Review Article

Comparing Normal Saline Application with No Application During Minimally Invasive Pneumoperitoneum Cholecystectomy Using Laparoscopic Techniques

Rabia Sana 1*, Amir Rathore 2

- 1 Allama Iqbal Medical College, Lahore, Pakistan; <u>rabiasana64@gmail.com</u>
- 2 Allama Iqbal Medical College, Lahore, Pakistan; amirrathore@gmail.com
- * Correspondence: <u>rabiasana64@gmail.com</u>

Abstract: The laparoscopic cholecystectomy was associated with several symptomatic therapies for gallstone disorders. The most popular method for doing this has been laparoscopic surgery. (Source:) In order to create enough work areas in the abdominal cavities, the first step in a laparoscopic cholecystectomy involves using gases to create a pneumoperitoneum using the verse's needles or through port holes in the abdominal wall. Intraabdominal pressures of 12–16 mmHg are typically regarded as sufficient for instrument visibility and manipulation. Standard pressure pneumoperitoneum in the post-operative period provides appropriate working space in this scenario, but new tendency needs to be employed for low pressure between 7-10mm Hg instead of normal pressures in an effort to decrease the consequences of pneumoperitoneum. Intraperitoneal saline washout following gall bladder retrieval combined with low-pressurized pneumoperitoneum was found to be an effective method for lowering analgesic consumption during the early stages of recovery following laparoscopic cholecystectomy, as well as postoperative pain and shoulder tip pain.

Keywords: normal saline application, no application, invasive pneumoperitoneum, cholecystectomy, laparoscopic techniques

1. INTRODUCTION

The preferred method of treating gallstone disease is laparoscopic cholecystectomy. This laparoscopic treatment involves three or four tiny incisions in order to remove the gall bladder. Numerous benefits come with laparoscopic procedures: fewer scars from the surgery, reduced pain following the procedure, shortened hospital stays, quicker healing, and improved cosmetic outcomes. Its benefits over an open cholecystectomy include less pain after surgery and a quicker return to work [1-4]. That being said, up to 80% of patients still experience excruciating pain following laparoscopic surgery and need to take pain medication. Pneumoperitoneum is created during laparoscopic cholecystectomy by using an automatic insufflator to create pressure in the abdominal or peritoneal cavity. By expanding the abdominal cavity, the pneumoperitoneum improves internal organ visibility and provides sufficient space for equipment movement. Adverse consequences of pneumoperitoneum include decreased pulmonary compliances, issues related to acidity, nausea, vomiting, and post-operative stiff shoulders. It was previously believed those intra-stomach pressures between 12 and 16 mmHg were adequate for instrument handling and vision [5]. Patients who have had a laparoscopic cholecystectomy report diaphragm stretch, peritoneal

