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Microbial and Clinical Characteristics in Hepatobiliary Surgery Patients: Analyzing Risk Factors and Antibiotic Resistance

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Abstract

Introduction: Bactibilia frequently complicates biliary obstruction, especially in malignant cases with drainage, and is associated with antimicrobial resistance, thereby posing significant therapeutic challenges. This study characterized the microbiological and clinical profiles, antibiotic resistance patterns, and associated risk factors in patients undergoing hepatobiliary surgery in Colombia.

Materials and Methods: We conducted a cross-sectional analytical study on 95 patients with positive bacterial cultures following surgery. The analysis included clinical and microbiological variables. For analytical purposes, patients were stratified into two groups: those with PBD and those without, allowing for the assessment of clinical and microbiological differences between the cohorts. We used chi-square tests, Student's t-tests, Mann–Whitney tests, and logistic regression.

Results: Of the 95 patients, 61.05% were men, with a median age of 67 years. Preoperative exposure to endoscopic retrograde cholangiopancreatography was significantly higher in patients with biliary pancreatitis (73.47%; p=0.001). *Escherichia coli* exhibited high resistance to ampicillin/sulbactam (74.29%) and ciprofloxacin (59.46%), while piperacillin/tazobactam (89.74%). Resistance to meropenem was notably associated with female sex (odds ratio [OR: 9.55; 95% confidence interval [CI], 1.12–80.9; P=0.038) and longer ICU stay (OR: 1.12; 95% CI, 1.00–1.24; P=0.038).

Discussion: This study reveals significant antibiotic resistance in *E. coli* and *K. pneumoniae*, especially in patients with preoperative biliary drainage. These findings highlight the importance of tailoring antibiotic prophylaxis based on preoperative cultures to effectively address antibiotic resistance in hepatobiliary surgery.

Keywords: antimicrobial drug resistance; infections; biliary tract surgical procedures; antimicrobial stewardship

Características microbianas y clínicas en pacientes sometidos a cirugía hepatobiliar: análisis de factores de riesgo y resistencia a antibióticos

Resumen

Introducción: La bactibilia complica frecuentemente las obstrucciones biliares especialmente en casos malignos con drenaje— y está asociada con la resistencia antimicrobiana, lo que genera importantes desafíos terapéuticos. Este estudio caracteriza los perfiles microbiológicos y clínicos, los patrones de resistencia a antibióticos y los factores de riesgo asociados en pacientes colombianos sometidos a cirugía hepatobiliar.

Materiales y métodos: Se llevó a cabo un estudio analítico de corte transversal en 95 pacientes que presentaron cultivos bacterianos positivos tras la cirugía. El análisis incluyó variables clínicas y microbiológicas. Para fines analíticos, los pacientes fueron estratificados en dos grupos: aquellos con drenaje biliar preoperatorio (PBD, por sus siglas en inglés) y aquellos sin él, lo que permitió evaluar las diferencias clínicas y microbiológicas entre las cohortes. Se utilizaron métodos estadísticos como la prueba de chi-cuadrado, la prueba t de Student, la prueba de Mann-Whitney y regresión logística.

Resultados: De los 95 pacientes, el 61.05% eran hombres, con una edad mediana de 67 años. La exposición preoperatoria a la colangiopancreatografía retrógrada endoscópica fue significativamente mayor en pacientes con pancreatitis biliar (73.47%, p = 0.001). *Escherichia coli* mostró una alta resistencia a ampicilina/sulbactam (74.29%) y ciprofloxacina (59.46%), mientras que *Klebsiella pneumoniae* presentó una resistencia considerable a ampicilina/sulbactam (92.31%) y piperacilina/tazobactam (89.74%). La resistencia a meropenem se asoció notablemente con el sexo femenino (OR: 9.55; IC 95%, 1.12–80.9; p = 0.038) y con una mayor estancia en la unidad de cuidados intensivos (OR: 1.12; IC 95%, 1.00–1.24; p = 0.038).

Discusión: El estudio revela una resistencia antibiótica significativa en *E. coli* y *K. pneumoniae*, especialmente en pacientes con drenaje biliar preoperatorio, lo cual se correlaciona con la gravedad de la infección y la duración de la estancia en la UCI. Estos hallazgos resaltan la importancia de personalizar la profilaxis antibiótica según los cultivos preoperatorios para abordar de manera efectiva la resistencia a los antibióticos en la cirugía hepatobiliar.

