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Surveillance of antimicrobial use in the hospital sector: a comparison between an Italian and a Chinese reality

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ABSTRACT:

Objective: The aim of this study was to compare the pattern and general trend of antibiotic consumption during the year 2015 between an Italian and a Chinese hospital to evaluate the variability in the pathogens present and in the resulting inpatient antimicrobial prescriptions.

Methods: This study was carried out at the University Hospital of Sassari (UHS, Sassari, Italy) and at the First Hospital of Qinhuangdao (FHQ, Hebei Province, China) from January to December 2015. The study compares data of antimicrobial consumption, the kind of infections and the number and type of pathogens.

Results: The overall consumption of antimicrobial agents at the UHS was 77.3 DDD/100 bed-days, while at FHQ it was only 40.8 DDD/100 bed-days. At the UHS, Co-amoxiclav was the penicillin most largely used as well as a b-lactamase inhibitor (16.5% of the total). At the FHQ, instead, the most common drugs used were first and second generation cephalosporins (19% of the total). Infections of the respiratory, urinary and gastroenteric tract were the first three most diagnosed infections. The most isolated bacteria type was *Escherichia coli* for both hospitals (14% of the total).

Conclusions: The study highlights the variation in antimicrobial prescriptions of different geographical regions. The consumption data revealed a conspicuous use of these drugs at the University Hospital of Sassari, which was nearly twice as high than that found at the Chinese hospital. Antimicrobials were prescribed in both hospitals mainly for respiratory tract infections and *Escherichia coli* was the main cause of infections in both hospitals.

Keywords: Antimicrobials, Consumption, Surveillance, Infection Control, Inpatient.

Key messages

What is already known on this subject

- The use of antibiotics and antimicrobial resistance is a great challenge for China and Italy;
- Consumption of antimicrobials in inpatients can be measured by using defined daily doses per 100 bed-days;
- Antimicrobial stewardship programs can control microbial resistance to antibiotics in inpatients.

What this study adds

- The variability in pathogens and resulting antimicrobial prescriptions in the hospital sector of two different geographical regions;
- Variation in antimicrobial prescription across different departments;
- The preponderance of Gram-negative bacteria in the Chinese reality and Gram-positive bacteria in the Italian hospital;
- Infections of the respiratory system are the most prevalent entity of all infections in both hospitals.

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INTRODUCTION

Antimicrobial resistance is one of the major problems in global public health. The inappropriate and widespread use of antimicrobial agents is the principal cause of the increasing presence of resistant pathogens[1,2]. Antimicrobial resistance results in increased morbidity, mortality, as well as in the rising cost of health care[3,4]. Antimicrobial stewardship programs can control the resistance of microbes in inpatients[5]. Integrating the surveillance of antimicrobial use with the observation of bacterial resistance rates can direct efforts to control resistance itself[6].

The European Centre for Disease Prevention and Control (ECDC) has confirmed that Italy presents one of the highest antimicrobial resistance rates in Europe. Moreover, the resistance levels appear higher in Central and Southern Italy than Northern Italy due to the higher consumption of antibiotics registered in these geographic areas. The ECDC reported of a positive trend in the resistance of Gram-negative species from 2012 to 2015[1]. This increase was shown to be related primarily to fluoroquinolones, third generation cephalosporins and aminoglycosides in *E. coli* and in *Klebsiella pneumoniae*. The resistance of *K. pneumoniae* to carbapenems was also reported for 2015 was 8.1%. In contrast, resistance of Gram-positive bacteria has remained basically stable.

Antimicrobial consumption in China is complex and still largely unexplored. Although there have been a number of studies conducted worldwide concerning the use of antibiotics, data from studies conducted in China are still very fragmented. Recently, the number of published reports on antibiotic consumption in China has greatly increased[7]. These studies presented a high degree of variability in terms of findings, settings and other study characteristics. However, a review based on data from 57 studies found that the use of antibiotics in China is proportionally high and excessive[8-10]. The choice of the antimicrobial drug varies across hospital levels and geographical regions. The percentage in use of antibiotics has shown fluctuations over time, which may be associated with changes in national healthcare policies. The National Antibacterial Resistance Surveillance Net (Mohnarin) was founded in 2005 to monitor nationwide bacterial resistance. It reported a higher prevalence of antibiotic resistance in China than in North America and Europe[11]. Successive reports indicated that multiple-drug resistant bacteria were common throughout the country[12].

