Received: 2018.05.19
Accepted: 2018.08.07
Published: 2018.11.28

Antimicrobial Resistance Profiles of Nosocomial Pathogens in Regional China: A Brief Report from Two Tertiary Hospitals in China

Authors' Contribution:

Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

BCDEF **Song Liu***
BCDEF **Meng Wang***
CF **Liming Zheng**
AG **Wenxian Guan**

Department of General Surgery, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, Jiangsu, P.R. China

* These authors contribute equally

Corresponding Authors:

Liming Zheng, e-mail: guan_wenxian@sina.com; Wenxian Guan, e-mail: guan_wenxian@sina.com

Source of support:

This study was supported by a grant from the National Natural Science Foundation of China (No. 81602103), the Natural Science Foundation of Jiangsu Province (No. BK20160114), the Distinguished Young Scholar Project of Medical Science and Technology Development Foundation of Nanjing Department of Health (JQX17005), the Key Project of Medical Science and Technology Development Foundation of Nanjing Department of Health (YKK16114), the Medical Research Program of Jiangsu Provincial Commission of Health and Family Planning (Q2017007), and the Wu Jieping Medical Foundation (320.2710.1817)

Background:

Antimicrobial resistance of nosocomial pathogens has become a worldwide problem that leads to major health-care and economic burdens. Regional antimicrobial resistance profiles are needed to inform selection of proper antimicrobial agents.

Material/Methods:

In collaboration with the Hospital Infection Control Office at our hospitals, we analyzed the constitution of nosocomial pathogens and the corresponding drug-resistance profiles. We paid particular attention to characteristics of pathogens that were derived from the bloodstream, and summarized the drug-resistance tendency of 2 specific bacteria within the most recent decade to reflect the development of resistance in regional China.

Results:

The most common types of nosocomial pathogens were *Escherichia coli* (859 isolates, 14.3%), *Staphylococcus aureus* (763 isolates, 12.7%), *Acinetobacter baumannii* (681 isolates, 11.3%), *Klebsiella pneumonia* (660 isolates, 11.0%), and *Pseudomonas aeruginosa* (654 isolates, 10.9%). The most common types of bloodstream-derived pathogens were *K. pneumoniae* (125 isolates, 16.3%), *E. coli* (118 isolates, 15.3%), *A. baumannii* (81 isolates, 10.5%), *Candida albicans* (57 isolates, 7.4%), *S. aureus* (45 isolates, 5.9%), *P. aeruginosa* (44 isolates, 5.7%), and *Enterobacterium spp.* (42 isolates, 5.5%). Distinct antimicrobial resistance profiles were observed between different pathogens as well as between bloodstream-derived and other sources of pathogens. The resistant rates of *A. baumannii* and *P. aeruginosa* to antimicrobial agents have been increasing during the most recent 10 years at our hospital.

Conclusions:

Our data demonstrated the characteristics of nosocomial infections and antibiotic resistance in regional China. The distinct resistance profile of each pathogen can help to tailor individual antimicrobial strategy. The emerging resistant rates to antimicrobials require reinforced actions for infection prevention and control.

MeSH Keywords:

Cross Infection • Drug Resistance, Microbial • Epidemiologic Studies

Full-text PDF:

<https://www.medscimonit.com/abstract/index/idArt/911229>

1771

—

2

18

Background

Antimicrobial resistance of nosocomial pathogens is becoming a global challenge that constrains the benefits of healthcare management and requires urgent actions. However, drug resistance profiles vary between western and eastern regions as well as between developed and developing countries. Regional resistance profiles are essential for selecting appropriate antibiotic therapy in designated areas. Evidence from Asia-Pacific area, especially from mainland China has not been fully obtained. Herein, we will characterize the antimicrobial resistance profile of nosocomial pathogens during a calendar year in 2 tertiary hospitals in east China. We will pay particular attentions to bloodstream-derived pathogenic strains that are theoretically more challenging. We will also illustrate antimicrobial-resistance trend of 2 specific pathogens (*Acinetobacter baumannii* and *Pseudomonas aeruginosa*) during the most recent 10 years in our hospitals, in a reflection of worsening drug-resistance situation in China.

Material and Methods

In collaboration with the Hospital Infection Control Office at our hospitals, all microbial data were retrieved from the Nosocomial Infection Surveillance System (NISS) and the Self-Report Infection System (SRIS). NISS is designed for real-time monitoring of newly emerging suspicious infections according to sample culture results of all types of body fluids, including sputum, incisional secretion, urine, blood, catheter tip, feces, and others. SRIS is dedicated to receiving reports from clinicians when suspicious healthcare-associated infection occurs even microbial evidence is absent. Every single infection was tracked and collected for analysis. All antimicrobial susceptibility tests in our hospitals were determined by the Clinical and Laboratory Standards Institute M100-S24 [1].