Palabras clave: resistencia a los fármacos antimicrobianos; infecciones; procedimientos quirúrgicos de las vías biliares; uso racional de los antimicrobianos

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Introduction

Bactibilia is defined as the colonization of microorganisms within the biliary tract, typically resulting from benign or malignant obstructive processes that disrupt bile flow[1,2]. In benign obstructions, bactibilia represents between 6% and 42% of uncomplicated cholelithiasis cases and 60% of choledocholithiasis cases[3]. In malignant obstructions, it occurs in 80 % approximately, although with preoperative biliary drainage (PBD), this incidence increases considerably (80–100%), as well as the bacterial resistance (50%) and the polymicrobial isolates (53%). However, some studies suggest that PBD has minimal impact on postoperative outcomes and carries risks of procedure-related complications[4,5]. Consequently, PBD is recommended for conditions such as pruritus, coagulopathy, cholangitis, renal failure, or delayed procedure by up to one week[6].

The debate persists because of the high morbidity rates (25–60%), which are broadly associated with postoperative infections and can increase healthcare costs by up to $15,366 per complication[7]. Bacterial resistance significantly contributes to the rising incidence of postoperative infectious complications, including intra-abdominal abscesses, surgical site infections, sepsis, and septic shock[5]. Straightforward PBD is associated with bacterial resistance that ranges from 20 to 70% across different antibiotic groups (e.g., first- and second-generation cephalosporins, ampicillin/sulbactam, cefotaxime), with a concerning prophylactic antibiotic resistance reported as high as 52% in some studies[4,8].

Given the concerning data on PBD and bacterial resistance, there is no consensus in the international guidelines on evaluating high-risk bacterial resistance groups to provide targeted antibiotic prophylaxis[9]. Thus, different experts and clinical practice guidelines recommend routinely assessing local microbiological profiles and postoperative statistics to adapt perioperative antibiotic strategies. In Colombia the information reported on microbiological profiles and resistance patterns is limited, which is particularly concerning given the critical importance of effective antimicrobial stewardship in infection control practices[10]. Therefore, this study aimed to address this gap by characterizing the microbiological and clinical profiles of patients undergoing hepatobiliary surgery and analyzing resistance patterns alongside their associated risk factors. We aimed to provide valuable insights that can inform early, effective, and safe antibiotic therapy guidelines in these surgical scenarios.

Materials and methods

A cross-sectional analytical study was conducted in a high-complexity institution in the metropolitan area of Bucaramanga, northeastern Colombia. All patients who underwent hepatopancreatobiliary surgical procedures between January and December 2023 were consecutively included in the study, resulting in a sample of 95 patients, each with at least one bilial culture recorded, and multiple microorganisms could be identified in each of these cultures. For further analysis, this study was approved by the Ethics Committee of the Cardiovascular Foundation of Colombia (approval number 07730), where patients were grouped into PBD and non-PBD groups, based on previous literature indicating differences in resistance and morbidity patterns between these groups (5). The inclusion criteria were as follows: adult patients (>18 years) who underwent hepatopancreatobiliary surgery with one recorded intraoperative bile culture.

Exclusion criteria: Patients with negative bile culture, emergency surgery (Protocols could not be followed).

Sociodemographic variables included age, sex, type of residence (rural or urban), and admission (first-time or readmission). Clinical variables encompassed a history of diabetes mellitus, obesity, hypertension, solid organ neoplasia, biliary or non-biliary infections, antibiotic therapy administered within 90 days, esophagogastroduodenoscopy, and abdominal surgery history. Perioperative variables involved hepatobiliary and pancreatic diagnoses, categorized as benign and malignant conditions; concomitant biliary infection, defined and scored according to the Tokyo Guidelines 2018; biliary stent use (endoscopic or percutaneous) with its duration, recorded based on the date of endoscopic retrograde cholangiopancreatography (ERCP) or percutaneous transhepatic catheter (PTC) placement. Surgical procedures were grouped into hepatectomy, pancreatoduodenectomy, cholecystectomy, and biliary reconstruction. Antibiotic prophylaxis was administered 30–60 min before surgery according to the surgeon´s decision and considering criteria such as preoperative biliary culture, active ongoing infection, or antibiotic allergies. Preoperative cultures were routinely collected for all patients as part of the institutional protocol prior to the initiation of postoperative antibiotic therapy. Postoperative antibiotic therapy was adjusted according to the culture results in case of an ongoing infection. The preoperative patient status was assessed using the American Society of Anesthesiologist classification (ASA).

