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Epidemiology and Risk Factors of Gall Stone in Dir Lower

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Abstract

This study evaluates patients diagnosed with Gall stone, focusing on their clinical presentations, medical histories, treatment regimens, and compliance. Patients ranged in age from 25 to 66 years, with a predominance of males (80%). The most common symptoms included flank pain, fever, urinary retention, and burning micturition. Diagnoses were mainly Gall stone stones, with 4 patients suffering from bilateral Gall stone calculi, while others had unilateral stones or hydronephroureter. Standard treatment involved IV fluids (N/S, Provas), antibiotics (Cefoperazone, Meronem), and pain relief medications (Tramadol, No Spa) at the ward level. Home treatment mirrored the ward regimen, with no significant drug interactions reported. Remarkably, 80% of the patients showed satisfactory compliance, though one patient demonstrated poor adherence.

Key words: Cholelithiasis, DHQ Timergara Teaching Hospital, Khyber Pakhtunkhwa

Introduction

Gallstones are one of the most common causes of gastrointestinal failure in the US and worldwide. Gallstones can lead to both chronic pain as well as episodic pain. They also create acute illnesses of the pancreatic, biliary, hepatic, and gastrointestinal tract. More than 6.3 million men and 14.2 million women aged 20 to 74 have gallstones in the United States. Up to 90% of people with gallstones are asymptomatic, but approximately 10% will develop symptoms within 5 years and 20% within 20 years following diagnosis. Gallstone disease is increasingly common with age. More than a quarter of women over the age of 60 have gallstones. Gallstones originate from metabolic, environmental and genetic factors; the composition of gallstones depends on the etiology [1]. Rapidly mobile, gallstones can move towards the entrance of the cystic duct, where they occlude bile flow and cause biliary colic. If the cystic duct is blocked for more than a handful of hours, the gallbladder becomes inflamed and susceptible to invasion by gut bacteria. When gallstones travel into a bile duct, biliary obstruction may result — with jaundice, abdominal pain, and cholangitis. Obstruction of the common bile duct can also cause pancreatitis. Patients with chronic gallstones may experience progressive fibrosis and decreased gallbladder motility. [1] Gopen, MD, and Jennifer G. Gill, MD Ultrasound is the modality of choice for gallstone detection; however, gallstones can be seen on computed tomography (CT), magnetic resonance imaging (MRI), and possibly x-rays, depending on calcium content. Management of gallstones is based on clinical severity and symptoms. Laparoscopic cholecystectomy is the accepted treatment for patients with symptomatic biliary colic or acute cholecystitis. Knowing this, one need not add that one million cholecystectomies are performed yearly in the United States, with half of those being attributable to biliary colic and chronic cholecystitis. [2] In the liver, primary bile acids are

derived from cholesterol. This vitamin C stimulates the conversion of cholesterol to bile acid via hydroxylation. These primary bile acids are transformed into secondary bile acids in the gut. Intestinal flora or hepatocytes further modify secondary bile acids into tertiary bile acids. Bile acids are amphipathic molecules possessing a hydrophilic hydroxyl group, a glycine or taurine side chain, and a hydrophobic steroid nucleus. [3] Gallstones comprise of bile products that precipitate out of solution, such as cholesterol, sonication products of red blood cells, and a combination of calcium bilirubin, phosphate, carbonate, palmitate, and cholesterol. These products are maintained in a mucin glycoprotein matrix as a nucleating agent for stone development. Various other substances (prostaglandins and arachidonoyl lethicin) encourage stone crystallization. [4] The most common type of gallstone consists predominantly of cholesterol. Black stones, which consist of calcium bilirubin, come from the hemoglobin metabolism. Brownstones, however, develop in the presence of bacterial or parasitic infection and are formed of a mixture of calcium substrates, including calcium bilirubin, calcium phosphate or palmitate, cholesterol, and bile. [4] Cholesterol stones are common among diabetic and metabolic dysfunctional patients. In contrast, black stones happen in those with inflammatory diseases like Crohn's disease or hemolysis, and brown-pigmented rocks are found in those with parasitic or bacterial infections and biliary strictures. [5]

