

## Original Article

# Microbiological profile and antibiotic susceptibility pattern in Blood stream infections in patients with Acute Cholangitis: A prospective observational study

\*Khan Md. Nazmus Saqeb

DOI: <https://doi.org/10.3329/bccj.v8i2.50022>**Abstract:**

**Background:** I analyzed the organisms isolated from the blood of patients with acute cholangitis and determined their antibiotic resistance characteristics. In addition, I evaluated risk factors associated with antibiotic-resistant bacteria and their impact on clinical outcomes.

**Methods:** 113 consecutive cases of acute cholangitis who met the diagnostic criteria were included in the study. Acute cholangitis was defined by TG18 criteria. Blood culture was obtained from every patient. The microbiological results of blood cultures & the antibiotic susceptibility pattern of the organisms were analyzed by SPSSv22.0. Multivariate analysis was performed to identify risk factors associated with antibiotic resistance & mortality.

**Result:** Among 113 patients, 71(62.8%) were male & the median age was 51 years. Choledocholithiasis was the most common underlying biliary disease followed by malignant and benign strictures. Severe cholangitis occurred in 17(15%) cases. 32(28.3%) cases had nosocomial infection. Causative organisms were isolated from 55(48.7%) of 113 blood cultures. *Escherichia coli* was the most common bacterium isolated (36.36%) from blood, followed by *Klebsiella pneumoniae* (23.64%), *Pseudomonas aeruginosa* (7.27%) & *Enterococcus* (7.27%). Anaerobic bacteria were isolated from 5(9.09%) specimens. Multiple organisms were isolated in 6(10.91%) specimens. Most organisms were susceptible to meropenem (86.7%), imipenem (83.1%), colistin (89.1%), amikacin (76.1%), piperacillin-tazobactam (79.6%) & polymyxin-B (83.3%). Multidrug resistant bacteria comprised 30.91% of blood isolates. Risk factors associated with antibiotic resistance were presence of an indwelling biliary device (OR:7.7), prior biliary intervention (OR:6.167) and a nosocomial source of infection (OR:9.09). Thirteen (11.5%) patients died from acute cholangitis. Risk factors associated with mortality were severe cholangitis (OR:6.9), malignant biliary obstruction (OR:8.4), nosocomial infection (OR:7.5) and isolation of multidrug resistant organisms in blood (OR:6.9).

**Conclusion:** *E. coli* was the most common organism isolated, followed by *Klebsiella*, *Pseudomonas* & *Enterococcus*. Colistin, meropenem, polymyxin-B, imipenem, amikacin & piperacillin-tazobactam were the most effective of all antibiotics. Risk factors associated with isolation of multidrug resistant bacteria from blood were presence of an indwelling biliary device, prior biliary intervention and a nosocomial source of infection. Risk factors associated with mortality were severe cholangitis, malignant biliary obstruction, nosocomial infection and isolation of multidrug resistant organisms in blood.

**Keywords:** Etiological spectrum, Microbiological profile, Antibiotic susceptibility pattern, Acute Cholangitis.

**Background:**

Acute cholangitis is a clinical entity caused by bacterial infection of the biliary system, most commonly secondary to partial or complete obstruction of the bile duct or hepatic ducts. The diagnosis is established by the characteristic clinical symptoms and signs of infection, abnormal laboratory studies suggestive of infection and biliary obstruction, and

abnormal imaging studies suggestive of biliary obstruction<sup>1</sup>. The main importance of this condition is that it is a very treatable condition if treated appropriately, but the mortality can be high if there is delay in treatment.

In approximately 85% of cases, cholangitis is caused by a stone embedded in the bile duct, with resulting bile stasis.<sup>2</sup> Other causes of bile duct obstruction that may result in cholangitis are neoplasms, biliary strictures, parasitic infections, and congenital abnormalities of the bile ducts.<sup>3</sup> The bacterial species most commonly cultured from the bile are *E. coli*, *Klebsiella*, *Pseudomonas*, *Proteus*, and enterococci. Anaerobic species such as *Bacteroides fragilis* and *Clostridium perfringens* are found in about 15% of appropriately cultured bile specimens.<sup>4</sup>

Diagnosis is made using the TG18 diagnostic criteria for acute cholangitis.<sup>5-7</sup> Because bacteria that ascend the biliary tree from duodenum is the main source of bacteriobilia, gram-negative enteric bacteria are the main pathogens

