



OPEN Distribution and drug resistance analysis of pathogens in early-stage digestive tract perforation complicated with peritonitis

Shuxiang Wang[✉] & Shuwen Yao

To investigate the distribution and drug resistance of pathogens associated with early-stage digestive tract perforation with peritonitis. A retrospective analysis was conducted on patients with digestive tract perforation and peritonitis at Huadu District People's Hospital of Guangzhou from Jan. 2020 to Aug. 2024. The selected patients were divided into two groups: the upper digestive tract (UDT) group and the lower digestive tract (LDT) group. General clinical characteristics and intraoperative secretions culture results were compared and analyzed. The study included 831 patients; 41.28% were in UDT group followed 58.72% in LDT group. 694 strains that isolated comprised 503 Gram-negative bacteria (GNB), 93 g-positive bacteria (GPB) and 98 fungi. Compared to LDT group, the UDT group had a higher positive rate of GPB and fungi but a lower positive rate of GNB. The most common pathogens among GNB were *E.coli*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae*; among GPB were *Streptococcus anginosus*, *Enterococcus aviae*, and *Streptococcus constellations*; among fungi were *Candida albicans*, *Candida glabrata*, and *Candida Cruxalis*. We further analyzed drug susceptibility results to related antibacterial drugs. The findings from this study have significant implications for guiding initial empirical antimicrobial therapy for patients with digestive tract perforation and peritonitis.

Keywords Digestive tract perforation, Peritonitis, Pathogen, Drug resistance

As defined by Sepsis-3, sepsis is life-threatening organ dysfunction caused by a dysregulated host response to serious infection¹, which usually progresses rapidly and leads to septic shock and multiple organ failure. Gastrointestinal perforation with peritonitis is a common acute abdominal disease and a frequent cause of sepsis and septic shock, with a mortality rate ranging from 8 to 25%^{2,3}. The prognosis of severe cases is influenced by age, with higher mortality rates being observed in the elderly population⁴. Early and effective anti-infective therapy plays a crucial role in improving patient outcomes⁵.

The increasing burden of antimicrobial resistance (AMR) poses a significant global health problem at present. A recent systematic analysis in *The Lancet* estimated that 4.71 million deaths were associated with bacterial AMR, of which approximately one-quarter of deaths were attributed to bacterial AMR⁶. Furthermore, the prevalence of AMR varies greatly across different regions and age groups^{6,7}, particularly affecting the elderly population aged over 70 years who are estimated to experience the highest proportion of drug-resistant related deaths in the future⁶. A multinational study involving 2,621 patients reported that the overall prevalence of AMR among ICU patients with abdominal infections was 26.3%⁸. Moreover, the AMR was identified as one of the independent risk factors for mortality⁸. The rational use of antibiotics, saving lives from infections, and reducing the occurrence of AMR remain ongoing challenges for clinicians. Therefore, regular monitoring and research on drug resistance are crucial.

In this trial conducted at Huadu District People's Hospital in Guangzhou from January 2020 to August 2024, patients with digestive tract perforation and peritonitis were selected to compare and analyze their general clinical characteristics and intraoperative secretion culture results. This study aims to understand pathogen distribution and drug resistance patterns, providing valuable guidance for empirical antibiotic use.

Department of Critical Care Medicine, Huadu District People's Hospital, Guangzhou, Guangdong, China. ✉email: wangshuxiang@hdhosp.cn

Material and methods

Study design

Patients with digestive tract perforation and peritonitis were retrospectively selected from Huadu District People's Hospital of Guangzhou, for a single-center analysis, from January 2020 to August 2024. Only patients who underwent emergency surgical treatment and had the location of perforation identified were included in this study. They were divided into two groups: the upper digestive tract (UDT) group and the lower digestive tract (LDT) group. The clinical characteristics collected for statistical analysis included age, gender, perforation location, cause of perforation, blood culture results, secretion culture results from aseptic surgery, and drug sensitivity information. This study was approved by the Ethics Committee of Huadu District People's Hospital of Guangzhou (NO. 2025007), and written informed consent was obtained from all patients. All methods were performed in accordance with the relevant guidelines and regulations.

Inclusion and exclusion criteria

Inclusion criteria: (1) Patients with peritonitis resulting from digestive-tract perforation, including the esophagus, stomach, duodenum, gallbladder, pancreas, small intestine, ileocecal part, colon, and rectum; (2) Emergency surgical treatment was performed and the site of perforation was identified. Exclusion criteria: (1) Age < 2 years; (2) Elective surgery or no surgery.

