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Clinical characteristics and antimicrobial patterns in complicated intra-abdominal infections: a 6-year epidemiological study in southern China

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ABSTRACT

Complicated intra-abdominal infection (cIAIs) are a common and important cause of morbidity worldwide. In this study, the clinical features, microbiological profiles, antimicrobial patterns and treatments of 3233 cIAI patients (mean age, 47.6 years; 54.7% male) with 3531 hospitalisations from 2008–2013 were retrospectively investigated. The most commonly isolated bacteria were *Escherichia coli* (47.6%), *Klebsiella pneumoniae* (16.9%), *Enterococcus faecalis* (10.4%) and *Pseudomonas aeruginosa* (8.8%). Ciprofloxacin, aminoglycoside (gentamicin), piperacillin/tazobactam and carbapenems exhibited activity against 53%, 76%, 88% and 100% of extended-spectrum β-lactamase (ESBL)-positive Enterobacteriaceae isolates, respectively. *Pseudomonas aeruginosa* isolates exhibited 100%, 95%, 88%, 71% and 76% susceptibility to aminoglycoside (gentamicin), ciprofloxacin, meropenem, imipenem and ceftazidime, respectively, and *Enterococcus* remained 100% susceptible to vancomycin and linezolid. β-Lactam antibacterials other than penicillin (specifically third-generation cephalosporins) and imidazole derivatives (ornidazole and metronidazole) were the most common first-line treatments. Patients subjected to regimen change after initial antibiotic treatment had predisposing conditions (e.g. older age, more severe co-morbidities) and a higher incidence of *P. aeruginosa* infection; in addition, these patients encountered a higher average cost of care and worse clinical outcomes compared with those without medication modification. Taken together, these findings indicate the importance of appropriate initial empirical therapy and suggest the use of combination therapy comprising cephalosporins and metronidazole.

1. Introduction

Intra-abdominal infections (IAIs) are a common cause of morbidity worldwide [1]. Complicated IAIs (cIAIs) extend beyond a single organ and cause either localised or diffuse peritonitis; accordingly, treatment involves both source control and antibiotic therapy [2,3]. Despite improvements in patient care, therapeutic failures continue to occur in patients with cIAIs [4]. Such infections often result in lengthy hospital stays, require multiple antibiotics and incur high healthcare costs [5,6].

Current available guidelines on the management of cIAIs have been predominantly written for the Western context. These guidelines recommend a wide range of first-line single or multiple antimicrobial agents based on patient characteristics (e.g. co-morbidities, immunosuppression, previous antibiotic exposure), expected involved pathogens (inferred by source and origin; community- or hospital-acquired status) and local resistance epidemiology [1,7–9]. Most recent guidelines also consider the antibiotic treatment of cIAIs from a microbiological point of view, particularly in terms of pathogens producing extended spectrum β-lactamases (ESBLs).

In Asia, the management of cIAIs remains challenging and differs from practices used in Western countries in several important ways. Despite the existence of Asian-specific guidelines on antimicrobial therapy for cIAIs [10], these guidelines and surveillance programmes should be improved and re-implemented based on information gathered through investigations conducted in China.

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To date, no studies have included a cost analysis of cIAI-associated hospital care in China, even though IAIs have been ranked as the second most common infectious cause of hospitalisation after respiratory infections.

To address these issues, the present study assessed the demographics, clinical features, antibiotic susceptibilities of pathogen isolates, antibiotic use and costs associated with the treatment of cIAIs in southern China with the intent to provide surveillance information and updated guidance regarding the antimicrobial management of cIAIs in similar hospital settings.

2. Methods

2.1. Study design

This 6-year, retrospective, incidence-based observational study was conducted based on electronic medical record (EMR) data of hospitalised patients from four hospitals (Dade Road General Hospital, Fangcun, University City and Ersha Island) belonging to a healthcare conglomerate, Guangdong Provincial Hospital of Chinese Medicine. This organisation, which was established in 1933 and is headquartered in the downtown area of Guangzhou city, Guangdong Province in southern China, is the largest healthcare conglomerate to practice both Chinese and Western medicine in China, with 3140 beds and more than 5 million outpatients and 70 000 inpatients each year. The hospitals comprising this organisation, a leader of clinical research in China, established EMR systems in 2003 and became the earliest EMR adopters among all hospitals nationwide.

