Assessment of Hepatic Biochemical Indices in Patients with Acute Cholecystitis

Galawesh Norri Taher[1] [1]Department of Nursing Techniques, Kirkuk Technical Institute, Northern Technical University, Iraq

Ozdan Akram Ghareeb[2] [2]Department of Community Health Techniques, Kirkuk Technical Institute, Northern Technical University, Iraq

ABSTRACT

Laboratory diagnosis of any pathological condition, including acute cholecystitis, contributes to the appropriate therapeutic management. Therefore, our study came to evaluate hepatic biochemical indicators in acute cholecystitis patients. This prospective study was conducted between January 2021 and July 2022 on 120 participants attended to private hospitals located in Kirkuk city, northern Iraq. Informed consent was obtained from each participant, and then the participants were divided into two groups, each group comprising 60 individuals, the first for control and the second for those diagnosed with acute cholecystitis. The biochemical analyzes of the liver indicators required for the study were performed after collecting the serums of all the participants. The laboratory results proved that the hepatic serum indices including ALT, AST, ALP, GGT, and total bilirubin in acute cholecystitis patients were significantly higher compared to the healthy participants. Thus, it was concluded that the apparent high levels of hepatic enzymes in the serum had a prominent role in diagnosing this disease.

Keywords: Biochemical analyzes, acute cholecystitis, hepatic indicators

Introduction

In general, acute cholecystitis (ACH) is caused by gallstones and may be up to 95% of cases although not all cases of gallstones present with symptoms of cholecystitis [1]. The main determinant of ACH pathology is obstruction of the cystic duct by gallstones, where this blockage causes the accumulation of bile in the gallbladder, which increases the pressure inside [2].An elevated concentration of bile, sometimes accompanied by bacterial infection or damage of gallbladder wall, may lead to inflammation of gallbladder known as cholecystitis [3]. This inflammation can minimize the normal blood pass to parts of the gallbladder, causing cells to die due to lack of oxygen [4,5]. Notably, the continuation of this obstruction with the patient not receiving early treatment leads to serious complications of this disease [6].Besides, there are other etiologies such as acalculous cholecystitis, gallbladder torsion and malignancy tumor [7]. Clinically, the patient with acute cholecystitis complains of acute pain in the right side of the abdomen, high temperature, and nausea that may coincide after eating [8]. In most patients, laparoscopic cholecystectomy, performed within less than a week of definitive diagnosis, is the treatment of choice for this acute disease [9].As for diagnosis of cholecystitis, it is mainly based on the apparent symptoms, in addition to laboratory tests, and ultrasound of the abdomen is usually used as well [10]. Hepatic indices levels may change due to the inflammatory process caused by cholecystitis, and some medical professionals have hypothesized that these alterations may help us predict gallstone obstruction in the common bilateral ducts and thus reduce the risks of surgical treatments [11,12]. Still, few studies

evaluating the effects of cholecystitis-related disorders on hepatic indices have reported different results [13-15]. Because we believe that the serum levels of liver enzymes in patients with cholecystitis may be abnormal. Therefore, we conducted the current study to evaluate the role of hepatic biochemical indicators in the diagnosis of acute cholecystitis.

Methods

This prospective study was conducted on 120 adult participants, 60 of whom were healthy as control and 60 others were diagnosed with acute cholecystitis by specialist physicians in the internal and/or surgical wards of private hospitals in Kirkuk, northern Iraq, during the period from January 2021 to July 2022, their ages ranged between 19 to 68 years old. The study included patients of both genders, ages 18 years and more, and they accepted to participate in the study. Individuals with any type of viral hepatitis, alcoholics, liver disease, and pancreatitis, pregnant women, less than 18 years of age, and refusing to enroll in this study were excluded. Of the total participants, 55 were men and 65 were women, and they were sectioned into (2) groups as follows:

- Group (control): It included 60 healthy individuals free of any disease, 33 of whom were men and 27 women, and a mean age was 42 years (age ranged between 29-52 years(.
- Group (Patients): It included 60 patients with acute cholecystitis, the men were about 33 compared to 27 women, while the mean age was about 42 years (ranging from 27-58 years).

Samples were collected by drawing blood (5ml) from all participants intravenously through a designated sterile glass tube. Then the blood was separated to obtain the serum after placing it in the centrifuge, where the serum was used to perform the biochemical tests. All patients underwent liver function tests in the form of alanine and aspartate aminotransferases (ALT, AST), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), and total bilirubin (TB). Laboratory results were processed as a statistical description by SPSS (IBM) version 26. Data were presented as mean and standard deviation. Independent sample variables (t-test) were comparison for both groups, with a significant p-value adopted at less than 5 percent.

