Medica Hospitalia
Journal of Clinical Medicine
Med Hosp 2024; vol 11 (2) : 220–225

OPEN ACCESS

Case Report

A 25-year-old Woman with Cholecystolithiasis, Cholecystitis, Choledocholithiasis, and Acute Hepatitis

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p-ISSN: 2301-4369 e-ISSN: 2685-7898
https://doi.org/10.36408/mhjcm.v11i2.930

Accepted: March 19th, 2024
Approved: June 06th, 2024

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Abstract

Background : Gallstone disease stands as the foremost gastrointestinal issue leading to hospital admissions, while also emerging as a substantial global public health concern, impacting approximately one-fifth of the population.
Case Report : A 25-year-old woman was admitted with abdominal pain with a history of gallstones. She had risk factors such as obesity with a Body Mass Index (BMI) of 35.3 and dyslipidemia. Further examination showed that she had acute hepatitis and choledocholithiasis. The patient underwent Endoscopic Retrograde Cholangiopancreatography (ERCP) with balloon extraction. The patient recovered from her condition then scheduled for cholecystectomy.
Conclusion : This case showed a relatively young female with cholecystolithiasis, cholecystitis, choledocholithiasis, and acute hepatitis presenting with colicky pain. Comprehensive management of gallstone diseases is essential to avert additional complications and the possibility of relapse, especially considering the young age of the patient.

Keywords : Cholecystolithiasis, Cholecystitis, Choledocholithiasis, Fatty liver

INTRODUCTION

Gallstones and cholelithiasis are common gastrointestinal problems in Europe, the USA, and other developed countries.[1–3] Gallstone disease has strong links with metabolic disorders such as obesity, dyslipidaemia, and type 2 diabetes, which also has a high prevalence.[1–3] The majority of people who have gallstones remain asymptomatic.[1–3] But gallstones can obstruct the cystic duct thus making the gallbladder distended.[1–3] Prolonged obstruction results in inflammation and infection of the gallbladder or the cystic duct, and even ischemia.[1–4] Repeated inflammation can result in chronic cholecystitis.[3,4] In this case, showed a comprehensive management of gallstone disease that is needed to prevent further complication that could be done currently in hospital in Central Java, Indonesia.

CASE REPORT

A 25-year-old woman was admitted to Emergency Room at Kariadi General Hospital with abdominal pain as the chief complaint. She felt abdominal pain especially in the epigastric and upper right quadrant 2 days before going to the emergency room. She felt the pain like being stabbed with a needle. The pain was not radiated into the shoulder or jaw. She felt the pain was constant and not influenced by activity. The patient also felt the pain worsen 5 hours before admission to the emergency room. The patient consumed over-the-counter pain medicine s but the pain persisted even though she consumed multiple over-the-counter pain drugs. The patient is also nauseated, vomiting, and perspiring.

The patient had a history of gallstones one year ago, from an ultrasound examination. The patient underwent an abdominal ultrasound examination one year ago due to abdominal pain that was like the current pain but milder. However, the patient never felt the pain again until 2 days before going to the emergency room, so the patient never followed up nor took any medications for the gallstone. The patient had not checked her lipid profile or her blood glucose levels. She worked as a cashier in Semarang City. She had no history of consuming alcohol.

In the emergency room, the patient's blood pressure was 120/80, the pulse rate was 96, the respiratory rate was 20, the temperature was 36.2°C, and the oxygen saturation was 99% room air. The visual

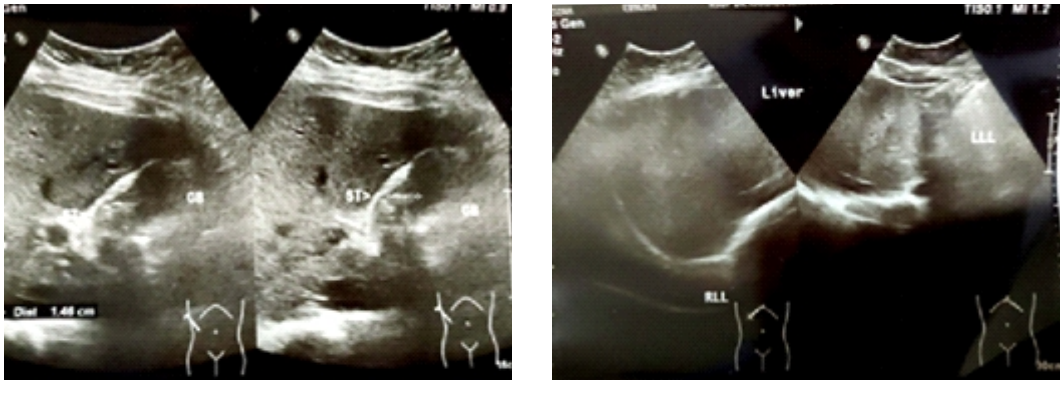

Figure 1. An abdominal ultrasound examination showed a grade II fatty liver and multiple cholecystolithiasis.

