

# Evaluation of Acalculous Cholecystitis, Diagnosis, and Management

Mohammed Jamil Addas<sup>1\*</sup>, Rashmah Mohammed Alshammari<sup>2</sup>, Abdullah Mahmoud Alokayli<sup>3</sup>, Abdalattif Kamel Bedaiwi<sup>3</sup>, Ahmed Mahmoud Ghabban<sup>4</sup>, Ali Mohammed Alasiri<sup>5</sup>, Kalil Mohammad AlKishan<sup>6</sup>, Nawaf Abdurraheem A Alhumairi<sup>7</sup>, Rasis Khalid Saleh Saber<sup>8</sup>, Ali Hanash Atef Alamri<sup>9</sup>, Amjed Naeem Alruwaili<sup>10</sup>

<sup>1</sup> Department of Medical Science, Faculty of Medicine, Jeddah University, Jeddah, Saudi Arabia. <sup>2</sup> Department of Medical Science, Faculty of Medicine, Alfaisal University, Riyadh, Saudi Arabia. <sup>3</sup> Department of Medical Science, Faculty of Medicine, Imam Mohammed Ibn Saud University, Riyadh, Saudi Arabia. <sup>4</sup> Department of Medical Science, Faculty of Medicine, Taibah University, Meddina, Saudi Arabia. <sup>5</sup> Department of Medical Science, Faculty of Medicine, Tabuk University, Tabuk, Saudi Arabia. <sup>6</sup> Department of Medical Science, Faculty of Medicine, Umm Al Qura University, Makkah, Saudi Arabia. <sup>7</sup> Department of Medical Science, Faculty of Medicine, Pavol Jozef Safarik University, Košice, Slovakia. <sup>8</sup> Department of Medical Science, Faculty of Medicine, Batterjee Medical College, Jeddah, KSA. <sup>9</sup> Emergency Department, Saudi Red Crescent Authority, Riyadh, Saudi Arabia. <sup>10</sup> Department of Emergency Medicine, King Abdullaziz Specialist Hospital, Aljouf, KSA.

## Abstract

**Background:** Around 10% of all cases of cholecystitis are related to the acalculous disease. Acalculous cholecystitis is traditionally known to occur in patients with critical illness and the symptoms may also be vague and intermittent. Therefore, diagnosing and treating such cases can be very difficult and challenging. **Objective:** In this review, we aimed to assess the published literature that discussed acalculous cholecystitis diagnosis and management. **Method:** PubMed database was used for articles selection, and the following keys were used in the MeSH ("Acalculous Cholecystitis "[Mesh]) AND ("Acalculous Cholecystitis management"[Mesh])). A total of 30 papers were reviewed and included in the review. **Conclusion:** An appropriate history, clinical findings, and laboratory data along with high suspicion index are factors needed in order to reach a correct and rapid diagnosis. These factors should be completed by imaging such as computed tomography and ultrasound. The initial step in treating acalculous cholecystitis should be antibiotics and source control. Then, cholecystectomy or drainage by percutaneous cholecystostomy can be done. Percutaneous cholecystostomy has shown a high success rate in controlling the cases of acalculous cholecystitis.

**Keywords:** Acalculous Cholecystitis, Management, Diagnosis

## INTRODUCTION

Obstruction of the biliary tract from stones is mostly the leading cause of acute cholecystitis <sup>[1]</sup>. Acute calculous cholecystitis is the second source of complicated intra-abdominal infection with a percentage of 18.5% <sup>[2, 3]</sup>. Nevertheless, around 10% of all cases of cholecystitis are related to acalculous disease <sup>[2, 4]</sup>. In this paper, we are going to review the literature that discussed acute acalculous cholecystitis.

## METHODOLOGY

PubMed database was used for articles selection, and the following keys were used in the MeSH ("Acalculous Cholecystitis "[Mesh]) AND ("Acalculous Cholecystitis management"[Mesh])). A total of 30 papers was reviewed and included in the review.

Inclusion criteria: the articles were selected according to the relevance to the project, which should include Acalculous Cholecystitis Management.

Exclusion criteria: all other articles that had no related aspect to the Acalculous Cholecystitis management as their primary endpoint or repeated studies.

## DISCUSSION

**Address for correspondence:** Mohammed Jamil Addas, Department of Medical Science, Faculty of Medicine, Jeddah University, Jeddah, Saudi Arabia.  
E-mail: mohd33.cp @ gmail.com

This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work noncommercially, as long as the author is credited and the new creations are licensed under the identical terms.

