Original Article

Causative Microorganisms Isolated from Patients with Intra-Abdominal Infections and Their Drug Resistance Profiles: An 11-Year (2011–2021) Single-Center Retrospective Study*

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Abstract

Objective To investigate the distribution and antimicrobial susceptibility of causative microorganisms recovered from patients with intra-abdominal infections (IAIs).

Methods A total of 2,926 bacterial and fungal strains were identified in samples collected from 1,679 patients with IAIs at the Peking Union Medical College Hospital between 2011 and 2021. Pathogenic bacteria and fungi were identified using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry. Antimicrobial susceptibility testing (AST) was performed using the VITEK 2 compact system and the Kirby–Bauer method. AST results were interpreted based on the M100-Ed31 clinical breakpoints of the Clinical and Laboratory Standards Institute.

Results Of the 2,926 strains identified, 49.2%, 40.8%, and 9.5% were gram-negative bacteria, gram-positive bacteria, and fungi, respectively. *Escherichia coli* was the most prevalent pathogen in intensive care unit (ICU) and non-ICU patients; however, a significant decrease was observed in the isolation of *E. coli* between 2011 and 2021. Specifically, significant decreases were observed between 2011 and 2021 in the levels of extended-spectrum β-lactamase (ESBL)-producing *E. coli* (from 76.9% to 14.3%) and *Klebsiella pneumoniae* (from 45.8% to 4.8%). Polymicrobial infections, particularly those involving co-infection with gram-positive and gram-negative bacteria, were commonly observed in IAI patients. Moreover, *Candida albicans* was more commonly isolated from hospital-associated IAI samples, while *Staphylococcus epidermidis* had a higher ratio in community-associated IAIs. Additionally, AST results revealed that most antimicrobial agents performed better in non-ESBL-producers than in ESBL-producers, while the overall resistance rates (56.9%–76.8%) of *Acinetobacter baumanmii* were higher against all antimicrobial agents than those of other common gram-negative bacteria. Indeed, *Enterococcus faecium*, *Enterococcus faecalis*, *S. epidermidis*, and *S. aureus* were consistently found to be susceptible to vancomycin, teicoplanin, and linezolid. Similarly, *C. albicans* exhibited high susceptibility to all the tested antifungal drugs.

Conclusion The distribution and antimicrobial susceptibility of the causative microorganisms from patients with IAIs were altered between 2011 and 2021. This finding is valuable for the implementation of evidence-based antimicrobial therapy and provides guidance for the control of hospital infections.

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Key words: Intra-abdominal infection; Causative microorganisms; Antimicrobial susceptibility testing; Gram-negative bacteria; Gram-positive bacteria

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INTRODUCTION

Intra-abdominal infections (IAIs) represent various conditions associated with pathological inflammation of the intra-abdominal organs or peritoneum[1] and are considered the second most common cause of mortality in the intensive care unit (ICU)[2]. Apart from surgical management, rapid and accurate identification of the causative microorganisms, as well as appropriate antimicrobial therapy, are critical for the diagnosis and treatment of IAIs. Appropriate antibiotic selection reduces the morbidity and mortality associated with IAIs, whereas excessive antimicrobial use can increase the emergence rate of antimicrobial-resistant strains[3]. Therefore, microbiological identification and antimicrobial susceptibility testing (AST) must be conducted prior to antibiotic therapy[4].

In this study, we analyzed the distribution and antimicrobial susceptibility of the causative microorganisms isolated from patients diagnosed with IAIs between 2011 and 2021 at the Peking Union Medical College Hospital (PUMCH) in China. Our findings will prove beneficial for informing the implementation of evidence-based antimicrobial use, while providing guidance for the control of nosocomial infections.

MATERIALS AND METHODS

Strains

A total of 2,926 pathogenic strains were isolated from patients with IAIs at the PUMCH between 2011 and 2021. Most of the IAI specimens were collected during surgical interventions, including collection of paracentesis samples, as well as sampling of abscesses or intra-abdominal organs, such as the small intestine, colon, pancreas, stomach, and liver. When the same type of sample was collected from one patient at different time points, only the first sample was included in the analysis. However, if samples were collected from different body parts of the same patient, they were regarded as independent samples and all samples were included in analysis. Thus, there were cases where one patient corresponded to multiple samples. Additionally, if multiple causative microorganisms were identified in one specimen, all microorganisms were considered, and if the same pathogens were identified in different samples of one patient, they would not be counted twice. The Ethics Committee of PUMCH approved this study and waived the need for consent due to its retrospective design (Ethics Approval Number: JS-2581). All patient data were anonymized prior to analysis.

Identification and Antimicrobial Susceptibility Testing

Pathogenic bacteria and fungi were identified using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS, bioMérieux Inc., Marcy l'Etoile, France). AST was carried out using a VITEK 2 compact system (bioMérieux Inc.) and the Kirby-Bauer method. Interpretation of the AST results was based on the clinical breakpoints of M100-Ed31 of the Clinical and Laboratory Standards Institute (CLSI) 2021[5]. *Staphylococcus aureus* (ATCC 29213 and 25923), *Streptococcus pneumoniae* (ATCC 49619), *Escherichia coli* (ATCC 25922 and 35218), *Pseudomonas aeruginosa* (ATCC 27853), *Klebsiella pneumoniae* (ATCC 700603), *Enterobacter cloacae* (ATCC 70032), and *Candida albicans* (ATCC 90028) were used as quality controls. The breakpoint of tigecycline used in this study was obtained from the United States Food and Drug Administration (FDA).

Statistical Analysis

Data were analyzed using WHONET 5.6 (World Health Organization Collaborating Centre for Surveillance of Antimicrobial Resistance). Descriptive analysis was conducted, and demographic and clinical data were summarized using percentages and mean ± standard deviation. Differences in incidence between hospital and community isolates and differences in susceptibility rates were assessed using the chi-squared test. *P*-values < 0.05 were considered statistically significant.

Data Availability

All data are incorporated into the article and its online Supplementary Table S1, available in www.besjournal.com.

RESULTS

Patient Characteristics

In this study, 2,926 isolates from 1,679 patients (age 57.2 ± 16.9 years) hospitalized at PUMCH between 2011 and 2021 with microbiologically proven IAIs were identified. Among 1,679 patients, 953 (56.8%) were men and 726 were (43.2%) women. The general demographic characteristics of the study population are summarized in Table 1. Patients aged ≥ 50 years accounted for 72.7% of the total IAI patient population, while those ≥ 65 years accounted for 36.8%. Of the 1,679 patients with IAIs, 92.0% (1,545/1,679) were treated in four departments: internal medicine (*n* = 457, 27.2%), surgical (*n* = 309, 18.4%), ICU (*n* = 362, 21.6%), and emergency (*n* = 417, 24.8%). Patients from other departments accounted for only 8.0% of the total number of patients.

