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The occurrence and antibiotic resistance pattern of *Klebsiella* isolates in burn patients in the North of Iran

Meysam Hasannejad-Bibalan[1], Ali Asqar Arabshahi[2], Nazanin Fathi[3], Mahsa Sadeghi[4], Mohammadreza Mobayen[4], Tofigh Yaghoubi[5], Reyhaneh Bonyad[5], Hadi Sedigh Ebrahim-Saraie[1*]

1. *Department of Microbiology, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran*
2. *Student Research Committee, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran*
3. *Department of Biology, Central Tehran Branch, Islamic Azad University, Tehran, Iran*
4. *Burn and Regenerative Medicine Research Center, Guilan University of Medical Sciences, Rasht, Iran*
5. *Razi Clinical Research Development Unit, Razi Hospital, Guilan University of Medical Sciences, Rasht, Iran*

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ABSTRACT

Klebsiella species are one the common bacterial etiology of burn related infections that may cause serious life threaten complications in patients. Antibiotic resistance challenge in recent years associated with increased mortality and treatment costs. Therefore, in order to optimize infection control policy and help with epidemiological data, the present study investigates the occurrence and antibiotic resistance pattern of *Klebsiella* isolates in burn patients in the North of Iran. This descriptive cross-sectional study was performed on burn patients hospitalized from March 2018 to March 2021 at Velayat Subspecialty Burn and Plastic Surgery Hospital in Rasht, the North of Iran. Standard microbiological producers were applied for the isolation and identification of *Klebsiella* isolates. Antibiotic resistance patterns were determined using the disk diffusion method. Of 594 clinical specimens, 61 cases (10.3%) were positive for *Klebsiella*. Among them, 42 samples (68.9%) were collected from intensive care units (ICUs) and 19 cases (31.1%) from internal wards. Also, 5 patients (8.2%) were related to ventilator-associated pneumonia (VAP). The highest level of antimicrobial resistance in *Klebsiella* isolates was toward imipenem (85.7%) and gentamicin (69.1%), respectively. While the highest level of susceptibility was to meropenem (63.6%). Regarding the significant prevalence and antibiotic resistance of in *Klebsiella* isolates among burn patients, more strict infection treatment protocols based on laboratory results can .prevent increased antibiotic resistance

Corresponding Author(s):
Dr. Hadi Sedigh Ebrahim-Saraie
Address: *Department of Microbiology, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran*
Tel: +98 13 33368540
E-mail: seddigh.hadi@gmail.com

1. Introduction

Nosocomial infections (NIs) or healthcare-associated infections (HAI), are those for which there is no evidence that the infection was present during admission. In other words, these infections are defined as those occurring within 48 to 72 hours of hospital admission, 3 days of discharge, or 30 days of an operation [1]. There has been a growing concern over nosocomial infections during the past decades, as this entity is closely related to antibiotic resistance [2]. HAI affects 3.2% of all hospitalized patients in the United States and 6.5% in the European Union [3]. In Iran, the overall rate of HAIs was estimated about 26.57 per 1000 patients (2.62%) [4].

The most prevalent types of NIs are urinary tract infections (UTI), bloodstream infections (BSI), surgical site infections (SSI), and ventilator-associated pneumonia (VAP) [5]. There have been many inclusive categorizations in terms of risk factors, but some of the main ones include advanced age, central venous catheter (CVC) use, admission to intensive care, emergency admission, impaired functional status and rapidly fatal underlying condition, and receiving intravenous antibiotics within the last 90 days [6, 7]. Bacteria, viruses, and fungi are the main responsible pathogens for nosocomial infections, while *C. difficile, Staphylococcus aureus*, *Klebsiella* spp., and *Escherichia coli* are the most frequently reported [8]. In studies conducted in Iran, *Klebsiella* spp*., Pseudomonas aeruginosa,* and *E. coli* were among the most prevalent pathogens [9].

