

Original Research Article

Bactibilia-effect on postoperative course and outcome in patients with bilio-pancreatic diseases

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ABSTRACT

Background: Bactibilia is detrimental to the outcomes of biliary tract surgery. The present study was undertaken to determine the microbial flora of bile and their significance to post-operative infectious complications and morbidity.

Methods: A retrospective study of patients with biliopancreatic diseases who underwent surgery from Jan 2017 to March 2020 in a tertiary care hospital were analyzed. The samples were assessed for bile microbiological flora, and a search for their possible link with post-operative infectious complications and morbidity was carried out.

Results: A total of 90 bile samples were assessed. The mean age of the study group was 51.8 SD-13.6 years with male predominance. Bactibilia was found in 39 cases (43.3%), mostly in patients with malignant diseases, older than 50 years and females. *Escherichia coli* was the most common organism. Post-operative infectious complications were seen in twenty cases, thirteen of them in bactibilia-associated patients, showing statistical significance. Statistical significance was found between the presence of pre-operative biliary stent and bactibilia and between diabetes mellitus and bactibilia. Nine out of 24 patients with comorbidities had post-operative infectious complications. No significant relationship was found between pre-operative jaundice and comorbidities with bactibilia.

Conclusions: The present study showed a statistically significant relationship between the presence of pre-operative biliary stent and bactibilia and also the incidence of post-operative infectious complications and bactibilia. Microbiological analysis of bile is a valuable tool in prognosticating the post-operative complications, thereby guiding us to provide adequate therapy and helps to establish local antibiotic guidelines.

Keywords: Bile, Bactibilia, Biliary stenting, Biliary microbial flora

INTRODUCTION

Bile in the bile ducts is usually sterile. Any disease process affecting the gall bladder or bile ducts causes colonizing of the bile, thus leading to bactibilia. In the circumstances of normal bile flow, bacteria in bile have no clinical significance. However, an obstruction causes an increase in biliary pressure, with a probable translocation of bacteria into the systemic stream. This causes cholangitis, ranging from local infection to severe sepsis and multi-organ dysfunction.¹ Ascending infection due to the reflux of duodenal contents is the prime reason followed by blood-borne or spread through portal venous

channels. The other predisposing conditions include critical illnesses such as trauma, burns, sepsis, HIV infection, immune-suppression, diabetes, non-biliary surgery and childbirth.²

Bactibilia is mainly caused by bacterial, followed by fungal organisms and rarely viral, with the most common agent being gram-negative bacteria.^{3,4} Bactibilia may increase the post-operative infectious complications, which in turn lead to a prolonged hospital stay and prolonged use of antibiotic therapy, ultimately resulting in increased costs.^{5,6}

Thus, this study aims to determine the various microbial flora in the bile of patients undergoing biliopancreatic surgeries and establish a statistical relation between bactibilia and post-operative infectious complications.

METHODS

The present study is a retrospective study carried out from 2016 to 2020 at a single center, NRI medical college and hospital, Guntur. The bile samples collected from all the patients undergoing any bilio-pancreatic surgeries during the study period were included. The bile was collected under sterile precautions from the common bile duct before the definitive procedure was carried out.

The inclusion criteria included patients above the age of 18 years, with an intra-operative collection of bile from the common bile duct alone. The exclusion criteria consisted of emergency surgeries, in which there might be a delay in the processing of the bile, and also case sheets containing incomplete medical details as per the study guidelines.

The data was collected retrospectively from the medical records of the patients who met the inclusion and exclusion criteria. Epidemiological data, comorbidities, nature of the illness, type of surgery underwent, post-operative outcomes were collected. Based on the above criteria, patients were grouped into two groups, group 1- patients with benign diseases and group 2- patients with malignant diseases (Table 1). The study parameters analyzed were age, sex, co-morbidities, pre-operative jaundice, pre-operative stenting, benign or malignant disease, bactibilia, post-operative infectious complications and post-operative duration of hospital stay (Figure 1).