Strain identification and sensitivity

The microbiological samples (Table 1) obtained from patients during emergency aseptic surgeries were subjected to strain identification and sensitivity testing through secretion culture at the Laboratory of Huadu District People's Hospital. The VITEK® MS instrument (BioMerieux, France) and the VITEK-2 Compact Automated Antimicrobial Susceptibility Testing (AST) systems were utilized for species identification and initial drug susceptibility testing. These systems automatically analyze and interpret the results. The generated report provides information on the species of bacteria cultured, the Minimum Inhibitory Concentration (MIC) values of tested antibiotics for drug sensitivity (via microbroth dilution), or the inhibition zone diameter (via disc diffusion), along with the corresponding sensitivity classification (e.g., sensitive, intermediate, drug resistant, etc.). For

	UGT group(n = 343)	LDT group(n = 488)	F/χ ²	p
Male, n(%)	279(81.34)	321(65.78)	23.536	< 0.001*
Age, years	54.90 ± 18.21	40.85 ± 17.86	0.724	< 0.001*
Location, n(%)				
Esophagus	7(2.04)	-		
Stomach	195(56.85)	-		
Duodenum	134(39.07)	-		
Gall bladder	6(1.75)	-		
Pancreas	1(0.29)	-		
Small intestine	-	40(8.20)		
Ileocecal junction	-	395(80.94)		
Colon	-	46(9.43)		
Rectum	-	7(1.43)		
Cause of perforation, n(%)				
Infection	6(1.75)	385(78.89)	478.071	< 0.001*
Ulceration	320(93.29)	11(2.25)	692.809	< 0.001*
Tumour	6(1.75)	29(5.94)	7.771	0.005*
Diverticulum	0	24(4.92)		
Ileus	0	6(1.23)		
Hernia	0	4(0.82)		
Traumatism	2(0.58)	7(1.43)	0.684	0.408
Foreign bodies' Injury	8(2.33)	7(1.43)	0.48	0.498
Iatrogenic injury	1(0.29)	7(1.43)	1.691	0.693
Unknown aetiology	0	8(1.64)		
Specimen submission, n(%)				
Blood culture submission	71(20.70)	51(10.45)	16.083	< 0.001*
Blood culture positive	11(15.49)	11(21.57)	0.387	0.534
Secretion culture submission	330(96.21)	473(96.93)	0.136	0.713
Secretion culture positive	141(42.73)	390(82.45)	135.187	< 0.001*
Mixed-infection secretions(≥ 2 pathogens)	27(19.15)	131(33.59)	9.653	0.002*

Table 1. Fundamental information in different groups. Notes: * and Bold type, Significant statistic value. Abbreviations: UGT, Upper Gastrointestinal Tract; LDT, Lower Digestive Tract.

specific strains such as carbapenem-resistant Enterobacteriaceae (CRE), other antibiotics like ceftazidime/avibactam may be included in the testing process.

Statistical analysis

The collected data were subjected to statistical analysis using SPSS 19.0, with the two-independent-sample t-test employed for measurement data and the Chi-square test used for enumeration data. Significance was determined by p values < 0.05 for two-tailed tests.

Results

831 patients that underwent the emergency surgery due to the perforation of digestive tract with peritonitis were included in this study. The UDT group (41.28%) accounted for 343 cases, age of which was 54.90 ± 18.29 (14 to 94); 81.34% were males and 18.66% females. The LDT group (58.72%) was with 488 cases; age of which was 40.85 ± 17.86 (4 to 85); 65.78% were males and 34.22% females. Compared with the LDT group, the proportion of males in the UDT group was statistically higher (81.31% vs. 65.78%, $p < 0.001$), and the average age was older ($p < 0.001$). (Table 1).

Location

Our study showed that, in the part of UDT perforation, the sources were most frequently located in stomach (56.85% of the patients) and duodenum (39.07%) followed by esophagus (2.04%), gallbladder (1.74%), and pancreas (0.29%); in LDT, they mainly located at the ileocecal part (80.94%) followed by colon (9.43%), small intestine (8.20%) and rectum (1.43%). (Table 1).

Cause of perforation

As our results, the most common cause of UDT perforation was gastric and duodenal ulcer, that of which occupied for 93.29% patients followed a small number of cases in the injury of foreign bodies in the digestive tract (2.33%), infection (1.75%), tumor (1.75%), trauma (0.58%), and iatrogenic injury (0.29%). On the other hand, the mainly cause of LDT was infection (78.89%) from both appendicitis and its' involving infection of adjacent tissue, and the others were tumors (5.94%), diverticulum (4.92%), ulcers (2.25%), trauma (1.43%), foreign body injury in digestive tract (1.43%), intestinal obstruction (1.23%), inguinal/internal hernia (0.82%) and iatrogenic injury (0.29%). Compared with the LDT group, the proportion accounted in ulcer (93.29% vs. 2.25%, $p < 0.001$) was significantly higher in UDT group, but that in infection (1.75% vs. 78.89%, $p < 0.001$) and tumor (1.75% vs. 5.94%, $p = 0.005$) was lower. There was no significant difference in the proportion of trauma, gastrointestinal foreign body injury or iatrogenic injury between the two groups. (Table 1).