**\*Principal & Corresponding Author:**

Dr. Khan Md. Nazmus Saqeb  
Assistant Professor  
Dept. of Gastrointestinal, Hepatobiliary & Pancreatic diseases  
Jahurul Islam Medical College & Hospital  
Bajitpur, Kishoreganj, Bangladesh.  
E-mail: [drsaqebk59@gmail.com](mailto:drsaqebk59@gmail.com)  
Phone: +8801715248062  
ORCID ID: <https://orcid.org/0000-0002-8080-947X>

associated with it.<sup>8</sup> Administration of broad-spectrum antibiotics is recommended until the results of culture are available.<sup>9</sup> However, in recent years, some studies have reported that isolates from acute cholangitis patients have changed due to the frequent use of biliary devices and prior exposure to antibiotics.<sup>10,11</sup> The major problem for infection control is the spread of extended spectrum- $\beta$ -lactamase (ESBL)-producing organisms in the community as well as in the nosocomial setting.<sup>12,13</sup> ESBL hydrolyzes cephalosporins and confers resistance to most  $\beta$ -lactams antibiotics. The rate of isolation of ESBL-producing gram negative bacteria is higher in Asia, including Korea, than in other regions.<sup>14</sup> In addition, the emergence of carbapenemase-producing bacteria is a major public health concern, because carbapenem is the most reliable therapeutic agent for ESBL-producing bacteria.<sup>15</sup>

Several other antibiotic resistant organisms like VRE, MRSA, VRSA & MDR *Acinetobacter* has also emerged as a public health concern. These bacteria may be intractable to the usual antibiotics and have a significant impact on clinical outcomes. Thus, a survey of the profile of organisms that cause acute cholangitis is needed for proper antibiotic selection. However, most of the few studies that have been published on this subject used only a small sample size, showing different results among them.<sup>16-21</sup>

Antibiotics and biliary drainage are two pillars of effective treatment of acute cholangitis. Early diagnosis prompt antibiotic therapy makes cure more likely. But delayed diagnosis and antibiotic resistance can make the situation worse. Moreover, the patterns of infective agents are changing over last few years and antibiotic resistance is increasing day by day. So, patterns of organisms and their resistance patterns need to be identified. This study aims at describing the patterns of organisms causing cholangitis along with their resistance patterns. Moreover, this study tries to figure out various risk factors responsible for development of resistant organisms and also tries to describe the risk factors which significantly affect the clinical outcome of acute cholangitis.

#### Methods:

This prospective and observational study was done in the department of Gastrointestinal, Hepatobiliary and Pancreatic Disorders (GHPD), Square Hospital (Dhaka, Bangladesh) from January, 2018 to August, 2019. 113 consecutive cases of acute cholangitis who met the diagnostic criteria were included in the study. Patients unwilling to give voluntary consent to participate in the study were excluded. Consecutive type of non-probability sampling technique was applied to enroll the patients. Prior to the commencement of this study, the research protocol was approved by the Ethical Review Committee (ERC) of the institution. The aims and objective of the study along with its procedure, risk and benefits were explained to the patients in easily understandable local language and then informed consent was taken from each patient. A predesigned structured questionnaire was used for recording all the data.

Acute cholangitis was diagnosed using the TG18 criteria<sup>5</sup>. Demographic data like age, sex, clinical data like presence of

abdominal pain, jaundice, fever, GCS score, vital parameters were recorded. Laboratory data like hemoglobin, white blood cell count, CRP, platelet count, blood C/S results, FBS, HbA1c, BUN, serum creatinine, serum bilirubin, AST, ALT, alkaline phosphatase, gamma-GT, USG of whole abdomen & ERCP findings were recorded. Severity of acute cholangitis was defined by TG 18 criteria. Blood culture was obtained from every patient. Usually 5 ml blood was obtained and transferred into aerobic and anaerobic blood culture bottles. And then was sent to the microbiology laboratory. Once in the microbiology laboratory blood cultures were analyzed using an automated system (BacTAlert 3D; bioMérieux, Marcy l'Etoile, France), and the isolates were identified by conventional methods including the Vitek system using a GNI or GPI card (bioMérieux, Hazelwood, MO, USA). Antibiotic susceptibility tests were conducted using either the Vitek system or the disc diffusion method according to the Clinical Laboratory Standards Institute (CLSI) guidelines.

