

Bile aspiration during ERCP in acute cholangitis

ALRAEINI A. A. T*, CHERKAOUI MALKI M, MECHHOR S, BENZZOUBEIR N, ERRABIH I and EL BACHA H

Hepato-gastro-enterology and proctology department (medicine B) - Ibn Sina university hospital center, Mohammed V University - Rabat – Morocco.

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Abstract

Background: Acute cholangitis is a biliary infection treated with antibiotics and biliary decompression, mainly via ERCP. Bile aspiration can identify pathogens but is not always recommended due to limited data. This study evaluated its clinical benefit.

Materials and Methods: We retrospectively included patients undergoing ERCP with bile aspiration for acute cholangitis (Jan 2023–Jul 2024). Data on clinical, biological, and bacteriological parameters were collected. The primary outcome was antibiotic adjustment based on bile cultures; secondary outcomes included hospital stay, 30-day recurrence, and mortality.

Results: Fifty-seven patients were included (mean age 61.6 ± 13.1 years; 56.1% female). ERCP indications were neoplasia (43.9%) and lithiasis (38.6%). Bile cultures were positive in 68.4%, mainly *Escherichia coli* and *Pseudomonas* spp. Antibiotic therapy was adjusted in 48.7% of patients; 26.3% were resistant to empirical therapy, while in 17.5% of sensitive cases therapy was changed to narrower-spectrum or switched to oral antibiotics. Prior biliary sphincterotomy was the only significant predictor of resistance (OR 11.7, $p = 0.047$). Mean hospital stay was 10 days; 30-day recurrence and mortality rates were 5% and 3.5%, respectively.

Conclusion: Bile aspiration during ERCP detected pathogens in two-thirds of cases and guided antibiotic adjustment in nearly half, improving management and allowing narrower-spectrum or oral therapy. Routine bile cultures are recommended, especially for patients undergoing repeated ERCP.

Keywords: Acute Cholangitis; Endoscopic Retrograde Cholangiopancreatography; Bile Culture; Antibiotics

1. Introduction

Acute cholangitis is an infection of the bile ducts, usually secondary to an obstruction, most commonly due to biliary stones, and can lead to severe sepsis. Blood cultures and bile aspiration cultures are the primary methods for identifying the pathogens responsible for acute cholangitis.

Under normal physiological conditions, the bile ducts are sterile. Any disruption of these physiological barriers can result in bile duct infection. In most cases, the source of infection originates from the duodenum, followed by hematogenous dissemination through the bloodstream [1].

Blood cultures performed before the start of antibiotic therapy have low sensitivity [2] [3]. However, bile cultures often identify the causative pathogens and frequently reveal polymicrobial growth, particularly in patients with an indwelling

* Corresponding author: ALRAEINI A. A. T

biliary stent [5]. This is consistent with the ascent of polymicrobial intestinal flora from the duodenum into the biliary tree, resulting in ascending cholangitis.

The initiation of empirical antibiotic therapy carries a risk of under-treatment or inadequate coverage due to increasing resistance to empirical regimens [6]. Identifying the causative pathogen is often challenging because of the low sensitivity of blood cultures. Bile aspiration is commonly performed for bacteriological analysis, and this method has demonstrated microbiological efficacy. However, it is not systematically performed and is not always mentioned in guidelines due to limited data on its clinical relevance.

The aim of this study was to evaluate the relevance and therapeutic impact of bile sampling during ERCP in patients with acute cholangitis.

2. Materials and Methods

A retrospective monocentric study was conducted between January 2023 and July 2024 in our interventional endoscopy unit at the Hepato-Gastroenterology Department (Medicine B), Ibn Sina university hospital center, Mohammed V University, Rabat, Morocco. All patients hospitalized for acute cholangitis diagnosed according to the Tokyo criteria and who underwent ERCP with bile aspiration were included. Data were collected on clinical, biological, and bacteriological parameters. Patients with missing data regarding clinical evolution, biological follow-up, bacteriological results, or antibiotic therapy were excluded.

The collected data included: date of admission, age, sex, smoking status, medical and surgical history, prior sphincterotomy, presence of a biliary stent, performance of sphincterotomy, placement of a biliary stent during ERCP, date of bile cultures and bacteriological results, type of empirical antibiotic therapy, time from admission to ERCP, total duration of antibiotic therapy, length of hospital stay, 30-day recurrence of cholangitis, and mortality rate.

