Original Article

Evaluation of the Antimicrobial Resistance Pattern of Nosocomial Infections in Patients Hospitalized in Chamran Heart Educational, Medical, and Research Center of Isfahan

Mehrnoush Dianatkhah[1,2], Zeinab Sadat Davoodi[3], Rasool Soltani[1], Fatemeh Shafiee[4], Alireza Hosseini[5]

[1]Department of Clinical Pharmacy and Pharmacy Practice, Isfahan University of Medical Sciences, Isfahan, Iran

[2]Chamran Cardiovascular Medical and Research Hospital, Isfahan, Iran

[3]Infectious Diseases and Tropical Medicine Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

[4]Department of Pharmaceutical Biotechnology, Isfahan University of Medical Sciences, Isfahan, Iran

[5]Department of Cardiac Surgery, Isfahan University of Medical Sciences, Isfahan, Iran

Received: 08-04-2024.
Revised: 26-04-2024.
Accepted: 05-05-2024.
Published: 08-08-2024.

ABSTRACT

Objective: According to the importance of evaluating the antimicrobial resistance pattern in the management of nosocomial infections (NIs), we decided to investigate the prevalence of antimicrobial resistance in Chamran Heart Hospital. **Methods:** This retrospective cross-sectional observational study was performed for 6 months from February to July 2022 at Shahid Chamran Hospital of Isfahan, Iran. All hospitalized patients with any NIs were eligible for the study. Clinical specimens were obtained from patients with NIs. All specimens underwent microbial culture, and if bacterial growth developed, differential tests were performed. Antibiotic susceptibility testing also was performed per the standards of Clinical and Laboratory Standards Institute, 2022. **Findings:** Out of 201 examined samples, urinary infection (34.83%), pneumonia (27.86%), and sepsis (13.43%) were reported to be the most prevalent infections. Among Gram-negatives (76.12%), *Citrobacter* spp. (26.37%), *Escherichia coli* (24.87%), and *Klebsiella* spp. (11.44%) were the most common pathogens. About 54.9% of *Citrobacter* spp., 33.3% of *E. coli*, and 45.45% of *Klebsiella* spp. were resistant to carbapenems. About 1.88% and 15% of *Citrobacter* spp. were identified as pan-drug-resistant bacteria and extensively drug-resistant (XDR), respectively. In addition, 4.34% of *Klebsiella* spp. were identified as XDR. Among Gram-positives (23.88%), *Enterococcus* spp. (8.95%) was identified as the most common pathogen, and the prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE) was 11.11% and 61.11%, respectively. **Conclusion:** In our study, carbapenem-resistant Enterobacteriaceae accounts for about 50% of all NIs. Moreover, despite the low prevalence of MRSA, VRE was reported to be high in our center when compared with other studies.

Keywords: *Antimicrobial resistance, nosocomial infection, prevalence*

Introduction

Nosocomial infections (NIs) which complicate the usual course of hospitalization are a major therapeutic issue[1-3] and are defined as infections that occur within 48 h after hospitalization, 3 days after discharge, or 30 days after surgery.[4] The prevalence of NIs depends on various factors, and there are from 1.5% to 26.1% in different countries, and the prevalence of these infections in Iranian hospitals has been reported as 1.3%–10%.[4]

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Quick Response Code:

Website: https://journals.lww.com/jrpp

DOI: 10.4103/jrpp.jrpp_25_24

NIs can increase mortality, the duration of treatment, hospitalization costs, and antibiotic resistance, especially in developing countries.[1,3,5-7] Several factors can be considered risk factors for NIs, such as suppression of

Address for correspondence:
Dr. Zeinab Sadat Davoodi,
E-mail: zdavoodi998@gmail.com

How to cite this article: Dianatkhah M, Davoodi ZS, Soltani R, Shafiee F, Hosseini A. Evaluation of the antimicrobial resistance pattern of nosocomial infections in patients hospitalized in Chamran Heart Educational, Medical, and Research Center of Isfahan. J Res Pharm Pract 2024;12:135-40.