Results

According to the results, there was a remarkable increase in ALT enzyme level in the serum of acute cholecystitis patients (125.34± 33.61), compared to healthy (48.79±13.83) control group (P = 0.000) , as display in figure (1)

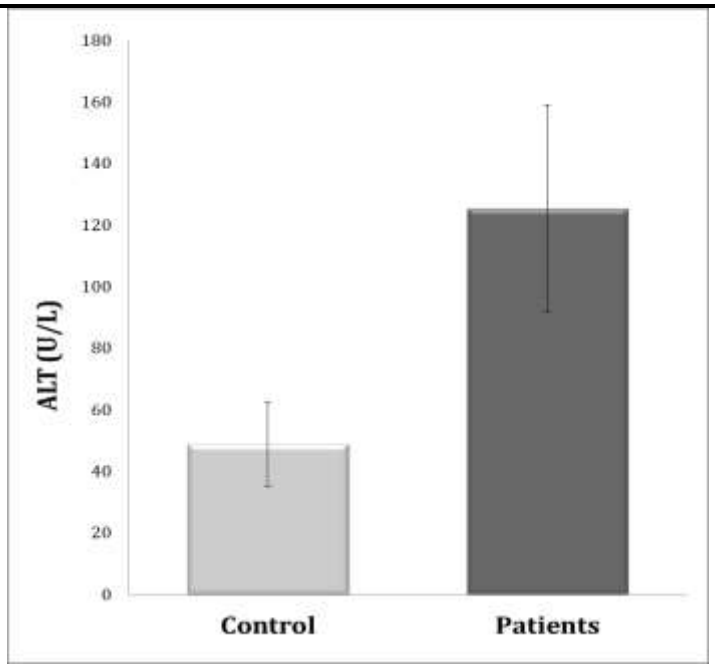

Figure 1: Serum ALT concentration in both study groups.

As for the serum level of AST enzyme in acute cholecystitis patients, it reached (118.49 ± 47.28) compared to the level of the control group, which was about (16.82±43.27), with a clear statistical difference (P =0.0001) between the two groups (Fig. 2).

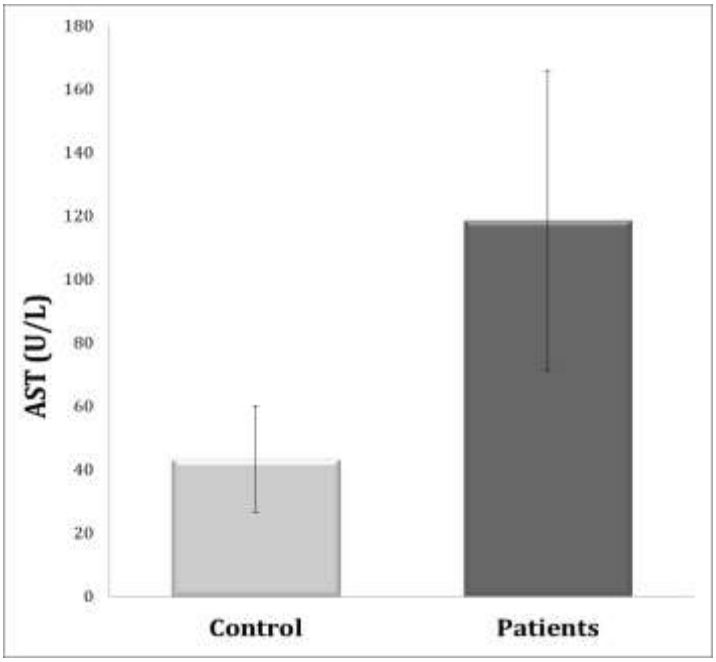

Figure 2: Serum AST concentration in both study groups.

