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ARTICLE

Current status and trends of antimicrobial resistance among clinical isolates in China: a retrospective study of CHINET from 2018 to 2022

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Abstract

Antimicrobial resistance (AMR) is a pressing issue in China, with antibiotic therapy becoming less effective against bacterial infections. To address this challenge, the China Antimicrobial Surveillance Network (CHINET) was established in 2005 to monitor antimicrobial resistance in the country. This study analyzed the CHINET data from teaching hospitals and evaluated the trends of AMR in China from 2018 to 2022. A range of 163,636 to 301,917 isolates was obtained per year, with the majority being Gram-negative bacilli (69.0% to 71.8%). The proportion of important multidrug-resistant pathogens remained stable over the years. While the analysis showed diverse AMR profiles for different bacterial species. Over the five years, generally decreased resistance rates were observed from the majority of the tested species. For example, resistance to ceftriaxone decreased in *Escherichia coli* and *Klebsiella pneumoniae*, while resistance to imipenem and meropenem decreased in *Pseudomonas aeruginosa*. Moreover, resistance to methicillin, gentamicin, fosfomycin, and clindamycin also decreased in clinical *Staphylococcus aureus* isolates. On the other hand, resistance levels of *Acinetobacter baumannii* remained stable. Our study provides a comprehensive overview of the AMR profiles of common bacterial species in China and highlights the ongoing efforts to address this challenge.

Keywords CHINET, *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *A. baumannii*, *S. aureus*, Antimicrobial susceptibility testing

Introduction

Antimicrobial resistance surveillance is essential in understanding the antimicrobial susceptibility of pathogenic bacteria and their resistance trends to important antimicrobial drugs. This is crucial for clinical anti-infection empirical management and precise treatment [1, 2]. In 2004, starting with eight hospitals, Huashan Hospital of Fudan University established the China Antimicrobial Surveillance Network (CHINET, www.chinets.com) [3]. Currently, the network has expanded to 71 hospitals across 29 provinces, municipalities and autonomous regions, including 55 tertiary and 16 secondary hospitals (or 51 general and 20 children's hospitals). The CHINET has established "CHINET Cloud", an online

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information system for antimicrobial susceptibility testing data, which provides a yearly release of surveillance data [3]. Thus far, the CHINET system has become one of the most influential antimicrobial surveillance networks in China. In 2018, CHINET reported the antimicrobial resistance trends of clinically important bacteria in China from 2005 to 2017 [4, 5]. In this study, we analyzed the antimicrobial susceptibility and resistance trends of clinically *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Staphylococcus aureus* isolated from 2018–2022. Our study highlights the current resistance trends in the above five target species, demonstrates the importance of bacterial surveillance studies, and plays a critical role in guiding empirical antimicrobial therapy in clinical practice.

Results

Percentage of targeted five bacterial species

The total number of bacterial isolates was 1,232,028, ranging from 163,636 to 301,917 per year (Fig. 1). The distribution of specimen sources for the different bacterial species varied considerably (Fig. 2). The main specimen sources for *E. coli* were urinary tract (48.0%, n = 112,487), blood (17.3%, n = 40,452) and respiratory tract (9.8%, n = 22,966). *K. pneumoniae* was mainly isolated from the respiratory tract (51.9%, n = 91,132), blood (16.1%, n = 28,270) and urinary tract (14.1%, n = 24,758). *P. aeruginosa* was mainly isolated from the respiratory tract (66.3%, n = 68,685), urinary tract (8.5%, n = 8,805) and pus (6.4%, n = 6,630). *A. baumannii* was mainly isolated from respiratory tract (76.6%, n = 75,414), blood (5.4%, n = 5,316) and urinary tract (4.8%, n = 4,725). *S. aureus* was mainly isolated from respiratory tract (38.7%, n = 44,059), pus (17.2%, n = 19,582) and blood (12.4%, n = 14,117). The ratio of Gram-negative bacilli and Gram-positive cocci was 69.0%–71.8% and 28.2%–31.0%, respectively (Fig. 1). There were no changes in the ratio between specimen types during the study period. The percentage of the five target species in the total number of all reported isolates is shown in Fig. 1 and Supplementary Appendix Table 1.

Escherichia coli

The resistance rates of *E. coli* to most antimicrobial agents decreased over the five years. Specifically, the resistance rate of clinical *E. coli* isolates to ceftriaxone decreased from 57.5% to 50.8% (Fig. 3). The rate of imipenem-resistant isolates also decreased from 2% in 2018 to 1.5% in 2022 (Fig. 3). Moreover, the resistance rates of *E. coli* to amikacin, piperacillin-tazobactam, cefoperazone-sulbactam, meropenem, ciprofloxacin and levofloxacin decreased from 2.7% to 2.2%, from 5.3% to 4.3%, from 6.5% to 5.5%, from 2.1% to 1.6%, from 66% to 61.4% and from 58.9% to 53.2%, respectively. Additionally, the resistance rates of *E. coli* to cefepime, cefoxitin, trimethoprim-sulfamethoxazole, and fosfomycin decreased from 27.3% to 25.1%, 13.5% to 9.7%, 56.2% to 51.8% and 5% to 4.4%, respectively. However, the resistance rates of colistin and tigecycline fluctuated around 1.0% and 0.1%, respectively. Notably, the resistance rate of *E. coli* to