There are several measures to quantify antimicrobial use in hospitalised populations. The World Health Organization (WHO) promotes the use of the Defined Daily Dose (DDD) methodology[13]. The definition of DDD "is the assumed average maintenance dose per day for a drug used for its main indication in adults". The hospital consumption of antimicrobials is calculated by summing the total number of grams of each antimicrobial used during the period of interest (usually 1 calendar year). The result is divided by the WHO-assigned DDD. DDDs per 100 bed-days is used to compare antimicrobial use between different hospitals. Formulary composition, antibiotic potency, and hospital census do not influence the result.

A large number of studies has demonstrated a higher presence of antimicrobial resistance in intensive care units than in general patient care departments[14,15]. Other surveys have also shown that the monitoring of hospital data can change the prescription in specific patient care areas[16-18]. One of the primary goals of these studies was to understand the connection between antimicrobial use and increasing resistance of pathogens as well as to define its relationship with individual patient care areas.

The aim of our study was, instead, to compare the pattern and trends of antibiotic consumption covering the year 2015 between an Italian and a Chinese hospital to evaluate the variability in pathogens and resulting inpatient antimicrobial prescriptions.

METHODS

This study was carried out at the University Hospital of Sassari (UHS, Sassari, Italy) and at the First Hospital of Qinhuangdao (FHQ, Hebei Province, China) from January to December 2015. The UHS is an acute care hospital, composed of 41 units. The number of beds of the UHS is 520. The First Hospital of Qinhuangdao is, instead, a general hospital, including more than 49 departments. The number of beds is 1670. Both hospitals include Medical, Surgical, Paediatric and Intensive Care Units.

The data were collected from patients of all age groups and gender, who were admitted at the two hospitals during the research period. Data included information concerning the hospitals' organization (number of beds, type and number of clinical departments) and consumption of drugs. The comparison between hospital complexes of the prescribed antimicrobial daily doses was carried out using the DDD methodology, which derived from the ATC/DDD Index 2016 made by the WHO Collaborating Centre for Drug Statistics Methodology. The DDD/100 bed-days parameter was calculated using the following formula: DDD/100 bed-days = [No. of units administered in the study period (mg) x 100] / [DDD (mg) x No. of days in study period x No. of beds x bed occupancy].

Data relative to antimicrobial consumption and infections of the UHS came from the Italian "Nuovo Sistema Informativo Sanitario" (NSIS) healthcare database. To be precise, we used information on hospital discharge parameters. Details were treated respecting each patient's privacy. Data relative to the number and type of pathogens of the UHS were collected, instead, using the Mercurio Database.

Data relative to antimicrobial consumption and infections of the FHQ derived from information on the local discharge parameters since no national database is available in China to date. The same was true also for the data relative to the number and type of pathogens that was obtained from local microbiological laboratories. The identification and antibiotic susceptibility were performed using the Vitek 2 system according to the guidelines of the Clinical and Laboratory Standards Institute (CLSI).

Antimicrobial consumption data were distinguished on the basis of the following parameters: ATC level 3, ATC level 5, type of clinical department (medical, surgical, paediatric and intensive care units) and route of administration.

RESULTS

The bed occupancy at the University Hospital of Sassari during 2015 was 75%, while it was 78% at the First Hospital of Qinhuangdao for the same study period.

The overall consumption of antimicrobial agents at the UHS was 77.3 DDD/100 bed-days in 2015 (Table 1). 55.6% of the total amount was composed by drugs belonging to the J01 class, which were largely represented by penicillins (24.760 DDD/100 bed-days) and other beta-lactam antibacterials (18.243 DDD/100 bed-days). The J01M class (quinolone antibacterials) ranked third, with a consumption of 9.6 DDD/100 bed-days.

The total consumption of antimicrobials at the FHQ was, instead, 40.79 DDD/100 bed-days in 2015 (Table 1). The most used class of antimicrobials at FHQ was the J01D class (22.99 DDD/100 bed-days), followed by J01C (6.7 DDD/100 bed-days) and J01M (4.61 DDD/100 bed-days).