Specimen submission

In comparing with the LDT group, the rate of the blood culture submission in UDT group was significantly higher (20.70% vs. 10.45%, $p < 0.001$); but that of the positive secretions culture (42.73% vs. 82.45%, $p < 0.001$) and the mixed- infection secretions (19.15% vs. 33.59%, $p = 0.002$) was lower. There was no significant difference in the rate of positive blood culture and secretion detection between groups. (Table 1).

Pathogen distribution

A total of 694 strains were isolated from secretions culture, 177 stains in UDT group and the other 517, respectively, in LDT group. 72.48% strains were Gram-negative bacteria (GNB), when 13.40% was Gram-positive bacteria (GPB) and 14.12% fungi. Compared with LDT group, the positive rate of GPB (20.34% vs. 11.03%, $p = 0.003$) and fungi (52.54% vs. 0.97%, $p < 0.001$) in UDT group was significantly higher; but that of GNB (27.12% vs. 88.01%, $p < 0.001$) was lower. The most common findings of GNB were *E. coli* (63.02%), *Pseudomonas aeruginosa* (PA) (13.92%) and *Klebsiella pneumoniae* (8.15%); that of GPB were *Streptococcus anginosus* (21.51%), *Enterococcus avium* (15.05%) and *Streptococcus constellations* (13.98%); of fungi were *Candida albicans* (55.10%), *Candida glabra* (19.39%) and *Candida clorunda* (14.29%). (Table 2).

Antimicrobial resistance

Main gram-negative bacteria

Overall 317 strains of *E. coli* were isolated from secretions culture, including 91 ESBL-positive, 8 multidrug-resistant organisms (MDROs) and 3 CRE. On the other hand, 41 strains of *Klebsiella pneumoniae* were isolated with 4 ESBL-positive but without MDROs/CRE. And both the ESBL-positive ($\chi^2 = 5.751$, $P = 0.016$) and drug-resistant (ESBL+/MDROs/CRE) strains ($\chi^2 = 7.713$, $P = 0.005$) were accounted for a higher proportion in *E. coli* than in *Klebsiella pneumoniae*. Regarding AMR patterns, high levels of drug resistance in *E. coli* were observed against cotrimoxazole, levofloxacin, as well as various cephalosporins such as cefuroxime, cefuroxime axetil and ceftiraxone (rates of resistance, 31.86% to 62.78%). On the other hand, *Klebsiella pneumoniae* displayed only moderate resistance against these drugs (12.2%–14.63%). However, both *E. coli* and *Klebsiella pneumoniae* demonstrated higher sensitivity rates towards carbapenems (99.05 and 100%), tigacycline (100%), cefoperazone-sulbactam (98.74% and 100%, respectively), amikacin (98.42% and 100%), as well as piperacillin/tazobactam (94.64% and 95.12%). (Table 3).

Furthermore, a total of 70 strains of PA that isolated from secretions cultures were without drug-resistant ones. Most antibacterial agents demonstrated higher sensitivity against PA, including piperacillin/tazobactam, ceftazidime, cefoperazone/sulbactam, cefepime, imipenem, meropenem, amikacin and tobramycin (rates of sensitivity, 95.71% to 100%). However, ticarcillin/clavulanate and levofloxacin displayed noticeable resistance rates (7.14% and 11.43%, respectively). Notably, the sensitivity rate of polymyxin against PA was only 1.43%, with an intermediate rate of 94.29%.

Pathogens	UGT group (n = 177)	LDTgroup (n = 517)	χ^2	p
GNB, n(%)	48(27.12)	455(88.01)	282.003	< 0.001*
E.coli	10(5.65)	307(59.38)		
Klebsiella pneumoniae	14(7.91)	27(5.22)		
Klebsiella oxytoca	2(1.13)	1(0.19)		
Pseudomonas aeruginosa	1(0.56)	69(13.35)		
Other Pseudomonas genera	1(0.56)	14(2.71)		
proteusbacillus vulgaris	1(0.56)	10(1.93)		
Other GNB	19(10.73)	27(5.22)		
GPB, n(%)	36(20.34)	57(11.03)	9.07	0.003*
Streptococcus anginosus	8(4.52)	12(2.32)		
Streptococcus salivarius	6(3.39)	1(0.19)		
Streptococcus mitis	6(3.39)	2(0.39)		
Streptococcus constellatus	0	13(2.51)		
Enterococcus avium	1(0.56)	13(2.51)		
Enterococcus faecalis	3(1.69)	3(0.58)		
Enterococcus faecium	1(0.56)	2(0.39)		
Staphylococcus aureus	6(3.39)	0		
Other GPB	5(2.82)	11(2.13)		
Fungus, n(%)	93(52.54)	5(0.97)	284.986	< 0.001*
Candida albicans	53(29.94)	1(0.19)		
Candida glabrata	17(9.60)	2(0.39)		
Candida tropicalis	4(2.26)	2(0.39)		
Candida krusei	14(7.91)	0		
Candida parapsilosis	4(2.26)	0		

Table 2. Pathogens distribution of secretions in different groups. Notes: * and Bold type, Significant statistic value. Abbreviations: UGT, Upper Gastrointestinal Tract; LDT, Lower Digestive Tract; GNB, Gram-Negative Bacterium; GPB, Gram-Positive Bacterium.

