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Original Research Article

Clinical and Microbiological Profile of Patients with Acute Bacterial Cholangitis at a Tertiary Care Centre in Northern India

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Abstract:

Introduction: The changing antimicrobial sensitivity pattern poses a great therapeutic challenge in the modern era. With the development of antibiotic resistance due to widespread injudicious use of antibiotics, we now have very limited antibiotics against certain pathogens, especially for fatal GI emergencies like acute cholangitis. We conducted a study to assess the microbial profile and the sensitivity pattern to antibiotics in patients who presented with acute bacterial cholangitis.

Methods: We enrolled all the patients admitted in our hospital between June 2023 to October 2023, who had acute bacterial cholangitis and were above 18 years of age. They were prospectively analyzed. Patient's clinical features, etiology, microbial profile and antibiotic sensitivity pattern were analyzed. As soon as patient underwent any procedure all cultures were obtained. Antibiotics were administered after collecting the bile for Culture and Sensitivity.

Results: Seventy six patients with acute cholangitis were evaluated. Choledocholithiasis, seen in 43 patients (56.6%) and malignancy seen in 29 patients (38.1%), were the most common factors precipitating acute cholangitis. Bile culture was positive in 62 of 76 patients (81.5%), and blood culture was positive in 23 of 76 (30.2%) patients. E. Coli followed by Klebsiella sps. were the most common organisms that were isolated from the bile culture. The organisms showed multi-drug resistance (MDR) pattern. The most common drugs to which these showed sensitivity were, Meropenem and Tigecycline.

Conclusions: With more community acquired pathogens being MDR/XDR, as shown in this study, there is a prompt need to revise the antibiotic policy depending on the local resistance pattern. Acute cholangitis, is a medical emergency and should be treated immediately with broad spectrum antibiotics and Endoscopic/Percutaneous intervention depending on the expertise.

Keywords: Endoscopic Retrograde Cholangiopancreatography, Percutaneous Transhepatic Biliary Drainage, Multiple drug resistance, extensively drug-resistant, Carcinoma gall bladder.

Introduction

Acute Cholangitis as defined by the Tokyo consensus is a bacterial infection of an obstructed biliary system [1]. Choledocholithiasis, malignancy followed by biliary strictures are the common predisposing factors [2, 3]. Patients with Acute cholangitis should be treated with a dual approach; immediate broad-spectrum empirical antibiotics followed by prompt decompression of the biliary system, either by Endoscopic or Percutaneous route. Antibiotics should be started as soon as patient is suspected of having cholangitis, and should be based on the local antibiotic resistance pattern. Antibiotic stewardship should be practiced and it should be changed as soon as the cultures are available. Injudicious use of antibiotics over the years has changed the antibiotic sensitivity pattern, with more cultures showing MDR/XDR pathogen. This necessitates an immediate review of the previously published guidelines and updating the existing empirical antibiotic policy [4–6]. In this study we have presented the clinical and microbial profile of patients admitted with acute bacterial cholangitis.

Materials and Methods

The present study is a cross-sectional study conducted in the gastroenterology department of SMS Medical College, Jaipur. We included all the patients, aged more than 18 years, admitted in gastroenterology department from June 2023 to October 2023 with acute cholangitis. Only patients who had not received antibiotics prior to Endoscopic retrograde cholangiopancreatography (ERCP) / Percutaneous transhepatic biliary drainage (PTBD) and had given written informed consent were included.

The diagnosis of acute cholangitis was based on the presence of clinical evidence of infection (fever and leukocytosis) in patients with biliary obstruction [7, 8]. Biliary obstruction was detected by elevated bilirubin, deranged SGOT/SGPT or serum alkaline phosphatase and dilated intra/extra-hepatic biliary system on imaging [7]. Ten milliliters of bile was collected during the ERCP, in a sterile tube using a sterile biliary cannula and sent immediately to microbiology laboratory for inoculation. Similarly during PTBD, 10 milliliters of bile was aspirated after the puncture and was sent for cultures.

Organ failure was defined as presence of any of the following features—hypotension (systolic blood pressure <90 mmHg), hypoxia (blood oxygen saturation <90%), renal failure (serum creatinine >1.5 mg/dl) and altered sensorium (Glasgow coma scale score <12) [8].

Approval was obtained from the institute review board and ethics committee prior to the study.

Statistical analysis: Data was analyzed using SPSS (Statistical Package for Social Sciences, release 11.0, standard version; SPSS Inc.). Categorical data is presented as proportions. Quantitative data is represented using means, median, standard deviation and range.

