RESEARCH ARTICLE

Comparative study on the changes of bacterial species and severity of antimicrobial resistance during 13 years

Huili Zhang[1☯]*, **Kairui Zhou**[1☯], **Xinglong He**[2], **Xin Yuan**[1]

1 Department of Pharmacy, The Second People's Hospital of Xinxiang, Xinxiang, Henan, China, **2** Clinical Laboratory, The Second People's Hospital of Xinxiang, Xinxiang, Henan, China

☯ These authors contributed equally to this work.

* zhlyzy218@163.com

Abstract

Background

With the widespread use of broad-spectrum antibiotics, the problem of bacterial resistance has become a global crisis. To monitor bacterial resistance in our hospital, the distribution of specimens, the detection of pathogens and their drug resistance from July 2005 to June 2007 (13 years ago) and July 2018 to June 2020 were compared and analyzed.

Methods

Ordinary specimens (such as sputum, urine, feces, and secretion) were inoculated in blood AGAR media, MacConkey medium, chocolate medium, double SS medium and selective culture medium. Blood, cerebrospinal fluid, pleural effusion, joint cavity effusion and other sterile body fluid samples were inoculated in aerobic and anaerobic blood culture flasks. Automatic microbial identification, drug sensitivity analysis and mass spectrometry analysis were used to determine their drug sensitivity.

Results

Compared with the results obtained 13 years ago, the number of specimens submitted for inspection in the past two years has increased significantly, exhibiting a growth rate of 283%. The changes in the pathogen species were obvious. Gram-positive cocci were the dominant bacteria 13 years ago, and Gram-negative bacilli were the dominant bacteria in the past two years. In addition, the resistance of several major Gram-negative bacilli to piperacillin/tazobactam, cefoperazone/sulbactam, meropenem and imipenem all showed an increasing trend.

Conclusion

The variety of pathogenic bacteria in our hospital has changed significantly in the past two years compared with that 13 years ago, and the clinical isolates of Gram-negative bacilli have increased significantly compared with Gram-positive cocci. In the clinical treatment of

anti-infective diseases, antimicrobial agents should be selected according to the bacterial
distribution characteristics and drug resistance in each hospital.

Introduction

The incidence of microbial infections has been increasing in the past several decades, and anti-
bacterial drugs are widely used clinically as the first-line therapy to inhibit the growth and
reproduction of bacteria; this, in turn, has led to the emergence of specific drugs and multidrug
resistance among various strains of microorganisms [1]. The problem of bacterial resistance
has become a global crisis; the World Health Organization (WHO) published the first global
antibiotic resistance report based on data from 114 countries around the world in 2014 [2]. In
2020, the WHO released an activity with the theme of "Unite to Protect Antimicrobial Drugs"
to raise the public and medical staff's awareness of the drug resistance crisis through extensive
publicity on the rational use of antimicrobial drugs. Resistance has important implications for
clinicians and patients due to a higher risk of inadequate treatment, an increased length of hos-
pital stay, and additional healthcare costs [3].

Among clinical isolates, the ratio of Gram-negative bacilli to Gram-positive cocci is approx-
imately 7 to 3 according to the CHINET surveillance from 2005 to 2017 and the CARSS sur-
veillance in 2016 [4, 5]. Multidrug-resistant Gram-negative bacterial infections are considered
one of the major threats to global health. They are the leading causes of nosocomial infections
around the world [6–8]. This makes it particularly important to monitor the distribution of
clinical isolates and the changes in drug resistance.

Among Gram-positive cocci and Gram-negative bacilli with high clinical isolation rate,
Staphylococcus aureus mainly produces three kinds of toxins (Pore-forming toxins, Exfolia-
tive toxins, Superantigens) to degrade host cells and weaken the body's response, thus caus-
ing skin and soft tissue infections and lung infections [9]. The virulence factors (toxins or
biofilm) of Gram-negative bacteria such as *Escherichia coli*, *Acinetobacter baumannii*, and *K.
pneumonia* can participate in bacterial adhesion, invasion, and escape from the host's
immune defense, causing the destruction of host cells or tissues, thus cause lung infection,
bloodstream infection, abdominal infection and urinary tract infection [10, 11]. These bacte-
ria can lead to multidrug resistance through hydrolase production, efflux pump overexpres-
sion or membrane pore protein mutation [12, 13]. Multidrug resistance has been increased
globally that is considered a public health threat. Several previous studies revealed the emer-
gence of multidrug-resistant bacterial pathogens from different origins especially fish, birds,
animals, and food chains which may be transmitted to human consumers resulting in severe
illness [14–16].

Here, the source and species of pathogen specimens, the number of detected pathogens and
the change of drug resistance in our hospital from July 2018 to June 2020 and from July 2005
to June 2007 were statistically analyzed. It provides a theoretical basis for clinicians to choose
antibacterial drugs, so as to reduce the unreasonable use of antibacterial drugs and effectively
control the bacterial drug resistance in our hospital.