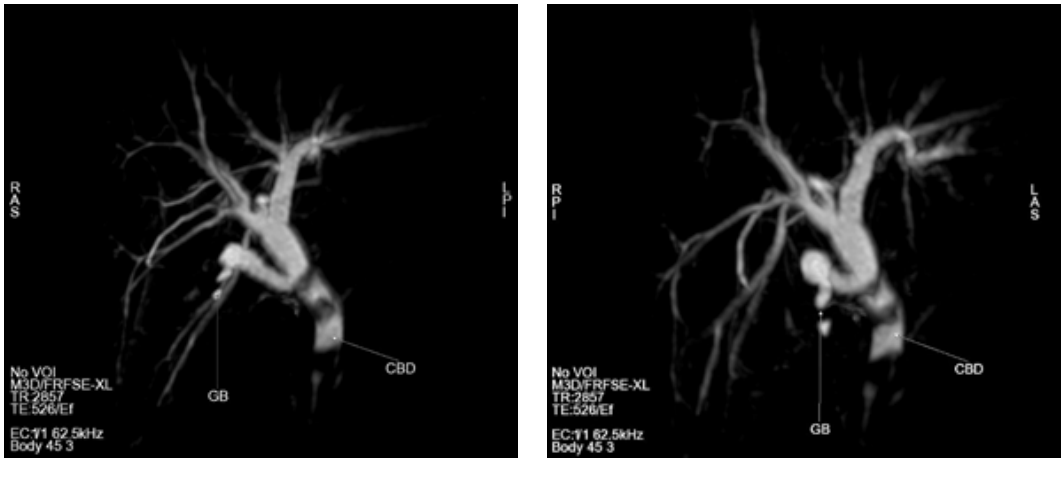

Figure 2. MRCP showed a widening of the intrahepatic and extrahepatic bile ducts.

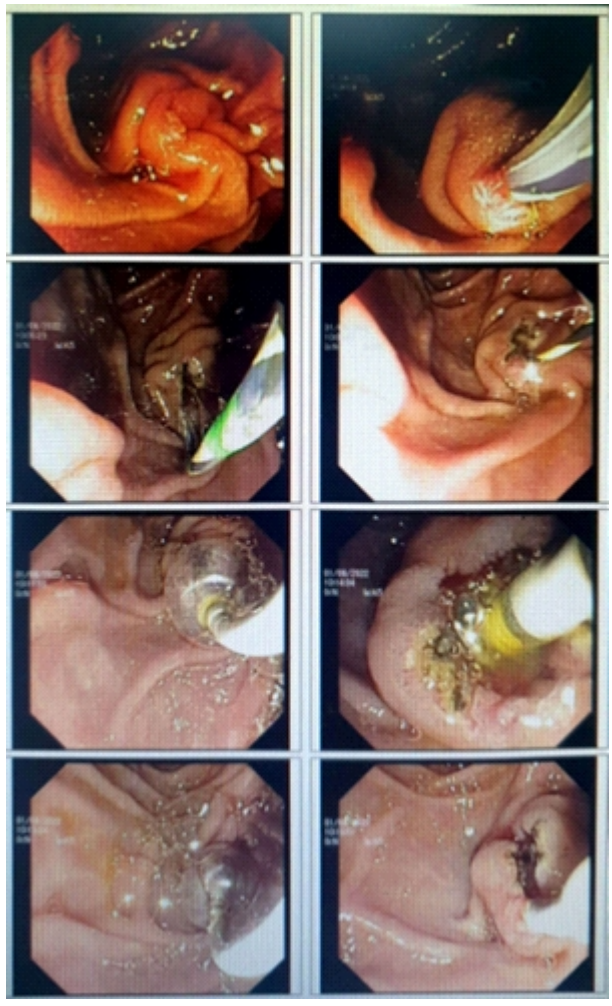

Figure 3. ERCP showed sludge in the common bile duct. Balloon extraction was performed.

analogue scale for abdominal pain is 6–7. The physical examination showed abdominal tenderness in the epigastric and upper right quadrant with positive Murphy's sign. The liver and spleen were not palpable. The patient was obese with a 95kg weight, 164cm height, and Body Mass Index (BMI) of 35.3. Then the patient was admitted to inpatient care and given ketorolac, metoclopramide, and hyoscine intravenously.