the immune system, old age, increasing the duration of hospitalization (stay more than 8 days in the hospital), invasive procedures, hospitalization in the intensive care unit (ICU), and the use of broad-spectrum antibiotics.[3,4,8] As a result of the high use of antimicrobial agents, infectious pathogens have changed to resistant bacteria, and this has caused a great problem in the control, prevention, and treatment of NIs.[9] The World Health Organization has named antibiotic resistance as one of the three major threats to human health.[10] The rapid spread of antimicrobial resistance and its economic burden has become a serious public health issue around the world. According to the Centers for Disease Control and Prevention (CDC) report, more than 70% of bacteria causing NIs are resistant to at least one of the drugs used to treat them, and these infections are more lethal than antibiotic-sensitive strains of the same species.[9] Since the pattern of microbial resistance determines the strategy of experimental treatment and antibiotic prophylaxis, it seems necessary to examine the pattern of microbial resistance with short intervals in medical centers.[11,12] Furthermore, based on the results of a systematic review study, monitoring the microbial prevalence pattern and microbial resistance of NI has a direct effect on reducing the rate of these infections.[7] Therefore, we decided to investigate the prevalence of NIs and the antibiotic resistance pattern at Shahid Chamran Heart Center in Isfahan, Iran.

Methods

This retrospective cross-sectional observational study was performed during 6 months from February to July 2022 at Shahid Chamran Hospital of Isfahan, Iran, affiliated to Isfahan University of Medical Sciences. The study was approved by the ethical committee of Isfahan University of Medical Sciences with the ethics ID IR.MUI.RESEARCH.REC.1400.406.

All hospitalized patients with NIs were eligible for the study. Clinical specimens (blood, urine, sputum or bronchoalveolar lavage fluid, and wound secretion) were obtained from patients with NI according to CDC definition, using standard methods and aseptic technique by the trained personnel and were immediately transported to the hospital's microbiology laboratory. All specimens underwent microbial culture, and if bacterial growth developed, differential tests were performed. Antibiotic susceptibility testing also was performed per the standards of the Clinical and Laboratory Standards Institute (CLSI, formerly National Committee for Clinical Laboratory Standards) guidelines (CLSI, 2022).[13] The resistant pattern of colistin and vancomycin was evaluated using the macrobroth dilution method, while other antibiotics were assessed by the disk diffusion method. Data analysis was done using Excel 2013.

Results

During the study period, 201 patients with NIs were recognized, of whom 107 (53.23%) were male and 94 (46.77%) were female. Most NIs were observed in ICUs (n = 105, 52.23%), followed by the pediatrics and the internal ward (n = 16, 7.96% each). Urinary tract infection (UTI) (n = 70, 34.83%) and pneumonia (n = 56, 27.86%) showed the most frequency, followed by bloodstream infection (n = 27, 13.43%) and catheter site infection (n = 16, 7.96%).

Table 1 shows the frequency of each pathogen as the causative agent of each evaluated NIs. Among Gram-negatives, *Citrobacter* spp. (n = 53; 26.37%) and *Escherichia coli* (n = 50; 24.87%), and among Gram-positives, *Enterococcus* spp. and *Staphylococcus* spp. were the most frequently isolated nosocomial pathogens.

Table 2 shows the resistance pattern of bacteria isolated from each infection site. As shown among the *Staphylococcus aureus*, the prevalence of methicillin-resistant *S. aureus* (MRSA) was 11.11%. Moreover, among the *Enterococcus* species, the prevalence of Vancomycin-Resistant Enterococcus (VRE) was 61.11%, and none of the *Staphylococcus* species was sensitive to penicillin.

This table also shows the resistance pattern of Gram-negative bacteria isolated from the infection site. As shown, 54.9% of *Citrobacter* species were resistant to carbapenem, and among the carbapenem-resistant species, 7.14%, 28.57%, 35.71%, and 10.71% were sensitive to third-generation cephalosporins, aminoglycosides, co-trimoxazole, and fluoroquinolones, respectively. The most sensitivity among carbapenem-resistant *Citrobacter* species was reported to colistin and co-trimoxazole (100% and 35%, respectively). In addition, 16.98% of all *Citrobacter* species were resistant to all four groups of mentioned antibiotics (multidrug resistance [MDR]).

