

Gallbladder and common bile duct actinomycosis: a comprehensive systematic review of literature

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Abstract

Gallbladder actinomycosis is a rare chronic bacterial infection caused by *Actinomyces* species, most commonly *Actinomyces israelii*. It is often diagnosed incidentally due to its nonspecific clinical presentation and unclear incidence. This systematic review aims to summarize the clinical presentation, diagnosis, and management of gallbladder and bile duct actinomycosis. A systematic literature search was conducted in Google Scholar to identify English-language studies reporting actinomycosis involving the gallbladder or bile duct on September 18, 2025. Studies describing the clinical presentation, diagnosis, and management of biliary actinomycosis were included. Studies involving other organs, review articles, editorials, conference abstracts without sufficient clinical data, non-English publications, and articles published in predatory journals were excluded. Data were extracted and analyzed descriptively according to PRISMA 2020 guidelines. Twenty-four studies reporting 25 patients were included. The mean age of the patients was 60.7 years, with 14 males (56%) and 11 females (44%). Isolated right upper quadrant pain was reported in 9 patients (36%). The gallbladder was the most commonly involved site in 20 patients (80%), followed by the common bile duct in 3 patients (12%), with combined gallbladder and common bile duct involvement and cystic duct remnant involvement in 1 patient each (4%). Acute cholecystitis was the most frequent initial diagnosis in 9 patients (36%). Surgical management, with or without adjunctive medical therapy, was the primary treatment modality in 23 patients (92%). Histopathological examination consistently demonstrated filamentous, Gram-positive branching bacilli in all 25 patients (100%). Gallbladder actinomycosis is rare and difficult to diagnose preoperatively. Histopathology confirms the diagnosis in most cases, and early recognition allows management with surgery and prolonged antibiotic therapy, which was associated with favourable outcomes.

Key words: actinomyces; actinomycosis; gallbladder; bile duct; cholecystitis.

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Introduction

Actinomycosis is a chronic infection caused by bacteria of the *Actinomyces* genus. These filamentous, Gram-positive, non-acid-fast, anaerobic organisms are part of the normal human flora.¹ *Actinomyces israelii* is the species most frequently identified.² Other species of *Actinomyces* that can cause the infection include *Actinomyces gerencseriae*, *Actinomyces naeslundii*, *Actinomyces viscosus*, *Actinomyces odontolyticus*, and *Actinomyces meyeri*.³ Although *Actinomyces* species are normal commensals, they can cause severe invasive disease under predisposing conditions. The infection most commonly involves the cervicofacial, respiratory, gastrointestinal and genitourinary organs.⁴ The global incidence of actinomycosis has been generally declining, except for abdominopelvic cases, which are slightly increasing. This rise is likely due to

more abdominal surgeries and trauma. Moreover, prolonged use of intrauterine contraceptive devices (IUDs) in females may increase the risk of infection.³ Less than one-third of cases involve the abdominopelvic region, with the infection most often occurring in the ileocecal area. Gallbladder involvement is extremely rare, and the infection is usually considered secondary to appendicitis, although it may also arise from a perforated intestinal ulcer or blunt abdominal trauma. Another possible route of infection is retrograde spread from the duodenum via the common bile duct or dissemination through the bloodstream.^{5,6} Gallbladder actinomycosis is most often identified incidentally during histopathological examination, accounting for approximately 5% of abdominal cases with involvement of the hepatobiliary system. Due to this rare occurrence, the true incidence has not been well established and remains unclear. Fewer than 1% of all actinomycosis cases have been reported to involve the gallbladder.^{1,4} Disruption of the mucosal barrier by trau-

ma, surgery, or infection permits tissue invasion, producing suppurative lesions that may progress to abscesses, sinus tracts, or a granulomatous reaction. Their discharge contains small yellowish “sulfur” granules. These granules are not confined to hepatic actinomycosis but occur throughout hepatobiliary actinomycosis, including gallbladder and common bile duct involvement; because most *Actinomyces* species do not survive in bile, their presence in biliary tissue indicates invasive infection rather than colonization, making histopathological demonstration the diagnostic hallmark.^{2,3} This study aims to systematically review the literature on biliary actinomycosis, a rare condition with uncertain incidence, to improve understanding of its presentation, diagnosis, and management.

Methods

Study protocols

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines.