**How to cite this article:** Jamil Addas, M., Mohammed Alshammari, R., Mahmoud Alokayli, A., Kamel Bedaiwi, A., Mahmoud Ghabban, A., Mohammed Alasiri, A. and et al. Evaluation of Acalculous Cholecystitis, Diagnosis, and Management. Arch Pharma Pract 2019;10(3):17-20.

Acute acalculous cholecystitis is the inflammation of the gallbladder without the presence of gallstone<sup>[5, 6]</sup>. Acalculous cholecystitis is prevalent mostly in critically ill patients, after cardiac surgery, severe trauma, abdominal vascular surgery, sepsis or burns<sup>[5, 7, 8]</sup>. Other causes of increasing the incidence of acalculous cholecystitis can be long periods of fasting, total parenteral nutrition, and drastic weight loss. Typically, acalculous cholecystitis affects older men more than females, which have predominance in calculous cholecystitis<sup>[8]</sup>.

The main pathophysiology of the disease is the hypo-motility of the gallbladder. This stasis of the gallbladder is caused by the lack of the stimulation of gallbladder resulting in the concentration of the bile salts. Then, the intraluminal pressure within the gallbladder will rise up leading to progressive ischemia and pressure necrosis. Eventually, gangrenous changes and perforation can result from progressive ischemia and they subsequently may lead to sepsis and shock<sup>[9]</sup>.

Cases of chronic acalculous cholecystitis have more insidious presentations. Symptoms are more prolonged and may be less severe. Symptoms may also be vaguer and more intermittent, despite patients can present with signs of acute biliary colic<sup>[10, 11]</sup>.

Moreover, because of this static condition, enteric pathogens will grow, for example, *Escherichia coli*, *Klebsiella*, *Bacteroides*, *Proteus*, *Pseudomonas*, and *Enterococcus faecalis*. This colonization of bacteria will also contribute to the inflammatory response. The exact cause of chronic acalculous cholecystitis is unknown but hypokinetic biliary dyskinesia results from decreased gallbladder emptying function among chronic patients. Several other factors can cause this condition, for example, hormonal changes, vasculitis, and decreased nerve innervation as a complication caused by conditions, such as diabetes<sup>[12, 13]</sup>.

Gastrointestinal disorders and cardiac events are strictly correlated. They often coexist and the differential diagnosis can be very difficult<sup>[14]</sup>. There are some cardiovascular disorders that can be associated with a hypovolemic state, such as acute myocardial infarction or acute heart failure. As mentioned earlier, this hypovolemic state can lead to ischemic damage to the gallbladder and its inflammation. Cases of aortic dissection have been reported that coexisted with acute acalculous cholecystitis. They suggested that the triad of stasis, ischemia, and sepsis was the pathophysiology behind these cases<sup>[15]</sup>.

The presentation of acalculous cholecystitis is similar to calculous cholecystitis. There are right upper quadrant pain, fever, and a positive murphy's sign<sup>[16]</sup>. Nevertheless, in critically ill patients, the diagnosis can be more difficult than in ambulatory patients because it may have non-specific symptoms, such as symptoms of sepsis, change in mental status, and overall worsening of the clinical course<sup>[17]</sup>. In

addition, the patient sometimes cannot express his abdominal discomfort.

There can be mild elevations in the liver function tests. However, jaundice is not usually caused directly by the disease at least not in the early stages<sup>[16]</sup>. The fulminant course of this disease is mostly associated with empyema, perforation, and gangrene and also significantly higher mortality and morbidity<sup>[5, 18]</sup>. As mentioned earlier, complicated diabetes as well as major cardiovascular disorders, autoimmune disease and AIDS are common predisposing factors<sup>[4, 19, 20]</sup>.

Patients are often asymptomatic. Clinical status and examination cannot be conclusive. Moreover, laboratory data may be entirely negative, not helpful or mild positive and nonspecific especially in late stages of the disease. The diagnosis of acute acalculous cholecystitis is difficult due to the overlapping with concomitant disorders, such as cardiovascular disorders. Early diagnosis and treatment can be useful, or, in certain cases, lifesaving<sup>[15]</sup>.