Materials and methods

Source of specimens

The research specimens were from the sterile body fluid samples (blood, cerebrospinal fluid,
pleural effusion, joint cavity effusion, etc.) and common specimens (sputum, urine, feces,

secretions, etc.) which sent by all clinical departments of our hospital to the microbiology room for bacterial culture from July 2018 to June 2020 and from July 2005 to June 2007. The examination was submitted in accordance with the normal procedures of clinical examination, and the collection and use of relevant test results and data were approved by the Medical Ethics Committee of our hospital.

Source of bacteria

The pathogenic bacteria detection results from our hospital's microbiology laboratory from July 2018 to June 2020 were selected to perform statistics and to compare and analyze the data from July 2005 to June 2007 [17].

Source of medium and reagent plate

The bacterial culture plate containing different media was purchased from Antu Bio-Engineering Co., LTD, Zhengzhou, China, and the random in vitro diagnostic reagent plate of the bacterial determination system was purchased from Deere Bio-Engineering Co., LTD, Zhuhai, China.

Isolation and identification of bacterial pathogens

Sterile body fluid specimens, such as blood, cerebrospinal fluid, pleural and ascites fluid, and joint cavity effusions, were inoculated into aerobic and anaerobic blood culture bottles and placed in a BD9120 automatic blood incubator. The blood bottle specimens were considered positive according to the normal specimen process. Various common specimens were inoculated on blood agar medium, MacConkey medium, chocolate medium, double SS medium, and other basic and selective media in a 35~37˚C, 5~10% CO_2 incubator for 18~24 h. Separately, according to the routine methods, Gram stain smears, oxidase tests, and thiolase tests were applied, and then we used a DL-96II automatic microorganism identification and drug sensitivity analyzer(the specimens from 2005 to 2007 used the Black Horse Bact-IST automatic microbial analysis system) and a VITEK MS mass spectrometer and proceeded according to the operating instructions. The bacteria were identified according to the biochemical reaction provided by the random in vitro diagnostic reagent plate of the bacterial determination system, and the semi-quantitative analysis of the MIC of antibacterial agents contained in the sensitive cards was performed. The results were analyzed according to the Clinical and Laboratory Standards Institute (CLSI) 2018 definitions [18].

Statistical analysis

Statistics on the source and number of pathogenic bacteria specimens and the type, number, and drug resistance of the pathogenic bacteria detected in the pathogenic microorganism laboratory from July 2018 to June 2020, a comprehensive analysis of the characteristics of the pathogenic bacteria detected in our hospital and the status of their antimicrobial resistance, and a comparative analysis with the data from July 2005 to June 2007 were performed to learn about the sources of pathogenic bacteria specimens, the changes in species over time, the number of pathogens detected and the changes in drug resistance over time in order to provide a reference for the rational application of antimicrobial drugs in the hospital. Office 2016 software was used to perform statistical analysis and to draw charts about the sources of the specimens, types, and numbers of pathogens.

Table 1. The distribution of specimen types before and after 13 years.

Specimen source	Number of bacteria 13 years ago	Percentage %	Number of bacteria at present	Percentage %	Rate of increase %
Sputum	1296	37.3	5450	41.3	320.5
Blood	956	27.8	4374	33.1	357.5
Urine	240	7.0	1066	8.1	344.2
Secretions	948	27.5	1676	12.7	76.8
Feces	--	--	153	1.2	--
Others	--	--	483	3.7	--
Total	3440	100	13202	100	283.8

Results

Distribution of the specimen types to be examined

Our hospital sent a total of 13,202 pathogenic bacteria cultures from July 2018 to June 2020, an increase of 283.8% compared with 13 years ago. The samples were still mainly sputum 41.3% (5,450/13202), blood 33.1% (4374/13202), secretions 12.7% (1676/13202) and urine 8.1% (883/13202) (Table 1), similar to the distribution of specimen types thirteen years ago.

Species and quantity of pathogenic bacteria

From July 2018 to June 2020, 2956 strains of pathogenic bacteria were cultured in our hospital, and 1616 strains were cultured 13 years ago, an increase of 82.92% over the previous period. The types and number of pathogenic bacteria detected are shown in Table 2. As shown in the table, thirteen years ago, the pathogen was identified in the majority of the Gram-positive cocci. The overall detection rate was 39.10% (*Staphylococcus aureus* 31.40%), and the Gram-negative bacilli overall detection rate was 32.50% (*Escherichia coli* 12.90%, *Pseudomonas aeruginosa* 11.40%, *Klebsiella pneumoniae* 8.20%). The detection rate of the *fungi* was also high, accounting for 18.20% of the total detected pathogens. From September 2018 to June 2020, Gram-negative bacilli were dominant, with a total detection rate of 62.86%, among which *K. Pneumoniae* was 22.83%, *P. Aeruginosa* was 17.66%, and *E. Coli* was 13.44%. The total detection rate of Gram-positive cocci was 19.35%, of which the detection rates of *S. Aureus* and *Coagulase-negative staphylococcus (CoNS)* were significantly lower than those 13 years ago, accounting for 9.91% and 3.38% of the total detected pathogens, respectively. The detection rate of fungi was also significantly lower than before.