Data sources and search strategy

A comprehensive literature search was conducted using the ‘Google Scholar’ to identify relevant English-language studies on actinomycosis involving the gallbladder and bile ducts, on September 18th, 2025. The search strategy included the following terms: “Actinomyces” OR “Actinomycosis” AND “Gallbladder” OR “Bile Duct” OR “Cholecystitis.” Boolean operators (AND, OR) were applied to optimize the search results. No restrictions were placed on the publication date.

Eligibility criteria

This systematic review included studies reporting at least one case of actinomycosis involving the gallbladder or bile duct. Eligible study designs comprised case reports and case series describing the clinical presentation, diagnosis, management, or outcomes of biliary actinomycosis. Studies were excluded if they involved actinomycosis affecting organs other than the gallbladder or bile duct, were review articles, editorials, were not published in the English language, or were published in non-recommended journals, as determined by cross-checking the journal against recognized lists of non-recommended publications.

Study selection and data extraction

Prior to full-text eligibility assessment, the titles and abstracts of all identified studies were independently screened to determine their relevance. Full texts of potentially eligible articles were subsequently reviewed in detail according to the predefined inclusion and exclusion criteria. The extracted variables included the author(s), year of publication, number of reported cases, patient age and sex, anatomical site, clinical presentation, past medical history, laboratory investigations, radiological findings, management approach, histopathological examination findings, and postoperative treatment, including follow-up data.

Data presentation

The collected data were organized in an Excel spreadsheet (Microsoft Excel, 2021) and analyzed descriptively using the Statistical Package for the Social Sciences (SPSS, version 27.0). Key results are presented as means, frequencies, and percentages.

Results

Study selection

A total of 44 records were identified through the systematic search. Eighteen records were removed before screening: 4 non-English publications, 2 available as abstracts only, and 12 for which the full text was not accessible. The titles and abstracts of the remaining 26 records were screened, and 1 was excluded as irrelevant. The full texts of the remaining 25 records were then assessed, of which 1 was excluded because it had been published in a non-recommended journal. All 24 remaining studies met the eligibility criteria, and none were excluded at this stage. This led to a final cohort of 24 studies (23 case reports and 1 case series). The PRISMA flow diagram, which illustrates the entire study selection process, is shown in Figure 1.

Characteristics of the included studies

The majority of studies included in this systematic review were case reports. A total of 25 patients were included in this study. Of these, 14 (56%) were male and 11 (44%) were female. The mean age of the patients was 60.7 years, with the age of one patient unknown. Among the 24 included studies, the United States contributed 6 (25.0%), followed by the United Kingdom and India with 3 each (12.5%). The past medical history of the patients varied. Eight patients (32%) had an unknown history, while 5 (20%) reported no prior medical conditions. Diabetes mellitus was present in 8 patients (32%), and hypertension in 4 patients (16%). Regarding clinical presentation, patients were distributed across three categories: 9 (36%) presented with isolated right upper quadrant (RUQ) pain, 7 (28%) with RUQ pain accompanied by other symptoms, and 9 (36%) with non-RUQ presentations (Table S1).

Main findings

According to laboratory findings, among patients with available data, hepatobiliary dysfunction was the predominant abnormality, observed in 10 patients (40%), most commonly as a cholestatic pattern (elevated ALP and/or GGT). Pancreatic enzyme elevations were rare (1 patient, 4%), as was viral hepatitis (1 patient, 4%), and interpretation was limited by the high proportion of missing data. Regarding the imaging findings, Uncomplicated acute cholecystitis was the most frequent radiological finding, reported in 9 patients (36%), followed by a gallbladder mass or lesion suspicious for carcinoma in 5 (20%), complicated cholecystitis in 4 (16%), and common bile duct stones or biliary obstruction in 3 (12%). The gallbladder was the most commonly involved site, affected in isolation in 20 patients (80%), followed by isolated common bile duct involvement in 3 patients (12%). One patient (4%) had combined gallbladder and common bile duct involvement, and 1 patient (4%) had actinomycosis of a cystic duct remnant. Acute cholecystitis, in 9 patients (36%), was the most frequent initial diagnosis, followed by gallbladder carcinoma in 3 patients (12%) (Table S2).

