Original Article

# Bacteriological Profile of Patients with Periampullary Cancer and Effect of Preoperative Biliary Drainage on Bacterial Flora

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## Abstract

**Aim:** This study aims to identify the frequency of bacteriobilia, commonly isolated bacteria and their antibiotic susceptibility pattern from cancer patients with periampullary carcinoma attending a regional cancer center in the North-East India. **Materials and Methods:** This was a retrospective 1-year study of patients with obstructive jaundice due to periampullary carcinoma treated between January 2018 and December 2018. Intraoperative bile samples were obtained for microbiological analysis after transection of the common bile duct. Bile specimens were transported to the microbiology laboratory, and processing was done according to the standard protocol used in our clinical microbiology laboratory. **Results:** Intraoperative bile samples were obtained from 27 patients, and in 21 (77.77%) patients, it was culture positive. Stenting was done in 10 (37.07%) patients, and in those who underwent stenting, microbial contamination of bile was increased significantly (80%) compared to 61.90% in those without stenting. Organisms isolated were *Escherichia coli* 9 (42.85%), *Klebsiella pneumonia* 7 (33.33%), *Pseudomonas* 3 (14.28%), and *Enterococcus cloacae* 2 (9.52%). Carbapenamase producing *E. coli* ($n$ = 1) and *K. pneumonia* ($n$ = 1) was isolated from the two stented patient and one was vancomycin-resistant enterococcus ($n$ = 1). **Conclusion:** Patients who underwent stenting for periampullary carcinoma had a significant risk for acquiring infection with multidrug-resistant bacteria.

**Keywords:** *Bactibilia, multidrug-resistant bacteria, periampullary carcinoma*

## Introduction

Human bile is normally sterile, and in healthy individual, daily excretion of bile helps in flushing out microorganisms entering the biliary tract. Isolation of microorganism in bile or bactibilia is related to infection, which results due to biliary tract obstruction, mass effect of tumor, and also due to interventions such as biliary stenting. Periampullary carcinoma is a heterogeneous group of neoplasms arising from the head of the pancreas, the distal common bile duct (CBD), and the duodenum. For nonmetastasizing cancer of the head of pancreas, surgical resection is the only curative treatment option.[1,2] Whether surgery should be performed immediately in patients with obstructive jaundice or after decompression of the bile duct has been debated extensively and is the subject of on-going studies. In 1935, Alan O. Whipple proposed a two-staged surgical strategy,[3] the rationale was to decompress the obstructed biliary tract and allow restoration of liver function, coagulopathy, and hemorrhagic diathesis. Nowadays, preoperative biliary drainage by endoscopic placement of an endobiliary stent into the CBD or through percutaneous transhepatic drainage of the biliary tract is usually performed.[1,4] Self-expanding metal stents have a higher patency rate and lower incidence of cholangitis than plastic stents.[1] There is increase in postoperative (infectious) complications in perioperative biliary drainage by a stent. Bacterial contamination of the biliary system with a bacterial flora that is resistant to antibiotics leads to an increased risk of postoperative infection.[4] Antibiotic prophylaxis based on preoperative bile cultures and short-term antibiotic treatment in patients who are at the risk of biliary contamination may reduce the chance of postoperative wound infections. Microorganisms gain access through either papilla of Vater or hematogenous route, which leads to bactibilia. Biliary obstruction causes an increase in ductal pressure, resulting in



