Original Article

Microbial Profile and Antibiotic Sensitivity in Duodenal Ulcer Perforation Peritonitis: Empirical vs. Culture-Guided Therapy—A Prospective Observational Study in Eastern Nepal

Ajit Khadga[1], Manish Kumar Mandal[2], Sachidanand Shah[1], Dipesh Shrestha[1], Sujita Khadga[3]

[1] Nobel Medical College Teaching Hospital, Kathmandu University, Biratnagar, Morang, Nepal

[2]Janaki Medical College, Tribhuvan University, Kshireshwornath, Dhanusha, Nepal

[3]Nepal Medical college, Attarkhel, Jhorpati-8, Kathmandu

ABSTRACT

BACKGROUND

Perforation peritonitis (PP) due to duodenal ulcer perforation (DUP) remains a major surgical challenge associated with considerable postoperative morbidity and mortality. Although empirical broad-spectrum antibiotics are routinely administered, their efficacy varies with evolving local resistance patterns. This prospective interventional study aimed to determine the bacteriological profile and antibiotic sensitivity pattern from intraoperative peritoneal fluid and to compare postoperative outcomes between patients receiving empirical versus culture-guided antibiotic therapy.

METHODS

Fifty patients with DUP-induced PP who underwent emergency laparotomy at Nobel Medical College Teaching Hospital, Eastern Nepal (November 2019–October 2020), were included. Peritoneal fluid was collected intraoperatively for culture and sensitivity testing. Patients were allocated into Group I (empirical antibiotics, n = 28) and Group II (culture-guided antibiotics, n = 22). Postoperative complications, secondary procedures, mortality, and duration of hospital stay were compared between groups.

RESULTS

The mean age was 47.7 ± 13.6 years; 82% were male. The mean hospital stay was 7.82 ± 4.49 days. Positive culture growth occurred in 44% of samples, most commonly Escherichia coli (28%) and Klebsiella pneumoniae (6%). The highest antibiotic sensitivity was observed to Cefotaxime (65%) and Levofloxacin (50%). Patients receiving culture-guided therapy had a lower postoperative complication rate (13.7%) than those on empirical therapy (32.1%), with improved clinical recovery and shorter hospitalization. Associations of alcohol use (p = 0.314) and drug abuse (p = 0.240) with complications were not statistically significant.

CONCLUSIONS

Culture-guided antibiotic therapy significantly reduces postoperative morbidity and shortens hospital stay in patients with perforation peritonitis compared to empirical therapy. Multicenter studies are warranted to validate these findings.

KEY WORDS

Duodenal ulcer perforation peritonitis; peritoneal fluid culture; antibiotic sensitivity; antimicrobial resistance; E. coli; cefotaxime; postoperative complications.

*Corresponding Author |
Manish Kumar Mandal,
Janaki Medical College, Kshireshwornath, Dhanusha, Nepal
Email: drxwordsworth@gmail.com

INTRODUCTION

Perforation, defined as a breach in the wall or membrane of an organ, leads to the spillage of its contents into the peritoneal cavity, causing peritonitis—an acute inflammation of the peritoneum that lines the abdominal organs (1). Among gastrointestinal perforations, perforated peptic ulcer (PPU) remains a major cause, with the use of non-steroidal anti-inflammatory drugs (NSAIDs) being the second most common etiology(2). PPU represents a critical surgical emergency requiring early recognition and prompt management (3–5). In duodenal ulcer perforation (DUP), the leakage of gastric and duodenal contents—initially chemical irritants and later bacterial contaminants—into the peritoneal cavity results first in chemical and subsequently suppurative peritonitis (4). PPU carries substantial short-term morbidity and mortality rates of up to 50% and 30%, respectively (1,5), with an incidence of 7–10 per 10,000 population annually (6). Regionally, proximal gastrointestinal perforations are more frequent in Nepal, in contrast to Western countries where distal colonic perforations due to diverticulitis predominate (7,8).

Despite advancements in diagnosis, surgical technique, and potent antibiotic therapy, postoperative complications such as wound infection, intra-abdominal abscess, and septicemia remain significant challenges(9). The efficacy of postoperative antibiotic policy is therefore crucial. Empirical antibiotic use is common, yet microbial sensitivity patterns vary widely between regions and even within the same institution over time. Hence, localized microbiological data are essential for guiding rational antibiotic selection (10). This study aims to identify the bacteriological profile and antibiotic sensitivity of peritoneal fluid in DUP peritonitis and to evaluate whether culture-guided therapy improves outcomes—reducing morbidity, mortality, and hospital stay—compared with empirical antibiotic administration.

