchey et al., (2014) which is suggestive of altered serum lipid levels, Devakiet al., (2011). The elevation of serum TC and TG levels in the GS patients may be due to an abnormal secretory mechanism for bile acids and phospholipids. A decreased production of bile acids and phospholipids (which solubilize cholesterol in the bile) would increase cholesterol precipitation, Al-Atrakchey et al., (2014). A higher level of serum TG may cause the GB hypomotility as TG reduces the GB sensitivity to cholecystokinin, which regulates the GB contraction. It is known that GB hypomotility is one of the main causes for cholesterol crystallization, Weerakoon et al., (2014). The patients with high serum cholesterol, LDL, and lower serum HDL levels may be expected to increase cholesterol excretion with the bile, Atamanalp et al., (2013) and that leads to creating the bile supersaturation with cholesterol. This changed pattern of unfavorable specific lipoprotein profile in the serum and the bile may be associated with the occurrence of cholesterol-related GS, Singh et al., (1997). In addition, the higher level of LDL is present either due to abnormal secretary functions and/or prolonged high fatty diet or down regulation of LDL-ApoB receptors by inhibition of LDL-ApoB receptor gene expression, Al-Atrakchey et al., (2014).

A routine LFT analysis for the pre-operative evaluation of uncomplicated symptomatic cholelithiasis usually comes out normal, Habib et al., (2009). Acute cholecystitis is the most common complication of cholelithiasis and about 95% of patients with acute cholecystitis have cholelithiasis. When a stone becomes persistently obstructs in the cystic duct that gives rise to stasis of Bile and impacted GS blocks the fluid from passing out of the gallbladder. This results in an irritation and inflammation of gallbladder and Bile stasis triggers release of the liver enzymes e.g., serum 5' NT, ALP, AST, ALT along with serum bilirubin level, Batta (2011); Fikry et al., (2014). The derangement of LFT observed in this study could be the result of recurrent biliary colic, which may have caused obstruction of bile flow, leading to cholestasis and change in liver function.

The present study revealed that the mean serum level of TP and ALB is significantly different in the case group than in the control group ($p<0.05$). As far as categorical analysis using cutoff values (Table 4) the serum level of TP in 7.5% of the cases was significantly higher ($p<0.05$), whereas the serum level of ALB was statistically insignificantly ($p>0.05$) lower only in 1.9% of cases (Table 5**)**. The increased level of TP observed in the case group during this study could be due to inflammation in the GB or resulting from cholecystitis. However, it was evident that the derangement in the serum levels did not have much impact on the synthetic functions of the liver. Whereas, other study reported that mean serum levels of total protein and albumin were lower in GS

disease than without GS disease, however the differences were statistically insignificant, Olokoba, et al., (2009).

It has been reported that jaundice is a common feature of Common bile duct (CBD) stones. However, jaundice could also be a manifestation of other GB disease. The difference in these two conditions is that the serum total bilirubin level is usually <4 mg/dL in GB disease without evidence of CBD stones, Changet al., (2009). A significant difference ($p<0.05$) was found in the mean serum level of TB, DB and IB between the case and control groups during this study. The categorical analysis using cutoff values (Table 4**)** indicated that significantly higher levels of TB (7.6%), DB (10.5%) and IB (11.4%) in the cases than in the controls. Research in the past has indicated that the mean serum levels of bilirubin (total and conjugated) were higher in individuals with GS disease than without GS disease, however the differences were statistically insignificant, Olokoba, et al., (2009).It is also reported that there is a degree of disturbance present in the cases of acute cholecystitis in the absence of clinical jaundice but in such cases the level of bilirubin is usually not very high and it is usually seen up to 2 mg/dl because the severity of inflammation does not influence the LFT parameters, Habib et al., (2009)and this is accordance with present findings.

In the present study higher mean serum level of ALP, ALT and AST were recorded for the case group than the control group. The differences were statistically significant ($p<0.05$) and this is consistent with the previous study, Batta (2011). However, other study reported that the mean serum ALP was not significantly elevated, Changet al., (2009). Similarly, the categorical association analysis using the cutoff values (Table4) revealed that the serum levels of ALP (17.1%) and ALT (16.2%)are significantly higher in the cases than in the controls ($p<0.05$), however the findings of AST (8.6%)statistically insignificant($p>0.05$).The previous study also has been reported that the significantly higher serum level of ALP and AST. The serum level of AST was significantly higher in compared to ALT in acute calculous cholecystitis patients. There is reported that, ALP is a non-specific indicator of cholestatic liver disease because of its multiple sources like bone, placenta beside its production from the biliary canalicular membrane, Fikry et al., (2014).However, production increases in tissues undergoing metabolic stimulation and levels rise as a result of increased synthesis and consequent release into the circulation, Limdi& Hyde, (2003)There is some degree of hepatocellular injury appeared which is transient, reactive phenomenon secondary to cholecystitis associated with cholelithiasis and this injury is return to normal within two weeks to one month after cholecystectomy, Fikry et al., (2014).

It is possible that inflammation in the gallbladder induces inflammation to the closely juxtapose neighboring liver tissue, resulting in generally two patterns of hepatocytes injuries. The first is hepatocellular damage that is demonstrated clinically by elevated levels

of the aminotransferases but with a relatively normal level of ALP. The second is cholestasis with an elevated ALP out of proportion of aminotransferases. The exact mechanism of hepatocellular damage in cholecystitis associated with cholelithiasis but without CBD stones are not totally understood. In addition, free radical reactions in GB have been demonstrated to occur in cholecystitis, suggesting that oxidative stress may be partially responsible for hepatocytes injuries, Chang et al., (2009).