Cases in which a single microorganism was identified from one patient were designated monomicrobial infection; whereas those with multiple microorganisms identified from one patient were deemed polymicrobial infection. Of the 1,679 patients, 959 (57.1%) had monomicrobial infection, and 720 (42.9%) had polymicrobial infection. Of the 720 patients with polymicrobial infection, 49.7% (358/720) were co-infected with gram-positive and gram-negative bacteria, 15.7% (113/720) were co-infected with more than one species of gram-negative bacteria, and 11.0% (79/720) were co-infected with more than one species of gram-positive bacteria. In addition, 22.8% (164/720) of the patients were co-infected with fungi and bacteria, and the remaining 0.8% (6/720) were co-infected with both anaerobic and aerobic bacteria.

Table 1. Demographic characteristics of the 1,679 patients included in the study

Demographic	Number	Proportion (%)
Overall	1,679	
Sex		
Male	953	56.8
Female	726	43.2
Age (years)		
0–18	33	2.0
19–49	425	25.3
50–64	603	35.9
≥ 65	618	36.8
Location		
Internal medicine departments	457	27.2
Surgical departments	309	18.4
Intensive care unit	362	21.6
Emergency departments	417	24.8
Other departments	134	8.0

Distribution of the Causative Microorganisms from 2011 to 2021

Of the 2,926 strains, 1,440 (49.2%) were identified as gram-negative bacteria. The top ten gram-negative bacteria, namely *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *Acinetobacter baumannii*, *E. cloacae*, *Stenotrophomonas maltophilia*, *K. oxytoca*, *Citrobacter freundii*, *Proteus mirabilis*, and *K. aerogenes* accounted for 83.6% of all gram-negative bacterial strains (Table 2). A total of 1,194 gram-positive bacteria were isolated, accounting for 40.8% of all strains, of which *Enterococcus* sp. and *Staphylococcus* sp. were the most common (76.9% of all gram-positive bacterial strains). The top ten gram-positive bacteria were *Enterococcus faecium*, *Enterococcus faecalis*, *Staphylococcus epidermidis*, *S. aureus*, *Streptococcus anginosus*, *Staphylococcus haemolyticus*, *Enterococcus gallinarum*, *Staphylococcus hominis*, *Enterococcus avium*, and *Streptococcus viridans, alpha-hem* (Table 2). Additionally, 278 (9.5%) fungi were isolated from patients with IAIs, including *C. albicans*, *C. glabrata*, *C. tropicalis*, and *C. parapsilosis*. Fourteen anaerobic bacteria were also isolated, namely *Bacteroides fragilis* (*n* = 7), *Fusobacterium* (*n* = 3), *Staphylococcus saccharolyticus* (*n* = 3), and *Actinomyces odontolyticus* (*n* = 1).

Causative microorganisms were deemed community-associated (CA) or hospital-associated (HA) when samples were collected ≤ 48 h or > 48 h after patients were admitted to the hospital, respectively[6]. Of the 2,926 isolated strains, 1,042 caused CA IAIs, while 1,710 strains caused HA IAIs (657 strains were isolated from ICU). Of note, the CA/HA infection classification of 174 strains isolated in 2011 could not be conducted due to lack of data. The distribution of microorganisms differed between

Table 2. Distribution of the 2,926 strains of causative microorganisms isolated from patients with intra-abdominal infections

Causative microorganism	Total strains (*n*, %)	HA (*n*, %)	CA (*n*, %)	*P* value
Gram-negative bacteria	1,440 (49.2)	862 (50.4)	500 (48.0)	0.472
Escherichia coli	369 (12.6)	202 (11.8)	140 (13.4)	0.270
Klebsiella pneumoniae	289 (9.9)	167 (9.8)	106 (10.2)	0.754
Pseudomonas aeruginosa	157 (5.4)	107 (6.3)	45 (4.3)	0.041
Acinetobacter baumannii	130 (4.4)	86 (5.0)	39 (3.7)	0.133
Enterobacter cloacae	99 (3.4)	63 (3.7)	26 (2.5)	0.097
Stenotrophomonas maltophilia	51 (1.7)	32 (1.9)	14 (1.3)	0.303
Klebsiella oxytoca	34 (1.2)	20 (1.2)	13 (1.2)	0.857
Citrobacter freundii	26 (0.9)	16 (0.9)	10 (1.0)	0.950
Proteus mirabilis	26 (0.9)	17 (1.0)	6 (0.6)	0.246
Klebsiella aerogenes	23 (0.8)	15 (0.9)	7 (0.7)	0.560
Others	236 (8.1)	137 (8.0)	94 (9.0)	0.395
Gram-positive bacteria	1,194 (40.8)	654 (38.2)	461 (44.2)	0.044
Enterococcus faecium	265 (9.1)	170 (9.9)	80 (7.7)	0.067
Enterococcus faecalis	211 (7.2)	149 (8.7)	49 (4.7)	< 0.001
Staphylococcus epidermidis	137 (4.7)	65 (3.8)	65 (6.2)	0.005
Staphylococcus aureus	104 (3.6)	57 (3.3)	42 (4.0)	0.358
Streptococcus anginosus	43 (1.5)	27 (1.6)	15 (1.4)	0.776
Staphylococcus haemolyticus	41 (1.4)	14 (0.8)	25 (2.4)	< 0.001
Enterococcus gallinarum	35 (1.2)	19 (1.1)	9 (0.9)	0.535
Staphylococcus hominis ss. hominis	31 (1.1)	17 (1.0)	14 (1.3)	0.405
Enterococcus avium	28 (0.9)	15 (0.9)	11 (1.1)	0.642
Streptococcus viridans, alpha-hem.	23 (0.8)	9 (0.5)	11 (1.1)	0.116
Others	276 (9.2)	112 (6.5)	140 (13.4)	< 0.001
Fungi	278 (9.5)	185 (10.8)	77 (7.4)	0.007
Candida albicans	152 (5.2)	101 (5.9)	39 (3.7)	0.017
Candida glabrata	45 (1.5)	30 (1.8)	14 (1.3)	0.412
Candida tropicalis	41 (1.4)	29 (1.7)	11 (1.1)	0.179
Candida parapsilosis	16 (0.6)	8 (0.5)	6 (0.6)	0.701
Clavispora lusitaniae	4 (0.1)	4 (0.2)	0 (0.0)	0.119
Pichia kudriavzevii	4 (0.1)	4 (0.2)	0 (0.0)	0.119
Aspergillus fumigatus	3 (0.1)	3 (0.2)	0 (0.0)	0.177
Candida sp.	3 (0.1)	1 (0.1)	2 (0.2)	0.304
Others	10 (0.4)	5 (0.3)	5 (0.5)	0.430
Anaerobe	14 (0.5)	9 (0.5)	4 (0.4)	0.599

Note. HA, hospital acquired; CA, community acquired. The frequency comparison (difference in incidence between hospital and community isolates) was performed using the chi-squared test, and *P*-values < 0.05 were considered to be statistically significant.