Postoperative variables included intensive care unit (ICU) admission, length of ICU stay, and total postoperative hospitalization days. Additional primary clinical variables, such as ICU readmission, death, and reoperation, were also recorded. Non-surgical infections were excluded as they were considered surgery-related complications. Microbiological variables included the isolated microorganism and antibiotic resistance. Microbiological analysis was performed based on the number of cultures obtained and reported. Bile samples were obtained under aseptic conditions after transection of the common bile duct using a syringe. The samples were cultured in accordance with the guidelines of the Institutional Medical Microbiology Department and the laboratory standards. Microorganism specimens and their corresponding resistance profiles were determined using the VITEK II system. Statistical analysis as the mean and median were calculated, along with measures of dispersion, including the standard

deviation or interquartile ranges, depending on the distribution of the variables. Categorical variables are presented as frequencies and percentages. Normality was assessed using the Kolmogorov-Smirnov test. Bivariate analysis was performed using antimicrobial resistance as the outcome variable, applying the chi-square test for categorical variables, the Student's t-test for continuous variables with a normal distribution, and the Mann-Whitney U test for those without a normal distribution. Additionally, a multivariate model using logistic regression was conducted to identify risk factors and independent predictors associated with antimicrobial resistance. Analyses were performed using Stata 16 software.

Ethical statement

This study was approved by the Ethics Committee of the Fundación Cardiovascular de Colombia (approval number 07730), which guarantees compliance with the highest national and international ethical standards in health research. All relevant ethical guidelines were rigorously followed, and all data collected were managed in accordance with personal data protection legislation. In addition, all participants provided informed consent, and their personal data were protected.

Results

A total of 95 patients were evaluated, of whom 61.05% were men. The median age was 67 years, with an interquartile range of 54–75 years. Of these, 51.57% were PBD patients, with a median age of 62 years (IQR: 52–75) and 70 years (IQR: 57–75) in the non-PBD group. Regarding medical history, comorbidities were similar in both groups, although hypertension was more prevalent in non-PBD at 47.83% (p= 0.193). Additionally, a history of previous abdominal surgeries was higher in PBD (36.73% vs. 17.39%, p = 0.035). The incidence of previous biliary infection (cholangitis or cholecystitis) and hepatectomies were significantly higher in PBD 61.22% (p < 0.001) and 18.37% (p = 0.01), respectively (Table 1).

According to the Tokyo criteria for the severity of biliary infection, most patients in the PBD group were classified as Tokyo 2 (57.69%), whereas most in the non-PBD were classified as Tokyo 1 (46.15%) (p=0.534). The administration of antibiotic prophylaxis in the non-PBD group was 86.86%, compared to 77.55% in the PBD group (p = 0.232). The most commonly used prophylactic antibiotics were ampicillin/sulbactam and cefazolin, which were more frequently administered in the non-PBD group compared to the PBD group (32.61% vs. 24.49% and 15.22% vs. 12.24%, respectively), with no statistically significant differences observed (p = 0.381 and p = 0.674, respectively). Regarding the ASA classification, the majority of PBD patients were classified as ASA III at 52.1%, similar to 52.17% in the non-PBD group (p=0.534). Postoperative complications occurred in 36.73% (p=0.379) of PBD patients, with ICU readmissions slightly higher in this group at 6.12% (p=0.699), as was mortality at 10.2% (p=0.518). Both groups had a median ICU stay of 3 days, although the interquartile

Table 1. Demographic, clinical, and postoperative Outcomes of Patients with and without Preoperative Biliary Drainage.