Table 2. The comparison of types and quantities of pathogenic bacteria before and after 13 years.

Species	Thirteen years ago	Percentage %	At the current time	Percentage %	The rate of change%
Staphylococcus aureus	508	31.4	293	9.91	-42.32
Coagulase negative staphylococcus	124	7.7	100	3.38	-19.35
Streptococcus	--	--	51	1.73	--
Enterococcus	--	--	128	4.33	--
Pseudomonas aeruginosa	184	11.4	522	17.66	183.70
Klebsiella pneumoniae	132	8.2	675	22.83	411.36
Escherichia coli	208	12.9	397	13.44	90.86
Acinetobacter baumannii	--	--	264	8.93	--
Fungus	304	18.8	134	4.53	-55.92
Other bacteria	156	9.6	392	13.26	151.28
Total	1616	100	2956	100	82.92

Table 3. The change in the resistance rate (%) of the main Gram-negative bacilli to common antibacterial drugs before and after 13 years.

Antibacterial drugs	*Pseudomonas aeruginosa*		*Klebsiella pneumoniae*		*Escherichia coli*		*Acinetobacter baumannii*	
	before	after	before	after	before	after	before	after
Ceftazidime	16.9	48.76	59.5	45.47	30.2	33.99	--	77.02
Aztreonam	32.5	42.56	65.8	--	33.3	--	--	--
Cefoperazone	62.3	--	76	--	70	--	--	--
Cefoperazone/Sulbactam	8.2	45.64	6.3	36.21	3.5	12.53	--	57.76
Cefotaxime	40.3	--	65.8	--	77.8	--	--	--
Cefepime	19.5	42.98	25.2	30.86	36.5	32.34	--	68.32
Imipenem	15.6	54.96	0	17.49	0	3.3	--	70.81
Meropenem	18.2	42.98	0	21.4	0	2.97	--	72.67
Piperacillin	54.5	53.72	69.4	--	71.4	--	--	--
Piperacillin/tazobactam	7.8	45.04	9.9	37.65	6.3	10.56	--	75.61
Amoxicillin Clavulanate potassium	--	--	80.2	--	79.4	--	--	--
Ampicillin	--	--	90.1	--	88.9	87.13	--	--
Ampicillin/Sulbactam	--	--	79.3	55.97	84.1	39.6	--	78.26
Ceftriaxone	--	--	74.5	53.5	85.7	59.74	--	81.37
Cefuroxime	--	--	82.9	56.58	87.3	63.04	--	--
Cefazolin	--	--	87.4	58.64	87.3	65.35	--	--
Polymyxin B	--	3.31	--	--	--	--	--	4.35
Amikacin	36.4	23.55	65.8	26.75	30.2	8.25	--	73.91
Gentamicin	81.8	42.15	80.2	44.44	68.3	45.87	--	80.75
Tobramycin	83.1	49.17	--	--	--	--	--	--
Netilmicin	77.9	--	70	--	55	--	--	--
Ciprofloxacin	66.2	44.21	51.4	47.12	81	65.68	--	78.26
Norfloxacin	67.5	43.15	55	--	85.7	--	--	--
Levofloxacin	49.4	45.45	53.9	42.39	80.4	62.71	--	71.43
Trimethoprim/sulfamethoxazole	100	--	57.5	53.29	82.5	69.31	--	73.91
Chloramphenicol	66.2	--	--	--	--	28.71	--	--
Macrodantin	--	--	45.9	23.25	22.2	4.62	--	--

Analysis of bacterial resistance

The drug resistance rates of the main Gram-negative bacilli and Gram-positive cocci detected in the microbiology laboratory of our hospital against common antibacterial drugs are shown in Tables 3 and 4. Resistance analysis was performed on the first four Gram-negative bacilli (*K. Pneumoniae*, *P. Aeruginosa*, *E. Coli*, *Acinetobacter baumannii*) and two Gram-positive cocci (*S. Aureus* and *CoNS*).

Klebsiella pneumoniae. Compared with 13 years ago, the resistance rate of *K. Pneumoniae* to piperacillin/tazobactam, cefoperazone/sulbactam, cefepime, meropenem, and imipenem has increased significantly. Among them, the resistance rates to meropenem and imipenem have increased from zero 13 years ago to 21.4% and 17.94% now; The resistance rate to cefoperazone/sulbactam, piperacillin/tazobactam and cefepime increased from the previous 6.3%, 9.9%, 25.2% to 36.21%, 37.65%, and 30.86%, respectively, and the rapid increase of resistance indicates that the resistance of *K. Pneumoniae* to antibiotics should not be ignored. The resistance rate to aminoglycosides (gentamicin, amikacin) and the first and second generation cephalosporins has declined.

