FREQUENCY AND ANTIMICROBIAL SUSCEPTIBILITY OF KLEBSIELLA SPECIES ISOLATED FROM URINE CULTURES AT A TERTIARY HEALTHCARE FACILITY OF LAHORE

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Abstract

Background and Objective: Klebsiella is found ubiquitously in nature and is a potential pathogen to infect different anatomic sites including urinary tract. Due to high resistance to antimicrobials it is considered as one of the most challenging pathogens. The study aimed to determine the frequency and antimicrobial sensitivity of Klebsiella species isolated from urine.

Methods: The data of urine cultures conducted during 1st Sep 2021 to 31st Aug 2022 was collected through Electronic Medical Record system. Uropathogens were recognized based on culture characteristics and biochemical tests with API-20E (bioMérieux) profile. Antibiotic susceptibility and extended spectrum beta-lactamase (ESBL) detection was performed by disc/combined disc diffusion using Kirby Bauer method.

Results: Of 2438 urine samples submitted for culture during the study period, 746 (30.6%) showed significant growth of a known uropathogen. The frequency of Klebsiella was 14.75% which was second most common uropathogen after E. coli (57.37%). Other isolates reported were Enterococcus (12.87%), Candida (8.71%), Pseudomonas (2.68%), Staphylococcus (1.48%), Proteus (1.07%) and Citrobacter species (1.07%). The isolates showed high sensitivity to imipenem (87.3%) followed by meropenem (85.5%), amikacin (84.6%) and fosfomycin (81.5%). A reduced sensitivity was observed against gentamicin (68.2%), piperacillin-tazobactam (61.8%), nitrofurantoin (58.2%) and cefotaxime (50%), but the least sensitivity was seen for ciprofloxacin (40.9%), cotrimoxazole (36.4%), cefuroxime (20%) and ampicillin (10%). Of all isolates 37 (33.6%) were ESBL producers.

Conclusion: Carbapenems, amikacin and possibly fosfomycin are the most efficient drugs for treating UTI due to Klebsiella species in our hospital setting. An on-going surveillance for ESBL producers as well as carbapenemase-producing Klebsiella pneumoniae (KPC) is needed.

Key words: Antibiotic susceptibility, Frequency, Klebsiella, UTI

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Numerous studies have well established the microbial etiology of urinary tract infection (UTI), with E. coli being the most common and Klebsiella the second commonest causative agent affecting individuals of all ages and genders, especially in hospitalized patients.[1,2] Females are more susceptible to such infections than males due to proximity of urethral orifice to the perianal area where E. coli, Klebsiella and other organisms of the gut flora are common.[3] The genus Klebsiella belongs to the Enterobacteriaceae family and has potential to cause a variety of infections including UTI, especially in hospitalized patients.[4] The virulence factors of Klebsiella include capsular polysaccharides, lipopolysaccharide (LPS), and iron-scavenging mechanisms. Being encapsulated, its capability

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to escape the defence mechanisms, its developing resistance against antimicrobials as well as the development of hypervirulent pathotypes have emerged as a main encounter in the healthcare industry. Such infections can occur everywhere in the body, including urinary tract infections. The most important species in this family causing opportunistic nosocomial infections is K. pneumoniae. It is a potential pathogen skilled to colonize, invade, and cause infections in different anatomical site. The other medically important species is K. oxytoca.

The Klebsiella species may have varying levels of resistance to antibiotics used in therapy as well as disinfectants used in hospitals. Many studies have shown a considerably high resistance to commonly used antimicrobials for K. pneumoniae urinary isolates.[5] Klebsiellae can produce extended-spectrum beta-lactamases (ESBLs) which enable these to get resistance against most beta-lactams, including cephalosporins and monobactams. However, carbapenems and cephamycins are not affected. The developing countries have witnessed an increased prevalence of ESBL-producing bacteria over the past several years.[6,7] Due to the acquisition of plasmids conferring multidrug resistance (MDR), nosocomial isolates are commonly resistant to a wide range of drugs.[8] Such ESBL isolates often carry genes which can confer resistance to other classes of antibiotics too including aminoglycosides, chloramphenicol, co-trimoxazole and fluoroquinolones.[9] Resultantly, many of such bacterial strains become MDR and infection by such highly resistant isolates upsurges the likelihood of treatment failure causing high mortality.[10,11] K. pneumoniae is amongst the important ESBL-producing members of Enterobacteriaceae with the prospective to cause a variety of infections, especially nosocomial, consequently resulting in higher mortality and morbidity in addition to higher healthcare overheads.[12]