Regarding the management approach, surgical management with or without concomitant medical treatment was the main treatment modality, performed in 23 patients (92%). In comparison, 1 patient (4%) underwent interventional procedures, and only 1 patient (4%) received medical treatment alone. Among the surgical group, cholecystectomy with an unspecified approach was performed in 6 patients (26.1% of total surgical cases), while open cholecystectomy was performed in 4 patients (17.4% of total surgical cases) (Table S3).

Postoperatively, β -lactam-based therapy (either alone or in combination) was the most commonly administered regimen, given in 12

patients (48%). The histopathological examination predominantly demonstrated filamentous, Gram-positive branching bacilli in all 25 patients (100%). This was followed by sulfur granules, which were observed in 16 patients (64%). The majority of patients (18; 72%) experienced an uneventful course or complete recovery (Table S4).

Discussion

Actinomycosis is caused by *Actinomyces* species, which are Gram-positive filamentous bacteria that were historically misidentified as fungi. The most commonly pathogenic species in humans are *Actinomyces israelii*, followed by *Actinomyces naeslundii*, *Actinomyces odontolyticus*. These bacteria are normally part of the oral cavity flora and, to a lesser extent, the gastrointestinal tract. They are typically of low virulence and need a breach of the mucosal barrier to invade deeper tissues and cause infection.¹⁶

In this cohort, right upper quadrant pain was the dominant presenting symptom (16 patients, 64%), the gallbladder was the most commonly affected site, and diabetes mellitus was the most frequently documented comorbidity. These patterns are illustrated by cases such as those of Mir *et al.*¹⁶ and Akbarzadeh-Jahromi *et al.*,¹⁷ in which right upper quadrant pain was accompanied by fever, nau-

sea, and jaundice, and mucosal disruption from gallstones or diabetes was proposed as a predisposing factor.

As emphasized by Ormsby *et al.*,¹⁸ accurate preoperative diagnosis of gallbladder actinomycosis is challenging, with only a few cases diagnosed prior to surgery. In almost all reported instances, actinomycosis was not suspected before the operation. Two patients were exceptions, in whom the organism was identified on endoscopic biopsy before or instead of surgery. This highlights the need to maintain a higher index of suspicion in atypical presentations. These findings are consistent with the results of the present study, in which just over a third of cases were preoperatively diagnosed as acute cholecystitis, while a few were diagnosed as carcinoma or chronic cholecystitis.

Elevated ALP levels were also observed in this systematic review, supporting the finding that hepatobiliary dysfunction is the predominant abnormality. This has been demonstrated by both Lee *et al.*¹⁹ and Han *et al.*,²⁰ who reported that despite the clinical and laboratory findings being generally nonspecific and the condition remaining a diagnostic challenge, elevated alkaline phosphatase levels were observed in affected patients.

Radiographic diagnosis of gallbladder actinomycosis remains inconclusive, as there are no distinct imaging features. The infection does not respect tissue planes, invades adjacent structures, and elicits