This study has been approved by the Ethics Committees of Nanjing Drum Tower Hospital and Jinling Hospital (DTW-2015-033-A). A written informed content was obtained from each patient when being admitted into our hospital.

Results

During 2015, a total of 5995 isolates of nosocomial pathogens were detected, including 1707 isolates of Gram (+) (28.5%) and 3870 isolates of Gram (–) (64.5%) bacteria as well as 418 isolates of fungi (7.0%). As shown in Figure 1A, the most common types of Gram (+) bacteria were *Staphylococcus aureus* (763 isolates, 12.7%), *Enterococcus spp.* (329, 5.5%), and *coagulase-negative Staphylococcus* (261 isolates, 4.4%). The most common types of Gram (–) bacteria were *Escherichia coli* (859 isolates,

14.3%), *A. baumannii* (681 isolates, 11.3%), *Klebsiella pneumoniae* (660 isolates, 11.0%), and *P. aeruginosa* (654 isolates, 10.9%). The most common type of fungi was *Candida albicans* (250 isolates, 4.2%).

The most common sources of nosocomial pathogens were sputum (2577 isolates, 43.0%), incisional secretion (773 isolates, 12.9%), blood (432 isolates, 7.21%), catheter tip (419 isolates, 6.99%), and urine (311 isolates, 5.19%). The other sources included feces, ascites, cerebrospinal fluid, hydrothorax, pharyngeal swab, and gastric fluid.

Figure 1B–1F show the antibiotics resistance profiles of the 5 most common nosocomial pathogens. For *E. coli* (Figure 1B), imipenem (96.8%), amikacin (96.2%), cefotetan (92.0%), and piperacillin/tazobactam (89.4%) exhibited high sensitivity rates, in contrast to ampicillin (11.5%) and ampicillin/sulbactam (20.4%) that demonstrated very low sensitivity rates. For *K. pneumoniae* (Figure 1C), all antimicrobial agents exhibited a medium sensitivity rate (40%–80%), among which amikacin held the highest sensitivity (77.9%) while ampicillin/sulbactam (36.8%) and ceftriaxone (40.0%) held the lowest sensitivity. For *A. baumannii* (Figure 1D), the sensitivity rate varied between 1.3% (ceftriaxone) and 36.8% (TMP-SMZ). A very high resistant rate was observed in the majority of antimicrobial agents, varying between 63% and 82%. For *P. aeruginosa* (Figure 1E), all enrolled antibiotics demonstrated similar sensitivities (approximately 50.0–78.0%) and resistant rates (21.0–44.0%). Notably, imipenem exhibited the lowest sensitivity (50.0%) and the highest resistant rate (43.2%) to *P. aeruginosa*. For *S. aureus* (Figure 1F), linezolid, vancomycin, quinupristin/dalfopristin, and tigecycline held nearly 100% sensitivities, in contrast to penicillin G (8.1%), clindamycin (34.2%), and erythromycin (31.1%) that held significantly low sensitivities to *S. aureus*.

We further analyzed the characteristics of pathogens derived from the bloodstream (Figure 2A). A total of 769 isolates were obtained in 2015, among which the most frequent pathogen types were *K. pneumoniae* (125 isolates, 16.3%), *E. coli* (118 isolates, 15.3%), *A. baumannii* (81 isolates, 10.5%), *C. albicans* (57 isolates, 7.4%), *S. aureus* (45 isolates, 5.9%), *P. aeruginosa* (44 isolates, 5.7%), and *Enterobacterium spp.* (42 isolates, 5.5%).

Interestingly, *A. baumannii* in the bloodstream (Figure 2B) exhibited a similar drug-resistance profile as *A. baumannii* derived from all resources in hospital (Figure 1D). In contrast, *P. aeruginosa* in the bloodstream (Figure 2C) demonstrated higher resistant rates to antibiotics than that derived from all other resources (Figure 1E), indicating that *P. aeruginosa* is more difficult to be eliminated from the bloodstream by antimicrobial agents.

Figure 1. Antimicrobial resistance profiles of nosocomial pathogens. Distribution of nosocomial pathogens in 2015 (A). Antimicrobial resistance of nosocomial *Escherichia coli* (B), of *Klebsiella pneumoniae* (C), of *Acinetobacter baumannii* (D), of *Pseudomonas aeruginosa* (E), and of *Staphylococcus aureus* (F) in 2015.