As mentioned earlier, acute acalculous cholecystitis arises in 0.2–0.4% of all critically ill patients and its mortality rate is 30 %. Delayed diagnosis directly increases mortality<sup>[21]</sup>. Early detection and early intervention will result in clinical improvement and better outcomes. Ultrasound is considered a useful tool in diagnosing cholecystitis in the emergency room. It is not only useful for acute gallbladder disease, but also for other conditions causing abdominal pain, becoming fundamental in the clinical practice. Ultrasound plays a key role in the acalculous cholecystitis diagnosis. It is simple, cost-saving, safe, radiation-free and rapid<sup>[15]</sup>. To confirm the diagnosis, ultrasound imaging can be combined with cholescintigraphy plus cholecystokinin (HIDA-CCK). Nevertheless, the diagnosis can be made if the ultrasound showed a distended gallbladder with inflammation and a thickened wall even without the presence of stones<sup>[16]</sup>. A highly thickened wall or the presence of fluid around the gallbladder in the ultrasound increases the specificity of the diagnosis. Abnormal ultrasound findings can be seen in critically ill patients without having acalculous cholecystitis. Therefore, ultrasound specificity might be low in such patients<sup>[22, 23]</sup>. On the other hand, CT detects gallbladder abnormalities more accurate than ultrasound particularly in critically ill patients despite CT's lack of specificity. There are many similarities between ultrasound and CT regarding the abnormal gallbladder findings. Pneumobilia is considered a highly specific finding for diagnosing acalculous cholecystitis. It is defined as the presence of gas in the gallbladder. However, if there are no abnormal gallbladder features detected in the imaging, it is associated with a high negative predictive value that mostly will rule out the diagnosis of acalculous cholecystitis<sup>[16, 24]</sup>.

A high suspicion index, along with an appropriate history, clinical findings, and laboratory data are needed to achieve a

correct and rapid diagnosis. However, they should be completed by ultrasound imaging. Proper diagnosis allows early treatment of acute acalculous cholecystitis, which reduces the risk of mortality and complications rate [16].

### Management

The initial step in treating acalculous cholecystitis should be similar to treating other infections, i.e. antibiotics and source control. Then, cholecystectomy or drainage by percutaneous cholecystostomy should be done [16].

Intravenous antibiotics administration early plays a critical role in fighting the infection and achieving source control. There are several recommended antibiotic agents for the initial empiric treatment of acalculous cholecystitis [25]. In mild to moderate infection, ceftriaxone, cefuroxime, and cefazolin are sound options. In severe infection or high-risk factors, such as end-organ disease, immunocompromise, and advanced age, cefepime, levofloxacin, piperacillin/tazobactam, ciprofloxacin, or carbapenems, each in combination with metronidazole are the recommended options. Carbapenems or piperacillin/tazobactam, each in combination with metronidazole are the advised options in patients with extended-spectrum beta-lactamase (ESBL)-producing organisms. The duration of antibiotic therapy is related to the control of the source and can be stopped 4-5 days after source control is achieved [25, 26].

Cholecystectomy was the historic treatment of acalculous cholecystitis because of the need to resect or debride the gallbladder in cases of gangrene or perforation [27-29]. However, minimally invasive alternatives, such as percutaneous cholecystostomy are now the recommended approach, especially for unstable patients [27, 30, 31].

The percutaneous cholecystostomy tube should be placed by the interventional radiologist to secure the drainage of the gallbladder [16]. Compared to open cholecystectomy, percutaneous cholecystostomy has shown lower morbidity, fewer admissions in the intensive-care unit, decreased length of stays, and lower costs [32]. Percutaneous cholecystostomy controls acalculous cholecystitis in more than 85% of the patients [33-35]. Moreover, the overall rate of complications of percutaneous cholecystostomy is approximately 2%, which is considered low especially that it is mostly used in critically ill patients [36, 37]. In percutaneous cholecystostomy, the gallbladder is usually intubated under laparoscopic or sonographic control by an anterolateral or anterior trans-hepatic approach to minimize bile leakage. A trans-peritoneal puncture can also be used. If percutaneous cholecystostomy is successful, rapid improvement is expected [27]. In addition, the percutaneous drain might be removed eventually in improved patients, which helps these patients to live comfortably without the burden of the drain and its care [16].

### CONCLUSION

An appropriate history, clinical findings, and laboratory data along with high suspicion index are factors needed in order to reach a correct and rapid diagnosis. These factors should be completed by imaging such as computed tomography and ultrasound.

The initial step in treating acalculous cholecystitis should be antibiotics and source control. Then, cholecystectomy or drainage by percutaneous cholecystostomy can be done. Percutaneous cholecystostomy has shown a high success rate in controlling cases of acalculous cholecystitis. Successful percutaneous cholecystostomy is associated with very good outcomes and rapid improvement.