All statistical analyses were performed using a statistical software package (SPSS version 22.0 for Windows; SPSS Inc., Chicago, IL, USA). Isolation rates of ESBL producers or carbapenemase producers (CRE), multidrug resistant (MDR) *Acinetobacter* species, MRSA, and Vancomycin-resistant *Enterococcus* (VRE) were recorded. Multivariate analysis was performed to identify risk factors associated with development of resistant bacteria and also to find out factors which could affect mortality. Continuous variables were expressed as medians, and categorical variables as frequencies and percentages. Statistical analysis was performed using Pearson's chi-square test. Odds ratio was calculated for each of the risk factors under evaluation. Statistical significance was defined as a p-value of <0.05.

#### Result:

A prospective observational study was carried out to see the etiological spectrum, microbiological profile & antibiotic susceptibility pattern of patients with acute cholangitis. Total 113 patients with acute cholangitis, who fulfilled the inclusion criteria, were included in this study. The result of the study is presented in following tables.

#### Discussion

Acute cholangitis is a clinical entity caused by bacterial infection of the biliary system, most commonly secondary to partial or complete obstruction of the bile duct or hepatic ducts. The diagnosis is established by the characteristic clinical symptoms and signs of infection, abnormal laboratory studies suggestive of infection and biliary obstruction, and abnormal imaging studies suggestive of biliary obstruction<sup>1</sup>.

The main importance of this condition is that it is a very treatable condition if treated appropriately, but the mortality can be high if there is delay in treatment. In approximately 85% of cases, cholangitis is caused by a stone embedded in the bile duct, with resulting bile stasis.<sup>2</sup> Other causes of bile duct obstruction that may result in cholangitis are neoplasms, biliary strictures, parasitic infections, and congenital abnormalities of the bile ducts.<sup>3</sup> Bile duct obstruction is necessary but not sufficient to cause cholangitis.

## Tables

**Table I: Demographic, clinical and microbiological characteristics of patients (n=113).**

Parameters	Result (%)
Median (95% CI) age (years)	51(25-94)
Male	71(62.8)
Etiology:	
Choledocholithiasis	68(60.2)
Malignant biliary obstruction	24(21.2)
Biliary stricture	10(8.8)
Parasite	3(2.7)
Infection of retained stent	5(4.4)
Severe cholangitis	17(15)
Positive blood culture	55(48.7)
Indwelling biliary device	25(22.1)
Prior biliary intervention done	33(29.2)
Source of infection:	
Community acquired	81(71.7)
Hospital acquired	32(28.3)
Number of organisms detected:	
Monomicrobial	49(89.09)
Polymicrobial	6(10.91)
Anaerobes	5(9.09)
Multidrug resistant strains on blood culture	17(30.91)
Death/Mortality	13(11.5)

**Table II: Organisms isolated from blood in patients with acute cholangitis.**

Organisms	N (%)
Gram negative aerobic bacteria	
Escherichia coli	20(36.36)
Klebsiella	13(23.64)
Pseudomonas	4(7.27)
Enterobacter	2(3.64)
Acinetobacter	1(1.82)
Gram negative anaerobic bacteria	
Bacteroides	2(3.64)
Gram positive aerobic bacteria	

Enterococcus	4(7.27)
Coagulase negative Staphylococcus	2(3.64)
Streptococcus viridans	1(1.82)
Streptococcus pneumoniae	2(3.64)
Gram positive anaerobic bacteria	
Clostridium perfringens	3(1.7)
Others	
Candida	1(1.82)

**Table III: Antibiotic susceptibility of organisms isolated from blood in patients with acute cholangitis.**

Antibiotic	Susceptibility (%)
Meropenem	86.7
Imipenem	83.1
Amikacin	76.1
Ceftazidime	60.2
Piperacillin-tazobactam	79.6
Cefepime	63.7
Linezolid	77
Vancomycin	9.7
Colistin	89
Polymyxin-B	83.3
Ceftriaxone	17.7
Levofloxacin	23.0
Ciprofloxacin	24.8
Gentamycin	37.7
Amoxicillin-clavulanic acid	11.5
Ampicillin	11.5

**Table IV: Frequency of isolation of multidrug resistant organisms from blood in patients with acute cholangitis.**

Organisms	N (%)
ESBL producing	11(20)
Carbapenem Resistant Enterobacteriaceae (CRE)	4(7.27)
Vancomycin Resistant Enterococcus (VRE)	1(1.82)
Multidrug resistant Acinetobacter	1(1.82)