irritations from carbonic acid through carbon dioxide, and activation of the sympathetic nervous system due to hypercarbia, which exacerbates local tissue inflammatory responses and ischemia of the splanchnic mucosa [6]. In around 35–60% of instances following a laparoscopic cholecystectomy, shoulder tip pain develops [7]. Pain is one of the primary causes of analgesic misuse, delayed discharge, and increased morbidity following laparoscopic cholecystectomy. Merely a handful of investigators observed that 80% of patients require opioid analgesia following laparoscopic surgeries [8]. The inhalation of CO2 in abdominal cavities might cause the liver and diaphragm areas to get stuck [9]. In order to restore the gas lost from the liver and reduce abdominal pain, it is advised to subdiaphragmatically infuse normal saline until the liver heals following the removal of the gall bladder [10]. Surgeons are in a unique position to handle issues when multivariate post-laparoscopic cholecystectomy pain management fails to yield the desired result because of very little adjustments in methods and corresponding improvements in results [11]. Analgesic medications, intraperitoneal anaesthesia, intraperitoneal salines, gas draining, warm gases, lower-pressure gases (12 mmHg), and the nitrous-oxides pneumoperitoneum have all been employed as analgesic treatments to alleviate this pain [12]. Lower pressure pneumoperitoneum is preferred over high pressure for the same reason, and it also has the advantage of enabling the establishment of a working area by withdrawing viscera [13]. Throughout the postoperative phase, there is an increasing trend to apply moderate pressure to the pneumoperitoneum to avoid injury. This pressure is typically between 7 and 10 mm Hg of standard pressure, while still maintaining adequate working space [14]. Comparable ratings for intraoperative complications indicate that the lower pressure approach is safer. Postoperative shoulder tip discomfort was significantly reduced in the low-pressure group (7-8 mm Hg) at 8% compared to the standard pressure group (12-14 mm Hg) at 32%, and fewer patients required postoperative analgesics [15]. Intraperitoneal saline washout in conjunction with low-pressured pneumoperitoneum was found to be more effective than lower-pressure pneumoperitoneum in reducing postoperative pain, shoulder tip pain, and analgesic consumptions during the initial recovery phase after laparoscopic cholecystectomy [16]. Studies show that lower pressure CO2 pneumoperitoneum lowers pain severity and shoulder tip discomfort following laparoscopic cholecystectomy. Although shoulder-tip discomfort is not as common, it can be lessened by including intraperitoneal normal saline infusions into lower-pressured CO2 pneumoperitoneum during laparoscopic cholecystectomy [17]. Another study found that in low-pressure pneumoperitoneum with normal saline washout, the incidence of shoulder tip discomfort was 1.6% lower than in low-pressure pneumoperitoneum alone, which had an incidence of 11.29%. In the same study [18], the analgesia demanding rate is significantly lower in lower pressured pneumoperitoneum with normal saline washout within twenty-four and forty-eight hours postoperatively compared to only low pressure pneumoperitoneum (70.9% vs. 90.3%; p=0.006 and 64.5% vs. 83.8%; p=0.013, respectively). The objective of the current review is to compare the outcomes of standard saline instillations vs those that do not require instillations after gall bladder removal in laparoscopic cholecystectomy with low-pressure pneumoperitoneum (defined as <12 mm Hg).

2. LITERATURE REVIEW

Globally, gallstones are quite common, occurring in 6% of men and 29% of women. The most successful treatment for gallbladder issues has been shown to be laparoscopic cholecystectomy. (Stones Gall) [19, 20]. Small spherical lumps called gallstones develop in the gallbladder sac as a result of abnormally elevated bile bilirubin or cholesterol levels. Around 10% to 20% of adults worldwide suffer from gallstones, and over 20% of those who have gallbladder stones will experience symptoms like