### REFERENCES

1. Bridges F, Gibbs J, Melamed J, Cussatti E, White S. Clinically diagnosed cholecystitis: a case series. *Journal of surgical case reports*. 2018 Feb 28;2018(2):rjy031.
2. Gomes CA, Junior CS, Di Saveiro S, Sartelli M, Kelly MD, Gomes CC, Gomes FC, Corrêa LD, Alves CB, de Fadel Guimarães S. Acute calculous cholecystitis: Review of current best practices. *World journal of gastrointestinal surgery*. 2017 May 27;9(5):118.
3. Sartelli M, Abu-Zidan FM, Catena F, Griffiths EA, Di Saverio S, Coimbra R, Ordoñez CA, Leppaniemi A, Fraga GP, Coccolini F, Agresta F. Global validation of the WSES Sepsis Severity Score for patients with complicated intra-abdominal infections: a prospective multicentre study (WISS Study). *World journal of emergency surgery*. 2015 Dec;10(1):61.
4. Barie PS. Acute acalculous cholecystitis. *J Am Coll Surg.* 1995;180:232-44.
5. Ganpathi IS, Diddapur RK, Eugene H, Karim M. Acute acalculous cholecystitis: challenging the myths. *Hpb*. 2007 Apr 1;9(2):131-4.
6. Rouieentan A, Nadri S, Niazi M, Mahmoudvand H. Comparing Complications of Open and Laparoscopic Cholecystectomy in Patients with Acute Cholecystitis in Western Iran. *Entomology and Applied Science Letters*. 2018 Jun 23;5(2):16-21.
7. McChesney JA, Northup PG, Bickston SJ. Acute acalculous cholecystitis associated with systemic sepsis and visceral arterial hypoperfusion: a case series and review of pathophysiology. *Digestive diseases and sciences*. 2003 Oct 1;48(10):1960-7.
8. Kalliafas S, Ziegler DW, Flancbaum L, Choban PS. Acute acalculous cholecystitis: incidence, risk factors, diagnosis, and outcome. *The American Surgeon*. 1998 May 1;64(5):471.
9. Jones MW, Ferguson T. *Acalculous Cholecystitis*. 2019.
10. Yi DY, Chang EJ, Kim JY, Lee EH, Yang HR. Age, predisposing diseases, and ultrasonographic findings in determining clinical outcome of acute acalculous inflammatory gallbladder diseases in children. *Journal of Korean medical science*. 2016 Oct 1;31(10):1617-23.
11. Le BB. Pathology of gallbladder and extrahepatic bile ducts. Case 1. Acalculous gangrenous cholecystitis. In *Annales de pathologie* 2014 Aug (Vol. 34, No. 4, pp. 271-278).
12. Walsh K, Goutos I, Dheansa B. Acute acalculous cholecystitis in burns: a review. *Journal of Burn Care & Research*. 2018 Feb 9;39(5):724-8.
13. Thampy R, Khan A, Zaki IH, Wei W, Korivi BR, Staerkel G, Bathala TK. Acute Acalculous Cholecystitis in Hospitalized Patients With Hematologic Malignancies and Prognostic Importance of Gallbladder Ultrasound Findings. *Journal of Ultrasound in Medicine*. 2019 Jan;38(1):51-61.
14. Manisty C, Hughes-Roberts Y, Kaddoura S. Cardiac manifestations and sequelae of gastrointestinal disorders. *British journal of cardiology*. 2009;16(4).
15. Tana M, Tana C, Cocco G, Iannetti G, Romano M, Schiavone C. Acute acalculous cholecystitis and cardiovascular disease: a land of confusion. *Journal of ultrasound*. 2015 Dec 1;18(4):317-20.
16. Balmadrid B. Recent advances in management of acalculous cholecystitis. *F1000Research*. 2018;7.