Pseudomonas aeruginosa. Compared with 13 years ago, the drug resistance rates of *P. Aeruginosa* to most antibacterial drugs were significantly increased, among which the drug

Table 4. The comparison of changes in the resistance rate (%) of the main G+ cocci to commonly used antibacterial drugs approximately 13 years ago.

Antibacterial drugs	Staphylococcus aureus		Coagulase negative staphylococcus	
	before	**after**	**before**	**after**
Azithromycin	45	74.16	80	78.95
Cefoxitin	--	25.85	--	6.6
Chloramphenicol	--	11	--	18.42
Clindamycin	37.5	72.25	--	60.23
Clarithromycin	45	75.12	80	77.63
Erythrocin	50	76.08	80	78.95
Macrodantin	75	2.87	80	13.16
Gentamicin	50	30.62	30	38.16
Levofloxacin	37.5	32.54	60	59.21
Linezolid	--	0	60	0
Moxifloxacin	--	30.62	--	48.68
Norfloxacin	62	37.32	--	43.16
Oxacillin	0	25.84	70	35.53
Penicillin	87.5	90.91	0	86.84
Rifampicin	--	13.4	97.9	15.79
Trimethoprim/sulfamethoxazole	75.5	40.19	--	55.26
Teicoplanin	--	0	80	0
Tetracycline	--	23.44	--	35.53
Tigecycline	--	0	--	0
Vancomycin	0	0	--	0
Amikacin	--	7.18	--	87.5

resistance rates to third- and fourth-generation cephalosporins, carbapenems, cefoperazone/sulbactam, and piperacillin/tazobactam were significantly higher than before, with drug resistance rates of > 40%. The drug resistance rate of aminoglycosides and quinolones decreased. The sensitivity to polymyxin B was still good.

Escherichia coli. Compared with 13 years ago, the drug resistance rates of *E. Coli* to meropenem and imipenem increased from zero resistance to 2.97% and 3.3%, respectively, maintaining a high sensitivity. It also maintains good sensitivity to cefoperazone/sulbactam and piperacillin/tazobactam. The drug resistance rate to first-, second-, and third-generation cephalosporins is still high. Resistance to aminoglycosides and quinolones also remains high.

Acinetobacter *Baumannii*. The drug resistance rate of *A. Baumannii* was not evaluated thirteen years ago. The analysis results of the last two years showed that the drug resistance rate of *A. Baumannii* to most antibacterial drugs was > 50%, and the drug resistance rate of carbapenem was > 70%, showing good sensitivity to polymyxin B.

Staphylococcus *Aureus*. Compared with 13 years ago, the resistance rate of *S. Aureus* to oxacillin increased from zero to 25.84%, the resistance rate to penicillin was more than 90%, and that to clindamycin, clarithromycin, erythromycin, azithromycin also increased, but no *S. Aureus* resistance to vancomycin, teicoplanin, linezolid, or tigecycline was found.

Coagulase-negative staphylococcus. Compared with 13 years ago, the drug resistance rate of *CoNS* to oxacillin increased from zero to 35.53%, and the drug resistance to penicillin, clarithromycin, erythromycin, and azithromycin was still high, with a drug resistance rate of > 75%. No *CoNS* resistant to vancomycin, teicoplanin, linezolid or tigecycline were found.

Discussion

Comparative analysis of the distribution of the types of specimens submitted for inspection found that our hospital prepared a total of 13,202 pathogenic bacteria cultures from July 2018 to June 2020, an increase of 283% from 13 years ago, indicating that the awareness and number of doctors in the hospital had been significantly increased. The specimens were mainly respiratory tract, blood, secretions and urine, which were similar to those 13 years ago.

Changes of pathogen species were detected. From July 2018 to June 2020, 2956 strains of pathogenic bacteria were cultured in our hospital, an increase of 82.92% compared with 13 years ago. The types of pathogenic bacteria changed significantly. Thirteen years ago, Gram-positive cocci were the majority, with a total detection rate of 39.10%, and the total detection rate of Gram-negative bacilli was 32.50%. In the past two years, Gram-negative bacilli were dominant, with a total detection rate of 62.86%, and the total detection rate of Gram-positive cocci was 19.35%. Similarly, the ratio of Gram-negative bacilli to Gram-positive cocci was approximately 7 to 3 according to CHINET surveillance from 2005 to 2017 and that obtained through CARSS surveillance in 2016 [4, 5]. Based on this result and previous experience, clinicians can determine the common pathogens of different diseases and choose effective antimicrobial treatment.