CA and HA IAIs (Table 2). The CA IAIs corresponded with a relatively higher proportion of aerobic gram-positive bacteria ($P < 0.05$) and a lower proportion of fungi ($P < 0.01$) compared with HA IAIs. The most common pathogens causing HA IAIs were *E. coli* (11.8%), *E. faecium* (9.9%), *K. pneumoniae* (9.8%), *E. faecalis* (8.7%), and *P. aeruginosa* (6.3%). Meanwhile, the most common pathogens causing CA IAIs were *E. coli* (13.4%), *K. pneumoniae* (10.2%), *E. faecium* (7.7%), *S. epidermidis* (6.2%), and *E. faecalis* (4.7%).

We also analyzed the prevalence of the top ten pathogens isolated from patients with IAIs between 2011 and 2021 (Figure 1). Specifically, a decreasing trend in *E. coli* was observed (from 16.6% to 8.4%), whereas an increasing trend was observed in *K. pneumoniae* (from 7.6% to 12.6%). Moreover, the isolation rate of *E. faecium* gradually increased and surpassed that of *E. faecalis*, with *E. faecium* consequently becoming the most frequently isolated gram-positive pathogen. The prevalence of other pathogens did not significantly change between 2011 and 2021 and ranged from 1.2% to 8.9%.

Prevalence of the Top Ten Pathogens Isolated from ICU and Non-ICU Departments

We compared the prevalence of the top ten pathogens isolated from ICU and non-ICU departments (Figure 2) and found that the prevalence of *E. faecium* (11.9%, ICU; 8.2%, non-ICU), *C. albicans* (8.7%, ICU; 4.2%, non-ICU), *A. baumannii* (6.5%, ICU; 3.8%, non-ICU), *C. glabrata* (3.7%, ICU; 0.9%, non-ICU), and *C. tropicalis* (2.4%, ICU; 1.1%, non-ICU) in the ICU patient samples were higher than those in the non-ICU patient samples. The prevalence of *S. aureus* (1.7%, ICU; 4.1%, non-ICU), and *S. epidermidis* (1.5%, ICU; 5.6%, non-ICU) in the non-ICU patient samples were relatively higher than those in the ICU patient samples. However, *E. coli* (14.8%, ICU; 12.0%, non-ICU), *E. faecalis* (6.2%, ICU; 7.5%, non-ICU), *K. pneumoniae* (10.8%, ICU; 9.6%, non-ICU), *P. aeruginosa* (5.2%, ICU; 5.4%, non-ICU), and *E. cloacae* (2.9%, ICU; 3.5%, non-ICU) showed similar prevalence in the ICU and non-ICU patient samples (Supplementary Table S1 and Figure 2).

Among the top ten causative microorganisms isolated from patients hospitalized in the ICU (Figure 3A), *E. coli* was the most prevalent, with isolation rates ranging from 10.0% to 22.2%, followed by *E. faecium* (7.6%–20.0%), *K. pneumoniae* (5.1%–20.0%), *C. albicans* (1.9%–21.7%), *A. baumannii* (0%–13.5%), *E. faecalis* (1.9%–8.7%), *P. aeruginosa* (1.9%–8.6%), *C. glabrata* (1.5%–7.7%), *E. cloacae* (1.3%–5.1%), and *C. tropicalis* (0%–4.3%). Moreover, we observed a decreasing trend in the isolation of *E. coli* and *A. baumannii*, and an increasing trend in the isolation of *E. faecium*, *K. pneumoniae*, and *C. albicans*.

Similarly, *E. coli* was the most prevalent pathogen isolated from patients hospitalized in the non-ICU wards with isolation rates ranging from 7.6% to 16.2%, followed by *K. pneumoniae* (7.0%–12.5%), *E. faecium* (2.3%–10.7%), *E. faecalis* (5.6%–13.1%), *S. epidermidis* (3.6%–8.7%), *P. aeruginosa* (1.5%–10.5%), *C. albicans* (2.7%–6.8%), *S. aureus* (1.7%–5.6%), *A. baumannii* (2.0%–5.9%), and *E. cloacae* (0.7%–5.6%; Figure 3B). A significant decrease was also observed in the prevalence of

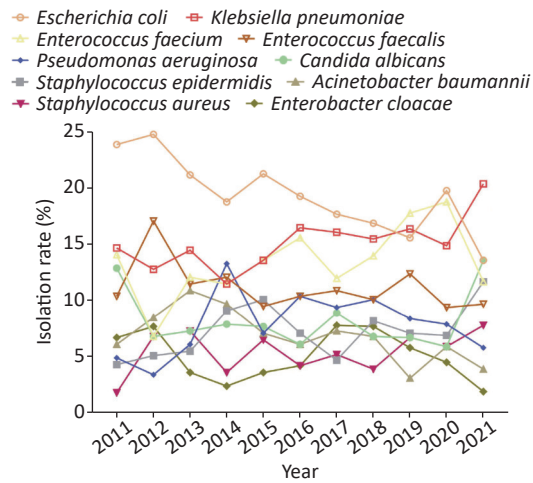


Figure 1. Trends in the prevalence of the top ten pathogens isolated from patients with intra-abdominal infections, 2011–2021.