17. Ryu JK, Ryu KH, Kim KH. Clinical features of acute acalculous cholecystitis. *Journal of clinical gastroenterology*. 2003 Feb 1;36(2):166-9.
18. Johnson LB. The importance of early diagnosis of acute acalculus cholecystitis. *Surgery, gynecology & obstetrics*. 1987 Mar;164(3):197-203.
19. Kamimura T, Mimori A, Takeda A, Masuyama J, Yoshio T, Okazaki H, Kano S, Minota S. Acute acalculous cholecystitis in systemic lupus erythematosus: a case report and review of the literature. *Lupus*. 1998 Jun;7(5):361-3.
20. Iannuzzi C, Belgithi J, Erlinger S, Menu Y, Fékété F. Cholangitis associated with cholecystitis in patients with acquired immunodeficiency syndrome. *Archives of Surgery*. 1990 Sep 1;125(9):1211-3.
21. Huffman JL, Schenker S. Acute acalculous cholecystitis: a review. *Clinical Gastroenterology and Hepatology*. 2010 Jan 1;8(1):15-22.
22. Pinto A, Reginelli A, Cagini L, Coppolino F, Ianora AA, Bracale R, Giganti M, Romano L. Accuracy of ultrasonography in the diagnosis of acute calculous cholecystitis: review of the literature. *Critical ultrasound journal*. 2013 Dec 1;5(S1):S11.
23. Boland GW, Slater G, Lu DS, Eisenberg P, Lee MJ, Mueller PR. Prevalence and significance of gallbladder abnormalities seen on sonography in intensive care unit patients. *American Journal of Roentgenology*. 2000 Apr;174(4):973-7.
24. Ahvenjarvi L, Koivukangas V, Jartti A, Ohtonen P, Saarnio J, Syrjala H, Laurila J, Ala-Kokko T. Diagnostic accuracy of computed tomography imaging of surgically treated acute acalculous cholecystitis in critically ill patients. *Journal of Trauma and Acute Care Surgery*. 2011 Jan 1;70(1):183-8.
25. Solomkin JS, Mazuski JE, Bradley JS, Rodvold KA, Goldstein EJ, Baron EJ, O'Neill PJ, Chow AW, Dellinger EP, Eachempati SR, Gorbach S. Diagnosis and management of complicated intra-abdominal infection in adults and children: guidelines by the Surgical Infection Society and the Infectious Diseases Society of America. *Surgical infections*. 2010 Feb 1;11(1):79-109.
26. Sawyer RG, Claridge JA, Nathens AB, Rotstein OD, Duane TM, Evans HL, Cook CH, O'Neill PJ, Mazuski JE, Askari R, Wilson MA. Trial of short-course antimicrobial therapy for intraabdominal infection. *New England Journal of Medicine*. 2015 May 21;372(21):1996-2005.
27. Barie PS, Eachempati SR. Acute acalculous cholecystitis. *Gastroenterology Clinics*. 2010 Jun 1;39(2):343-57.
28. Glenn FR, Becker CG. Acute acalculous cholecystitis. An increasing entity. *Annals of surgery*. 1982 Feb;195(2):131.
29. Hashemian M, Jourian J, Lashkarizadeh MR. Comparing the effects of clonidine and pregabalin on postoperative shivering and pain in patients undergoing laparoscopic cholecystectomy. *Pharmacophore*. 2017 Jan 1;8(4):76-81.
30. Granlund A, Karlson BM, Elvin A, Rasmussen I. Ultrasound-guided percutaneous cholecystostomy in high-risk surgical patients. *Langenbeck's archives of surgery*. 2001 Apr 1;386(3):212-7.
31. Davis CA, Landercasper J, Gundersen LH, Lambert PJ. Effective use of percutaneous cholecystostomy in high-risk surgical patients: techniques, tube management, and results. *Archives of Surgery*. 1999 Jul 1;134(7):727-32.
32. Simorov A, Ranade A, Parcells J, Shaligram A, Shostrom V, Boilesen E, Goede M, Oleynikov D. Emergent cholecystostomy is superior to open cholecystectomy in extremely ill patients with acalculous cholecystitis: a large multicenter outcome study. *The American Journal of Surgery*. 2013 Dec 1;206(6):935-41.
33. Akhan O, Akinci D, Özmen MN. Percutaneous cholecystostomy. *European journal of radiology*. 2002 Sep 1;43(3):229-36.
34. Lee MJ, Saini S, Brink JA, Hahn PF, Simeone JF, Morrison MC, Rattner D, Mueller PR. Treatment of critically ill patients with sepsis of unknown cause: value of percutaneous cholecystostomy. *AJR*. *American journal of roentgenology*. 1991 Jun;156(6):1163-6.
35. VanSonnenberg E, D'Agostino HB, Goodacre BW, Sanchez RB, Casola G. Percutaneous gallbladder puncture and cholecystostomy: results, complications, and caveats for safety. *Radiology*. 1992 Apr;183(1):167-70.
36. Noh SY, Gwon DI, Ko GY, Yoon HK, Sung KB. Role of percutaneous cholecystostomy for acute acalculous cholecystitis: clinical outcomes of 271 patients. *European radiology*. 2018 Apr 1;28(4):1449-55.
37. Kirkegård J, Horn T, Christensen SD, Larsen LP, Knudsen AR, Mortensen FV. Percutaneous cholecystostomy is an effective definitive treatment option for acute acalculous cholecystitis. *Scandinavian Journal of Surgery*. 2015 Dec;104(4):238-43.