**Table V: Association of presence of indwelling biliary device with development of drug resistance in organisms causing acute cholangitis. (n=113)**

Indwelling biliary device	Multidrug resistant organisms		Total	p-value
	Present	Absent		
Present	10	15	25	<0.001
Absent	7	81	88	
<b>Total</b>	17	96	113	

**Table VI: Association of prior biliary intervention with development of drug resistance in organisms causing acute cholangitis (n=113).**

Prior biliary intervention	Multidrug resistant organisms		Total	p-value
	Present	Absent		
Present	11	22	33	<0.001
Absent	6	74	80	
<b>Total</b>	17	96	113	

**Table VII: Association of hospital acquired infection with development of drug resistance in organisms causing acute cholangitis (n=113).**

Source of infection	Multidrug resistant organisms		Total	p-value
	Present	Absent		
Hospital acquired	12	20	32	<0.001
Community acquired	5	76	81	
<b>Total</b>	17	96	113	

**Table VIII: Multivariate analysis of risk factors associated with development of multidrug resistance in organisms causing acute cholangitis.**

Variable	P value	Odds ratio	95% CI
Indwelling biliary device	0.001	7.7	(2.5-23.45)
Prior biliary intervention	0.001	6.167	(2.05-18.58)
Hospital acquired infection	0.001	9.09	(2.87-28.57)

**Table IX: Association of severity of cholangitis with mortality in patients with acute cholangitis. (n=113)**

Severity of cholangitis	Death		Total	p-value
	Yes	No		
Severe	6	11	17	<0.001
Mild or moderate severe	7	89	96	
<b>Total</b>	13	100	113	

**Table X: Association of malignant biliary obstruction with mortality in patients with acute cholangitis. (n=113)**

Malignant biliary obstruction	Death		Total	p-value
	Yes	No		
Present	8	16	24	<0.001
Absent	5	84	89	
<b>Total</b>	13	100	113	

**Table XI: Association of source of infection with mortality in patients with acute cholangitis. (n=113)**

Source of infection	Death		Total	p-value
	Yes	No		
Hospital acquired	9	23	32	<0.001
Community acquired	4	77	81	
<b>Total</b>	13	100	113	

**Table XII: Association of infection with multidrug resistant organisms & mortality in patients with acute cholangitis. (n=113)**

MDR organisms	Death		Total	p-value
	Yes	No		
Present	6	11	17	<0.001
Absent	7	89	96	
<b>Total</b>	13	100	113	

**Table XIII: Multivariate analysis of risk factors associated with mortality in patients with acute cholangitis.**

Variable	P value	Odds ratio	95% CI
Severe cholangitis	0.001	6.935	(1.97-24.39)
Malignant biliary obstruction	0.001	8.4	(2.43-28.99)
Hospital acquired infection	0.001	7.5	(2.12-27.03)
Infection with multidrug resistant organisms	0.001	6.9	(1.97-24.39)

Cholangitis is relatively common in patients with choledocholithiasis and nearly universal in patients with a post-traumatic bile duct stricture, but is seen in only 15% of patients with neoplastic obstruction of the bile duct. It is most likely to result when a bile duct that already contains bacteria becomes obstructed, as in most patients with choledocholithiasis and stricture but in few patients with neoplastic obstruction. Malignant obstruction is more often complete than obstruction by a stricture or a bile duct stone and less commonly permits reflux of bacteria from duodenal contents into the bile ducts.<sup>4</sup>

The bacterial species most commonly cultured from the bile are *E. coli*, *Klebsiella*, *Pseudomonas*, *Proteus*, and enterococci. Anaerobic species such as *Bacteroides fragilis* and *Clostridium perfringens* are found in about 15% of appropriately cultured bile specimens. Anaerobes usually accompany aerobes, especially *E. coli*.<sup>4</sup> Symptoms indicative of suspected acute biliary infection are fever, chills, abdominal pain, jaundice, nausea, vomiting, and disturbance of consciousness. If even one of these symptoms is present, acute biliary infection is suspected and it is necessary to proceed to diagnosis.<sup>22</sup> Vital signs include blood pressure, heart rate, respiration rate, temperature, urine volume, oxygen saturation (SpO<sub>2</sub>), and consciousness level.

The consultation should include a detailed medical history of the timing of the appearance of symptoms and their nature.