Epidemiology

In the United States, about 14 million women and 6 million men ages 20 to 74 have gallstones. Symptomatic gallstones led to 2 million ambulatory care visits in 2023, 1 million emergency department visits, 605,000 laparoscopic cholecystectomies (280,000 inpatient) and 49,000 open cholecystectomies(inpatient). The prevalence of gallstone disease increases with age, and intervention for gallstones has been growing among older adults, Hispanics, and females. Some report that gallstones in Indigenous Americans are as high as 70%. [6] Most cholesterol gallstones are increasing in Westernized countries all around the world today. It is considered that this type of gallstone influences 20% of the European population. [7] 10% of those with gallstones become symptomatic within 5 years of diagnosis, 20% within 20 years, with a yearly incidence of 1% to 2%. [8] In 1% to 2% symptomatic patients with gallstones, complications arise, often due to common duct stones. [2] The prevalence of common duct stones found during a cholecystectomy is reported to be between 5% and 15% and increases with age. The Swedish registry noted a prevalence of common duct stones found during 11% of interoperative cholangiograms in patients with symptomatic gallstones. [9] Several factors are associated with an increased prevalence of gallstones. In Western countries, most (75%) of gallstones are cholesterol stones linked with metabolic derangements (dyslipidemia, diabetes, obesity, and insulin resistance) and high-saturated-fat, low-fiber, high-sugar diets. Other associations include a sedentary lifestyle and diseases, including weight loss or very low caloric diets, which impair gallbladder contraction and increase biliary cholesterol secretion. 3[11] The genetic contribution to gallstone risk is estimated to be between 25% to30%. [5] High estrogen levels have been linked to increased bile cholesterol and decreased gallbladder contractility. Women of reproductive age or those on estrogen-containing birth control medication are twice as likely to form gallstones than men. [12]

Treatment / Management

Cholecystectomy laparoscopic is the first treatment of symptomatic gallstones. Open cholecystectomy is reserved for when laparoscopic cholecystectomy is not possible or safe. However, in acute cholecystitis, unstable patients, or poor surgical candidates, interventional radiology can place a cholecystostomy tube as either a temporizing or palliative measure. [9]

Preoperative, postoperative, or intraoperative ERCP (endoscopic retrograde cholangiopancreatography) can be performed to extract common bile duct stones, or they can be extracted intraoperatively by laparoscopic or open common bile duct exploration. In a common bile duct exploration, the common duct is accessed through the cystic duct and visualized fluoroscopically or directly through a choledochotomy and a choledochoscope. The choledochoscope needs a second monitor, and fluoroscopy uses radiation, but both works. [23] Although standard duct incision can lead to post-incision duct stenosis, it needs to be meticulously closed. The common bile duct may be connected to the bowel in a side-to-side anastomosis or a Roux-en-Y choledochojejunostomy to prevent stenosis. Otherwise, a T-tube may be used to control the opening of the duct. Nonetheless, duct intubation, bacterial translocation into the biliary tree, and duct displacement resulting in bile peritonitis can be the risks of the procedure [39]. Intraoperative ERCP is a combined laparoscopic-endoscopic approach to this problem. In this technique, a guidewire is advanced through the cystic duct across the Ampulla of Vater into the duodenum and captured by a snare through the endoscope. The sphincterotome is then passed over the guidewire to do sphincterotomy and stone removal. [9] This technique allows for decreased hospitalization, reduced price, and less anesthesia but demands more technical skill and staff coordination. [9] Cholangitis must be treated urgently by relieving the obstruction - with endoscopic instrumentation (ERCP), percutaneous transhepatic intervention, or surgery - and giving early antibiotics. Cholecystectomy should be performed after acute illness recovery. 7 There is little use of pharmacological, mechanical treatment for gallstones due to low efficacy. [2] Like Lithotripsy, it does not prevent stones from forming; trained personnel are needed to perform the procedure. And, after October 2023, lithotripsy only plays a minor role in a multi-modal á-la-carte concept for challenging stones. Haemobilia due to erosion, hematoma, portal vein or hepatic artery transection, post-Whipple hemorrhage, post-cholecystectomy hemorrhage, or infection with neurotoxic clostridium (also known as airspace infection) all can take place within the common duct [48]. Mechanical Lithotripsy can be performed as a secondary maneuver after failed sphincterotomy for common duct stones, or electrohydraulic Lithotripsy or laser lithotripsy can be used to attempt to pulverize stones beneath fluoroscopy. Laser therapy is, however, costly and constrained by high heat. Extracorporeal shockwave Lithotripsy can be performed to treat difficult common duct stones, but efficacy is low []. [7] During shockwave lithotripsy, most operators utilize compressible water-filled bags in an external position to the body, but this is painful, and analgesia is needed for the counterpart of the procedure. Extracorporeal shock-wave therapy is contraindicated in the absence of portal thrombus and umbilical varices and can result in arrhythmias, haemobilia, cholangitis, pancreatitis, ileus and biliary colic. [9] Ursodeoxycholic acid (ursodiol) is a bile acid used to dissolve bile stones and treat liver pathology (biliary cirrhosis).[9] It can be given daily with the aim of gallstone dissolution, but the dissolution rate is 35 and a leaner control group in a cohort of 4699 laparoscopic cholecystectomies performed over 19 years. (27) found a direct association between frailty as assessed using the Modified Frailty Index and postoperative morbidity and mortality rates following laparoscopic cholecystectomy for acute cholecystitis. Fugazzola et al. created a preoperative risk score for patients undergoing cholecystectomy for acute calculous cholecystitis using a multicenter observational study from September 2021 to September 2022 involving 1253 patients from 79 centers [28]. Findings revealed a 30-day mortality rate of 6.6 % and 30-day mortality of 1%. [29]