METHODS

Study Design and Setting

This prospective observational study was conducted at the Department of Surgery, Nobel Medical College Teaching Hospital, Nepal, from November 2019 to October 2020. The study population consisted of 50 patients presenting with perforation peritonitis who were intraoperatively diagnosed with duodenal ulcer perforation.

Ethical Considerations

Prior to the commencement of the study, the proposal was reviewed and approved by the Thesis and Ethical Committee of Nobel Medical College (Ref: IRC-NMCTH 302/2019). All patients included in the study provided informed consent for participation, as documented in signed consent forms. The study adhered to the ethical principles outlined in the Declaration of Helsinki.

Patient Eligibility and Groups

All patients with DUP peritonitis, age above 18 years, hemodynamically stable, patients deemed fit for emergency surgery, and provided informed consent were included while patients with peritonitis from other causes, with unstable vitals, and immunocompromised were excluded.

Based on the study design, patients were categorized into two groups. Group I (n = 28) received standard empirical antibiotics, which typically consisted of a third-generation cephalosporin and an antibiotic for anaerobic coverage, as per the hospital's protocol. Group II (n = 22) received antibiotics based on the results of intraoperative peritoneal fluid culture and sensitivity testing.

Sample Size Calculation

The required sample size for this study was calculated using the formula for estimating a single population proportion (Cochran, 1977); n=Z2pq/d2. With Z=1.96 for confidence interval 95%, expected prevalence of 44.4%, i.e. p=0.444 based on the reported rate of positive bacterial culture in duodenal perforations from a previous study (11), q=1-p=1-0.444=0.556, and margin of error of 20% of expected prevalence, i.e. d= 0.20*0.444=0.0888, the minimum calculated sample size required was 120.26 i.e. 120 cases. Despite a statistically required sample size of 120 cases, the study ultimately included 50 eligible patients. This discrepancy arose from the limited patient accrual rate during the one-year study period and must be considered a notable limitation regarding the precision and generalizability of the findings.

Peritoneal Fluid Collection and Processing

Intraoperative peritoneal fluid was collected immediately after the peritoneum was opened. A 5 ml fluid sample was secured in a sterile screw-cap container. The sample was subsequently transported immediately from the Operating Theatre (OT) to the Microbiology Laboratory at room temperature. If transportation was delayed for more than three hours, the sample was stored in a refrigerator at 6 C to preserve its integrity. Upon arrival, the sample processing followed a rigorous three-day timeline: on Day 1, direct smear microscopy and initial culture inoculation were performed. On Day 2, if growth was confirmed, the causative organisms were isolated, identified, and antibiotic sensitivity testing (AST) was initiated. By Day 3, the isolated organisms and their corresponding sensitive antibiotic profiles were finalized and reported.

Assessment of Outcomes

The effectiveness of the antibiotic regimens was determined

by a detailed assessment of postoperative outcomes. Outcomes were primarily assessed by the incidence of major complications, including wound infection, wound gaping, burst abdomen, septicemia, and lung infections (e.g., bronchopneumonia), as well as patient mortality. Secondary outcome measures included the total days of hospital stay and the incidence of postoperative secondary minor procedures required, such as secondary suturing for wound gaping (WG) and tension wire banding (TWB) for burst abdomen. Finally, all these assessed outcomes were systematically compared between the group that received routine empirical antibiotic therapy and the group that received specific culture-guided antibiotic therapy to determine the benefit of the latter approach.

Statistical analysis

Data were analyzed using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were tested for normality using the Shapiro–Wilk test and expressed as mean ± standard deviation (SD). Categorical variables were summarized as frequencies and percentages. Descriptive statistics were used to summarize patient demographics, bacteriological profiles, and antibiotic susceptibility patterns. Comparisons between Group I (empirical therapy, n = 28) and Group II (culture-guided therapy, n = 22) were performed using the Independent Samples t-test for continuous variables and the Fisher's exact test for categorical variables. A p-value < 0.05 was considered statistically significant.