Table 1: Primary division of study population (Group 1 vs group 2).

Variables	Group 1 (Benign)	Group 2 (Malignant)	Total
No. of cases	42	48	90
Pre-op jaundice	10	25	35
Pre-op biliary stent	21	16	37
Bactibilia	18	21	39
Post-op infections	7	13	20
Post-op duration of stay mean (days)	8.38	11.79	10.08 (avg)

In the current study, jaundice was considered if serum total bilirubin levels are more than 1.5 mg/dl, while the patient was considered to have a fever if the axillary body temperature is $\geq 37.8^{\circ}$ C at least 48 hours after surgery. Patients with purulent discharge from the surgical wound were categorized as having surgical site infections and were treated accordingly.

The empirical antibiotics given to the study population were cefoperazone with sulbactam, with or without metronidazole, given at the time of induction of anesthesia and continued post-operatively for 3-5 days. Amikacin was given to patients at high risk of developing post-operative infectious complications like pre-operative cholangitis.

Sample processing

The bile samples were received in the Bacteriology laboratory in liquid medium in blood culture bottles. The bottles were incubated for 24 hours at 37° C. The following day, samples were inoculated on blood agar and MacConkey agar and incubated overnight at 37° C aerobically. All the culture plates were examined for visible growth. The colonies were identified as per standard microbiological procedure and automated identification system Vitek 2. Antibiotic sensitivity testing of the microorganisms was done by fully automated Vitek 2 (biomerieux, Germany), and the results were interpreted as minimum inhibitory concentration for every antibiotic tested, as per the recommended guidelines by the CLSI 2021 (Clinical laboratory standards institute).

Statistical analysis

The data collected in the current study was statistically analyzed in the SPSS software. The qualitative variables were analyzed through Pearson’s chi-square test or T-test, at a 95% confidence level. A probability of 0.05 or less was accepted as being statistically significant.

RESULTS

A total of 114 case records were identified during the study period, among which 90 case records met the study

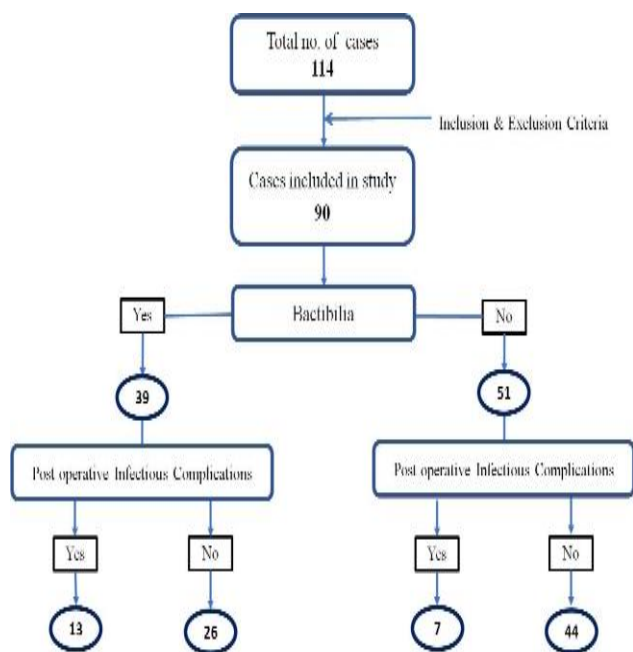


Figure 1: Study design.

protocols. The mean age is 51.8 years (SD 13.6 years, range: 15-89). Majority were men (n=47) and older than 50 years (n=57). Comorbidities were found in 24 patients, and diabetes mellitus was the most common. Among the total 90 cases, 42 belong to the benign disease category (group 1), and 48 had malignant diseases (group 2). Among the benign diseases, choledocholithiasis with cholelithiasis is most common (n=23), and perampullary carcinoma (n=38) was the commonest in the malignant group. The most common procedures done were Whipples surgery (n=46), CBD exploration±choledochoduodenostomy (n=28), and hepaticojejunostomy (n=10).

