Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE

DOI: 10.53555/jptcp.v29i04.4388

ANALYSIS OF SERUM PATTERN OF CHOLESTEROL, LIPASE AND LIVER ENZYMES TO DIFFERENTIATE THE DIAGNOSIS OF ACUTE CHOLECYSTITIS FROM ACUTE PANCREATITIS

Swastika[1], Dr Subhadip Bag[2*], Dr Anil Kumar Munta[3]

[1]MBBS student 2019 batch, Madhubani Medical College, Bihar
[2*]Senior Resident, Dept of Community Medicine, Madhubani Medical College, Bihar
[3]Professor, Dept of Biochemistry, Madhubani Medical College

***Corresponding Author:** Dr Subhadip Bag
* Senior Resident, Dept of Community Medicine, Madhubani Medical College, Bihar

Abstract:

Introduction: Acute cholecystitis and acute pancreatitis, two very common but serious condition of human, often present with similar symptoms and even have overlapping positive biochemical diagnostic test. Though Ultrasonography can be used as a diagnostic tool to differentiate, but sometimes even it fails to identify the gallstone which may lead to confuse the clinician. All these lead to delay in accurate diagnosis and treatment initiation. This present study analyses the role of serum cholestatic and pancreatic pattern to diagnose gall stone disease and acute pancreatitis early and accurately.

Methods: This case-control study was conducted in Madhubani Medical college, Bihar. Study participants were distributed in 3 groups (n= 40) ie. patients of Acute Cholecystitis, acute pancreatitis and control group. Blood samples were taken from them and various biochemical parameters were studied. Data were interpreted in SPSS version 16.

Results: Liver enzymes, lipid profile and lipase were significantly increased in both the experimental groups i.e. acute cholecystitis and acute pancreatitis. Receiver Operator Curves were plotted for each biochemical marker. The maximum AUC seen for ALP (1.0), LDL (0.98) and VLDL (0.91) for acute cholecystitis whereas Lipase and TG has the highest AUC for diagnosing acute pancreatitis. All the bio-marker were plotted for Acute pancreatitis and acute cholecystitis with Cut off for Sensitivity and Specificity.

Conclusions: ALP, LDL and VLDL can predict acute pancreatitis and lipase and TG can predict the status of acute cholecystitis. It gives the basic analytical report that may help the clinician for the prompt management without undergoing for radiological observations, biopsies or any surgical interventions for the individual.

Introduction

Cholelithiasis (gallstones disease-GSD), is one of the prominent disorders facing mankind. It may occur anywhere within the biliary system and specific terminology is used depending on their location: cholecystolithiasis (gallstones within the gallbladder), choledocholithisis (in bile ducts),biliary microlithiasis (if the gallstones <3 mm in diameter) etc. The majority of gallstones are either cholesterol, pigment stones (black or brown composed of calcium bicarbonate) or mixed type.

Apart from several risk factors, women are probably at increased risk because estrogen stimulates the liver to remove more cholesterol from blood and divert it into the bile [1].
The gall stones (GS) not only affect the biliary tree but also the hepatic parenchyma [2].Alanine and aspartate transaminases are produced from hepatocytes and alkaline phosphatase is mainly from biliary epithelium. Biliary colic is the upper abdominal pain due to passage of a gallstone through the cystic duct and these symptoms often confuse for acute pancreatitis [3]. It is evidenced that gallstone pancreatitis is associated with the rise of lipase and other pancreatic enzymes [4]. Studies reported that the liver enzymes are elevated in both pancreatitis and gallstone disease [5].At the same time, several studies reporting that concerned to biliary and gallbladder disease, the rise of alkaline phosphatase typically represents a "cholestatic" pattern and frequently patients present with a "mixed" picture of elevation in all three liver enzymes [6, 7]. Hence, all these diversified patterns leave the clinician in diagnostic dilemma initially. Ultrasonography is the key diagnostic test used to identify the presence of stones, however sometimes it unnoticed the small stones or sludge [8].
Therefore the present study will analyse the serum cholestatic and pancreatic pattern for the differential diagnosis of gall stone disease and acute pancreatitis accurately. Early intervention in these cases not only retards the unwanted effects but also provides the prompt treatment and prevents the associated clinical complications.