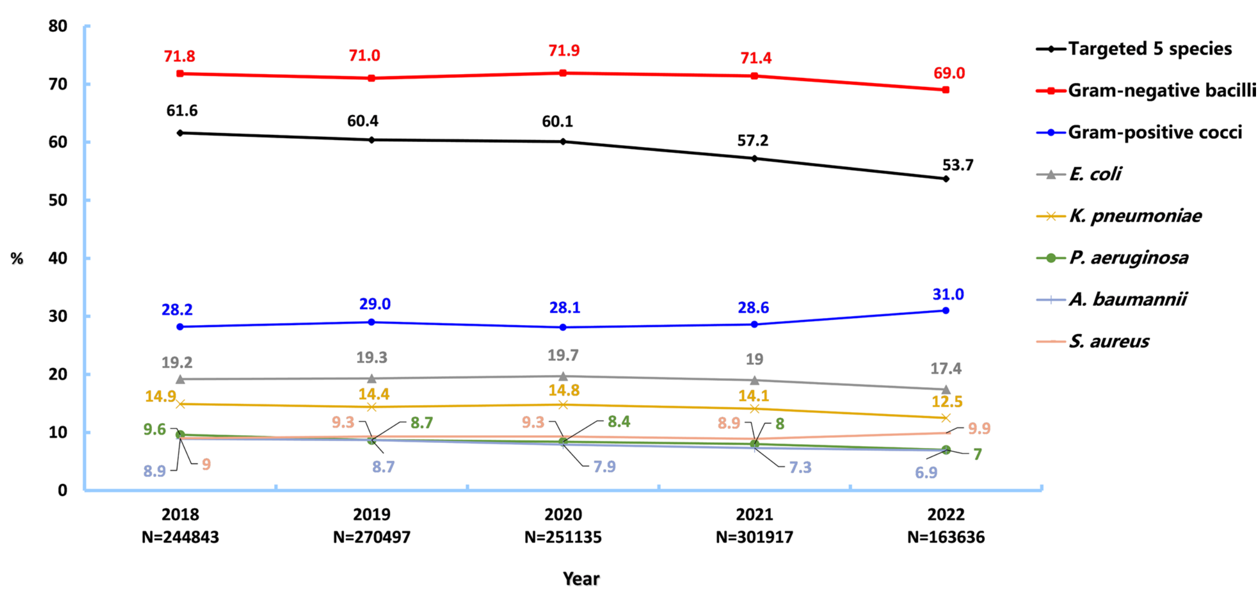

Fig. 1 Percentages of Gram-negative bacilli, Gram-positive cocci, and targeted five species among total number of all reported isolates