Results

102 patients with cholangitis were screened. Out of these, 76 were included in the study. Out of 102 patients, 26 patients were excluded, 16 had received antibiotics before, 4 had a severe form of cholangitis, and 6 patients refused for intervention. A flow chart of recruited patients is shown below (Fig. 1).

The demographic, clinical, laboratory and etiological profile of all patients is shown in Table 1. The mean age was 46.3 ± 8.6 years and showed a male predominance, i.e. 41 out of 76 patients (53.9%). Fever, jaundice, and abdominal pain were the most common presenting symptoms. Twenty-five (13.5%) patients had diabetes mellitus.

All patients had undergone ultrasonography of the abdomen for the diagnosis (n = 76). Dilated CBD and dilated intrahepatic biliary radicles (IHBR) were seen on USG in 62 of 76 (81.5%) patients. The mean CBD diameter on USG was 8.6mm. MRCP was done in all patients, especially in the malignant etiology group, to look for the type of block. Choledocholithiasis in 43 of 76 (56.6%) and malignancy in 29 of 76 (38.1%) patients were the most common etiologies, precipitating acute cholangitis. Biliary stricture was seen in 4 patients, with 2 patients having post cholecystectomy stricture and 2 having chronic pancreatitis. Therapeutic procedure in the form of ERCP was attempted in 64/76 patients (84.2%). Technical success was achieved in 58/64 patients (90.6%). Percutaneous transhepatic biliary drainage was done in all the remaining patients. Bile culture was positive in 62 of 76 patients (81.5%), and blood culture was positive in 23 of 76 (30.2%).

Aerobic blood culture was sent in 76 patients. Cultures were positive in 23/76 (30.2%) patients and were predominantly monomicrobial in 21/23 patients. E. coli was the predominant organism in 15 out of 23, followed by Klebsiella sps. in 6, Pseudomonas in 3, and Acinetobacter in 1. Bile culture was also sent in all 76 patients before starting antibiotics. Bile culture was positive in 62 of 76 (81.5%) patients. E. coli in 39 of 62 (62.9%), followed by Klebsiella sp in 14 of 62 (22.6%), were the predominant organisms. Other organisms isolated were Pseudomonas in 7, Acinetobacter in 2, Enterococci in 2, and Staphylococcus in 1.The results of antibiotic sensitivity was to our surprise. Most of the pathogens were MDR/XDR. Details have been given in the Table 3 below. Most of the E. coli and Klebsiella sps., were resistant to third generation cephalosporins and most of the fluoroquinolones. Pseudomonas was resistant to fluoroquinolones, and had intermediate sensitivity to piperacillin and tazobactam. All these organisms were uniformly susceptible to carbapenems. Enterococcus had high sensitivity to linezolid, vancomycin, and teicoplanin.

Therapeutic procedure in the form of ERCP was attempted in 64 of 76 patients (84.2%). Technical success was achieved in 58 of 64 patients (90.6%). Interventions done during ERCP were the placement of double pigtail plastic biliary stent in 42 of 58 patients (72.4%), nasobiliary drain placement in 4 of 58 (6.9%) and biliary SEMS placement in 12 of 58 (20.6%) patients. In patients who had technical failure during ERCP, 5 Patients had gastric outlet obstruction and one had failed cannulation. In 18 patients who underwent percutaneous transhepatic biliary drainage (PTBD), technical success was seen in all the patients.

The indications of PTBD were: Type III hilar block in 5 patients; Type IV hilar block in 3; gastric outlet obstruction in 5; failed cannulation in 1; and 3 patients refused for ERCP and 1 had surgically

altered biliary anatomy. Bilateral PTBD was done in 2, because of the underlying malignant etiology.

