Available online at www.ijpcr.com
International Journal of Pharmaceutical and Clinical Research 2016; 8(6): 538-542

ISSN- 0975 1556

Research Article

Prevalence of *Klebsiella* Bacteriuria and Antimicrobial Susceptibility in a Tertiary Care Hospital, Tiruchirapalli, India

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Available Online: 8th June, 2016

ABSTRACT
Urinary tract infection is a common health issue encountered in medical practice and leads to frequent antibiotic prescription in outpatient department strains of *Klebsiella* are challenging for the clinicians when it is become a multidrug resistant *Klebsiella* either inside the hospital or in outpatient department. Thus this study has its own objective to determine the prevalence of *Klebsiella* bacteriuria among urine samples received in Clinical Microbiology Laboratory from February 2012 to June 2015. A battery of 3,958 urine samples was included. All the urine samples which are having the criteria for inclusion were subjected for bacteriological screening. Further confirmation performed by microscopy, biochemical tests and special staining. Among the urine samples processed, 170 samples supported *Klebsiella* sp isolation. Further, species level determination resulted *K. pneumoniae* (116) and *K. oxytoca* (54). All the isolates were subjected to antimicrobial susceptibility test. This study revealed that *Klebsiella pneumoniae* isolation from UTI in this region is predominant.

Keywords: *Klebsiella*, bacteruria, prevalence, antimicrobial susceptibility test

INTRODUCTION

Urinary tract infections (UTIs) are very common reason for consultation and antibiotic prescription in current practice[1,2]. Excessive and/or inappropriate use of antibiotics in treating UTIs is responsible for the emergence and spread of multi-drug resistant (MDR) urinary bacteria. UTIs caused by MDR *Klebsiella pneumonia* isolates are a major public health problem, since the therapeutic options significantly reduced and more challenging in clinical scenario. Moreover, MDR pathogens resulting in high morbidity and mortality as they reflect in increased hospital stay and treatment expenditure[3]. The development of drug-resistant pathogens in patients with serious infections such as UTIs has generally been ascribed to the widespread use of antimicrobial agents and the limited availability of infection prevention and control programs. As a result, it is increasingly common to encounter individuals infected with bacterial pathogens that are resistant to almost all currently available antibiotics. Of particular concern in the healthcare setting is the emergence of resistant gram-negative pathogens, including drug resistant *K. pneumoniae*. While antibiotic resistance was previously noted mainly in nosocomial UTIs, it is nowadays also frequently observed in community-acquired UTIs[1,2].

Globally, nonsusceptibility of urinary *K. pneumoniae* to commonly used oral and parenteral antimicrobial agents is rapidly increasing and shows large variation temporally and regionally[4]. Empirical antibiotic therapy is based on epidemiological data that are updated and adapted geographically[5]. Thus, it is of great importance for institutions to know the local antibiotic resistance patterns of each region in order to implement suitable infection control measures and develop a rational antibiotic policy with local recommendations for antibiotic use. These surveillance data are also used to assess the effectiveness of the measures taken and to identify new points for intervention to control bacterial resistance. Unlike most developed countries, we unfortunately do not yet have nationwide surveillance programs for monitoring antimicrobial resistance. However, surveillance studies of bacterial resistance are among the most important measures in terms of controlling the spread of resistant bacteria. Therefore, the objectives of this regional study were to analyze the prevalence of *Klebsiella* sp prospectively and to determine the antibiotic resistant pattern that add valuable data to assist the medical community in the development of a plan for a rational use

Table 1: Results of culture

Results of culture	Number of samples	Percentage
Significant bacteriuria (*Klebsiella*)	163	4.1
Insignificant bacteriuria (*Klebsiella*)	7	0.2
Other isolates	356	9.0
Commensals	565	14.3
Sterile	2867	72.4
Total	3958	100

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Table 2: Distribution of *Klebsiella* positive samples with respect to the patients' age