Antibiotic resistance continues to be a major threat in the treatment of nosocomial infections. Unfortunately, previous reports indicated the high rate of NIs and antibiotics resistance in Iranian hospital [10, 11]. In previous the Organisation for Economic Co-operation and Development (OECD) research, the impact of antimicrobial resistance and its burden has been intensely investigated, with estimations of about $3.5 billion a year for 33 studied countries, and $2 billion a year in the United States alone [12]. Worth mentioning is the need for proper training of hospital staff for biosafety, proper waste management, and healthcare reforms and making a general reduction of nosocomial infections. Therefore, in order to optimize infection control policy and help with epidemiological data, the present study investigates the occurrence and antibiotic resistance pattern of *Klebsiella* isolates in burn patients in the North of Iran.

2. Materials and Methods

2.1. Study design and subjects

This retrospective cross-sectional study was conducted from March 2018 to March 2021 at Velayat Subspecialty Burn and Plastic Surgery Hospital in Rasht, the North of Iran. All patients with suspected infections occurring following their admission were included. During the study, all the demographic and clinical data of the patients sustaining infections were gathered, including age, sex, admission duration, and outcome. The exclusion criteria were incomplete medical records. The Ethics Committee of Guilan University of Medical Sciences approved the study design (IR.GUMS.REC.1400.280). All personal details of patients were kept strictly confidential.

2.2. Specimen and bacterial identification

Swabs or aspiration samples were collected and transferred to the microbiology laboratory using aseptic conditions. For the isolation and recognition of the *Klebsiella* spp*.,* standard procedures were carried out. Concisely, burnt site wound samples were inoculated into the blood and MacConkey agars and incubated aerobically at 37 °C for 24–48 h. The identification of the *Klebsiella* spp. was based on standard microbiological procedures, including reaction in Triple Sugar Iron Agar, Simmons' citrate agar, Christensen's urea agar, Indole test, Methyl red, and Voges-Proskauer tests. Antimicrobial susceptibility was determined and interpreted using the disk diffusion method on Mueller–Hinton agar (Merck, Germany) based on the Clinical and Laboratory Standards Institute (CLSI) recommendations.

2.3. Statistical analyses

The analyses were accomplished by using SPSS™ software, version 24.0 (IBM Corp., USA). Continuous variables were expressed as the mean ± standard deviation, and categorical variables were expressed as percentages and numbers.

3. Results

During the study period, 594 clinical specimens were obtained from hospitalized burn patients, of which 61 cases (10.3%) were due to *Klebsiella* isolates. Among these 61 cases, 44 samples (72.1%) and 17 cases (27.9%) were related to men and women. The mean age of patients was 39.15 ± 18.48 years (age range 2 to 84 years), and the mean hospital stay was 4.18 ± 4.43 days. Most of these samples were obtained from burn injury with 26-50% total body surface area (TBSA), and the 19-55 years old age group. Among them, 42 samples (68.9%) were collected from intensive care units (ICUs) and 19 cases (31.1%) from internal wards. Also, 5 cases (8.2%) of these infections were related to ventilator-associated pneumonia (VAP) patients. The outcome of 42.6% of patients was death, while 57.4% of patients were discharged.

The highest level of antimicrobial resistance in *Klebsiella* isolates was against imipenem (85.7%) and gentamicin (69.1%), respectively. In addition, the highest level of susceptibility was observed to meropenem (63.6%). Table 1 shows the patterns of antibiotic resistance of *Klebsiella* isolates.

Table 1: Antibiotic susceptibility results of 61 clinical isolates of *Klebsiella*

Class	Antibiotics	Resistant		Sensitive		Total
		No.	%	No.	%	No.
Cephalosporins IV	Cefepime	41	67.6	20	32.4	61
Cephalosporins III	Ceftazidime	41	67.9	20	32.1	61
Carbapenem	Meropenem	22	36.4	39	63.6	61
Carbapenem	Imipenem	52	85.7	9	24.3	61
Aminoglycosides	Amikacin	25	40.8	36	59.2	61
Aminoglycosides	Gentamicin	42	69.1	19	30.9	61
Aminoglycosides	Tobramycin	37	60.6	24	39.4	61
Quinolones	Ciprofloxacin	38	63	23	37	61

