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Trends and relationship between antimicrobial resistance and antibiotic use in Xinjiang Uyghur Autonomous Region, China: Based on a 3 year surveillance data, 2014–2016

Haishaerjiang Wushouer[a], Zhao-Xia Zhang[b], Jian-Hua Wang[c], Ping Ji[b], Qing-Fang Zhu[c], Renagu Aishan[d], Lu-Wen Shi[a,e,*]

[a] Department of Pharmacy Administration and Clinical Pharmacy, Peking University Health Science Center, Beijing, China
[b] Department of Laboratory Medicine, First Affiliated Hospital of Xinjiang Medical University, Urumchi, China
[c] Department of Pharmacy, First Affiliated Hospital of Xinjiang Medical University, Urumchi, China
[d] Department of Clinical Medicine, Xinjiang Medical University, Urumchi, China
[e] International Research Center of Medical Administration (IRCMA) of Peking University, Beijing, China

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ABSTRACT

Purposes: The objective of the study was to identify the trends and relations between antimicrobial resistance (AMR) and antibiotic use in the Xinjiang Uyghur Autonomous Region in Western China from 2014 to 2016.
Methods: A retrospective, descriptive analysis of AMR prevalence, and trends and relations between AMR and antibiotic use during the 3-year period was performed.
Results: Third-generation cephalosporin-resistant *Escherichia coli* was the most prevalent resistant pathogen in terms of both resistance density and resistance proportion. A significant correlation was found between resistance density of third-generation cephalosporin-resistant *Klebsiella pneumoniae* and the use of beta-lactam–beta-lactamase inhibitor combinations (cc = 0.63, p = 0.03), quinolones (cc = 0.60, p = 0.04), and carbapenems (cc = 0.76, p = 0.004), among which only beta-lactam–beta-lactamase inhibitor combinations showed a significant correlation with third-generation cephalosporin-resistant *E. coli* (cc = 0.63, p = 0.03). For carbapenem-resistant *Pseudomonas aeruginosa*, not only carbapenem use (cc = 0.65, p = 0.02) but also penicillin (cc = 0.76, p = 0.004) and quinolone (cc = 0.69, p = 0.01) use showed significant correlation. A strong correlation was observed between the resistant proportion of third-generation cephalosporin-resistant *E. coli* and only the use of beta-lactam–beta-lactamase inhibitor combinations (cc = 0.61, p = 0.03).
Conclusion: The association between antibiotic use and AMR, especially the implication of the difference in resistance density and resistance proportion, is crucial for local physicians and decision-makers to better use of antibiotics and allocate healthcare resources more effectively, as well as to better implement antimicrobial stewardship and effective infection control strategies.

Introduction

Antimicrobial resistance (AMR) in a wide range of infectious agents is a growing global health threat [1]. Because of AMR, including multidrug resistance, the efficacy of antibiotics is currently threatened by pathogens like *Staphylococcus aureus*, Enterobacteriaceae, and *Acinetobacter baumannii* [2–5]. AMR can have an adverse effect on patients by affecting clinical outcomes such as morbidity and mortality and by incurring a significant economic burden [6,7]. It has been estimated that the global economic cost of AMR could be up to 100 trillion US dollars [8].

One of the most important factors responsible for the emergence of resistance is irrational use of antibiotics [9]. Such use can increase selective pressure, which is the key determinant of the emergence of AMR [10]. Hence, it is important to identify the spatial and temporal trends and relations between AMR and antibiotic use not only to better understand the epidemiology and burden of AMR but also to better implement antibiotic-use monitoring.

* Corresponding author at: 38 Xueyuan Road, Beijing, 100191, China. Fax: +86 1082805019.
E-mail address: shiluwen211@163.com (L.-W. Shi).

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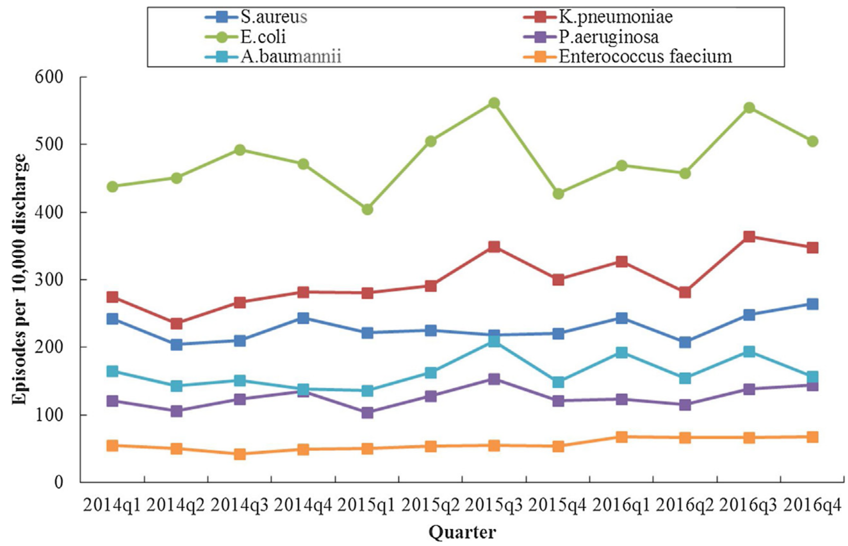