Complications

This appears to be associated with gallbladder inflammation from gallstones, which can lead to acute and chronic cholecystitis, empyema, gangrenous cholecystitis and emphysematous cholecystitis. These stones can become wedged in the common bile duct, leading to obstruction, jaundice, dilation of the biliary tree proximally to the obstruction, and pancreatitis or cholangitis. 30[32] Gallstones may also externally compress a bile duct, such as the common bile duct or hepatic duct, from inside the cystic duct or gallbladder neck, which is known as Mirizzi syndrome. Gallstones can become impacted within the gallbladder, setting up erosion through the wall, leading to a cholecystoenteric fistula between the gallbladder and the bowel, frequently the duodenum (Bouveret syndrome). Gallstone ileus occurs in 0.3% to 0.5% of patients with gallstones and can cause an ileus in the small bowel. Centre for Evidence Synthesis in Epidemiology, re BRAND 8 [33] ERCP has procedural morbidity such as duodenal and bile duct injury, haemobilia, pancreatitis and rare case-report of pulmonary bile embolism after ERCP for gallstone pancreatitis. [9] Cholecystectomy can lead to complications either at the time of surgery or afterwards, such as injury to a bile duct or bowel, retained stones in the common bile duct, incisional hernia, and chronic right upper quadrant pain. [34] A higher intake of monounsaturated fats, fiber, olive oil, omega-3 fatty acids and vegetable proteins protects against gallstones. Polyunsaturated fatty acids may promote gallbladder emptying, and vegetable protein, fruits and vegetables rich in vitamin C and coffee may promote gallbladder motility. Exercise also may prevent gallstones from forming. [7] A diet higher in refined sugars, fructose, and fast food, with low fiber and vitamin C uptake, and a context of higher insulin needs increase the gallstone risk. [11] In the latter circumstance, asymptomatic choledocholithiasis is treated conservatively. [35] Gallstones during pregnancy are associated with worse maternal and neonatal outcomes, such as preterm birth. Cholecystectomy can be performed safely during the early and mid-stages of pregnancy. [10] Gallstones can be asymptomatic, can be symptomatic with a varying degree of severity and may lead to sub-acute or severe illness. Gallstones detected on imaging may or may not be clinically troublesome. In these cases, when symptomatic, the decision for intervention must be a joint conversation between the interprofessional team and the patient, along with the primary care team, surgeon (if appropriate), radiologist and, if needed, a gastroenterologist/ERCP endoscopist. It is usually helpful to get a general surgeon involved early. If gallstones lead to intermittent or persistent symptoms, early treatment decreases the requirement for emergency department care and reduces the risk of complications. [36]

Methodology

This is mainly a retrospective observational study, with concurrent data collection, to review cases of bladder stones at a tertiary care center. Being retrospective, the authors had access to a long patient history, ultimately providing insight into long-term trends in treatment, outcomes, and recurrence. This setup allows one to track trends in gall bladder stone development, previous treatment efficacy, and prevalence of risk factors. At the same time, featuring current data from outpatient visits serves a dynamic function, providing contemporary information about treatment protocols, diagnostic procedures, and patient demographics. These methods [historical documents versus contemporary data aggregation] allow for an inclusive sampling of data points, strengthening the validity of findings across temporal contexts. This study has a similar design to previous work, where retrospective data is required to analyze trends. Still, there is a need for real-time data to provide accurate insights when conducting analysis [7]. This study was conducted in DHQ-TTH Timeragra Dir upper.

The target population was patients diagnosed with gallbladder stones who attended the hospital's nephrology and urology outpatient clinics. INCLUSION CRITERIA: Patients treated during this period with a confirmed diagnosis of gallbladder stones and attended outpatient consultations. To ensure data integrity, patients who failed to provide consent and/or had incomplete medical records were excluded. A convenience sampling method was used to select 40 study participants. This sample size was considered adequate for exploratory analysis of the data and consistent with other studies in urology and nephrology research [12]. Data was obtained through various means, including detailed information about patient demographics, clinical histories, and treatment plans.

Methods:

A structured questionnaire was used to obtain vital patient data, including demographic information (age, sex, and contact number), clinical indications (chief complaints and investigation results), and personal and family history, including diagnoses and treatment plans. Interviews and qualitative insights. Interviews, when performed with a portion of the patients, enabled qualitative insights into their medical histories, lifestyle domains, and experiences with treatment. The data were drawn from hospital records, laboratory reports, and patient contacts. They were recorded using Performa, which was used to record all possible information for analysis. Demographic data, clinical data, past medical history, management details, and other relevant information were entered on Performa and included in the appendices for reference. This extensive data collection process identified all relevant variables for later data analysis 8. Data is analyzed with the help of SPSS (Statistical Package for the Social Sciences) and Microsoft Excel. Descriptive statistics were used to summarize demographic data, such as age, gender, and medical history. This enabled basic and descriptive knowledge of the characteristics of the sample. Inferential statistics were used for trend and correlation analysis in the dataset. The goal was to investigate associations of patient characteristics (age, gender, lifestyle) with treatment outcomes. Analyses: Chi-square tests, t-tests, and ANOVA were assessed. The data analysis cycle guaranteed an adequate interrogation of treatment algorithms, patient demographics and clinical outcomes7. The study received ethical approval from the Ethics Committee of Dir L Timergara Teaching Hospital General and Teaching Hospital. All participants were informed of the study's aim, methods, and potential harm and provided informed consent. Patient privacy & confidentiality were maintained by anonymizing and removing personal identifiers from the dataset. This methodology met the ethical principles for conducting medical research and protected the privacy and security of patient data. Ethical approval for this study was granted by the HSPH Review Board, which agreed to implement ethical guidelines based on the Declaration of Helsinki as the principles to follow regarding medical research involving human subjects 7.

Results and Discussion

Case No. 1: a 55-year-old male with the chief complaints of flank pain, fever, urinary retention, scrotal swelling, and burning micturition. He had a past medical history of hypertension. On investigations, he had a WBC count of $10.3 \times 10^3/mm^3$, hemoglobin of 13.1 g/dl, and platelets of 409K. Gall stone function tests were normal (creatinine: 1.0 mg/dl and urea: 49 mg/dl). The diagnosis was a 4mm calculus ±grade IV hydronephroureter, and PCNL was planned. The patient was treated with acetaminophen, intravenous saline, and antibiotics (Cefoperazone + Sulbactam). No side effect was observed, and proper compliance of the patient was noted with the prescribed medication. Case 2: 45-year-old man with flank pain, fever, burning, Nausea and vomiting. He had PCNL 3 weeks ago and pyelolithotomy 12 years ago in his medical