Patients should be asked about their previous medical history and regular medications. In the physical examination, the evaluation and measurement of the patient's state of consciousness goes without saying, and the presence or absence of yellowing of the palpebral conjunctiva, the location and severity of tenderness, and whether or not there are any symptoms of peritoneal irritation must always be confirmed.

Blood tests including white blood cell count, platelet count, C-reactive protein (CRP), albumin, alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), aspartate aminotransferase (AST), alanine aminotransferase (ALT), bilirubin, blood urea nitrogen (BUN), creatinine, prothrombin time (PT), and PT-international normalized ratio (INR) are carried out for the purpose of diagnosis and severity grading, and blood gas analysis should also be performed.<sup>22</sup> If a high fever is present, blood culture should preferably be performed at this point. In terms of diagnostic imaging, abdominal ultrasound and computed tomography (CT) are useful for the diagnosis of acute biliary infection, and at least one of these should be performed. Abdominal ultrasound in particular is minimally invasive, widely used, simple, and cheap, and should therefore be performed first in patients with suspected biliary infection, despite disadvantages including the fact that the results are easily affected by the operator's skill and the patient's condition.<sup>7</sup> Inflammation in acute cholangitis is

difficult to assess on diagnostic imaging, but it is possible to evaluate dilatation of the bile duct, or bile congestion due to occlusion/ stenosis of the bile duct or biliary calculus and its cause<sup>22</sup>. Males and females are equally affected. The average age of patients presenting with acute cholangitis is 50 to 60 years. Diagnosis is made using the TG18 diagnostic criteria for acute cholangitis.<sup>5-7</sup>

After the definitive diagnosis of acute cholangitis & severity assessment, initial treatment including the infusion of sufficient fluids and antibiotic and analgesic administration should be started, with careful monitoring of blood pressure, heart rate, and urine volume. In the case of serious deterioration, such as the appearance of shock (hypotension), disturbance of consciousness, acute dyspnea, acute renal dysfunction, hepatic dysfunction, or disseminated intravascular coagulation (DIC) (reduced platelet count), emergency biliary drainage should be considered alongside appropriate organ support and respiratory/circulatory management (such as artificial ventilation, tracheal intubation, and the use of hypertensive agents)<sup>22</sup>.

Biliary drainage and antibiotics are the two key pillars of the treatment of acute cholangitis. If blood culture has not been performed as part of the initial response, it should be carried out before antibiotic administration. If biliary drainage is performed, bile samples must always be sent for culture. Because bacteria that ascend the biliary tree from duodenum is the main source of bacteriobilia, gram-negative enteric bacteria are the main pathogens associated with it.<sup>8</sup> Administration of broad-spectrum antibiotics is recommended until the results of culture are available.<sup>9</sup> However, in recent years, some studies have reported that isolates from acute cholangitis patients have changed due to the frequent use of biliary devices and prior exposure to antibiotics.<sup>10,11</sup>

The major problem for infection control is the spread of extended spectrum- $\beta$ -lactamase (ESBL)-producing organisms in the community as well as in the nosocomial setting.<sup>12,13</sup> ESBL hydrolyzes cephalosporins and confers resistance to most  $\beta$ -lactams antibiotics. The rate of isolation of ESBL-producing gram negative bacteria is higher in Asia, including Korea, than in other regions.<sup>14</sup> In addition, the emergence of carbapenemase-producing bacteria is a major public health concern, because carbapenem is the most reliable therapeutic agent for ESBL-producing bacteria.<sup>15</sup> Several other antibiotic resistant organisms like VRE, MRSA, VRSA & MDR Acinetobacter has also emerged as a public health concern.

Antibiotic-resistant bacteria such as ESBL or carbapenemase producers, VRE, and MRSA are recalcitrant to clearance with the most commonly employed antibiotics.<sup>23</sup> VRE and MRSA play only a minor role in acute cholangitis; however, antibiotic resistance mediated by production of ESBL and/or carbapenemase has become an obstacle to treating acute cholangitis.<sup>12,15</sup> The antimicrobial surveillance studies has revealed a generalized rise in antibiotic resistance over time.<sup>23</sup> Recent data from the global Study for Monitoring Antimicrobial Resistance Trends showed that in the

Asia-Pacific region and in Latin America, 40% and 30% of *E. coli* and *Klebsiella* spp. respectively, from patients with intra-abdominal infections were ESBL-positive.<sup>24</sup> These data showed antibiotic-resistant bacteria were frequently isolated in acute cholangitis patients, suggesting the importance of recognizing recent changes in antibiotic-resistant profiles in these patients.