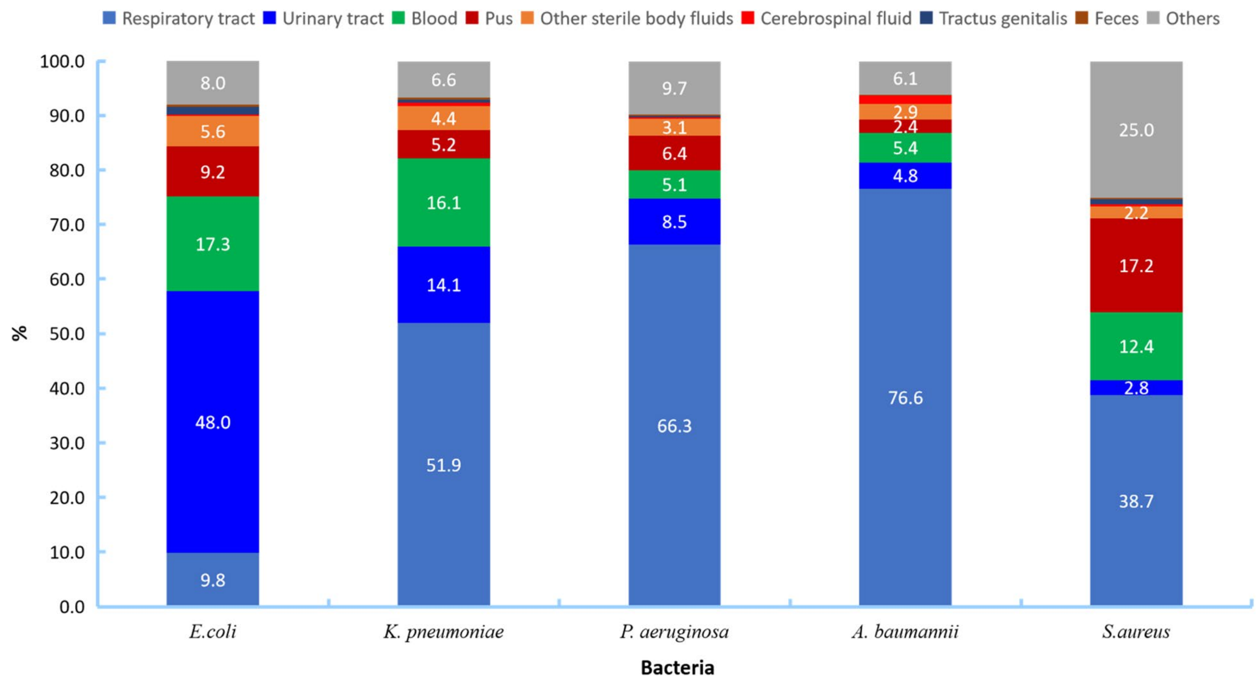

Fig. 2 Prevalence of *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *A. baumannii*, and *S. aureus* among specimen type

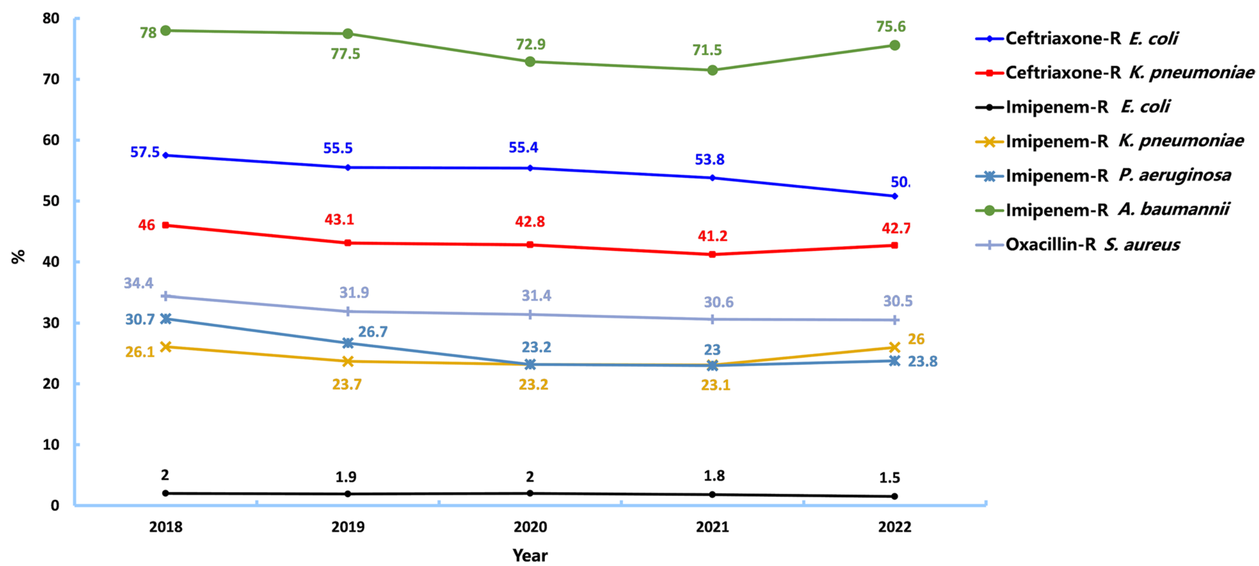

Fig. 3 Rates of ceftriaxone-resistant *E. coli* and *K. pneumoniae*, imipenem-resistant Gram-negative bacilli, and oxacillin-resistant *S. aureus* clinical isolates from 2018 to 2022

polymyxin B increased from 0.7% in 2018 to 1.0% in 2022 (Fig. 4 and Supplementary Appendix Table 2).

Klebsiella pneumoniae

The resistance rate of *K. pneumoniae* isolates to ceftriaxone decreased from 46.0% to 42.7% during the five-year period (Fig. 3). While *K. pneumoniae* isolates showed a relatively stable resistance rates to imipenem, meropenem, amikacin, piperacillin-tazobactam, cefepime and tigecycline (Figs. 3 and 5). While the resistance rates to cefoperazone-sulbactam, levofloxacin and trimethoprim-sulfamethoxazole decreased from 33% to 30.9%, from 38% to 35.2% and from 38.2% to 32.9% respectively. However, a significant decrease