Also, results recorded a considerable raise (P=0.000) in the activity of ALP enzyme in the serum of acute cholecystitis patients (133.61±36.03), compared to control individuals (82.95±17.11), as shown in figure (3)

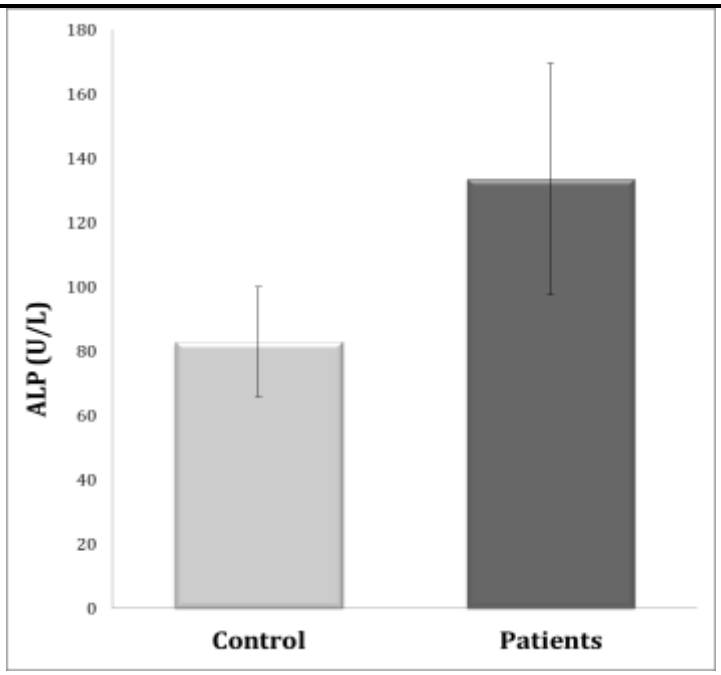

Figure 3: Serum ALP concentration in both study groups.

Besides, our results also demonstrated a clear increase (P =0.0001) in GGT enzyme levels in serum of patients (71.46±21.13) compared to healthy group (42.66±9.90), as shown in figure (4).

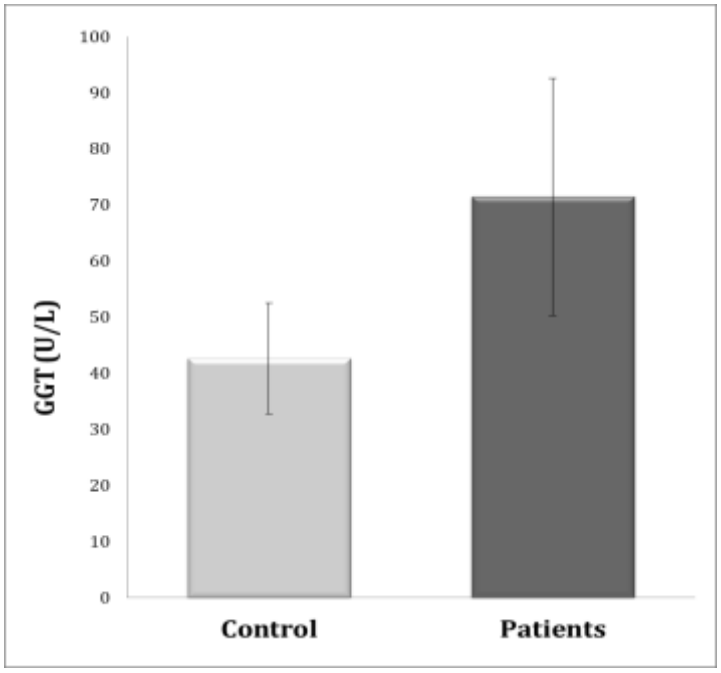

Figure 4: Serum GGT concentration in both study groups.

The last figure (5) shows the obvious high concentration of total bilirubin in the serum (P =0.000) of patients group (1.53±0.49) compared to the control group (1.02 ±0.27).