cholecystitis or biliary colic mostly as adults. Gallstone disorders are defined as conditions where symptoms or complications arise from stones that are present in the biliary tracts or gallbladders; however, individuals who have asymptomatic gallstones are not considered to have gallstone diseases. Gallstone disease is one gastrointestinal issue that has a high socioeconomic cost [21]. Gallstones are categorised according to their composition and location. Cholesterol makes up the majority of almost 90% of stones. Black and brown colour stones are other varieties, although they make up less than 10% [22]. There are two types of biliary tract stones: extrahepatic (choledocholithiasis) and intrahepatic (hepatolithiasis). When a gallbladder is surgically removed, or when secondary stones from the gallbladder flow into the common bile duct, they can be distinguished in the biliary tract. Gallstones are explained in Primer, along with the present principles for managing them and future approaches to treating common disorders [23]. A tiny organ, the gallbladder is joined to the liver's right lobe. It features an internal hollow area that can hold up to 50 millilitres of bile. It has a pear form and thin walls, but it is pliable. It is situated in a shallow depression known as the cystic fossa on the inferior surface of the liver. It is separated into three sections: the fundus, body, and neck, and it is located posterosuperior to the IVC. The neck narrows and continues as a cystic duct, which joins with the hepatic duct to form the common bile duct. The fundus of the gall bladder is spherical and faces the abdominal wall. The body is located in the cystic fossa. The inferior surfaces of the gallbladders are covered by the peritoneum. Without peritoneums, its superior surface relates to the liver. Occasionally, it may be suspended by a mesentery from the liver and covered by the visceral peritoneum, which could cause the gall bladder to torsion [24]. The gallbladder fundus extends below the tip of the ninth costal cartilages and as far as the front edge of the liver surface. The porta hepatis is superomedially directed by the gallbladder's neck. Gall bladder inflammation can cause adhesions to form with nearby structures and can also erode their walls. Gallstones can slide or pass through the duodenum and encase intestinal blockages (gallstone ileus). In the small intestine's distal region. 97% of the bile that comes from the liver is water, 1%-2% is bile salt, and 1% is pigment. Storing bile is one of the gallbladder's primary purposes. Bile is concentrated by a factor of ten by the processes of active reabsorption of water, sodium chloride, and bicarbonates; mucus secretion makes the bile viscous [25]. There are involuntary muscles in the gallbladder and sphincter Oddi, but there are only sporadic muscular fibres in the remaining portion of the biliary tract. Columnar epithelium lines the inside of the biliary system and gallbladder, and the mucosa of the gallbladder has many goblet cells that secrete mucus (26]. Oral cholecystograms and intravenous cholangiography are no longer used in the industrialised world. Currently, endoscopic retrograde cholangiopancreatography, percutaneous transhepatic cholangiography, and ultrasound are the imaging modalities employed for anatomical elaboration. A non-invasive method that offers great anatomical detail is MRCP [27]. The right hepatic arteries, a branch of the common hepatic arteries located in the calot triangle, are the primary source of cystic arteries, which supply the gallbladder with blood. Normally, it passes behind the common hepatic duct, ascends to the cystic duct, passes through the gallbladder neck, and then splits off into tiny sections along its body to nourish the gallbladder. Nonetheless, the structural variances in the origin of cystic arteries are often observed. It may come from the gastroduodenal artery, the trunk of the hepatic arteries, or the left hepatic artery. Furthermore, the gall bladder can be reached by the cystic artery running in front of the common hepatic duct. No matter where the cystic artery originates, it almost always occurs within the cystohepatic trigone. Additionally, the right hepatic artery may send many arterial twigs to the gallbladder through the gallbladder bed; these twigs are occasionally seen during a laparoscopy [28]. When the gallbladder is not severely inflamed, the several veins draining it can be seen during a laparoscopy as they travel along the artery twigs to the gallbladder fossa. Rarely, if a cystic vein is present, the gallbladder's blood is drained into the right portal vein [29]. Worldwide, gallstone disease is a prevalent ailment. There are notable regional variations in the occurrence of gallstone disease. Among Western countries, gallstone disease is rather frequent; among men, the incidence ranges from 7.9 to 16.60 percent [30]. In Asians, it spans from approximately 3% to 15%; in Africans, it is essentially nonexistent (<5%); in China, it varies from 4.21 to 11% [31]. Gallstone disease is also fairly frequent in several ethnic groups. For instance, American Indian boys and girls are affected in proportions of 29.50% and 64.10%, respectively, and Mexican Americans are affected in proportions of 8.90% and 26.70% [32]. The prevalence of gallstone illnesses ranges from 10% to 20%, making them prevalent and expensive. Analysing asymptomatic situations that lead to early therapies and the prevention of serious outcomes is the importance of early screening [33]. According to US epidemiological data, 20 million Americans may be affected by cholelithiasis. In Russia, 15.8% of digestive system disorders are gallbladder-related, and in Moscow, that number might reach 22% [34]. Gallstones are becoming more common among Pakistani citizens. Gallstones were reported to be surgically treated in 9.03% of cases in Southern Sindh, with women 3.3 times more likely than men to get gallstones. According to a recent study conducted in Karachi, 10.2% of people had gallstone disease [35]. Whereas Europe and the USA have recorded eighty percent of cholesterol stones, Asia has reported eighty percent of pigment stones. Five to ninety percent cholesterol is made up of phospholipid, biles acid, calcium salt, bile pigment, and other substances. Gallstone formation is often preceded by the formation of biliary sludge, a viscous mixture of cholesterol crystals, glycoproteins, and calcium deposit. Biles that are supersaturated with cholesterol comprise the bulk of stones found in the United States. The overproduction of cholesterol brought on by altered hepatical cholesterol metabolisms is the main cause of this hypersaturation, which results from the concentration of cholesterol being higher than its solubility percentages. An imbalance between pronucleating (which encourages crystallisation) and antinucleating (which prevents crystallisation) proteins speeds up the bile's cholesterol crystallisation [40]. Biliary epithelial cells release mucin, which is broken down by lysosomal enzymes. If this breakdown is prevented, cholesterol crystals may form. Excessive sphincter contraction, loss of gallbladder muscle wall motility, extended bile stasis with inadequate reservoir function, and bile flow all contribute to the buildup of bile and the development of stones. Bilirubin stones can also occasionally arise from red blood cell lysis. Increased enterohepatic bilirubin circulation and biliary tract infections are two theories for the development of bilirubin stones. Bilirubin stones, also known as pigment stones, are more frequent in Asians and Africans and are associated with biliary system infections and chronic hemolytic diseases [41]. Both calculus and acalculus can have cholecystitis. It involves stone impaction in the cystic duct, Hartmann's pouche, or gallbladder neck. On the other hand, as the gallbladder's pressure increases, its walls harden, the blood