Many K. pneumoniae strains have developed high resistance to antibiotics due to their capability to form an enzyme known as a carbapenemase. Such K. pneumoniae carbapenemase producing strains are stated as KPC. These are hard to treat since these have high levels of resistance to multiple antibiotics. In fact more infections caused by Klebsiella are because of multi-drug-resistant hypervirulent (MDR-hv) strains.[13-16] Klebsiella, therefore, creates problems for physicians due to multi-drug resistance displayed by this bacterium. Of particular concern is an important emergent tendency in ESBLs producing Klebsiellae and carbapenem-resistance ratio in Klebsiella urinary isolates that are often resistant to other routinely used antibiotics too.[17] The resulting limitations on the therapeutic choices mandate innovative actions for the management of Klebsiella nosocomial infections. The identification of ESBLs and KPC producing bacteria is essential for applicable antibiotic use and infection control practices to reduce the spread of these strains. The current study designed to determine the frequency of Klebsiella isolates causing UTIs and to find out their antibiotic susceptibility so as to provide guidelines to our physicians for appropriate antibiotic treatment.

METHODS

Institutional Review Board approved the study vide Letter No. SMDC-IRB/AL/151/2021 Dated 28.08.2021. The data of the isolates from urine samples was collected through Electronic Medical Record (EMR) system of the hospital from 1st Sep 2021 to 31st Aug 2022. During the study period, a total 2438 samples of urine for cultures from both in-patients and out-patients of all ages and genders were submitted to Shalamar Hospital Laboratory. The uropathogens were recognized by culture characteristics and biochemical tests including API-20E (BioMérieux). Antibiotic susceptibility and extended spectrum beta-lactamase (ESBL) detection was performed by disc/combined disc diffusion tests using Kirby Bauer method. The data analysis involved transcription, primary data inspection, and content analysis. Statistical analysis was done by descriptive statistics using ratio and percentages. Microsoft Excel was used to make tables and charts. Qualitative variables were expressed as rates and percentages.

RESULTS

Out of all 2438 samples, 746 (30.6%) showed sig-

nificant growth of a known uropathogen. Table-1 shows the types and frequency of all uropathogens isolated. The overall isolation rate of Klebsiella spp was 4.5%. However, amongst all uropathogens, the frequency of Klebsiella was 14.75% which was second most common uropathogen after E. coli (57.37%). The other uropathogens reported were Enterococcus spp (12.87%), Candida spp (8.71%), Pseudomonas spp (2.68%), Staphylococcus spp (1.48%), Proteus spp (1.07%) and Citrobacter spp (1.07%).

Table 1: *Types and frequency of all uropathogens isolated (n=746)*

Uropathogen	No. of Positive Cultures	Percentage
1. *E. coli*	428	57.37%
2. Klebsiella spp.	110	14.75%
3. Enterococcus spp.	96	12.87%
4. Candida spp.	65	8.71%
5. Pseudomonas spp.	20	2.68%
6. Staphylococcus spp.	11	1.48%
7. Proteus spp.	8	1.07%
8. Citrobacter spp.	8	1.07%
Total	**746**	**100%**

