



## 19 Years Old Male Patient with Cholelithiasis: A Case Report

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### ABSTRACT

Cholelithiasis refers to the formation of hardened deposits of digestive fluid, known as gallstones, which can develop in the gallbladder, bile duct, or both. This study aims to analyze the factors contributing to the occurrence of cholelithiasis in young patients, specifically 19-year-old males, and identify the clinical symptoms and associated examination results. A 19-year-old male patient visited the Internal Medicine Polyclinic with the main complaint of right upper abdominal pain radiating to the back. He also experienced nausea and vomiting. The patient frequently consumed high-fat foods. On physical examination, the patient's height was 171 cm, weight 74 kg, and BMI 25.34 kg/m<sup>2</sup> (overweight). Abdominal examination revealed a positive Murphy's sign. Laboratory tests showed total cholesterol of 216 mg/dl, LDL 158 mg/dl, HDL 38 mg/dl, and triglycerides 86 mg/dl. An abdominal ultrasound indicated thickened gallbladder walls, a single stone measuring approximately 0.82 cm by 1.17 cm, accompanied by sludge, and calcification in the right lobe of the liver. The patient was treated with Ursodeoxycholic Acid (UDCA) 250 mg twice daily and Atorvastatin 10 mg once daily. Cholelithiasis is a multifactorial condition, influenced by several factors, commonly referred to as the "4F" factors: female gender, age over 40, fertility (being in the fertile period), and fat (obesity). Other contributing factors include age, genetics, and race. Children and adolescents may develop gallstones due to increased consumption of fat, refined carbohydrates, and low fiber intake. Overweight and obesity are significant risk factors because they increase the secretion of intrahepatic cholesterol, which promotes gallstone formation. The treatment of cholelithiasis can be classified into non-surgical and surgical approaches.

**Keywords:** cholelithiasis, risk factors, obesity

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### INTRODUCTION

Cholelithiasis, commonly known as gallstones, refers to the formation of stones composed of cholesterol, bilirubin, or bile (Kumar, 2016; Lammert et al., 2016; Littlefield & Lenahan, 2019; Swarne et al., 2021; Zeng et al., 2021). These stones harden and develop within the gallbladder, an organ responsible for storing bile that is released under specific conditions. Cholelithiasis is a common disease in the population with a prevalence of 5%-22%, especially in the middle-aged female population. The prevalence varies between populations, the prevalence of cholelithiasis is around 10% in the adult population in the United States, and around 6%-22% in the Western European population, while the prevalence of cholelithiasis in the Asian population ranges from 3%-16%.

In developing countries like Indonesia, it is estimated that 10–15% of the adult population is affected by gallstones. A study by researchers involving 192 patients diagnosed with cholelithiasis revealed that the majority were women (67.71%), while men accounted for 32.29%. The highest prevalence was observed among individuals aged 40 years (80.46%). Additionally, there has been a noticeable shift in gallbladder disease occurrences among Millennials (aged 25–32 years) and Generation Z (aged 10–25 years), potentially influenced by changes in lifestyle and genetic factors. This case report discusses a 19-year-old male patient diagnosed with cholelithiasis.

This study aims to analyze the factors that contribute to the occurrence of cholelithiasis in young patients, specifically 19-year-old males. In addition, this study also aims to identify clinical symptoms and examination results associated with cholelithiasis in the context of demographics and

lifestyle. It is hoped that the results will provide a better understanding of cholelithiasis in young populations and aid in the development of more effective prevention strategies.

## CASE REPORT

A 19-year-old male patient came to the Internal Medicine Polyclinic of Wangaya Regional Hospital on July 15th, 2024 with a main complaint of right upper abdominal pain since 1 week before going to the hospital. The pain was felt penetrating to the back. The abdominal pain was felt especially when consuming oily foods and high fat content foods. The patient often felt nauseous and vomited about 1-2 times a day. Before the right upper abdominal pain, the patient felt epigastrium pain 1 day earlier. The patient's stomach was not enlarged. The patient also said he had fever that started in the beginning of the right upper abdominal pain. The fever had been felt for 4 days. When the patient came to the hospital, the patient no longer had a fever but the abdominal pain was still felt intermittently. When he had a fever, the patient said there were no nosebleeds, bleeding gums, blackish stools, and red spots on the skin. The patient's stool was not pale in color, there was no diarrhea and the patient's urine were not dark colored like tea. The patient's eyes were not yellow. The patient did not experience any weight loss. The patient often consumed high-fat foods such as goat meat, offal, and fried foods. There was no history of hypertension and diabetes. None of his family members had similar complaints. The patient only consumed Paracetamol 3x500 mg and Antacid 3xC1 to relieve his fever and stomachache.