About 62.5% of *Pseudomonas aeruginosa* were resistant to carbapenem and the most sensitivity among this species was reported to aminoglycosides (87.5%).

Carbapenem resistance was reported in up to 45.45% of *Klebsiella* species. Among the carbapenem-resistant species, 60%, 40%, 40%, and 40% were sensitive to third-generation cephalosporins, aminoglycosides, fluoroquinolones, and co-trimoxazole, respectively.

According to Table 2, 33.33% of *E. coli* were resistant to carbapenem and among the carbapenem-resistant species, 6.67%, 40%, 13.33%, and 6.67% were sensitive to third-generation cephalosporins, aminoglycosides, fluoroquinolones, and co-trimoxazole, respectively.

Table 1: Frequency of isolated pathogens from each nosocomial infection

Pathogen	Total	NI				
		UTI, *n* (%)	Pneumonia, *n* (%)	BSI, *n* (%)	SSI, *n* (%)	Wound infection, *n* (%)
Citrobacter spp.	53	11 (15.71)	21 (37.5)	6 (22.22)	3 (37.5)	5 (71.43)
Escherichia coli	50	39 (55.71)	9 (16.07)	0	0	0
Klebsiella spp.	23	12 (17.14)	6 (10.71)	3 (11.11)	0	0
Enterococcus spp.	18	5 (7.14)	2 (3.57)	4 (14.81)	2 (25)	0
CoNS	17	2 (2.86)	1 (1.78)	7 (25.39)	1 (12.5)	1 (14.28)
Staphylococcus aureus	11	0	3 (5.36)	3 (11.11)	1 (12.5)	0
Acinetobacter spp.	9	0	9 (16.07)	0	0	0
Pseudomonas aeruginosa	8	0	2 (3.57)	1 (3.7)	0	1 (14.28)
Enterobacter spp.	7	1 (1.43)	2 (3.57)	1 (3.7)	0	0
Moraxella	3	0	1 (1.78)	1 (3.7)	0	0
Micrococcus	2	0	0	1 (3.7)	1 (12.5)	0
Total	201	70 (100)	56 (100)	27 (100)	8 (100)	7 (100)

CoNS=Coagulase-negative *staphylococcus*, UTI=Urinary tract infection, BSI=Bloodstream infection, SSI=Surgical site infection, NI=Nosocomial infection

Table 2: Antibiotic resistance pattern of bacteria isolated from infection

Microorganism	Antibiotics	*n*	Susceptibility		
			Sensitive, *n* (%)	Intermediate, *n* (%)	Resistant, *n* (%)
Staphylococcus aureus	Penicillin	11	0	0	11 (100)
	Tetracycline	4	1 (25)	0	3 (75)
	Cefoxitin	9	8 (88.89) (MSSA)	0	1 (11.11) (MRSA)
	Clindamycin	10	6 (60)	0	4 (40)
	Co-trimoxazole	9	9 (100)	0	0
	Vancomycin	11	11 (100)	0	0
CoNS	Penicillin	17	0	0	17 (100)
	Cefoxitin	17	9 (52.94)	0	8 (47.06)
	Clindamycin	16	3 (18.75)	0	13 (81.25)
	Co-trimoxazole	13	10 (76.92)	0	3 (23.1)
	Erythromycin	16	3 (18.75)	0	13 (81.25)
	Vancomycin	17	17 (100)	0	0
Enterococcus spp.	Penicillin	18	8 (44.45)	0	10 (55.56)
	Ampicillin	18	8 (44.45)	0	10 (55.56)
	Ciprofloxacin	4	0	2 (50)	2 (50)
	Tetracycline	5	0	0	5 (100)
	Vancomycin	18	7 (38.8)	0	11 (61.11) (VRE)
Citrobacter spp.	Cefotaxime	53	12 (22.64)	0	41 (77.36)
	Ceftriaxone	53	12 (22.64)	0	41 (77.36)
	Ciprofloxacin	38	12 (31.58)	6 (15.79)	20 (52.63)
	Co-trimoxazole	42	26 (61.9)	2 (4.76)	14 (33.3)
	Carbapenem	51	9 (17.65)	14 (27.45)	28 (54.9)
	Aminoglycoside	49	24 (48.98)	6 (12.24)	19 (38.77)
Escherichia coli	Cefotaxime	50	13 (26)	0	37 (74)
	Ceftriaxone	50	13 (26)	0	37 (74)
	Ciprofloxacin	38	10 (26.31)	4 (10.53)	24 (63.16)
	Co-trimoxazole	39	14 (35.9)	0	25 (64.1)
	Carbapenem	45	18 (40)	12 (26.67)	15 (33.3)
	Aminoglycoside	48	35 (72.93)	0	13 (27.08)
Klebsiella spp.	Cefotaxime	23	13 (56.52)	0	10 (43.48)
	Ceftriaxone	23	13 (56.52)	0	10 (43.48)
	Ciprofloxacin	19	10 (52.63)	0	9 (47.37)
	Co-trimoxazole	19	13 (68.42)	0	6 (31.58)

