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Developing A Surgical Rationale of Bile Culture and Sensitivity to Guide Targeted Antibiotics in Laparoscopic Cholecystectomy in a Tertiary Care Hospital in Nepal

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ABSTRACT

Introduction

Laparoscopic cholecystectomy is the standard surgical treatment for benign gallbladder conditions. Traditionally, antibiotics have been used empirically in patients to lower the risk of post operative complications. Earlier routine use of antibiotic has now been replaced with single dose preoperative antibiotic. But, the emergence of anti-microbial resistant organisms has raised concerns regarding the use of broad spectrum antibiotics including ceftriaxone to all cases.

Methods

This is a single-centered, prospective study. Data collection was done between January 2025 to April 2025. There were 148 patients included in the study. Single dose ceftriaxone was given at induction. Bile was collected during the intraoperative period and culture was sent. Association of bile C/S with various preoperative and postoperative factors were analyzed.

Results

In our study, bile culture was positive in 11 of 148 patients (7.4%). Escherichia coli and klebsiella pneumoniae were the predominant isolates (72%). No significant association of the bile culture colonization was observed with either age, gender or BMI. Those who were immunocompromised had higher bile culture microbial growth rates (21.1% vs. 5.4 %; p = 0.036). Signficantly higher culture growth rates were also noted in infective cases (29.4%). Among the cases that had growth on bile culture, 100% of the organisms were resistant to the routinely used prophylactic antibiotic.

Conclusion

Routine bile culture positivity in laparoscopic cholecystectomy is low in our study when prophylactic ceftriaxone was given. While additional prophylactic antibiotics may not be universally required, selective use of antibiotic other than ceftriaxone is justified in high-risk groups such as diabetic patients or those with infective pathology.

Keywords

Bile culture; laparoscopic cholecystectomy; surgical site infection

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INTRODUCTION

Laparoscopic cholecystectomy (LC) is the standard surgical treatment for many benign gallbladder disorders[1]. Globally 6% of people have gall stones while developing countries have higher prevalence upto 15%[2]. Therefore, LC is a common surgery in our part of world.

Laparoscopic cholecystectomy has risk of complications including postoperative infection. To prevent these, surgeons have been using antibiotics. There are studies which support use of empirical antibiotic in LC. However many oppose their routine use, but support its use in high risk patients like acute cholecystitis, immunocompromised patients etc. Surgical Infection Society Guidelines recommend against the routine use of pre and post operative antibiotics unless associated with acute cholecystitis[3]. The emergence of anti-microbial resistant (AMR) organisms has raised concerns regarding the rampant use of antibiotics[4].

In acute cholecystitis, bile fluid can harbor multiple pathogenic organisms. Escherichia coli is the most common organism which accounts for 25-50 % of cases, followed by klebsiella and enterococcus.[5,6] At the same time, AMR has crippled the developing nations. Data reports 19579 deaths associated with and 4707 deaths attributed to bacterial AMR in Nepal in the year 2021 alone[7,8].

Therefore, we need to develop our own rationale for using antibiotics in routine surgeries like LC, so that we can balance between avoidance of the postoperative complications, and at the same time decrease AMR and maintain antibiotic stewardship which is the current worldwide concern. This study aims to develop a surgical rationale of prescribing appropriate antibiotic based on culture and sensitivity at our centre, to those patients who require it.

METHODS

This is a single centre cross-sectional study. The study was approved by the Institutional Review Committee. Patients who underwent LC during the period of January 2025 to April 2025 in the Department of GI and General surgery were included in the study.

Patients with benign gallbladder disease diagnosed as acute and chronic cholecystitis, gall bladder stone, polyps, adenomyomatosis etc. who underwent elective LC were included in the study. Patients were admitted a day prior to surgery. Written consent was taken and confidentiality and anonymity was maintained. Preoperative ceftriaxone 1 g IV was administered at induction, around 30 minutes before incision. Surgery was performed and bile aspiration was done only after retrieving the intact gallbladder from the umbilical port after the completion of surgery. Patient demographics, preoperative, intraoperative and postoperative variables were noted. Bile culture data (organism and antibiotic susceptibility) were collected.

Bile aspiration was not done if there was intraoperative bile spillage due to any reason. One ml sample of bile was aspirated in a sterile syringe and then sent immediately to the microbiology laboratory. In the microbiology lab, samples were inoculated onto blood agar, mac-conkey agar and other selective media as required and tests done accordingly. Antibiotic sensitivity was performed in those with positive culture using Kirby-Bauer disk. Culture sensitivity(C/S) results were collected later and analyzed with various pre and post op parameters.