One study showed that the risk factors for carbapenem-resistant *E. coli* acquisition are previous use of carbapenem and metronidazole, presence of a biliary drainage catheter, and prior hospital stay.<sup>25</sup> Nosocomial infection has been introduced as a risk factor in previous studies of antibiotic-resistant organisms.<sup>23,25</sup> Infection by antibiotic-resistant bacteria typically has a poor outcome.<sup>25,26</sup> These bacteria may be intractable to the usual antibiotics and have a significant impact on clinical outcomes. Thus, a survey of the microbiological profile of acute cholangitis along with their antibiotic susceptibility pattern, is needed for proper antibiotic selection. However, most of the few studies that have been published on this subject used only a small sample size, showing different results among them.<sup>16-21</sup>

In this study, the median age of patients was 51 years & 71 (62.8%) of them were male. The underlying biliary diseases were choledocholithiasis in 68 (60.2%) patients, and malignant and benign strictures in 24 (21.2%) and 10 (8.8%) patients, respectively. Severe cholangitis occurred in 17 (15%) cases. 81 (71.7%) cases developed cholangitis in community setting & 32 (28.3%) cases had nosocomial infection. History of prior biliary intervention was found in 33 (29.2%) cases, while an indwelling biliary device was found in 25 (22.1%) cases. Goo JC et al.<sup>27</sup> in their study found that the underlying biliary diseases were choledocholithiasis in 187 (54.0%) patients, and malignant and benign strictures in 146 (42.2%) and 13 (3.8%) patients, respectively. They also found that severe cholangitis occurred in 107 (24.7%) cases & 367 (84.8%) cases developed cholangitis in community setting.

In this study, causative organisms were isolated from 55 of 113 (48.7%) blood cultures. *Escherichia coli* was the most common bacterium isolated and was present in 36.36% of blood. The four most common bacterial species isolated from blood were *E. coli* (36.36%), *Klebsiella pneumoniae* (23.64%), *Pseudomonas aeruginosa* (7.27%) & *Enterococcus* (7.27%). Anaerobic bacteria (*Bacteroides fragilis* & *Clostridium perfringens*) were isolated from only five (9.09%) blood specimens. Multiple organisms were isolated in 6 (10.91%) specimens. Goo JC et al.<sup>27</sup> in their study found that causative organisms were isolated from 266 of 419 (63.4%) blood cultures. *Escherichia coli* was the most common bacterium isolated and was present in 40% of blood. The four most common bacterial species isolated from blood were *E. coli*, *Klebsiella pneumoniae*, *Enterococcus* spp., and *Pseudomonas aeruginosa*.

Anaerobic bacteria (*Bacteroides fragilis*) were isolated from only five blood specimens. The rates of multiple organism

isolation were 49 of 266 (18.4%) in blood. In our study, most organisms were susceptible to meropenem (86.7%), imipenem (83.1%), colistin (89.1%), amikacin (76.1%), piperacillin-tazobactam (79.6%) & polymyxin-B (83.3%). Organisms were least susceptible to ciprofloxacin (24.8%), ceftriaxone (17.7%), levofloxacin (23.1%), gentamycin (37.7%), ampicillin (11.5%) & amoxicillin-clavulanic acid (11.5%). Kaya M et al.<sup>28</sup> in their study found a low resistance to meropenem, amikacin and imipenem. There was high resistance for gentamicin (47%), ciprofloxacin (48%), levofloxacin (49%), ceftazidime (54%), ampicillin (79%), cefotaxime (86%) and ampicillin/sulbactam (89%).

In our study, the multidrug resistant bacteria isolated from blood included 11 ESBL-producing bacteria, 4 carbapenemase-producing organisms (CRE), 1 VRE & 1 MDR Acinetobacter. Multidrug resistant bacteria comprised 30.91% of blood isolates. Risk factors associated with isolation of multidrug resistant bacteria from blood were presence of an indwelling biliary device (OR:7.7), prior biliary intervention (OR:6.167) and a nosocomial source of infection (OR:9.09). Goo JC et al.<sup>27</sup> in their study found that antibiotic-resistant bacteria isolated from blood included 20 ESBL-producing and 4 carbapenemase-producing organisms. Those isolated from bile included 34 ESBL-producing bacteria, 13 carbapenemase-producing bacteria, 3 MDR Acinetobacter, 1 VRE, and 1 MRSA. Resistant bacteria comprised 7.4% of blood isolates. Risk factors associated with ESBL or carbapenemase-producing organisms from blood were prior biliary intervention (p=0.016) and nosocomial infection (p=0.048).