Antibacterial drugs	E.coli (n = 317)			Klebsiella pneumoniae (n = 41)		
	S(%)	I(%)	R(%)	S(%)	I(%)	R(%)
Amoxicillin/clavulanic acid	80.76	10.09	9.15	87.80	7.32	4.88
Piperacillin/tazobactam	94.64	1.89	3.47	95.12	4.88	0.00
Cefuroxime	63.09	3.79	33.12	80.49	4.88	14.63
Cefuroxime axetil	62.15	4.42	33.44	82.93	2.44	14.63
Cefoxitin	87.70	4.42	7.89	92.68	2.44	4.88
Ceftazidime	80.44	9.15	10.41	95.12	0.00	4.88
Ceftriaxone	68.14	0.00	31.86	87.80	0.00	12.20
Cefperazone/sulbactam	98.74	0.32	0.95	100.00	0.00	0.00
Cefepime	81.70	0.00	9.78	95.12	0.00	2.44
Ertapenem	99.05	0.00	0.95	100.00	0.00	0.00
Imipenem	99.05	0.32	0.63	100.00	0.00	0.00
Amikacin	98.42	0.63	0.95	100.00	0.00	0.00
Levofloxacin	24.29	43.85	31.86	78.05	12.20	9.76
Tigecycline	100.00	0.00	0.00	100.00	00.00	00.00
Cotrimoxazole	37.22	0.00	62.78	85.37	00.00	14.63

Table 3. Antimicrobial resistance of E.coli and Klebsiella pneumoniae. Notes: Bold type, high drug resistance rate (> 30%) Abbreviations: S, Susceptible; I, Intermediate; R, Resistant.

Main gram-positive bacteria

Twenty strains of Streptococcus anginosus were isolated, and they exhibited significant resistance to erythromycin and clindamycin (40% and 60%, respectively). However, they showed sensitivity to levofloxacin, vancomycin, cefepime, and cefotaxime (95%–100%).

Thirteen strains of *Streptococcus constellatus* that isolated demonstrated high resistance rates to erythromycin and clindamycin (both 76.92%), but better sensitivity rates to levofloxacin, chloramphenicol, vancomycin, ceftriaxone, ampicillin, and cefotaxime (92.31%–100%).

Moreover, fourteen strains of *Enterococcus aviae* exhibited high resistance rates (28.57%–71.43%) to various antibiotics including penicillin, ampicillin, gentamicin, and erythromycin; however they displayed excellent sensitivity rates to linezolid, teicoplanin, vancomycin, and tigacycline (all 100%).

Fungus

The common fungi isolated from secretions were combined into 54 strains of *Candida tropicalis*, 19 strains of *Candida glabrata*, and 14 strains of *Candida creososa*. Sensitivity results revealed that *Candida tropicalis* exhibited high sensitivity rates (96.3%–100%) to flucytosine, fluconazole, itraconazole, and voriconazole; while *Candida glabrata* showed sensitivity to flucytosine and voriconazole (94.74% and 100%). Only Voriconazole demonstrated sensitivity against *Candida krusei* (Table 4).

Discussion

Perforation of digestive tract with peritonitis is a common cause of sepsis. Compared to UDT, LDT perforation has higher morbidity and mortality rates. Early effective anti-infective treatment can reduce the mortality in critically ill patients⁵. The aim of this study was to investigate the distribution and drug resistance of pathogens associated with gastrointestinal perforation and subsequent peritonitis, providing a basis for selecting early antibiotics for patients in this area. A total of 831 cases were collected in this study including 343 cases in UDT group and 488 cases in LDT group. Notably, demographic differences were observed between the two groups: the UDT group had a higher proportion of males and older individuals compared to the LDT group. The causes of perforation were varied, including infection, ulcer, tumor, diverticula, intestinal obstruction, inguinal/internal hernia, trauma, injury from foreign bodies in the digestive tract, iatrogenic injury, and unknown causes. However, the distribution of these causes varied significantly across different regions. In a clinical retrospective study published in Front Surg, it was observed that 350 patients with perforated peritonitis were predominantly males at Darbhanga Medical College and Hospital in India. The most common causes of perforation were duodenal ulcer (50%), typhoid fever (20%), traumatic injury, appendicitis, and tuberculosis⁹. In contrast, our study revealed that the largest proportion of cases involved appendicitis and adjacent infections (46.33%), followed by gastroduodenal ulcers (38.51%). Tumors accounted for 4.21% of cases, while diverticulum accounted for 2.89%. Traumatic injuries were rare, and there were no reported cases of typhoid fever or tuberculosis. Compared with LDT group, the UDT group had a higher incidence of ulcers but lower rates of infections and tumors. Interestingly, case reports on digestive tract perforation frequently mentioned foreign body injuries such as chicken bones, fish bones, rabbit bones, toothpicks, magnet balls, etc.^{10–15} Additionally, digestive tract perforation occasionally occurred as a complication of certain diseases like mediastinal emphysema, Rapunzel syndrome, Ehlers-Danlos syndrome, Schönlein-Henoch disease, and Peutz-Jeghers syndrome^{16–20}.