supply is decreased, and exudate may accumulate. It might be persistent, with recurrent episodes of acute inflammation that could eventually result in chronic cholecystitis. Compared to non-diabetics, patients with diabetes experience acute cholecystitis more frequently, which can lead to problems. If the inflamed gallbladder is left untreated, necrosis and gangrene could develop, which could result in sepsis symptoms. Gallbladder perforation is an uncommon but potentially fatal illness that can result from improper management of cholecystitis. Gallstone pancreatitis can result from gallstones that dislodge from the pancreatic duct in cholecystitis and lodge below the sphincter of Oddi [42]. Gallstones without symptoms hardly ever cause issues. Additionally uncommon are symptomatic gallstones that lead to major problems. Gallstones with symptoms almost seldom cause death. Any location in the biliary system where a gallstone blockage occurs can result in the development of symptoms. The cystic duct is typically blocked, which can result in pain, inflammation, or both. Choledocholithiasis, in which stones pass through the cystic duct, develops in about 10% of cases [43]. Roughly 1 in 10 people will experience a gallbladder perforation that results in life-threatening complications, people with diabetes mellitus or those who wait too long to seek care or do not react to therapy are more likely to experience this illness. After the gallbladder is punctured, pain may momentarily subside, but this creates a dangerous and deceptive scenario since a widespread abdominal infection subsequently arises [44]. Gallbladder pus can develop in 2% to 3% of people with acute cholecystitis who have pain lasting more than a few days. A physical examination is frequently insufficient to determine the underlying cause of life-threatening illnesses, particularly when the infection spreads to other body areas [45]. The inflamed gallbladder adheres to the surrounding tissue and may puncture, allowing the organs to communicate with one another. Gallstones can occasionally slip into the small intestine in these patients, causing dangerous conditions that may need to be investigated right away [46]. Gallstone ileus is the term for the gastrointestinal system blockage caused by gallstones. It usually affects those over 65 and can occasionally be fatal. Depending on the degree of obstruction, surgical alleviation of impaction is the primary course of treatment in order to remove it [47]. Blockage-related cholegitis is a common and dangerous illness. In 75% of instances, the infection can be cured with prompt treatment; but, if the condition worsens, the infection may spread and become life-threatening. To open and drain the ducts, endoscopic sphincterotomy or surgical intervention will be needed. 48]. Because the pancreatic duct joins the common bile duct before entering the duodenum, stones in the common bile duct typically cause pancreatitis in patients. The pancreatic duct can get blocked by stones that frequently travel into and impede the lower portion of the common bile duct [49]. When ducts are clogged, the active enzyme cannot reach the duodenum and instead damages the pancreas, resulting in acute pancreatitis. When germs cause purulent swelling in the liver and bile channel, rising cholangitis happens. Cancer of the gallbladder is an uncommon disease [50]. Because most individuals with gallstones present asymptomatic, gallbladder illnesses may be equated with gallstones. These stones are quiet, easily discovered, and don't need long-term care. Most likely due to stone impaction in the cystic duct, patients with symptomatic gallstones typically report with recurrent episodes of discomfort in the right side hypochondrium and epigastrical region. Severe upper abdomen discomfort and nausea or vomiting may occur, and these symptoms may worsen over the course of many hours to around half an hour. Boas' sign, or hyperesthesia beneath the right scapula blade, can occasionally occur in patients. Particularly after a heavy dinner at night, episodic pain frequently happens [51]. Severe pain in the right hypochondrium region accompanied by fever, nausea, leucocytosis, and vomiting is caused by gallbladder wall inflammations. Without medical attention, the condition may infrequently go away and even perforate, but it can also cause gangreneous gallbladder. Less frequently, stones enter the common bile duct, obstructing it and resulting in cholestasis symptoms [52]. Extrinsic compression of the common hepatic duct from impacted stones in the cystic ducts and Hartmann's pouche in the gall bladder (Mirrizi syndrome) can result in obstructive jaundice[53]. Cholangitis is brought on by even little bile flow obstructions. A common bile duct stone typically results in pain in the right hypochndrial or epigastric region, although it can also be painless. By blocking the primary pancreatic ducts as they flow from the neighbouring common bile duct at Ampulla to Vater in the second section of the duodenum, stones in the common bile duct might momentarily produce acute pancreatitis. Stones may occasionally fistulate straight from the gallbladder into the duodenum during the quiet inflammatory phase [54]. If this stone impacts the duodenum, it can cause obstructions known as Bouveret's syndromes. Alternatively, it can damage the narrowest portion of the small intestine, which can result in an obstruction known as gallstone ileus [55]. Upper abdomen pain can be a symptom of both intra- and extra-abdominal diseases, and cholelithiasis and these conditions frequently coexist. Other diagnoses to take into account include pancreatitis (acute or chronic), hepatitis, dyspepsia, GERD, gastric ulcer disease, bronchopneumonia, oesophageal spasm, heart discomfort, and diabetic ketoacidosis. A thorough history and physical examination direct additional investigation [56]. The current diagnostic techniques for gallstone diseases are less invasive than previous techniques, despite the fact that gallstone incidence is substantial and only a small percentage of patients exhibit symptoms [57]. In cases of complicated cholelithiasis, a complete blood count, a liver function test, and measurements of serum lipase and amylase are advised. Cholangitis and cholecystitis can both have abnormal liver profiles. A disturbed liver profile or elevated blood lipase and amylase raise the possibility of gallstone-induced pancreatitis. A perforated or gangrenous gallbladder may be indicated by an increased total leukocyte count [58]. A variety of imaging techniques can be used to diagnose gallbladder problems, however HIDA scans and ultrasonography are the most frequently employed. Gallstones and their size, quantity, thickness of the gallbladder wall, pericholecystic fluid, and Murphy's sign-the patient's unpleasant reaction upon contact with the ultrasonographic probe—are all significant findings from ultrasonography. In almost 90% of patients who are fasting, ultrasound provides a correct diagnosis; nevertheless, in 50% of cases, stones in the common bile duct may go unnoticed [59]. Acute cholecystitis is diagnosed by hepatobiliary-iminodiacetic acid scan, which evaluates gallbladder function. It offers better than 95% accurate diagnosis in ambulatory situations. However, it may result in 30% to 40% false positive results in hospitalised patients receiving whole parentral feeding; in these situations, ultrasonography is preferred. HIDA scan results are deemed abnormal if the radioactive tracer does not visualise the gallbladder and instead travels progressively through the bile ducts or is identified as coming from the biliary system [60]. Using magnetic resonance imaging (MRCP), gallstones in the bile duct and other biliary system anomalies can be found. Although MRCP has a sensitivity of about 98%, it is solely useful for diagnosis and offers no treatment benefit for choledocholithiasis patients [60].