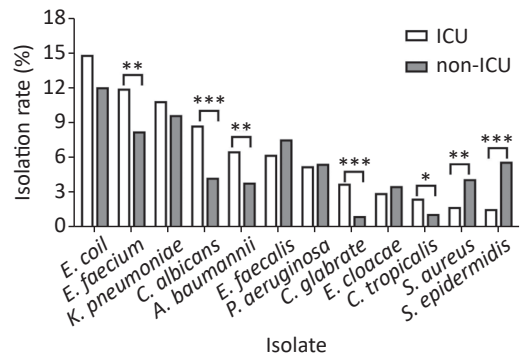


Figure 2. Comparison of the prevalence of the top ten pathogens isolated from intensive care unit (ICU) and non-ICU patients, 2011–2021. Data was analyzed with a chi-squared test. $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$.

E. coli in the non-ICU patient samples, similar to that observed in the ICU patient samples. Meanwhile, other pathogens isolated from non-ICU samples exhibited only minor fluctuations in prevalence from 2011 to 2021.

Antimicrobial Susceptibility of Clinically Important Gram-negative Pathogens (2011–2021)

The antimicrobial susceptibility profiles of the clinically important gram-negative pathogens are shown in Table 3. The resistance rate of *E. coli* to ampicillin was 75.0%, which was the highest among all tested antibiotics. The β-lactam/β-lactamase inhibitor piperacillin/tazobactam was more effective than ampicillin/sulbactam against both *E. coli* ($P < 0.001$) and *K. pneumoniae* ($P < 0.001$). The resistance rates of *E. coli* to piperacillin/tazobactam and ampicillin/sulbactam were 10.9% and 36.6%, respectively, and those of *K. pneumonia*e were 10.0% and 26.0%, respectively. With regard to quinolone antibiotics, *E. coli* and *K. pneumoniae* showed similar resistance to levofloxacin (55.2% and 18.7%, respectively) and ciprofloxacin (57.9% and 26.2%, respectively). Moreover, both *E. coli* and *K. pneumoniae* exhibited greater susceptibility to ceftazidime (third-generation cephalosporin) than that to cefazolin (first-generation cephalosporin; $P < 0.001$ and $P < 0.05$, respectively). Regarding the third-generation cephalosporins, *E. coli* and *K. pneumoniae* showed lower resistance to ceftazidime than that to ceftriaxone ($P < 0.001$) and cefotaxime ($P < 0.001$). With respect to carbapenems, both *E. coli* and *K. pneumoniae* exhibited similar resistance to ertapenem (4.4% and 8.5%, respectively), imipenem (2.2% and 7.7%, respectively), and meropenem (2.7% and 7.4%, respectively). Although *K. pneumoniae* showed greater resistance to carbapenems than that by *E. coli*, the resistance rates to most other drugs in the spectrum were higher in *E. coli* than that in *K. pneumonia*. The resistance rate of *E. coli* to aztreonam (38.9%) was higher than that to ceftazidime (28.1%; $P < 0.05$) but lower than those to cefotaxime (56.5%; $P < 0.01$) and ceftriaxone (51.4%; $P < 0.05$). In comparison, the resistance rate of *K. pneumoniae* was also lower to aztreonam (17.1%) than that to cefotaxime (27.9%; $P < 0.05$). Although *E. coli* and *K. pneumoniae* exhibited high resistance rates (55.2% and 25.5%, respectively) to trimethoprim/sulfamethoxazole, they showed high susceptiblility rates to cefoxitin, amikacin, and tigecycline.

The resistance rates of *E. cloacae* to piperacillin/tazobactam (23.5%), aztreonam (35.1%), ceftriaxone (39.4%), and ceftazidime (37.4%) were significantly higher than those of *K. pneumoniae* (10.0%, 17.1%, 22.1%, and 17.8%, respectively).

The resistance rates of *P. aeruginosa* to all tested antimicrobial agents were < 35%. The resistance rates of *P. aeruginosa* to levofloxacin (13.5%) and ciprofloxacin (11.6%) were lower than that observed in *Enterobacteriales*. With respect to carbapenems, *P. aeruginosa* exhibited higher resistance rates to imipenem (32.7%) than that to meropenem (20.4%).

The overall resistance rates of *A. baumanmii* to all antimicrobial agents were higher than those of *E. coli*, *K. pneumoniae*, *E. cloacae*, and *P. aeruginosa*. However, trimethoprim/sulfamethoxazole (56.9%), tigecycline (7.7%), and ampicillin/sulbactam (66.9%) exhibited relatively superior activity compared to that by other antimicrobial agents. Moreover, *A. baumanmii* exhibited similar resistance rates to levofloxacin and ciprofloxacin, and imipenem and

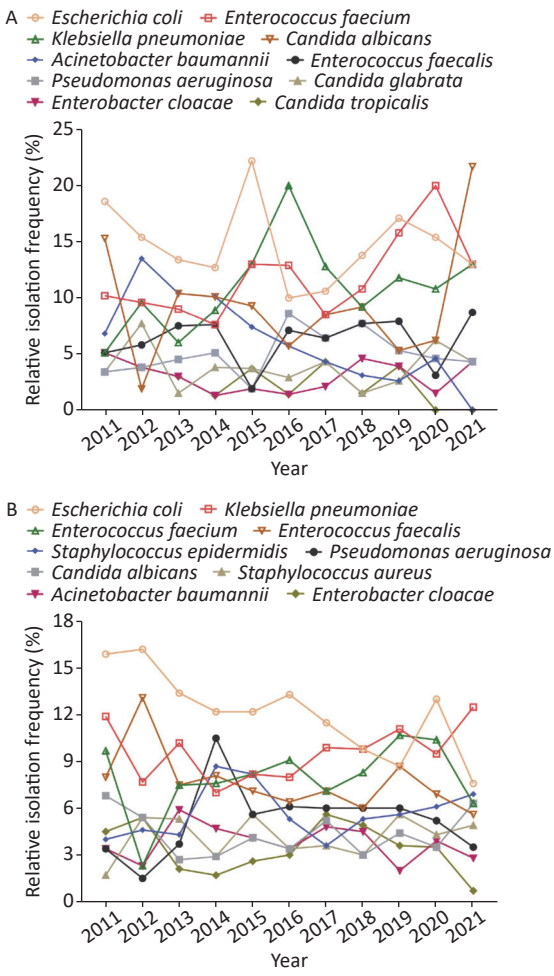


Figure 3. Trends in the prevalence of the top ten pathogens isolated from ICU (A) and non-ICU (B) patients, 2011–2021.

meropenem.