During the physical examination, the patient was awake and aware, with a Glasgow Coma Scale (GCS) score of E4V5M6. Vital signs included a blood pressure of 123/85 mmHg, a heart rate of 85 beats per minute, a respiratory rate of 20 breaths per minute, a body temperature of 36°C, and an SpO<sub>2</sub> of 98% on room air. The patient's height was 171 cm, weight was 74 kg, and their Body Mass Index (BMI) was 25.34, which falls within the overweight category. On general status examination the patient's pupils were isocor, there were no icteric sclera, anemic conjunctiva, exophthalmos eyes, nostrils breathing, and cyanosis on the lips. Thorax examination included heart and lung examination within normal limits. During the abdominal examination, the patient displayed tenderness in the epigastric region and right upper quadrant, along with a positive Murphy's sign. Bowel sounds were normal, and there were no indications of hepatomegaly or splenomegaly. Examination of the extremities found both acral warm, no edema and Capillary Refill Time (CRT) <2 seconds.

Additional examinations were performed on the patient which includes bilirubin profile, lipid and uric acid profile, liver function test, and abdominal Ultrasonography (USG). The bilirubin profile examination showed total bilirubin of 0.55 mg/dl, direct bilirubin of 0.2 mg/dl, indirect bilirubin of 0.35 mg/dl. The lipid profile examination showed increased total cholesterol of 216 mg/dl, increased direct LDL of 158 mg/dl, decreased direct HDL of 38 mg/dl, and triglycerides of 86 mg/dl. The patient's uric acid examination showed 6.2 mg/dl. The patient's liver function examination showed SGPT of 16 and SGOT of 13. The patient's abdominal Ultrasonography (USG) examination showed the patient's gallbladder within normal size, thickened walls, there was single stone in the gallbladder measuring about 0.82 cm and 1.17 cm, accompanied by sludge, and there was calcification in the right lobe of the liver. The internist gave the patient Ursodeoxycholic Acid (UDCA) 2x250 mg PO and Atorvastatin 1x10 mg PO for 30 days. The patient was scheduled for a clinical evaluation 1 month later and abdominal ultrasound evaluation 2 months later.

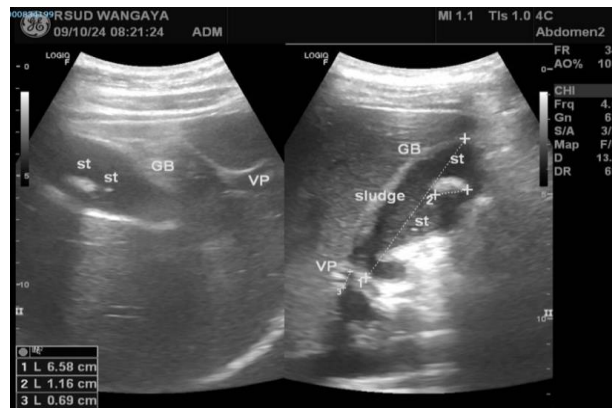


Figure 1. Ultrasonography of the patient's gallbladder.