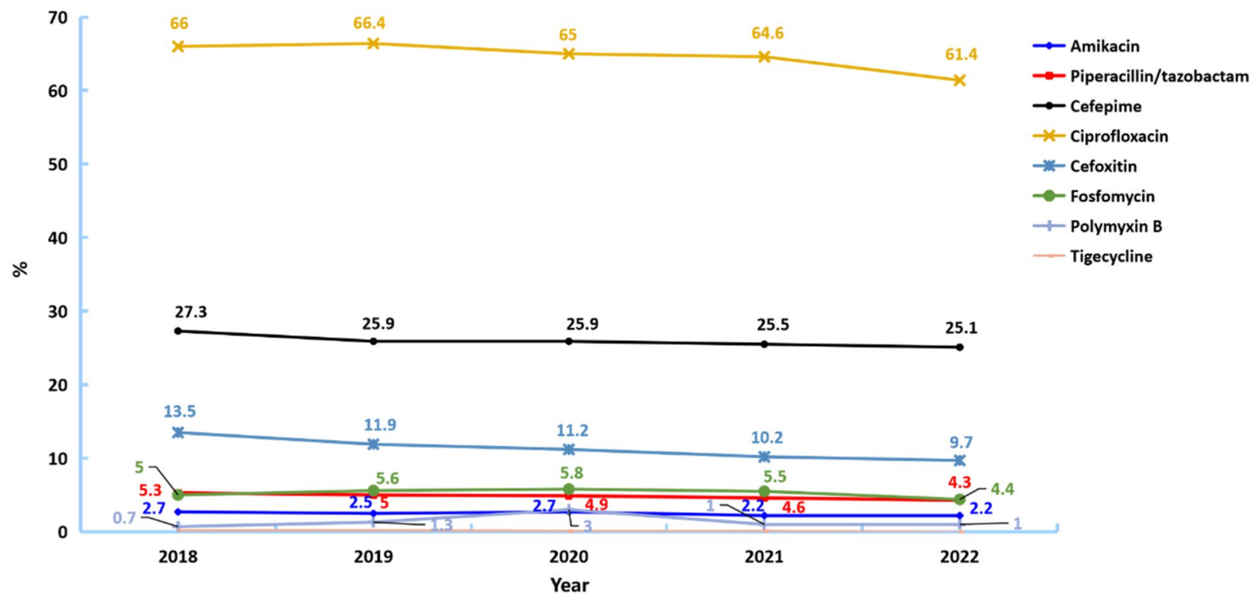

Fig. 4 Resistance profile of *E. coli* for eight representative antimicrobial agents

in resistance was observed for ceftazidime-avibactam and ciprofloxacin, from 9.8% to 4.8% and from 50.2% to 38.3%, respectively. A significant increase in resistance was observed for polymyxin B, from 1.0% to 5.1%. The resistance rate of *K. pneumoniae* to cefoxitin increased from 25.2% to 27.9%. Colistin and tigecycline resistance rates fluctuated around 2.5% and 4.0%, respectively. (Fig. 5 and Supplementary Appendix Table 3).

Pseudomonas aeruginosa

P. aeruginosa resistance decreased for all antimicrobial agents, during the five-year period. The rates of imipenem- and meropenem-resistant isolates decreased from 30.7% to 23.8% and from 25.8% to 19.2%, respectively, during the 5-year sampling period (Fig. 3 and Supplementary Appendix Table 4). Resistance to ceftazidime-avibactam significantly decreased from 11.1%

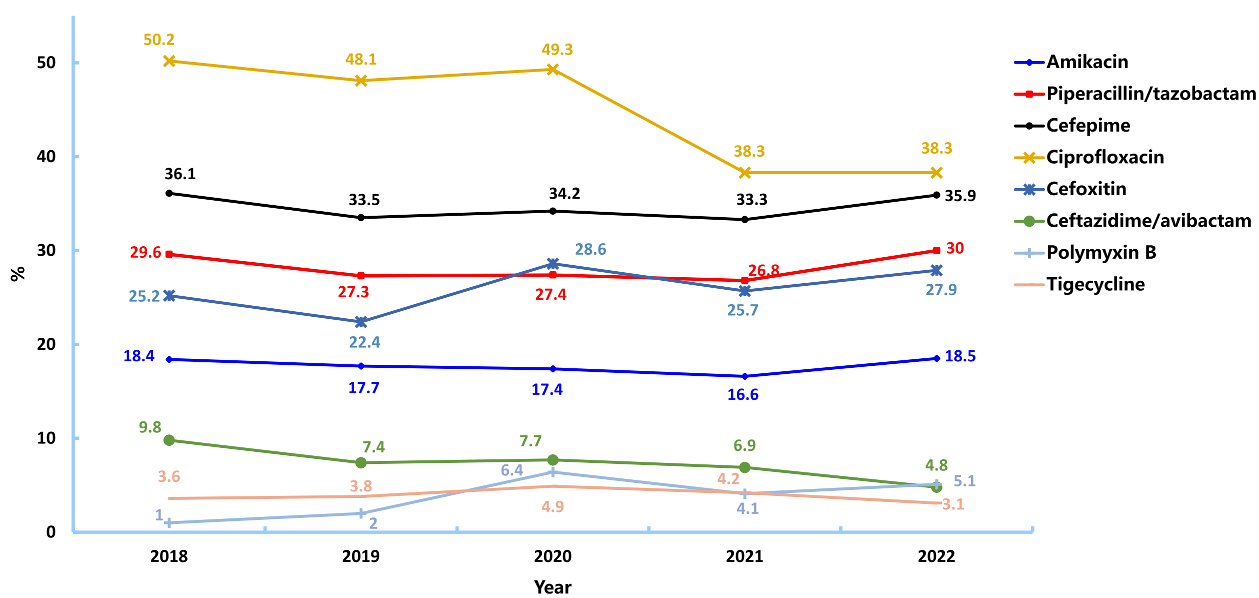

Fig. 5 Resistance profile of *K. pneumoniae* for eight representative antimicrobial agents