In addition, 173 (46.9%) *E. coli* and 34 (11.8%) *K. pneumoniae* isolates produced extended-spectrum β-lactamases (ESBLs). Importantly, most of the antimicrobial agents performed better against non-ESBL-producers than against ESBL-producers, with the exception of ertapenem, imipenem, and meropenem, for which the susceptibility of both ESBL-producers and non-ESBL-producers was similar (Figure 4). Amikacin, cefoxitin, and piperacillin/tazobactam also performed well against ESBL-producers, showing high susceptibility rates of 90.7%, 73.3%, and 79.8%, respectively, in *E. coli* and 85.3%, 77.8%, and 70.6%, respectively, in *K. pneumoniae* (Figure 4).

Antimicrobial Susceptibility of Clinically Important Gram-positive Pathogens

Vancomycin, teicoplanin, and linezolid were consistently effective against *E. faecium*, *E. faecalis*, *S. epidermidis*, and *S. aureus* (Figure 5). The susceptibility rates of *E. faecium* and *E. faecalis* to ciprofloxacin were < 50%, whereas those of *S. epidermidis* and *S. aureus* were < 65% (Figure 5). The resistance rates of *E. faecalis* to most antimicrobial agents were significantly lower than those of *E. faecium*, save for tetracycline, tigecycline, and linezolid. The resistance rates of *E. faecium* to vancomycin and linezolid were 3.4% and 0.4%, respectively, and those of *E. faecalis* were 0.5% and 2.4%, respectively. Ceftaroline, rifampin, and tigecycline showed strong activity against *S. epidermidis* and *S. aureus*. The resistance rates of *S. epidermidis* to most antimicrobial agents were higher than those of *S. aureus*, excluding tetracycline and clindamycin.

Changes in the Prevalence of Multidrug-resistant Bacteria between 2011 and 2021

A significant decrease was observed in the levels

Table 3. Antimicrobial susceptibility testing results of clinically important gram-negative pathogens isolated from patients with intra-abdominal infections

Drug	*E. coli* (*n* = 369)			*K. pneumoniae* (*n* = 289)			*E. cloacae* (*n* = 99)			*P. aeruginosa* (*n* = 157)			*A. baumanmii* (*n* = 130)		
	%R	%I	%S	%R	%I	%S	%R	%I	%S	%R	%I	%S	%R	%I	%S
Ampicillin	75.0	2.8	22.2	–	–	–	–	–	–	–	–	–	–	–	–
Ampicillin/sulbactam	36.6	18.7	44.7	26.0	6.6	67.3	–	–	–	–	–	–	66.9	2.4	30.6
Piperacillin/tazobactam	10.9	4.6	84.5	10.0	3.9	86.1	23.5	6.2	70.4	11.6	9.0	79.4	72.2	4.8	23.0
Aztreonam	38.9	3.9	57.2	17.1	2.1	80.7	35.1	2.1	62.9	21.2	15.9	62.9	–	–	–
Trimethofrim/sulfamethoxazole	55.2	1.4	43.4	25.5	2.5	72.0	8.2	2.0	89.8	–	–	–	56.9	6.0	37.1
Ciprofloxacin	57.9	11.8	30.3	26.2	12.1	61.7	15.2	13.1	70.7	11.6	3.9	84.5	70.5	0.8	28.7
Levofloxacin	55.2	13.1	31.7	18.7	9.2	72.1	10.5	9.5	80.0	13.5	8.4	78.1	68.8	2.3	28.9
Cefazolin	63.2	15.8	21.1	28.2	20.5	51.3	–	–	–	–	–	–	–	–	–
Ceftriaxone	51.4	0.8	47.8	22.1	1.4	76.5	39.4	2.1	58.5	–	–	–	72.7	25.3	2.0
Ceftazidime	28.1	8.6	63.3	17.8	0.7	81.5	37.4	3.0	59.6	13.4	3.4	83.2	70.4	0.8	28.8
Cefepime	31.0	14.3	54.7	16.0	3.9	80.1	13.5	16.7	69.8	9.7	9.0	81.3	68.2	2.3	29.5
Cefotaxime	56.5	0.8	42.7	27.9	2.2	69.8	42.6	4.9	52.5	–	–	–	76.8	21.2	2.0
Cefoxitin	15.8	7.2	77.0	16.0	1.1	83.0	–	–	–	–	–	–	–	–	–
Cefuroxime	54.0	2.0	44.0	24.6	2.9	72.4	–	–	–	–	–	–	–	–	–
Tigecycline	0.0	0.7	99.3	2.5	9.0	88.5	4.0	10.7	85.3	–	–	–	7.7	30.0	62.3
Gentamicin	45.5	0.8	53.7	14.6	0.4	85.0	11.2	1.0	87.8	9.6	0.7	89.6	71.2	1.9	26.9
Ertapenem	4.4	0.6	95.0	8.5	0.4	91.1	8.4	10.5	81.1	–	–	–	–	–	–
Imipenem	2.2	0.8	97.0	7.7	0.4	91.9	6.1	4.1	89.8	32.7	0.6	66.7	70.8	1.5	27.7
Meropenem	2.7	0.5	96.7	7.4	0.4	92.2	5.2	0.0	94.8	20.4	7.9	71.7	70.1	0.8	29.1
Amikacin	4.9	1.9	93.2	5.6	0.4	94.0	2.0	2.0	95.9	6.5	0.0	93.5	64.0	0.8	35.2

Note. R: resistant; S: susceptible; I: intermediate.

of ESBL-producing *E. coli* (from 76.9% to 14.3%) and *K. pneumoniae* (from 45.8% to 4.8%) between 2011 and 2021 (Figure 6A). Moreover, the prevalence of carbapenem-resistant *E. coli* (Figure 6B) and *K. pneumoniae* (Figure 6C) fluctuated annually over the 11 years. Specifically, carbapenem-resistant *E. coli* was less common than carbapenem-resistant *K. pneumoniae*, with a slightly higher prevalence of ertapenem-resistant isolates in several years compared with imipenem- and meropenem-resistant isolates. Similarly, the prevalence of vancomycin-resistant *E. faecium* and *E. faecalis* fluctuated between 2011 and 2021 (Figure 6D); however, vancomycin-resistant *E. faecium* was more common than vancomycin-resistant *E. faecalis*. Due to insufficient data, changes in the prevalence of methicillin-resistant *S. aureus* (MRSA) and *S. epidermidis* (MRSE) were not assessed.