Review of literature

Cholelithiasis or gallstones disease is one of the striking and major afflictions leading to surgical intervention in modern society. Biliary sludge can be considered as the precursor for the occurrence of gall stones but basically it occurs due to the accustomed deposits of digestive fluid within the biliary system. Deposition of digestive fluid within the gallbladder is known as cholecystolithiasis and within the bile ducts, choledocholithiasis. Gallstones are caused by the combined factors that include inherited body chemistry, obesity, gallbladder motility, pregnancy, nutritional factors (like low intake of calcium, magnesium, and vitamin C and low fluid consumption etc. Apart from these general risk factors gallstone risk increases for female gender is more prone (especially before menopause) because of hormone estrogen as this hormone stimulates the liver to eliminate more cholesterol from blood and drain it into bile. North Indian population have higher chance of having gallstones disease. The prevalence of the cholelithiasis is more in Bihar rather than the other states of the nation [9].
The inflammation of gall bladder which occurs due to the obstruction of cystic duct by gall stones or may be by biliary sludge impactation at neck of gall bladder. Cholelithiasis further leads to acute cholecystitis and acute pancreatitis. Acute inflammatory response occurs due to the increase of intra luminal pressure within the gallbladder, together with cholesterol and supersaturated bile and synthesis and secretion of prostaglandins I2 and E2 also triggers this response [10]. Acute Pancreatitis is inflammatory condition of pancreas which may occur due to the obstruction of common bile duct on impinge on main pancreatic duct by gallstones and it may also occur due to the backflow of bile into pancreatic duct. The incidence of occurrence in male population is 10% - 30% that is higher than female. The activation of trypsin and lack of pancreatic clearance of active trypsin triggers the inflammatory response of pancreas [11].
The epidemiological screening method to correctly determine the disease is ultrasonography. For the assessment of cholecystitis the following tests can be done like Blood examination: increase white blood cell (WBC) count may be the indication of an infection. Increased levels of liver enzymes can aid the doctor for making the diagnosis. Computerized tomography (CT) scans and ultrasound

Lipid profile

A panel of blood tests used to find dyslipidaemias. The lipid profile typically includes Low density lipoprotein (LDL) High density lipoprotein (HDL), Triglycerides and Total cholesterol. This test is used to identify cardiovascular disease and pancreatitis. (SIDHU)

Liver enzymes

This is also referred as hepatic panel comprises transaminases like aspartate transaminase (AST or SGOT), alanine transaminase (ALT or SGPT) and alkaline phosphatase (ALP) are useful biomarkers of liver injury in a patient with some degree of intact liver function. The liver enzymes are importance in detection of hepatic involvement in some diseases can be of crucial importance ([12].

Lipase

Lipase is an enzyme that breaks down triglycerides into free fatty acids and glycerol. Lipases are present in pancreatic secretions and are responsible for fat digestion. The detection of serum lipase is importance of pancreatitis, crohn's disease, celiac diseases and others (pirahanchi).

Aim and objectives

The aim of the current study is to analyse the serum pattern of cholesterol, lipase and liver enzymes to differentiate the diagnosis of acute cholecystitis from acute pancreatitis

1. To evaluate and compare the serum cholesterol, liver and pancreatic enzymes for their role in the cholecystitis and acute pancreatitis
2. To correlate and analyse the serum pattern of the markers separately in the respective diseases to check the feasibility as an indicator to differentiate and assessing the disease.
3. To establish a cut off for these markers independently to identify and to differentiate the disease at initial stages.

Materials and methods

Selection of participants

This case and control study was carried out at Madhubani Medical College (MMC), Madhubani, Bihar. The approval of ethical clearance was obtained from the Institutional Ethical Committee. The informed consent was obtained from all the age and gender matched participants or their attendants in the respective groups (n=40) i.e., control group, individuals with acute cholecysytits and acute pancreatitis. The age group of 30 to 50 years will be chosen for the study.