Age group (in years)	Distribution of *Klebsiella* positive samples in years				
	2012	2013	2014	2015*	Total
1 - 10	-	1	2	2	5
11 - 20	1	-	5	4	10
21 - 30	1	7	4	5	17
31 – 40	6	5	12	8	31
41 - 50	5	7	12	9	33
51 - 60	7	7	7	5	26
61 - 70	8	5	6	7	26
71 - 80	8	4	2	6	20
81 - 90	-	-	1	1	2
Total	36	36	51	47	170

*Upto June only

of therapeutics including antimicrobial agents in the treatment of UTIs due to *K. pneumoniae*.

MATERIALS AND METHODS

This was a prospective study which was conducted in the Department of Microbiology in Chennai Medical College Hospital and Research Centre, Tiruchirapalli, India over a period of 3 years and 5 months, starting from February 2012 to June 2015.

Study area and patients

A battery of 3,958 urine samples received in the Clinical Microbiology Laboratory was included. All the urine samples which were having the criteria for inclusion were subjected for bacteriological screening.

Specimen collection

After getting clearance from the Institutional ethical committee, this study was conducted. Urine samples were collected by standard mid-stream clean catch/ catheterized/ suprapubic method in sterile, wide mouthed containers that were covered with tight-fitting lids.

Culture

The samples were processed by using standard microbiological procedures. The specimens were inoculated on dried plates of Nutrient agar, MacConkey agar and Blood agar (in 5-10% CO_2 atmosphere) by standard loop method and the plates were incubated at 37°C overnight. The isolates were confirmed by using standard bacteriological identification techniques. Culture results were interpreted as significant and insignificant according to the standard criteria.

Biochemical confirmation

After colony determination and microscopy, the isolates were confirmed by biochemical methods and special staining technique (capsular staining) to confirm capsulated *Klebsiella* species).

Antimicrobial Susceptibility test

Antimicrobial Susceptibility test was performed using Kirby-Bauer disc diffusion method and interpretation was done according to Clinical and Laboratory Standards Institute (formerly NCCLS) guidelines[6,7,8]. The antibiotics included tested were ampicillin (10mcg), amoxyclav (20/10mcg), amikacin (30mcg), gentamycin, cefipime (30mcg), ceftriaxone (30mcg), cefuroxime (30mcg), cefotaxime, ceftazidime, cefoxitin, cefeperazone-sulbactam, piperacillin-tazobactam, ciprofloxacin (5mcg), co-trimaxazole (25mcg), norfloxacin (10mcg),