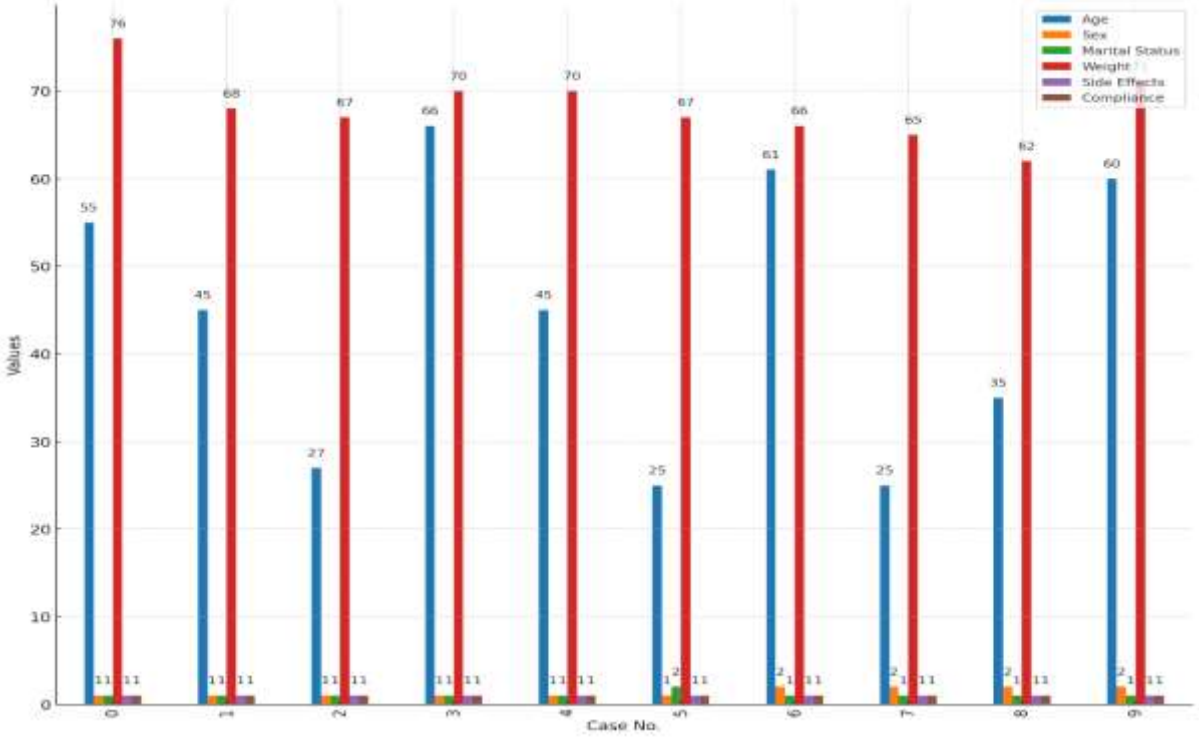
history. Laboratory investigations revealed a count of 8.515 × 10^3/mm^3, hemoglobin 8.4 g/dl, and creatinine level of 2.35 mg/dl. He was found to have a 5.5mm calculus and moderate hydronephroureter, warranting the removal of a DJ stint. Further treatment with Cefoperazone + Sulbactam (2g BD-IV), acetaminophen and intravenous fluids were given. Bakht Shaheen complied satisfactorily and completely recovered with no major side effects. Case no. 3_27-year-old man who presented with left flank pain, Nausea, and vomiting. There was a need for PCNL surgery performed a year ago. Investigations showed a white blood cell (WBC) count of 6.3 × 10^3/mm^3 hemoglobin of 13.1 g/dl and normal Gall stone function (creatinine 0.90 mg/dl). The diagnosis made was left Cholelithiasis; PCNL was advised. He started on Cefoperazone + Sulbactam (2g BD-IV), Tramadol for pain relief and antiemetics. The treatment you recommended made sense, and the patient was treated with complete recovery without any drug interactions and complied with the treatment plan perfectly. Case No. 4: A 66-year-old man was referred with flank pain, urinary retention, scrotal swelling, and burning micturition. He had a history of cardiac condition and obstructive uropathy. Laboratory tests showed WBC8.5 × 10^3/mm^3, hemoglobin 10.1 g/dl, and normal Gall stone function (creatinine 0.85 mg/dl). He was subsequently diagnosed with a left Gall stone with obstructive uropathy; PCNL was advised for him. Repeated blood and urine cultures were negative throughout his hospital stay, while the patient was treated with Cefoperazone + Sulbactam, Ringer's lactate, and Tramadol for pain control. He was compliant and had a satisfactory response to treatment. Case No. 5: a 45-year-old man came in with flank pain, fever, pain, Nausea and vomiting. He was diagnosed with PCN for 3 weeks, then pyelolithotomy 12 years in the past. Her blood tests showed a WBC count of 12900 × 10^3/mm^3, hemoglobin of 8.5 g/dl, and platelets of 597K. Gall stone function tests showed creatinine and urea of 2.3 mg/dl and 82.7 mg/dl, respectively. He had been diagnosed with bilateral Gall stone stones. She was treated with Meropenem, acetaminophen, and IV fluids. And although he failed to comply with Cefoperazone, he had a gratifying convalescence, and the regimen was tailored for maximum effect. Case No. 6—A 25-year-old man presented with bilateral flank pain, urinary retention, and anemia. Laboratory findings revealed an 18000/mm^3 white blood cell (WBC) count and 9 g/dl hemoglobin, 6.3 mg/dl serum calcium. He was found to have bilateral Gall stone calculi and obstructive uropathy. Shujaat was managed with Tramadol for pain, Cefoperazone + Sulbactam, calcium gluconate for Hypocalcemia and the rest of the supportive care. He had minimal compliance with his treatment, and his anemia could have been better managed for better recovery. Case No.7: 61-year-old female, Flank pain, frequency and N&V. Her investigation showed high blood sugar (RBS: 190 mg/dl) and Gall stone insufficiency (creatinine: 2.7 mg/dl, urea: 74 mg/dl). She has multiple gall balladry stones. They received treatment for pain with Cefoperazone and Tramadol. Shazia faithfully followed her treatment plan and made a good recovery. Case No. 8: 25-year-old female with flank pain, weakness, and urinary retention. Her investigations revealed normal WBC and hemoglobin; Gall stone function tests showed elevated creatinine (3.74 mg/dl) and urea (90 mg/dl). X-ray: Left gall balladeer stone...for treating Solifenacin, Ciprofloxacin, other supportive. Her condition improved, although she continued to struggle with compliance. Case No.9: A 35-year-old woman with right flank pain, vomiting, and burning sensations. Laboratory tests revealed normal WBC and hemoglobin levels with low serum calcium (7.2 mg/dl), indicating some complications. Rishma was found to have a right Gall stone and Hypocalcemia. She administered Ciprofloxacin, Tramadol for pain, and calcium supplements. The treatment worked, and she followed the prescribed plan. Case No. 10: A 60-year-old woman with diabetes and hypertension presented with dysuria, anorexia, and flank pain. Investigations showed WBC count:10.3 × 10^3/mm^3, hemoglobin: 12.9

g/dl, creatinine: (2.35 mg/dl). She was also found to have bilateral Gall stone stones. He was treated with Tamsulosin for urinary retention, Ciprofloxacin, and other supportive treatments. Gul Bano had comorbidities like diabetes and hypertension, but her treatment was well-managed — and she recovered after following her prescribed regimen.

Conclusion

Proper treatment protocols for these cases were implemented for each patient according to their conditions. Management included Cefoperazone and Meropenem for infections, Solifenacin for urinary retention, and Tramadol for pain control. For most patients, appropriate treatment and scrupulous monitoring led to acceptable outcomes.

Patient Demographics, Clinical Characteristics, and Treatment Outcomes for Gall bladder Stone Cased Timergara Dir L.