The patient undertook a laboratory examination. The patient had leucocytosis with leukocytes 14.700. The patient also had elevated liver function test parameters. The Aspartate Aminotransferase (AST) was 748 U/L, the Alanine Aminotransferase (ALT) was 545 U/L, the Alkaline Phosphatase was 151 U/L, and the Gamma GT was 488 U/L. We calculated the r-factor to differentiate between cholestatic and hepatocellular injury, and it was 8.2, which is consistent with a hepatocellular injury pattern. The total bilirubin was 2.92 mg/dL with direct bilirubin 1.95 mg/dL and indirect bilirubin 0.97 mg/dL. The albumin and globulin were normal.

Because the laboratory showed hepatocellular injury, the patient was tested with immunoserology tests, and the HBsAg, anti-HCV, and IgM anti-HAV were all negative. The patient was also scheduled for an abdominal ultrasound examination.

On the second day of inpatient care, the pain persisted. The patient was given ampicillin-sulbactam 1.5 grams three times intravenously and ursodeoxycholic acid twice daily.

From the ultrasound examination, there was a grade II fatty liver without widening of the portal vein. The intrahepatic and extrahepatic bile ducts were normal. There was also multiple cholecystolithiasis (maximum size was 1.46cm). The spleen size was normal, and the splenic vein was not widened.

The patient was also tested for a urinalysis and lipid profile. The urinalysis findings were normal. The total cholesterol was 174, triglyceride was 200, HDL cholesterol was 22, and direct LDL was 79.

On the fourth day of inpatient care, the third day of

antibiotics given, the symptoms decreased significantly. The patient was not vomiting, and the pain was reduced significantly. Then, the patient was programmed for Magnetic Resonance Cholangiopancreatography (MRCP) to find any stone in the bile duct.

From the MRCP, there were multiple filling defects on the distal common bile duct (maximum size was 1.4x1.1cm), and multiple filling defects in the vesica velea (maximum size was 1.1x1.0cm). There was also a widening of the right hepatic duct (0.8cm diameter), left hepatic duct (0.7cm diameter), common hepatic duct (1.4cm diameter), and common bile duct (1.2cm diameter). There was no widening of the pancreatic duct. It also showed the gallbladder was in normal size with thickening of its wall.

The liver function test was evaluated on the fifth day of inpatient care. The AST was 38 U/L, the ALT was 184, the ALP was 126, and the GGT was 55. The total bilirubin was 1.9 mg/dL with direct bilirubin at 1.3 mg/dL and indirect bilirubin at 0.6.

On the eighth day of inpatient care, the patient underwent *Endoscopic Retrograde Cholangiopancreatography* (ERCP). The mucosa of the ampulla was not oedematous and hyperaemic. There was no tumour or mass. There was bile surrounding the mucosa. Cannulation was performed, and a guide wire was entered. When the contrast entered, the common bile duct was widened, and a filling defect on the distal common bile duct. Sphincterotomy was performed, followed by sweeping with a balloon extractor multiple times, and the sludge came out without stone.

On the ninth day of inpatient care, one day after ERCP, the pain was gone, and the patient was not vomiting. The patient was discharged.

Ten days after discharge, the patient went to the outpatient clinic and was tested with a liver function test. The test came out normal. The AST was 11 U/L, the ALT was 16 U/L, the Alkaline Phosphatase (ALP) was 77 U/L, the Gamma-GT (GGT) was 60 U/L, and the total bilirubin was 0.9. The resulting culture from bile acid was Proteus vulgaris, sensitive to ampicillin-sulbactam which was given intravenously during the outpatient stay. She did not feel any abdominal pain or vomiting. The patient was given ursodeoxycholic acid twice daily and was educated to lose weight and avoid food with high cholesterol and saturated fats. To prevent further complications, the patient was then scheduled for cholecystectomy.