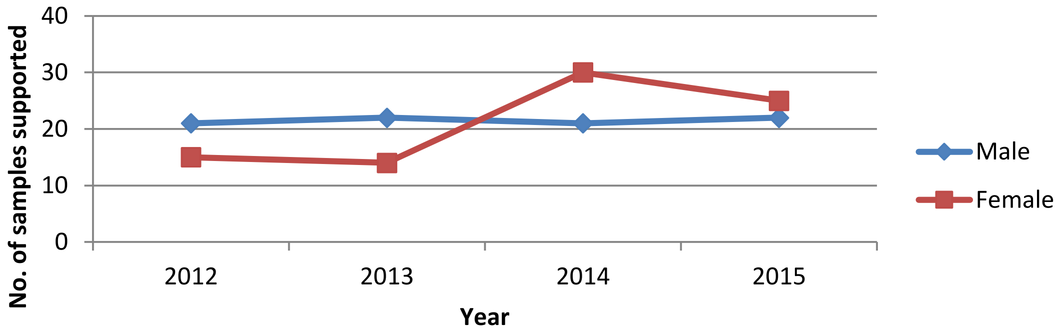

Figure 1: Gender wise distribution of positive *Klebsiella* cultures

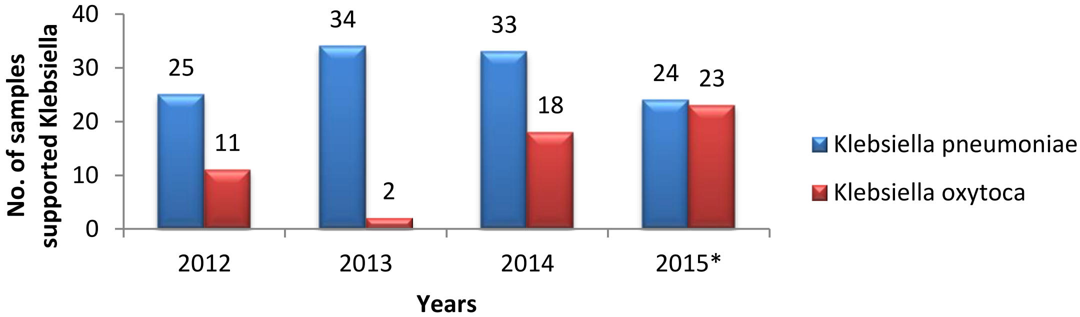

Figure 2: Distribution of *Klebsiella* species

Table 3: Antibiotic resistance pattern of the *Klebsiella* isolates

Antibiotics	Percentage distribution of antibiotic resistance among *Klebsiella* isolates			
	2012 (n=36)	2013 (n=36)	2014 (n=51)	2015 (n=47)
Penicillin Group				
Ampicillin	36 (100)	36 (100)	51 (100)	47 (100)
Cotrimoxazole	19 (52.8)	19 (52.7)	20 (39.2)	24 (51)
Fluroquinolones				
Norfloxacin	29 (80.5)	22 (61.1)	28 (45.1)	25 (53.2)
Ciprofloxacin	17 (47.2)	21 (58.3)	34 (33.3)	27 (57.4)
Levofloxacin	13 (36.1)	12 (33.1)	40 (21.6)	26 (55.3)
Aminoglycosides				
Gentamicin	18 (50)	16 (44.4)	32 (37.3)	22 (46.8)
Amikacin	13 (36.1)	8 (22.2)	11 (21.6)	13 (27.7)
II generation cephalosporin				
Cefuroxime	29 (80.5)	24 (66.6)	32 (62.7)	32 (66)
III generation cephalosporin				
Cefatoxime	28 (77.8)	24 (66.6)	19 (62.7)	33 (70.2)
Ceftriaxone	28 (77.8)	24 (66.6)	31 (60.8)	33 (70.2)
Ceftazidime	28 (77.8)	24 (66.6)	30 (58.8)	28 (59.6)
IV generation cephalosporin				
Cefipime	28 (77.8)	24 (66.6)	28 (54.9)	26 (55.3)
β lactum and β lactamase inhibitors				
Amoxycillin – clavulanic acid	34 (94.4)	35 (97.2)	42 (82.4)	45 (95.7)
Cefaperazone - sulbactum	12 (33.3)	15 (41.7)	12 (23.5)	18 (38.3)
Piperacillin - tazobactam	9 (25)	11 (30.6)	14 (27.4)	14 (29.8)
Carbapenem				
Imepenem	2 (5.5)	1 (2.7)	0	5 (10.7)
Meropenem	2 (5.5)	1 (2.7)	0	5 (10.7)
Ertapenem	2 (5.5)	1 (2.7)	0	5 (10.7)

[Figure in parenthesis denoted percentages]

levofloxacin (5mcg), ertapenam, imipenem (10mcg) and meropenem (10mcg) (Himedia, India).