For nearly two years, the top five pathogens identified in the hospital were *K. Pneumoniae*, *P. Aeruginosa*, *E. coli*, *S. Aureus*, and *A. Baumannii*, and one of the five CHINET statistics in the first half of 2020 (*E. coli*, *K. Pneumoniae*, *S. Aureus*, *P. Aeruginosa*, and *A. Baumannii*) were the same but in a different order. In addition, according to CHINET statistics, since 2017, the isolation rate of *K. Pneumoniae* in respiratory specimens has exceeded that of *A. Baumannii*, rising to first place [19, 20].

An analysis of pathogen resistance to common antibacterial drugs detected in our hospital was conducted. Antibiotic-resistant nosocomial infections pose a serious clinical challenge to doctors in the ICU and other departments, increasing morbidity, mortality, length of stay, and health care costs [21, 22]. At present, antibiotic resistance in our hospital is quite serious, especially in the ICU. The detection rate of *S. Aureus* and *CoNS* resistant to oxacillin was significantly higher than that thirteen years ago, and the detection rate of carbapenem-resistant Gram-negative bacilli was significantly increased. Care should be taken to consider multidrug-resistant bacteria when treating infections in patients in the ICU. Among the Gram-negative bacilli, the drug resistance rate of *P. Aeruginosa* to most antibacterial drugs was significantly increased, the drug resistance rate to third- and fourth-generation cephalosporins, carbapenems, cefoperazone/sulbactam, and piperacillin/tazobactam was significantly increased compared with that before, with a drug resistance rate of $> 40\%$. The WHO reported in 2017 that carbapenem-resistant *P. Aeruginosa* was listed in the "critical" group for which new antibiotics were urgently required [23]. It is suggested that clinicians should avoid using the third and fourth generation cephalosporins and their compound preparations when treating *P. Aeruginosa* infection. The detection rates of carbapenem-resistant *K. Pneumoniae* and *A. Baumannii* were also significantly increased. The drug resistance rates of *K. Pneumoniae* to meropenem and imipenem increased from zero thirteen years ago to 21.4% and 17.94%, respectively, while the drug resistance rate of *A. Baumannii* to carbapenems was $> 70\%$. Colistin maintained very high in vitro antimicrobial activity against *P. Aeruginosa* and *A. baumannii* (more than 95% of isolates exhibited susceptibility at all timepoints). *K. Pneumoniae* and *P. Aeruginosa* were highly resistant to aminoglycosides thirteen years ago in our hospital. In recent years, due to their toxicity and side effects, aminoglycosides have mainly been used to jointly control infections of multidrug resistant bacteria [24]. Therefore, the antimicrobial resistance of *K. Pneumoniae* and *P. Aeruginosa* to aminoglycosides has decreased in our hospital in the last two

years. *E. Coli* was highly sensitive to meropenem and imipenem, with a sensitivity rate of > 96%. Although the detection rate of Gram-positive cocci in our hospital was significantly lower than that 13 years ago, its resistance to oxacillin increased significantly, and the resistance rate of *S. Aureus* to oxacillin increased from zero to 25.84%; penicillin, clarithromycin, erythromycin, and azithromycin resistance remained high. No resistance was found against vancomycin, teicoplanin, and linezolid. Vancomycin has historically been the drug of choice for the treatment of methicillin-resistant *S. Aureus* infections, but its increased use has already led to vancomycin-intermediate *S. aureus* (VISA) as well as vancomycin-resistant *S. aureus* (VRSA) in certain parts of the world [25–27].

Challenges posed by multidrug resistant and pandrug resistant bacteria have become evident in recent years with the proliferation of various multidrug-resistant Gram-negative bacteria, such as extended-spectrum beta-lactamase (ESBL)-producing Enterobacterales, carbapenem-resistant Enterobacterales (CRE), carbapenem-resistant *Acinetobacter baumannii* (CRAB), carbapenem-resistant *P. Aeruginosa*, and other carbapenem-resistant Gram-negative bacteria, has introduced new challenges to clinical anti-infectious disease treatment and hospital infection control [28–32]. According to the statistics, approximately 50% of *K. pneumoniae* strains produce ESBLs, and a marked change is that carbapenem-resistant *K. pneumoniae* (CRKP) increased from 3.0% in 2005 to 20.9% in 2017 [4]. In China, the dominant genotype of CRKP is *K. Pneumoniae* carbapenemase-2 (KPC-2), accounting for approximately 70% of cases [33]. Because carbapenem-resistant Gram-negative bacilli are usually extensively drug-resistant, infections caused by these drug-resistant bacteria are difficult to treat, including challenges related to diagnosis and treatment, and they cause increased morbidity and mortality [34, 35].