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki (and subsequent revisions) and the current norms for observational studies. The protocol was reviewed and approved by the Ethical Committee of Guangdong Provincial Hospital of Chinese Medicine. Due to the retrospective nature of the study, informed consent was not deemed necessary. All patient data were anonymised and de-identified prior to analysis.

2.2. Patient selection

Patients were identified by searching the EMRs of participating hospitals for discharge diagnoses suggestive of cIAI. Doctors and experts were consulted to ensure that the selected diagnoses were appropriate and applicable for infection. Most diagnoses of cIAIs can be mapped to the International Classification of Diseases 9th revision (ICD-9) codes: 540–543 (Appendicitis); 562 (Diverticula of intestine); 567 (Peritonitis and retroperitoneal infections); 569 (Other disorders of intestine); 575 (Other disorders of gallbladder); and 576 (Other disorders of biliary tract). Patients were eligible for inclusion if they had been hospitalised between 1 January 2008 and 31 December 2013.

2.3. Patient analysis

Each patient's EMR was subjected to a review of demographic information (patient age, sex, dates of hospitalisation and discharge, education level, occupation, medical insurance, marital status), co-morbidities (immunosuppression, malignancy, organ dysfunction, poor nutritional status, cardiac disease), patient lifestyle factors (smoking, alcohol use), primary and secondary discharge diagnoses, primary surgical procedures, laboratory and microbiology results (number, type and results), antibiotic therapy type and duration, status of switching to second-line antibiotic drugs, length of hospital stay and discharge status (alive or dead). The hospital ward of admission and in-hospital transfers [to other wards or to the intensive care unit (ICU)] were also recorded.

2.4. Pathological diagnosis

Bacterial species can be identified according to their unique activities, such as physiological reactions and metabolites. Accordingly, microbiological tests based on Gram staining, microscopic observation of bacterial morphotypes, characteristics in culture medium and various specific biochemical reactions were applied to identify bacteria according to Clinical and Laboratory Standards Institute (CLSI) procedures [11]. The hospitals mainly incorporated an automatic bacterial identification and susceptibility analysis system (MicroScan® WalkAway® 96 Plus; Beckman Coulter, Brea, CA). Antibiotic resistance testing was also performed according to CLSI procedures [12], and micro-organisms were tested using a susceptibility panel. The empirical antibiotic treatment principle was based on Antibacterial Drug Selection Guidelines established by the Chinese Medical Association.

2.5. Medication analysis

Only antibacterial antibiotics were analysed (ATC code J01), and regimens were considered modified if new antibiotics were administered to the patient beyond 3 days after admission.

2.6. Outcome measurement

The assessed factors included patient characteristics, pathogen characteristics, antibiotic susceptibility and clinical outcomes (length of hospital stay, recurrence rate and mortality rate). All analyses were descriptive in nature. First-line empirical antibiotic therapy was defined as effective if all isolated bacteria were sensitive to at least one of the antibiotics administered to patients documented as infection-positive. Alternatively, in patients without bacterial culture data, empirical therapy was deemed effective when a patient recovered from infection using a selected regimen.

2.7. Cost analysis

The overall cost of medications during each hospitalisation was defined as the sum of costs calculated for each type of medicine (Western or herbal medicine) received by the patient during the hospitalisation period. The costs of examination (laboratory and instrumental tests), treatment, diagnosis (including specialists' consultancies) and bed fees were directly recorded and assessed by referring to fees for service providers. Costs related to primary surgical procedures were included in treatment and were independent of the choice of antibiotic therapy.

2.8. Statistical analysis

All descriptive statistical analyses were conducted using R3.1.1 software (The R Project for Statistical Computing; https://cran.r-project.org/). Continuous variables are expressed as the mean ± standard deviation or 95% confidence intervals, and categorical variables as number of events and percentage. Student's *t*-test, the Wilcoxon rank-sum test or χ^2 test were used as appropriate for univariate statistical analysis in which baseline characteristics and outcomes of the clinical success and failure groups were compared. Fisher's exact test was used to assess the differences in categorical variables between groups. A *P*-value of <0.05 was considered statistically significant.