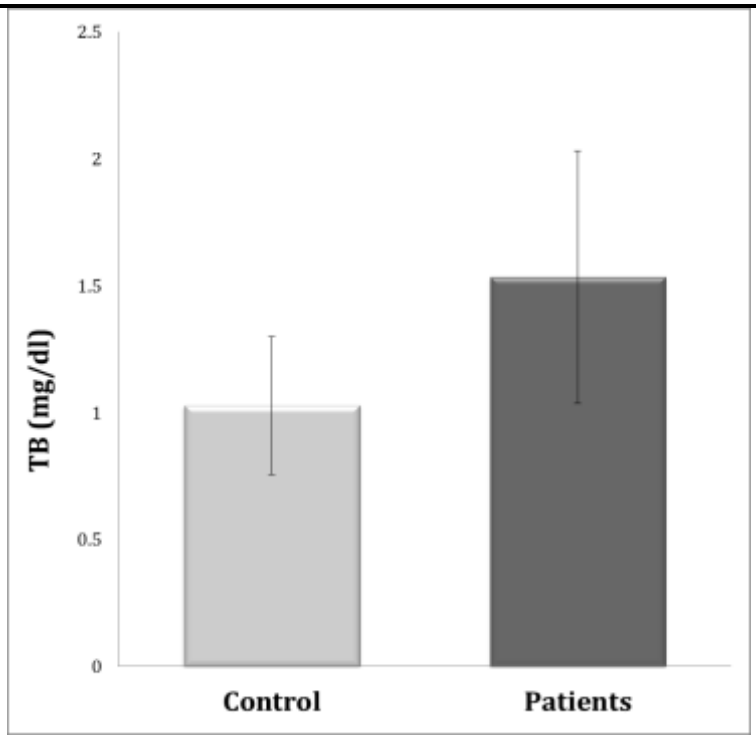

Figure 5: Serum TB concentration in both study groups.

Discussion

Acute cholecystitis, known as inflammation that may develop over a period of hours, is the most common complication of cholelithiasis [16]. It occurs when the cystic duct of the gallbladder becomes obstructed, causing bile to stagnate and release liver enzymes into the blood. This obstruction also prevents fluid from passing out, causing irritation and swelling of the gallbladder [17,18]. Liver serological enzymes testing are used as a routine assessment for the diagnosis of cholecystitis for the purpose of checking the workable situation of the liver [19]. In a retrospective study, Song et al. (2014) analyzed the clinical characteristics of 424 patients with acute cholecystitis. They found that about (42%) of them did not suffer from cholelithiasis compared to (58%) patients with cholelithiasis, and they noticed a correlation of rising liver enzymes concentrations in patients with cholelithiasis, especially in patients without cholelithiasis [20]. The serum concentrations of ALT, AST, and ALP in our study patients were significantly increased when compared with healthy controls. This indicated the presence of liver cell injury in acute cholecystitis patients [21]. Although Aspartate amino transferase (AST) is found in various parts of the human body, it is found in abundance in the liver and skeletal muscles [22]. It is used in combination with other liver enzymes such as alanine transaminase (ALT) as a clinical sign of liver damage [23]. It should be noted that zone 3 of the hepatic acinus contains the highest concentration of AST, and any damage to this region leads to an increase in the concentration of this enzyme in the blood [24]. In the liver, alkaline phosphatase (ALP) is found on the canalicular membrane of hepatocytes. A high serum level usually indicates bile duct obstruction or epithelium damage, cholestasis, and the development of inflammatory processes in the liver [25,26]. The mechanism of high alkaline phosphatase has been associated with the enhanced synthesis and release of cell membranes by the detergent action of retained bile salts [27]. In previous review on this topic (2018), Vagvala and O'Connor emphasized that liver enzyme abnormalities typically appear in either of two types: hepatocyte injury or cholestasis. They indicated that hepatocyte injury is usually a disproportionate elevation of AST and ALT for ALP, while cholestasis is indicated by a disproportionate elevation of ALP for AST and

ALT. Besides, cases of acute cholecystitis usually appear with elevated levels of these enzymes as well as total bilirubin [28]. Amirthalingam and companions found, in their study (2017) on (149) patients with acute cholecystitis in an emergency situation, an increase in serum concentrations of liver enzymes, especially ALP, with the severity of the disease [29]. Gamma-glutamyl transferase is an enzyme found throughout the body, though mostly found in the liver. It may leak into the bloodstream in cases of liver damage, so high levels of this enzyme in the blood may be a sign of liver disease or bile duct damage [30]. Often evaluation of this enzyme is not sufficient to diagnose the accurate etiology of hepatic disorders. Therefore it is usually performed alongside or after other hepatic indicator assessments [31].In a previous retrospective study by Ahn et al.(2016), they analyzed (854) patients acute cholecystitis who attended the emergency ward, values of liver function tests were considered reliable predictors especially with gallstone obstruction, and gamma-glutamyl transpeptidase was the most reliable variable[15]. In a systematic review, Chen et al. (2020) examined data from 19 studies that represented approximately 4,057 patients suffering from acute cholecystitis, and calculated the mean diameter of common bile duct stones and liver function test values for patients with both conditions. They found that serum liver enzyme values were high, and GGT enzyme was the most susceptible and specific indication of biliary obstruction in the setting of acute cholecystitis [32]. Total bilirubin is a combination of direct and indirect bilirubin, it is a compound result from normal catabolic pathway to break down hemoglobin required to eliminate waste products from the body, which is formed as a result of the destruction of aging or abnormal erythrocytes [33]. In general, bilirubin builds up in the blood serum when the gallbladder is obstructed as it cannot drain properly. An augmentation in the bilirubin concentration in the serum of patients with acute cholecystitis indicates obstruction of the bile ducts due to gallstones [34,35].