Figure 2D and 2E demonstrate the resistance trend of *A. baumannii* and *P. aeruginosa* during the recent 10 years in our hospital. Notably, the resistant rate of *A. baumannii* has been dramatically increasing in the last decade (Figure 2D). Specifically, the resistant rate of *A. baumannii* to imipenem was 33.3% in 2006 and was elevated to 83.2% in the last year of the study. The resistant rate to piperacillin/tazobactam increased from 44.8% to 78.4%, the rate to ceftazidime increased from 65.0% to 83.6%, the rate to cefepime increased from 70.1% to 81.4%, and the rate to amikacin increased from 69.5% to 77.2%. The only exception was levofloxacin, for which the resistant rate was 65.5% in 2006, and has been fluctuating between 34.4% and 67.4% within the recent decade.

The resistant rate of *P. aeruginosa* to imipenem has been increasing as well, which was 30.3% in 2006 and 45.6% in 2015.

In contrast, the resistant rate of *P. aeruginosa* to piperacillin/tazobactam, ceftazidime, cefepime, and amikacin arrived at its peak in 2009, and has been decreasing in the past 6 years. The latest resistant rate to these 4 antibiotics was between 22.0~31.0% (Figure 2E).

Discussion

Antimicrobial resistance has been emerging as one of the major challenges to global physicians, microbiologists, and pharmacologists. Failure of clearance of pathogens by current antimicrobial agents causes increased mortality and morbidity, and leads to dramatic healthcare, economic, and social burdens. Besides, nosocomial infection (also referred to as hospital-acquired infection) is different from community-acquired

Figure 2. Antimicrobial resistance profiles of *Acinetobacter baumannii* and *Pseudomonas aeruginosa*. Distribution of nosocomial pathogens derived from bloodstream (**A**). Antimicrobial resistance of *Acinetobacter baumannii* (**B**) and of *Pseudomonas aeruginosa* (**C**) derived from bloodstream in 2015. Trends of antimicrobial resistance of *Acinetobacter baumannii* (**D**) and of *Pseudomonas aeruginosa* (**E**) between 2006 and 2015.

infection, and is usually more difficult to be resolved because of enhanced exposure to antibiotics. Failure of nosocomial infection control can result in serious public health events as well as heavy social and economic burdens [2]. Therefore, understanding regional antimicrobial resistant characteristics of nosocomial pathogens, especially recent trends of their resistant profiles can provide critical information for clinical drug selection, future drug development, and legislation reinforcement of nosocomial infection control.

Current literature does not provide enough information about healthcare-associated infections in Asia-Pacific developing countries [3–6]. Very few literature reports provide relevant data for mainland China. Wang et al. conducted a calendar-year prevalence survey in a single city of southeast China [7]. They reported that lower respiratory tract infection, urinary tract infection, surgical site infection, and bloodstream infection

were the most common types of infections and accounted for the majority of nosocomial infections, which was similar to our findings. They found that Gram-negative bacteria (especially *E. coli* and *A. baumannii*) were the most common isolated pathogens. Compared to their study, we further described the detailed resistance profile of the most common pathogen, and emphasized the characteristics of pathogens in bloodstream infections. We also analyzed the resistance trend of *A. baumannii* and *P. aeruginosa* during the most recent decade to draw attention to the emerging resistance rates of serious pathogens.

Recently, Li et al. reported their surveillance data of nosocomial infections specifically from intensive care units (ICUs) in east China [8]. They summarized the most common pathogens in ICUs and the associated carbapenem-resistant rates. Although their targeted surveillance in ICUs was important, they did not collect relevant data from general wards and did not provided

resistant profiles for antimicrobials other than carbapenem. In 2014, a nationwide cross-sectional survey of nosocomial infections was conducted in China [9]. More recently, Wang et al. conducted a meta-analysis of the prevalence of nosocomial infections in China [10]. Both of these studies compared the prevalence among different wards or hospitals, and summarized the most common types and pathogens of nosocomial infections, which were similar to previous reports in the literature [7]. Both studies emphasized the overall prevalence in large populations. Nevertheless, these studies did not provide details about resistant profiles for individual antimicrobials and therefore, failed to help tailor clinical antimicrobial strategies.

In our current study, we briefly summarized the distribution of nosocomial pathogens and their corresponding antimicrobial profiles in the east tertiary Chinese hospitals. Due to flexible healthcare referral policy in China [11,12], our hospital receives patients from all over the nation. Therefore, our data could potentially reflect at least regional data, and theoretically, national characteristics of nosocomial infections and antibiotic resistance.

Blood stream infection is theoretically more life-threatening since pathogens are more easily spread systemically and invade corresponding organs. Therefore, we paid particular attention to the 2 bloodstream-derived pathogens *A. baumannii* and *P. aeruginosa*, and analyzed their antimicrobial resistant trends in the most recent decade. Our data clearly showed that the resistance of *A. baumannii* is becoming increasingly serious in China, in accordance to recent emergence of multidrug resistant, extensive drug resistant, and pandrug resistant isolates of *A. baumannii* around the world [13,14].

