

Relation of Intra-Operative Bile Culture with Post-Operative Complications in Patients Undergoing CBD Exploration for Choledocholithiasis at Tertiary Centre

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Introduction: Choledocholithiasis are present in around 5 to 20 % of cases of patients with cholelithiasis. These stones are mostly removed either surgically or endoscopically. Routine bile culture is sent during operative management of biliary tree. This study aims to recognize the organisms predominantly present in bile along with its relations to the post operative septic complications.

Methods: This was a hospital-based Prospective Analytical Study of patients who underwent Common Bile Duct exploration in the Department of Surgery, Dhulikhel Hospital, Kathmandu University Hospital from 2019 to 2021 A.D.

Results: Total forty patients were enrolled in this study, with mean age of 52 years. The mean length of hospital stay was 7.48 days. The bile culture positivity was seen in 77.5% cases with predominantly Gram-negative organisms like *E coli* and *Klebsiella*. Aminoglycoside had good sensitivity against these biliary organisms. The surgical site infection was seen in 67.5% patients.

Conclusion: This study showed that many of the patients had positive bile culture sent intra-operatively. However, there is no association of the positivity with post operative complications. The predominant organisms were Gram negative and the effective antibiotics were aminoglycosides including gentamicin and amikacin.

Keywords: aminoglycosides, bile culture, CBD exploration, choledocholithiasis, surgical site infection.

Surgical removal of gallbladder is the definitive treatment for symptomatic gallstones. Laparoscopic cholecystectomy is the standard of care.¹ In cases of acute inflammation of gallbladder, analgesia with intravenous antibiotics is used.² Common bile duct stones can be removed with a preoperative or postoperative Endoscopic Retrograde Cholangiopancreatography (ERCP) or operatively with a single stage common bile duct exploration. Common Bile Duct (CBD) exploration can be performed via laparoscopic approach or open.^{3,4} Although Laparoscopic CBD exploration is recommended, due to technical expertise and equipment availability, open CBD exploration are still performed at a significant proportion in many centers worldwide.³ Though bile is sterile, the biliary infection can be caused by any type of organisms ranging from aerobic gram positive to gram negative to anaerobic organisms. E.coli, Klebsiella and Streptococcus are the common organisms.⁵ Infected bile or bile-contaminated operations are reported to have a higher incidence of septic complications than non-bile contaminated operations.^{4,5} During the post-operative

period, surgical site infections are seen in around 2.6 % patients undergoing different surgeries in Nepal.⁶ The United States Centers for Disease Control and Prevention (CDC) has developed criteria that define SSI as infection related to an operative procedure that occurs at or near the surgical incision within 30 days of the procedure.⁷

Infections in the biliary tree contribute both to formation of CBD stones and its complication like cholangitis or hepatic abscesses.² Knowing the organisms is crucial in management of patient undergoing biliary surgeries.³ Thus, routine bile culture is sent intra-operatively during biliary surgery. The use of antibiotics prophylaxis as well as during post-operative period is necessary in patients undergoing CBD exploration.⁸ This study aims to recognize the organisms predominantly present in bile along with its relations to the post operative complications in patients undergoing CBD exploration.

Methods

This was a hospital-based prospective analytical study including patients undergoing CBD exploration for CBD stones at Dhulikhel Hospital, Department

of Surgery, Kathmandu University Hospital, Kavre, Nepal. Consecutive Sampling Technique is used where all the patients meeting the inclusion criteria were taken as samples during the study period. Patients of age more than 16 years planned for CBD exploration were taken into the study. Those cases where bile sample were not taken were excluded. Data was collected using the proforma form. After selection of the samples, consent was obtained from the patients or relatives and they were enrolled in the study. With the help of Proforma, patient's demographic details, the pre-operative, intra-operative and post-operative information were filled. Patients underwent CBD exploration as per departmental procedures. Pre-operative antibiotics were given which included cephalosporins (Cefotaxime 1gm or Cefazolin 2gm) and aminoglycosides (Amikacin 500mg) along with Metronidazole 500mg. Bile cultures were sent during intra-operative period and sent in a sterile medium to Department of Microbiology. During post operative period, patients were monitored regularly including the vitals charting and assessment of post operative complications. Bile culture reports were traced from the microbiology department on second postoperative day. The culture and sensitivity pattern of the bile was recorded.

