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Original Research Article

Antibiotic resistance pattern in *Klebsiella pneumoniae* strains isolated from children with urinary tract infections from Tabriz hospitals

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ABSTRACT

The aim of this study was to evaluate the resistance pattern and susceptibility of some antibiotics to *K. pneumoniae* isolated from urinary tract infections. In this descriptive cross-sectional study, 165 *K. pneumoniae* strains were collected from Tabriz hospitals during six months and were identified by standard laboratory tests in a dedicated environment. Antibiotic resistance assay was performed by disk diffusion method. The highest resistance of *K. pneumoniae* isolates to tetracycline antibiotics (71.5 %), ciprofloxacin (56.9 %) and ceftriaxone (41.8 %) and the highest sensitivity to gentamicin (87.9 %), imipenem (85.5 %) and Cefepime (81.8 %) obtained. With increasing prevalence of antibiotic resistance, early detection of antibiotic resistant strain is necessary to select appropriate treatment and prevent spread of antibiotic resistance.

***Keywords*:** *Klebsiella pneumoniae*, urinary tract infection, antibiotic resistance pattern

INTRODUCTION

Klebsiella pneumoniae, Gram-negative bacilli, Non-motile, non-spore is as a saprophytic microorganism exists in the nasopharynx and human intestine [1-2]. This organism forms part of the natural microflora of the human body, and about one-third of people are intestinal carriers of the germ, and one of the common causes of nosocomial infections [3-4]. Urinary tract infections are one of the most common types of nosocomial infections [5]. These infections are usually characterized by microbiological features.

The presence of more than 10^5 microorganisms per ml of urine along with up to two bacterial species indicates bacterial infection of the urinary tract [6-7]. In the United States, the prevalence of *K. pneumoniae* clinical infections in long-term care hospitals was higher than in short-term intensive care units in 2013 [8]. Clinically, *K. pneumoniae* strain is widely colonized in hospitalized patients and is more commonly seen in immunocompromised individuals such as diabetics or patients with acquired immunodeficiency and the elderly and children [9-10]. Severe *Klebsiella* epidemics usually occur in neonates and more endemic infections in the kidney disease ward. Although *K. pneumonia* accounts for a small proportion of pneumonia cases, its mortality rate is high and about 90 % [11-12]. The high resistance of *Klebsiella* to antibiotics and their rapid spread to different parts of the hospital created major problems in treatment and cause septicemia and death [13-14]. Some organisms are inherently resistant to a number or all of the antimicrobial agents, and some organisms are resistant to other organisms by mutation mechanisms and the release of resistance genes from other organisms. Increased emergence of multidrug resistance among hospital isolates, especially *K. pneumoniae*, has limited treatment options for the treatment of infections caused by these bacteria [15]. With the widespread use of antibiotics in Iran and the increased risk of drug resistance, the objectives of this study were to determine the antibiotic resistance profile of *K. pneumoniae* clinical isolates to the most commonly used drugs for the treatment of this bacterium.

MATERIALS AND METHODS

This descriptive cross-sectional study was conducted over a six-month period from April to September in 2019. 421 specimens of children with urinary tract infections (inpatient and outpatient) were isolated in Tabriz hospitals using routine laboratory methods, microscopic examination, colonization and growth characteristics in MacConkey medium as well as biochemical tests including lactose and glucose fermentation ability, citrate utilization ability in Simon citrate medium, MRVP, motility, sulfur reduction, indole production, urease enzyme, lysine decarboxylase and orentin decarboxylase were identified. All *K. pneumoniae* isolates were stored at -78 °C in BHI medium containing 15 % glycerol until subsequent tests. Afterwards, antibiotic resistance pattern of *K. pneumoniae* isolates by CLSI agar disc diffusion method was compared to 10 antibiotic discs including ceftriaxone (30 µg), ciprofloxacin (30 µg), cefazolin (30 µg), cefotaxime (30 µg).

Gentamicin (10 µg), tetracycline (75 µg), cefepime (30 µg), imipenem (10 µg), ceftazidime (30 µg) and amikacin (30 µg) were determined by Padtan Teb Company. Antibiogram results of each sample were compared after 24 h of incubation at 37 °C according to CLSI table and recorded as sensitive (S), semi-sensitive (I) and persistent (R) [16]. At this stage, isolates that were resistant to at least three antibiotics from different families were selected as MDR strains. In order to control the quality of antibiogram steps in each of the tests with clinical isolates of *K. pneumoniae*, the sensitivity test was performed exactly on the standard strain *K. pneumoniae* ATCC 700603 and the results were compared with standard values. The obtained data were analyzed by SPSS software.

RESULTS

Among 421 samples studied, 165 were positive for *K. pneumoniae* (39.2 %), 89 of which were female (53.9 %) and 76 were male (46.1 %). Outpatient ward was 119 samples (72.1 %) and inpatient ward 46 samples (27.8 %). Mean age of patients was 7.6 ± 2.8 years from minimum 5 years up to 13 years. According to antibiotic susceptibility test, *K. pneumoniae* had the highest resistance to tetracycline antibiotics (71.5 %), ciprofloxacin (56.9 %) and ceftriaxone (41.8 %) and the highest antibiotic susceptibility to gentamicin (87.8 %), imipenem (85.4 %), and cefepime (81.8 %) showed.