Discussion

The objective of this study was a review of the prevalence, types, diagnostic modalities, treatment options, and management of gallbladder stone disease in a tertiary care setting in Dir L Timergara Teaching Hospital General and Teaching Hospital. The results of this study explain the increased activity of pathophysiological significance of gallbladder stones, their epidemiology, effects on health and quality of life, as well as on other eco-metric parameters in modern society. With the increasing incidence of gallbladder stones globally it is important to assess these factors to reduce the burden of public health and to improve the standards of patient care. Data was carefully collected from approximately 40 cases, including both inpatient admissions and outpatient visits. The diagnosis is made through various investigations such as blood investigations (Complete Blood Count, Gall stone and Liver Function Tests), urine analysis (calcium and uric acid levels), and imaging (ultrasound and CT-). Instead, these diagnostic methods enabled a precise evaluation of the stone's chemical composition, dimensions, and anatomical locations, which was paramount in choosing the optimal treatment regimen. Management approaches were case-dependent; pharmacotherapy and surgical intervention was among the various options. In pharmacological cases, the patients were given drugs for infections (antibiotics), anti-inflammatories, analgesics/anti-spasmodic to relieve

pain, and muscle relaxants to pass the stone. Drugs to change the urinary pH were also utilized when warranted, underscoring the need for individualized medication adjustments to enhance therapy outcomes. PCNL was chosen for larger or obstructive stones requiring surgical intervention in the current study, with the placement of DJ stents in some cases for postoperative urinary drainage. Postoperatively, patients undergoing operative treatment only were monitored for one to two days to track recovery and fine-tune medications as needed. Overall, the treatment plans in most cases were effective and prescriptions were generally appropriate concerning dosing, formulation, and absence of important drug interactions. However, prescription errors were noted in some cases (contraindications of drug combinations [e.g., ciprofloxacin + olanzapine] and some untreated comorbidities). The necessity of careful review of prescriptions especially applies to patients with complex medical histories or those on multiple medications. This study emphasizes the significance of distinguishing between stone types (calcium oxalate, calcium phosphate, uric acid, cystine, and struvite stones), which is a very important finding. Each has its own set of risk factors, dietary recommendations, and treatment protocols. Alas, there were often no individualized dietary and therapeutic recommendations for stone types. With targeted management plans including diet changes and patient education, the treatment can be maximized and disease recurrence avoided, leading to higher long-term patient outcomes. Therefore, this investigation highlights the importance of broad diagnostic and tailored therapeutic strategies for treating gallbladder stones. Healthcare professionals can improve therapeutic success, reduce recurrence, and better quality of life among affected individuals by utilizing individualized treatment plans based on stone type and patient-specific factors.

References

[1] Khan, S. R., Pearle, M. S., Robertson, W. G., Gambaro, G., Canales, B. K., Doizi, S., & Tiselius, H. G. (2016). Gall balladery stones. Nature Reviews Disease Primers, 2(1), 1-23.

[2] Kumar, S. B. N., Kumar, K. G., Srinivasa, V., & Bilal, S. (2012). A review on urolithiasis. International Journal of Universal Pharmacy and Life Sciences, 2(2), 269-280.

[3] Parmar, M. S. (2004). Gall balladery stones. Biomedical Journal, 328(7453), 1420-1424.

[4] Kirkali, Z., Rasooly, R., Star, R. A., & Rodgers, G. P. (2015). Urinary stone disease; progress, status, and needs. Urology, 86(4), 651-653.

[5] Xu, H., Zisman, A. L., Coe, F. L., & Worcester, E. M. (2013

[6] Gall balladr stones; an update on current pharmacological management and future directions. Expert Opinion on Pharmacotherapy, 14(4), 435-447.

[7] Heilberg, I. P., & Schor, N. (2006). Gall stone stone disease; causes, evaluation, and medical treatment. Arquivos Brasileiros de Endocrinologia & Metabologia, 50(6), 823-831.

[8] Eknoyan, G. (2004). History of urolithiasis. Clinical Review in Bone and Mineral Metabolism, 31(2), 177-185.

[9] Lopez, M., & Hoppe, B. (2010). History, epidemiology, and regional diversities of urolithiasis. Pediatric Nephrology, 25(1), 49-59.

[10] Robertson, W. G. (1990). Epidemiology of urinary stone disease. Urological Research, 18(1), S3-S8.

[11] Kodama, H., & Ohno, Y. (1989). Descriptive epidemiology of urolithiasis. Hinyokika Kiyo. Acta Urologica Japonica, 35(6), 923-934.

[12] Singh, K. B., & Sailo, S. (2013). Understanding epidemiology and etiological factors of urolithiasis; an overview. Scientific Visualization, 13(4), 169-174.

[13] Knoll, T. (2010). Epidemiology, pathogenesis, and pathophysiology of urolithiasis. European Urology Supplements, 9(12), 802-806.

