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The prevalence and antibiotic susceptibility pattern of carbapenem-resistant *Enterobacteriaceae* in an Iranian burn center

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ABSTRACT

Carbapenems are a class of β-lactam antibiotics that are commonly used to treat multidrug-resistant (MDR) Gram-negative bacteria. However, the emergence of carbapenem-resistant strains and rapid spread across all continents become a major public health concern. In this regard, we aimed to investigate the prevalence and antibiotic resistance pattern of carbapenem-resistant *Enterobacteriaceae* (CRE) in an Iranian burn center. This retrospective cross-sectional study was performed during three years from March 2018 to March 2021 on burn victims who referred to a burn specialist hospital in the North of Iran. All bacterial isolates were differentiated and confirmed by standard microbiology methods. Disc diffusion method was applied to determine the antibiotic susceptibility pattern. CRE was defined as an isolate resistant to imipenem or/and meropenem. Totally, 33 out of 127 (26%) *Enterobacteriaceae* samples were resistance to carbapenem. Also, 66.7% of CRE were isolated from ICU and 33.3% from surgery ward. The majority of CRE (66.7%) was associated with surgical site infections (SSIs). The most prevalent CRE among the clinical samples was *Klebsiella* spp. (75.8%), followed by *Escherichia coli* (12.1%), Proteus spp. (9.1%), and *Enterobacter* spp. (3%), respectively. The antibiotic susceptibility pattern showed amikacin with 53.3% susceptibility as the most effective agents against CRE isolates. Despite the low level of CRE in our study, the high level of drug resistance among these isolates necessitating the use of unique infection control strategies and rigorous adherence to these guidelines.

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1. Introduction

Healthcare-associated infections (HAIs), also known as nosocomial infections, are a public health concern, because they are linked to additional medical complications, and increased morbidity and mortality. These infections frequently occur after hospitalization and the symptoms appear after 48-72 hours [1, 2]. The prevalence of HAIs is about less than 10% in developed and slightly more in developing countries [3], also depending on the type of infection, the mortality rates ranges from 2.3% to 14.4% [4]. The risk for HAIs depends on the facility's infection control practices, the patient's immunological condition, and the community's prevalence of various pathogens. Other risk factors that are important in causing HAIs are staying in an intensive care unit (ICU), Immunosuppressive drugs, the age and sex of the patient [5-7].

The most challenging HAIs can be caused by the presence of invasive devices including catheter-associated bloodstream infection (CABSI), ventilator-associated pneumonia (VAP), and catheter-associated urinary tract infection (CAUTI) [8, 9]. The most frequently isolated microorganisms in HAIs are *Escherichia coli*, Methicillin-resistant *Staphylococcus aureus* (MRSA), *Pseudomonas aeruginosa*, and other non-pseudomonas Gram-negative bacteria [10]. The impact of HAIs is not limited to the patient's level but also affects the community because it is associated with multidrug-resistant (MDR) infections [11]. Unfortunately, antimicrobial resistance in HAIs has increased dramatically within the past decade, such infections usually originate endogenously from the microbial components of the individual's microbiome. Many of which are showing a natural resistance against a few antibiotics and can subsequently cause infections that are difficult or even impossible to treat [12].

Carbapenems are a class of atypical β-lactam antibiotics that are used to treat HAIs caused by multidrug-resistant (MDR) organisms. Carbapenems are also safer to use than other last-line medications like polymyxins because they have fewer side effects. However, the emergence of CRE and rapid spread across all continents, primarily among Gram-negative bacteria become a major public health concern [13-15]. In this regard, we aimed to investigate the prevalence and antibiotic resistance pattern of carbapenem-resistant *Enterobacteriaceae* (CRE) in an Iranian burn center.

2. Material and methods

2.1 Study design

This retrospective cross-sectional study was performed during three years from March 2018 to March 2021 on burn victims who referred to a burn specialist hospital in the North of Iran. The demographic and clinical information of patients whose culture results are positive for CRE was entered during the study. This information includes age, gender, underlying diseases, burn percentage, and duration of hospitalization.