Table 1. Antibiotic profile of *K. pneumoniae* strains isolated from urinary tract infections

Antibiotics	Sensitive(S)	Intermediate(I)	Resistant(R)
ceftriaxone	41.20	16.97	41.83
ciprofloxacin	30.91	12.12	56.97
cefazolin	64.84	11.52	23.64
cefotaxime	48.48	16.37	35.15
Gentamicin	87.86	6.06	6.07
tetracycline	21.21	7.27	71.52
cefepime	81.82	5.45	12.73
imipenem	85.46	8.48	6.06
ceftazidime	76.37	5.45	18.18
amikacin	57.57	12.73	19.70

DISCUSSION

However, many researchers have focused on antibiotic resistance in bacteria isolated from patients in hospitals as well as bacteria that have a direct detrimental effect on human health, but the spread of resistance to antibiotics is a natural ecological phenomenon that has evolved for billions of years [17-18]. In the present study, out of 421 urine samples of inpatient and outpatient urinary tract pathogens, 165 samples of *K. pneumoniae* were positive (39.1 %). 89 of which were female (53.9 %) and 76 were male (46.0 %). Khalili reported 82.8 % of positive urine cultures for females and 17.2 % for males [19]. The results of this study indicate that girls are more boys to urinary tract infections, including *K. pneumoniae* than men. There can be several reasons, one of which being the shortness of the urethra and the closeness of the mouth to the anus in girls. In contrast to the different anatomical systems of the male urinary tract with prostate secretions containing bactericidal substances. Collectively, they can play an important role in preventing the invasion of pathogenic bacteria [20]. The increased use of antibiotics in recent years has led to the emergence and spread of resistant bacteria, especially MDR multidrug resistant strains.

Today, treatment of many infections caused by important pathogens such as *K. pneumoniae* is associated with many problems and increases the risk of death.

According to the results of this study, tetracycline (71.5 %), ciprofloxacin (56.9 %) and ceftriaxone (41.8 %) were the most resistant isolates of *K. pneumoniae*. In Paterson study, *K. pneumoniae* strains isolated from patients with bacteremia, 5.5 % of the isolates were resistant to ciprofloxacin. In another study in Turkey, 42 % of the isolates were resistant to ciprofloxacin. In Argentina, the United States and Taiwan, 15, 9 and 6 % of *K. pneumoniae* isolates were resistant to ciprofloxacin, respectively. Other studies have not reported ciprofloxacin resistance in South Africa, Australia and Belgium [21]. According to research by Amirmozafari, resistance to cefixime, ceftriaxone, cefotaxime, ceftazidime, ceftizoxime 100 % and drug resistance to tetracycline has been reported to be 80 % [22]. In 2015, Roudbari reported resistance of *K. pneumoniae* to antibiotics cefazolin, cefepime, ceftazidime, trimethoprim sulfamethoxazole, 54.44, 49.46, 45.19, and

46.2 %, respectively [23]. Tavakol and Momtaz reported resistance to tetracycline (72 %) and ciprofloxacin (54 %) and sensitivity to gentamicin (92 %) and cefepime (86 %), respectively [6]. Taslima in 2007 reported in Bangladesh the resistance of this bacterium to ceftazidime (36 %), gentamicin (27 %), tetracycline (27 %), and ciprofloxacin (45 %) [20]. Yousefi in Borujerd and Hamadan hospitals, resistance of *K. pneumoniae* to cefixime antibiotics 46.7 %, ceftriaxone 43.3 %, azetronam 43.3 %, cefotaxime 41.7 %, cotrimaxazole 40.8 %, ceftazidime 36.7 % and sensitivity to imipenem antibiotics 0 %, ciprofloxacin 16.7 %, cefepime 25 % and gentamicin 26.7 % reported [24]. In 2011, Langarizadeh reported the antibiotic resistance pattern of 72 *K. pneumoniae* strains isolated from urine samples as follows: amoxicillin 98.6 %, co-trimoxazole 95.8 %, nitrofurantoin 94.4 %, ceftazidime 80.5 %, cephalothin 77.7 %, gentamicin 73.6 %, tetracycline 72.2 %, nalidixic acid 58.3 %, chloramphenicol 48.6 %, norfloxacin, amikacin and ciprofloxacin 43.0 % and imipenem 1.4 % [25]. Therefore, according to the results of the present study, the resistance of the isolates compared to the mentioned studies has some differences that can be attributed to the sample size or the sampling method.

In the present study 88 (53.3 %) of 165 *K. pneumoniae* isolates were MDR multiple drug resistance samples. This rate was 55 % and 67.9 % in the Hashemizadeh study, in 2013 and Langarizadeh study in 2011, respectively, which is higher than the present study [25-26]. The prevalence of these strains has many causes and may be due to incorrect administration of antibiotics in the treatment of various infections or transmission of resistance genes by various transport agents such as R plasmids, bacteriophages, transposons and integrons [27].

CONCLUSION

This finding indicated that the antibiotic resistance of *K. pneumoniae* strains was very high in the study area, which, if not adequately addressed, will have irreparable health and therapeutic consequences in the near future. Therefore, it is imperative that the treatment regimen used by physicians was based on the results of the antibiogram performed by the clinical microbiology laboratory.

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