to 6.3%. Furthermore, the resistance rates to cefoperazone-sulbactam, piperacillin-tazobactam, ceftazidime, ciprofloxacin and amikacin decreased from 17.1% to 15%, 16.7% to 13.5%, 19.3% to 14.9%, 24.1% to 15.3%, and 6.2% to 3.8%, respectively. The resistance rates of colistin and polymyxin B fluctuated around 1.5% and 0.5% respectively (Fig. 6 and Supplementary Appendix Table 4).

Acinetobacter baumannii

During the five-year period, the resistance levels of *A. baumannii* isolates to imipenem and meropenem remained relatively stable, decreasing from 78% to 75.6% and from 78.8% to 76.6%, respectively (Fig. 3). Resistance to cefoperazone-sulbactam, amikacin, and levofloxacin increased from 52.5% to 58.7%, 57.8% to 59.2% and 61.5% to 63.1%, respectively. Resistance to ampicillin-sulbactam, piperacillin-tazobactam, ceftazidime, ciprofloxacin, and tigecycline decreased from 72.6% to 68.7%, from 77.9% to 77.4%, from 77.7% to 74.5%, from 79.1% to 75.4% and from 5.1% to 2.5%, respectively. Colistin and polymyxin B resistance rates were fluctuated around 1% and 0.5%, respectively (Fig. 7 and Supplementary Appendix Table 5).

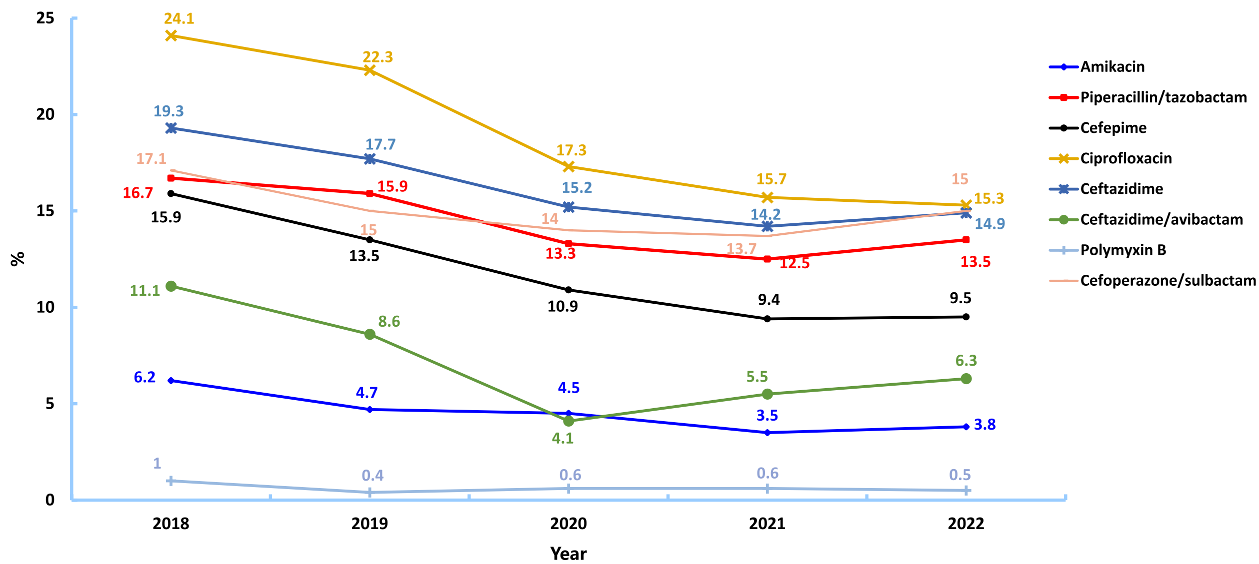

Fig. 6 Resistance profile of *P. aeruginosa* for eight representative antimicrobial agents