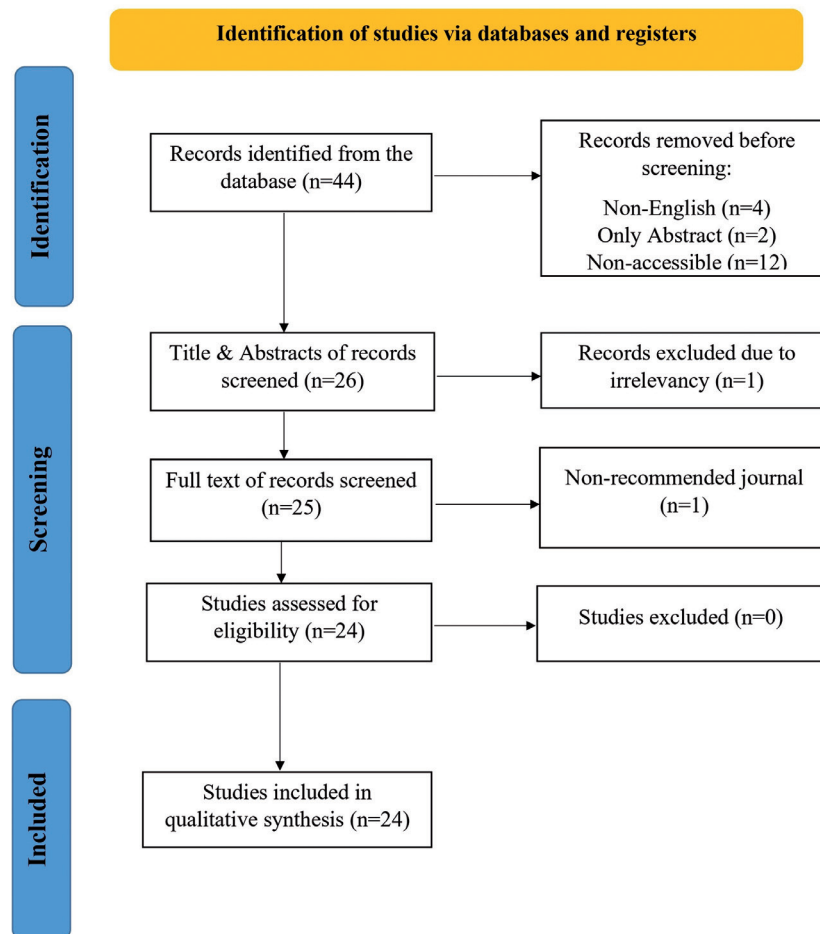


Figure 1. Study selection PRISMA flow chart.

a fibrotic reaction, producing tumor-like lesions that can be mistaken for carcinoma.^{22,23} In this systematic review, imaging most often showed features of acute cholecystitis, while a gallbladder mass mimicking carcinoma was reported in one fifth of patients.

Most actinomycete species do not survive in bile salts, with the exception of certain strains of *Actinomyces naeslundii*. This highlights that the presence of sulfur granules in the gallbladder generally indicates invasive infection rather than mere colonization.¹⁷ According to this review, these granules are the second most frequently observed histopathological finding, after the filamentous, Gram-positive, branching bacilli. Other features that have been reported include chronic inflammatory changes, micro abscess formation, and granulomas.

Cholecystectomy followed by prolonged antibiotic therapy was the predominant management strategy in this review (23 patients, 92%), as exemplified by Akbarzadeh-Jahromi *et al.*,¹⁸ although the antibiotic regimen and duration were unspecified in several reports.

The increased vascularity and tissue thickening following actinomycosis infection raises the necessity for a long-term course of high-dose antibiotic treatment. Among the beta-lactams, penicillin is the drug of choice for all actinomycotic infections, including gallbladder actinomycosis. After surgical removal of the infected organ, antibiotic therapy should be initiated within 1-14 days postoperatively and continued for a period of 6 to 12 months.²⁴ In line with this approach, the majority of patients in this systematic review received beta-lactams alone or in combination, mostly in the form of penicillin, with a treatment duration of around 3 to several months in some cases. However, a few studies employed shorter courses of antibiotics, lasting less than 3 months.

An uneventful course or complete recovery was documented in 18 patients (72%), including the case of Sullivan *et al.*,²⁴ in whom preoperative symptoms resolved completely.

This systematic review has several limitations. First, the available evidence is limited to case reports and small case series, which restricts the ability to draw strong causal inferences and limits the generalizability of the findings. Second, full texts of 14 potentially relevant reports could not be obtained, as institutional subscription and interlibrary loan access were unavailable. Third, the overall sample size was small due to the rarity of gallbladder and bile duct actinomycosis. Fourth, several studies had incomplete clinical, laboratory, imaging, and follow-up data, which limited the ability to perform more detailed analyses. Finally, one limitation of this review is that the search was conducted in Google Scholar alone; the search string and number of records screened are reported in full to permit the closest possible approximation.

Conclusions

Gallbladder actinomycosis is a rare but clinically significant cause of biliary disease. Preoperative diagnosis remains challenging because of nonspecific clinical, laboratory, and radiological findings, and it may mimic gallbladder carcinoma. Definitive diagnosis rests on demonstration of the organism, usually by histopathological identification of filamentous bacteria and occasionally by culture; sulfur granules support the diagnosis but are not required. This review underscores the importance of maintaining a high index of suspicion in patients with predisposing factors, as timely recognition and management with cholecystectomy and appropriate antibiotic therapy are associated with favorable outcomes.

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Online supplementary material:

Table S1. Demographic data of the included studies.

Table S2. Laboratory findings, imaging findings and radiological classification, and anatomical site of involvement.

Table S3. Management and outcome.

Table S4. Summary of patient-level variables.

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