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bacterial proliferation and dissemination.[5] Eventually, the bacteria presumably translocate into the circulation causing a systemic infection. The most common type of biliary tract infection is aerobic bacterial infection, with a Gram-negative preponderance. Uncommon causative agents are Gram-positive bacteria, anaerobes, viruses, and fungus.[6] The typical Gram-negative enteric aerobes are *Escherichia coli*, *Klebsiella* species, and Proteus species, while *Pseudomonas aeruginosa*, *Enterococcus faecalis* are less commonly cultured.[7] It is well-known that bactibilia is more common after endoscopic stent insertion than open surgery for pancreatic cancer.[8] Similarly, study has shown that increase of *E. coli* in bile leads to a decrease in patient survival.[9] The aim of this study was to characterize the bacterial flora in the bile of patients with periampullary cancer who did or did not undergo biliary stenting, and to assess whether there were differences in antibiotic resistance patterns in these two groups of patients attending a regional cancer center in North-East India. The resultant data will prove beneficial in identifying the causative agents of bile infection in our hospital setting. It will further help in instituting accurate antibiotic therapy, betterment of infection control protocols, and finally, prevent prolonged hospital stay of patients.

## Materials and Methods

This was a prospective study conducted in the microbiology department, of a tertiary care cancer center in North East India. The study was carried over 1 year from January 2018 to December 2018. All intraoperative bile samples were obtained for microbiological analysis after transection of the CBD. Bile specimens were transported to the microbiology laboratory, and processing was done according to the standard protocol used in our clinical microbiology laboratory. The bile samples were received in the bacteriology laboratory in liquid medium in blood culture bottles. The bottles were incubated for 24 h at 37°C. Next day samples were inoculated on blood agar and MacConkey agar and incubated overnight at 370°C aerobically. All plates were examined for visible growth. The colonies were identified as per the standard microbiological procedure. Antibiotic sensitivity testing of the microorganisms was done by modified Kirby-Bauer disc diffusion method on Mueller-Hinton agar, and the results were interpreted as was recommended by the Clinical Laboratory Standards Institute Guidelines.

## Results

The present study included 27 patients. Of them, 20 (74.07%) were male and 7 (25.92%) were female. Maximum number of patients 17 (62.96%) were in the age group of 35–50 years, followed by – 10 (37.03%) in the age group of 61–65 years. Comorbid conditions were seen in 22 of our patients and out of them 3 postoperative patients who underwent stenting presented with sepsis [Table 1]. Out of the 27 intraoperative bile samples, 21 (77.77%) were culture positive [Table 2]. Of 27 patients, 17 were nonstented and 10 patients were stented. In patients who underwent stenting, microbial contamination of bile was increased significantly ($n$ = 8, i.e., 80% compared to $n$ = 13, i.e., 76.5% in those without stenting [Table 2]. Criteria for stenting were as follows: the presence of cholangitis, serum bilirubin >15 mg/dl, serum albumin <3 g/dl, and these features were observed in 10 of our patients [Table 3]. Following organisms were isolated from the bile samples – *E. coli* 9 (42.85%), *Klebsiella pneumonia* 7 (33.33%), *Pseudomonas* 3 (14.28%), and *Enterococcus cloacae* 2 (9.52%) [Table 4]. *E. coli* was the most common isolate in the stented patients, the common bacterial isolates from bile like *E. coli* was replaced by *P. aeruginosa* and *E. faecalis* in stented patients [Table 5]. These bacterial isolates were also associated with a high incidence of antimicrobial resistance against commonly prescribed antibiotics such as ceftriaxone (67%) and piperacillin–tazobactam (33%). carbapenamase producing

**Table 1: Clinical profile of patients**

| Clinical profile | *n* |
|---|---|
| Age (years) | |
| 35-50 | 17 |
| 61-65 | 10 |
| Gender | |
| Male | 20 |
| Female | 7 |
| Comorbidity | 22 |
| HTN | 16 |
| DM | 5 |
| COPD | 1 |
| Smoker | 9 |
| EtOH use | 7 |
| Sepsis (postoperative) | 3 |

COPD: Chronic obstructive pulmonary disease,
HTN: Hypertension, DM: Diabetes mellitus, EtOH: Ethyl alcohol