Contd...

Table 2: Contd...

Microorganism	Antibiotics	*n*	Susceptibility		
			Sensitive, *n* (%)	Intermediate, *n* (%)	Resistant, *n* (%)
	Carbapenem	22	9 (40.9)	3 (13.64)	10 (45.45)
	Aminoglycoside	23	16 (69.56)	0	7 (30.43)
Acinetobacter spp.	Ceftazidime	9	0	0	9 (100)
	Ciprofloxacin	9	0	0	9 (100)
	Co-trimoxazole	9	0	0	9 (100)
	Carbapenem	9	0	0	9 (100)
	Aminoglycoside	9	0	0	9 (100)
Pseudomonas aeruginosa	Ceftazidime	6	4 (66.67)	2 (33.33)	0
	Ciprofloxacin	5	4 (80)	0	1 (20)
	Carbapenem	8	1 (12.5)	2 (25)	5 (62.5)
	Aminoglycoside	8	7 (87.5)	0	1 (12.5)
Enterobacter spp.	Cefotaxime	7	3 (42.86)	0	4 (57.14)
	Ceftriaxone	7	3 (42.86)	0	4 (57.14)
	Ciprofloxacin	5	3 (60)	0	2 (40)
	Co-trimoxazole	7	5 (71.43)	0	2 (28.57)
	Carbapenem	7	1 (14.28)	2 (28.57)	4 (57.14)
	Aminoglycoside	7	4 (57.14)	0	3 (42.86)
Moraxella spp.	Co-trimoxazole	3	3 (100)		

MSSA=Methicillin-sensitive *staphylococcus aureus*, MRSA=Methicillin-resistant *staphylococcus aureus*, VRE=Vancomycin-resistant enterococci

Carbapenem resistance was reported in up to 57.14% of *Enterobacter* species. Among the carbapenem-resistant species, 50%, 50%, 25%, and 50% were sensitive to third-generation cephalosporins, aminoglycosides, fluoroquinolones, and co-trimoxazole, respectively.

About 80% of *Acinetobacter* species were reported as MDR and 20% as extensively drug-resistant (XDR) (resistant to all antibacterial categories including colistin).

Discussion

In our study, the most prevalent NIs was UTI (34.83%), followed by pneumonia (27.86%). As could be expected, the highest prevalence of NIs occurred in the ICUs of the hospital.

Surprisingly, *Citrobacter* spp. was the most common pathogen in our study, which is not a common finding in similar studies. According to a study that was conducted from 2009 to 2014 in Taiwan, most of the patients who were infected with *Citrobacter* spp. infection was over 60 years old and had significant underlying diseases such as high blood pressure, diabetes, chronic kidney disease, and coronary artery disease.[14] These results are consistent with other studies.[15-18] Similarly, in our study, elderly patients who had underlying diseases were more susceptible to *Citrobacter* infection, and according to the results of our study, most of the patients who were infected with this infection had similar risk factors such as high blood pressure, diabetes mellitus, history of coronary artery bypass surgery, and kidney failure.