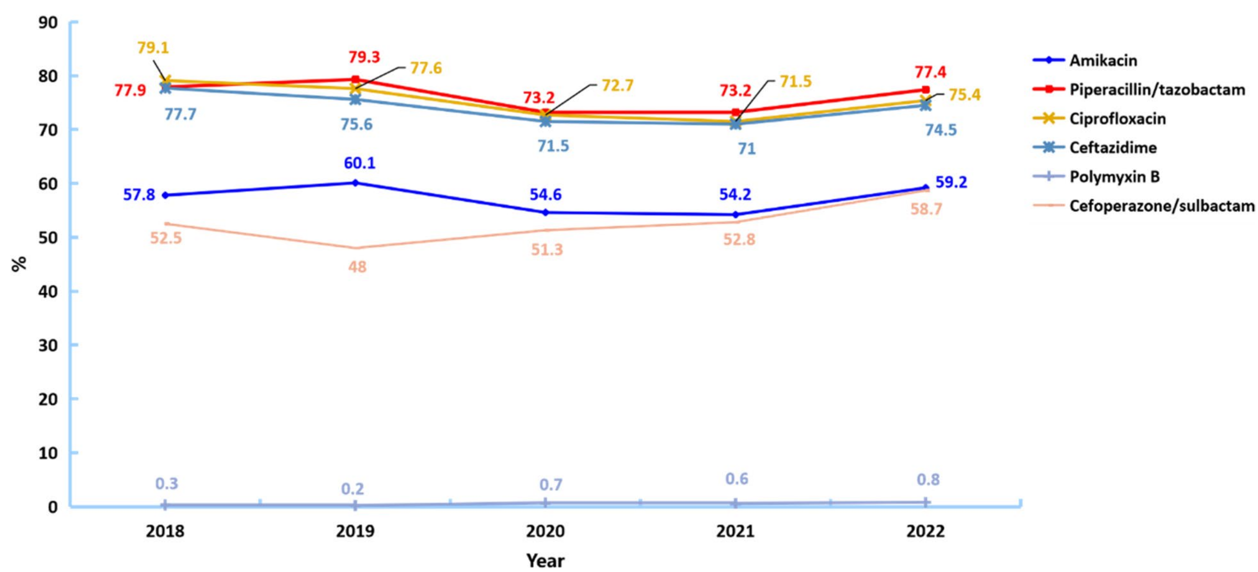

Fig. 7 Resistance profile of *A. baumannii* for six representative antimicrobial agents

Staphylococcus aureus

The prevalence of methicillin resistance in *S. aureus* isolates decreased from 34.4% in 2018 to 30.5% in 2022 (Fig. 3). Furthermore, a significant reduction in resistance rates was noted for several antibiotics. For instance, the percentage of *S. aureus* isolates resistant to gentamicin, fosfomycin and clindamycin decreased from 17%, 13%, and 38.9% to 8.4%, 3.4%, and 26.7%, respectively. Similarly, resistance rates to rifampicin, ciprofloxacin, trimethoprim-sulfamethoxazole, and erythromycin decreased from 4.9% to 1.7%, 19.5% to 12.7%, 14.7% to 10.4% and 64.3% to 52.7% respectively. Notably, no isolates were observed resistant to vancomycin and linezolid. On the other hand, resistance rates to teicoplanin and tigecycline remained relatively low, fluctuating around 0.1% and 0.3%, respectively (Fig. 8 and Supplementary Appendix Table 6).

Discussion

In summary, the resistance status and trends of most antimicrobials against the five target species were relatively stable. The resistance level of some antimicrobials showed a decreasing trend, but each species still had its characteristic antimicrobial resistance. For *E. coli*, the resistance trends of all cephalosporins were relatively stable and decreased to some extent. For the third-generation cephalosporins, the resistance rate in China showed a decreasing trend, whereas the resistance rate increased in the EU/EAA in 2001 to 2018, which kept below 15% [6]. The resistance rates of carbapenems, amikacin, polymyxin B, colistin, fosfomycin, and partial β-lactam-β-lactamase inhibitor combinations remained relatively low, the sensitivity of tigecycline was above 99.7%.

Conversely, the overall resistance status of *K. pneumoniae* was more severe than that of *E. coli*. The resistance rates of carbapenems have been increasing since the CHINET surveillance data were collected in 2005. According to CHINET data from 2018 to 2022, the resistance rates of carbapenems, including ertapenem, imipenem and meropenem, increased significantly, up to 26.9%, 26% and 27.5%, respectively. Compared with CHINET data from 2005 to 2017 [5], the resistance to carbapenems still grew rapidly. Compared with the resistance status of carbapenems from several global surveillance studies [7, 8], the resistance rates of carbapenems ranged from 3.5% to 8.4% in Latin America, 3.2% to 3.7% in Europe, 1.2% to 1.9% in North America, and some countries had higher proportions of carbapenem-resistant *K. pneumoniae* > 40%, including India (54.9%), Greece (53.6%), Argentina (46.4%). Therefore, the carbapenem resistance rates in China remained at the hyper-average level in a global context. In addition, only colistin, polymyxin B, ceftazidime-avibactam, and tigecycline maintained relatively high susceptibility to *K. pneumoniae*. It should be noted that the increasing trends of polymyxin B resistance were observed in both *K. pneumoniae* (from 1% to 5.1%) and *E. coli* (from 0.7% to 1%) isolates during 2018–2022. As China approved the use of polymyxin B in clinics in 2017 [9], further surveillance of polymyxin B resistance in both *K. pneumoniae* and *E. coli* in Chinese clinics is urgently needed to ensure the prudent use of this last resort antimicrobial agent.