RESULTS AND DISCUSSION

Among 3,958 urine samples screened, significant *Klebsiella* bacteriuria was found in only 170 (4.3%) samples and depicted in table 1. Among positive cultures which were obtained, all supported to monobacteriuria. Highest incidence (33%) was reported in the age group of 41-50 years (Table 2). The sexwise distribution of the positive *Klebsiella* isolates was depicted in figure 1. Overall, 170 *Klebsiella* isolates were determined in this study. Among them, *K. pneumoniae* isolates were possible to 116 samples and 54 samples supported *K. oxytoca* (Figure 2). The distribution of *K. pneumoniae* was observed as 25, 34, 33 and 24 in 2012, 2013, 2014 and 2015 respectively. *Klebsiella pneumonaie*, the most common isolate, was found to be sensitive to carbapenems (Imipenem, meropenem and ertapenam) followed by amikacin and levofloxacin. *K. oxytoca*, the second most frequent organism which was grown on culture while sensitivity to the abovesaid antibiotics. In this study, we are not concentrating the species variations among the *Klebsiella* isolates for sensitivity pattern. High resistance pattern was observed among ampicillin, amoxycillin-clavulanic acid, norfloxacin, cefuroxime and other third generation cephalosporins (Table 3). The distribution of multi drug resistance (MDR) was also determined and analyzed the sensitivity to carbapenem group of antibiotics. The overall determination of MDR among *Klebsiella* isolates was depicted in figure 3. It was observed that there is an increase MDR yearly and also increasing resistance of carbapenem (Figure 4).

This study was carried out to determine the prevalence of *Klebsiella* isolates among the urine samples processed in the Department of Microbiology, Chennai Medical College Hospital and Research Centre, Tiruchirapalli, India. The percentage of susceptibility of *K. pneumoniae* and *K. oxytoca* isolates to the antibiotics which are commonly used to treat *Klebsiella* infections as shown in table 3. The most predictable and primary etiological bacteria involved in urinary tract infections (UTI) are *Escherichia coli* followed by *K. pneumoniae* in both outpatient and inpatient[9,10].

Lot of research papers are published related to *E. coli* infections among urinary tract infectious patients. Thus in this present study we concentrating on *Klebsiella* species as the observable bacterial isolates from urine samples and this finding is not observed in other studies that compared. In general, the prevalence of UTI occurred more in females than in males due to shorter urethra, closer proximity to the perirectal area in females. But in this study, the prevalence was found to be more or less equal. Most of the studies suggested that UTIs are more frequent in females than males during childhood[11,12,13]. Out of 170 *Klebsiella* isolates, 116 of *K. pneumoniae* and 54 of *K. oxytoca* were recorded.