Data was collected and Statistical analysis was performed using IBM SPSS version 26. Categorical variables, including bile culture results, were analyzed using chi-square or Fisher's exact test as appropriate. A p-value < 0.05 was considered statistically significant.

RESULTS

There were total 148 patients included in the study. Out of these total patients, 11 (7.4 %) had positive bile culture after 48 hours of innoculation. There were more females when compared to males. There was no difference in bile culture positivity among the different age groups categories. Similarly there was no difference in bile culture growth between males and females, or among different BMI categories as shown in the table 1.

Among these total patients who underwent LC, 11 % were preoperative or intraoperatively diagnosed as infective conditions (acute cholecystitis or empyema GB). These patients had a higher rate of bile culture growth (29.4%) when compared to those with non-infective conditions (4.6%), ($p = 0.0033$).

The patients with concomittant CBD stones(4%) underwent preop. ERCP and biliary drainage in this study. These kinds of preoperative biliary intervention were numerically associated with higher culture positivity in this study. Although numerically a higher proportion of patients who underwent preoperative ERCP had positive bile cultures (33.3% vs. 6.3%), the sample size was too small to draw definitive conclusions. Therefore, no statistically robust inference can be made regarding the impact of preoperative biliary intervention on bile colonization.

Those who had intraoperative drain requirement showed a higher rate of bile culture positivity, (28.6%) compared to those not requiring drains intraopertively(3.9%),($p = 0.0012$). Therefore need of intraopertive drain was associated with

Table 1. Demographic and preoperative variables

Variables	Categories	Total number of patients n(%)	Growth in culture n(%)	p-value
Age (years)	18-40	46(31.1%)	4(8.7%)	0.48
	41-70	88(59.4%)	5(5.7%)	
	>70	14(9.5%)	2(14.3%)	
Gender	Male	41(27.7%)	3(7.3%)	0.97
	Female	107(72.3%)	8(7.5%)	
BMI (kg/m^2)	<18.5	29(19.6%)	3(10.3%)	0.69
	18.5-24.99	87(58.8%)	5(5.7%)	
	25-29.99	28(18.9%)	3(10.7%)	
	>30	4(2.7%)	0	

Table 2. Periopertive factors

Variables	Categories	n(%)	Growth in culture n(%)	p-value
Surgical condition	Infective	17(11.5%)	5(29.4%)	0.003
	Non infective	131(88.5%)	6((4.6%)	
Preoperative billiary intervention	Yes	6(4.1%)	2(33.3%)	0.064
	No	142(95.9%)	9(6.33%)	
Drain placement (Intraoperative)	Yes	21(14.2%)	6(28.6%)	0.001
	No	127(85.8%)	5((3.9%)	
Gall bladder content	Single calculi	34(23%)	5(14.7%)	0.099
	Multiple calculi	108((73%)	5(4.6%)	
	Polyp/adenomyomatosis	6(4%)	0(0%)	
Hospital stay	=<3 days	133(89.9%)	7(5.3%)	0.015
	>3 days	15(10.1%)	4(26.7)	
Diabetes Mellitus	Yes	19 (12.8%)	4(21.1%)	0.036
	No	129(87.2%)	7(5.4%)	

presence of organism in the culture of bile from the gallbladder. Similarly, patients who stayed in the hospital for more than three days demonstrated a higher rate of bile culture positivity (26.7%) than those discharged within three days (5.3%), and this difference was statistically significant (p = 0.015) as shown in table 2.

Regarding gallstone characteristics, 23% of the total patients who underwent LC had a single stone, 73% had multiple stones, and 4% had polypoid or adenomyomatous changes. Although bile culture positivity was numerically higher in patients with single stones (14.7%) compared to those with multiple stones (4.6%), this association was not statistically significant (p = 0.099). Therefore the content of the gallbladder, whether stones or polyps did not influence the presence of organisms in the bile in this study.

Ninteen of the patients had diabetes mellitus (DM). None were taking immunosuppresants. These patients had more culture positivity (21.1% vs. 5.4%, p = 0.036) when compared to other non-diabetic patients. Thus, patients with DM had a higher bacterial growth in bile during LC suggesting higher rates of possible gallbladder infections.