Bile for culture was collected using a biliary catheter immediately after obtaining biliary access. Biliary cannulation was performed with a sphincterotome; the first 5 mL of bile aspirate were discarded, and the subsequent 3–4 mL was collected using a separate syringe. Samples were cultured for both aerobic and anaerobic growth.

2.1. Judgment Criteria

The primary judgment criterion was the concordance between the empirical antibiotic administered and the results of the antibiogram. Secondary judgment criteria included the assessment of hospital stay duration, mortality rate, and 30-day recurrence of cholangitis.

2.2. Statistical Analysis

Continuous variables were reported as means with standard deviations or as medians with interquartile ranges. Predictive factors were analyzed using logistic regression, with a p-value < 0.05 considered statistically significant. All analyses were performed using Jamovi software, version 2.3.28.

The study protocol was approved by the ethics committee.

3. Results

3.1. Demographic and clinical characteristics of patients

Our study included 57 patients. The mean age was 61.6 ± 13.1 years, and 56.1% were female. Diabetes was present in 19.3% of cases. According to the Tokyo classification, acute cholangitis severity was grade I in 21.1%, grade II in 56.1%, and grade III in 22.8% of patients. Regarding the etiology of cholangitis, neoplasia accounted for 43.9%, lithiasis for 38.6%, and other causes for 17.6% of cases. Additionally, 14% of patients had a history of prior biliary sphincterotomy (Table 1).

Table 1 Demographic and Clinical Characteristics of Patients

Variables	Observations (n = 57)
Age, mean (SD)	61.6 (13.1)
Male, n (%)	25 (43.9%)
Female, n (%)	32 (56.1%)
Diabetes, n (%)	11 (19.3%)
Symptoms, n (%)	
Fever	42 (73.7%)
Jaundice	57 (100%)
Abdominal pain	47 (82.5%)
Charcot's triad, n (%)	37 (65%)
Cholangitis grade (Tokyo classification 2018), n (%)	
Grade I	12 (21.1%)
Grade II	32 (56.1%)
Grade III	13 (22.8%)
Etiology of cholangitis, n (%)	
Neoplasia *	25 (43.9%)
Lithiasis	22 (38.6%)
Sclerosing cholangitis	4 (7.0%)
Cystic echinococcosis	3 (5.3%)
Non-tumoral stenosis	2 (3.5%)
Hepatic abscess	1 (1.8%)
Prior biliary sphincterotomy, n (%)	8 (14%)
Biliary stent in place, n (%)	7 (12.3%)

* Pancreatic tumors, cholangiocarcinomas, liver metastases, duodenal tumors, gallbladder tumor

4. Management

All patients received empirical antibiotic therapy upon admission. The empirical antibiotics were a combination of third-generation cephalosporins and metronidazole in 49 (85.9%) cases, amoxicillin/clavulanic acid in 4 (7%) cases, a combination of ciprofloxacin and metronidazole in 2 (3.5%) cases, imipenem/cilastatin in 2 (3.5%) cases, and a combination of ceftazidime and vancomycin in 1 (1.75%) case. The mean time from admission to ERCP was 2.95 ± 1.62 days.

4.1. Bacteriological Results of Bile Culture

Bile cultures were negative in 18 (32%) cases and positive in 39 (68%) cases (**Figure 1**). The main pathogens identified in positive samples were *Escherichia coli* in 30.7% of cases, *Pseudomonas aeruginosa* in 25.6%, Gram-positive bacteria (*Enterococcus* and *Streptococcus*) in 20.4%, *Enterobacter* in 12.8%, *Klebsiella pneumoniae* in 12.8%, other bacteria in 17.9%, and polymicrobial infections in 12.3%. A combination of Gram-negative and Gram-positive bacteria was observed in 1 case (*E. coli* and *Enterococcus faecalis*) (**Table 2**).