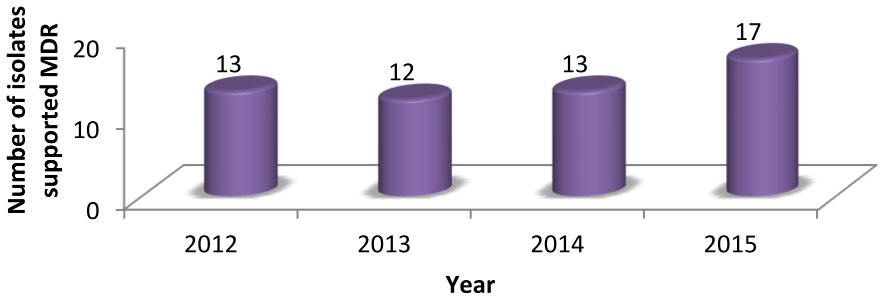

Figure 3: Carbapenem resistance among MDR *Klebsiella* strains

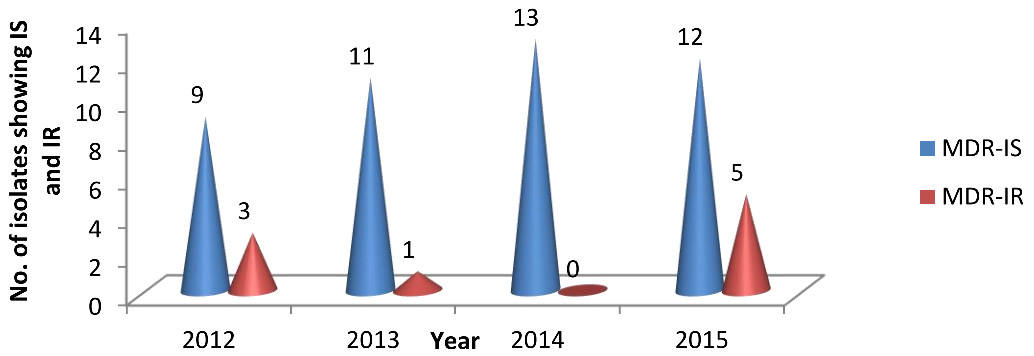

Figure 4: Carbapenem resistance among MDR *Klebsiella* strains
[IR – Imepenem Resistant; IS – Imipenem Sensitive]

Most of the studies suggested that the older men of 61 – 70 years were observed positive to *K. pneumoniae* urinary culture, mainly due to prostate obstruction or subsequent instrumentation like catheter[14]. Other study suggested that the incidence of UTI in females was more at an earlier age compared to that in males[13]. Antibiotic resistance is a major clinical problem in treating *Klebsiella* infections and the issue was increasing over the years where the resistance rates vary from country to country[15].

K. pneumoniae is becoming resistant to co-trimoxazole and norfloxacin due to use for a long period and must have been abused and a result the organisms must have developed a different mode of action[13]. Overall resistance to various generations of cephalosporins and penicillins alone was high on account of the production of extended spectrum β lactamases (ESBLs) by the bacteria involved. Based on the observations of this study, we recommend the use of levofloxacin, ciprofloxacin or 3rd generation cephalosporins along with β lactamase inhibitors (clavulanate or sulbactam) against infection caused by *Klebsiella* species after proper laboratory investigation. The posological determination and incidence of toxicity subsequently reduced with the usage of piperacillin or cephalosporins[3]. Furthermore, carbapenem groups including imepenem, carbapenem etc showed very effective but relatively expensive. The restriction in procurement and indiscriminate use are making the organisms susceptible to it. Hence, there is a need to emphasize the rational use of antimicrobials and strictly adhere to the concept of reserve drugs to minimize the misuse of available antimicrobials. Carbapenem (imipenem or meropenem) and amikacin or gentamicin should be considered as a reserved drug for the treatment of severe nosocomial infections caused by *K. pneumoniae*. In fact, the irrational and inappropriate use of antibiotics is responsible for the development of resistance of the Enterobacteriaceae family including *K. pneumonia*[12]. In addition, regular antimicrobial susceptibility surveillance is essential for endemic monitoring of the resistance patterns. An effective national and state level antibiotic policy and draft guidelines should be introduced to preserve the effectiveness of antibiotics and for better patient management[5,15]. Though carbapenem resistance was observed among the MDR *Klebseilla*, there is no observation of pan drug resistance in this study. Further, the carbapenem resistance strains were found to be sensitive to colistin and tigecycline.

In vitro sensitivity is an important factor yet other factors given below should also be seriously considered in selecting the antimicrobial agents for an infection. For example cost of drugs for complete treatment, route of administration (oral, parenteral etc.), age (if the patient is neonate chloramphenicol is contraindicated) and pregnancy (tetracyclines are contraindicated). Other factors like allergic reactions to drugs like β lactam antibiotic, kinetics of drugs and its concentration at the target site and mode and frequency of administration, bactericidal or bacteriostatic, efficacy/safety ratio, immunological status of the patient, MDR should also be considered[9,11].

Most of the isolates had a high level of resistance further laboratory evidence of infection and antibiotic susceptibility testing should be carried out to help in the choice of systemic drugs. Continuous monitoring of antimicrobial susceptibility pattern in individual settings together with their judicious use is emphasized to minimize emergence of drug resistant bacteria. Thus, it is highly recommended that practicing physicians should become aware of the magnitude of the existing problem of antimicrobial resistance and help in fighting this deadly threat by rational prescribing.

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