**Table 2: Patient profile and culture isolates**

| | |
|---|---|
| Total number of bile sample received | 27 |
| Total number of culture-positive | 21 |
| Total number of culture-negative | 6 |
| Total number of patients undergoing stenting | 10 |
| Total number of culture-positive in stented patient (%) | 8 (80) |
| Total number of nonstented patients | 17 |
| Total number of culture-positive in nonstented patient (%) | 13 (61.90) |

**Table 3: Indication of stenting in the study patients**

| Parameters | Number of patients |
|---|---|
| Presence of cholangitis | 10 |
| Serum bilirubin >15 mg/dl | 8 |
| Albumin level <3 g/dl | 9 |
| Both raised bilirubin >15 and albumin <3 | 6 |

**Table 4: Organisms isolated from bile samples**

| Organisms | Number of isolates |
|---|---|
| *Escherichia coli* | 9 |
| *Klebsiella pneumoniae* | 7 |
| *Pseudomonas aeruginosa* | 3 |
| *Enterococcus faecalis* | 2 |

**Table 5: Organisms isolated from stented and nonstented patients**

| Organisms | Stented patients | Nonstented patients |
|---|---|---|
| *Escherichia coli* | 1 | 8 |
| *Klebsiella pneumoniae* | 2 | 5 |
| *Pseudomonas aeruginosa* | 3 | - |
| *Enterococcus faecalis* | 2 | - |
| No growth (%) | 2 (20) | 4 (23.52) |

*E. coli* ($n$ = 1) and *K. pneumonia* ($n$ = 1) isolates from the two stented patients. Another clinical isolate from a stented patient was vancomycin-resistant enterococcus (VRE, $n$ = 1).

Antimicrobial susceptibility pattern observed in the study was as follows: Gram-negative isolates showed the highest sensitivity to meropenem, imipenem, netilmicin, and amikacin. In the present study, most of the *E. coli* were imipenem (88.89%), meropenem (88.89%), ertapenem (77.78%), piperacillin–tazobactam (55.56%), amikacin (77.78%), netilmicin (89%), gentamicin (88.89%), and cefepime (55.56%), respectively. Moreover, most of the *K. pneumonia* were sensitive to imipenem (89%), meropenem (89%), ertapenem (89%), Piperacillin–tazobactam (67%), amikacin (89%), netilmicin (78%), and gentamicin (89%), respectively. In the present study, among the three *P. aeruginosa* isolates, all were sensitive to imipenem, meropenem, two were resistant to piperacillin–tazobactam and one isolate was resistant to amikacin, netilmicin, and gentamicin and cefepime, respectively. Among the Gram-positive isolates, in the present study, out of the two *E. faecalis* isolated from stented patient one was resistant to vancomycin but sensitive to teicoplanin and linezolid, the other isolate was sensitive to vancomycin but showed resistance to piperacillin–tazobactam, ciprofloxacin, and chloramphenicol, both the isolates showed high level of aminoglycoside resistance.

In the present study, most of the E *coli* were sensitive to imipenem (88.89%), meropenem (88.89%), ertapenem (77.78%), piperacillin–tazobactam (55.56%), amikacin (77.78%), netilmicin (89%), gentamicin (88.89%), and cefepime (55.56%), respectively.

In the present study, most of the *K. pneumonia e* were sensitive to imipenem (89%), meropenem (89%), ertapenem (89%), piperacillin–tazobactam (67%), amikacin (89%), netilmicin (78%), and gentamicin (89%), respectively.

### Antibiotic sensitivity profile of *Pseudomonas aeruginosa*

In the present study, three of the *P. aeruginosa* all were sensitive to imipenem, meropenem, two were resistant to piperacillin–tazobactam and one isolate was resistant to amikacin, netilmicin, and gentamicin and cefepime, respectively.

### Antibiotic sensitivity profile of *Enterococcus faecalis*

In the present study, out of the two *E. faecalis* isolated from stented patient one was resistant to vancomycin but sensitive to teicoplanin and linezolid, the other isolate was sensitive to vancomycin but showed resistance to piperacillin–tazobactam, ciprofloxacin, and chloramphenicol, both the isolates showed high-level aminoglycoside resistance.