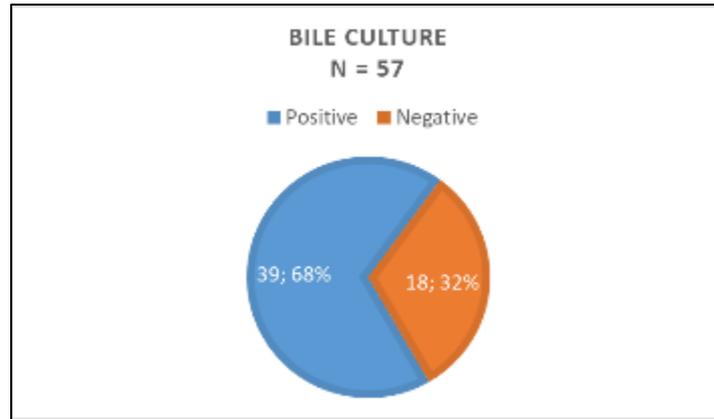


Figure 1 Bile Fluid Culture Results

Table 2 Pathogens Identified in Bile Culture

Identified Pathogens N = 39 (%)	
<i>Escherichia coli</i>	12 (30.7%)
<i>Pseudomonas aeruginosa</i>	10 (25.6%)
<i>Klebsiella pneumoniae</i>	5 (12.8%)
<i>Enterococcus faecalis</i>	4 (15.3%)
<i>Enterococcus faecium</i>	1 (2.56%)
<i>Enterococcus gallinarum</i>	1 (2.56%)
<i>Enterobacter hormaechei</i>	2 (5.12%)
<i>Enterobacter cloacae</i>	1 (2.56%)
<i>Enterobacter spp</i>	2 (5.12%)
<i>Providencia rettgeri</i>	1 (2.56%)
<i>Providencia alcalifaciens</i>	1 (2.56%)
<i>Proteus mirabilis</i>	1 (2.56%)
<i>Pseudomonas mosselii</i>	1 (2.56%)
<i>Pseudomonas putida</i>	1 (2.56%)
<i>Streptococcus mitis</i>	1 (2.56%)
<i>Streptococcus species</i>	1 (2.56%)
<i>Stenotrophomonas maltophilia</i>	1 (2.56%)
<i>Acinetobacter baumannii</i>	1 (2.56%)
Polymicrobial	7 (12.3%)

4.2. Antibiogram results and antibiotic therapy modification based on bile culture

Antibiotic susceptibility testing showed that bile pathogens were sensitive to empirical antibiotics in 51.3% of cases and resistant in 48.7% of cases.

A modification of antibiotic therapy based on the bile antibiogram was performed in 26.3% of patients with resistant pathogens, among whom 9 patients had experienced clinical deterioration, while no antibiotic change was made in 4 patients due to clinical and biological improvement.

Furthermore, in cases where pathogens were sensitive, antibiotic therapy was occasionally adjusted, allowing a switch to narrower-spectrum or oral antibiotics in 10/57 (17.54%) cases (Figure 2).

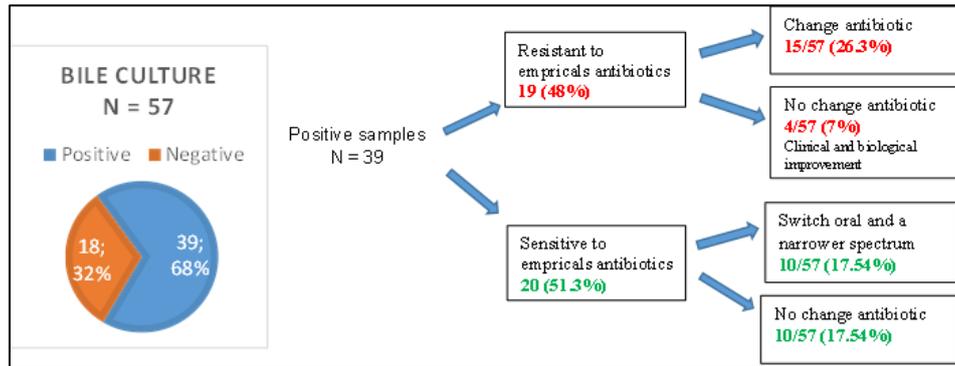


Figure 2 Antibiogram results and antibiotic therapy modifications based on antibiogram findings

In our study, the mean duration of antibiotic therapy was 13 ± 3 days, the mean hospital stay was 9.45 ± 3.75 days, the 30-day recurrence rate was 5%, and the mortality rate was 3.5%.

4.3. Characteristics of patients with resistant pathogens:

A total of 19 patients were included, with a mean age of 61.1 ± 11.9 years. Eight patients (42%) had grade III cholangitis. The median C-reactive protein (CRP) level was 126 [78–194] mg/L. The main pathogen identified was Pseudomonas aeruginosa in 8 cases (42%), and 7 patients (36.3%) had a history of prior biliary sphincterotomy (Table 3).