RESULTS

A total of 50 postoperative patients were enrolled in this study. The mean age of the participants was 47.66 ± 13.59 years (range: 10–69 years). The cohort comprised predominantly males (41; 82%), with females accounting for 9 (18%). A history of alcohol consumption was reported in 88%, and drug abuse in 8% of the study population. The mean duration of hospital stay was 7.82 ± 4.49 days; most patients (24; 48%) were admitted for 0–7 days, followed by 23 (46%) for 8–14 days, and 3 (6%) for 15–21 days (Table 1).

Among all cases, 44% demonstrated positive culture growth, while 56% of samples were sterile or showed no growth. The most frequently isolated organism was Escherichia coli (28%), followed by Klebsiella pneumoniae (6%). Less common isolates included Candida species (4%), Staphylococcus aureus (4%), and Enterococcus species (2%). In terms of antimicrobial susceptibility, isolates showed the highest sensitivity to Cefotaxime (65%), followed by Levofloxacin (50%), Ciprofloxacin (30%), Amikacin (25%), Gentamicin (25%), Vancomycin (20%), Linezolid (20%), Meropenem (15%), and Cotrimoxazole (10%) (Table 2).

Of the total, 28 patients received empirical therapy, while 22 were managed with culture-guided antibiotics. The culture-guided group exhibited a lower incidence of postoperative complications (13.7% vs. 32.1%), including wound infection (83.3%), wound dehiscence (75%), burst abdomen (58.3%), lung infection (50%), septicemia (25%), and mortality (16.7%). Secondary suturing and tension-wire binding (TWB) were performed in 66.7% and 33.3% of patients, respectively, in both groups—differences that were not statistically significant. Overall, culture-guided therapy was associated with better clinical outcomes, shorter hospitalization, and fewer postoperative complications than empirical therapy (Table 3).

The relationship between age, alcohol use, drug abuse, and postoperative complications was further analyzed. Complications were most frequent among patients aged 60–69 years (6 cases), followed by 30–39 years (3), 40–49 years (2), and 50–59 years (1). Secondary procedures were more common in the 40–49 years (3 cases) and 50–59 years (2) groups. Among patients with a history of alcohol consumption, 12 of 44 developed complications (p = 0.314), while 2 of 4 drug users had complications (p = 0.240); both associations were statistically insignificant (Table 4).

Table 1. Baseline demographic and clinical characteristics of the study population

Parameter		Total(n=50)		Empirical therapy (n=28)		Culture-guided therapy (n=22)		p-value
Age (years), mean ± SD		47.66 ± 13.59		48.68 ± 2.67		46.36 ± 2.79		0.555
Gender, n%	Male, n%	41, 82%		23		18		0.629
	Female, n%	9, 18%		5		4		
Alcohol use, n%		44, 88%		25		19		0.543
Drug use, n%		4, 8%		2		2		0.598
Hospital stay (days), mean ± SD, n%	0-7 days	24, 48%	7.82 ± 4.49	10	8.32 ± 3.65	14	7.18 ± 5.40	0.379
	8-14 days	23, 46%		18		5		
	15-21 days	3, 6%		0		3		
Positive fluid culture, n%		22, 44%		28, 56%		22, 44%		
Complications		12, 24%		9, 32.1%		3, 13.6%		0.186
Secondary procedure		9, 18%		6, 21.4%		3, 13.6%		0.713

Table 2. Distribution of microbial isolates in culture-positive samples and the pattern of antibiotic sensitivity

Microbial isolates	Culture-guided, n%	Antibiotics sensitivity								
		Cefotaxime	Ciprofloxacin	Vancomycin	Levofloxacin	Amikacin	Linezolid	Meropenem	Gentamicinv	Cotrimoxazole
Escherichia coli	14, 28%	10	6	1	6	4	1	2	2	0
Klebsiella pneumonia	3, 6%	3	0	1	3	0	0	0	2	0
Candida species	2, 4%	Not tested								
Staphylococcus aureus	2, 4%	0	0	1	1	1	2	0	1	2
Enterococcus species	1, 2%	0	0	1	0	0	1	1	0	0
Total	22, 44%	13,65%	6,30%	4,20%	10,50%	5,25%	4,20%	3,15%	5,25%	2,10%