The monitoring of bacterial resistance in medical institutions, regions, and nationwide is helpful to grasp the sensitivity of clinically important pathogenic bacteria to antibacterial drugs and to provide a basis for the empirical treatment of infections. Our data show significant changes and trends in the drug resistance of clinically important pathogenic bacteria, which provides a reference for hospitals to comprehensively understand drug resistance. To promote the rational use of antimicrobial drugs and to reduce the occurrence of drug resistance, personnel at all levels should be trained in the clinical application and management of antimicrobial drugs. In addition, while selecting antibacterial drugs based on the results of drug sensitivity, it is also recommended to combine pharmacokinetic/pharmacodynamic (PK/PD) data and MIC determination to calculate the correct dose of antibacterial drugs for each patient [36].

Conclusion

The variety of pathogenic bacteria in our hospital has changed significantly in the past two years compared with that 13 years ago, and the clinical isolates of Gram-negative bacilli have increased significantly compared with Gram-positive cocci. In the clinical treatment of anti-infective diseases, antimicrobial agents should be selected according to the bacterial distribution characteristics and drug resistance in each hospital. In addition, bacterial resistance monitoring at the hospital level is an important part of antimicrobial management measures in China, and local antimicrobial resistance data are crucial to guide the rational use of antimicrobial agents.

Acknowledgments

Author Contributions

Conceptualization: Huili Zhang.

Data curation: Huili Zhang, Kairui Zhou.

Investigation: Huili Zhang, Kairui Zhou.

Methodology: Xinglong He.

Project administration: Huili Zhang.

Resources: Huili Zhang, Xinglong He.

Supervision: Huili Zhang, Xin Yuan.

Validation: Huili Zhang, Kairui Zhou.

Visualization: Huili Zhang, Kairui Zhou.

Writing – original draft: Kairui Zhou, Xin Yuan.

Writing – review & editing: Huili Zhang, Kairui Zhou.

References

1. Wasfi R, Elkhatib WF, Ashour HM. Molecular typing and virulence analysis of multidrug resistant Klebsiella pneumoniae clinical isolates recovered from Egyptian hospitals. Sci Rep. 2016 Dec 22; 6:38929. https://doi.org/10.1038/srep38929 PMID: 28004732.

2. Abdula N, Macharia J, Motsoaledi A, Swaminathan S, VijayRaghavan K. National action for global gains in antimicrobial resistance. Lancet. 2016 Jan 9; 387(10014):e3–5. https://doi.org/10.1016/S0140-6736(15)00668-6 Epub 2015 Nov 18. PMID: 26603924.

3. van der Steen M, Leenstra T, Kluytmans JA, van der Bij AK; ISIS-AR study group. Trends in Expanded-Spectrum Cephalosporin-Resistant Escherichia coli and Klebsiella pneumoniae among Dutch Clinical Isolates, from 2008 to 2012. PLoS One. 2015 Sep 18; 10(9):e0138088. https://doi.org/10.1371/journal.pone.0138088 PMID: 26381746.

4. Hu F, Zhu D, Wang F, Wang M. Current Status and Trends of Antibacterial Resistance in China. Clin Infect Dis. 2018 Nov 13; 67(suppl_2):S128–S134. https://doi.org/10.1093/cid/ciy657 PMID: 30423045.

5. Zhou M, Wang Y, Liu C, Kudinha T, Liu X, Luo Y, et al. Comparison of five commonly used automated susceptibility testing methods for accuracy in the China Antimicrobial Resistance Surveillance System (CARSS) hospitals. Infect Drug Resist. 2018 Aug 30; 11:1347–1358. https://doi.org/10.2147/IDR.S166790 PMID: 30214255.

6. Poza M, Gayoso C, Gómez MJ, Rumbo-Feal S, Tomás M, Aranda J, et al. Exploring bacterial diversity in hospital environments by GS-FLX Titanium pyrosequencing. PLoS One. 2012; 7(8):e44105. https://doi.org/10.1371/journal.pone.0044105 Epub 2012 Aug 29. PMID: 22952889.

7. Exner M, Bhattacharya S, Christiansen B, Gebel J, Goroncy-Bermes P, Hartemann P, et al. Antibiotic resistance: What is so special about multidrug-resistant Gram-negative bacteria? GMS Hyg Infect Control. 2017 Apr 10; 12:Doc05. https://doi.org/10.3205/dgkh000290 PMID: 28451516.

8. Pritsch M, Zeynudin A, Messerer M, Baumer S, Liegl G, Schubert S, et al. First report on bla NDM-1-producing Acinetobacter baumannii in three clinical isolates from Ethiopia. BMC Infect Dis. 2017 Mar 1; 17(1):180. https://doi.org/10.1186/s12879-017-2289-9 PMID: 28249575.