Inclusion criteria and exclusion criteria

The participants of the corresponding groups who have fulfilled the diagnostic criteria of the respective diseases will be included. Individuals with smoking, alcoholism, pregnancy, cardiac ailments will be excluded.

Parameters

1. FBS
2. Liver enzymes (AST, ALP and ALT)
3. Lipid profile
4. Lipase

FBS: analysed by Glucose oxidase and peroxidase method (GOD-POD)

Liver enzymes SGOT, SGPT were analysed by IFCC method (kinetic) and ALP by Tris carbonate method.

Lipid Profile: The serum total cholesterol was estimated by cholesterol oxidase and peroxidase method (CHOD-POD). Hydrogen peroxide is formed during the cholesterol oxidation and in turn this oxidises the chromogen to produce pink colour). Serum triglyceride was estimated by Trinder method (dynamic extended stability with lipid clearing agent. The HDL cholesterol was analysed by Phosphotungstic Acid Method. Chylomicrons, LDL and VLDL are precipitated from serum by phosphotungstate. The HDL cholesterol remains unaffected in the supernatant and is estimated with enzymatic cholesterol method. The serum **LDL cholesterol and serum VLDL cholesterol** were measured by indirect method in accordance with Friedewald formula.

Lipase: Estimated by advanced homogenous micelle technology

Sample collection

A detailed clinical examination was recorded with reference to age, sex, family and clinical history from all the participants. 5ml of blood sample was collected. Their fasting blood samples were collected and analysed for plasma glucose, liver enzymes, lipid profile and lipase.

Statistical analysis

All the statistical analysis was carried out by using SPSS (Statistical Package for Social Sciences) trial version 16 in MS excel 2007. The quantitative variables were expressed as Mean and Standard deviation. $p<0.05$ is considered as statistically significant.

Kruskal Wallis test was used for mean comparison between the groups and receiver operator characteristic (ROC) curve was used to identify the optimal cut off values

Results

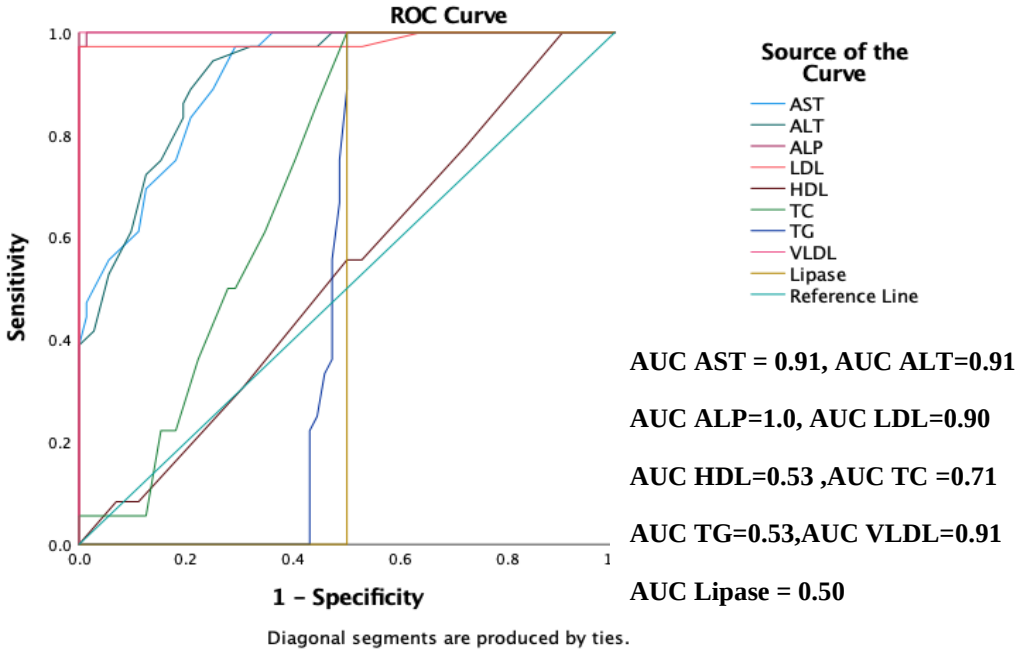
The descriptive and mean of various biomarker are among different group are shown in Table 1.There is statistical difference of mean values of Liver enzyme , Lipid profile and Lipase biomarker among the groups. The ROC curve for diagnostic maker with AUC is shown in Figure 1. Sensitivity and Specificity and cut off of biomarker are shown in Table 2.