This study design approved by the regional ethics committee of Guilan University of Medical Sciences (IR.GUMS.REC.1400.462). Because of the retrospective nature of study, the committee waived the need for informed consent. However, all patients' personal information will remain confidential.

2.2 Microbiological methods

All samples as a part of the routine laboratory process were taken from patients and transferred to the microbiology laboratory of studied hospital. Then the samples were immediately cultured in blood agar and McConkey agar and incubated at 37 °C for 24 hours. Plates, where bacteria did not grow, were incubated for another 24 hours. After bacterial growth, all samples were differentiated and confirmed by standard microbiology methods include, Gram stain, catalase test, oxidase test, citrate utilization test, indole test, motility test, methyl red (MR) test, Voges-Proskauer (VP) test, triple sugar iron (TSI) agar test, and urease test. Disc diffusion method was applied to determine the antibiotic susceptibility pattern on Mueller–Hinton agar (Merck, Germany) according to the Clinical and Laboratory Standards Institute (CLSI) recommendations. Also, the selection of antimicrobial disks (Padtanteb, Iran) and interpretation of results for each pathogen was also based on CLSI guidelines. *Escherichia coli* ATCC 25922 were used for the standard control strains. CRE was defined as an isolate resistant to imipenem or/and meropenem.

2.3 Statically analysis

All data sorted and included in SPSS™ software, version 24 (IBM Corp., USA) for analysis. For data analysis, descriptive statistics in terms of relative frequency were applied. To describe the results, mean ± standard deviation for continuous variables and percentages of the group for categorical variables were used.

3. Results

During the study period, a total of 127 *Enterobacteriaceae* were isolated from clinical samples. Of which, 33 out of 127 (26%) isolates were CRE. The mean hospital stay was 25.3 ± 63.3 days. Also, 66.7% of CRE were isolated from ICU and 33.3% from surgery ward. The majority of CRE (66.7%) was associated with surgical site infections (SSIs). In addition, most of the CRE was isolated from patients with burn percentages between 25 and 50. The detailed results of patients infected with CRE presented in Table 1. The most prevalent CRE among the clinical samples was *Klebsiella* spp. (75.8%), followed by *Escherichia coli* (12.1%), *Proteus* spp. (9.1%), and *Enterobacter* spp. (3%), respectively. The antibiotic susceptibility pattern showed amikacin with 53.3% susceptibility as the most effective agents against CRE isolates. The full antibiotic susceptibility pattern of CRE isolates presented in Table 2.

Table 1. Demographic and clinical characteristics of 33 patients infected with CRE

Gender	
Male	69.7
Female	30.3
Age (year)	
Mean ± SD	41.2 ± 19.6
Min - Max	4 - 85
Source of isolation (%)	
ICU	66.7
Surgery ward	33.3
Type of infection (%)	
SSIs	66.7
BSI	12.1
UTI	12.1
VAP	9.1
Burn percentage (%)	
1-25	18.2
26-50	54.5
51-75	15.2
76-100	12.1
Outcome (%)	
Death	42.4
Discharged	57.6

Table 2. Antibiotic susceptibility pattern of CRE isolates

Antibiotics	Resistant (%)	Intermediate (%)	Susceptible (%)
Cefotaxime	100	0	0
Ciprofloxacin	95.6	0	4.4
Gentamicin	89.7	3.4	6.9
Cefepime	68.2	9.1	22.7
Ceftazidime	68.4	5.2	26.4
Tobramycin	47.6	23.8	28.6
Amikacin	20	26.7	53.3

4. Discussion

A serious consequence in burn patients is burn wound infection (BWI), which can cause an increasing degree of burn wound depth, healing delay, graft loss, and sepsis [16]. Healthcare facilities are increasingly hosting CRE, which are linked to high mortality rates [17].

Although the prevalence of carbapenem-resistant is increasing, this rate in our study was not remarkable. Among the 127 collected *Enterobacteriaceae* isolates, only 26% were resistant to carbapenem. However, this rate is higher than the 13% obtained by Dahab et al. in 2017 and 8.5% by Aminu et al. in 2019. The emergence of CRE during a course of treatment could pose a substantial risk of treatment failure [18].