## Discussion

The present study was done to identify the frequency of bactibilia, the most commonly isolated bacteria and their antibiotic susceptibility pattern from cancer patients with periampullary carcinoma attending a regional cancer center in North-East India. Bacteriological profile of the patient with and without biliary stent was demonstrated. In the present study, 27 bile samples were analyzed for the presence of microorganisms, out of which 21 (77.7%) showed bacterial growth. This finding was similar to a study by Scheufele *et al*.[4] However, a study conducted by Capoor *et al*. found a lower rate of bacterial growth in 32%.[6] In general, enteric Gram-negative aerobes such as *E. coli* and *Klebsiella*, were most frequently found isolates, whereas *Pseudomonas* was less frequently isolated.[10-13] The findings of our study showed *E. coli* 9 (42.8%) was the most common bacteria isolated followed by *K. pneumonia* 7 (33.3%), *Pseudomonas* 3 (14.28%), and *E. faecalis* 2 (9.5%). It was seen that in stented patients, the common bacterial isolates from bile like *E. coli* was replaced by *P. aeruginosa* and *E. faecalis*. Furthermore, these patient groups had greater risk of postoperative infection with multidrug-resistant bacteria. Normally, the patient undergoing stenting was associated with increased infection rate, and also with more antibiotic-resistant bacteria in the bile. The presence of antibiotic-resistant bacteria in the bile will warrant changing the type of perioperative antibiotics used for prophylaxis or treatment of infections. In the present study, bacterial isolates were detected in the bile of almost 80% of stented patients, and three patients presented with postoperative sepsis. It was observed that the use of preoperative biliary stenting significantly increased postoperative infectious complications. Similar observation was made by Jinkins *et al*.[14]

*Enterococcus* species was isolated from one stented patient which one was VRE. Nomura *et al*. also found that the presence of enterococci in the bile was associated with increased postoperative complications.[10] Antibiotic sensitivity of Gram-negative isolates revealed maximum sensitivity to ertapenem, imipenem, and meropenem,

which was similar to a study by Ahmed *et al*.[5] This showed that carbapenems were extremely effective against Gram-negative bacterial infection. The aminoglycosides such as netilmicin, amikacin, and gentamicin also showed good sensitivity profile. However, antimicrobial resistance to second- and third-generation cephalosporins had increased while fourth-generation cephalosporins showed a good promise against Gram-negative organisms. Similar findings were seen by Parekh *et al*.[7] The present study also showed that isolates were least sensitive to amoxicillin-clavulanic acid and ampicillin and second-generation cephalosporins. Another important finding was emerging resistance against piperacillin–tazobactam which is the common preoperative empirical drug of choice. The three *P. aeruginosa* were isolated, and all were sensitive to imipenem, meropenem, two were resistant to piperacillin–tazobactam and one isolate was resistant to amikacin, netilmicin, gentamicin, and cefepime, respectively. The two *E. faecalis* were isolated from stented patient one was resistant to vancomycin but sensitive to teicoplanin and linezolid, the other isolate was sensitive to vancomycin but showed resistance to piperacillin–tazobactam, ciprofloxacin, and chloramphenicol. Both the isolates showed high-level aminoglycoside resistance, similar to what Sharma *et al*. observed.[15]

## Conclusion

Our results indicate that patients undergoing biliary stenting there is a risk of acquiring multidrug-resistant infection with atypical biliary bacterial isolates. A bile sample for microbiological analysis is desirable, as it leads to an accurate selection of antibiotics for the treatment of patient with biliary obstruction. Thus, a regular update of antibiotic policy based on institutional antimicrobial susceptibility data will aid choosing the most appropriate antibiotics for the empirical therapy of biliary infection in patients with periampullary carcinoma.

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### Conflicts of interest

There are no conflicts of interest.

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