The ROC curve with AUC for diagnosis of Acute Pancreatitis is shown in figure 2.Senstivity and specificity and cut of biomarker are shown in Table 3.

Table 1: Comparison of Mean between Group

Variable	Control Group	Acute Cholecystitis	Acute Pancreatitis	KW-H /df/p value
Age Mean± SD	40.2 ± 6.3	40.1 ± 6.6	40.2 ± 6.5	0.052/2/**0.974**
FBS (mg/dl) Mean± SD	78.1 ± 5.1	81.5 ± 5.1	79.7 ± 7.0	5.365/2/0.068
AST (U/L) Mean± SD	33.6 ± 5.5	82.5 ± 6.3	73.8 ± 6.3	**81.4/2/<0.001**
ALT(U/L) Mean± SD	31.5± 4.8	78.1 ± 6.7	69.4 ± 6.6	**81.6/2/<0.001**
ALP (U/L) Mean ± SD	100.0 ± 15.5	179.3 ± 8.5	144.8 ± 7.7	**95.0/2/<0.001**
LDL(mg/dl) Mean ± SD	54.9 ± 7.9	140.9 ± 7.7	113.6 ± 8.1	**95.0/2/<0.001**
HDL(mg/dl) Mean ± SD	49.1 ± 7.4	37.6 ± 5.1	33.5 ± 4.8	**93.7/2/<0.001**
TC(mg/dl) Mean ± SD	152.7 ± 17.7	210 ± 45.1	220 ± 40.1	**95.1/2/<0.001**
TG (mg/dl) Mean ± SD	133.2 ± 7.7	200.5 ± 4.9	372.1 ± 9.4	**95.1/2/<0.001**
VLDL (mg/dl) Mean ± SD	26 ± 1.5	40.1 ± 0.98	34.4 ± 1.87	**95.1/2/<0.001**
Lipase (U/L) Mean ± SD	113.5 ± 1.8	155.2 ± 5.6	181.5 ± 6.9	**95.1/2/<0.001**