Table 3 Characteristics of Patients with Antibiotic-Resistant Pathogens

Variables	Observations (n = 19)
Age, mean (SD)	61.3 (11.8)
Male, n (%)	11 (57.9%)
Diabetes, n (%)	4 (21.1%)
Cholangitis grade III, n (%)	8 (42.1%)
Etiologies, n (%)	
Neoplasia	12 (63.2%)
Lithiasis	4 (21.1%)
Mean CRP [IQR]	126 [78–194] mg/L
Pathogens, n (%)	
Pseudomonas aeruginosa	8 (42.1%)
Escherichia coli	4 (21.1%)
Klebsiella pneumoniae	3 (15.9%)
Gram-positive bacteria	3 (15.9%)
Mean duration from admission to ERCP	2.58 ± 1.65 days
Prior biliary sphincterotomy, n (%)	7 (36.3%)

4.4. Predictive Factors of Positive Bile Culture and Resistance to Empirical Antibiotic Therapy:

We studied the predictive factors for a positive bile culture (Table 4). In univariate analysis, cholangitis grade I (OR = 2.33, $p = 0.031$) and lithiasis etiology (OR = 1.72, $p = 0.005$) were significant. However, after multivariate analysis, no factor remained statistically significant.

Table 4 Statistical Analysis of Predictors of a Positive Bile Culture

Univariate analysis				Analyze multivariate			
predictor	OR	95% CI	p	Predictor	OR	95% CI	p
Age	1.014	[0.9714 - 1.06]	0.534	Sex	0.770	[0.1856 - 3.20]	0.720
Sex	1.90	[0.593 - 6.08]	0.280	Diabetes	0.316	[0.0621 - 1.60]	0.164
Diabetes	0.473	[0.123 - 1.82]	0.276	Cholangitis grade I	0.229	[0.0448 - 1.17]	0.076
Cholangitis grade I	0.231	[0.0609 - 0.887]	0.031	Cholangitis grade III	1.594	[0.2425 - 10.48]	0.627
Cholangitis grade II	1.44	[0.468 - 4.42]	0.526	Lithiasis	0.138	[0.0122 - 1.56]	0.109
Cholangitis grade III	3.14	[0.618 - 15.99]	0.168	Neoplasia	0.876	[0.0737 - 10.41]	0.917
Duration of ATB before ERCP	0.912	[0.645 - 1.29]	0.599				
Lithiasis	0.172	[0.0511 - 0.581]	0.005				
Neoplasia	2.74	[0.818 - 9.15]	0.102				
Prior biliary sphincterotomy	2.31	[0.000 - 0.9]	0.994				

We also performed a statistical analysis (Table 5) to identify predictors of pathogen resistance to empirical antibiotic therapy. Both univariate and multivariate analyses revealed that a history of biliary sphincterotomy was a significant predictor of resistance to empirical antibiotic treatment (OR 11.7, $p = 0.047$).

Table 5 Statistical Analysis of Predictors of a Pathogen Resistant to Empirical Antibiotic Therapy

Univariate Analysis				Multivariate Analysis			
Predictor	OR	95% CI	p	Predictor	OR	95% CI	p
Age	0.988	[0.940 – 1.04]	0.611	Sex	1.110	[0.2311 – 5.33]	0.897
Sex	2.062	[0.575 – 7.39]	0.266	Cholangitis grade II	0.238	[0.0283 – 2.00]	0.186
Diabetes	2.400	[0.385 – 14.97]	0.349	Cholangitis grade III	1.212	[0.1033 – 14.22]	0.878
Cholangitis grade I	1.687	[0.249 – 11.42]	0.592	Lithiasis	3.380	[0.3046 – 37.5]	0.321
Cholangitis grade II	0.224	[0.062 – 0.94]	0.041	Neoplasia	1.402	[0.145 – 13.55]	0.770
Cholangitis grade III	4.121	[0.894 – 19.00]	0.069	Previous biliary sphincterotomy	11.726	[1.034 – 132.88]	0.047
Duration of antibiotics before ERCP	0.830	[0.556 – 1.24]	0.364				
Lithiasis	2.700	[0.697 – 10.46]	0.151				
Neoplasia	0.477	[0.132 – 1.72]	0.258				
Previous biliary sphincterotomy	11.083	[1.208 – 101.6]	0.033				

In our study, the mean duration of antibiotic therapy was 13 ± 3 days, the mean length of hospital stay was 9.45 ± 3.75 days, the 30-day recurrence rate was 5%, and the mortality rate was 3.5%.