DISCUSSION

Advanced age, female sex, a diet high in carbohydrates and low in fiber, obesity, and genetic factors are all risk factors for gallstone disease. This patient, although relatively young age, is obese with a BMI of 35. Obesity will activate the pathogenic pathways that lead to gallstone formation, including abnormal gallbladder emptying, increased cholesterol crystallization tendency, stone aggregation, and supersaturation of bile with cholesterol. Gallstones that include pigment reveal problems with bilirubin metabolism.[1–3]

Gallstone prevention includes frequent, healthful activity, a nutritious diet, and maintaining a normal body weight. Additionally, ursodeoxycholic acid aids in preventing the growth of cholesterol crystals in bile. A diet high in vitamin C or regular vitamin C supplementation (500 mg 4 times per day) may prevent gallstone development.[1–3]

Gallstones may go undiscovered or discovered accidentally in asymptomatic patients or produce colicky pain as complications emerge. The characteristic of colicky pain is episodic attacks of severe pain in the right upper abdominal quadrant of the epigastrium for at least 15–30 minutes with radiation to the right back or shoulder and a positive reaction to analgesics. Laboratory tests from uncomplicated symptomatic gallbladder stones are within normal values in most patients. Diagnosis can be achieved from abdominal ultrasonography to *computed tomography* (CT), *magnetic resonance cholangiopancreatography* (MRCP), and cholecystography.[1–3]

Acute cholecystitis is the most common complication of gallstones, occurring in about 10% of the patients with symptomatic gallstones, and represents one-third of all surgical emergency hospital admissions. The stones obstruct the cystic duct thus causing inflammation.[1,2]

Acute cholecystitis symptoms include strong pain that gets worse with time and radiates to the right shoulder or interscapular region. These symptoms are frequently accompanied by fever, nausea, and vomiting. Murphy's sign, which manifests as pain in the right upper abdominal quadrant and tenderness on palpation (but not the left), is a highly sensitive and specific diagnostic indicator. White blood cell counts and C-reactive protein levels are frequently elevated. Gallstones, a swollen gallbladder, a thicker (>4mm) gallbladder wall, and pericholecystic fluid can all be found with abdominal ultrasound, and sonographic Murphy's sign (intensified pain upon probe pressure directly over the gallbladder) may be present.[1,4,5]

Ursodeoxycholic acid should only be used to treat symptomatic patients who have tiny stones that are known to have originated from gallbladder sludge or cholesterol. Every time, the patient should be made aware of the possibility of a curative cholecystectomy in advance. Nonsteroidal anti-inflammatory drugs are the best therapy option for biliary colic. In addition to adding spasmolytics (e.g. butyl scopolamine), opioids such as buprenorphine may be utilized if the pain is exceptionally bad. Buprenorphine is best suited because it appears to contract the sphincter Oddi less than morphine. Empirical antibiotics must be given right away

in cases of acute cholecystitis with symptoms of sepsis, cholangitis, abscess, or perforation.[1,3]

Given that almost half of patients with symptomatic cholecystolithiasis experience recurrent colic, cholecystectomy may be necessary depending on the frequency and severity of symptomatic episodes. Bile acid dissolution therapy with *Ursodeoxycholic Acid* (UDCA) and *Extracorporeal Shock Wave Lithotripsy* (ESWL) is one of the alternatives to surgery, although these treatments have a poor rate of cure, high risk of gallstone recurrence, and ineffectiveness in reducing symptoms and consequences following medical treatment. In carefully chosen individuals, the cure rate for gallstones is only 27% after UDCA and only 55% after ESWL, and the recurrence rate was >40% following complete stone disintegration or ESWL for 4 years.[1,4,5]

Although cholecystectomy is the preferred course of treatment, the advantages of surgery for acute calculous cholecystitis have never been well investigated. While doing a cholecystectomy in the event of acute cholecystitis reduces further bouts of gallstone-related disease, it is important to be aware of the relatively high complication rate, especially in high-risk individuals. Therefore, it is important to carefully explore your options before having surgery. However, leaving the gallbladder in place runs the risk of causing recurring gallstone-related illness.[6]

Loozen *et al* (2016) said, in their research from 1841 patients in randomized controlled trials and 14 non-randomized studies, that conservative treatment of acute cholecystitis seems feasible and safe, especially in patients with mild disease. And less than 25% of the patients appear to experience recurrent gallstone-related illness during long-term follow-up without surgery.[6]