[14] Coe, F. L., Parks, J. H., & Asplin, J. R. (1992). The pathogenesis and treatment of gall balladery stones. New England Journal of Medicine, 327(16), 1141-1152.

[15] Moe, O. W. (2006). Gall balladery stones; pathophysiology and medical management. The Lancet, 367(9507), 333-344.

[16] Reynolds, T. M. (2005). Chemical pathology clinical investigation and management of Cholelithiasis. Journal of Clinical Pathology, 58(2), 134-140.

[17] Park, S., & Pearle, S. (2007). Pathophysiology and management of calcium stones. Urologic Clinics of North America, 34(3), 323–334.

[18] Griffith, D. P. (1978). Struvite stones. Gall balladery International, 13(5), 372-382.

[19] Ratkalkar, V. N., & Kleinman, J. G. (2011). Mechanisms of stone formation. Clinical Reviews in Bone and Mineral Metabolism, 9(3), 187-197.

[20] Courbebaisse, M., Prot-Bertoye, C., & Daudon, M. (2020). Cholelithiasis; from mechanisms to preventive medical treatment. Néphrologie & Thérapeutique, 16(1), 65-75.

[21] Prien, E. L., & Prien Jr, E. L. (1968). Composition and structure of urinary stone. The American Journal of Medicine, 45(5), 654-672.

[22] Sofia, N. H., & Walter, T. M. (2016). Prevalence and risk factors of gall balladery stone. Global Journal for Research Analysis, 5(3), 2-16.

[23] Miller, N. L., & Lingeman, J. E. (2007). Management of gall bladder stones. Bio Medical Journal, 334(7591), 468-472.

[24] Frassetto, L., & Kohlstadt, I. (2011). Treatment and prevention of balladery stones; an update. American Family Physician, 84(11), 1234-1242.

[25] Tsai TJ, Chan HH, Lai KH, Shih CA, Kao SS, Sun WC, Wang EM, Tsai WL, Lin KH, Yu HC, Chen WC, Wang HM, Tsay FW, Lin HS, Cheng JS, Hsu PI. Gallbladder function predicts subsequent biliary complications in patients with common bile duct stones after endoscopic treatment. BMC Gastroenterol. 2018 Feb 27;18(1):32.

[26] Shenoy R, Kirkland P, Hadaya JE, Tranfield MW, DeVirgilio M, Russell MM, Maggard-Gibbons M. Management of symptomatic cholelithiasis: a systematic review. Syst Rev. 2022 Dec 12;11(1):267. [

[27] Di Ciaula A, Garruti G, Frühbeck G, De Angelis M, de Bari O, Wang DQ, Lammert F, Portincasa P. The Role of Diet in the Pathogenesis of Cholesterol Gallstones. Curr Med Chem. 2019;26(19):3620-3638.

[28] Rebholz C, Krawczyk M, Lammert F. Genetics of gallstone disease. Eur J Clin Invest. 2018 Jul;48(7):e12935.

[29] E S, Srikanth MS, Shreyas A, Desai S, Mehdi S, Gangadharappa HV, Suman, Krishna KL. Recent advances, novel targets and treatments for cholelithiasis; a narrative review. Eur J Pharmacol. 2021 Oct 05;908:174376.

[30] Unalp-Arida A, Ruhl CE. Burden of gallstone disease in the United States population: Prepandemic rates and trends. World J Gastrointest Surg. 2024 Apr 27;16(4):1130-1148.

[31] Gutt C, Schläfer S, Lammert F. The Treatment of Gallstone Disease. Dtsch Arztebl Int. 2020 Feb 28;117(9):148-158.

[32] Fujita N, Yasuda I, Endo I, Isayama H, Iwashita T, Ueki T, Uemura K, Umezawa A, Katanuma A, Katayose Y, Suzuki Y, Shoda J, Tsuyuguchi T, Wakai T, Inui K, Unno M, Takeyama Y, Itoi T, Koike K, Mochida S. Evidence-based clinical practice guidelines for cholelithiasis 2021. J Gastroenterol. 2023 Sep;58(9):801-833.

[33] Cianci P, Restini E. Management of cholelithiasis with choledocholithiasis: Endoscopic and surgical approaches. World J Gastroenterol. 2021 Jul 28;27(28):4536-4554.

[34] Di Ciaula A, Wang DQ, Portincasa P. An update on the pathogenesis of cholesterol gallstone disease. Curr Opin Gastroenterol. 2018 Mar;34(2):71-80.

[35] Kotrotsios A, Tasis N, Angelis S, Apostolopoulos AP, Vlasis K, Papadopoulos V, Filippou DK. Dietary Intake and Cholelithiasis: A Review. J Long Term Eff Med Implants. 2019;29(4):317-326.

[36] Han JH, So H, Bang SJ, Nah YW. [Surgical Removal of a Huge Common Bile Duct Stone]. Korean J Gastroenterol. 2024 May 25;83(5):200-204.