The results showed that the most common CRE were *Klebsiella pneumoniae* with 75.8% and *E. coli* with 12.1%. A previous Iranian meta-analysis study showed the pooled prevalence of carbapenem-resistant *K. pneumoniae* and *E. coli*, 24% and 5%, respectively [19].

Also, according to our results, the most of CRE were isolated from the ICUs. This was in line with the study conducted by Correa et al., which showed that the highest CRE infection rate was in ICUs [20].

Among antibiotics tested for CRE the most effective antibiotics were aminoglycosides, particularly amikacin. Despite the several similar reports, antibiotic susceptibility patterns can be varied based on used antimicrobial stewardship, time and geographical area [21-23].

Retrospective studies are not without limitations. First of all, we have only record the pattern of locally available antibiotics. Second, the study performed in a tertiary care hospital; however, this was the only referral burn center in our region.

Despite the low level of CRE in our study, the high level of drug resistance among these isolates necessitating the use of unique infection control strategies and rigorous adherence to these guidelines.

Authors' contributions

Study design and supervision: MM, MG. Data collection and analysis of results: RA, SK. Drafting the article: SK, FK, MM, MG. Critically revisions: FK, SK. All authors read and approved the final version of article.

Conflict of interests

None to be declared.

Ethical declarations

This study design approved by the regional ethics committee of Guilan University of Medical Sciences (IR.GUMS.REC.1400.462).

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References

1. Sartelli M, Bartoli S, Borghi F, Busani S, Carsetti A, Catena F, et al. Implementation Strategies for Preventing Healthcare-Associated Infections across the Surgical Pathway: An Italian Multisociety Document. Antibiotics (Basel). 2023;12(3). DOI: 10.3390/antibiotics12030521 PMID: 36978388
2. Liu JY, Dickter JK. Nosocomial Infections: A History of Hospital-Acquired Infections. Gastrointest Endosc Clin N Am. 2020;30(4):637-52. DOI: 10.1016/j.giec.2020.06.001 PMID: 32891222
3. Khan HA, Baig FK, Mehboob R. Nosocomial infections: Epidemiology, prevention, control and surveillance. Asian Pacific Journal of Tropical Biomedicine. 2017;7(5):478-82. DOI: 10.1016/j.apjtb.2017.01.019
4. Al-Tawfiq JA, Memish ZA. Mass gathering medicine: 2014 Hajj and Umra preparation as a leading example. Int J Infect Dis. 2014;27:26-31. DOI: 10.1016/j.ijid.2014.07.001 PMID:

25128639
5. Khan KS, Reed-Embleton H, Lewis J, Saldanha J, Mahmud S. Does nosocomial COVID-19 result in increased 30-day mortality? A multi-centre observational study to identify risk factors for worse outcomes in patients with COVID-19. J Hosp Infect. 2021;107:91-4. DOI: 10.1016/j.jhin.2020.09.017 PMID: 32950587
6. Wang L, Du KN, Zhao YL, Yu YJ, Sun L, Jiang HB. Risk Factors of Nosocomial Infection for Infants in Neonatal Intensive Care Units: A Systematic Review and Meta-Analysis. Med Sci Monit. 2019;25:8213-20. DOI: 10.12659/MSM.917185 PMID: 31675354
7. Girou E, Stephan F, Novara A, Safar M, Fagon JY. Risk factors and outcome of nosocomial infections: results of a matched case-control study of ICU patients. Am J Respir Crit Care Med. 1998;157(4 Pt 1):1151-8. DOI: 10.1164/ajrccm.157.4.9701129 PMID: 9563733
8. Edwardson S, Cairns C. Nosocomial infections in the ICU. Anaesthesia & Intensive Care Med. 2019;20(1):14-8. DOI: 10.1016/j.mpaic.2018.11.004
9. Urrea M, Pons M, Serra M, Latorre C, Palomeque A. Prospective incidence study of nosocomial infections in a pediatric intensive care unit. Pediatr Infect Dis J. 2003;22(6):490-4. DOI: 10.1097/01.inf.0000069758.00079.d3 PMID: 12799503
10. Issler-Fisher AC, McKew G, Fisher OM, Harish V, Gottlieb T, Maitz PK. Risk factors for, and the effect of MRSA colonization on the clinical outcomes of severely burnt patients. Burns. 2015;41(6):1212-20. DOI: 10.1016/j.burns.2015.03.003 PMID: 26150350
11. Blot S, Depuydt P, Vandewoude K, De Bacquer D. Measuring the impact of multidrug resistance in nosocomial infection. Curr Opin Infect Dis. 2007;20(4):391-6. DOI: 10.1097/QCO.0b013e32818be6f7 PMID: 17609598
12. Sikora A, Zahra F. Nosocomial infections StatPearls [Internet]: StatPearls Publishing; 2022.
13. Wang Q, Zhang Y, Yao X, Xian H, Liu Y, Li H, et al. Risk factors and clinical outcomes for carbapenem-resistant Enterobacteriaceae nosocomial infections. Eur J Clin Microbiol Infect Dis. 2016;35(10):1679-89. DOI: 10.1007/s10096-016-2710-0 PMID: 27401905
14. Nguyen M, Joshi SG. Carbapenem resistance in Acinetobacter baumannii, and their importance in hospital-acquired infections: a scientific review. J Appl Microbiol. 2021;131(6):2715-38. DOI: 10.1111/jam.15130 PMID: 33971055
15. Nordmann P, Poirel L. Epidemiology and Diagnostics of Carbapenem Resistance in Gram-negative Bacteria. Clin Infect Dis. 2019;69(Suppl 7):S521-S8. DOI: 10.1093/cid/ciz824 PMID: 31724045
16. Church D, Elsayed S, Reid O, Winston B, Lindsay R. Burn wound infections. Clin Microbiol Rev. 2006;19(2):403-34. DOI: 10.1128/CMR.19.2.403-434.2006 PMID: 16614255
17. Sievert DM, Ricks P, Edwards JR, Schneider A, Patel J, Srinivasan A, et al. Antimicrobial-resistant pathogens associated with healthcare-associated infections: summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2009-2010. Infect Control Hosp Epidemiol. 2013;34(1):1-14. DOI: 10.1086/668770 PMID: 23221186
18. Aminu BM, Khadija ML. Antibacterial activity of local honey against Carbapenem Resistant enterobacteriaceae isolated from infected wounds. Bayero J Pure & Applied Sci. 2019;12(1):13-7. DOI: 10.4314/bajopas.v12i1.3S
19. Nasiri MJ, Mirsaeidi M, Mousavi SMJ, Arshadi M, Fardsanei F, Deihim B, et al. Prevalence and Mechanisms of Carbapenem Resistance in Klebsiella pneumoniae and Escherichia coli: A Systematic Review and Meta-Analysis of Cross-Sectional Studies from Iran. Microb Drug Resist. 2020;26(12):1491-502. DOI: 10.1089/mdr.2019.0440 PMID: 32348701
20. Correa AAF, Fortaleza C. Incidence and predictors of health care-associated infections among patients colonized with carbapenem-resistant Enterobacteriaceae. Am J Infect Control. 2019;47(2):213-6. DOI: 10.1016/j.ajic.2018.08.007 PMID: 30279017
21. Armin S, Fallah F, Karimi A, Karbasiyan F, Alebouyeh M, Rafiei Tabatabaei S, et al. Antibiotic Susceptibility Patterns for Carbapenem-Resistant Enterobacteriaceae. Int J Microbiol. 2023;2023:8920977. DOI: 10.1155/2023/8920977 PMID: 36860272
22. Davari N, Khashei R, Pourabbas B, Nikbin VS, Zand F. High frequency of carbapenem-resistant Enterobacteriaceae fecal carriage among ICU hospitalized patients from Southern Iran. Iranian J Basic Med Sci. 2022;25(12):1416.
23. Bahrami S, Shafiee F, Hakamifard A, Fazeli H, Soltani R. Antimicrobial susceptibility pattern of carbapenemase-producing Gram-negative nosocomial bacteria at Al Zahra hospital, Isfahan, Iran. Iran J Microbiol. 2021;13(1):50-7. DOI: 10.18502/ijm.v13i1.5492 PMID: 33889362