in the proforma form. During post-operative period patients received empiric antibiotics which included Cephalosporins (Cefotaxime), Aminoglycosides (Amikacin) and Metronidazole and later effective antibiotics were given according to the culture and sensitivity of the bile culture report. All these data were recorded in the proforma form. The patients were followed up upto 30 days and were contacted by phone after discharge during this period.

Data was collected according to the proforma form, and entered in Microsoft Access and Microsoft Excel 2010. Analysis was done using Statistical Package for Social Sciences (SPSS) version 22. Chi-square test was used and P-value less than 0.05 were considered as statistically significant.

Results

The total patients that were included in this study were 40, who underwent CBD exploration for choledocholithiasis during the study period. The age of patients ranges from 20 to 75 years with mean age of 52 years (SD=13.05). Majority of the patients i.e. 47.5% fall in the age group of 40 to 59 years. Out of these cases, 65% were females.

Fifty percent i.e., twenty patients with CBD stone had developed acute cholangitis in the past thus explaining the

CBD Exploration for Choledocholithiasis

Age Group (years)	Gender		Total (%)
	Female (%)	Male (%)	
20-39	6(25)	3(18.8)	9(22.5)
40-59	10(41.7)	9(56.2)	19(47.5)
60+	8(33.3)	4(25)	12(30)
Total	24(100)	16(100)	40(100)

Table 1: Age and gender wise distribution of patients undergoing CBD exploration

Organisms	Number	Percentage
E coli	27	87.09
Enterococcus	8	25.80
Klebsiella	6	19.35
Pseudomonas	4	12.90
Salmonella typhi	1	3.22
Salmonella paratyphi	1	3.22
MRSA	1	3.22
Proteus	1	3.22
Enterobacteriaceae	1	3.22

Table 2: Organisms present in bile culture study sent during CBD exploration

need of early ERCP in majority of cases. Out of 40 patients, 31 (77.5%) had positive bile culture. In total, fifty organisms were isolated from the 31 positive cultures.

Among positive bile cultures, E coli, Enterococcus and Klebsiella were common pathogens shown in **Table 2**. 45% of cultures had polymicrobial growths.

Surgical Site Infection	Culture Positive		Total (%)	P-value
	Yes (%)	No (%)		
Seen	22 (70.9)	5 (55.6)	27 (67.5)	0.755
Not Seen	9 (29.1)	4 (44.4)	13 (32.5)	
Total	31 (100)	9 (100)	40 (100)	

Table 3: Surgical site infections in the CBD exploration cases

Post-operative Systemic Complications	Culture Positive		Total (%)	P-value
	Yes (%)	No (%)		
Seen	8 (25.8)	1 (11.1)	9 (22.5)	0.353
Not Seen	23 (74.2)	8 (88.9)	31 (77.5)	
Total	31 (100)	9 (100)	40 (100)	

Table 4: Post-operative systemic complications following CBD exploration.