The etiological culture test is considered one of the most crucial diagnostic tests for infectious diseases, and positive blood/secretion cultures in patients with peritonitis and sepsis are typically associated with a higher mortality risk²¹. In our study, a total of 694 strains were isolated from secretion cultures; 177 strains were identified in UDT group, while 517 strains in LDT group, respectively; 72.48% belonged to GNB followed 13.40% GPB and 14.12% fungi. When comparing UDT to LDT results, the rates of positive culture findings, mixed infections, and GNB in the LDT group were higher; but that of GPB and fungal infection were lower. GNB, such as *E. coli*, PA, and *Klebsiella pneumoniae*, and GPB, including *Streptococcus anginosus*, *Enterococcus avium* and *Streptococcus constellatus* were identified as the primary pathogens. For fungi, *Candida albicans*, *Candida glabrata*, and *Candida krusei* were the predominant species.

E. coli, a common pathogen in gastrointestinal infections, is a significant contributor to mortality. It ranked second only to *Staphylococcus aureus* as the most prevalent cause of fatal peritoneal and abdominal infections with 30.4% of *E. coli*-related deaths occurring through such infections, followed by bloodstream infections (25.1%)²². In our analysis of drug resistance of common GNB, we observed a higher prevalence of ESBL-positive and drug-resistant strains of *E. coli*. The drugs exhibiting greater resistance were cotrimoxazole, quinolones, second-generation cephalosporins and ceftriaxone. Conversely, carbapenems, tigacycline, cefoperazone sulbactam, amikacin, piperacillin and tazobactam demonstrated good sensitivity towards *E. coli* and *Klebsiella pneumoniae*. Additionally, PA is also a common pathogen associated with infection and mortality rates²². Previous studies have indicated a low isolation rate of PA in abdominal infections but a high incidence rate in intensive care units (ICUs)²³. However, in our study, the positive culture rate for PA was found to be second

Antibacterial agents	Candida tropicalis (n = 54)			Candida glabrata (n = 19)			Candida krusei (n = 14)		
	S(%)	I(%)	R(%)	S(%)	I(%)	R(%)	S(%)	I(%)	R(%)
Flucytosine	98.15	0.00	1.85	94.74	5.26	0.00	28.57	71.43	5.10
Fluconazole	100.00	0.00	0.00	0.00	100.00	0.00	0.00	21.43	78.57
Itraconazole	96.30	3.70	0.00	0.00	84.21	15.79	21.43	57.14	21.43
Voriconazole	100.00	0.00	0.00	100.00	0.00	0.00	100.00	0.00	0.00

Table 4. Antimicrobial resistance of fungus. Notes: Bold type, high drug resistance rate (> 20%) Abbreviations: S, Susceptible; I, Intermediate; R, Resistant.

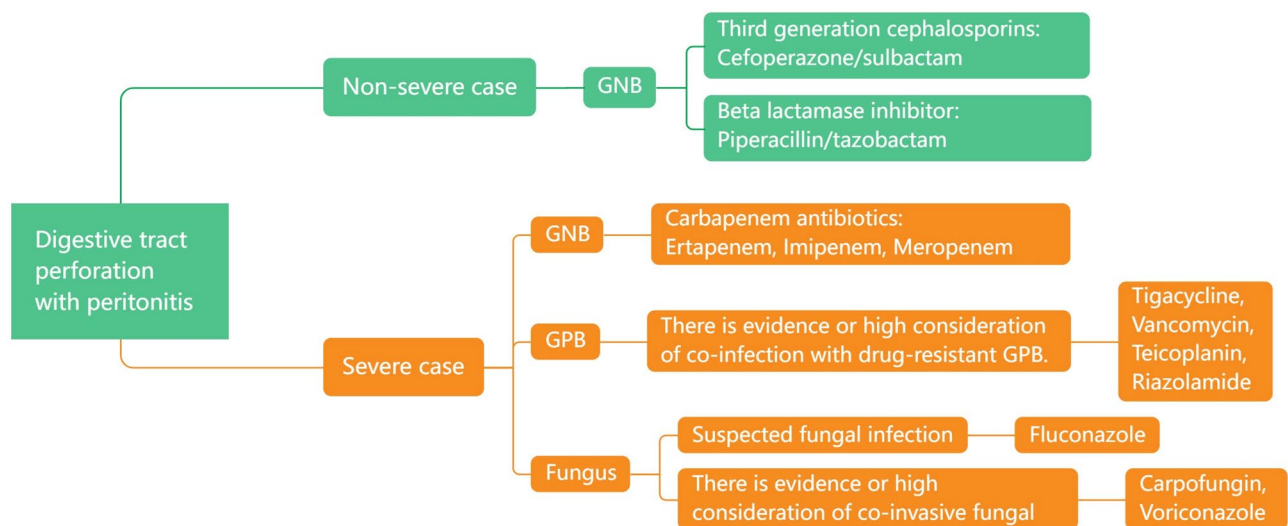


Fig. 1. Early antibiotic selection strategy Notes: The Green-Strategy was applied to the cases of non-severe digestive tract perforation complicated with peritonitis, while the Orange-Strategy to severe cases. GNB, Gram-negative bacterium; GPB, gram-positive bacterium.