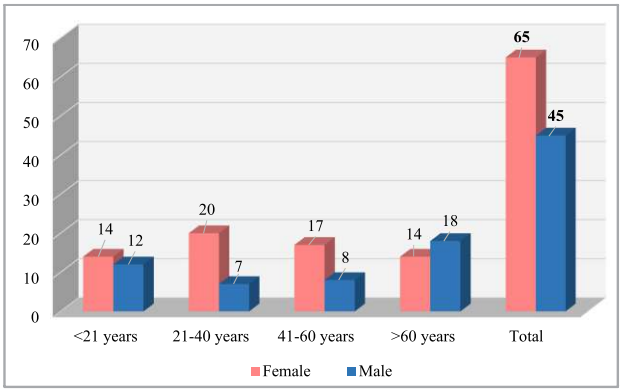

Figure-1: *Age and gender-wise distribution of patients with Klebsiella UTI*

Figure-1 shows gender-wise distribution of Klebsiella isolates in different age groups of patients. Amongst samples showing positive cultures of Klebsiella species, 65 (59.1%) belonged to female and 45 (40.9%) to male patients. Moreover, the frequency of UTI caused by Klebsiella species varied in different age groups. The isolation rate of Klebsiella species in female patients having UTI were higher in their younger and adult age groups. Two important species of Klebsiella isolated were K. pneumoniae 92 (83.6%) and K. oxytoca 18 (16.4%).

Figure-2 shows antimicrobial susceptibility of Klebsiella species isolates against commonly used antibiotics which varied significantly with the type of antibiotic tested. The isolates showed maximum sensitivity to imipenem (87.3%) followed by meropenem (85.5%), amikacin (84.6%) and fosfomycin (81.8%). A reduced sensitivity was observed against gentamicin (68.2%), piperacillin-tazobactam (61.8%), nitrofurantoin (58.2%) and cefotaxime (50%), but the least sensitivity was seen for ciprofloxacin (40.9%), cotrimoxazole (36.4%), cefuroxime (20%) and ampicillin (10%). Of all isolates 37 (33.6%) were ESBL producers.

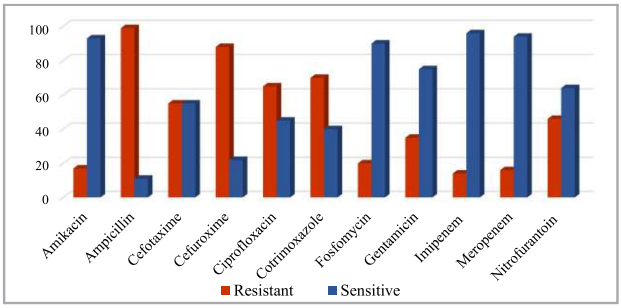

Figure-2: *Antimicrobial susceptibility of Klebsiella isolates (n=110)*

DISCUSSION

Infections of the urinary tract (UTIs) have been documented as the second most common infections in humans.[18] Microbial etiology of UTIs has been well established, with Klebsiella being the second commonest causative agent after Escherichia coli. Klebsiella is an important bacterial pathogen which is ubiquitous in different environments, particularly in healthcare hubs. Irrespective of advances in healthcare field this multidrug resistant pathogen is responsible for nosocomial infections of grave nature. The current study mainly focused on the description of antimicrobial susceptibility profile of Klebsiella species recovered from urine specimens. The relative frequency of this pathogen as compared to other pathogens isolated was also observed. Out of all, 30.6% samples showed significant growth of a known uropathogen. The recovery rate of uropatho-

gens found in the present study is in accord with several such studies showing an overall similar prevalence of UTI.[19,20] However, many other studies have shown variable frequency. For example one study conducted in Ethiopia has documented an overall occurrence of UTI in the region as 90.1%.[21]. Similarly, another study conducted in Eastern Nepal has documented an overall prevalence of UTI as 82.3%.[22] Our study has shown the frequency of Klebsiella amongst all uropathogens as 14.75% which was the second most common uropathogen. This finding of Klebsiella being the second commonest genus of the Enterobacteriaceae family after E. coli has been described in many studies conducted previously.[22,23] In a meta-analysis, the results of several studies pooled for knowing the frequency of K. pneumoniae in positive clinical isolates was found to be 16%.[24]