In this case, the patient came with severe abdominal pain that persisted after the administration of nonsteroidal anti-inflammatory drugs and spasmolytics. Positive Murphy's sign and elevated white blood cell count were present. MRCP also showed a thickening of the gallbladder wall. So, the patient has acute cholecystitis due to cholecystolithiasis. After several days of antibiotics and symptomatic treatments, the symptoms were reduced significantly.[1,7,8]

As many as 3–16% of patients with gallbladder stones also have *Common Bile Duct* (CBD) stones, depending on their age. They either migrate from the gallbladder (secondary stones) or less frequently grow from scratch in the bile duct, as in the case of CBD dilatation with stasis (primary stones). Acute biliary discomfort, induced by CBD distention following partial or total obstruction, is a common sign of CBD stones. It might be difficult to distinguish the pain from the pain caused by gallbladder stones.[1,7,8]

Patients with symptomatic CBD stones may have altered liver biochemical tests, such as elevated serum bilirubin concentrations, as well as ALT, AST, gamma-GT, and ALP.[1,7]

Abdominal ultrasound has a high sensitivity for detecting CBD dilatation, which is an indirect indicator of CBD stones. Even in dilated CBD, stones may be seen clearly in ultrasound examination. CBD stones larger than 5 mm can be found with EUS and MRCP in patients who may have CBD stones but with an inconclusive abdominal ultrasound. For detecting CBD dilation, CT imaging is also highly sensitive. It also evaluates other possible causes of upper abdominal pain and gallstone complications. And lastly, ERCP has a very high sensitivity for detecting CBD stones.[1,7–9]

Although there may be a spontaneous passage to the small bowel in many cases, there is a high chance of biliary discomfort and related issues such as pancreatitis, cholangitis, and jaundice. Therefore, it is generally agreed that symptomatic choledocholithiasis should be treated. Endoscopic sphincterotomy and stone removal are currently the preferred approaches in most countries.[1,7–9]

In a condition where gallbladder stones and bile duct stones occur simultaneously, current studies show that laparoscopic cholecystectomy is recommended within 72 hours after ERCP and leads to significantly fewer recurrent biliary events as compared to delayed laparoscopic cholecystectomy (after 6–8 weeks). Cholecystectomy and ERCP are not recommended to be performed on the same day.[1]

This patient also had acute hepatitis with a marked increase in transaminase levels. The AST was 748 U/L, the ALT was 545 U/L, the Alkaline Phosphatase was 151 U/L, and the Gamma GT was 488 U/L. Examination of hepatitis A, hepatitis B, and hepatitis C were all negative. The patient had a history of taking over-the-counter pain medication due to abdominal pain, and the transaminase levels came back to normal after cessation of the drug, which may indicate drug-induced liver injury. The patient also had a fatty liver in the abdominal ultrasound, which may cause elevated transaminase levels. The patient is also obese, which is also a risk factor for developing inflammation easier than non-obese patients, due to the build-up of pro-inflammatory cytokines, such as TNF-α.

There are two types of drug-induced liver injury (DILI). Intrinsic DILI is typically dose-related and occurs in a large proportion of individuals exposed to the drug (predictable) and onset is within a short period (hours to days). Idiosyncratic DILI is usually not dose-related, occurs in only a small proportion of exposed individuals (unpredictable), and exhibits a variable latency to onset of days to weeks. DILI is diagnosed by one of the following thresholds: i) ≥ 5x Upper Limit Normal (ULN) elevation in ALT, ii) ≥ 2 x ULN elevation in ALP (particularly with accompanying elevations in concentrations of gamma-glutamyl transferase (GGT) in the absence of known bone pathology driving the rise in ALP level), or iii) ≥ 3 x ULN elevation in ALT and simultaneous elevation of bilirubin

concentration exceeding 2 x ULN. However, diagnosis of DILI has to be done after excluding other causes of liver injury, such as autoimmune hepatitis.[10,11]

A recent systematic review and meta-analysis of the prevalence of metabolic-associated fatty liver disease in the Asia-Pacific region is 29.62%. Obesity is the most common risk factor for fatty liver. Type 2 diabetes mellitus, high serum triglycerides, and low serum high-density lipoprotein (HDL) levels are also common in patients with fatty liver.[12,13]