only to that of *E. coli* among the most prevalent GNB. In terms of PA resistance analysis, it still exhibited good sensitivity towards various antibiotics except polymyxin, and drug-resistant ones were rare. A cross-country systematic analysis in 2019 within the Americas region revealed that bacterial resistance was linked to 569,000 deaths, *E. coli*, *Klebsiella pneumoniae* and PA being major pathogens⁷. Therefore, in clinical practice, to reduce the risk of infection-related mortality, the initial selection of antibiotics should avoid those with high resistance and instead opt for antibiotics demonstrating better sensitivity. As for the duration of antibacterial drug use, no conclusive evidence has been established⁵. The extent of severe abdominal infection's AMR varies significantly across different regions. The overall rate of bacterial drug resistance was 26.3%, with refractory GNB accounting for 4.3%⁸. Among GNB, carbapenems exhibited a higher resistance rate compared to other antibiotics⁶. For the treatment of intraperitoneal infections caused by CRE, antimicrobial therapy focuses on antibacterial agents such as Tigacycline, Elacycline, Ceftazidime/avibactam, as well as novel carbapenem/beta-lactamase inhibitors like Meropenem/vabobactam, Imipenem/cilastatin/relebactam²⁴.

The common GPB associated with abdominal infection include streptococcus and Enterococcus²⁵, among which enterococcus is associated with 30-day mortality in patients with severe abdominal infection²⁶. However, there are variations in the distribution of strains across different studies. Previous research indicated that Enterococcus faecalis was the most prevalent GPB associated with digestive tract perforation and peritonitis²⁷. In contrast, our study found Streptococcus anginosus, Enterococcus avium and Streptococcus constellatus to be the most common GPB. Erythromycin and clindamycin exhibited high resistance against Streptococcus anginosus and Streptococcus constellatus; therefore, they should be avoided clinically whenever possible. On the other hand, levofloxacin and vancomycin demonstrated higher sensitivity when tested against all three bacteria. For Enterococcus aviae infections, linezolid, teicoplanin, vancomycin, and tigecycline were found to be ideal treatment options with a 100% sensitivity rate.

Patients with fungal peritonitis complicated by sepsis and septic shock have a higher mortality rate²⁸, an increased risk of postoperative complications, delayed postoperative recovery and longer hospital stays compared to those without it²⁹. A serum 1,3-β-D-glucan level <3.3 pg/ml and a peritoneal level <45 pg/ml, combined with a low peritonitis score (<3), are associated with a lower likelihood of abdominal fungal infection, which helps avoid unnecessary treatment with antifungal drugs³⁰. Our study found that patients with UDT perforation complicated by peritonitis had a significantly higher positive rate (52.54% vs. 0.97%, $p < 0.001$) for culture fungi in secretions during operation. Candida species were the only fungi cultured from secretions, predominantly Candida albicans, Candida glabrata, and Candida krusei. In clinical practice, not all positive fungal cultures require antifungal therapy; however appropriate antifungal therapy reduces the risk of death within 30 days for severe surgical abdominal candidiasis³¹. Echinocandin is recommended as first-line treatment for aggressive candida infections in critically ill patients while fluconazole is used as preventive treatment^{28,32}. Recent literature suggests adding amphotericin B liposomes as another option for treating abdominal candida infections³³. The results of fungal susceptibility testing demonstrated that common broad-spectrum antifungal drugs exhibited high efficacy against the majority of Candida albicans strains, with the exception of Candida glabra and Candida cloris. Notably, voriconazole displayed sensitivity towards all these strains, making it an optimal choice for initial treatment of abdominal fungal infections.

According to the previous literature review and the results of this study, we prepared an antibiotic selection strategy for early digestive tract perforation complicated with peritonitis. (Fig. 1).

Our study had some limits. Firstly, it was a retrospective study conducted at a single center, which involving a limited number of regions and cases. Consequently, it lacked diversity and was susceptible to selection bias,

which might have affected the accuracy of the results. Secondly, the specimens of secretions used in our study were extracted during early operations, excluding those re-examined during disease progression or prolongation. The collection of late specimens may have better reflected the changes in strain and drug sensitivity caused by widespread and sustained use of antibacterial drugs as well as disease progression, thereby providing greater guidance for treatment adjustments in later stages. Finally, efforts such as multi-center collaboration, expanding the sample size, and analyzing the long-term outcomes of drug-resistant bacteria will be the critical directions for our future research.

