

# **Research Article**

# ANALYSIS OF BACTERIAL CHOLANGITIS IN PATIENTS ATTENDING TERTIARY HEALTH CARE CENTRE IN NORTH INDIA

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Abstract- Introduction: Acute bacterial cholangitis is defined as infection either in the inflamed biliary ductal system or in the biliary obstruction. The rational of this study was to identify the microbiological organisms responsible for causing biliary cholangitis and the emergence of drug resistance in these organisms. Materials and Methods: This retrospective study was done in the Department of Microbiology of Tertiary care Super speciality Hospital in North India. All cases of cholangitis due to various causes were included during the study period. Bile samples from clinically suspected cholangitis cases were collected under sterile conditions and standard bacteriological tests were performed for identification and appropriate statistical methods were employed. Result: In the present study involving 175 patients, 57% presented with acute cholangitis, 38% with chronic cholangitis and 5% with malignancy. A total of 50.3% of the bile samples among suspected cholangitis patients were positive for aerobic culture. Gram negative bacteria were the predominant pathogens responsible for cholangitis than Gram positive bacteria. *Escherichia coli* (52.1%) was the predominant microorganism among Gram positive and Gram-negative bacteria followed by *Pseudomonas aeruginosa* (9.6%) and *Acinetobacter baumannii* (8.5%). Polymicrobial infection was reported in 3.2% of the bile culture positive cases of cholangitis. Conclusion: Gram negative bacteria demonstrated maximum resistance to  $\beta$ -lactam group and cephalosporin group of drugs followed by aminoglycosides. Emerging multiple drug resistance strains and polymicrobial etiology reflects therapeutic failure. Incorporating a proper antibiotic policy can help clinicians in early and prompt treatment of cholangitis cases.

### Keywords- Bile culture, cholangitis, ESBL

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#### Introduction

Acute cholangitis results from bacterial or nonbacterial infection in an inflamed and obstructed biliary ductal system [1]. Cholelithiasis especially in common bile duct, neoplasms and strictures in biliary ductal system are the common predisposing factors causing increased intraluminal pressure. The bacteria gains entry through the biliary tract either by retrograde ascent from duodenum or during some instrumentation for removal of stones or stent placement for stricture [2]. The most common organisms isolated in bile are *Escherichia coli, Klebsiella* spp., *Enterobacter* spp and *Pseudomonas* spp. Initial therapy includes empiric broad-spectrum antibiotics and prompt decompression of the biliary system [3]. Change of antibiotics if necessary is altered according to blood/bile culture reports. Widespread and indiscriminate use of antibiotics over the years has altered the sensitivity pattern of micro-organisms and with the emergence of drug resistance; there is a necessity to bring change in empirical antibiotic policy [4]. The present study was conducted to determine the microbiological profile of the bile and antibiotic susceptibility obtained in cholangitis cases in our geographic area.

#### **Materials and Methods**

It is a retrospective hospital-based study of 12 months involving the Departments of Gastroenterology and Microbiology of tertiary healthcare super speciality hospital in North India.

All cases of cholangitis due to various causes diagnosed in the Department of Gastroenterology were included during the study period. The clinical presentations including fever, jaundice, abdominal pain, pruritus, history of previous gall stones, medical treatments and endoscopic or surgical interventions were recorded. During OPD visits or surgical intervention, bile for culture was taken either from common bile duct or from the gall bladder. Cultures were performed within an 1-2 hour of collection. The bile sample was inoculated onto the Sheep blood agar, MacConkey's agar and Robertson cooked meat broth incubated at 37°C for 24 hours. Bacteria isolated aerobically were identified and the antibiogram pattern of the isolates carried out using standard Kirby Bauer technique and interpreted according to CLSI criteria. Extended Spectrum Beta Lactamase (ESBL) production was tested by disk diffusion method using cefotaxime (30 µg) vs cefotaxime/clavulunic acid (30/10 µg). Regardless of zone diameters, a ≥5 mm increase in a zone diameter of an anti-microbial agent tested with clavulunic acid versus its zone size when tested alone, indicated ESBL production as in CLSI phenotypic method. Klebsiella pneumoniae ATCC 700603 strain was used as positive control for ESBL production and Escherichia coli ATCC 25922 as negative control for ESBL production. Metallo-beta Lactamase (MBL) production was detected in imipenem-resistant isolates by phenotypic tests. The Imipenem(IMP)-EDTA combined disc test was used.