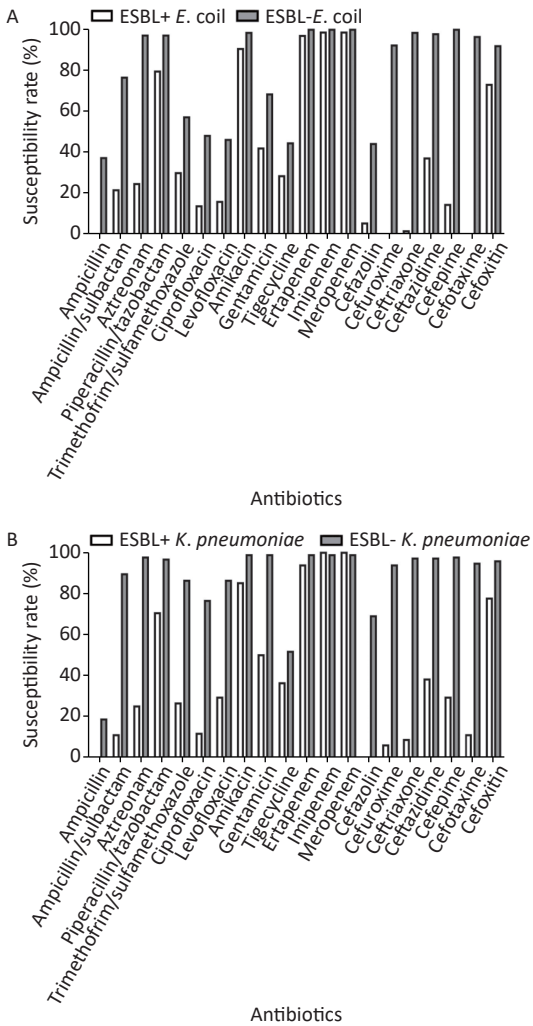


Figure 4. Antimicrobial susceptibility of extended-spectrum β-lactamase (ESBL)-producing and non-ESBL-producing *Escherichia coli* (A) and *Klebsiella pneumoniae* (B).

Fungal Resistance Rates

A total of 278 fungal strains were isolated, 152 of which were *C. albicans*, which exhibited high susceptibility to all tested antifungal drugs. Fluconazole and voriconazole showed the susceptibility rate of 99.3%.

DISCUSSION

IAIs are the second most common cause of infections in the ICU with a mortality rate higher than that of other infections[7]. Although most patients are treated with antibiotics (98.1%), only two-thirds undergo microbial cultures, indicating

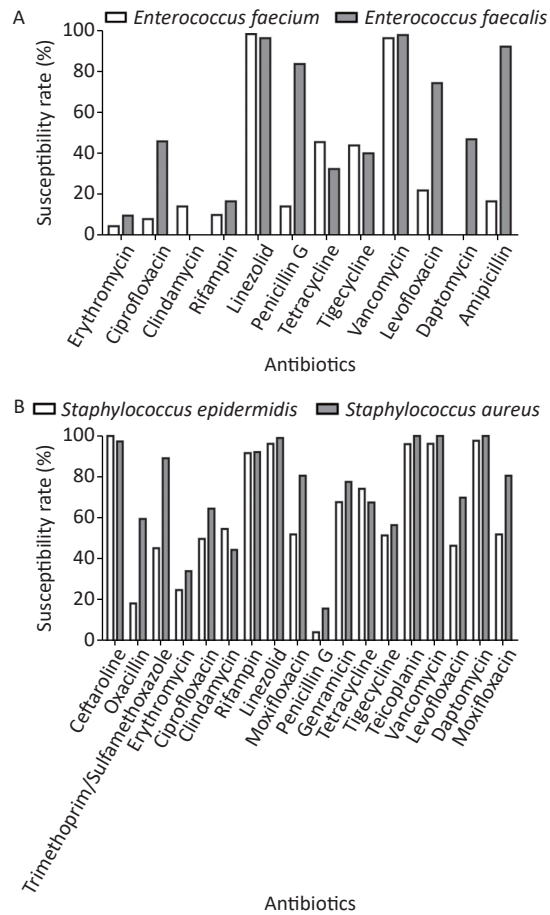


Figure 5. Antimicrobial susceptibility of clinically important gram-positive pathogens. (A) *Enterococcus faecium* and *Enterococcus faecalis*, (B) *Staphylococcus epidermidis* and *Staphylococcus aureus*.

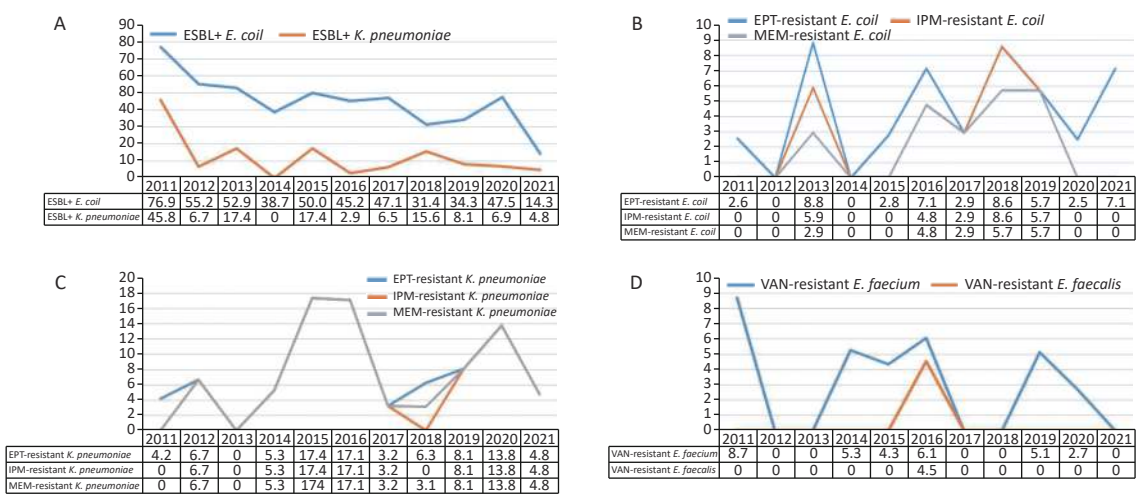
that empirical antimicrobial treatments are commonly applied in clinical practice, thus, highlighting the importance of local AST results. The current study explored the relative frequency and trends in antimicrobial susceptibility of causative microorganisms isolated from 1,679 patients with IAIs at the PUMCH from 2011 to 2021. A total of 2,926 strains were detected.