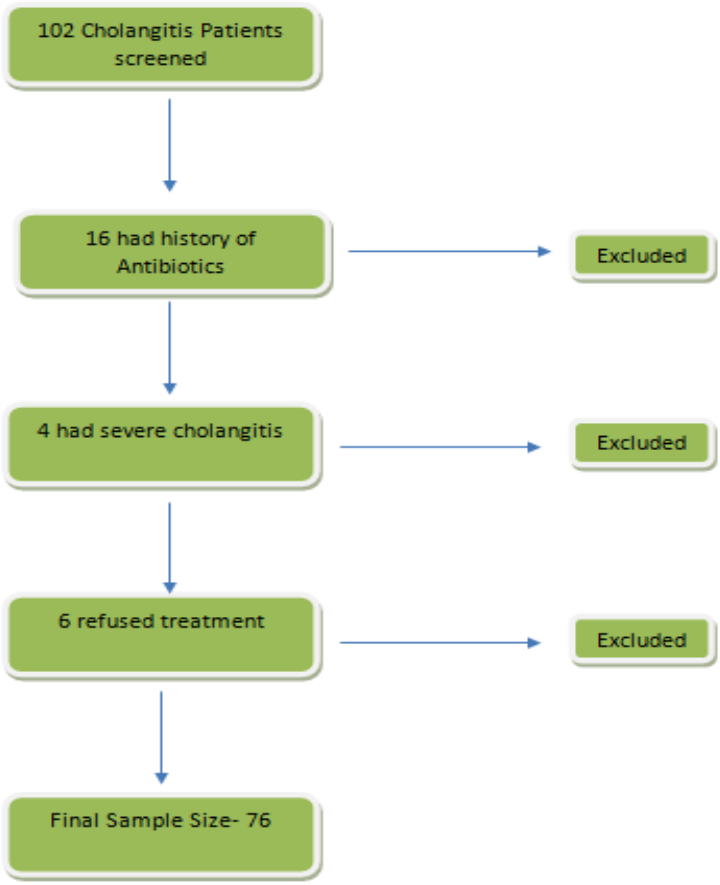

Figure 1: Flow Chart of Patients Selection

Table 1: Clinical Profile of Acute Bacterial Cholangitis Patients

Variable	
Mean Age (in yrs)	46.3± 8.6
Sex (Males)	41/76 (53.9%)
Signs/Symptoms	
Pain	42/76 (55.2%)
Jaundice	76/76 (100%)
Fever	70/76 (92.1%)
Grade of Cholangitis	
Mild Cholangitis	51/76 (67.1%)
Moderate Cholangitis	25/76 (32.8%)
Malignant	
Benign	47/76 (61.8%)
Malignant	29/76 (38.1%)
Diagnosis	
Choledocholithiasis	43/76 (56.6%)
Benign CBD Stricture	4/76 (5.2%)
Ca GB	15/76 (19.7%)
Ca HOP	8/76 (10.5%)
PACA	2/76 (2.6%)
Others	4/76 (5.2%)
Procedures	
Therapeutic ERCP	64/76 (84.2%)
Technical Success	58/64 (90.6 %)

DPT	42/58 (72.4%)
NBD	4/58 (6.9%)
SEMS	12/58 (20.6%)
PTBD	18/76 (23.6%)

Table 2: Result of Microbial Isolates from Cultures

Distribution of Organism	Bile Culture	Blood Culture
Positive	62/76(81.5%)	23/76(30.2%)
Monomicrobial	59/62 (95.1%)	21/23 (91.3%)
E. Coli	39/62(62.9%)	15/23 (65.2%)
Klebsiella	14/62 (22.6%)	6/23 (26.0%)
Pseudomonas	7/62 (11.3%)	3/23 (13.0%)
Acinetobacter	2/62 (3.2%)	1/23 (4.3%)
Enterococci	2/62 (3.2%)	0
Staphylococcus	1/62 (1.6%)	0

Table 3: Antibiotic Sensitivity Pattern

Antibiotic	Sensitivity (Bile Culture)
Colistin	62/62 (100%)
Polymyin B	62/62 (100%)
Meropenem	57/62 (91.9%)
Imipenem	55/62 (88.7%)
Piperacillin + Tazobactam	49/62 (79.0%)
Cefoperazone + Sulbactam	41/62 (66.1%)
Aminoglycosides	41/62 (66.1%)
Linezolid	3/3 (100%)
Vancomycin	3/3 (100%)
Teicoplanin	3/3 (100%)
Cefotaxime	30/62 (48.3%)
Ceftazidime	26/62(41.9%)
Ampicillin	6/62 (9.6%)

Discussion

Acute cholangitis is a life-threatening medical emergency in gastroenterology, defined by the Tokyo consensus as a bacterial infection of an obstructed biliary system requiring emergency care. Charcot's triad, comprising fever, jaundice, and abdominal pain, were the commonest symptoms seen in our patients, as seen in other studies [1, 2]. In our study, all the patients had jaundice, followed by fever in 92% of the patients and pain in the abdomen in 55%. In this study, the commonest etiology for biliary obstruction was choledocholithiasis in 43 of 76 patients (56.6%). This was similar to other studies that have been previously published in India and around the world [2, 7]. In a study by Agarwal et al. from India, the reported incidence of choledocholithiasis as a cause of biliary obstruction resulting in cholangitis was around 70% of their 175 patients.In the same study, the incidence of malignant biliary obstruction was around 21% [2].