P. aeruginosa is widely distributed in nature, whereas serious infections with *P. aeruginosa* are predominantly hospital

acquired [15]. *P. aeruginosa* becomes especially problematic when it develops resistance to multiple classes of antibiotics, even during the course of infection control. Our data demonstrated a fluctuating resistant rate of *P. aeruginosa* to individual types of antibiotics in the recent 10 years in China, which is in accordance to data reported from hospitals in the United States [16]. However, the prevalence of multi-drug resistant strains of *P. aeruginosa* becomes a more serious therapeutic challenge, especially in ICUs [17,18]. The ability to rapidly develop resistance to different drugs during treatment makes the management of *P. aeruginosa* a global challenge, although the trend to antibiotic resistance was unstable in the most recent decade, according to our study.

We are aware of our study limitations. First, this was a descriptive epidemiological study based on data collected from regional hospitals. Due to unavailable follow-up data, we failed to evaluate the impact of nosocomial infections on clinical prognosis in these patients. Second, the antimicrobial resistant profile varies between primary and tertiary healthcare facilities; therefore, our data cannot represent situations in community settings or in primary and secondary hospitals in China.

Conclusions

Our data demonstrated the characteristics of nosocomial infections and antibiotic resistance in regional China. The distinct resistance profile of each pathogen can help to tailor individual antimicrobial strategies. The emerging resistant rates of nosocomial pathogens to antimicrobials requires reinforced actions for infection prevention and control. Future multicenter studies in China are needed to describe national epidemiology of nosocomial infection and drug resistance status.

References:

- Clinical and Laboratory Standards Institute: Performance standards for antimicrobial susceptibility testing: twenty-fourth informational supplement. CLSI document M100-S24. Wayne, PA: CLSI, 2014
- Sun B: Nosocomial infection in China: Management status and solutions. *Am J Infect Control*, 2016; 44: 851–52
- World Health Organization. Report on the burden of endemic health care-associated infection worldwide: Clean care is safer care. 2011, Geneva
- World Health Organization: The burden of health care-associated infection worldwide: A summary. 2010, Geneva
- Zaidi AK, Huskins WC, Thaver D et al: Hospital-acquired neonatal infections in developing countries. *Lancet*, 2005; 365: 1175–88
- Shears P: Poverty and infection in the developing world: Healthcare-related infections and infection control in the tropics. *J Hosp Infect*, 2007; 67: 217–24
- Wang J, Hu J, Harbarth S et al: Burden of healthcare-associated infections in China: Results of the 2015 point prevalence survey in Dong Guan City. *J Hosp Infect*, 2017; 96: 132–38
- Li Y, Cao X, Ge H et al: Targeted surveillance of nosocomial infection in intensive care units of 176 hospitals in Jiangsu province, China. *J Hosp Infect*, 2018; 99: 36–41
- Ren N, Wen X, Wu A: Nationwide cross-sectional survey on healthcare-associated infection in 2014. *Chin J Infect Control*, 2016; 15: 83–87
- Wang J, Liu F, Tartari E et al: The prevalence of healthcare-associated infections in Mainland China: A systematic review and meta-analysis. *Infect Control Hosp Epidemiol*, 2018; 39: 701–9
- Eggleston K, Ling L, Qingyue M et al: Health service delivery in China: A literature review. *Health Econ*, 2008; 17: 149–65
- Henderson GE, Cohen MS: Health care in the People's Republic of China: A view from inside the system. *Am J Public Health*, 1982; 72: 1238–45
- Chinese XDR Consensus Working Group, Guan X, He L, Hu B et al: Laboratory diagnosis, clinical management and infection control of the infections caused by extensively drug-resistant Gram-negative bacilli: A Chinese consensus statement. *Clin Microbiol Infect*, 2016; 22(Suppl. 1): S15–25
- Magiorakos AP, Srinivasan A, Carey RB et al: Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: An international expert proposal for interim standard definitions for acquired resistance. *Clin Microbiol Infect*, 2012; 18: 268–81
- National Nosocomial Infections Surveillance (NNIS) System report, data summary from October 1986–April 1998, issued June 1998. *Am J Infect Control*, 1998; 26: 522–33

16. Lister PD, Wolter DJ, Hanson ND: Antibacterial-resistant *Pseudomonas aeruginosa*: Clinical impact and complex regulation of chromosomally encoded resistance mechanisms. Clin Microbiol Rev, 2009; 22: 582–610
17. Obritsch MD, Fish DN, MacLaren R, Jung R: National surveillance of antimicrobial resistance in *Pseudomonas aeruginosa* isolates obtained from intensive care unit patients from 1993 to 2002. Antimicrob Agents Chemother, 2004; 48: 4606–10
18. Livermore DM: Multiple mechanisms of antimicrobial resistance in *Pseudomonas aeruginosa*: Our worst nightmare? Clin Infect Dis, 2002; 34: 634–40