4. Discussion

Recent studies have shown that multidrug-resistant *K. pneumoniae* isolates have increased among burn patients in Iran [13]. Given the importance of nosocomial infections, detecting the pattern of common microorganisms and their resistance algorithm in hospital settings can improve treatment decisions [14]. It has been shown that *K. pneumoniae* is usually isolated from burn wound infections as the second most common pathogen [14, 15]. The prevalence of this bacterium in our study was 10.3%. Other studies in India, Tanzania, and Pakistan, reported the prevalence of *Klebsiella* spp. isolated from burn wounds ranging from 15.19% to 28% [15-18].

VAP is one of the most common nosocomial infections among burn patients admitted to intensive care units [19]. In our study, 8.2% of *Klebsiella* infections was linked with a VAP episode. Previously, a study by Sanchez et al., showed pneumonia as the most common clinical diagnosis [20]. Other reports suggest that burn patients with VAP have more recovery time, longer mechanical ventilation, and increased mortality [21].

Given the high resistance of isolates to multiple antibacterial agents, choosing the proper antimicrobial is a significant challenge for physicians [19]. There are many variations in antibiotic resistance in different studies. This study found high resistance to imipenem (85.7%). Consistent with our results, a recent systematic review and meta-analysis concluded that the prevalence of carbapenem-resistant *Klebsiella pneumoniae* is alarmingly high in the majority of Iranian hospitals [18]. Carbapenems have emerged as a primary factor in managing infections caused by *Klebsiella*. However, the acquisition of resistance mechanisms, including extended spectrum beta-lactamase (ESBL), has increased resistance to these antibiotics and limited treatment options [22]. Similar to our results, Ahanjan et al. reported high percentages of isolates' resistance to cephalosporins [23]. Our study showed that azithromycin and meropenem antibiotics with sensitivity (68.2%) and (63.6%) were the most effective antibiotics against *Klebsiella* isolates. If we look at Klebsiella resistance over the years, its resistance to most antibiotics has not diminished [15]. Experimental treatment and drug administration without microbial culture, overuse, and inappropriate use of broad-spectrum antibiotics are the main reasons for the increase in antibiotic resistance and treatment failure [24]. Control measures such as hand hygiene, isolation, close epidemiological surveillance, minimization of exposure to risk factors, selection of appropriate medication, and, if possible, initiation of treatment after determining the antibiotic profile can, to some extent, prevent the increase and spread of the resistant species. It should be noted that without applying the basic rules of hygiene and efficient use of disinfectants, the circulation of bacteria in the hospital cannot be effectively stopped [25] We have shown that *K. pneumoniae* remains an important isolate of burn wound infection and continues to be isolated from burn wound infections. Also, resistance to common antibiotics appears to be increasing [15]. Differences in the prevalence and susceptibility of bacteria isolated from burn wounds have been attributed to differences in treatment methods in different geographical locations. Since bacterial strains and antibiotic resistance are often subtle differences in different burn units, this study must be performed separately at each burn center to achieve a targeted clinical application using their results.

As the limitations of retrospective and monocentric studies, the results cannot be generalized. However, to achieve generalized results, it is necessary to conduct more similar studies with higher sample size and multicenter.

Regarding the significant prevalence and antibiotic resistance of in *Klebsiella* isolates among burn patients, more strict infection treatment protocols based on laboratory results can prevent increased antibiotic resistance. Hopefully, still some of the locally available antibiotics are effective for treatment of *Klebsiella* infections in burn patients.

Authors' contributions

Study design and concept: MH, TY, MM, HS. Data collection and analysis: MS, RB, MM. Drafting and critical revisions: AA, MS, NF, MH, TY, HS. All authors read and approved the final version of manuscript.

Conflict of Interest

The authors have no conflicts of interest to declare.

Ethical declarations

The Ethics Committee of Guilan University of Medical Sciences approves the research protocol (approval code: IR. GUMS. REC.1400.280).

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