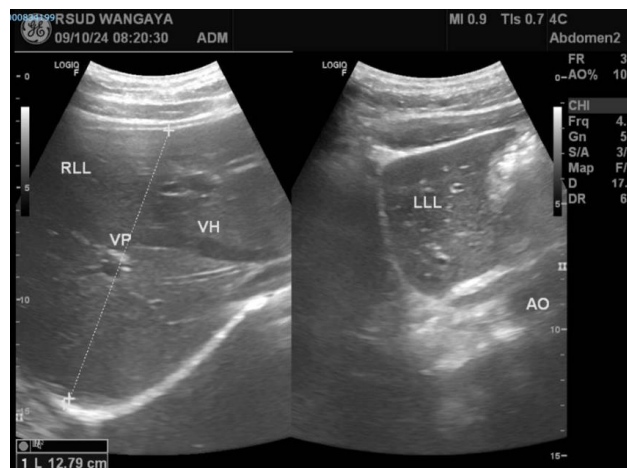


Figure 2. Ultrasonography of the patient's liver

## RESULTS AND DISCUSSION

Cholelithiasis refers to the formation of hardened deposits of digestive fluid, known as gallstones, which can develop in the gallbladder, bile duct, or both. It is a common condition and is classified into three types: cholesterol stones (containing over 70% cholesterol), pigment stones (containing less than 30% cholesterol), and mixed stones. Cholesterol stones are the most common type which are generally oval, multifocal or mulberry in shape and contain more than 70% cholesterol. Pigment stones consist of brown pigment and black pigment. Calcium bilirubin pigment stones (brown pigment) are generally brown or dark brown, soft, easily crushed and contain calcium bilirubinate as the main component, brown pigment stones are formed due to stasis factors and bile duct infections. Black pigment stones are usually found in patients with chronic haemolysis or liver cirrhosis and consist of polymerized bilirubin derivatives. Mixed stones are a mixture of cholesterol containing calcium (Adhata et al., 2022).

Approximately 10%-15% of cholelithiasis are asymptomatic, 10%-20% of them develop symptoms within 5-20 years. Biliary colic typically presents as pain in the upper right quadrant of the abdomen, persisting for over 30 minutes. This pain frequently radiates to the back and is typically accompanied by nausea and vomiting (Kristianus et al., 2022). Symptoms usually arise after consuming fatty or spicy foods, as fatty foods can trigger gallbladder contractions. About an hour after eating such foods, individuals may experience intense, dull pain that can last between 1 to 5 hours (Lysandra et al., 2022). Cholelithiasis can show atypical symptoms such as dyspepsia accompanying biliary colic complaints or even being the main complaint. These atypical symptoms can make it difficult for clinicians to distinguish symptomatic cholelithiasis from functional dyspepsia (Kristianus et al., 2022). Diagnosing cholelithiasis can be challenging due to the significant variation in symptoms between patients under and over 30 years old. In younger patients, the diagnosis is further complicated by increased pain radiation. Additionally, symptoms such as intolerance to fatty

foods, dyspepsia, belching, and flatulence, along with related conditions, are less common in this age group (Kazi et al., 2022). Our patient had a main complaint of right upper abdominal pain which was felt penetrating to the back. The abdominal pain was felt especially when consuming oily foods and high fat content foods. The patient often felt nauseous and vomited about 1-2 times a day. Our patient symptoms are typical for cholelithiasis even though he is 19 years old which usually had atypical symptoms.

Cholelithiasis is a multifaceted condition influenced by various factors. Its occurrence is commonly linked to four key risk factors, often summarized as the "4F": being female, aged over 40 (forty), within the fertile period (fertile), and obesity (fat) (Lysandra et al., 2022). Among the general population, gender appears to be the major risk factor, with women being more susceptible to gallstones than men (Dewi & Yusmaidi, 2024). Additionally, factors such as obesity, rapid weight loss, glucose intolerance, insulin resistance, high sugar intake, alcohol consumption, diabetes mellitus, hypertriglyceridemia, certain medications, and pregnancy also contribute to the development of cholelithiasis. The formation of gallstones is influenced by four primary contributing factors (Dewi & Yusmaidi, 2024):

- a. Supersaturation of cholesterol in bile
- b. Contribution to the precipitation of cholesterol and the formation of crystallization nuclei.
- c. Impairment of basic gallbladder function (contraction, absorption, secretion, etc.)
- d. Impaired enterohepatic circulation of bile acids.