Conclusions

Through this study, we found an increase in the activities of the biochemical indicators of the following liver enzymes: ALT, AST, ALP, GGT, and total bilirubin in patients with acute cholecystitis compared to healthy individuals, so that these tests can be adopted as an accurate diagnostic for acute cholecystitis cases.

References

1- Yokoe M, Takada T, Hwang TL, Endo I, Akazawa K, Miura F, Mayumi T, Mori R, Chen MF, Jan YY, Ker CG. Descriptive review of acute cholecystitis: Japan-Taiwan collaborative epidemiological study. Journal of Hepato-biliary-pancreatic Sciences. 2017 Jun;24(6):319-28.

2- Housset C, Chrétien Y, Debray D, Chignard N. Functions of the Gallbladder. Compr Physiol. 2016 Jun 13;6(3):1549-77.

3- Katabathina VS, Zafar AM, Suri R. Clinical presentation, imaging, and management of acute cholecystitis. Techniques in vascular and interventional radiology. 2015 Dec 1;18(4):256-65.

4- Gross AR, Bacaj PJ, Williams HJ. Educational Case: Gallstones, Cholelithiasis, and Cholecystitis. Academic Pathology. 2020 Sep 10;7:2374289520951902.

5- Bruni A, Garofalo E, Zuccalà V, Currò G, Torti C, Navarra G, De Sarro G, Navalesi P, Longhini F, Ammendola M. Histopathological findings in a COVID-19 patient affected by ischemic gangrenous cholecystitis. World Journal of Emergency Surgery. 2020 Dec;15(1):1-8.

6- González-Castillo AM, Sancho-Insenser J, Miguel-Palacio D, Morera-Casaponsa JR, Membrilla-Fernández E, Pons-Fragero MJ, Pera-Román M, Grande-Posa L. Mortality risk estimation in acute calculous cholecystitis: beyond the Tokyo Guidelines. World Journal of

Emergency Surgery. 2021 Dec;16(1):1-0.
7- Kimura Y, Takada T, Kawarada Y, Nimura Y, Hirata K, Sekimoto M, Yoshida M, Mayumi T, Wada K, Miura F, Yasuda H. Definitions, pathophysiology, and epidemiology of acute cholangitis and cholecystitis: Tokyo Guidelines. Journal of hepato-biliary-pancreatic surgery. 2007 Jan;14(1):15-26.
8- Gallaher JR, Charles A. Acute Cholecystitis: A Review. JAMA. 2022 Mar 8;327 (10) : 965-75.
9- Sultan AI, Ali SH, Ghareeb OA. Port Site Consequences After Laparoscopic Cholecystectomy Using an Open Versus Closed Approach of Pneumoperitoneum. Cureus. 2022 Jul 1;14(7).
10- Lammert F, Gurusamy K, Ko CW, Miquel JF, Méndez-Sánchez N, Portincasa P, Van Erpecum KJ, Van Laarhoven CJ, Wang DQ. Gallstones. Nature reviews Disease primers. 2016 Apr 28;2(1):1-7.
11- Yasukawa K, Shimizu A, Kubota K, Notake T, Sugenoya S, Hosoda K, Hayashi H, Kobayashi R, Soejima Y. Clinical characteristics and management of acute cholecystitis after cardiovascular surgery. Journal of Hepato-Biliary-Pancreatic Sciences. 2021 Feb;28(2):211-20.
12- Zare M, Kargar S, Akhondi M, Mirshamsi MH. Role of Liver Function Enzymes in Diagnosis of Choledocholithiasis in Biliary Colic Patients. Acta Medica Iranica. 2011;49(10):663-6.
13- Zhang HC, Wang LS, Miller E. Hepatobiliary and Pancreatic Adverse Events. InImmunotherapy 2021 (pp. 339-355). Springer, Cham.
14- Zgheib H, Wakil C, Shayya S, Mailhac A, Al-Taki M, El Sayed M, Tamim H. Utility of liver function tests in acute cholecystitis. Annals of hepato-biliary-pancreatic surgery. 2019 Aug;23(3):219.
15- Ahn KS, Yoon YS, Han HS, Cho JY. Use of liver function tests as first-line diagnostic tools for predicting common bile duct stones in acute cholecystitis patients. World journal of surgery. 2016 Aug;40(8):1925-31.
16- Adachi T, Eguchi S, Muto Y. Pathophysiology and pathology of acute cholecystitis: A secondary publication of the Japanese version from 1992. Journal of Hepato-Biliary-Pancreatic Sciences. 2022 Feb;29(2):212-6.
17- Ahmed M. Acute cholangitis-an update. World journal of gastrointestinal pathophysiology. 2018 Feb 15;9(1):1.
18- Haas I, Lahat E, Griton Y, Shmulevsky P, Shichman S, Elad G, Kammar C, Yaslovich O, Kendror S, Ben-Ari A, Paran H. Percutaneous aspiration of the gall bladder for the treatment of acute cholecystitis: a prospective study. Surgical Endoscopy. 2016 May;30(5):1948-51.
19- Kassem AA, Fikry A, Shahin D, Salah HA. Elevated liver enzymes in patients with cholecystitis. AAMJ. 2011 Sep;9(3):2.
20- Song SH, Kwon CI, Jin SM, Park HJ, Chung CW, Kwon SW, Ko KH, Hong SP. Clinical characteristics of acute cholecystitis with elevated liver enzymes not associated with choledocholithiasis. European journal of gastroenterology & hepatology. 2014 Apr 1;26(4):452-7.
21- Kohli VK, Kohli C, Singh A. Liver and Biliary Tract. InComprehensive Multiple-Choice Questions in Pathology 2022 (pp. 93-104). Springer, Cham.
22- Jung SY, Yun HH, Lim JH, Lee DH, Seo SB, Baek JY, Lee J, Yoo K, Kim H, Kim HL, Lee JH. Hepatocyte-specific deletion of Bis causes senescence in the liver without deteriorating hepatic function. Biochemical and Biophysical Research Communications. 2022 Sep 3;619:42-8.
23- Ramadhan SA, Ghareeb OA. Efficiency of Cichorium Intybus in Reducing Hepatotoxicity Induced by Zinc Oxide Nanoparticles. Annals of Medical and Health Sciences Research. 2022 May;12(3):93-96 .
24- El Okle OS, Lebda MA, Tohamy HG. Thiamethoxam-induced biochemical, hormonal and histological alterations in

