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Original Article

Antimicrobial Stewardship and Resistance Patterns in Ganjavian Hospital, Dezful, Southwest of Iran: A Two-Year Analysis

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Abstract

Background: Antimicrobial stewardship studies are essential to prevent microbial resistance, ensure proper antimicrobial use, and reduce treatment costs. This study aimed to examine the prescription trends of eight costly antimicrobial agents, including carbapenem (imipenem/meropenem), voriconazole, vancomycin, liposomal amphotericin B, colistin, linezolid, teicoplanin, and caspofungin, at Ganjavian hospital in Dezful.

Methods: This cross-sectional study collected prescription forms for the eight targeted antimicrobials from March 2018 to March 2020. The recorded data included patient information, microbiological findings, infection sites, and details of antimicrobial use.

Results: The analysis of 200 patients revealed that the most common infection sites were the bloodstream (41%), respiratory system (24.5%), and unidentified sources (13%). The majority of patients were admitted to internal wards (29.5%), general intensive care units (25.5%), and neonatal intensive care units (13%). The predominant bacterial isolates were *Escherichia coli* (19.5%), *Acinetobacter baumannii* (14.5%), *Pseudomonas aeruginosa* (12.5%), and *Staphylococcus aureus* (11.5%). Multidrug-resistant (MDR) bacteria caused 53% of infections, and 33.5% were caused by bacteria resistant to all tested antimicrobials.

Conclusion: MDR bacteria pose a significant challenge, underscoring the critical need for nosocomial infection control, antimicrobial stewardship, and continuous monitoring of antimicrobial resistance patterns in this medical center.

Keywords: Antimicrobial stewardship, Drug resistance, Intensive care units, Cross infection

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Introduction

Antimicrobial resistance has emerged as a pressing global health concern. The misuse of antimicrobials, often due to unnecessary usage or incorrect selection of the drug, route of administration, dose, or duration, is a significant contributing factor (1). One of the key benefits of antimicrobial stewardship is the enhancement of patient outcomes, the efficient management of resources, and the decrease in healthcare costs.

In recent years, resistant nosocomial (hospital-acquired) infections have become a prominent cause of in-hospital mortality, and this trend is expected to escalate in the foreseeable future. The prevalence of causative pathogens varies depending on the geographical location, type of hospital, and characteristics of the population (2). Nosocomial infections are typically caused by more resistant microorganisms, resulting in prolonged hospital stays and the employment of broad-spectrum and combination antimicrobials. Studies have shown that 7% of developed nations and 10% of developing countries experience nosocomial infections (3). Alarmingly, more than 700 000 deaths occur each year due to infection with resistant bacteria, and it is estimated that these cases will reach 10 million deaths by 2050 (4).

Given the significance of the rational administration of antimicrobials to optimize the expenditure of health services and reduce microbial resistance, the deputy responsible for the treatment, in collaboration with

the Food and Drug Organization and the Association of Infectious and Tropical Diseases of the Ministry of Health in Iran, has developed and compiled a comprehensive set of guidelines for the prescription of eight costly antimicrobials. These include carbapenem (imipenem/meropenem), voriconazole, vancomycin, liposomal amphotericin B, colistin, linezolid, teicoplanin, and caspofungine.

This research endeavor sought to examine the prescription trends of eight costly antimicrobial agents, carbapenem (imipenem/meropenem), voriconazole, vancomycin, liposomal amphotericin B, colistin, linezolid, teicoplanin, and caspofungin, within the confines of Ganjavian Hospital located in Dezful.

Materials and Methods

Data Collection

The present study is a cross-sectional descriptive epidemiological study. The prescription forms of eight pricey antimicrobials, including vancomycin, liposomal amphotericin B, imipenem/meropenem, teicoplanin, linezolid, caspofungin, colistin, and voriconazole, were amassed for patients hospitalized at Ganjavian hospital in Dezful from March 2018 to March 2020. All the pertinent details encompassed within the forms, such as the file number, administration date, patient ward, age, gender, pregnancy status, lactation, microbiological findings encompassing the type of isolated pathogen, sample type, antimicrobial susceptibility test results (AST), potential site of infection, as well as the dosage and duration of treatment, were extracted. The data extraction process was thoroughly performed to ensure accuracy and dependability. The hospital staff and medical records were also consulted to cross-check and verify any inaccurate or missing information.