The common risk factors for cholelithiasis include pregnancy (where progesterone reduces gallbladder motility, leading to stasis), obesity, genetic predisposition, the use of certain medications (such as estrogens, fibrates, and somatostatin analogs), gallbladder stasis, metabolic syndrome, rapid weight loss, prolonged fasting, surgeries involving the biliary system, Crohn's disease, and bowel resections (Lysandra et al., 2022). Our patient is a 19 years old male which is not related to the major risk of cholelithiasis such as "female" and "forty", but still on the risk of "fertile" and "fat".

Other contributing factors include age, genetic predisposition, and race. The detection rate of gallstones increases with age, with higher rates observed in each decade after age 20 (Dewi & Yusmaidi, 2024). While gallstone disease is common in young adults between the ages of 20 and 40, symptoms usually do not appear until later in life. Western studies indicate that 4-20% of cholecystectomy procedures are conducted on individuals under 30 years old (Kazi et al., 2022). People aged >40 years are more likely to develop cholelithiasis than those of younger ages due to increased cholesterol secretion into the bile with increasing age (Adhata et al., 2022). It is believed that the cholesterol content in bile increases with age, as dyslipoproteinemia leads to higher cholesterol excretion into the bile, while the synthesis of bile acids decreases due to reduced activity of the enzyme cholesterol 7 $\alpha$ -hydroxylase (CYP7A1) (Dewi & Yusmaidi, 2024). As people age, several physiological changes occur, such as atherosclerosis, reduced testosterone levels in men, and a decline in estrogen levels in women. These changes imply that lower testosterone levels in men may be connected to the formation of gallstones (Shabanzadeh et al., 2017).

Cholelithiasis is uncommon in children, but when it does occur, it is often linked to factors such as haemolytic disease, a history of Total Parenteral Nutrition (TPN) therapy, Wilson's disease, cystic fibrosis, and the use of certain medications. In children aged 1-5 years, cholelithiasis is commonly associated with haemolytic disease, while in adolescents, it is more likely to be related to obesity, pregnancy, and medication use (Adhata et al., 2022).

Another factor that affects cholesterol supersaturation in bile is gender. Female gender is recognized as a significant risk group for cholelithiasis, with a risk 2-3 times higher in women of reproductive age compared to men. Pregnancy, especially in multiparous women, also contributes to the formation of gallstones due to hormonal changes (Dewi & Yusmaidi, 2024). Lack of physical activity increases the risk of cholelithiasis because the gallbladder contracts less (Adhata et al., 2022). Most pediatric studies also show a female predominance in cholelithiasis cases. The increased prevalence of gallstones in girls may be associated with puberty and hormonal changes, especially the rise in estrogen production. Estrogens bind to estrogen receptors (ERs) in the liver, leading to an increase in cholesterol secretion into the bile, which in turn promotes the formation of gallstones (Zdanowicz et al., 2022). In men, the likelihood of developing cholelithiasis may increase due to variations in body weight, independent of their Body Mass Index (BMI) (Dewi & Yusmaidi, 2024).

Cholelithiasis is believed to be greatly influenced by a diet rich in meat, animal fats, and fried foods. Saturated fat is found in fried foods and animal fats. Consuming foods heavy in refined sugar and saturated fat may raise the risk of developing a gallstone (Lysandra et al., 2022). Children and adolescents are more likely to develop gallstones due to their increased consumption of fat, highly refined carbohydrates, fructose, and poor fiber content. These dietary practices lead to increased biliary cholesterol levels and the production of gallbladder mucus induced by hypertriglyceridemia (Zdanowicz et al., 2022). Our patient often consumed high-fat foods such as goat meat, offal, and fried foods. On the laboratory examination showed increased total cholesterol of 216 mg/dl, increased direct LDL of 158 mg/dl, decreased direct HDL of 38 mg/dl which indicates the patient had dyslipidemia.