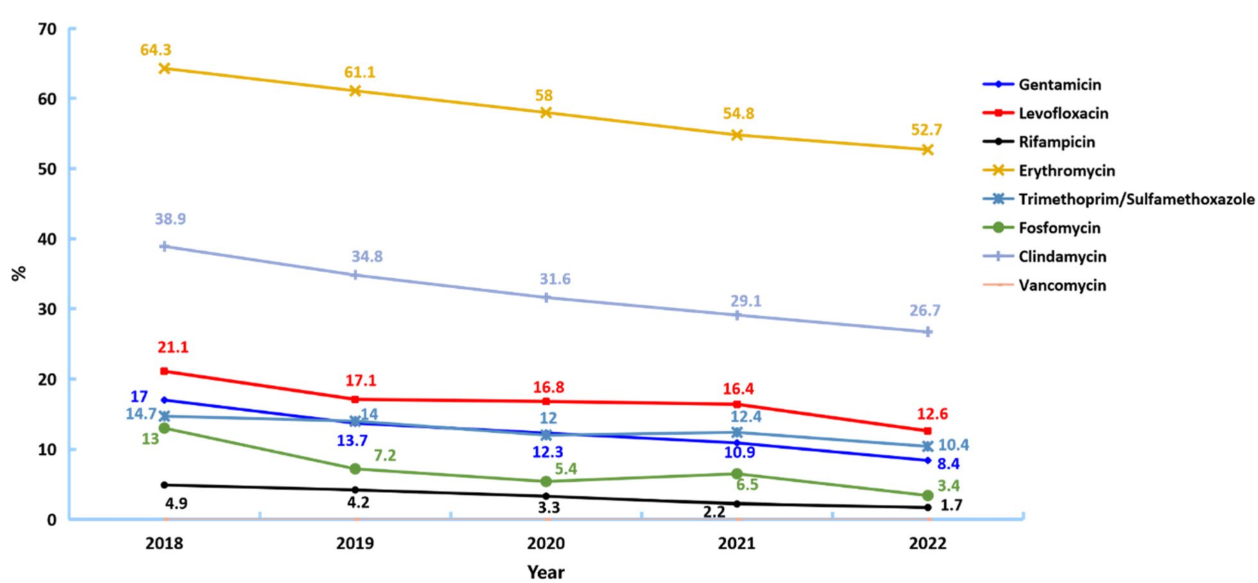

Fig. 8 Resistance profile of *S. aureus* for eight representative antimicrobial agents

For *P. aeruginosa*, resistance levels decreased for most antimicrobials. In addition, *P. aeruginosa* is a common pathogen associated with carbapenem-resistant phenotypes and showed resistance rates of around 20% to 30%. Currently, the Antimicrobial Testing Leadership and Surveillance (ATLAS) programme is investigating resistance patterns of *P. aeruginosa* in the Asia–Pacific region from 2015 to 2019, and the overall rate of carbapenem-resistant *P. aeruginosa* was 18.9%, ranging from the lowest in Australia (6.5%) to the highest in India (29.3%) [10]. There is no doubt that the resistance of *A. baumannii* to most antimicrobials, including carbapenems and β-lactam-β-lactamase inhibitor combinations, remains at high levels. While the proportion of carbapenem resistance in clinical *A. baumannii* isolates in European countries varied from 10% to 30% in Germany, it was relatively lower than in China ranging from 75.6% to 78.8% [11]. Regarding the prevalence of MRSA in China, the detection rate of MRSA has continuously decreased from 69.0% in 2005 to 30.5% in 2022. Data from EARS-Net showed that the prevalence of MRSA in European countries also showed a significant decreasing trend, from 24.4% in 2005 to 14.1% in 2018 [12].

From the above analysis of the five target bacterial species, the most intuitive change is that antimicrobial resistance showed a decreasing trend for some species. This is a positive confirmation of the work that has been done to address the serious antimicrobial resistance status. Over the past decade, China has established a relatively comprehensive management system and technical support framework for antimicrobial stewardship [13]. Firstly, based on One Health, several guidelines and documents are issued and strictly implemented to regulate the use of antimicrobials in both humans and animals and to strengthen antimicrobial surveillance in the environment. Secondly, antimicrobial resistance surveillance networks, such as CHINET and CARSS, established in China, provide high-quality, comprehensive and real-time surveillance data, which are essential to reducing the burden of antimicrobial resistance [14]. Third, professional staff training and advanced techniques also provide more opportunities to identify unusual resistance phenotypes, genotypes of resistance genes, or other resistance mechanisms, so that precision therapy can be used to reduce the burden of antimicrobial use.