The organism isolated from the bile culture specimen were analyzed. Among the 11 patients with positive bile cultures, escherichia coli (45.4%) was the most

Table 3. Microbiological profile

Organism	Number (%) (n=11)	Resistant to ceftriaxone(n)
Klebsiella oxytoca	2 (18.2%)	2
Escherichia coli	5(45.4%)	3
Klebsiella pneumoniae	3(27.3%)	2
Acinetobacter	1(9.1%)	Intrinsically resistant

common organism isolated, followed by klebsiella pneumoniae (27.3%). All isolates showed resistance to third-generation cephalosporins, particularly ceftriaxone, highlighting the predominance of ceftriaxone-resistant gram-negative organisms in biliary infections (Table 3).

DISCUSSION

In Laparoscopic cholecystectomy, as a standard protocol, patients receive prophylactic antibiotics approximately within thirty minutes prior to the incision, usually at the time of induction. However, amidst the worldwide surge of AMR, routine use of ceftriaxone as prophylactic antibiotic to all LC, requires a critical evaluation.

There were total 148 patients included in the study who underwent LC during the study peroid at our center. Our study observed female predominance(72% females) among patients undergoing LC, which was consistent with the findings of Darkahi et al and Matsushima et al [9,10]. Among these pt who underwent LC, 11.5% had infective pathology diagnosed clinically (preop or intraoperatively). But even among these infective patients diagnosed clinically, 30% patients had documented bile culture positivity. This finding is consistent with other studies which show similar results, with 35% to 65% positive bile culture in infective cases[9,11,12]. This suggests that only few cases undergoing LC with ceftriaxone as prophylactic antibiotic harbour contaminated bile. Gram negative bacteria, E coli, Klebsiella were the most common organism isolated from bile culture in our study which is backed up by various other researches[13,14]. Although all isolates in our study were monomicrobial, existing literature with significant polymicrobial infection are present. Studies also show polymicrobial infections significantly associated with age, pre-operative ERCP, associated comorbidities and immunocompromised status[6,14,15].

A cross-sectional analysis by Mahafzah et al., with 1248 laparoscopic cholecystectomy cases represents age, gender, preoperative ERCP, associated morbidities and infective cases to be the independent predictors of bile culture positivity[14]. While our data presents a higher rate of bile culture positivity among the patients undergoing pre-operative biliary intervention, this did not achieve any statistical significance. Positive bile culture after pre-operative biliary interventions are likely attributable to the effects of endoscopic sphincterotomy and biliary stenting, which predominantly alter the biliary flora and susceptibility to infection[16,17].

We used prophylactic antibiotic in all cases. However, whether to use antibiotics prophylactically is also a debate. Researches show role of antibiotics in laparoscopic cholecystectomy. A systemic review by Matsui et al, implies that antibiotics significantly reduce the risk of post-operative complications. Another meta-analysis also corroborates similar results[18,19].However, there is a meta-analysis, showing no significance of prophylactic use of antibiotics to prevent complications[20]. Further, several studies in literature have underscored the limited benefit of prophylactic antibiotic use[21,22,23]. However, we did not omit the use of preoperative antibiotic as this is the standard protocol at our centre. Bile culture in our study showed 7% culture positivity in spite of using ceftriaxone as prophylactic antibiotic. Therefore we can assume that 7% of patients need additional or different prophylactic antibiotics. Also among these culture positive cases, 100% had resistance to ceftriaxone which is being regularly used. So there is a question of choice of antibiotics in these culture positive cases. Meanwhile, the global surge of AMR is emerging[24]. The resistant patterns however differs based on local resistance pattern, differences in prescribing patterns and prior use of antibiotics[25,26] This underlines the significance of proper antibiotic use in our setting.

A key limitation of our study is the single-center design. It was a hospital based study and there were only few positive bile cultures which may have introduced selection bias.

CONCLUSION

In our study, few of the patients undergoing laparoscopic cholecystectomy had positive bile

cultures mainly E. coli and klebsiella which were commonly resistant to ceftriaxone, the drug most often given before surgery. This makes it clear that routine use of ceftriaxone offers little benefit in preventing infections in these patients.

These findings call for a shift in practice. Rather than prescribing antibiotics across the board, their use should be targeted, especially for higher-risk patients such as those who have DM or present with infection at the time of surgery. Building stronger antibiotic stewardship practices is crucial so that we use these medicines wisely, avoid unnecessary exposure, and keep them effective for the patients who truly need them.

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CONFLICT OF INTEREST

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