Variable	non-PBD n=46 (%)	PBD n=49 (%)	p-value
Age (median- IQR)	70 (57-75)	62 (52-75)	0.337
Sex (woman)	24 (52.17)	34 (69.39)	0.086
Residential Zone (Urban)	35 (76.09)	40 (81.63)	0.508
Referral	23 (50)	28 (57.14)	0.485
Readmission	12 (26.09)	11 (22.45)	0.679
Medical history			
Obesity	8 (17.39)	10 (20.41)	0.708
Hypertension	22 (47.83)	17 (34.69)	0.193
Diabetes Pre-Operative	13 (28.26)	10 (20.41)	0.372
Malignant Neoplasia	7 (15.22)	4 (8.16)	0.283
Previous Biliary Infection	10 (21.74)	16 (32.65)	0.233
Exposure to Antibiotics in the Last 90 Days	14 (30.43)	19 (38.78)	0.394
Pre-ERCP	18 (39.13)	36 (73.47)	0.001
Previous Abdominal Surgery	8 (17.39)	18 (36.73)	0.035
Diagnostic			
Cholelithiasis	29 (63.04)	31 (63.27)	0.982
Neoplasia	21 (45.65)	15 (30.61)	0.131
Biliary infection	11 (23.91)	30 (61.22)	<0.001
Fistula	9 (19.57)	8 (16.33)	0.681
Peri-Operative			
Biliary Stent User	4 (8.7)	40 (81.63)	<0.001
Cholecystectomy	26 (56.52)	35 (71.43)	0.13
Biliary Tract Exploration or Re-exploration	30 (65.22)	36 (73.47)	0.383
Biliary Reconstruction	22 (47.83)	26 (53.06)	0.61
Hepatectomy	1 (2.17)	9 (18.37)	0.01
Pancreatoduodenectomy	12 (26.09)	6 (12.24)	0.085
Antibiotic prophylaxis	40 (86.86)	38 (77.55)	0.232
Most common antibiotics for prophylaxis			
Ampicillin/Sulbactam	15 (32.61)	12 (24.49)	0.381
Cefazolin	7 (15.22)	6 (12.24)	0.674
Risk stratification			
ASA			0.534
I	2 (4.35)	2 (4.08)	
II	18 (39.13)	20 (40.82)	
III	24 (52.17)	27 (55.1)	
IV	2 (4.35)	0 (0)	
TOKYO			0.212
1	6 (46.15)	5 (19.23)	
2	5 (38.46)	15 (57.69)	
3	2 (15.38)	6 (23.08)	
Post-Operative			
Postoperative Complications	13 (28.26)	18 (36.73)	0.379
ICU Readmission	2 (4.35)	3 (6.12)	0.699
Mortality	3 (6.52)	5 (10.2)	0.518
Days in ICU (median - IQR)	3 (2-4)	3 (2-8)	0.709
Days in Hospital (median -IQR)	10 (3-18)	9 (7-18)	0.573

ERCP: Endoscopic Retrograde Cholangiopancreatography; IQR: Interquartile Range

range was broader in the PBD group (IQR: 2-8). The length of hospitalization was greater in non-PBD at 10 days (IQR: 3-18) (p=0.534) (Table 1).

In the group without biliary drainage, *Klebsiella pneumoniae* was isolated in 50% of the cases, followed by *Escherichia coli* (30.77%), *Enterobacter cloacae* complex (5.77%), and *Klebsiella oxytoca* (3.85%). In contrast, in the group with preoperative biliary drainage, *Escherichia coli* was the most prevalent (38.89 %), followed by *Klebsiella pneumoniae* (27.78%), and *Klebsiella oxytoca* (7.41%) (Table 2, Figure 1).

In the evaluation of resistance patterns among various Gram-negative microorganisms to multiple antibiotics, distinct patterns were observed. In the evaluation of *E. coli,* we found a high resistance to ampicillin/sulbactam (74.29%), followed by ciprofloxacin (59.46%). *Klebsiella pneumoniae* showed resistance, with 92.31% to ampicillin/sulbactam and 89.74% to piperacillin/tazobactam. Similarly, *Klebsiella oxytoca* demonstrated a 100% resistance to ampicillin/sulbactam. Notably, *Enterococcus faecalis* had a low prevalence. The details of other microorganisms are presented in Table 3.