3. CONCLUSION

following gall bladder retrieval, instilling normal saline during a low pressure pneumoperitoneum laparoscopic cholecystectomy improves shoulder tip pain, post-operative stomach pain, and the need for further analgesic medication following the procedure.

REFERENCES

- [1] Taki-Eldin A, Badawy AE. Outcome of laparoscopic cholecystectomy in patients with gallstone disease at a secondary level care hospital. ABCD Arq Bras Cir Dig (São Paulo). 2018 (1): e1347.
- [2] Cassata G, Palumbo V, Cicero L, De Luca A, Damiano G, Fazzotta S: A New Device for Close Laparoscopy Pneumoperitoneum. SMIT. 2018;25(6):570-7.
- [3] Mahajan S, Shankar M, Garg VK, Gupta V, Sorout J. Intraoperative safety of low pressure pneumoperitoneum cholecystectomy: a comparative study. ijSurgery. 2017;4(11):3679-84.
- [4] Gohil A. Comparison of low pressure versus standard pressure pneumoperitoneum for elective laparoscopic cholecystectomy in a tertiary care institute of western India. ijSurgery. 2018;5(5):1776-80.
- [5] Hua J, Gong J, Yao L, Zhou B, Song Z. Low-pressure versus standard-pressure pneumoperitoneum for laparoscopic cholecystectomy: a systematic review and meta-analysis. AJS. 2014;208(1):143-50