In our study, a total of 13 out of 113 patients died during admission with acute cholangitis. Eight patients with biliary malignancy, four with choledocholithiasis & one from infection of a retained stent expired during their hospital admission with acute cholangitis. Risk factors associated with mortality were severe cholangitis (OR:6.9), malignant biliary obstruction (OR:8.4), nosocomial infection (OR:7.5) and isolation of multidrug resistant organisms in blood (OR:6.9). Goo JC et al.<sup>27</sup> in their study found that a total of 33 out of 346 patients died during acute cholangitis cases. They concluded that risk factors associated with mortality were malignant biliary obstruction, severe cholangitis, nosocomial infection, and isolation of antibiotics-resistant bacteria in bile or blood, which is similar to our study.

## Conclusion

The causative organisms of acute cholangitis & their antibiotic susceptibility pattern is changing over time. E. coli was the most common organism isolated from the blood samples of patients with acute cholangitis, followed by Klebsiella, Pseudomonas & Enterococcus. Anaerobes were isolated in only 5 cases. Colistin, meropenem, polymyxin-B, imipenem, amikacin & piperacillin-tazobactam were the most effective of all antibiotics acting against organisms causing acute cholangitis. Organisms were least susceptible to ciprofloxacin, ceftriaxone, levofloxacin, gentamycin, ampicillin & amoxicillin-clavulanic acid. Risk factors associated with isolation of multidrug resistant bacteria from

blood were presence of an indwelling biliary device (OR:7.7), prior biliary intervention (OR:6.167) and a nosocomial source of infection (OR:9.09). And risk factors associated with mortality were severe cholangitis (OR:6.9), malignant biliary obstruction (OR:8.4), nosocomial infection (OR:7.5) and isolation of multidrug resistant organisms in blood (OR:6.9).

## References

1. Wada K, Takada T, Kawarada Y, Nimura Y, Miura F, Yoshida M, Mayumi T, Strasberg S, Pitt HA, Gadacz TR, Büchler MW, Belghiti J, de Santibanes E, Gouma DJ, Neuhaus H, Dervenis C, Fan ST, Chen MF, Ker CG, Bornman PC, Hilvano SC, Kim SW, Liau KH, Kim MH. Diagnostic criteria and severity assessment of acute cholangitis: Tokyo Guidelines. *J Hepatobiliary Pancreat Surg* 2007; 14: 52-58.
2. Lillemoe K. Surgical treatment of biliary tract infections. *Am Surg* 2000; 66:138-44.
3. Tenner S and Steinbergh WM 2016, 'Gallstone Disease', in Feldman, M, Friedman, LS and Brandt, LJ (eds), Sleisenger and Fordtran's Gastrointestinal and Liver Disease, pp.1130, Elsevier, Philadelphia.
4. Tenner S and Steinbergh WM 2016, 'Gallstone Disease', in Feldman, M, Friedman, LS and Brandt, LJ (eds), Sleisenger and Fordtran's Gastrointestinal and Liver Disease, pp. 1131, Elsevier, Philadelphia.
5. Kiriya S, Takada T, Strasberg SM, Solomkin JS, Mayumi T, Pitt HA, et al. New diagnostic criteria and severity assessment of acute cholangitis in revised Tokyo Guidelines. *J Hepatobiliary Pancreat Sci.* 2012; 19:548-56.
6. Kiriya S, Takada T, Strasberg SM, Solomkin JS, Mayumi T, Pitt HA, et al. TG13 guidelines for diagnosis and severity grading of acute cholangitis (with videos). *J Hepatobiliary Pancreat Sci.* 2013; 20:24-34.
7. Kiriya S, Kozaka K, Takada T, Strasberg SM, Pitt HA, Gabata T, et al. Tokyo Guidelines 2018: diagnostic criteria and severity grading of acute cholangitis (with videos). *J Hepatobiliary Pancreat Sci.* 2018; 25:17-30.
8. Sung JY, Leung JW, Shaffer EA, Lam K, Olson ME, Costerton JW. Ascending infection of the biliary tract after surgical sphincterotomy and biliary stenting. *J Gastroenterol Hepatol* 1992; 7:240-245.
9. Bornman PC, van Beljon JI, Krige JE. Management of cholangitis. *J Hepatobiliary Pancreat Surg* 2003; 10:406-414.
10. Rerknimitr R, Fogel EL, Kalayci C, Esber E, Lehman GA, Sherman S. Microbiology of bile in patients with cholangitis or cholestasis with and without plastic biliary endoprosthesis. *Gastrointest Endosc* 2002;56: 885-889.
11. Choi SH, Lee JE, Park SJ, et al. Emergence of antibiotic resistance during therapy for infections caused by Enterobacteriaceae producing AmpC beta-lactamase: implications for antibiotic use. *Antimicrob Agents Chemother* 2008; 52:995-1000.
12. Pitout JD, Nordmann P, Laupland KB, Poirel L. Emergence of Enterobacteriaceae producing extended-spectrum beta-lactamases (ESBLs) in the community. *J Antimicrob Chemother* 2005; 56:52-59.
13. Rodríguez-Baño J, Alcalá JC, Cisneros JM, et al. Community infections caused by extended-spectrum beta-lactamase-producing Escherichia coli. *Arch Intern Med* 2008; 168:1897-1902.
14. Hawkey PM. Prevalence and clonality of extended-spectrum beta-lactamases in Asia. *Clin Microbiol Infect* 2008;14 Suppl 1:159-165.