In patients with *E. coli* and PBD, a higher percentage of resistance to all antibiotics was observed, except for meropenem. This difference was statistically significant for ceftriaxone, cefepime, and ceftazidime. In contrast, in patients with *K. pneumoniae*, there was variation in the resistance profiles between patients with PBD and those without PBD, with no statistically significant differences found (Table 4).

In the multivariate analysis of resistance to different antibiotics, certain variables were found to be significantly associated with resistance to meropenem. Specifically, women had a higher probability of developing resistance, with an odds ratio (OR) of 9.55 (95% CI, 1.12-80.9; P=0.038). Likewise, patients with longer ICU stays were also more likely to acquire infections caused by microorganisms resistant to piperacillin (OR, 1.12 [95% CI, 1.00–1.24]; p=0.038) (Table 5).

Table 2. Distribution of the most frequent microorganisms in patients with and without preoperative biliary drainage

Microorganism	non-PBD n (%)	PBD n (%)	p value
Klebsiella pneumoniae	26 (50)	15 (27.78)	0.030
Escherichia coli	16 (30.77)	21 (38.89)	0.302
Klebsiella oxytoca	2 (3.85)	4 (7.41)	0.372
Enterobacter cloacae complex	3 (5.77)	1 (1.85)	0.287
Aeromonas hydrophila	1 (1.92)	2 (3.7)	0.524
Pseudomonas aeruginosa	0 (0)	3 (5.56)	0.135
Citrobacter freundii	0 (0)	2 (3.7)	0.265
Morganella morganii spp	1 (1.92)	1 (1.85)	0.735
Aeromonas sobria	1 (1.92)	0 (0)	0.484
Citrobacter amalonaticus	1 (1.92)	0 (0)	0.484
Enterococcus faecalis	0 (0)	1 (1.85)	0.516
Enterococcus gallinarum	0 (0)	1 (1.85)	0.516
Proteus hausseri	1 (1.92)	0 (0)	0.484
Proteus vulgaris	0 (0)	1 (1.85)	0.516
Candida albicans	0 (0)	1 (1.85)	0.516
Candida tropicalis	0 (0)	1 (1.85)	0.516

Discussion

Our findings describe the clinical and microbiological characteristics of patients undergoing hepatobiliary surgery in a high-complexity setting in Colombia. The demographic distribution was predominantly female, in contrast to other studies, where men typically predominate[4,11]. Notably, the microbial profile observed in our study differs from that commonly reported in large case series, where *Enterococcus spp.* and *Enterobacter spp.* are frequently the most prevalent pathogens. This variation may be attributable to differences in local antimicrobial use, patient population characteristics, or institutional infection control practices. Furthermore, the predominance of certain gastrointestinal tract enterobacteria could be influenced

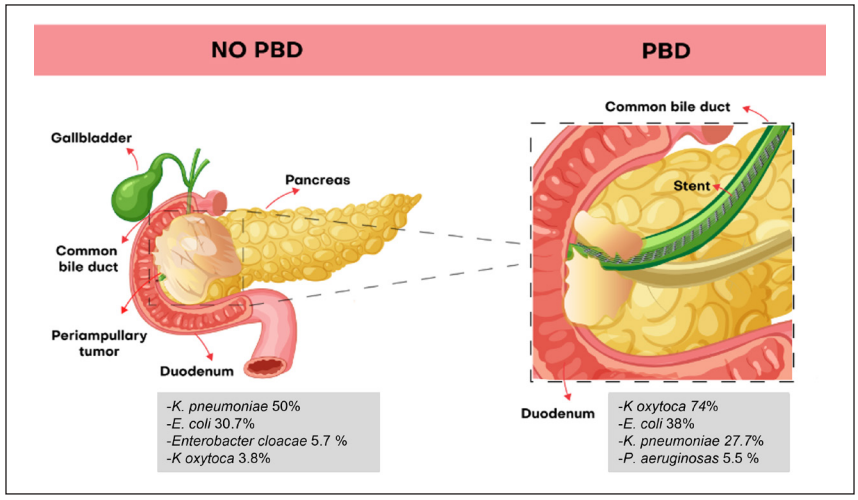

Figure 1. Most frequent microorganisms in PBD and no-PBD groups

Table 3. Resistance profile of gram-negative and gram-positive bacilli in all patients.