Inclusion Criteria

All patients who were admitted to Ganjavian Hospital during that specific time frame and received one or more antimicrobials that were of high cost were included in the study.

Exclusion Criteria

Forms that had incomplete or deficient information were not taken into consideration in the study.

Statistical Analysis

The primary objectives of the study were to determine the frequency of sources of infection, the most affected wards, the type of pathogen, the results of microbial susceptibility, and the rationale for administering expensive antimicrobials. The standard deviation was used to describe variables, while frequencies and percentages were utilized to analyze qualitative variables. The Kolmogorov-Smirnov test was performed to determine the normality of the variables. In addition, the data were analyzed using the chi-square test and t-test. The statistical analysis was performed using SPSS (version 22), considering a significance level of 0.05.

Results

The prescriptions of two hundred patients who were admitted to the hospital were thoroughly analyzed, covering a wide age range from one to ninety-three years old. These patients were treated with a minimum of one out of eight highly costly antimicrobials. The most prevalent sources of infection were the bloodstream (41%), the respiratory system (24.5%), and origins that could not be identified (13%). Our findings indicated that there was no statistically significant correlation between the gender of the patients and the location of the infection (a 95% confidence interval, $P=0.6$). The majority of the patients were admitted to the internal ward (29.5%), general intensive care units (ICUs, 25.5%), and neonatal ICU (13%), the details of which are provided in Table 1.

There was a correlation between the source of infection among patients and the specific ward they were in ($P<0.05$). The initial sites of infection observed in the internal ward primarily comprised bloodstream infections. On average, it took 7.8 ± 6.1 days from the time of hospitalization for an infection or positive culture to be detected in patients. Notably, *Escherichia coli* (19.5%), *Acinetobacter baumannii* (14.5%), *Pseudomonas aeruginosa* (12.5%), and *Staphylococcus aureus* (11.5%) were the most prevalent bacterial strains responsible for the prescription of costly antimicrobials. Other bacteria included *S. epidermidis* (11%), *Klebsiella pneumoniae* (8%), *Stenotrophomonas maltophilia* (5.5%), *Enterococcus* sp. (5%), gram-negative bacilli (4.5%), *Streptococcus* sp. (4%), *S. pneumoniae* (3%), *Citrobacter freundii* (1.5%), *Shigella* (1%), and *S. saprophyticus* (0.5%). Vancomycin and meropenem exhibited the highest incidence of prescriptions for patients, with 144 and 115 patients, respectively (Table 2). Based on the results, 97 cases (48.5%) were reported as nosocomial infections, with *A. baumannii* being the most prevalent bacteria.

Based on the results of the AST, multidrug-resistant (MDR) bacteria were responsible for infection in 53% of patients, and 33.5% of the isolated bacteria demonstrated resistance to all antibiotics. Notably, 14.5% of patients received treatment without the availability of AST results. The most notable rates of resistance to carbapenems were observed in *S. maltophilia* (81.8%), *A. baumannii* (65.51%), and *K. pneumoniae* (31.25%). Additionally, 70% of *Enterococcus* spp. isolates were vancomycin-resistant enterococci (VRE).

It is imperative to acknowledge that within the confines of this research, throughout two years of meticulous examination, no instances were observed wherein the administration of the liposomal amphotericin B, linezolid, caspofungin, and voriconazole antimicrobials was prescribed.

Discussion

The findings of this study highlight the significance

Table 1. Frequency Distribution of Sources of Infection Among Hospitalized Patients by Ward

Sources of Infection/ Inpatient Ward	Respiratory	Urinary System	Cardiovascular	Abdomen	Skin/Soft Tissue	Bloodstream infection	Unknown	Total	*P* Value
Internal ward	6	7	1	5	0	32	8	59	0.001
Pediatric	0	0	0	0	0	5	1	6	
Isolate pediatric	1	1	0	0	0	5	0	7	
Neurosurgery	1	0	0	0	0	3	1	5	
General surgery	1	0	0	2	4	4	1	12	
General ICU	28	8	0	0	0	7	8	51	
Neonatal ICU	5	1	0	1	0	16	3	26	
ICU heart	0	1	0	3	1	0	2	7	
Orthopedic	5	1	0	5	0	6	1	18	
Obstetrics and gynecology	2	0	0	2	0	4	1	9	
Total	49	19	1	18	5	82	26	200	

Note. ICU: Intensive care unit.