Bactibilia was found in 39 bile samples (43.3%). The majority were females (54%) with a mean age of 50 years. In the 39 samples, 21 were from patients with malignant disease (p=0.93). In the patients with bactibilia, 16 (41.02%) had jaundice, and 22 (56.4%) patients underwent endoscopic retrograde cholangiopancreatography (ERCP) with biliary stenting pre-operatively. Thirteen patients had comorbidities, among which diabetes mellitus was most common, which is seen in 12 (30.7%) patients. Statistical significance was found between the presence of pre-operative biliary stent and bactibilia (p=0.009) and also between diabetes mellitus and bactibilia (p=0.049). There was no statistical relationship between the presence of comorbidities and bactibilia (p=0.211) and the presence of pre-operative jaundice and bactibilia (p=0.716). Patients with bactibilia had an increased post-operative stay, which was significant statistically (p=0.015) (Table 2).

In the 39 bile samples with bactibilia, forty-three bacterial cultures came out to be positive as a result of simultaneous growth of two organisms in 4 bile samples. *E. coli* was the most frequently isolated bacteria (60.5%), followed by *Klebsiella pneumoniae* (16.2%) and *Pseudomonas aeruginosa* (11.6%) (Table 3).

Table 2: Distribution of variables in the study population.

Variables	Culture-positive, (n=39) (%)	Culture-negative, (n=51) (%)	P value
Age: mean (years)	49.7	52.5	0.93846
Gender: Male/female	18/21	29/22	0.31352
Comorbidities	13 (33.3)	11 (21.5)	0.21105
Diabetes mellitus	12 (30.7)	7 (13.7)	0.04960
Pre-op jaundice	16 (41)	19 (37)	0.71614
Pre-op biliary stent	22 (56.4)	15 (29.4)	0.00989
Post-op infectious complications	13 (33.3)	7 (13.7)	0.02661
Post-op duration of stay-mean (days)	11.36	9.31	0.01572

Table 3: Distribution of micro-organisms.

Identified bacteria	Benign group	Malignant group	Total
<i>Escherichia coli</i>	11	15	26
<i>Klebsiella sp.</i>	4	3	7
<i>Pseudomonas</i>	1	4	5
<i>Enterococcus sp.</i>	3	0	3
<i>Enterobacter sp.</i>	0	1	1
<i>Proteus vulgaris</i>	0	1	1
Total	19	24	43

Post-operative infectious complications were found in 20 patients, of which 13 of them had bactibilia, which resulted in a statistically significant relationship between bactibilia and the incidence of post-operative infectious complications (p=0.026), and *E. coli* being the most identified organism (n=8). Mono microbial growth was seen in 11 patients, while two organisms were grown in the culture of 2 cases. The presence of pus at the wound site was the most identified complication (n=12), while fever was recorded in 4 patients. Two patients developed bile leak, and an equal number developed an enterocutaneous fistula. Statistical significance was found between the presence of comorbidities (n=24) and the post-operative infectious complications (p=0.036) and also between post-operative duration of stay as well as post-operative infectious complications (p<0.00001) (Table 4).

Table 4: Correlation between post-operative infectious complications and study parameters.

Variables	Post-operative infectious complications		P value
	Present (n=20) (%)	Absent (n=70) (%)	
Age: mean (years)	50.6	52.2	0.32405
Gender: Male/female	10/10	37/33	0.82151
Comorbidities	9 (45)	15 (21.4)	0.03552
Diabetes mellitus	7 (35)	12 (17)	0.08438
Pre-op jaundice	10 (50)	25 (35.7)	0.24777
Pre-op biliary stent	11 (55)	26 (37)	0.15231
Bactibilia	13 (65)	26 (37)	0.02661
Post-op duration of stay-mean (days)	14.15	9.07	<0.00001

DISCUSSION

Post-operative infectious complications are detrimental to the outcomes of biliary tract surgeries. The present study was carried to reaffirm the implicative role of bactibilia and to assess the usefulness of an empirical antibiotic regime based on the local antibiogram. The present study was a retrospective analysis of 90 patients who underwent biliary tract surgeries at our institute. In the present study, most of the patients belonged to the age group of above 50 years. A few of the previous studies showed a synergistic association with the older age group and bactibilia.⁷⁻⁹ However, in the present study, we have not found any such association. Furthermore, we did not find any association between the patient's sex and bactibilia.