Gram Negative Microorganism	SAM		CZO		FEP		CRO		TZP		CIP		MEM		CAZ	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
E. coli	26/35	74.3	11/19	57.9	9/33	27.3	8/23	34.8	13/32	40.6	22/37	59.5	1/35	2.78	11/35	31.4
K. pneumoniae	36/39	92.3	13/16	81.3	15/39	38.5	4/19	21.1	35/39	89.7	17/39	43.6	9/39	23.08	17/39	43.6
K. oxytoca	4/4	100	0/1	0.0	0/5	0.0	0/1	0.0	4/5	80.0	2/6	33.3	2/5	40.0	2/6	33.3
C. freundii	-	-	1/1	100	2/0	0.0	0/1	0.0	2/2	100	0/2	0.00	1/2	50.0	0/2	0.0
E. cloacae complex	-	-	3/3	100	1/4	25.0	-	-	2/3	66.7	1/4	25.0	0/4	0.00	2/4	50.0
M. morganii ssp	2/2	100	1/1	100	-	-	-	-	0/2	0.0	1/2	50.0	0/2	0.0	1/2	50.0
P. hausseri	1/1	100	-	-	0/1	0.0	1/1	100	0/1	0.0	0/1	0.00	0/1	0.0	0/1	0.0
P. vulgaris	0/1	0.0	-	-	0/1	0.0	-	-	0/1	0.0	0/1	0.00	0/1	0.0	0/1	0.0
P. aeruginosa	0/2	0.0	-	-	3/3	100	-	-	2/2	100	2/3	66.7	3/3	100	2/3	66.7
A. hydrophila	-	-	2/2	100	-	-	-	-	1/2	50.0	-	-	1/3	33.3	-	-
Aeromonas sobria	-	-	-	-	0/1	0.0	-	-	1/1	100	-	-	1/1	100	-	-
Citrobacter amalonaticus	-	-	-	-	0/1	0.0	-	-	0/1	0.0	0/1	0.00	0/1	0.0	0/1	0.0

Escherichia coli (E. coli), Klebsiella pneumoniae (K. pneumoniae), Klebsiella oxytoca (K. oxytoca), Citrobacter freundii (C. freundii), Enterobacter cloacae complex (E. cloacae complex), Morganella morganii ssp (M. morganii spp), Proteus hausseri (P. hausseri), Proteus vulgaris (P. vulgaris), Pseudomonas aeruginosa (P. aeruginosa), Aeromonas hydrophila (A hydrohila) SAM: ampicilina sulbactam, CZO: cefazolina, FEP:cefepime, CRO: ceftriaxona, TZP: piperacilina/tazobactam, CIP: ciprofloxacina, MEM: meropenem, CAZ: ceftazidime, VAN: vancomicina

Table 4. Comparison of Antibiotic Resistance in *Escherichia coli* and *Klebsiella pneumoniae* Isolates Between PBD and Non-PBD Patients

	Escherichia coli				*Klebsiella pneumoniae*			
AB	**non-PBD**	**PBD**	**Δ%**	**p value**	**non-PBD**	**PBD**	**Δ%**	**P value**
SAM	9/15 (60%)	17/20 (85%)	25	0.100	23/25 (92%)	13/14 (92.86%)	0.86	0.711
CZO	4/9 (44.44%)	7/10 (70%)	25.56	0.255	8/9 (88.89%)	5/7 (71.43%)	-17.46	0.400
FEP	1/14 (7.14%)	8/19 (42.11%)	34.97	0.03	10/25 (40%)	5/14 (35.71)	-4.29	0.533
CRO	1/10 (10%)	7/13 (53.85%)	43.85	0.038	3/11 (27.27%)	1/8 (12.50%)	-14.77	0.426
TZP	4/13 (30.77%)	9/19 (47.37%)	16.6	0.285	23/26 (88.46)	12/13 (92.31%)	3.85	0.593
CIP	7/16 (43.75%)	15/21 (71.43%)	27.68	0.087	10/25 (40%)	7/14 (50%)	10	0.3936
MEM	1/15 (6.67%)	0/21 (0%)	-6.67	0.471	6/25 (24%)	3/14 (21.43)	-2.57	0.592
CAZ	2/15 (13.33%)	9/20 (45%)	31.67	0.049	10/25 (40%)	7/14 (50%)	10	0.395

AB: Antibiotic, SAM: ampicilina sulbactam, CZO: cefazolina, FEP:cefepime, CRO: ceftriaxona, TZP: piperacilina/tazobactam, CIP: ciprofloxacina, MEM: meropenem, CAZ: ceftazidime, VAN: vancomicina. **Δ%** :Absolute difference in proportions.

by regional microbiological epidemiology or alterations in biliary flora resulting from prior interventions[12–16]. Recognizing these distinctions is essential for optimizing empirical antimicrobial therapy and informing prophylactic antibiotic strategies in hepatobiliary surgical patients.