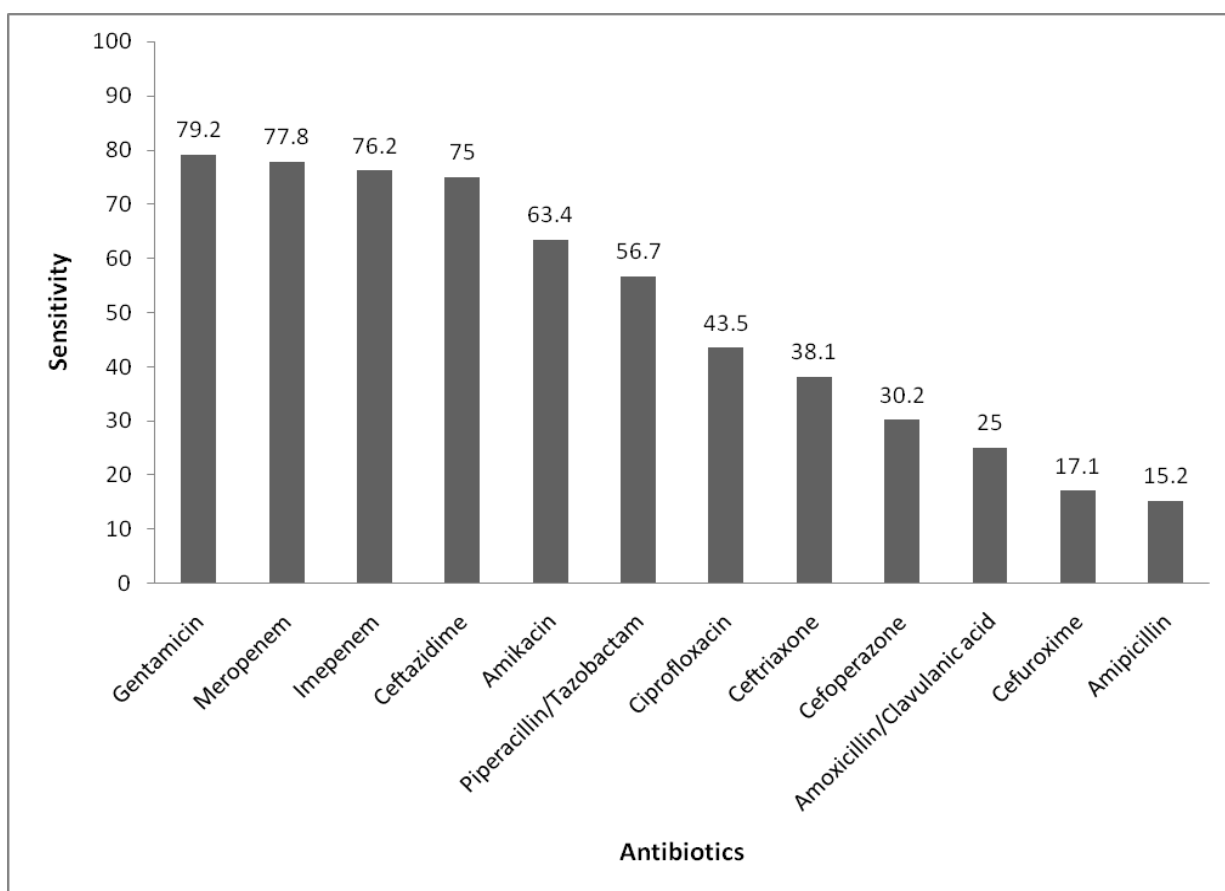


Figure 1: Bar Diagram showing the antibiotic sensitivity pattern for organisms cultured in bile

Amikacin, Gentamicin and Carbapenems were the antibiotics having good sensitivities to the organisms cultured in bile. Gentamicin was sensitive in 79.1% of cultures followed by Carbapenems in 77.8%. 63.4% of organisms were sensitive to Amikacin. Ceftazidime (75%) was sensitive drug against Pseudomonas organisms. There was high resistance noted in Ampicillin (84.7%), Amoxycyclav (75%), and Ceftriaxone (61.9%) shown in **Figure 1**.

Surgical site infection was seen in 67.5% patients in the post-operative period when followed up to 30 days. Majority of cases i.e. 62.5% of cases had superficial surgical site infection. There was no statistically significant correlation between positive bile culture and surgical site infection (P-value 0.755) as shown in **Table 3**.