Fig. 1. Incidence (episodes per 10,000 discharged) of all infections caused by the six major pathogens.

China is estimated to be the second largest consumer of antibiotics in the world [11]. How antibiotics are used in China is crucial for global health care and the management of AMR. Since the implementation of new reform initiatives in April 2009, China's healthcare system has adopted a series of measures on antibiotic stewardship for limiting antibiotic use [12,13].

Although estimates have been made for some regions of China concerning the trends of antibiotic use and prevalence of resistance [13–17], analysis of the trends and relations between AMR and antibiotic use in the Xinjiang Uyghur Autonomous Region, a multiethnic population area in Western China, has largely been overlooked. Our study was aimed at describing and analyzing the trends and relations between antibiotic use and AMR in Xinjiang, using surveillance data for the 3-year period from 2014 to 2016.

Materials and methods

Study design

We retrospectively analyzed the aggregated quarterly surveillance data on antibiotic use and AMR from the surveillance network of participating hospitals in Xinjiang from 2014 to 2016. Data on inpatient-care settings from 36 participating hospitals across the region, which contain full records of antibiotic use and AMR for the study period, were extracted from two separate online electronic databases, respectively.

Settings

The Xinjiang Uyghur Autonomous Region is a provincial inland area of 1,660,000 km^2. Located in Northwest China, the region has 23 million inhabitants (a 2014 estimate). A regional surveillance network devoted to antibiotic use and AMR was established after a decision made by the central government in 2005. The initiative has grown in scope and size as part of the national surveillance system for antibiotic use and AMR [18]. The estimated coverage of the surveillance network is 50% of all discharged inpatients in the region as of 2014 [19].

Antibiotic use

Quarterly data on antibiotic use were extracted from prescriptions for inpatients. Antibiotics were categorized according to the Anatomic Therapeutic Chemical (ATC) classification system, expressed in defined daily doses (DDDs) as a measurement unit, following the recommendation of the World Health Organization [20]. Antibiotic use was converted into the number of DDDs per 1000 patient-days (pd) for regional and national comparisons.

Antibiotic resistance

Quarterly AMR data consisted of routine antibiotic susceptibility test (AST) results, reported to the network, for six major bacterial species (*S. aureus*, *Pseudomonas aeruginosa*, *Enterococcus faecium*, *Escherichia coli*, *Klebsiella pneumonia*, *and A. baumannii*) from all sample sources (e.g., blood, cerebrospinal fluid, bone marrow, pleural effusion, urine, and ascites) causing infections. Duplicate isolates, defined as the isolates of the same species that showed the same susceptibility results at the same site for each patient within 7 days, were excluded. AST was performed as per routine laboratory methods at each hospital, and all the hospitals adhered to Clinical and Laboratory Standards Institute (CLSI) guidelines. Minimum inhibitory concentration (MIC) assays were performed as confirmation tests for most of the drugs. The hospitals that did not perform MIC assays employed the disc diffusion method. The AST results were ascertained according to agreed protocols, and general quality and comparability of these data were evaluated by annual internal and external quality assessment exercises [15,18]. Both the proportion and density of the resistant isolates were used in the analysis for different epidemiological interpretations [21].

Statistical analysis

Quarterly incidence rates of infections with the six major bacterial species were expressed as episodes per 10,000 discharged patients. The resistance proportion was calculated by dividing the number of resistant isolates by the total number of the isolates of the same species tested against the corresponding antibiotic multiplied by 100%. Incidence density of resistant isolates was expressed as the number of resistant isolates per 1000 pd. The Spearman correlation coefficient was calculated for the association of quarterly antibiotic use and resistance. Linear regression analysis was applied to determine the trends in patient-days, trends in resistance density, and trends in antibiotic use with time. Trends in the resistance proportion were determined by the Cochrane–Armitage test. A difference with $p < 0.05$ was considered to indicate statistically significant, and all the analyses were conducted in Microsoft Excel 2013 and STATA 14.0 (StataCorp LLC, Texas, USA).

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