Conclusion: The findings of this study partially reflect the current distribution of pathogens and the patterns of AMR and sensitivity in gastrointestinal perforation and peritonitis in the north of Guangzhou, China. These results are highly significant for guiding early empirical antibiotic therapy.

Data availability

All data that used or analysed during the current study are available from the corresponding author.

Received: 24 October 2024; Accepted: 14 May 2025

Published online: 19 May 2025

References

1. Singer, M. et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA* **315**, 801. <https://doi.org/10.1001/jama.2016.0287> (2016).
2. Amini, A. & Lopez, R. *Duodenal Perforation*. (Treasure Island (FL): StatPearls Publishing, Jan) (2024).
3. Yadav, D. & Garg, P. K. Spectrum of perforation peritonitis in delhi: 77 cases experience. *Indian J. Surg* **75**, 133–137 (2013).
4. Arvaniti, K. et al. Epidemiology and age-related mortality in critically ill patients with intra-abdominal infection or sepsis: an international cohort study. *Int. J. Antimicrob. Agents* **60**, 106591. <https://doi.org/10.1016/j.ijantimicag.2022.106591> (2022).
5. Evans, L. et al. Surviving sepsis campaign: International guidelines for management of sepsis and septic shock 2021. *Intensive care Med.* **47**, 1181–1247. <https://doi.org/10.1007/s00134-021-06506-y> (2021).
6. Collaborators, G. A. R. Global burden of bacterial antimicrobial resistance 1990–2021: a systematic analysis with forecasts to 2050. *Lancet (London, England)* **404**, 1199–1226 (2024).
7. collaborator, A. r. The burden of antimicrobial resistance in the Americas in 2019: a cross-country systematic analysis. *Lancet regional health. Americas* **25**, 100561. <https://doi.org/10.1016/j.lana.2023.100561> (2023).
8. Blot, S. et al. Epidemiology of intra-abdominal infection and sepsis in critically ill patients: “AbSeS”, a multinational observational cohort study and ESICM Trials Group Project. *Intensive Care Med.* **45**, 1703–1717. <https://doi.org/10.1007/s00134-019-05819-3> (2019).
9. Hameed, T., Kumar, A., Sahni, S., Bhatia, R. & Vidhyarthi, A. K. Emerging Spectrum of Perforation Peritonitis in Developing World. *Front. Surg.* **7**, 50. <https://doi.org/10.3389/fsurg.2020.00050> (2020).
10. Mačiulienė, A. et al. Predictors of 30-Day In-Hospital mortality in patients undergoing urgent abdominal surgery due to acute peritonitis complicated with sepsis. *Med. Sci. Monitor : Int. Med. J. Exp. Clinic. Res.* **25**, 6331–6340. <https://doi.org/10.12659/msm.915435> (2019).
11. Kanamalla, K., Salamone, F. J. & Vargas, J. (2021) Perforated sigmoid colon in the setting of chicken bone ingestion and diverticulitis: A case report. *Ann. Med. Surg.* **68**, 102650. <https://doi.org/10.1016/j.amsu.2021.102650> (2021).
12. Krieger, T., Majernik, J. & Ninger, V. Perforation of descending colon diverticulum by swallowed rabbit bone - A case report. *Rozhledy v chirurgii : mesicnik Ceskoslovenske chirurgicke spolecnosti* **100**, 94–96 (2021).
13. Evola, G. et al. Accidentally ingested wooden toothpick, perforation of a sigmoid diverticulum and mimicking acute colonic diverticulitis: A case report and literature review. *Int. J. Surg. Case Rep.* **104**, 107945. <https://doi.org/10.1016/j.ijscr.2023.107945> (2023).
14. Peyron, P. A., Villard, C. & Baccino, E. Fatal bowel perforation caused by ingestion of high-powered magnets in a 6-year-old boy. *Int. J. Legal Med.* **138**, 1659–1662. <https://doi.org/10.1007/s00414-024-03188-1> (2024).
15. Yamashita, K. et al. A rare case of perforation of a colorectal tumor by a fish bone. *Clin. J. Gastroenterol.* **15**, 598–602. <https://doi.org/10.1007/s12328-022-01622-8> (2022).
16. de Oliveira, M. F. A. & Rodrigues, M. A. M. Peutz-Jeghers syndrome: an unusual autopsy finding in pregnancy. *Autops. Case Rep.* **11**, e2021279. <https://doi.org/10.4322/acr.2021.279> (2021).
17. Alotaibi, A. E., AlAamer, O. H., Bawazeer, M. A. & Alzahrani, A. A. Gastric perforation leading to the diagnosis of classic Ehlers-Danlos syndrome: a case report. *J. Med. Case Rep.* **15**, 537. <https://doi.org/10.1186/s13256-021-03108-6> (2021).
18. Sert, O. Z. Multiple small bowel perforation in a young adult female due to Rapunzel Syndrome. *Ann. Italiani di Chirurgia* **9**, 1–4 (2020).
19. Vasileva, A. V., Chakarov, I. & Chakarova, P. Modern diagnostic methods for early assessment of the abdominal involvement in Schönlein-Henoch disease. *Folia Med.* **66**, 73–79. <https://doi.org/10.3897/folmed.66.e113993> (2024).
20. Pachowska, K. et al. Pneumomediastinum as a complication of colon perforation - a case report. *Polski merkuriusz lekarski : organ Polskiego Towarzystwa Lekarskiego* **47**, 226–228 (2019).
21. Sim, J., Hong, S. S., Kwak, J. Y. & Jung, Y. T. Prediction of culture-positive sepsis and selection of empiric antibiotics in critically ill patients with complicated intra-abdominal infections: a retrospective study. *Europ. J. Trauma Emergency Surg : official Publication Europ. Trauma Soc.* **48**, 963–971. <https://doi.org/10.1007/s00068-020-01535-6> (2022).
22. Global mortality associated with 33 bacterial pathogens in 2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet (London, England)* **400**, 2221–2248. [https://doi.org/10.1016/s0140-6736\(22\)02185-7](https://doi.org/10.1016/s0140-6736(22)02185-7) (2022).
23. Chou, J., Knight, P. H. & Sawyer, R. G. Is the isolation of pseudomonas aeruginosa associated with outcomes from intra-abdominal infection? no, but the receipt of an empiric anti-pseudomonal agent is. *Surg. Infect.* **22**, 675–679. <https://doi.org/10.1089/sur.2020.396> (2021).
24. Fiore, M. et al. Spontaneous bacterial peritonitis due to carbapenemase-producing Enterobacteriaceae: Etiology and antibiotic treatment. *World J. Hepatol.* **12**, 1136–1147. <https://doi.org/10.4254/wjh.v12.i12.1136> (2020).
25. Mehta, N. Y., Lotfollahzadeh, S. & Copelin, I. E. in *StatPearls* (StatPearls Publishing, Copyright © 2024, StatPearls Publishing LLC., 2024).
26. Morvan, A. C. et al. Impact of species and antibiotic therapy of enterococcal peritonitis on 30-day mortality in critical care-an analysis of the OUTCOMEREA database. *Critical care (London, England)* **23**, 307. <https://doi.org/10.1186/s13054-019-2581-8> (2019).
27. Wang, H., Liu, X., Bi, H., Tang, Y. & Wang, D. Clinical analysis of septic shock caused by acute upper and lower gastrointestinal perforation. *Zhonghua wei zhong bing ji jiu yi xue* **32**, 943–946. <https://doi.org/10.3760/cma.j.cn121430-20200417-00312> (2020).
28. Hasibeder, W. & Halabi, M. Candida peritonitis. *Minerva Anestesiol* **80**, 470–481 (2014).