As reported in Table 2, Co-amoxiclav was the penicillin most largely adopted at UHS together with a b-lactamase inhibitor (12.7 DDD/100 bed-days; 16.5% of the total). Ampicillin/Sulbactam and Levofloxacin ranked in second and third position, respectively (5.9 and 5.6 DDD/100 bed-days, respectively). The Cephalosporin class (J01D) was represented by 4 drugs: Ceftriaxone, Meropenem, Cefazolin and Cefixime. When drug consumption was considered by department, Co-amoxiclav confirmed to be the most used drug in the Medical, Surgical and Pediatric Units while Amphotericin-B ranked first in the Intensive Care Unit.

Interestingly, three types of cephalosporins ranked in the first three positions at FHQ and more specifically: Cefuroxime (4.71), Cefazolin (4.62) and Cefoxitin (4.14). Thus, the drugs most commonly adopted at FHQ were first and second generation cephalosporins (Table 2).

When the consumption of antimicrobial agents was considered dividing by hospital unit (Figure 1), at UHS the medical and surgical units resulted to consume the major part of the total antimicrobials (UHS: 36.702 and 31.652 DDD/100 bed-days; FHQ: 16,145 and 19,311 respectively).

During 2015, 20.056 inpatients were recorded at UHS, of which 1316 were diagnosed with infectious diseases. The number of days of hospitalization was 12.149. The most common infections were those of the respiratory tract (508 patients), followed by infections of the urinary (N=157) and gastroenteric tract (N=155; refer to Table 3 for more details). For the same study period, 49.016 inpatients were recorded at FHQ, of which 6214 were diagnosed with infectious diseases (12.6%). The most diagnosed infections in FHQ were those of the respiratory tract (3376 patients), followed by infections of the gastroenteric tract (N=1288).

Finally, the total pathogens isolated in 2015 by the Departments of the University Hospital of Sassari figured as 6299. The most common pathogen isolated was *Escherichia coli* (14.45%), the bacterium responsible for the infections of the gastroenteric and urinary tracts as well as secondary meningitis (Table 4). The second most frequently isolated pathogen was *Streptococcus agalactiae* (8.91%), which was the common cause of respiratory tract infections. *Enterococcus faecalis* was isolated in only 8.72% of cases. For the same time frame, a total of

Table 1. DDD/100 bed-days by class of antimicrobials between the two hospitals. Antimicrobial types are listed in the Table from the most to the less consumed for each hospital.

(DDD/100 BED-DAYS)	ATC 3 DESCRIPTION	ATC 3	HOSPITALS
24.760	Beta-lactam antibacterials, penicillins	J01C	UHS
18.243	Other beta-lactam antibacterials	J01D	
9.590	Quinolone antibacterials	J01M	
5.979	Macrolides, lincosamides and streptogramins	J01F	
5.249	Drugs for treatment of tuberculosis	J04A	
5.128	Antimycotics for systemic use	J02A	
3.948	Other antibacterials	J01X	
2.880	Aminoglycoside antibacterials	J01G	
1.065	Tetracyclines	J01A	
0.437	Sulfonamides and trimethoprim	J01E	
77.30	**UHS Total**	**UHS Total**	
22.99	Other beta-lactam antibacterials	J01D	FHQ
6.70	Beta-lactam antibacterials, penicillins	J01C	
4.61	Quinolone antibacterials	J01M	
1.83	Drugs for treatment of tuberculosis	J04A	
1.58	Other antibacterials	J01X	
1.56	Macrolides, lincosamides and streptogramins	J01F	
0.90	Antimycotics for systemic use	J02A	
0.59	Aminoglycoside antibacterials	J01G	
0.05	Tetracyclines	J01A	
40.79	**FHQ Total**		

Table 2. The top 10 antimicrobials consumed in the two hospitals. Antimicrobial types are listed in the Table from the most to the less consumed for each hospital.