During post-operative period 42.5% of patients developed fever. Out of 40 cases, nine patients (22.5%) developed post-operative systemic complications. There were 12.5% of cases who developed chest complications mostly atelectasis and pneumonia. Urinary tract infections were seen in ten percent of cases. One case developed postoperative intra-abdominal collection secondary to stent migration that also developed post-operative pneumonia. Twenty six percentage of cases with positive bile culture developed post operative complications however this

association was not statistically significant (P-value 0.353) shown in **Table 3**. There was no mortality during the study period.

Discussion

In our study, mean age of all patients was 52 ± 13.05 years, where majority were under the range of 40-59 years (47.5%). These findings were comparable to the study performed by De Silva et al in 2019 where mean age was 53.6 years and the maximum range of patients falls under 40 60 years.⁹ The male to female ratio observed in our study also showed that females have higher risk of having choledocholithiasis similar to previous other studies.

Acute cholangitis is one of the severe complications of choledocholithiasis which occurred in 50% of patients. In a study by Salvador et al choledocholithiasis was the most common underlying biliary disease which was more likely to be associated with cholangitis.¹⁰ The reported acute cholangitis was 25.3% as shown by De Silva et al in their study.⁹

Though bile is a sterile body fluid, cultures sent during CBD exploration in this study were positive in 31 (77.5%) cases. This data is similar to the findings in the study done by Salvador et al. showing 78% of positive bile cultures.¹⁰ Among these, 45% of cultures had polymicrobial growths. In the study done by Flores et al.

had shown 42.1% of polymicrobial organisms growth.¹¹

The predominant organisms were Gram negative organism. *E.coli* and *Klebsiella* were the two most commonly seen organisms in this study (52.9% and 11.8%). Similar findings were noted in the study conducted by Flores et al and Chang et al.^{11,12} *E coli* (36%) and *Klebsiella* (15%) were the common gram-negative organisms noted by Chang et al.¹²

The common gram-positive organism seen in bile was *Enterococci* occurred in 15.8%. In the study done by Flores et al, this organism was present in 17.2% of positive bile cultures.¹¹

Different factors have been proposed regarding the causes of infection in the biliary tree. There is also a potential risk in patients who undergo endoscopic treatment for choledocholithiasis to have biliary tree infection.^{13, 14} The enteric organisms can migrate during endoscopic manipulation.⁵ In our setting, many of the patients had undergone endoscopic attempt for removal of choledocholithiasis, with multiple attempts in some cases. This might be a reason for positive bile culture in high proportion of cases.

The culture of the bile had gram negative pathogens as predominant organisms. Thus, antibiotics used pre-operatively and during post operative period should be effective in covering these organisms.

Also, there were good proportions of polymicrobial growth, which necessitates using combination of drugs in treating them effectively. Aminoglycosides i.e amikacin and gentamicin had good sensitivities against biliary flora as shown in this study. Other effective drugs include Piperacillin/Tazobactam and ciprofloxacin. Thus, empirical treatment with ciprofloxacin or piperacillin/tazobactam can be done and if necessary, an aminoglycoside can be added based on severity of infection. Melzer et al and Salvador et al also concluded that aminoglycosides as sensitive antibiotics for biliary organisms.^{10, 15}

There was no association noted in the study regarding the positivity of bile culture with post-operative systemic complications. Similar conclusions were drawn in study done by Chandrakasan et al.¹⁶ Other papers, though old ones had concluded the Same.^{17, 18}

There were 67.5% of cases with surgical site infection, which is a high proportion of operated cases. This finding was also not statistically correlated with the bile culture status. Willis et al in his paper also showed no relevancy.¹⁹

Conclusion

This study showed that that many of the patients had positive bile culture sent during in-operative period. The

predominant organisms were Gram negative and the effective antibiotics were aminoglycosides like gentamicin and amikacin. A significant proportion had surgical site infection. There was no statistic significant correlation between positivity of bile culture with post-operative local and systemic complications. Many of patients had surgical site infection, which necessitates further studies to carry out to evaluate the cause and also improve the current rate.

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