5. Discussion

Pathogen identification and targeted antibiotic therapy are the cornerstone of treating severe bacterial infections. In acute cholangitis, blood cultures have low sensitivity. Our study demonstrates good sensitivity of bile sampling.

In a retrospective study, Chandra, Subhash, et al., showed that bile cultures had twice the sensitivity of blood cultures (78% vs. 32%) for identifying the causative pathogens in cholangitis [7]. Other studies reported similar or even higher sensitivities for pathogen identification via bile culture obtained during ERCP for cholangitis, ranging from 68.1% to 91.8% [8], [9], [10], [11].

Digestive-origin pathogens are the most frequently identified, with *Escherichia coli* (25%–50%) ranking first, followed by *Klebsiella* species (15%–20%) and *Enterobacter* species (5%–10%). *Enterococcus* is the most common Gram-positive bacterium causing cholangitis, present in 10%–20% of patients. Anaerobes are detected in 5%–10% of cases and are usually associated with mixed infections [12], [13].

The presence of *Pseudomonas* often reflects prior biliary instrumentation and varies from 0% to 25% [14], [15].

According to the Tokyo guidelines, broad-spectrum empirical antibiotic therapy is recommended as first-line treatment [17], [18]. Sensitivity of pathogens to this empirical therapy is highly variable (25%–64%) [9], [10], [11], highlighting the need to adapt empirical antibiotic regimens.

Bile sampling increases pathogen detection sensitivity and allows for narrower-spectrum antibiotic therapy. The main factors influencing resistance to empirical antibiotics are previous biliary procedures and patient age, as confirmed in several studies [8], [9], [11].

In a retrospective study conducted by Stathopoulos et al., including 405 patients, antibiotic therapy was modified in 26.4% of cases thanks to bile sampling. Predictive factors for resistance were age over 60 years, presence of a biliary stent, and previous sphincterotomy [8].

In a study including 721 patients, Gromski et al. reported that extended-spectrum beta-lactamases (ESBLs) and carbapenem resistance were found in 7.9% and 3.6% of Enterobacteriaceae, respectively [11].

Risk factors for bacteriobilia include orthotopic liver transplantation, steroid therapy, placement of biliary stents, and repeated biliary interventions [16]. Other studies have reported that the presence of a biliary stent and prior endoscopic biliary sphincterotomy are predictive factors for a positive bile culture [8], [9], [11]. In our study, no risk factor was statistically significant.

Empirical antibiotic regimens generally include a third-generation cephalosporin or a quinolone in combination with metronidazole, which is currently recommended as first-line broad-spectrum therapy for biliary infections [17].

The sensitivity to empirical antibiotic therapy varies across studies; in our study, it was 51.3%. In other studies, it ranged between 25%, 60%, 64%, and 88% [9], [10], [11].

According to the Tokyo Guidelines, the choice of antimicrobial agents is based on the severity of acute cholangitis. It is recommended that empirically administered antibiotics be adjusted according to the identified causative microorganisms and their antimicrobial susceptibility [18].

In our series, antibiotic therapy was modified based on bile culture antibiograms in 26.3% of patients whose pathogens were resistant to empirical antibiotics, among which clinical deterioration was observed in 9 cases. In 4 cases, no change was made due to clinical and biological improvement. Furthermore, in sensitive samples, antibiotic adjustments were made in 17.54%, allowing de-escalation to narrower-spectrum antibiotics or oral administration.

In our study, the predictive factor for resistance to empirical antibiotics was a prior biliary sphincterotomy ($p = 0.047$; odds ratio = 11.7). Other studies have also identified age over 60, prior sphincterotomy, and the presence of a biliary stent as predictors of resistance [8], [11].

In our cohort, the mean duration of antibiotic therapy and hospitalization, as well as the rates of recurrence and mortality, were similar to those reported in the literature [12], [19], [20].

Limitations of our study include its single-center and retrospective design.

6. Conclusion

During ERCP for acute cholangitis, bile aspiration identified a pathogen in over two-thirds of cases in our study. It allowed adjustment of antibiotic therapy in half of the patients, facilitating better management of severe sepsis, particularly in cases involving multi-drug-resistant pathogens. In other cases, it enabled narrower-spectrum antibiotics and oral administration. Bile cultures should be routinely performed during ERCP for acute cholangitis, especially in patients undergoing repeated ERCPs, to ensure more effective antimicrobial therapy.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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