University Hospital of Sassari		
DDD/100 BED-DAYS	**ATC 5 DESCRIPTION**	**ATC 5**
12.74	Amoxicillin, Clavulanic Acid	J01CR02
5.90	Ampicillin, Sulbactam	J01CR01
5.56	Levofloxacin	J01MA12
4.50	Clarithromycin	J01FA09
4.39	Ceftriaxone	J01DD04
3.86	Meropenem	J01DH02
3.79	Piperacillin. Tazobactam	J01CR05
3.78	Ciprofloxacin	J01MA02
3.56	Cefazolin	J01DB04
3.06	Cefixime	J01DD08
The first hospital of Qinhuangdao		
DDD/100 BED-DAYS	**ATC 5 DESCRIPTION**	**ATC 5**
4.71	Cefuroxime	J01DC02
4.62	Cefazolin	J01DB04
4.14	Cefoxitin	J01DC01
3.45	Piperacillin and enzyme inhibitor	J01CR05
3.08	Meropenem	J01DH02
2.73	Levofloxacin	J01MA12
2.27	Cefoperazone combinations	J01DD62
1.66	Moxifloxacin	J01MA14
1.16	Amoxicillin	J01CA04
1.13	Amoxicillin and enzyme inhibitor	J01CR02

2589 strains of pathogens were isolated at the FHQ. The most common pathogen isolated figured again as *E. coli* (14.41%). The second most frequently isolated bacterium, instead, was *Pseudomonas aeruginosa* (12.44%), followed by *Acinetobacter baumannii* (11.74%).

DISCUSSION

The comparison of antimicrobial consumption between the two hospitals showed a wide use of these products by the University Hospital of Sassari, which appeared to be nearly twice as high than that found in the Chinese hospital. Even the analysis of the type of antibiotics used showed a higher consumption of protected penicillins and quinolones in Sassari's hospital departments. In the Chinese hospital, instead, first and second generation cephalosporins ranked higher than in the Italian hospital.

Antimicrobials were mainly used by the medical departments at the UHS, as opposed to the surgical departments at the FHQ. A detailed analysis comparing pathogen-directed antibiotic treatments with empirical broad-spectrum antibiotic treatments is in plan to follow this study.

Among the pathogens isolated, *Escherichia coli* figured as the most common cause of hospital infections in both health institutions. Interestingly, our study highlighted the preponderance of Gram-negative bacteria

Table 3. Number and frequency (%) of the top 3 infection types for which antimicrobial agents were adopted divided by hospital.

University Hospital of Sassari		
Ratio (%)	**N**	**Type of infection**
38.60	508	Respiratory tract
11.93	157	Urinary tract
11.78	155	Gastroenteric tract
The first hospital of Qinhuangdao		
Ratio (%)	**N**	**Type of infection**
54.32	3376	Respiratory tract
20.72	1288	Gastroenteric tract
2.22	138	Urinary tract

Table 4. Number and frequency (%) of the top 3 pathogens isolated and responsible of the infections divided by hospital.

University Hospital of Sassari		
Ratio (%)	**N**	**Pathogens**
14.45	910	*Escherichia coli*
8.91	561	*Streptococcus agalactiae*
8.72	549	*Enterococcus faecalis*
The first hospital of Qinhuangdao		
Ratio (%)	**N**	**Pathogens**
14.41	373	*Escherichia coli*
12.44	322	*Pseudomonas aeruginosa*
11.74	304	*Acinetobacter baumannii*

in the Chinese reality, while at UHS we also detected the presence of Gram-positive bacteria (*Streptococcus agalactiae* and *Enterococcus faecalis*). Antimicrobials were prescribed in both hospitals mainly for respiratory tract infections; urinary tract infections ranked second for the Italian hospital, which was substituted by gastrointestinal infections for the Chinese hospital.

CONCLUSIONS

Collecting and monitoring data concerning antimicrobial consumption is fundamental for the surveillance of antimicrobial use and to predict antimicrobial resistance. Within a wide range of infectious diseases, antimicrobial resistance is becoming an increasing threat for public health in many countries and multiple sectors. Very high rates of resistance have been observed in bacteria that cause common infections (i.e. urinary tract infections, pneumonia). Data on the resistance patterns shows that the proportion of resistant strains to commonly used antibacterial drugs exceeded 50% for bacteria like *E. coli*, *K. pneumoniae* and *S. aureus*[19]. Coordinated action and surveillance systems are thus required to minimize the emergence and spread of antimicrobial resistance.

Conflict of Interests:
The Authors declare that they have no conflict of interests.

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