Two important species of genus Klebsiella detected in the present study were K. pneumoniae (83.6%) and K. oxytoca (16.4%). This finding has been documented in many previous analogous studies. One such study has reported that among Klebsiella species isolated, 89% were K. pneumoniae and 11% were K. oxytoca. Majority of uropathogens were recovered from women samples. This result is in concordance with results of several such studies conducted previously. In a cumulative manner, the females belonging to younger and adult age groups accounted for a substantial number of isolates. Female to male ratio was highest in age bracket of 21–60 years and low in the age lot of beyond 60 years. The possible explanation for this high number in younger and adult females could be because the women are in their child-bearing age, sexually more active and therefore, more prone to get UTIs. Klebsiella species are generally resistant to quite a lot number of antibiotics. This is believed to be a plasmid-mediated effect. Length of hospitalization period and undertaking aggressive procedures are risk factors for getting infections with such resistant strains. The present study has demonstrated that antimicrobial susceptibility of Klebsiella isolates against commonly used antibiotics varied significantly with the type of antibiotic tested. The isolates showed maximum sensitivity to carbapenems followed by amikacin and fosfomycin. A relatively reduced sensitivity was observed against gentamicin, piperacillin-tazobactam and nitrofurantoin. However, a much reduced sensitivity was seen against cefotaxime, ciprofloxacin and cotrimoxazole, whereas least sensitivity was noticed for cefuroxime and ampicillin. A similar study has documented multi-drug resistant K. pneumoniae amongst clinical isolates from Balochistan, where resistance to amoxicillin and 3rd generation cephalosporins have been reported as 100%, followed by 76.2% resistance to fluoroquinolones and gentamicin, 66.7% to co-trimoxazole and 23.8% to piperacillin-tazobactam respectively.[25] Such array of antimicrobial resistant Klebsiellae in present study can be related to widespread inappropriate uses of antimicrobials.

The high drug-resistance prospective of Klebsiellae are of great public health apprehension. Multidrug resistance in such nosocomial bacteria are transforming these pathogens into supergerms and consequently making their control tougher. Our study has demonstrated that of all Klebsiella isolates 33.6% were ESBL producers. The isolation frequency of ESBL producing Klebsiella in our healthcare facility is less as compared to many other centers.[26] The possible explanation for this relatively low occurrence of ESBL producing pathogens in our set-up may be credited to the stringent infection prevention and control measures implemented by hospital infection control committee. Carbapenems are usually reserved for treating ESBL producing bacterial strains. Such bacteria have various resistance mechanisms to carbapenems. The most important mechanism is production of enzyme carbapenemase.[27] The commonest carbapenemase include K. pneumoniae carbapenemase (KPC). These KPCs are important not only because of carbapenem-resistance, but also because they are frequently not detected by customary sensitivity testing and therefore, retain an extraordinary potentiality for spreading. Thus such pathogens pose challenges in infection prevention as well as treatment due to restricted choices for antibiotics. The most appropriate treatment policy for KPC-pro-

ducing pathogens has yet to be well-defined; however, possible treatment include amikacin, polymyxins and tigecycline. Since carbapenem-resistance is being increasingly reported, the microbiology section of diagnostic laboratory has a key role in the detection of carbapenemase-producing strains to aid in treatment selection and help in infection control.

The limitations of the study were that it was a laboratory based study and limited to the cases for which cultures were requested. Because of the small sample size, the findings of this study may not be representative of the entire population. In order to elucidate the actual resistance pattern in our community, we recommend performing a larger-scale investigation. Moreover, we must detect carbapenemase-producing Klebsiella in routine settings. There is also a need for physicians to be more aware of and curb the injudicious use of antibiotics.

CONCLUSION

Klebsiella species were amongst the important causes of urinary tract infection in patients reporting to our healthcare facility. This study has provided important facts on antimicrobial resistance among Klebsiella species. The possible choices for the treatment of ESBL-producing isolates could be amikacin and carbapenems. Due to a high level of antimicrobial resistance amongst these uropathogens, it is vigilant to advise antibiotic therapy, preferably after culture and sensitivity testing since antibiotic resistance is becoming a huge public health concern that can lead to limited options for drug treatment.

Ethical Approval:
The ethical Approval was obtained vide letter no. SMDC-IRB/AL/151/2021

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