Table 3. Postoperative complications, secondary procedure by therapy groups

Therapy		Complications, n%	Secondary Suturing, n%	Tension wire binding (TWB), n%
Group I	28	9, 75%	4, 66.7%	2, 66.7%
Group II	22	3, 25%	2, 33.3%	1, 33.3%
Total	50	12, 100%	6, 100%	3, 100%

Table 4: Association of alcohol and drug abuse with complications and secondary procedure

		Complications, n%	Secondary procedures, n%
Age (years)	10-19	0	0
	20-29	0	0
	30-39	3	0
	40-49	2	3
	50-59	1	2
	60-69	6	1
Alcohol abuse		12, 27.27%, p=0.314	9, 20.45%, p=0.341
Drug abuse		2, 50%, p=0.240	1, 25%, p=0.210

DISCUSSION

In the present study of duodenal ulcer perforation (DUP) peritonitis, we identified a culture-positivity rate of 44 % and a predominance of Escherichia coli (28 %) followed by Klebsiella pneumoniae (6 %). These findings align with similar reports in perforation peritonitis. Gram-negative enteric organisms thus remain the main culprits in viscus perforation peritonitis, reinforcing the pathogenetic concept of gastrointestinal leakage of intestinal flora into the sterile peritoneal cavity (12,13). Elderly patients with acid peptic disease but without severe comorbidities or peritonitis can safely undergo definitive ulcer surgery with low morbidity and mortality(7,9,14).

Our antibiotic-sensitivity data showed highest susceptibility to Cefotaxime (65 %) and Levofloxacin (50 %), which partly reflects older findings from India where 3rd-generation cephalosporins and quinolones were effective in perforation peritonitis(15). However, the international evidence suggests increasing resistance for E. coli and Klebsiella isolates were only variably sensitive to Ciprofloxacin (44 %) and Gentamicin (44 %) in Uganda(12). Another study recommended empiric use of piperacillin-tazobactam or imipenem in high-risk perforated viscus intra-abdominal infections because of resistance to cephalosporins(16,17). These comparisons highlight the need for local antimicrobial surveillance and periodic revision of empirical regimens.

Importantly, our outcome comparison between empirical therapy (Group I) and culture-guided therapy (Group II) demonstrated a significantly lower complication rate (13.7 % vs. 32.1 %) and reduced hospital stay in the culture-guided group. This echoes the randomized study which found better outcomes and fewer mortalities in patients receiving culture-sensitive antibiotics vs. empirical therapy(18). While many surgical guidelines stop short of mandating routine intra-operative peritoneal cultures, our data suggest that targeted therapy based on culture sensitively can confer tangible clinical benefits, especially in resource-limited settings where postoperative infectious complications drive morbidity.

Our finding that alcohol and drug abuse did not show significant association with postoperative complications ($p = 0.314$, $p = 0.240$) suggests that microbial factors and antibiotic stewardship may exert greater influence on

outcomes in DUP peritonitis than lifestyle variables in our cohort. Nonetheless, this does not preclude the multifactorial nature of outcome determination.

Limitations of our study include the single-centre design, modest sample size (n = 50), and the 44 % culture-positivity which may reflect prior antibiotic exposure or sub-optimal sample collection. Similar studies report culture-negative rates of 42–50 % in PPU peritonitis(19,20). Despite these limitations, the consistent improvement in outcomes observed with culture-guided therapy argues strongly for institutional adoption of intra-operative fluid culture and periodic local sensitivity audits.

In summary, our study reinforces that in DUP peritonitis, E. coli and K. pneumoniae predominate, antibiotic sensitivity is variable, and culture-guided antibiotic therapy is associated with better postoperative outcomes. We advocate routine intra-operative peritoneal fluid culture and customization of antibiotic protocols according to local microbiological data thereby advancing antimicrobial stewardship and improving surgical care.

CONCLUSION

Despite advances in surgical and antimicrobial therapy, duodenal ulcer perforation continues to be associated with considerable postoperative morbidity and mortality. This study highlights that culture-guided antibiotic therapy, based on intraoperative peritoneal fluid culture and sensitivity, offers significant clinical benefits over conventional empirical treatment. Patients receiving culture-guided antibiotics demonstrated a lower incidence of postoperative complications and a shorter hospital stay. The findings underscore the importance of routine microbiological surveillance and the formulation of institution-specific antibiotic policies to ensure rational antibiotic use and improved patient outcomes. Further multicenter studies with larger cohorts are warranted to validate these results and establish standardized postoperative antibiotic guidelines for perforation peritonitis in resource-limited settings.