9. Grumann D, Nübel U, Bröker BM. Staphylococcus aureus toxins—their functions and genetics. Infect Genet Evol. 2014 Jan; 21:583–92. https://doi.org/10.1016/j.meegid.2013.03.013 Epub 2013 Mar 26. PMID: 23541411.

10. Ruer S, Pinotsis N, Steadman D, Waksman G, Remaut H. Virulence-targeted Antibacterials: Concept, Promise, and Susceptibility to Resistance Mechanisms. Chem Biol Drug Des. 2015 Oct; 86(4):379–99. https://doi.org/10.1111/cbdd.12517 Epub 2015 Feb 6. PMID: 25589217.

11. Theuretzbacher U, Piddock LJV. Non-traditional Antibacterial Therapeutic Options and Challenges. Cell Host Microbe. 2019 Jul 10; 26(1):61–72. https://doi.org/10.1016/j.chom.2019.06.004 PMID: 31295426.

12. Naparstek L, Carmeli Y, Chmelnitsky I, Banin E, Navon-Venezia S. Reduced susceptibility to chlorhexidine among extremely-drug-resistant strains of Klebsiella pneumoniae. J Hosp Infect. 2012 May; 81(1):15–9. https://doi.org/10.1016/j.jhin.2012.02.007 Epub 2012 Mar 30. PMID: 22463977.

13. Clancy CJ, Chen L, Shields RK, Zhao Y, Cheng S, Chavda KD, et al. Epidemiology and molecular characterization of bacteremia due to carbapenem-resistant Klebsiella pneumoniae in transplant recipients. Am J Transplant. 2013 Oct; 13(10):2619–33. https://doi.org/10.1111/ajt.12424 Epub 2013 Sep 6. PMID: 24011185.

14. Abolghait SK, Fathi AG, Youssef FM, Algammal AM. Methicillin-resistant Staphylococcus aureus (MRSA) isolated from chicken meat and giblets often produces staphylococcal enterotoxin B (SEB) in non-refrigerated raw chicken livers. Int J Food Microbiol. 2020 Sep 2; 328:108669. https://doi.org/10.1016/j.ijfoodmicro.2020.108669 Epub 2020 May 20. PMID: 32497922.

15. Algammal AM, El-Sayed ME, Youssef FM, Saad SA, Elhaig MM, Batiha GE, et al. Prevalence, the antibiogram and the frequency of virulence genes of the most predominant bacterial pathogens incriminated in calf pneumonia. AMB Express. 2020 May 29; 10(1):99. https://doi.org/10.1186/s13568-020-01037-z PMID: 32472209.

16. Algammal AM, Mabrok M, Sivaramasamy E, Youssef FM, Atwa MH, El-Kholy AW, et al. Emerging MDR-Pseudomonas aeruginosa in fish commonly harbor oprL and toxA virulence genes and blaTEM, blaCTX-M, and tetA antibiotic-resistance genes. Sci Rep. 2020 Sep 29; 10(1):15961. https://doi.org/10.1038/s41598-020-72264-4 PMID: 32994450.

17. Zhang Huili, Song Junhua, Zhang Jing. Analysis of Pathogenic bacteria Distribution and Drug-resistance in Clinical Samples. Chinese pharmacy. 2008; 19(26): 2041–2043.

18. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing. 2018, M100–S28. https://doi.org/10.1016/j.diagmicrobio.2018.07.016 PMID: 30149988

19. Hu Fupin, Guo Yan, Zhu Demei, Wang Fu, et al. Bacterial resistance surveillance in CHINET tertiary hospitals in 2019.Chin J Infect Chemother. 2020; 20(3):233–243.

20. Hu F, Guo Y, Yang Y, Zheng Y, Wu S, Jiang X, et al. Resistance reported from China antimicrobial surveillance network (CHINET) in 2018. Eur J Clin Microbiol Infect Dis. 2019 Dec; 38(12):2275–2281. https://doi.org/10.1007/s10096-019-03673-1 Epub 2019 Sep 2. PMID: 31478103.

21. Exner M, Bhattacharya S, Christiansen B, Gebel J, Goroncy-Bermes P, Hartemann P, et al. Antibiotic resistance: What is so special about multidrug-resistant Gram-negative bacteria? GMS Hyg Infect Control. 2017 Apr 10; 12:Doc05. https://doi.org/10.3205/dgkh000290 PMID: 28451516.

22. Johnson AP. Surveillance of antibiotic resistance. Philos Trans R Soc Lond B Biol Sci. 2015 Jun 5; 370 (1670):20140080. https://doi.org/10.1098/rstb.2014.0080 PMID: 25918439.

23. Tacconelli E, Carrara E, Savoldi A, Harbarth S, Mendelson M, Monnet DL, et al. Discovery, research, and development of new antibiotics: the WHO priority list of antibiotic-resistant bacteria and tuberculosis. Lancet Infect Dis. 2018 Mar; 18(3):318–327. https://doi.org/10.1016/S1473-3099(17)30753-3 Epub 2017 Dec 21. PMID: 29276051.