Figure 1: ROC curve for Acute Cholecystitis



AUC AST = 0.91, AUC ALT=0.91

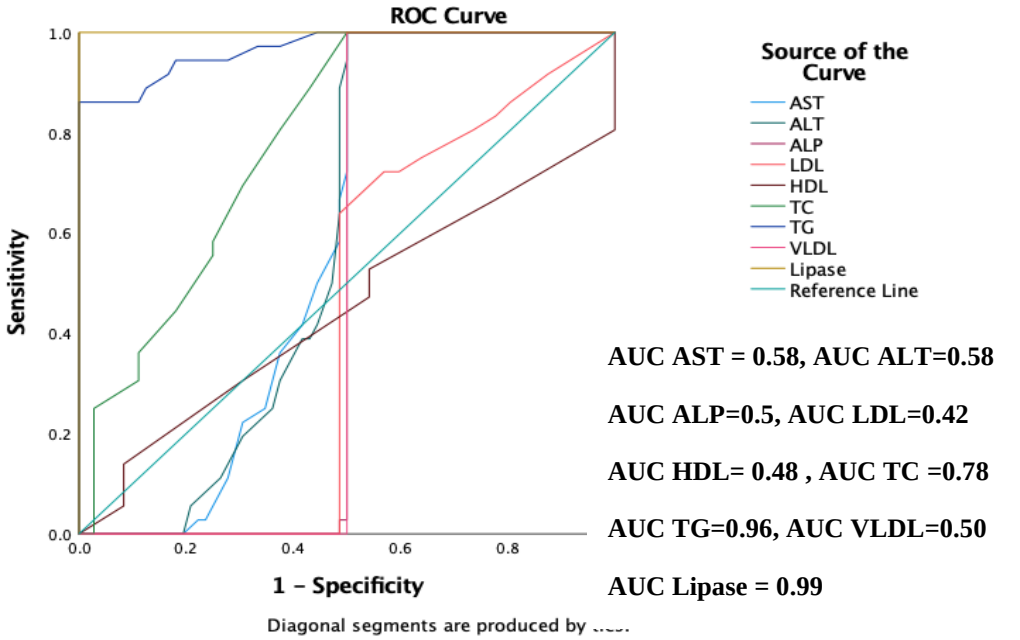
AUC ALP=1.0, AUC LDL=0.90

AUC HDL=0.53 ,AUC TC =0.71

AUC TG=0.53,AUC VLDL=0.91

AUC Lipase = 0.50

Figure 2: ROC curve for Acute Pancreatitis



AUC AST = 0.58, AUC ALT=0.58

AUC ALP=0.5, AUC LDL=0.42

AUC HDL= 0.48 , AUC TC =0.78

AUC TG=0.96, AUC VLDL=0.50

AUC Lipase = 0.99

Table 2 : Bio Marker for Acute Cholecystitis with Cut off with Sensitivity and Specificity

LAB PARAMETER	CUT OFF VALUE (UNITS)	SENSTIVITY	SPECIFICTY
AST (U/L)	75.5	83%	80%
ALT (U/L)	71.5	83%	80.6%
ALP (U/L)	157	100%	98.6%
LDL (mg/dL)	126	100%	100%
HDL (mg/dL)	7 or less	100%	100%
TC (mg/dL)	397	100%	100%
TG (mg/dL)	191	100%	100%
VLDL (mg/dL)	38.2	100%	100%
LIPASE (U/L)	147	94.4	50%

Table 3 : Bio Marker for Acute pancreatitis with Cut off with Sensitivity and Specificity

LAB PARAMETER	**CUT OFF VALUE (UNITS)**	**SENSTIVITY**	**SPECIFICTY**
AST (U/L)	73.5	58.3%	48.6%
ALT (U/L)	67.5	63%	51.4%
ALP (U/L)	143	58.3%	50%
LDL (mg/dL)	115.5	50%	50%
HDL(mg/dL)	7 OR LESS	100%	100%
TC (mg/dL)	203	100%	50%
TG (mg/dL)	150	100%	50%
VLDL (mg/dL)	30	100%	50%
LIPASE (U/L)	166.5	100%	100%

Discussion

Acute cholecystitis is one of the most common clinical conditions and sometimes it may be confused with other illnesses such as peptic ulcer disease, irritable bowel disease, and cardiac disease. Chronic and acute pancreatitis can also mimic gallbladder disease. According to the findings obtained from the Table I, the parameters of liver enzymes, lipid profile and lipase were significantly increased in both the experimental groups i.e. acute cholecystitis and acute pancreatitis. There are no accurate methods of differentiating acute biliary pancreatitis. Obstructions of biliary ducts, idiopathic pancreatitis may be related with biliary origin which needs identification for acute treatment. Cut-off points of admission biochemical markers with sensitivity, specificity, positive predictive value and negative predictive value were determined after identification of significant variables. Receiver Operator Curves were plotted for each biochemical marker. Increased Alkaline Phosphatase, total bilirubin, direct bilirubin, amylase and lipase levels may be used in prediction of biliary pancreatitis [13].

