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Original article

Evaluation of the Antimicrobial Resistance of *Klebsiella pneumoniae* by E-Test Method in Khatam_ol_Anbia Hospital, Tehran, Iran, during 2015

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Background: Gram-negative organisms producing Extended-spectrum beta-lactamases (ESBLs) are presented as a global problem. *Klebsiella pneumoniae* is considered as one of the most important microorganism of this group. The prevalence rate of *K. pneumoniae* species is increasing, and this increase is higher in the ESBL group, indicating the increase in antibiotic resistance. We must have sufficient knowledge about regional antibiotics resistance in order to monitor the prevalence rate and antimicrobial resistance among the isolates by appropriate treatment. In this regard, the objective of our study was to evaluate antimicrobial susceptibility among *K. pneumoniae* isolates by E-test method in Khatam ol Anbia hospital during 2015.

Materials and methods: This descriptive cross-sectional study was carried out during 2015. All clinical samples were collected from intensive care unit (ICU) and general wards of Khatam ol Anbia hospital. All of the *K. pneumoniae* strains were detected by biochemical and microscopic tests. Antimicrobial susceptibility and minimum inhibitory concentration (MIC) were determined by disk diffusion and E-test methods. Descriptive statistics was used to analyze data.

Results: About 62 *K. pneumoniae* strains were isolated from clinical samples of ICU and general wards during one year. Of these, 38 (61.3%) isolates were isolated from intensive care unit, and 24 (38.7%) isolates were isolated from the general wards. In this review, the least resistance was related to colistin (4.8%) and Amikacin (14.5%), respectively, and the most resistance was observed to the antibiotics of ciprofloxacin (66.1%), ceftriaxone (62.9%) and gentamicin (59.7%), respectively. Resistance to imipenem was observed in 38.7% of the isolates.

Conclusion: The current study demonstrates that antibiotic resistance pattern is changing, and resistance to imipenem and colistin is rising, so this should be considered as a serious risk for admitted patients in hospital.

Key words: Klebsiella pneumoniae, Antimicrobial resistance, E-test

1. Background

Klebsiella pneumoniae is one type of Gram-negative bacteria, which is known as an urgent threat to human health due to the emergence of multidrug-resistant strains associated with hospital outbreaks and hypervirulent strains associated with severe community-acquired infections (1). *Klebsiella* can lead different types of healthcare-associated infections such as pneumonia, bloodstream infections, wound or surgical site infections, and meningitis. *K. pneumoniae*, widely considered as an opportunistic pathogen, can be carried asymptomatically in the intestinal tract, skin, nose, and the throat of healthy individuals (2-3). Recently, the high prevalence rate of MDR *K. pneumoniae* species has been turned out to be worldwide. Some of the *Klebsiella* bacteria have become highly resistant to antibiotics. In recent years, by increasing the emergence of MDR *K. pneumoniae* species worldwide, this kind of infections have few treatment options (4-5) with a mortality rate upwards of 50% (6).

The greater adhesiveness and presumably invasiveness of the strains could have a vital role in the recurrent of the infections and persistence of the *K. pneumoniae* strains despite appropriate antibiotic treatment (7). However, unlike the adhesion ability, the invasive capacity of *K. pneumoniae* strains in causing liver infections (8-9) and urinary tract infections (10) is still controversial and requires further study.

Unlikeness, since the early 1970s, after *K. pneumoniae* was established in the hospital environment, epidemiology and its spectrum of infections significantly have changed and this microorganism became a leading cause of nosocomial infections, especially in developed western countries. In fact, its considerable efficiency in colonization accompanied by acquired resistance to antibiotics, has enabled *K. pneumoniae* strains to persist and spread rapidly in healthcare settings. the urinary tract, wounds, lungs, abdominal cavity, intra-vascular devices, surgical sites, soft tissues, and subsequent bacteremia infection were the most common healthcare-associated infections caused by this agent (2, 10).

K. pneumoniae outbreaks effective control requires a detailed understanding of antimicrobial drug resistance in this organism. We evaluated the prevalence rate of *K. pneumoniae* antimicrobial drug resistance in Khatam-Ol- Anbia hospital by E-test method.

2. Objectives

This study was performed in order to investigate the antibiotic resistances in *K. pneumoniae* by using E-test at the Khatam-ol-Anbia hospital during 2015. To deal with the aforementioned issues, our objective was to learn about the antibiotic resistances in every region, choose the correct treatment, and take the necessary steps to prevent further resistances, thereby reducing morbidity and mortality.

3. Materials and Methods

This was a cross-sectional study. During the project, samples containing isolated *K. pneumoniae* strains were sent to the Khatam-ol-Anbia hospital laboratory in Tehran, Iran during 2015. Traditional culture and biochemical identification tests were used for examination (11). The confirmed clinical isolates of *K. pneumoniae* were stored in Tryptic soy broth (HiMedia, India) and 15% glycerol at the temperature of -70°C.