For detection of metallobetalactamase, Imipenem(IMP)-EDTA combined disk test was employed for test organisms. Culture positive isolates were inoculated on to plates of Mueller Hinton agar as recommended by the CLSI using lawn culture method. After 24hours of incubation at 37°C the inhibitory zones of the imipenem and Imipenem(IMP)-EDTA disks were compared. In the combined disc test, if the increase in inhibition zone with the imipenem and EDTA disc was found to be  $\geq$ 7 mm than the imipenem disc alone, it was considered as metallobetalactamase producing organism. The study was conducted after taking the approval of the institutional ethics committee. Statistical analysis was done by using proportion of sensitive, resistant and intermediate antibiotic sensitivity of bacteria. Statistical package SPSS Version 16 was used to do the analysis.

### Results

In the present study during the time period of 1 year a total of 175 patients presented with features of acute or chronic cholangitis. The highest distribution of cholangitis was seen in the fourth decade of life with the median age being 38.7 years. The most common clinical presentations were abdominal pain, weight loss, fever and jaundice (63%). Leucocyte count was raised in 88.7% of the cases. Most of the patients had cholestatic jaundice and Alkaline Phosphatase (ALP) was significantly high in patients with malignancy or biliary obstruction. Among 175 clinically suspected cholangitis patients included in the study, 88 patients showed evidence of bacterial growth (94 isolates) yielding an infection rate of 50.3% (46.8% Monomicrobial and 3.2% polymicrobial).





Fig-3 Distribution of ESBL producing Isolates in positive bile culture patients



Fig-4 Distribution of MBL producing Isolates in positive bile culture patients



Fig-5 Antibiotic susceptibility pattern in Gram Negative organisms

A total of 45.1% of the polymicrobial infection was seen during the primary drainage of the biliary tract. Among positive culture cases, male and female patients were 55 (62.5%) and 33 (37.5%) respectively with male to female ratio of 1.6:1. Gram negative bacteria were the predominant pathogens responsible for cholangitis than Gram positive bacteria. Escherichia coli (52.1%) was the most commonly isolated bacteria followed by Pseudomonas aeruginosa (9.6 %) and Acinetobacter baumannii (8.5%). Among Gram positive cocci, bactobilia was caused by 4% of Enterococcus faecium isolates and 1% of Staphylococcus aureus isolate in acute cholangitis cases. Among all the gram negative isolates 20.5% were ESBL producer. Escherichia coli was the predominant microorganism producing extended spectrum beta lactamases in 65% of positive ESBL cultures followed by *Enterobacter cloacae* (15%). Among pathogenic growth on bile culture 14.4% of them were Metallo beta-lactamase producer, most commonly isolated organism responsible for MBL producer was Pseudomonas aeruginosa (29%) followed by Citrobacter freundii (22%). Among total positive bile culture in the present study 0.5% were both ESBL and MBL producers. Gram negative bacteria demonstrated maximum resistance to β-lactam group and cephalosporin group of drugs (40%) followed by aminoglycosides like amikacin (22%) and gentamicin (25%). Among 4 isolates of Enterococcus faecalis (1 isolate was High Level Aminoglycoside Resistant) and 1 isolate of Methicillin resistant Staphylococcus aureus was obtained. Gram positive bacteria showed maximum resistance to penicillin and erythromycin followed by fluoroquinolones.

### Discussion

In untreated acute cholangitis and chronic cholangitis cases infected bile plays an important role as risk factor in increasing rate of complications such as bacteraemia, wound infection and intra-abdominal sepsis. In the present study a positive bile culture rate of 50.3% was observed in clinically suspected cholangitis disease. Our results are comparable with results of study by Gomi, *et al.*, [6] who showed 23-46% culture positive rates in symptomatic cholelithiasis and cholangitis cases. The Gramnegative organisms formed 95% of the bactobilia isolates in which *E. coli* (52%), *Pseudomonas aeruginosa* (10%), *Enterobacter* spp (10%) and *Acinetobacter baumannii* (9%) were the most common organisms.