rats. Int J Toxicol Pharmacol Res. 2016;8:320-5.
25- Ando Y, Ahn J. Approach to the patient with abnormal liver chemistries or jaundice. Yamada's Textbook of Gastroenterology. 2022 Apr 15:720-32.
26- Taher GN , Ghareeb OA . Adverse effects of iron oxide nanoparticles on some biochemical markers and ameliorative effect of Silymarin. *Biochemical and Cellular Archives*. 2022; 22(1): 1829-1832.
27- Khanna R, Gautam V. Progressive Familial Intrahepatic Cholestasis. InGI Surgery Annual 2022 (pp. 95-126). Springer, Singapore.
28- Vagvala SH, O'Connor SD. Imaging of abnormal liver function tests. Clinical liver disease. 2018 May;11(5):128.
29- Amirthalingam V, Low JK, Woon W, Shelat V. Tokyo Guidelines 2013 may be too restrictive and patients with moderate and severe acute cholecystitis can be managed by early cholecystectomy too. Surgical endoscopy. 2017 Jul;31(7):2892-900.
30- Shyamkrishnan R, Saharia GK, Panda S, Mangaraj M. Evaluation of Homocysteine and Gamma-Glutamyl Transferase Concentrations As Markers of Chronic Kidney Disease: An Indian Perspective. Cureus. 2022 Mar 8;14(3).
31- Liao M, Qin W, Liao Y, Yao R, Yu J, Liao W. Prognostic value of gamma-glutamyl transpeptidase to lymphocyte count ratio in patients with single tumor size≤ 5 cm hepatocellular carcinoma after radical resection. Frontiers in Oncology. 2019 May 21;9:347.
32- Chen H, Jorissen R, Walcott J, Nikfarjam M. Incidence and predictors of common bile duct stones in patients with acute cholecystitis: a systematic literature review and meta-analysis. ANZ journal of surgery. 2020 Sep;90(9):1598-603.
33- Ngashangva L, Bachu V, Goswami P. Development of new methods for determination of bilirubin. Journal of pharmaceutical and biomedical analysis. 2019 Jan 5;162:272-85.
34- Rouma BS, Meier DE, Fitzgerald TN. Cholelithiasis (Gallstones). InPediatric Surgery 2020 (pp. 865-871). Springer, Cham.