24. Hawkey PM, Warren RE, Livermore DM, McNulty CAM, Enoch DA, Otter JA, et al. Treatment of infections caused by multidrug-resistant Gram-negative bacteria: report of the British Society for Antimicrobial Chemotherapy/Healthcare Infection Society/British Infection Association Joint Working Party. J Antimicrob Chemother. 2018 Mar 1; 73(suppl_3):iii2–iii78. https://doi.org/10.1093/jac/dky027 PMID: 29514274.

25. Tenover FC, Biddle JW, Lancaster MV. Increasing resistance to vancomycin and other glycopeptides in Staphylococcus aureus. Emerg Infect Dis. 2001 Mar-Apr; 7(2):327–32. https://doi.org/10.3201/eid0702.010237 PMID: 11294734.

26. Trakulsomboon S, Danchaivijitr S, Rongrungruang Y, Dhiraputra C, Susaemgrat W, Ito T, et al. First report of methicillin-resistant Staphylococcus aureus with reduced susceptibility to vancomycin in Thailand. J Clin Microbiol. 2001 Feb; 39(2):591–5. https://doi.org/10.1128/JCM.39.2.591-595.2001 PMID: 11158112.

27. Centers for Disease Control and Prevention (CDC). Staphylococcus aureus resistant to vancomycin—United States, 2002. MMWR Morb Mortal Wkly Rep. 2002 Jul 5; 51(26):565–7. PMID: 12139181.

28. Tacconelli E, Cataldo MA, Dancer SJ, De Angelis G, Falcone M, Frank U, et al. ESCMID guidelines for the management of the infection control measures to reduce transmission of multidrug-resistant Gram-negative bacteria in hospitalized patients. Clin Microbiol Infect. 2014 Jan; 20 Suppl 1:1–55. https://doi.org/10.1111/1469-0691.12427 PMID: 24329732.

29. Wright H, Bonomo RA, Paterson DL. New agents for the treatment of infections with Gram-negative bacteria: restoring the miracle or false dawn? Clin Microbiol Infect. 2017 Oct; 23(10):704–712. https://doi.org/10.1016/j.cmi.2017.09.001 Epub 2017 Sep 8. PMID: 28893690.

30. Horcajada JP, Montero M, Oliver A, Sorlí L, Luque S, Gómez-Zorrilla S, et al. Epidemiology and Treatment of Multidrug-Resistant and Extensively Drug-Resistant Pseudomonas aeruginosa Infections. Clin Microbiol Rev. 2019 Aug 28; 32(4):e00031–19. https://doi.org/10.1128/CMR.00031-19 PMID: 31462403.

31. Morency-Potvin P, Schwartz DN, Weinstein RA. Antimicrobial Stewardship: How the Microbiology Laboratory Can Right the Ship. Clin Microbiol Rev. 2016 Dec 14; 30(1):381–407. https://doi.org/10.1128/CMR.00066-16 PMID: 27974411.

32. Wong D, Nielsen TB, Bonomo RA, Pantapalangkoor P, Luna B, Spellberg B. Clinical and Pathophysiological Overview of Acinetobacter Infections: a Century of Challenges. Clin Microbiol Rev. 2017 Jan; 30 (1):409–447. https://doi.org/10.1128/CMR.00058-16 PMID: 27974412.

33. Zhang R, Liu L, Zhou H, Chan EW, Li J, Fang Y, et al. Nationwide Surveillance of Clinical Carbapenem-resistant Enterobacteriaceae (CRE) Strains in China. EBioMedicine. 2017 May; 19:98–106. https://doi.org/10.1016/j.ebiom.2017.04.032 Epub 2017 Apr 26. PMID: 28479289.

34. Centers for Disease Control and Prevention (CDC). Guidance for control of infections with carbapenem-resistant or carbapenemase-producing Enterobacteriaceae in acute care facilities. MMWR Morb Mortal Wkly Rep. 2009 Mar 20; 58(10):256–60. PMID: 19300408.

35. Pachori P, Gothalwal R, Gandhi P. Emergence of antibiotic resistance Pseudomonas aeruginosa in intensive care unit; a critical review. Genes Dis. 2019 Apr 17; 6(2):109–119. https://doi.org/10.1016/j.gendis.2019.04.001 PMID: 31194018.

36. Delattre IK, Taccone FS, Jacobs F, Hites M, Dugernier T, Spapen H, et al. Optimizing β-lactams treatment in critically-ill patients using pharmacokinetics/pharmacodynamics targets: are first conventional doses effective? Expert Rev Anti Infect Ther. 2017 Jul; 15(7):677–688. https://doi.org/10.1080/14787210.2017.1338139 Epub 2017 Jun 19. PMID: 28571493.