The distribution of pathogens differs between countries and regions[8-10], and the initial selection of anti-infection schemes differs among doctors. The 2007–2016 national multi-center study of the Chinese Antimicrobial Resistance Surveillance of Nosocomial Infections (CARES), which included 2,756 patients with IAIs, reported that gram-negative and gram-positive bacteria accounted for 70.8% and 29.2% of all isolates, respectively[11]. In contrast, as a single-center study, the proportion of gram-negative and gram-positive bacteria in our study was similar (49.3% *vs.* 40.7%). Additionally, the most common pathogens identified in the CARES study were *E. coli* (33.4%), *K. pneumoniae* (10.8%), and *E. faecium* (10.7%)[11], similar to that found in the current study. Meanwhile, according to the Study for Monitoring Antimicrobial Resistance Trends (SMART) in North America from 2005 to 2010, the most frequently isolated gram-negative pathogens from IAIs were *E. coli*, *K. pneumoniae*, and *P. aeruginosa*[12].

Polymicrobial infections are common in IAIs, particularly those involving co-infection with gram-positive and gram-negative bacteria. In the current study, some patients were found to be co-infected with aerobic bacteria, anaerobic bacteria, or fungi. Moreover, certain differences were noted in pathogen distribution between HA IAIs and CA IAIs. For example, *C. albicans* was more prevalent in HA IAIs, while *S. epidermidis* was more commonly isolated from CA IAIs. Additionally, the proportion of gram-positive bacteria was relatively higher in CA IAIs than that in HA IAIs. Nevertheless, *Enterobacteriales* remain the most prevalent bacteria in all IAIs, of which *E. coli* was the most common species.

Guidelines reported by the World Society of Emergency Surgery (WSES) suggest that IAIs should be managed with either single or multiple antibiotic regimens. Beta-lactam/beta-lactamase inhibitor combinations, including amoxicillin/clavulanate, ticarcillin/clavulanate, and piperacillin/tazobactam, have exhibited *in vitro* activity against gram-positive, gram-negative, and anaerobic bacteria[13]. Indeed, most isolates of *E. coli* and other *Enterobacterales* remain susceptible to third-generation cephalosporins. In the current study, the prevalence of the top ten pathogens isolated from patients with IAIs from 2011 to 2021 revealed a significant decrease in *E. coli* and significant increase in *K. pneumoniae*. Meanwhile, the isolation of *E. faecium* gradually increased, ultimately becoming the most common gram-positive pathogen. These trends may prove detrimental to current infection control measures as *K. pneumoniae* and *E. faecium* are reportedly more resistant to multiple antimicrobial agents than other *Enterobacterales* and gram-positive bacteria.

The current drug resistance levels in China



	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
ESBL+ *E. coil*	76.9	55.2	52.9	38.7	50.0	45.2	47.1	31.4	34.3	47.5	14.3
ESBL+ *K. pneumoniae*	45.8	6.7	17.4	0	17.4	2.9	6.5	15.6	8.1	6.9	4.8

	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
EPT-resistant *E. coil*	2.6	0	8.8	0	2.8	7.1	2.9	8.6	5.7	2.5	7.1
IPM-resistant *E. coil*	0	0	5.9	0	0	4.8	2.9	8.6	5.7	0	0
MEM-resistant *E. coil*	0	0	2.9	0	0	4.8	2.9	5.7	5.7	0	0

	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
EPT-resistant *K. pneumoniae*	4.2	6.7	0	5.3	17.4	17.1	3.2	6.3	8.1	13.8	4.8
IPM-resistant *K. pneumoniae*	0	6.7	0	5.3	17.4	17.1	3.2	0	8.1	13.8	4.8
MEM-resistant *K. pneumoniae*	0	6.7	0	5.3	174	17.1	3.2	3.1	8.1	13.8	4.8

	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
VAN-resistant *E. faecium*	8.7	0	0	5.3	4.3	6.1	0	0	5.1	2.7	0
VAN-resistant *E. faecalis*	0	0	0	0	0	4.5	0	0	0	0	0

Figure 6. Changes in the prevalence of multidrug-resistant bacteria from 2011 to 2021. ESBL+ *Escherichia coli* and ESBL+ *Klebsiella pneumoniae* (A), carbapenems-resistant *E. coli* (B) and *K. pneumoniae* (C), vancomycin-resistant *Enterococcus faecium* and *E. faecalis* (D), 2011–2021.

require urgent attention and development of appropriate mitigating strategies, particularly as the prevalence of ESBL-producing isolates is significantly higher than that reported in other regions[14]. And *P. aeruginosa* and *A. baumannii* exhibited multi-drug resistance, with the prevalence in *A. baumannii* found to be significantly higher than that in *P. aeruginosa*. Although the China Antimicrobial Surveillance Network (CHINET) has reported that the prevalence of MRSA has significantly decreased in China from > 50% to ~30%[15,16], the isolation of carbapenem-resistant *Enterobacteriales* has rapidly increased, becoming a refractory problem.

Given that ESBL-encoding genes are encoded on plasmids, drug resistance can be transmitted through transformation, transduction, or translocation. Indeed, ESBL-producing bacteria often carry multiple drug-resistant genes[17]. The present study showed that the prevalence of ESBL-producing *E. coli* and *K. pneumoniae* was 46.9% and 11.8%, respectively. Moreover, ESBL-producing *Enterobacterales* isolates had higher drug resistance rates than non-ESBL-producing isolates. The resistance rates to gentamicin, ampicillin/sulbactam, trimethoprim/sulfamethoxazole, aztreonam, and cephalosporin were > 50.0% in ESBL-producing *K. pneumonia*. Moreover, the resistance rates to cephalosporins, were > 50% in ESBL-producing *E. coli*. In contrast, carbapenems had the highest susceptibility against *Enterobacteriales*, with resistance rates to imipenem, meropenem, and ertapenem in *E. coli* and *K. pneumonia* being < 10.0%. Considering that both bacterial species exhibited higher susceptibility to piperacillin/ tazobactam and amikacin, these antibiotics may prove to be effective treatment options.

P. aeruginosa and *A. baumannii* are the most commonly detected non-fermentative bacteria, however, *P. aeruginosa* is more virulent and is more prone to accruing resistance. In the current study, *P. aeruginosa* exhibited > 90% susceptibility to amikacin, while its resistance rates to imipenem and meropenem were 32.7% and 20.4%, respectively. Pakyz et al. reported that nosocomial infections with *P. aeruginosa* have a significant linear relationship with carbapenem usage, and restricted carbapenem usage will reduce the occurrence of drug resistance[18]. As for the treatment of infections caused by *P. aeruginosa*, early effective antimicrobial therapy is crucial. The combination of antimicrobial agents may act synergistically to reduce the occurrence of drug resistance.