From the above analysis, it can be concluded that the resistance status of clinical isolates in China remains serious. Some important multidrug-resistant bacteria, such as carbapenem-resistant *K. pneumoniae*, carbapenem-resistant *P. aeruginosa* and carbapenem-resistant *A. baumannii*, are widespread in China and have been highlighted as an urgent threat to global public health [15]. As this type of multidrug-resistant bacteria spreads around the world in the absence of alternative drugs, patients are often left without effective treatment, resulting in significant morbidity and mortality. New antibiotics and drug combinations based on antimicrobial susceptibility testing have been developed to address this threat, including ceftazidime-avibactam, meropenem-vaborbactam, cefiderocol, and others [16–18].

From the retrospective study of CHINET, we can learn the holistic antimicrobial resistance profile of China. First, CHINET consists of 71 hospitals from 29 provinces, municipalities and autonomous regions covering 960 million people in China. Second, CHINET conducts active surveillance studies and responds to the comprehensive status and trends of antimicrobial resistance in China. Third, hospital-level surveillance of bacterial resistance is needed as part of antimicrobial stewardship activities in China, as local data on antimicrobial resistance are critical to guide the rational use of antimicrobials, such as the empirical use of antimicrobials for hospital-acquired and ventilator-associated pneumonia [19]. The present study still has some limitations, including the short time period, which covered variations in many antimicrobials, and the large fluctuations over time. Finally, there is a need to strengthen the CHINET surveillance system, especially for important drug-resistant pathogens, and to conduct molecular biological studies to clarify the susceptibility of different genotypes of strains to antibacterial agents, especially new antibacterial agents, in order to understand the epidemiological characteristics of important drug-resistant bacteria. With the development of molecular biology techniques, a promising approach that combines the resistant phenotype with the genotype of virulence and resistance genes, which can be an effective strategy to reduce the burden of antimicrobial use.

Conclusion

The antimicrobial resistance status of clinical isolates in China remains stable but serious. Although the isolation rate of MRSA is decreasing, the Gram-negative bacilli have higher antimicrobial resistance profiles, especially ceftriaxone-resistant *E. coli*, carbapenem-resistant *K. pneumoniae*, carbapenem-resistant *P. aeruginosa* and multidrug-resistant *A. baumannii*. These pose great challenges to antimicrobial chemotherapy in clinics in China. We need to strengthen the CHINET surveillance system and make efforts to curb the rise of antimicrobial resistance.

Materials and methods

Bacterial strains and species identification

All clinical isolates of *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *A. baumannii* and *S. aureus* collected from outpatients and inpatients in 71 hospitals were included in CHINET for five years between 2018–2022. To avoid duplicate counts, only one isolate of the same species was included per patient per year based on their personal identification code and hospital. Species identification was performed at each participating site and confirmed by the central laboratory using matrix-assisted laser desorption ionisation-time of flight mass spectrometry (BioMérieux, Marcy I'Etoile, France). *E. coli* ATCC 25922, *P. aeruginosa* ATCC 27853 and *S. aureus* ATCC 29213 were used as quality control strains for antimicrobial susceptibility testing to ensure the reproducibility of the testing procedure.

Antimicrobial susceptibility testing

According to a CHINET uniform protocol, antimicrobial susceptibility testing was performed using automated systems, supplemented by a disc diffusion method for some antimicrobial agents that were not available in automated systems. Quality control and test results were interpreted according to Clinical and Laboratory Standards Institute (CLSI) 2022 breakpoints for all agents tested, except for tigecycline and polymyxin B [20]. Tigecycline minimum inhibitory concentrations (MICs) were interpreted using US Food and Drug Administration (FDA) MIC breakpoints for which CLSI criteria were not available [21]. Colistin and polymyxin B were interpreted using the European Committee on Antimicrobial Susceptibility Testing (EUCAST) MIC interpretive breakpoints for colistin [22]. During the 5-year sampling period, the methods used were consistent in all participating hospitals.

Data analysis

Data were collected in a standardized format from microbiology laboratories and entered into a central database using WHONET software [23]. Statistical analysis and calculations were performed using the WHONET software.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s44280-023-00009-9.

Additional file 1: Table 1. Percentages of targeted 5 species among total number of all reported isolates. **Table 2.** Resistance rates and susceptibility rates of *E. coli* to antimicrobial agents. **Table 3.** Resistance rates and susceptibility rates of *K. pneumoniae* to antimicrobial agents. **Table 4.** Resistance rates and susceptibility rates of *P. aeruginosa* to antimicrobial agents. **Table 5.** Resistance rates and susceptibility rates of *A. baumannii* to antimicrobial agents. **Table 6.** Resistance rates and susceptibility rates of *S. aureus* to antimicrobial agents.

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Authors' contributions

F.H., Y.G. and D.Z. designed the study. W.Y., L.D., S.W., R.H., D.Y., and Y.Y. performed the experiments and wrote the manuscript. All authors contributed to the article and approved the submitted version.

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Availability of data and materials

The datasets used or analyzed during the current study are available in CHINET, www.chinets.com.

Declarations

Ethics approval and consent to participate
The study protocol was approved by the Institutional Review Board of Huashan Hospital, Fudan University (no. 2019–460).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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