Table 2. Frequency of Use of Each Antibiotic and the Average Dose Prescribed by Different Bacteria

Antibiotic	Most Abundant Bacteria	Frequency (%)	Average Dose Prescribed ± SD	Lowest Dose	Highest Dose
Vancomycin	*S. aureus*	21 (14.5)	27.3 ± 17.8	1	64
	S. epidermidis	20 (13.8)	20.7 ± 16.9	1	74
	Enterococcus spp.	6 (4.16)	25.8 ± 23.6	1	66
	E. coli	19 (13.1)	19.8 ± 13.1	2	44
	A. baumannii	23 (19.1)	23.6 ± 16.0	2	60
Imipenem	*E. coli*	9 (28.1)	37.6 ± 20.4	5	64
	P. aeruginosa	6 (18.7)	45.1 ± 21.9	1	79
Meropenem	*E. coli*	25 (21.7)	22.4 ± 19.7	3	78
	A. baumannii	22 (13.9)	28.1 ± 19.3	1	71
Teicoplanin	*P. aeruginosa*.	2 (33.3)	5.0 ± 2.8	3	7
Colistin	*A. baumannii*	6 (40.0)	42.0 ± 20.0	24	72
	K. pneumoniae	4 (26.6)	31.2 ± 32.1	3	75

Note. SD: Standard deviation.

of certain Gram-negative bacteria, such as *E. coli*, *A. baumannii*, and *P. aeruginosa*, followed by *S. aureus* as a Gram-positive bacterium, in driving the prescription of expensive and broad-spectrum antibiotics. These microorganisms are commonly associated with nosocomial infections, making them pivotal in clinical settings. While antibiotic sensitivity patterns are influenced by local factors, the rise of MDR bacteria suggests that these organisms may increasingly contribute to in-hospital morbidity and mortality, warranting focused attention within healthcare systems.

International authorities consistently caution against the inappropriate use of antimicrobials and the proliferation of MDR bacteria. Studies indicate that a significant proportion (40%-70%) of antimicrobial prescriptions in long-term care facilities do not align with guidelines, emphasizing the need for judicious prescribing practices (5). A critical consideration for optimizing treatment efficacy lies in interpreting AST results. Notably, empirical treatment without AST guidance was observed in 29 patients in our study. Common factors contributing to antibiotic resistance include unwarranted prescriptions, misuse, incorrect dosing or administration routes, and timing errors (4).

Studies conducted by Ghanbari et al at Shariati hospital in Iran and Rahimi et al in Hamedan, Iran, revealed a higher prevalence of nosocomial infections in internal wards and ICUs (6,7). The primary sites of nosocomial infections identified across various studies include bloodstream infections, urinary tract infections, ventilator-associated pneumonia, and surgical site infections (8,9), which is in line with our observations.

In various studies, *S. aureus*, particularly methicillin-resistant *S. aureus*, *K. pneumoniae*, *A. baumannii*, *P. aeruginosa*, and *Enterococcus* spp., have been identified as the most prevalent nosocomial pathogens. MDR Acinetobacter is notably significant in cases of hospital-acquired pneumonia and ventilator-associated pneumonia (10,11). The analysis of the study results suggests that factors such as prolonged hospital stays, underlying illnesses, and improper catheter use significantly contribute to infections in internal wards. Additionally, the use of costly antibiotics, mechanical ventilation, especially prolonged intubation, ICU duration, and extended catheter use are

key factors in nosocomial infections and MDR bacteria in ICUs. It is crucial for healthcare providers to receive training on sterile catheter placement, judicious catheter use, and early extubation protocols to reduce ICU stays.

The predominant pathogens identified in this investigation necessitating expensive antimicrobials include *E. coli*, *A. baumannii*, *P. aeruginosa*, *S. aureus*, *K. pneumoniae*, and *S. maltophilia*. Vancomycin, imipenem, and meropenem were the most commonly prescribed antimicrobials, with vancomycin notably overused despite limited *S. aureus* cultures. While *S. aureus* isolates have shown sensitivity to vancomycin (12), their excessive initial use raises concerns for future resistance development. Notably, a significant proportion of *A. baumannii* and *S. maltophilia* isolates exhibited carbapenem resistance, emphasizing the challenge of MDR-Acinetobacter treatment.