- [6] Bhattacharjee HK, Jalaludeen A, Bansal V, Krishna A, Kumar S, Subramanium R. Impact of standard-pressure and low-pressure pneumoperitoneum on shoulder pain following laparoscopic cholecystectomy: a randomised controlled trial. Surg endosc. 2017;31(3):1287-95.
- [7] Choi GJ, Kang H, Baek CW, Jung YH, Kim DR. Effect of intraperitoneal local anesthetic on pain characteristics after laparoscopic cholecystectomy. WJG. 2015;21(47):13386.
- [8] Pryor A, Gracia G. Abdominal access techniques used in laparoscopic surgery. UpToDate version. 2015;22.
 - (https://www.academia.edu/download/58186213/Abdominal_access_techniques_used_in_lapar oscopic_surgery_-_UpToDate.pdf)
- [9] Esmat ME, Elsebae MM, Nasr MM, Elsebaie SB. Combined low pressure pneumoperitoneum and intraperitoneal infusion of normal saline for reducing shoulder tip pain following laparoscopic cholecystectomy. World J Surg. 2006;30(11):1969-73.
- [10]Yao L, Wang Y, Du B, Song J, Ji F. Comparison of postoperative pain and residual gas between restrictive and liberal fluid therapy in patients undergoing laparoscopic cholecystectomy. Surgical Laparoscopy, Endoscopy & Percutaneous Techniques. 2017;27(5):346-50.
- [11]Al-Shammari AJ, Alobaidi QA, Al-Faham AM. Intra-Peritoneal normal saline installation minimize post laparoscopic cholecystectomy shoulder pain in patient admitted to diwaniya teaching hospital. Indian J Public Health Res Dev. 2018;9(10):862-6.
- [12] Celarier S, Monziols S, Francois MO, Assenat V, Carles P, Capdepont M. Randomized trial comparing low-pressure versus standard-pressure pneumoperitoneum in laparoscopic colectomy: PAROS trial. Trials. 2020;21(1):1-7.
- [13] Fitzgibbons Jr RJ, Annibali R, Litke BS. Gallbladder and gallstone removal, open versus closed laparoscopy, and pneumoperitoneum. AJS. 1993;165(4):497-504.
- [14] Gohil A. Comparison of low pressure versus standard pressure pneumoperitoneum for elective laparoscopic cholecystectomy in a tertiary care institute of western India. IJS. 2018;5(5):1776-80.
- [15]Zaman M, Chowdhary K, Goyal P. Prospective randomized trial of low pressure pneumoperitoneum for reduction of shoulder tip pain following laparoscopic cholecystectomy: a comparative study. World J Lap Surg. 2015;8(1):13-5.
- [16] Barczyński M, Konturek A, Herman RM. Superiority of preemptive analgesia with intraperitoneal instillation of bupivacaine before rather than after the creation of pneumoperitoneum for laparoscopic cholecystectomy: a randomized, double-blind, placebo-controlled study. Surg Endosc. 2006;20(7):1088-93.
- [17]Saadati K, Razavi MR, Salman DN, Izadi S. Postoperative pain relief after laparoscopic cholecystectomy: intraperitoneal sodium bicarbonate versus normal saline. Gastroenterol hepatol bed bench. 2016;9(3):189-96.
- [18]Barczyński M, Herman RM. Low-pressure pneumoperitoneum combined with intraperitoneal saline washout for reduction of pain after laparoscopic cholecystectomy: a prospective randomized study. Surg Endosc. 2004;18(9):1368-73.
- [19]Salih ZM, Arif SH, Sulayvani FK. Intraperitoneal instillation of normal saline to decrease shoulder pain following laparoscopic cholecystectomy. DMJ. 2014;8(1):42-50.