Overweight and obesity are major risk factors for cholelithiasis, with a BMI of 27.5 kg/m<sup>2</sup> serving as a key threshold. Obesity results in increased synthesis and secretion of cholesterol into the bile, with the amount of cholesterol produced directly correlating to excess body weight. The risk of cholelithiasis is further elevated by significant fluctuations in body weight and frequent cycles of weight gain and loss. The Adrenergic Receptor Beta-3 (ADRB3), which is expressed in adipose tissue, plays a role in regulating lipolysis. It is also present in gallbladder tissue, where it influences gallbladder contractions (Dewi & Yusmaidi, 2024). A diet high in fiber, vegetable proteins, nuts, calcium, and vitamin C, along with the consumption of coffee and alcohol, and regular physical activity, may help reduce the risk of gallstone formation (Bojazyah & Bohlala, 2024). Our patient BMI is 25,34 kg/m<sup>2</sup> which indicates him that he is in the overweight category, but usually BMI >27,5 kg/m<sup>2</sup> has bigger risk of developing cholelithiasis. Our patient said that he rarely eats vegetables and no past history of alcohol consumption to reduce the risk of developing cholelithiasis.

Obesity is associated with increased cholesterol secretion in the liver, contributing to gallstone formation. Furthermore, the distribution of fat in the body, especially visceral fat, has been linked to gallstone development. Visceral fat releases vasoactive substances into the portal venous system, which activate macrophages and trigger the release of inflammatory cytokines such as TNF- $\alpha$  and IL-6. These cytokines reduce the levels of adiponectin, a hormone produced by fat cells that enhances insulin sensitivity and promotes fatty acid oxidation, offering protective benefits against diabetes and atherosclerosis (Hendarto et al., 2023).

Children who are obese, with an average BMI of 21.5, are at a significantly higher risk of developing choledocholithiasis compared to those with a normal BMI. Furthermore, children with symptomatic cholecystitis and a BMI of 23 or higher are at an even greater risk of choledocholithiasis, exhibiting symptoms at a much higher frequency than both the general and obese populations. A high-fat diet seems to trigger a series of events leading to the formation of gallstones and their movement into the biliary system. First, bile becomes supersaturated due to increased cholesterol absorption by the liver or elevated de novo cholesterol synthesis. Second, cholesterol directly affects the plasma membranes of smooth muscle cells in the gallbladder wall, leading to impaired contraction and dysmotility. Additionally, elevated levels of cholecystokinin in obese children play a significant role in stimulating postprandial gallbladder emptying (Frybova et al., 2018).

Cholesterol in the liver can move through the biliary tract to the small intestine, where it is partially reabsorbed and then enters the bloodstream through the lymphatic system, eventually returning to the liver. The body obtains cholesterol from two main sources: biosynthesis and absorption. Cholesterol biosynthesis primarily occurs in the liver, where acetyl-CoA is converted into cholesterol through enzymatic reactions. The key enzymes involved in this process include 3-Hydroxy-3-Methylglutaryl-CoA Reductase (HMGCR) and squalene monooxygenase. Some of the cholesterol produced in hepatocytes is converted into bile salts, while the remaining cholesterol is transported into the biliary tract by ABCG5/8 transporters. In the bile, phospholipids form microclumps that are secreted into the intestine. Both biosynthetic and dietary cholesterol are absorbed by the Niemann–Pick C1-Like Protein1 (NPC1L1) on intestinal epithelial membranes, esterified by ACAT (Acyl-Coenzyme-A: cholesterol acyltransferase), and then enter the bloodstream via the lymphatic system. Eventually, these cholesterol molecules are taken up by the liver as chylomicrons (Sun et al., 2022).

In pediatric patients with cholesterol and pigment gallstones, the RNA expression levels of ABCG5 and ABCG8 were observed to be elevated in those with cholelithiasis. Additionally, children with cholesterol stones exhibited lower levels of plant sterols (such as campesterol and sitosterol) and higher levels of cholesterol precursors compared to both healthy controls and those with pigment stones. These observations account for the increased cholesterol content in cholelithiasis (Zdanowicz et al., 2022). We still do not know what kind of stones does our patient have due to the patient did not undergo cholecystectomy.

Evidence suggests that adipokines and hepatokines play a role in the development of cholelithiasis in children. Increased levels of chemerin, retinol-binding protein 4 (RBP-4), and fibroblast growth factor 21 (FGF-21) have been found in children with cholelithiasis. In lean children, only chemerin showed a significant increase in those with cholelithiasis. Chemerin may act as both a pro-inflammatory and anti-inflammatory molecule. Additionally, elevated expression of several interleukins (IL-1, IL-4, IL-6, IL-7, IL-8, and IL-17A) has been observed in cases of calculous cholecystitis (Zdanowicz et al., 2022).