In a similar study conducted in Taiwan on 112 patients presenting with cholangitis, choledocholithiasis was seen in 54.6% of cases and malignancy in 25% [7]. In our study, malignant obstruction was seen in 29 of 76 patients (38.1%), with carcinoma gall bladder being the most common. This could be due to the high prevalence of CaGB in northern India. All these patients were subjected to urgent ERCP/PTBD, and bile cultures were aspirated before the administration of a single dose of antibiotics. A blood culture was also obtained. Immediately after drawing the cultures, the patient received IV broad-spectrum antibiotics based on our local resistance pattern.

Bile in a normal biliary tract is in a sterile state [9]. Any obstruction to the biliary tract leads to bacterial colonization of the bile [10, 12], leading to an ascending infection. There is also evidence of bile being infected by the portal blood flow. The presence of obstruction, along with infected bile, leads to an increase in the common bile duct pressure, which results in reflux of bile into the liver sinusoids, resulting in acute cholangitis, cholangiolar abscess, bacteremia, sepsis, and septic shock [1].

In our study, the aerobic bile culture was aspirated either via ERCP or PTBD. All the patients had cholangitis, with no history of any endoscopic or radiological intervention and no history of antibiotics. The present study showed bile culture to be positive in 62 of 76 (81.5%) patients and

blood culture in 23 of 76 (30.2%). This was similar to the study by Bae et al., who reported positive bile culture in 71.7% of cases and positive blood culture in 31.3% of cases [12]. The bile culture aspirated was predominantly monomicrobial in 59 of 62 (95.1%). The most common organism isolated from bile culture was E. coli, seen in 39 of 62 (62.9%), followed by Klebsiella sps. in 14 of 62 patients (22.6%). Other organisms isolated were Pseudomonas in 7, Acinetobacter in 2, Enterococci in 2, and Staphylococcus in 1. Similarly, blood culture, it was predominantly monomicrobial, i.e. in 21 of 23 patients. E. coli was the predominant organism, in 15 out of 23, followed by Klebsiella in 6, Pseudomonas in 3, and Acinetobacter in 1.

This was similar to the previously published studies [6, 12–14, 16, 17]. The gram-positive organism Enterococcus was seen almost exclusively in bile in 2 patients. Anaerobic cultures from bile and blood are uncommon, seen in less than 15%, in most of the reports [7, 12, 13]. The common organism leading to bacterial cholangitis has remained the same over the decade, as seen in most of the studies, but what has changed dramatically is the antibiotic susceptibility. [16, 18, 19]. Initially, in the 1990s, ampicillin and gentamicin were the agents of choice.

These drugs were associated with significant nephrotoxicity, and hence their use is now discouraged. A study by Shivaprakasha et al. on biliary bacterial isolates of 128 patients showed high resistance of gram-negative bacilli to ampicillin (92.4%), cephalexin (82.46%), ciprofloxacin (68.42%), and piperacillin (64.33%) [6]. In a study by M.K. Sahu et al., it was seen that the resistance pattern has shifted drastically, and more organisms are becoming resistant to third generation cephalosporins. Cefotaxime: 71.4% vs. 15.7%; ceftazidime: 80% vs. 21.1%.

When we compared this to our study, the sensitivity of Gram-negative bacteria to polymyxins and carbapenems is still very good, but it has decreased significantly to third- and fourth generation cephalosporins. [6, 9, 13, 15].

In our study, only 48% of gram-negative bacteria isolates had sensitivity to cefotaxime, and to ceftazidime, it was even lower, i.e., 41.9%. Enterococcus, a gram-positive organism isolated from blood or bile culture, had good sensitivity to vancomycin, linezolid, and teicoplanin.

Conclusion

With the increasing prevalence of MDR/XDR pathogens in the bile culture of patients with acute cholangitis, there is an immediate need to revise the antibiotic policy depending on the local resistance pattern. With more community-acquired pathogens being MDR/XDR, as shown in this study, it poses a serious threat to the healthcare system. Immediate attention should be given to this changing spectrum. Acute cholangitis, is a medical emergency and should be treated immediately with broad-spectrum antibiotics and endoscopic or percutaneous intervention, depending on the expertise.

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