Regarding bacterial resistance, our study revealed high rates for commonly used antibiotics, including ampicillin/sulbactam, ciprofloxacin, cefazolin, and ceftriaxone, particularly affecting *E. coli* and *K. pneumoniae*. These findings are consistent with the significant resistance reported in other studies[1,13]. However, the distinct microbiota observed in our study may account for the additional percentage of resistance.

Several factors have been consistently associated with bacterial resistance in the literature. For instance, the presence of biliary tract infection has been linked to higher rates of resistance to antibiotics, such as piperacillin/tazobactam, in patients with cholangitis than in those without the infection[13]. Our study demonstrated a higher percentage of resistance in the PBD group, which was not correlated with the presence of biliary infection but rather with the severity of the infectious process. Another factor described is the duration of preoperative biliary drainage, which has been associated with increased resistance to second-generation cephalosporins[9]. However, our findings did not show any impact of drainage duration on resistance rates. Our analysis revealed that both woman and undergoing

hepatectomy were independently associated with resistance to broad-spectrum antibiotics, such as meropenem and cefepime. Additionally, resistance to meropenem was associated with a longer stay in the intensive care unit, which aligns with the expected consequences of antibiotic resistance. This resistance is primarily associated with multidrug-resistant (MDR) microorganisms, which have high mortality rates[17].

In subgroup analyses, several studies have identified preoperative biliary drainage (PBD) as a risk factor for increased antimicrobial resistance[18]. This association is presumed to be causal, as illustrated by a Finnish study showing a marked rise in resistance to second-generation cephalosporins shortly after PBD placement[9]. Likewise, other series have reported increased resistance to commonly used prophylactic agents, such as ampicillin/sulbactam[1]. These findings raise concerns about the potential reduced efficacy of empirical prophylaxis and standard therapeutic strategies, particularly in patients with prior biliary instrumentation. In response to this challenge, various authors have proposed alternative approaches, including the addition of aminoglycosides, such as gentamicin, to broaden antimicrobial coverage[19], the use of combination therapy, such as piperacillin/tazobactam with vancomycin, to reduce infectious complications[20], and the implementation of targeted prophylaxis based on biliary culture results, a strategy already in use at our institution[21,22].

Having a prior PBD before surgery allows for adjustment of prophylactic therapy based on the microorganism identified in the biliary tract, a strategy known as targeted prophylaxis. A meta-analysis demonstrated that this approach reduces surgical site infections by 20%[23]. This strategy could be particularly relevant given the high resistance rates to SAM, second-, third-, and fourth-generation cephalosporins, and piperacillin/tazobactam. This leaves meropenem and other non-beta-lactam antibiotics, such as aminoglycosides and quinolones, as alternatives, which have their own pharmacokinetic challenges and potential side effects[14].

Currently, international guidelines recommend empirical antimicrobial prophylaxis regimens for biliary tract manipulation based on microbiological profiles commonly reported in large case series, where *Enterococcus spp.* and *Enterobacter spp.* predominate[24]. However, our findings reveal a different microbial profile, with a high prevalence of multidrug-resistant enterobacteria, especially *E. coli* and *K. pneumoniae*, which significantly limits the effectiveness of standard prophylactic regimens[25]. This mismatch between international recommendations and local resistance profiles may increase the risk of postoperative infections, ICU readmissions, and mortality, particularly in high-complexity surgical settings.