Based on our results, *Citrobacter* spp. was most sensitive to co-trimoxazole (61.9%) and most resistant to third-generation cephalosporins such as cefotaxime or ceftriaxone (77.36%). In a study of Korea in 2018 which evaluated patients from 2007 to 2017, 83.3%, 97%, and 100% of *Citrobacter* species were sensitive to co-trimoxazole, amikacin, and imipenem, respectively.[15] Similarly, in a study conducted in Taiwan, 72.2% of *Citrobacter* species were sensitive to co-trimoxazole,[14] and in Rajabi's study which was conducted in Kerman, the sensitivity of *Citrobacter* to co-trimoxazole was 93.7%.[4] The high percentage of *Citrobacter* sensitivity to co-trimoxazole can be related to the less prevalent use of this antimicrobial agent in Iran.

Another considerable result of our study is the point that *P. aeruginosa* was more sensitive to ceftazidime in comparison with carbapenem, which can be a result of the high use of carbapenem antibiotics and less prevalent use of ceftazidime.

MRSA is one of the most prevalent pathogens causing NIs.[19-21] In the present study, 11 cases of *S. aureus* were detected, and only one of them (11.11%) was MRSA, while in most studies, the number of MRSA species is reported to be around 50% of all *S. aureus*. For example, the prevalence of MRSA in the study which was conducted by Masoudifar *et al.* and Soltani *et al*. was reported to be 49% and 52.6%.[22,23] In our study, 61.11% of *Enterococcus* spp. were resistant to vancomycin. Similarly, in Masoudifar's study, 56.56% of *Enterococcus* spp. were resistant to vancomycin.[22]

In our study, the frequency of pan-drug-resistant and XDR *Citrobacter* was 1.88% and 15%, respectively, and the frequency of XDR *Klebsiella* was reported to be 4.34%. In Migliara's study that was conducted in Italy, *Acinetobacter baumannii* and *Klebsiella pneumoniae* had the highest MDR rates with 100% and 94%, respectively, and about 47% of *P. aeruginosa* were also reported as MDR.[24] In Davoudi's study, all cases of *Acinetobacter* were reported as MDR.[19] In our study, all cases of *Acinetobacter* were resistant to all tested antibiotics except colistin. Colistin sensitivity can be related to less and controlled use of this antimicrobial agent in Iran. The highest prevalence of NIs which caused by *Acinetobacter* spp. is related to the respiratory, especially in patients with mechanical ventilation.[25] To reduce the number of MDR microorganisms, it is necessary to choose antibiotics more carefully for the prophylaxis and treatment besides, the surgical environment should be aseptic, and wound management should be done properly.[26]

Among the limitations of the study, it can be said that in some cases, antibiotic treatment was started before the culture was sent to the laboratory, and as a result, many of those cultures were false negatives. Furthermore, due to the limitations of the hospital's facilities, it was not possible to use the methods of determining antibiotic sensitivity with broth microdilution method and Minimum Inhibitory Concentration (MIC) determination to report more accurate results of antibiotic resistance. However, our study emphasizes the importance of correct antibiotic de-escalation according to the result of cultures to prevent the overuse of antibiotics and antimicrobial resistance.

In our study, carbapenem-resistant Enterobacteriaceae accounts for about 50% of all NIs. Moreover, despite the low prevalence of MRSA, VRE was reported to be high in our center when compared with other studies. So, our study emphasizes the importance of correct antibiotic de-escalation according to the result of cultures in order to prevent over use of antibiotics and antimicrobial resistance.

Authors' Contribution

All authors contributed to the idea of the research, design of the study, data analysis, and manuscript preparation.

Financial support and sponsorship

This study was financially supported by the vice chancellery for research and technology of Isfahan University of Medical Sciences.

Conflicts of interest

There are no conflicts of interest.

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