From the Figure 1, it was evident that the receiver operator characteristic curve (ROC) analysis of the markers demonstrated the area under the curve (AUC) for acute cholecystitis.. Our results showed that the serum concentrations of all three markers were significantly higher with several studies (bullet). Among the liver and lipid parameters that are analysed in the current study, the maximum the AUC for the parameters seen for ALP (1.0) and LDL (0.98) indicating significant diagnostic ability for acute cholecystitis rather than other markers and our study is correlating with several studies (Figure 1) [14].

This study also demonstrated in Figure 2, that lipase can be treated as promising marker that has the highest AUC with the greatest sensitivity and specificity in diagnosing the acute pancreatitis. To differentiate the acute cholecystitis from acute pancreatitis the levels of serum ALP, LDL and VLDL can be considered as good predictors. The serum lipase (166.5 U/L) and serum TG (150 mg/dl) level above the cut off value to predict the acute pancreatitis (Table 2 and 3)

In this study, the performance of PCT, hs-CRPand WBC in diagnosing infected diabetic foot ulcer was evaluated. Our results showed that the serum concentrations of all three markers were signiℵcantly higher in IDFU compared to NIDFU group. This study also demonstrated that hs-CRP has the highest AUC and the greatest sensitivity and speciℵcity in detecting infection in DFU. In this study, the performance of PCT, hs-CRP and WBC in diagnosing infected diabetic foot ulcer was evaluated. Our results showed that the serum concentrations of all three markers were signiℵcantly higher in IDFU compared to NIDFU group. This study also demonstrated that hs-CRP has the highest AUC and the greatest sensitivity and speciℵcity in detecting infection in DFU. In this study, the performance of PCT, hs-CRP and WBC in diagnosing infected diabetic foot ulcer was evaluated. Our results showed that the serum concentrations of all three markers were signiℵcantly higher in IDFU compared to NIDFU group. This study also demonstrated that hs-CRP has the highest AUC and the greatest sensitivity and speciℵcity in detecting infection in DFU. In this study, the performance of PCT, hs-CRP and WBC in diagnosing infected diabetic foot ulcer was evaluated. Our results showed that the serum concentrations of all three markers were signiℵcantly higher in IDFU compared to NIDFU group. This study also demonstrated that hs-CRP

has the highest AUC and the greatest sensitivity and speci ﬁ city in detecting infection in DFU. In this study, the performance of PCT, hs-CRP and WBC in diagnosing infected diabetic foot ulcer was evaluated. Our results showed that the serum concentrations of all three markers were signi ﬁ cantly higher in IDFU compared to NIDFU group. This study also demonstrated that hs-CRP has the highest AUC and the greatest sensitivity and speci ﬁ city in detecting infection in DFU.

In this study, the performance of PCT, hs-CRP and WBC in diagnosing infected diabetic foot ulcer was evaluated. Our results showed that the serum concentrations of all three markers were signi ﬁ cantly higher in IDFU compared to NIDFU group. This study also demonstrated that hs-CRP has the highest AUC and the greatest sensitivity and speci ﬁ city in detecting infection in DFU.

Summary

- The present study was under taken to observe the levels of markers to differentiate acute cholecystitis from acute pancreatitis
- Among the parameters, both the liver, hepatic enzymes and lipase showed highly significant elevation in the acute cholecystitis and acute pancreatitis.
- The AUC for the parameters TAG (0.96) and lipase (1.0) with more AUC having significant diagnostic ability rather than other parameters to evaluate the acute pancreatitis and the parameters ALP (1.0), LDL (0.98) and VLDL (0.91) having more AUC with diagnostic ability of acute cholecystitis
- Based on AUC, the cut off values of these markers has been established for ALP (157), TAG (191) and VLDL (38.2) which helps in the prediction acute cholecystitis and for lipase (166.5) along with TAG (150) helps in understanding acute pancreatitis and beyond these optimum cut off values, these markers gives an idea in understanding the progression of the disease

Conclusion

Gall stone disease is one of the significant diseases that occur anywhere in the biliary tree. The symptoms of biliary colic are often correlated with acute pancreatitis which puts the clinician dilemma. Hence there is a need to observe the pattern analysis and to establish a optimum cut off for serum markers to differentiate acute cholecystitis from acute pancreatitis independently. The combination markers ALP and VLDL can differentiate the acute pancreatitis from cholelithiasis and lipase and TAG can predict the status of acute cholecystitis. This study gives the basic analytical report that may help the clinician for the prompt identification, diagnosis and improved treatment protocol without undergoing for radiological observations, biopsies or any surgical interventions for the individual.