15. Falagas ME, Rafailidis PI, Kofteridis D, et al. Risk factors of carbapenem-resistant *Klebsiella pneumoniae* infections: a matched case control study. *J Antimicrob Chemother* 2007; 60:1124-1130.
16. Heo JH, Lee JH, Lee MY, et al. Bacterial identification in bile and blood of patients with acute cholangitis from benign and malignant bile duct obstruction. *Korean J Gastroenterol* 2002; 40:53-59.
17. Flores C, Maguilnik I, Hadlich E, Goldani LZ. Microbiology of choledochal bile in patients with choledocholithiasis admitted to a tertiary hospital. *J Gastroenterol Hepatol* 2003; 18:333-336.
18. Englesbe MJ, Dawes LG. Resistant pathogens in biliary obstruction: importance of cultures to guide antibiotic therapy. *HPB (Oxford)* 2005; 7:144-148.
19. Melzer M, Toner R, Lacey S, Bettany E, Rait G. Biliary tract infection and bacteraemia: presentation, structural abnormalities, causative organisms and clinical outcomes. *Postgrad Med J* 2007; 83:773-776.
20. Demirbağ AE, Karademir A, Parlak E, et al. Multidrug resistance of isolated microorganisms in occluded bile duct stents. *Turk J Gastroenterol* 2007; 18:33-40.
21. Bae WK, Moon YS, Kim JH, et al. Microbiologic study of the bile culture and antimicrobial susceptibility in patients with biliary tract infection. *Korean J Gastroenterol* 2008; 51:248-254.
22. Miura F, Takada T, Strasberg SM, Solomkin JS, Pitt HA, Gouma DJ, et al. TG13 flowchart for the management of acute cholangitis and cholecystitis. *J Hepatobiliary Pancreat Sci.* 2013; 20:47-54.
23. Hawkey PM, Jones AM. The changing epidemiology of resistance. *J Antimicrob Chemother* 2009;64 Suppl 1: i3-i10.
24. Guembe M, Cercenado E, Alcalá L, Marín M, Insa R, Bouza E. Evolution of antimicrobial susceptibility patterns of aerobic and facultative gram-negative bacilli causing intra-abdominal infections: results from the SMART studies 2003-2007. *Rev Esp Quimioter* 2008; 21:166-173.
25. Jeon MH, Choi SH, Kwak YG, et al. Risk factors for the acquisition of carbapenem-resistant *Escherichia coli* among hospitalized patients. *Diagn Microbiol Infect Dis* 2008; 62:402-406.
26. Falagas ME, Karageorgopoulos DE. Extended-spectrum beta-lactamase-producing organisms. *J Hosp Infect* 2009; 73:345-354.
27. Goo JC, Seong MH, Shim YK, et al. Extended Spectrum-β-Lactamase or Carbapenemase Producing Bacteria Isolated from Patients with Acute Cholangitis. *Clin Endosc* 2012; 45:155-160.
28. Kaya M, Beştaş R, Bacalan F, et al. Microbial profile and antibiotic sensitivity pattern in bile cultures from endoscopic retrograde cholangiography patients. *World J Gastroenterol* 2012; 18(27): 3585-3589.