[37] Hirajima S, Koh T, Sakai T, Imamura T, Kato S, Nishimura Y, Soga K, Nishio M, Oguro A, Nakagawa N. Utility of Laparoscopic Subtotal Cholecystectomy with or without Cystic Duct Ligation for Severe Cholecystitis. Am Surg. 2017 Nov 01;83(11):1209-1213.

[38] Ruhl CE, Everhart JE. Gallstone disease is associated with increased mortality in the United States. Gastroenterology. 2011 Feb;140(2):508-16.

[39] Thapar VB, Thapar PM, Goel R, Agarwalla R, Salvi PH, Nasta AM, Mahawar K., and IAGES Research Collaborative Group. Evaluation of 30-day morbidity and mortality of laparoscopic cholecystectomy: a multicenter prospective observational Indian Association of Gastrointestinal Endoscopic Surgeons (IAGES) Study. Surg Endosc. 2023 Apr;37(4):2611-2625.

[40] Nassar AHM, Khan KS, Ng HJ, Sallam M. Operative Difficulty, Morbidity and Mortality Are Unrelated to Obesity in Elective or Emergency Laparoscopic Cholecystectomy and Bile Duct Exploration. J Gastrointest Surg. 2022 Sep;26(9):1863-1872.

[41] Fagenson AM, Powers BD, Zorbas KA, Karhadkar S, Karachristos A, Di Carlo A, Lau KN. Frailty Predicts Morbidity and Mortality After Laparoscopic Cholecystectomy for Acute Cholecystitis: An ACS-NSQIP Cohort Analysis. J Gastrointest Surg. 2021 Apr;25(4):932-940.

[42] Fugazzola P, Cobianchi L, Di Martino M, Tomasoni M, Dal Mas F, Abu-Zidan FM, Agnoletti V, Ceresoli M, Coccolini F, Di Saverio S, Dominioni T, Farè CN, Frassini S, Gambini G, Leppäniemi A, Maestri M, Martín-Pérez E, Moore EE, Musella V, Peitzman AB, de la Hoz Rodríguez Á, Sargenti B, Sartelli M, Viganò J, Anderloni A, Biffl W, Catena F, Ansaloni L., S.P.Ri.M.A.C.C. Collaborative Group. Prediction of morbidity and mortality after early cholecystectomy for acute calculous cholecystitis: results of the S.P.Ri.M.A.C.C. study. World J Emerg Surg. 2023 Mar 18;18(1):20.

[43] Del Vecchio Blanco G, Gesuale C, Varanese M, Monteleone G, Paoluzi OA. Idiopathic acute pancreatitis: a review on etiology and diagnostic work-up. Clin J Gastroenterol. 2019 Dec;12(6):511-524.

[44] Brägelmann J, Barahona Ponce C, Marcelain K, Roessler S, Goeppert B, Gallegos I, Colombo A, Sanhueza V, Morales E, Rivera MT, de Toro G, Ortega A,

Müller B, Gabler F, Scherer D, Waldenberger M, Reischl E, Boekstegers F, Garate-Calderon V, Umu SU, Rounge TB, Popanda O, Lorenzo Bermejo J. Epigenome-Wide Analysis of Methylation Changes in the Sequence of Gallstone Disease, Dysplasia, and Gallbladder Cancer. Hepatology. 2021 Jun;73(6):2293-2310.

[45] Sohail Z, Shaikh H, Iqbal N, Parkash O. Acute pancreatitis: A narrative review. J Pak Med Assoc. 2024 May;74(5):953-958.

[46] Zaher EA, Ebrahim MA, Al Salman O, Patel P, Alchalabi M. Bigger Than a Hen's Egg: A Case of Bouveret Syndrome. Cureus. 2024 Apr;16(4): e58742.

[47] Knapik M, Okoń K, Ulatowska-Białas M. Fatal pulmonary bile embolism associated with acute pancreatitis - a case report and review of the literature. Pol J Pathol. 2024;75(1):54-57.

[48] Field X, Tong C, Cox S, Crichton J, Goodwin B, Welsh F, Cha R. Outcomes of asymptomatic common bile duct stones detected at intraoperative cholangiography. N Z Med J. 2024 May 17;137(1595):73-79.

[49] Patel SS, Kohli DR, Savas J, Mutha PR, Zfass A, Shah TU. Surgery Reduces Risk of Complications Even in High-Risk Veterans After Endoscopic Therapy for Biliary Stone Disease. Dig Dis Sci. 2018 Mar;63(3):781-786.

[50] Genser L, Vons C. Can abdominal surgical emergencies be treated in an ambulatory setting? J Visc Surg. 2015 Dec;152(6 Suppl):S81-9.

[51] Coleman J. Bile duct injuries in laparoscopic cholecystectomy: nursing perspective. AACN Clin Issues. 1999 Nov;10(4):442-54.