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The clinical samples were collected from the patients in intensive care unit (ICU) and general wards of Khatam ol Anbia hospital. Antibiotic susceptibility testing was performed on Mueller–Hinton medium (bioMérieux), and the results were interpreted using Clinical and Laboratory Standards (CLSI) guidelines. Minimum inhibitory concentrations (MICs) were determined for colistin, ceftriaxone, cefepime, gentamicin, amikacin, ciprofloxacin, imipenem, and piperacillin by E-test (bioMérieux) method. Antimicrobial agent MICs were evaluated according to the Clinical and Laboratory Standards Institute guidelines (CLSI)(12).

Statistical analysis was performed using the SPSS software (v. 21; SPSS Inc., Chicago, IL, USA).

4. Results

In this study, 34 (54.8%) patients were men, and 28 (45.2%) patients were female. The percentage of samples obtained from the ICU and general wards was 61.3 and 38.7%, respectively. Distribution of clinical samples was as follow: urine 20 (32.3%) cases, sputum 17 (27.4%) cases, blood 4 (6.5%) cases, and bronchoalveolar lavage (BAL) 21 (33.89%) cases.

In this study, 62 *K. pneumoniae* strains were isolated from patients. The highest rates of resistance were belonged to ciprofloxacin (66.1%) and ceftriaxone (62.9%). The lowest rates were belonged to amikacin (14.5%) and colistin (4.8%). The resistance pattern of antibiotics is listed in Table 1.

Table 1: The resistance pattern of antibiotics.

Antibiotic	Sensitive	Intermediate	Resistance
Ceftriaxone	21(33.9)	2(3.2)	39(62.9)
Cefepime	37(59.7)	2(3.2)	23(37.1)
Gentamicin	25(40.3)	---	37(59.7)
Amikacin	53(85.5)	---	9(14.5)
Ciprofloxacin	21(33.9)	---	41(66.1)
Imipenem	38(61.3)	---	24(38.7)
Piperacillin	36(58.1)	2(3.2)	24(38.7)
Colistin	59(95.2)	---	3(4.8)

5. Discussion

Currently, the presence of MDR (multi drug resistance) bacteria is considered as a major problem in treating infectious diseases. During the past few years, the growing epidemic of infections caused by multidrug-resistant (MDR) Gram-negative bacteria, most importantly *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Klebsiella pneumoniae*, and *Escherichia coli* strains, has led to the revival of polymyxins as the last-resort treatment option worldwide (13-15)**.**

Among the most common pathogens isolated in intensive care units (ICUs) *Klebsiella* spp. have important role, and *K. pneumoniae* is the most frequently encountered carbapenemase-producing *Enterobacteriaceae* (16). Increasing antimicrobial drug resistance, including carbapenem-resistant *K. pneumoniae* (CRKP), accounts for substantial increase in illness and death.

Data from the global SENTRY Antimicrobial Surveillance Program (2006–09), which includes different centers in North America, Europe, Latin America, and the Asia-Pacific region, revealed that the overall colistin resistance rate in *K. pneumoniae* was 1.5% (17).

In three studies were reported trends in the prevalence rate of colistin resistance (18-20) , which confirmed increases in resistance. In one study in Greece, the overall prevalence rate of colistin resistance among *K. pneumoniae* isolates during 2005–2008 was 10.5%, although no resistance was observed during 1996–1998. It was reported that colistin resistance had increased at an alarming rate from 1% in 2005 to 19% in 2008. It was also reported that colistin resistance among isolates non-susceptible to imipenem had risen from 14% in 2005 to 34% in 2008. An epidemiological study of *K. pneumoniae* resistance to colistin in one region of Tunisia showed that the prevalence rate increased from 0.4% in 2005 to 1.9% in 2009. Trends towards increased colistin resistance were also confirmed by the report of the worldwide SENTRY Antimicrobial Surveillance Program, which is from 1.2% in 2006 to 1.8% in 2009 (17).

The clinician is often faced with a gram stain of a body fluid showing large, encapsulated, gram negative rods and many suspect Klebsiella colonies; however, the choice of antibiotic therapy may be difficult before the antimicrobial susceptibility pattern of the organism is known.

In another prospective study on hospital-acquired infections was done in Rome during January 2002–December 2004, after *Pseudomonas* (25%), *K. pneumoniae* was shown as the second most frequent Gram-negative species (11%)(21). In recent meta-analysis covering studies (2000–2010) on Gram-negative wound infections in hospitalized adult burn patients, *K. pneumoniae* has been reported as one of the most common Gram-negative pathogens after *P. aeruginosa* (22).

6. Conclusion

This study documents the growing incidence of ciprofloxacin resistance among *K. pneumonia* isolates. Antibiotic resistance among nosocomial pathogens have particularly been challenging in three aspects: the rising emergence of resistance to the newest antibiotics; the presence of antibiotic resistance genes on bacterial plasmids, which may be transferred among different bacterial species; and the spread of resistant bacteria among patients not only in the hospital but also in the community.

Conflict of interests

The authors declare that they have no conflicts of interest.

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Authors' Contribution

The core idea of this work came from Davood Yadegarynia and Sara Rahmati Roodsari. Zahra Arab-Mazar collected the data and acted as technical and material support.

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