Although there are no national studies available for comparing our resistance profile in patients with similar characteristics, data from GREBO (the Group for the Control of Bacterial Resistance in Bogotá) show lower resistance rates for *E. coli* (27.3%) and K. pneumoniae (58%)[26]. These figures are based predominantly on urine and blood samples, highlighting the significant gap in resistance rates between national data and the specific scenario of high-complexity abdominal surgery. At

Table 5. Multivariate Logistic Regression of Risk Factors for Antibiotic Resistance in Hepatobiliary Surgery Patients

Variable	Cefepime resistance		Piperacillin/tazobactam resistance		Ciprofloxacin resistance		Meropenem resistance	
	OR(IC 95%)	p-value	OR(IC 95%)	p-value	OR(IC 95%)	p-value	OR (IC 95%)	p-value
Age	1.02 (0.98 to 1.07)	0.163	0.87 (0.78 to 0.98)	0.024	1.00 (0.97 to 1.03)	0.705	0.99 (0.93 to 1.05)	0.783
Sex (man)	2.03 (0.54 to 7.63)	0.294	1.66 (0.13 to 20.23)	0.687	2.26 (0.81 to 6.24)	0.115	9.55 (1.12 to 80.9)	0.038
Hepatectomy	46.1 (2.81 to 756.7)	0.007	–	–	–	–	–	–
Exploration of bile ducts and re-exploration	0.049 (0.005 to 0.421)	0.006	–	–	–	–	–	–
Hospital stay	–	–	1.24 (1.02 to 1.50)	0.024	–	–	–	–
Obesity	–	–	–	–	0.26 (0.06 to 0.99)	0.049	–	–
Intensive care unit stay	–	–	–	–	–	–	1.12 (1.00 to 1.24)	0.038
Chronic kidney disease	–	–	–	–	–	–	99.17 (3.74 to 2628.1)	0.006
Drainage	–	–	–	–	–	–	16.57 (1.34 to 204.4)	0.028

the departmental level, the problem of bacterial resistance is evident, as reflected in our results, which show an increase in multidrug-resistant enterobacteria. This situation complicates the development of recommendations for optimal prophylaxis and treatment of patients with complex conditions and high morbidity in the hepatobiliary surgery service[27]. There is an urgent need for a robust bacterial resistance surveillance system and the implementation of optimized antimicrobial use programs[28]. Additionally, targeted prophylactic therapies should be analyzed and adapted to these specific scenarios.

Limitations

The main limitations of this study include its cross-sectional design, which does not allow for the establishment of causality, and the relatively small sample size, which may affect the generalizability of the results. Additionally, although relevant clinical and microbiological variables were included, long-term follow-up studies are recommended to assess the impact of antimicrobial resistance in patients. The inclusion of patients from a single center may also limit the extrapolation of the findings to other populations. Finally, heterogeneity in preoperative treatments and the duration of preoperative biliary drainage may have introduced biases into the results, highlighting the need for additional studies to confirm these findings.

In conclusion, this study revealed high rates of antimicrobial resistance in patients undergoing hepatobiliary surgery, particularly among those with preoperative biliary drainage. *E. coli* and *K. pneumoniae* were the predominant pathogens, showing significant resistance to commonly used antibiotics such as ampicillin/sulbactam and piperacillin/tazobactam. These findings underscore the need to tailor prophylactic strategies to local microbiological profiles and to strengthen antimicrobial stewardship and surveillance programs.

Ethical considerations

Protection of persons. Participation in the study adhered to the principle of respect for persons. All eligible participants were included based on predefined inclusion criteria, and their autonomy and dignity were respected throughout the research process. Given the retrospective design and the use of secondary clinical data, no direct interventions or modifications to standard medical care were performed. The study was classified as minimal risk in accordance with applicable regulatory frameworks.

Protection of vulnerable populations. The study population included patients who may be considered vulnerable due to their clinical condition. To ensure their protection, no experimental procedures were conducted, and data collection was limited to information obtained during routine clinical care. The study did not involve coercion, undue influence, or differential treatment, and safeguards were implemented to protect participants' rights, autonomy, and well-being.

Confidentiality and privacy. Confidentiality and privacy of participant information were strictly maintained. All data were anonymized prior to analysis, and personal identifiers were removed or replaced with unique study codes. Access to the database was restricted to authorized members of the research team. No identifiable personal information is disclosed in any reports, publications, or presentations derived from this research. Data were stored in secure, password-protected systems in accordance with institutional policies and national data protection regulations.

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