References

1. Maple JT, Ikenberry SO. ASGE Standards of Practice Committee;. The role of endoscopy in the management of choledocholithiasis. *Gastrointest Endosc*. 2011; 74(4):731-744.
2. Patel G , Jain A, Singh M , Garg M , Karim T, Dey S. Liver biopsy in gall stone disease: a prospective study in patients undergoing cholecystectomy . Int Surg J. 2018; 5 (1):286-291.
3. Elad R, Shimon S, Bernardo M, Tali B, Todd Z, Adrian R, Yoav L. Enzyme pattern of biliary colic: A counterintuitive picture. World J Hepatol. 2016; 8(36): 1629-1636.
4. Sato A, Hashimoto M, Sasaki K, Matsuda M, Watanabe G. Elevation of Pancreatic Enzymes in Gallbladder Bile Associated with Heterotopic Pancreas. A Case Report and Review of the Literature. J Pancreas. 2012; 13(2):235-238.
5. Tetangco EP, Shah N, Arshad HM, Raddawi H. Markedly Elevated Liver Enzymes in Choledocholithiasis in the absence of Hepatocellular Disease: Case Series and Literature Review. J Investig Med. 2016; 4(2):2324709616651092.

6. Videhult P, Sandblom G, Rudberg C, Rasmussen IC. Are liver function tests, pancreatitis and cholecystitis predictors of common bile duct stones? Results of a prospective, population-based, cohort study of 1171 patients undergoing cholecystectomy. HPB (Oxford). 2011; 13(8):519–527.
7. Eula P, Natasha S, Hafiz M, Hareth R. Markedly Elevated Liver Enzymes in Choledocholithiasis in the absence of Hepatocellular Disease: Case Series and Literature Review. J Investig Med High Impact Case Rep. 2016;4 (2): 1-3
8. Sanders G, Kingsnorth A. Biliary colic/cholecystitis Biliary colic and cholecystitis share a spectrum of symptoms, and no exact time course or definition exists to separate them. Br Med J. 2007; 335 (7614):295-9.
9. Wadhwas, V., Jobanputra, Y., Gard, S.K., Parwardhan, S., Mehta, D., Sanaka. Nationwide trends of hospital admissions for acute cholecystitis in the United States. Gastroenterology Report
10. Pamuk B, Yilmaz H, Kebapçilar L, Kirbiyik H, Alacacioğlu A, Bozkaya G, Pamuk G, Demirpence M. The effect of orlistat and weight loss diet on plasma ghrelin and obestatin. J Res Med Sci. 2018;23:95.
11. Gupta KK, Ali S, Sanghera RS. Pharmacological Options in Atherosclerosis: A Review of the Existing Evidence. CardiolTher. 2019 ;8(1):5-20
12. Waldmann E, Parhofer KG. Apheresis for severe hypercholesterolaemia and elevated lipoprotein(a). Pathology. 2019;51(2):227-232Gupta KK, Ali S, Sanghera RS. Pharmacological Options in Atherosclerosis: A Review of the Existing Evidence. CardiolTher. 2019 ;8(1):5-20
13. Ismail OZ, Bhayana V. Lipase or amylase for the diagnosis of acute pancreatitis? ClinBiochem. 2017 ;50(18):1275-1280.
14. M S Padda , S Singh, S J Tang, D C Rockey. Liver test patterns in patients with acute calculous cholecystitis and/or choledocholithiasis. Aliment Pharmacol Ther. 2009 1;29(9):1011-8.