In total, 24 patients had comorbidities, diabetes mellitus (n=19) being the most common. In the present study, no statistically significant relation was observed between comorbidities and bactibilia (p=0.21105). However, diabetes mellitus alone has shown to be an individual risk factor for bactibilia (p=0.0460). These results are in concordance with other studies, such as by Hickman et al who associated bactibilia with diabetes mellitus.¹⁰ Pre-operative biliary stenting was also found to be an independent risk factor for bactibilia (p=0.00989). This observation was consistent with the findings of Galili et al and can be mainly attributed to the fact that sphincterotomy may lead to ascending infections from the intestinal lumen into the common bile duct.¹¹ In the present study, we found that there was no significant association between presence of pre-operative jaundice and bactibilia, whereas a study conducted by Galili et al found to have association between 2 variables.¹¹

The bacteriological profile of our bactibilia was comparable with that reported in the literature.^{7,12} The predominantly found organisms were the *Escherichia coli* and *Klebsiella* species among the benign group, and *E. coli* and *Pseudomonas* were the most commonly found in the malignant group. In the present study, monomicrobial cultures were seen in 35 (89.74%) patients, with *E. coli* and *Klebsiella* species being the most common similar to studies done elsewhere.^{13,14} Monomicrobial infections pose a challenge for the choice of the antimicrobial drug because many antibiotics cover predominantly either gram-positive or gram-negative bacteria but not both.¹⁴

In the present study, a total of 20 patients developed post-operative infectious complications. Among these, 13 patients had bactibilia. This may suggest that patients with bacteria in their bile tend to have a higher incidence of infective complications post-operatively. This phenomenon is upheld in the present study as well, as there was a statistically significant correlation between bactibilia and post-operative complications in the study population. The aforementioned trend can be strengthened by some significant results shown in other studies.^{5,6,11,15} In the current study, there was no statistical

correlation between patient's age and sex with post-operative complications. The presence of comorbidities showed a positive correlation, while diabetes as such showed no correlation with the incidence of complications. This is somewhat controversial, as diabetes is usually associated with infective complications and can be a bias due to the limited sample size. Pre-operative jaundice and pre-operative biliary stenting showed no association with post-operative complications. In the current study, there was a clear statistically significant relation to state that both bactibilia and post-operative complications resulted in an extended post-operative hospital stay of the patients.

Although there was no statistical relationship between the complications and variation in the empirical antibiotics given and their culture sensitivities patterns, the antibiotic regime followed at our study place had prevented post-operative infectious complications in about 66% of patients included in the study. Microbiological analysis of bile is a valuable diagnostic tool that aids to provide adequate therapy and helps to establish local antibiotic guidelines for management of biliary tract infections.¹⁶

The limitations of the present study were that it was a single centre, retrospective study and the emphasis was on the local microbiota. We would require a more extensive multi-center prospective study to analyze larger populations and thence put forward a typical empirical antibiotic regimen.

CONCLUSION

The present study reaffirmed the significant relationship between pre-operative stenting and bactibilia and between bactibilia and post-operative infectious complications. Antibiotic prophylaxis is essential and should be considered before any surgical or non-surgical interventions to the biliary tracts. The primary intention is to lessen the systemic, intraperitoneal, and wound sepsis caused by microorganisms released from the biliary tract. Microbiological analysis of bile is valuable tool in prognosticating post-op complications, thereby guiding us to provide appropriate therapy and helps to establish local antibiotic guidelines in management of infectious complications after biliopancreatic interventions.

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