- [20] Mukhtar Z, Masood HM, Akbar A, Gondal KM, Afzal A, Naveed M. Comparison of Direct Pressure versus Electrocauterization of Liver Bed for Bleeding Control in Laparoscopic Cholecystectomy. Annals of King Edward Medical University. 2021 Jul 9;27(2).
- [21]Portincasa P, Moschetta A, Petruzzelli M, Palasciano G, Di Ciaula A, Pezzolla A. Symptoms and diagnosis of gallbladder stones. Best Practice & Research Clinical Gastroenterology. 2006 Jan 1;20(6):1017-29.
- [22] Tazuma S. Epidemiology, pathogenesis, and classification of biliary stones (common bile duct and intrahepatic). Best practice & research Clinical gastroenterology. 2006 Jan 1;20(6):1075-83.
- [23]Vítek L, Carey MC. New pathophysiological concepts underlying pathogenesis of pigment gallstones. Clinics and research in hepatology and gastroenterology. 2012 Apr 1;36(2):122-9.
- [24] Stringer MD. Gallbladder and extrahepatic bile ducts. Bergman's Comprehensive Encyclopedia of Human Anatomic Variation. 2016 Jul 5:1261-71.
- [25] Housset C, Chrétien Y, Debray D, Chignard N. Functions of the Gallbladder. Compr Physiol. 2016 Jun 13;6(3):1549-77.
- [26] Mahadevan V. Anatomy of the gallbladder and bile ducts. Surgery (Oxford). 2020 Aug 1;38(8):432-6.
- [27] Sherlock S, Dooley J. Diseases of the liver and biliary system. John Wiley & Sons; 2008 Apr 15.
- [28] Wise PE, Holzman MD. Surgical anatomy of the gallbladder, liver, and biliary tree. InLaparoscopic Surgery of the Abdomen 2004 (pp. 73-86). Springer, New York, NY.
- [29]The numerous veins draining gallbladder run along the arterial twigs to the gallbladder fossa which are visible during laparoscopy if it is not grossly inflamed. Rarely if cystic vein present it drain blood from gallbladder to the right branch of portal vein
- [30]Shaffer EA. Epidemiology of gallbladder stone disease. Best practice & research Clinical gastroenterology. 2006 Jan 1;20(6):981-96.
- [31] Gleibermann L. Blood pressure and dietary salt in human populations. Ecology of food and nutrition. 1973 Jan 1;2(2):143-56.
- [32] Modlin IM, Lye KD, Kidd M. A 5-decade analysis of 13,715 carcinoid tumors. Cancer: Interdisciplinary International Journal of the American Cancer Society. 2003 Feb 15;97(4):934-59.
- [33] Reshetnyak VI. Concept of the pathogenesis and treatment of cholelithiasis. World journal of hepatology. 2012 Feb 27;4(2):18.
- [34] Reshetnyak VI. Concept of the pathogenesis and treatment of cholelithiasis. World journal of hepatology. 2012 Feb 27;4(2):18.
- [35] Bilal M, Haseeb A, Saad M, Ahsan M, Raza M, Ahmed A, Shahnawaz W, Ahmed B, Motiani V. The prevalence and risk factors of gallstone among adults in Karachi, south Pakistan: A population-based study. Glob J Health Sci. 2016;9(4):106-4.
- [36] Nakeeb A, Comuzzie AG, Martin L, Sonnenberg GE, Swartz-Basile D, Kissebah AH, Pitt HA. Gallstones: genetics versus environment. Annals of surgery. 2002 Jun 1;235(6):842-9
- [37]Konner M, Eaton SB. Paleolithic nutrition: twenty-five years later. Nutrition in Clinical Practice. 2010 Dec;25(6):594-602.
- [38]Ruiz-Núñez B, Pruimboom L, Dijck-Brouwer DJ, Muskiet FA. Lifestyle and nutritional imbalances associated with Western diseases: causes and consequences of chronic systemic low-grade