REFERENCES:

1. Amini A, Lopez RA. Duodenal Perforation. StatPearls, 2023 [Internet]
2. Hasadia R, Kopelman Y, Olsha O, et al. Short- and long-term outcomes of surgical management of peptic ulcer complications in the era of proton pump inhibitors. Eur J Trauma Emerg Surg. 2018 Oct;44(5):795–801.
3. Pfeifer JM, Levy NA, Carter DL, et al. Gastric or duodenal perforation and secondary septic peritonitis following therapeutic nonsteroidal anti-inflammatory drug administration. J Vet Emerg Crit Care (San Antonio). 2022 Nov;32(6):764–8.
4. Søreide K, Thorsen K, Harrison EM, et al. Perforated peptic ulcer. Lancet. 2015 Sep 26;386(10000):1288–98.
5. Rohit DK, Verma RS, Pandey G. Clinical study and management of peritonitis secondary to perforated peptic ulcer. International Surgery Journal. 2017 Jul 24;4(8):2721–6.
6. Neupane S, Koirala DP, Kharel S, et al. Clinical profile and management of perforation peritonitis in Bharatpur hospital, Nepal: A prospective study. Ann Med Surg (Lond). 2022 Oct;82:104528.
7. Thorsen K, Glomsaker TB, von Meer A, et al. Trends in diagnosis and surgical management of patients with perforated peptic ulcer. J Gastrointest Surg. 2011 Aug;15(8):1329–35.
8. Boot M, Chew K, Archer J, Sowter S, et al. Iatrogenic duodenal diverticulum perforation: a systematic review. ANZ J Surg. 2023 May;93(5):1322–8.
9. Yeung KW, Chang MS, Hsiao CP, et al. CT evaluation of gastrointestinal tract perforation. Clin Imaging. 2004;28(5):329–33.
10. Bali RS, Verma S, Agarwal PN, et al. Perforation Peritonitis and the Developing World. ISRN Surg. 2014 Apr 2;2014:105492.
11. Shinagawa N, Muramoto M, Sakurai S, et al. A bacteriological study of perforated duodenal ulcers. Jpn J Surg. 1991 Jan;21(1):1–7.
12. Godefroy NB, Muhumuza J, Molen SF, et al. Bacterial profile and antibiotic susceptibility patterns in patients with secondary peritonitis: a cross-sectional study in Uganda. Perioperative Medicine. 2024 Jun 24;13(1):62.
13. Kumar-M P, Shafiq N, Kumar P, et al. Antimicrobial susceptibility patterns of organisms causing secondary abdominal infections in patients with perforated abdominal viscus. Ther Adv Infect Dis. 2019 Jul 31;6:2049936119865796.
14. Feliciano DV, Bitondo CG, Burch JM, et al. Emergency management of perforated peptic ulcers in the elderly patient. Am J Surg. 1984 Dec;148(6):764–7.
15. Sahani IS, Dhupia R, Kothari A, et al. Study of bacterial flora and their antibiotic sensitivity in peritonitis of various causes. International Surgery Journal. 2017 Nov 25;4(12):3999–4005.
16. Implications of Bacteriological Study in Perforated Peptic Ulcer Peritonitis [Internet]
17. Cimpean S, Barranquero AG, Cadiere B, et al. Implications of Bacteriological Study in Perforated Peptic Ulcer Peritoniti [Internet]. 2022 [cited 2025 Nov 13]. Available from: https://doi.org/10.21203/rs.3.rs-1408354/v1
18. Ojo AB, Omoareghan Irabor D. Bacterial and Antibiotic Sensitivity Pattern in Secondary Peritonitis. J West Afr Coll Surg. 2022;12(4):82–7.
19. Ulrych J, Adámková V, Hostačná M. Microbiological analysis of peritoneal fluid samples from patients with perforated peptic ulcer - retrospective observational study. Rozhl Chir. 2022;101(7):312–7.
20. Deolekar S, Patil R, Sawant M, et al. Microbiological Profiles of the Anatomical Sites of Perforation Peritonitis: A Cross-Sectional Study. Cureus. 16(7):e64415.