The emergence of carbapenem-resistant *A. baumannii* during the coronavirus disease 19 pandemic underscores the evolving resistance patterns in *Acinetobacter* (13). Treatment of MDR-Acinetobacter poses a formidable challenge, with recommendations suggesting alternative regimens such as polymyxins, high-dose ampicillin-sulbactam with additional agents, or newer antibiotics. Considering the escalating resistance, refraining from carbapenem use for Acinetobacter infections without susceptibility confirmation is advised to mitigate resistance risks and optimize treatment outcomes.

The management of nosocomial infections caused by *S. maltophilia* is frequently challenging and is associated with a significant mortality rate. In instances of intricate and severe cases, it is advised to employ combined antimicrobial therapies; however, certain studies have shown that monotherapy can also be effective (14). Although there is no definitive treatment for *S. maltophilia*, trimethoprim-sulfamethoxazole (TMP/SMX) has consistently served as the primary drug, with certain beta-lactams being utilized as alternative options. Nevertheless, the correlation between clinical response and in vitro susceptibility is not always favorable (15). Our investigation has demonstrated that carbapenems are not a viable choice for treating *S. maltophilia* infections, whereas a regimen containing TMP/SMX can be deemed an appropriate treatment modality (with a susceptibility rate of over 90% to TMP/SMX). It appears that to impede the development of further resistance, the utilization of quinolones and TMP/SMX for treating *S. maltophilia* infections should be approached with greater caution and should align more closely with the results obtained from AST.

Usually, when we have carbapenem-resistant gram-negative bacteria, colistin can be used as a treatment option. In other words, based on the available evidence, colistin is the last treatment option for MDR Gram-negative bacteria such as *A. baumannii*, *P. aeruginosa*, and *K. pneumoniae* (16). In the study by Ranjan et al, 9% of carbapenem-resistant Enterobacteriaceae isolates were resistant to colistin (17). Although in this study, more than 85% of *P. aeruginosa* and 77% of Gram-negative bacilli have been sensitive to colistin, resistance to these organisms is increasing. In our study, the most common use of the colistin antibiotic was for the treatment of *A. baumannii* and *K. pneumoniae* infections, and the highest average dose of this antibiotic was related to *A. baumannii* (average: 42 doses), indicating that patients received the drug for a relatively long time (about 2 weeks). It seems that if the administration of this drug is not managed, we will probably witness more resistance to this valuable drug in the future. Considering that about 81% and 69% of cases of *Pseudomonas* and *Klebsiella* were susceptible to carbapenems, the administration of colistin is not initially recommended for the treatment of these organisms.

Enterococcus spp. is one of the major pathogens of nosocomial infections, and its prevalence in the healthcare setting is increasing. The World Health Organization has put VRE at the top of the list because there are limited treatment options for them (18). According to the results of the AST test, Kelly et al used daptomycin to treat bloodstream infections due to VRE (19). Unfortunately, in our study, 70% of enterococcal isolates were resistant to vancomycin. In the future, this hospital will face a serious challenge in treating VRE infections. We think this bacterium is a serious concern and requires prompt and sustained action to ensure that the problem does not grow. Additionally, to treat this resistant organism, we should look for new, effective antibiotics.

Limitations

- Some of the relevant forms were not properly completed by the doctors, so we had to extract the necessary information from the patient's medical records.
- The analysis was performed based on the available data since the AST was not performed for all of the considered antibiotics.

Conclusion

The two-year analysis of antimicrobial stewardship and resistance patterns at Ganjavian Hospital in Dezful, Southwest Iran, highlights the pressing challenge of MDR bacteria. The findings underscore the critical importance of robust antimicrobial stewardship practices, vigilant nosocomial infection control measures, and ongoing monitoring of antimicrobial resistance patterns to effectively combat the emergence and spread of resistant pathogens in the hospital setting.

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Competing Interests

The authors declare no conflict of interests.

Ethical Aproval

This research was confirmed by the Ethics Committees of Dezful University of Medical Sciences, Dezful, Iran (IR.DUMS.REC.1398.057).

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