This patient had hepatic steatosis detected by abdominal ultrasound, obesity (BMI of 35.3), high triglycerides (200), and low LDL (22). Therefore, the patients need further examination for advanced fibrosis risk assessment. Using transaminase levels in inpatient care, the patient's FIB-4 score was normal, therefore it is best to repeat non-invasive tests at an interval of 2–3 years. If there is an intermediate or high risk, liver biopsy or imaging may be done to assess the fibrosis stage or disease activity. Therapeutic options for fatty liver include lifestyle modification and exercise, metabolic risk management (e.g. dyslipidaemia, hypertension), and drugs such as pioglitazone or vitamin E. If the patient develops cirrhosis, management of cirrhosis must be done, including varices screening and treatment, HCC surveillance, or liver transplantation if indicated and feasible.[12,13]

CONCLUSION

Gallstones are common gastrointestinal problems and have strong links with metabolic disorders such as obesity and dyslipidaemia. This case showed a relatively young female with symptomatic cholelithiasis and choledocholithiasis with colicky pain. Gallstones may lead to cholecystitis, cholangitis, or even pancreatitis. Metabolic disorders also link with the fatty liver which may later cause liver fibrosis and liver failure. This patient's biggest risk factor is obesity with metabolic syndrome. Elaborate management of metabolic syndrome since adolescence is needed to prevent many diseases, like gallstones and their complications.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest. Informed Consent was acquired from the patient.

REFERENCES

1. EASL Clinical Practice Guidelines on the prevention, diagnosis and treatment of gallstones. 2016.
2. Portincasa P, Di Ciaula A, De Bari O, Garruti G, Palmieri VO, Wang DQH. Management of gallstones and its related complications. Vol. 10, Expert Review of Gastroenterology and Hepatology. Taylor and Francis Ltd; 2016. p. 93–112.
3. Gutt C, Schläfer S, Lammert F. The treatment of gallstone disease. Dtsch Arztebl Int. 2020 Feb 28;117(9):148–58.
4. Mou D, Tesfasilassie T, Hirji S, Ashley SW. Advances in the management of acute cholecystitis. Vol. 3, Annals of Gastroenterological Surgery. Wiley-Blackwell Publishing Ltd; 2019. p. 247–53.
5. Gomes CA, Junior CS, di Saveiro S, Sartelli M, Kelly MD, Gomes CC, *et al*. Acute calculous cholecystitis: Review of current best practices. World J Gastrointest Surg. 2017;9(5):118.
6. Loozen CS, Oor JE, van Ramshorst B, van Santvoort HC, Boerma D. Conservative treatment of acute cholecystitis: a systematic review and pooled analysis. Surg Endosc. 2017 Feb 1;31(2):504–15.
7. Molvar C, Glaenzer B. Choledocholithiasis: Evaluation, treatment, and outcomes. Semin Intervent Radiol. 2016 Dec 1;33(4):268–76.
8. Cai JS, Qiang S, Bao-Bing Y. Advances of recurrent risk factors and management of choledocholithiasis. Vol. 52, Scandinavian Journal of Gastroenterology. Taylor and Francis Ltd; 2017. p. 34–43.
9. Buxbaum JL, Abbas Fehmi SM, Sultan S, Fishman DS, Qumseya BJ, Cortessis VK, *et al*. ASGE guideline on the role of endoscopy in the evaluation and management of choledocholithiasis. Gastrointest Endosc. 2019 Jun 1;89(6):1075–1105.e15.
10. Andrade RJ, Aithal GP, Björnsson ES, Kaplowitz N, Kullak-Ublick GA, Larrey D, *et al*. EASL Clinical Practice Guidelines: Drug-induced liver injury. J Hepatol. 2019 Jun 1;70(6):1222–61.
11. Devarbhavi H, Aithal G, Treeprasertsuk S, Takikawa H, Mao Y, Shasthry SM, *et al*. Drug-induced liver injury: Asia Pacific Association of Study of Liver consensus guidelines. Hepatol Int. 2021 Apr 1;15(2):258–82.
12. Chalasani N, Younossi Z, Lavine JE, Charlton M, Cusi K, Rinella M, *et al*. The Diagnosis and Management of Nonalcoholic Fatty Liver Disease: Practice Guidance From the American Association for the Study of Liver Diseases. Hepatology. 2018;67(1):328–57.
13. Eslam M, Sarin SK, Wong VWS, Fan JG, Kawaguchi T, Ahn SH, *et al*. The Asian Pacific Association for the Study of the Liver clinical practice guidelines for the diagnosis and management of metabolic associated fatty liver disease. Vol. 14, Hepatology International. Springer; 2020. p. 889–919.