29. Nyumura, Y. et al. Pathophysiology and surgical outcomes of patients with fungal peritonitis from upper gastrointestinal tract perforation: a retrospective study. *Surg. Today* <https://doi.org/10.1007/s00595-024-02851-9> (2024).
30. Novy, E. et al. Combination of serum and peritoneal 1,3-beta-D-glucan can rule out intra abdominal candidiasis in surgical critically ill patients: A multicenter prospective study. *Critical care (London England)*. **27**, 470. <https://doi.org/10.1186/s13054-023-04761-7> (2023).
31. Yan, T. et al. Appropriate Source Control and Antifungal Therapy are Associated with Improved Survival in Critically Ill Surgical Patients with Intra-abdominal Candidiasis. *World J. Surg.* **44**, 1459–1469. <https://doi.org/10.1007/s00268-020-05380-x> (2020).
32. Pemán, J. et al. Jávea consensus guidelines for the treatment of Candida peritonitis and other intra-abdominal fungal infections in non-neutropenic critically ill adult patients. *Rev. Iberoam. Micol.* **34**, 130–142 (2017).
33. Maseda, E. et al. Critical appraisal beyond clinical guidelines for intraabdominal candidiasis. *Critical care (London, England)* **27**, 382. <https://doi.org/10.1186/s13054-023-04673-6> (2023).

Author contributions

S.W. and S.Y. designed the study. S.Y. collected and assembled the data. S.W. and S.Y. performed the statistical analysis and wrote the manuscript, and S.W. prepared table 1–4. All authors reviewed the manuscript.

Funding

This research was supported by the Key Discipline Project (Grant No. YNZDXK202202, 2022–2025) of the Huadu District People's Hospital and the Huadu District General Medical Research Special Project (Grant No. 23-HDWS-006), Guangzhou.

Declarations

Competing interests

The authors declare no competing interests.

Additional information

Correspondence and requests for materials should be addressed to S.W.

Reprints and permissions information is available at www.nature.com/reprints.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Open Access This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by-nc-nd/4.0/>.

© The Author(s) 2025