- inflammation in an evolutionary context. The Journal of nutritional biochemistry. 2013 Jul 1;24(7):1183-201.
- [39] Alsaif FA, Alabdullatif FS, Aldegaither MK, Alnaeem KA, Alzamil AF, Alabdulkarim NH, Aldohayan AD. Incidence of symptomatic cholelithiasis after laparoscopic sleeve gastrectomy and its association with rapid weight loss. Saudi Journal of Gastroenterology: Official Journal of the Saudi Gastroenterology Association. 2020 Mar;26(2):94.
- [40] Wolpers C, Hofmann AF. Solitary versus multiple cholesterol gallbladder stones. The clinical investigator. 1993 Jun;71(6):423-34.
- [41] Aishwarya VL. Association of Cholelithiasis, Choledocholithiasis and Hypothyroidism (Doctoral dissertation, Thanjavur Medical College, Thanjavur).
- [42] Guglielmi FW, Boggio-Bertinet D, Federico A, Forte GB, Guglielmi A, Loguercio C, Mazzuoli S, Merli M, Palmo A, Panella C, Pironi L. Total parenteral nutrition-related gastroenterological complications. Digestive and Liver Disease. 2006 Sep 1;38(9):623-42.
- [43] Williamson RC, Jiao LR. Open biliary operations. General Surgical Operations. 2006;4:375-96.
- [44] Tazuma S. Epidemiology, pathogenesis, and classification of biliary stones (common bile duct and intrahepatic). Best practice & research Clinical gastroenterology. 2006 Jan 1;20(6):1075-83.
- [45]BREWER GE. Differential Diagnosis in Diseases of the Gall Bladder and Ducts. The Boston Medical and Surgical Journal. 1903 May 14;148(20):526-33.
- [46]Önder A, Kapan M, Ülger BV, Oğuz A, Türkoğlu A, Uslukaya Ö. Gangrenous cholecystitis: mortality and risk factors. International surgery. 2015 Feb;100(2):254-60.
- [47] Robson AM. Lectures on Diseases of the Gall Bladder and Bile Ducts: Delivered at the Royal College of Surgeons of England. British medical journal. 1897 Mar 3;1(1889):641.
- [48] Kjaer DW, Kruse A, Funch-Jensen P. Endoscopic gallbladder drainage of patients with acute cholecystitis. Endoscopy. 2007 Apr;39(04):304-8.
- [49] Adsay NV. GALLBLADDER, EXTRAHEPATIC. Sternberg's diagnostic surgical pathology. 2004;1:1775.
- [50] Nuño-Guzmán CM, Marín-Contreras ME, Figueroa-Sánchez M, Corona JL. Gallstone ileus, clinical presentation, diagnostic and treatment approach. World journal of gastrointestinal surgery. 2016 Jan 1;8(1):65.
- [51]Bergman JJ, van der Mey S, Rauws EA, Tijssen JG, Gouma DJ, Tytgat GN, Huibregtse K. Long-term follow-up after endoscopic sphincterotomy for bile duct stones in patients younger than 60 years of age. Gastrointestinal endoscopy. 1996 Dec 1;44(6):643-9.
- [52] Adamek HE, Albert J, Weitz M, Breer H, Schilling D, Riemann JF. A prospective evaluation of magnetic resonance cholangiopancreatography in patients with suspected bile duct obstruction. Gut. 1998 Nov 1;43(5):680-3.
- [53]Pilli HP, Payala V. Infections of Biliary Tract. InGallstones-Review and Recent Progress 2021 Dec 8. IntechOpen.
- [54] Friedman GD. Natural history of asymptomatic and symptomatic gallstones. The American journal of surgery. 1993 Apr 1;165(4):399-404.
- [55] Guzman D, Abramo TJ. Sorting out problems manifested by peritoneal irritation. Clinical Pediatric Emergency Medicine. 2002 Mar 1;3(1):22-32.

- [56] Baer HU, Matthews JB, Schweizer WP, Gertsch P, Blumgart LH. Management of the Mirizzi syndrome and the surgical implications of cholecystcholedochal fistula. Journal of British Surgery. 1990 Jul;77(7):743-5.
- [57]Pidlaoan V, Krishna SG. Management of medical complications of gallstone disease. InMultidisciplinary Management of Common Bile Duct Stones 2016 (pp. 113-127). Springer, Cham.
- [58] Revzin MV, Scoutt L, Smitaman E, Israel GM. The gallbladder: uncommon gallbladder conditions and unusual presentations of the common gallbladder pathological processes. Abdominal imaging. 2015 Feb;40(2):385-99.
- [59] Dube C, Bursey RF, Champion MC, Fardy JM, Grégoire S, MacIntosh DG, Patel DG, Rostom A, Saloojee N, Scully LJ, Sekar AS. Common symptoms and signs in Gastroenterology. Thomson ABR, Shaffer EA. First principles of gastroenterology: The Basis of Disease and Approach to Managment. 5th ed. Canada: Janssen Ortho. 2011:5-11.
- [60] Attasaranya S, Fogel EL, Lehman GA. Choledocholithiasis, ascending cholangitis, and gallstone pancreatitis. Medical Clinics of North America. 2008 Jul 1;92(4):925-60.