In previous studies. Gram negative enteric aerobes accounted for 70-78% of positive bile cultures, in which E. coli and Klebsiella spp were the most common [6]. This study was conducted in a tertiary care super speciality setup with an in house microbiology laboratory, which may have led to better isolation of the pathogens without any delay in transport. We also recovered four isolates which are both ESBL and MBL producers, in critically ill patients. Most of the polymicrobial infections (3.2%) were seen among cases of gall stone obstruction, malignancy or previous instrumentation of the biliary ductal system. According to Wu, et al.,[7] the stone may be acting as a source of infection with the bacteria entrapped in the core. In such cases, it becomes pivotal to remove the stones before initiating antibiotic therapy. Cholecystitis due to Candida spp is a rare disease [8] and in our study we found only one isolate from immunosuppressed patient due to malignancy and had previous history of invasive procedures like stent placement in biliary ductal system. This focuses the critical role of early diagnosis of fungal infection in case of cholangitis and the need for early antifungal treatment to prevent complications like fungaemia and death in patients who may not respond to antibiotics and biliary drainage. However, in our study there was absence of anaerobic infections in cholangitis cases. In this study sensitivity for ampicillin-sulbactam was only 50%. Cephalosporins showed a very poor sensitivity of 58-66%. However, piperacillin-tazobactum, cefaperazonesulbactum, imipenem and meropenem had an efficacy ranging from 74% to 81%. Aminoglycosides (gentamicin and amikacin) had poor coverage ranging from 65-68%, and guinolones (ciprofloxacin and ofloxacin) had good coverage ranging from 79% to 81%. The isolates from symptomatic and complicated choledocholithiasis or cholangitis were resistant to many high end antibiotics as in the study by Abeysuriya, et al[9]. A total of 65% of E. coli, 25% of Enterobacter spp 5% of Klebsiella isolates and 5% of Acinetobacter baumannii isolates were ESBL producers. These isolates were usually from patients previously treated with antibiotics, which may have caused selection of resistant gut flora in these patients. Microbiology of cholangitis has not changed drastically but the emergence of drug resistance like ESBL, MBL, AmpC, HLAR, MRSA etc., among these organisms has been a matter of concern. Due to high rate of resistance as seen in our study, ampicillin or ampicillin sulbactam should not be a choice of empirical antibiotic. Polymicrobial infection justifies the selection of these broadspectrum antibiotics [10,11]. But as long as there is biliary obstruction, the concentration and excretion of the antibiotic will not be accurate. Therefore, this necessitates effective antimicrobial activity against potential causative organisms, immediate biliary decompression, the severity of the cholecystitis, and the local susceptibility pattern must be taken into consideration when prescribing drugs[12]. Prior studies have observed excellent responses with piperacillin-tazobactam and meropenem with quinolones for Gram negative isolates and vancomycin for Grampositive isolates being preferred.

### Conclusion

Selection of empirical antibiotic is critical and crucial in patients of complicated cholangitis cases. In our study, we have found multidrug resistant isolates of *Escherichia coli, Klebsiella* spp and *Pseudomonas aeruginosa. Acinetobacter* spp, which is an unusual pathogen, was also recovered from the bile. Therefore, in cases with history of prior instrumentation, hospitalisation, sepsis with co-morbid conditions like malignancy, combination drugs like piperacillin-tazobactum may be considered as the empirical antibiotic of choice. Effective management of cholangitis involves three steps: appropriate resuscitation, initiation of broad spectrum antibiotics to address the systemic infection and definitive biliary decompression. Emphasis should be on developing local antibiotic sensitivity data since significant number of cases of cholangitis show polymicrobial aetiology and high rate of antibiotic resistance.

Application of research: The data helps to select the empirical antibiotics depending on the individual cases.

**Research Category:** Bacterial Cholangitis and drug resistance

#### Abbreviations

ESBL: Extended spectrum betalactamase MBL: Metallobetalactamase HLAR: High Level Aminoglycoside Resistance.

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### Author Contributions: All author equally contributed

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Ethical approval: The Study was conducted after getting ethical approval from Institute Ethics Committee.

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