Nosocomial infections with *A. baumannii* and MRSA are most commonly caused by iatrogenic factors (including medical personnel, medical apparatus, and instruments)[19]. In the current study, the resistance rates of *A. baumannii* to gentamicin, piperacillin/tazobactam and carbapenem were determined to be > 70.0%. Therefore, treatment of *A. baumannii* infections should be performed according to the results of AST.

No vancomycin- or daptomycin-resistant *Staphylococcus* sp. was isolated in this study, indicating that both of these drugs remain effective alternatives for treating serious *Staphylococcus* infections. However, *Staphylococcus* sp. had a resistance rate of > 60% compared with traditional antibacterial drugs, such as penicillin and erythromycin. Additionally, the resistance rates of *E. faecium* and *E. faecalis* to vancomycin and linezolid were < 4%, thus, highlighting their therapeutic efficacy.

Certain limitations were noted in the current study. First, although data were collected over an 11-year period, the number of identified causative microorganisms was small. Second, this was a single-center study, therefore, the findings may not be applicable to other regions.

CONCLUSION

Our data demonstrates that the antimicrobial resistance patterns of causative microorganisms in our hospital is constantly evolving. To ensure the safety and effectiveness of pathogen-specific antimicrobial treatment, it is necessary to continually update the antimicrobial susceptibility spectrum data, monitor isolated bacteria, and minimize the use of ineffective antimicrobial agents in the treatment of IAIs.

CONFLICTS OF INTEREST

None declared.

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CONTRIBUTORS

DING Rui designed the study, conducted the study, analyzed the data, and wrote the manuscript. MA Rui Rui conducted the study, contributed to the acquisition of data, and approved the final

manuscript. LIU Ya Li helped design the study, has seen the original study data, reviewed the analysis of the data, and approved the final manuscript. ZHAO Ying, GUO Li Na, DOU Hong Tao, SUN Hong Li, LIU Wen Jing, ZHANG Li, WANG Yao, and LI Ding Ding contributed to the acquisition of data, analysis and interpretation, and approved the final manuscript. YI Qiao Lian, and XU Ying Chun designed the study and approved the final manuscript.

DISCLOSURES

The authors have no conflicts of interest to disclose.

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REFERENCES

1. Menichetti F, Sganga G. Definition and classification of intra-abdominal infections. J Chemother, 2009; 21 Suppl 1, 3–4.
2. Sudhaharan S, Kanne P, Vemu L, et al. Bacteriological profile of intra-abdominal infections in a tertiary care hospital. Iran J Microbiol, 2018; 10, 208–14.
3. Armstrong C. Updated guideline on diagnosis and treatment of intra-abdominal infections. Am Fam Physician, 2010; 82, 694–709.
4. Sartelli M, Catena F, Ansaloni L, et al. Complicated intra-abdominal infections in a worldwide context: an observational prospective study (CIAOW Study). World J Emerg Surg, 2013; 8, 1.
5. Humphries R, Bobenchik AM, Hindler JA, et al. Overview of changes to the clinical and laboratory standards institute performance standards for antimicrobial susceptibility testing, M100, 31st Edition. J Clin Microbiol, 2021; 59, e0021321.
6. Zhang S, Huang WX. Epidemiological study of community- and hospital-acquired intraabdominal infections. Chin J Traumatol, 2015; 18, 84–9.
7. De Waele J, Lipman J, Sakr Y, et al. Abdominal infections in the intensive care unit: characteristics, treatment and determinants of outcome. BMC Infect Dis, 2014; 14, 420.
8. Shree N, Arora BS, Mohil RS, et al. Bacterial profile and patterns of antimicrobial drug resistance in intra-abdominal infections: current experience in a teaching hospital. Indian J Pathol Microbiol, 2013; 56, 388–92.
9. Zhang SY, Ren LL, Li YS, et al. Bacteriology and drug susceptibility analysis of pus from patients with severe intra-abdominal infection induced by abdominal trauma. Exp Ther Med, 2014; 7, 1427–31.
10. Zhao CJ, Chen HB, Wang H, et al. Analysis of pathogen spectrum and resistance of clinical common organisms causing bloodstream infections, hospital-acquired pneumonia and intra-abdominal infections from thirteen teaching hospitals in 2013. Natl Med J China, 2015; 95, 1739–46. (In Chinese)
11. Zhang JG, Zhao CJ, Chen HB, et al. A multicenter epidemiology study on the risk factors and clinical outcomes of nosocomial intra-abdominal infections in China: results from the Chinese Antimicrobial Resistance Surveillance of Nosocomial Infections (CARES) 2007-2016. Infect Drug Resist, 2018; 11, 2311–9.
12. Babinchak T, Badal R, Hoban D, et al. Trends in susceptibility of selected gram-negative bacilli isolated from intra-abdominal infections in North America: SMART 2005-2010. Diagn Microbiol Infect Dis, 2013; 76, 379–81.
13. Sartelli M, Coccolini F, Kluger Y, et al. WSES/GAIS/SIS-E/WSIS/AAST global clinical pathways for patients with intra-abdominal infections. World J Emerg Surg, 2021; 16, 49.
14. Zhang H, Yang QW, Liao K, et al. Antimicrobial Susceptibilities of aerobic and facultative gram-negative bacilli from intra-abdominal infections in patients from seven regions in China in 2012 and 2013. Antimicrob Agents Chemother, 2016; 60, 245–51.
15. Hu FP, Guo Y, Zhu DM, et al. Resistance trends among clinical isolates in China reported from CHINET surveillance of bacterial resistance, 2005-2014. Clin Microbiol Infect, 2016; 22 Suppl 1, S9-14.
16. Hu FP, Zhu DM, Wang F, et al. Current status and trends of antibacterial resistance in China. Clin Infect Dis, 2018; 67, S128–34.
17. Zahar JR, Lesprit P. Management of multidrug resistant bacterial endemic. Med Mal Infect, 2014; 44, 405–11.
18. Pakyz AL, Oinonen M, Polk RE. Relationship of carbapenem restriction in 22 university teaching hospitals to carbapenem use and carbapenem-resistant Pseudomonas aeruginosa. Antimicrob Agents Chemother, 2009; 53, 1983–6.
19. Lima AL, Oliveira PR, Paula AP. Acinetobacter infection. N Engl J Med, 2008; 358, 2846.