## CONCLUSION

The study included only the patients that had cholesterol gallstone. The stones were inspected visually and the cases that had other types of stones were excluded from the study. A major proportion of the participating patients (41%) were between 30-40 years in age group (Mean ± SD = 35.10 ± 3.47). The gallstones predominantly occur in the female patients (M:F = 1:4.25) and that cholesterol gallstones are formed due to derangement in the lipid composition of the blood. The abnormally and significantly higher levels of TC, TG, LDL, and VLDL and the lower level of HDL observed in the patients compared to the corresponding values in the control group. It was also evident from the findings of the study that the GS patients have a significantly higher level of the atherogenic index. Similarly, it was observed that the GS patients have a chance of biliary cholestasis and derangement of liver function, as suggested by their significantly high levels of TP, bilirubin, ALP, ALT, and AST. However, this does not seem to have impact on the synthetic functions of the liver.

## LIMITATIONS

1. The gallbladder stones were identified to be cholesterol GS by visual inspection, not by chemical analysis.
2. Many factors (e.g., high fatty diet, less physical activity, parity, alcohol consumption, ethnic and genetic variations) could have effects on both lipoprotein metabolism and GS disease. These factors were not considered in this study.
3. Serum LDL level could not be measured by the direct method.
4. LFT is not specific for the liver only. A decreased level of serum albumin, for example, may be observed in chronic diseases, or an elevated level of aminotransferases may be observed in cardiac diseases. Similarly, whether an elevated level of ALP was of liver origin or bone origin could not be specified.

## REFERENCES

Al-Atrakchey RN, Taher MA, Saeed IN. Lipid profile and fasting blood sugar analysis in patients with Cholelithiasis. *Iraqi J Pharm Sci* 2014; 23(2): 51-6.

Aslam HM, Saleem S, Edhi MM, Shaikh HA, Hafiz M, Saleem M. Assessment of gallstone predictor: comparative analysis of ultrasonographic and biochemical parameters. *Int Arch Med* 2013; 6: 17.

Atamanalp SS, Keles MS, Atamanalp RS, Acemoglu H, Laloglu E. The effects of serum cholesterol, LDL, and HDL levels on gallstone cholesterol concentration. *Pak J Med Sci* 2013; 29: 187-90.

Batta A. Cholecystitis and an enzyme study. *Int J Cur Biomed Phar Res* 2011; 1: 11-4.

Chang C-W, Chang W-H, Lin C-C, Chu C-H, Wang T-E, Shih S-C. Acute transient hepatocellular injury in cholelithiasis and cholecystitis without evidence of choledocholithiasis. *World J Gastroenterol* 2009; 15: 3788-92.

Channa NA, Shaikh HR, Khand FD, Bhanger MI, Laghari M. Association of gallstone disease risk with serum level of alkaline phosphatase. *J Liaquat Univ Med Health Sci* 2005; 4: 18-22.

Channa NA, Khand F, Ghanghro AB, Soomro AM. Quantitative analysis of serum lipid profile in gallstone patients and controls. *Pak J Anal Environ Chem* 2010; 11: 59-65.

Chuang S-C, Hsi E, Wang S-N, Yu M-L, Lee K-T, Juo S-HH. Polymorphism at the mucin-like protocadherin gene influences susceptibility to gallstone disease. Clinica Chimica Acta 2011; 412: 2089-93.

Devaki RN, Virupaksha H, Rangaswamy M, Deepa K, Goud B, Nayal B. Correlation of serum lipids and glucose tolerance test in cholelithiasis. *Int J Pharm Bio Sci* 2011; 2: 224-8.

Fikry A.A, Kassem A.A, Shahin D, Salah H.A. Elevated liver enzymes in patients with cholecystitis. *J Surgery* 2014; 2: 38-41.

Getachew A. Epidemiology of gallstone disease in Gondar University Hospital, as seen in the department of radiology. *Ethiop J Health Dev* 2008; 22: 206-11.

Greenberger N J, Paumgartner G. Diseases of the gallbladder and bile ducts. Harrison's principles of internal medicine (17th ed.). New York: McGraw-Hill 2008: 1991-2001.

Habib L, Mirza MR, Channa MA, Wasty WH. Role of liver function tests in symptomatic cholelithiasis. *J Ayub Med Coll Abbottabad* 2009; 21: 117-9.

Kumar D & Nagaraj. Undisputable behaviour of lipid profile in cholelithiatic gall bladder. *J Biomed Pharma Res* 2014; 3(4): 54-57.

Limdi J, Hyde G. Evaluation of abnormal liver function tests. *Postgrad Med J* 2003; 79: 307-12.

Olokoba A, Bojuwoye B, Olokoba L, et al,. Relationship between Gallstone disease and liver enzymes. *Res J Med Sci* 2009; 3: 1-3.

Pradhan S.(a) Study of Helicobacter hepaticus in gallbladders with cholelithiasis and its sensitivity pattern. *Kathmandu Univ Med J* 2009; 7: 125-8.

Pradhan SB, Joshi M, Vaidya A. (b) Prevalence of different types of gallstone in the patients with cholelithiasis at Kathmandu Medical College, Nepal. *Kathmandu Univ Med J* 2009; 7: 268-71.

Reshetnyak VI. Concept of the pathogenesis and treatment of cholelithiasis. *World J Hepatol* 2012; 4: 18-34.

Singh V, Zaidi SA, Singh VS. Lipids in biliary lithogenesis. *JPak Med Assoc* 1997; 47: 253-5.

Weerakoon HT, Ranasinghe S, Navaratne A, Sivakanesan R, Galketiya KB, Rosairo S. Serum lipid concentrations in patients with cholesterol and pigment gallstones. *BMC Research Notes* 2014; 7: 548.