Moreover, abnormal drug concentrations in the biliary tract can play a role in the development of cholelithiasis. Ceftriaxone, a third-generation cephalosporin, is excreted into the biliary system, and its interaction with calcium may cause calcium-ceftriaxone complexes to precipitate, which could contribute to gallstone formation (Zdanowicz et al., 2022). Our patient did not had any history of consuming ceftriaxone or other cephalosporins.

Management of cholelithiasis is divided into 2, namely non-surgical and surgical management. Non-surgical management can be done with supportive management and diet, 80% of cholelithiasis patients recover with rest, IV fluids, nasogastric suction, analgesics and antibiotics. Oral dissolution therapy is the destruction of stones by administering oral medication, this medication can destroy stones in 60% of cholelithiasis patients, the criteria for media dissolution are stone diameter <20mm, number of stones <4 stones, good bladder function and patent cystic duct, but in children this therapy is not recommended except for children at high risk for surgery (Adhata et al., 2022). Ursodeoxycholic acid (UDCA) is an oral bile acid that decreases cholesterol secretion by reducing the cholesterol concentration in bile within the gallbladder. It is effective in dissolving gallstones and is approved for clinical use. However, due to the widespread use of laparoscopic cholecystectomy and limited awareness among clinicians regarding its benefits, the current role of UDCA in treating symptomatic gallstones remains unclear (Hall et al., 2023). UDCA therapy is recommended for asymptomatic patients. However, in pediatric practice, a significant number of patients with symptomatic cholelithiasis are treated with UDCA for litholysis (Diez et al., 2021). Contact dissolution is a way to destroy stones by inserting a solvent fluid into the gallbladder through a percutaneous catheter through the liver or nasobiliary catheter, the solution used is methyl-terbutyl-ether which is inserted into the gallbladder and is able to destroy gallstones within 24 hours. Extracorporeal Shock Wave Lithotripsy (ESWL) uses high amplitude sound waves to destroy stones, but this method is not recommended in children because of the high recurrence rate (Adhata et al., 2022). We gave our patient UDCA 2x250 mg due to no indication of cholecystectomy. Our patient gallstone size is less than 2.50 cm and it is not multiple stones. We also gave the patient Atorvastatin 2x10 mg to the cholesterol levels as it can prevent the stone to develop even bigger in size.

Complications arising from the enlargement of gallstones can include cholecystitis, cholangitis, choledocholithiasis, gallstone pancreatitis, and cholangiocarcinoma (Lysandra et al., 2022). In some severe cases may require cholecystectomy (Ali et al., 2021). Surgery is infrequently necessary for asymptomatic cholelithiasis. However, patients with large gallstones (larger than 2.50 cm), congenital hemolytic anemia, non-functioning gallbladders, or those undergoing bariatric surgery or colectomy may need to undergo a preventive cholecystectomy (Bojazyah & Bohlala, 2024). Cholecystectomy in patients under the age of 30 is generally associated with low morbidity and no reported mortality (Kazi et al., 2022). Surgical management is divided into open cholecystectomy and laparoscopic cholecystectomy. Open cholecystectomy is the gold standard for patients with symptomatic cholelithiasis, complications that can occur are bile duct injury and the most common indication is recurrent biliary colic followed by acute cholecystitis. Indications for laparoscopic cholecystectomy are patients with symptomatic cholelithiasis without acute cholecystitis.

Cholecystectomy is the gold standard for the management of symptomatic cholelithiasis (Adhata et al., 2022).

## CONCLUSION

This study showed that cholelithiasis can occur in young patients, including a 19-year-old male, although the condition is more common in older populations. Factors contributing to the development of cholelithiasis in this patient included a high-fat diet and obesity, which increased cholesterol levels in the bile. The patient's clinical symptoms, such as right upper abdominal pain and nausea, were consistent with those of cholelithiasis, although at a young age they are often less characteristic. The results of this study emphasize the importance of awareness of the risk of cholelithiasis among young individuals and the need for more effective prevention approaches, including education on healthy eating and weight management, to reduce the incidence of cholelithiasis in this population.

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