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Research Article

Prevalence and Antimicrobial Susceptibility Pattern of *Klebsiella pneumoniae* Causing Urinary Tract Infection and issues Related to the Rational Selection of Antimicrobials

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Abstract: Antimicrobial resistance is not only increasing the healthcare costs, but also the severity and death rates from certain infections that could have been avoided by prudent and rational use of the existing and newer antimicrobial agents. Prudent and rational use of antimicrobial is possible by forming local, national and global wide Antibiogram. Urinary tract Infection (UTI) is among the most common infections described in outpatient department and hospitals inpatients. *Klebsiella pneumoniae* (*K. pneumoniae*) accounts for 2nd highest organism isolated from urine samples of UTI patients after *Escherichia coli*. The present study is undertaken to determine the antimicrobial susceptibility pattern of K.pneumoniae isolated from urine samples of UTI patients of Peoples College of Medical Science & Research Centre and hospital. Between January 2010 and December 2011, a total of 1450 urine specimens processed in the laboratory, of which 65 (15.4%) yielded *K. pneumoniae*. Organisms were identified by conventional methods. Antimicrobial susceptibility testing was done by the disk diffusion methods. K.pneumoniae is showing good antimicrobial susceptibility for imipenem, gatifloxacin, amikacin, gentamicin, ampicillin/Sulbactam, levofloxacin and amoxicillin/clavulinic acid.
An attempt has been made in this study to recognize the K.pneumoniaein patients of UTI of tertiary care hospital, Bhopal M.P.; to record the antibiogram and probable drug of choice for K.pneumoniae considering the antibiotic susceptibility testing, cost, side effects and many other factors.
Keywords: UTI, *K. pneumoniae*, antibiotic susceptibility testing, antimicrobial resistance, rational selection of antimicrobials

INTRODUCTION

A urinary tract infection (UTI) remains a major clinical problem over 50 years after the introduction of anti-microbial therapy. This is partly because of the emergence of increasing rates of drug resistance in UTI. The increasing prevalence of antibiotic resistance has been reported from various countries including India [1-3]. Urinary tract infection is the second infection in human. Urinary infections cause fewer complications than nosocomial infections, but they occasionally can cause bacteremia and death. Gram negative bacteria play an important role in UTI. It has been estimated that more than 7 million visits to emergency units and 100,000 in hospitals occurs annually in the USA [4].

Escherichia coli remained the most common causative agent of uncomplicated UTI for many years with 75-90% causes of UTI infection [5-7]. *Klebsiella pneumonia* accounts for 2nd highest organisms. The other gram negative pathogens causing UTI are *Proteus mirabilis* and *Pseudomonas aeruginosa*, however, *Enterococci* and coagulase negative *Staphylococci* are the most frequently encountered gram positive bacteria in UTI [8].

K. pneumonia is important opportunistic nosocomial pathogens causing a variety of infections including urinary tract infections (6-17 %), pneumonia (7-14 %), septicemia (4-15 %), wound infections (2-4 %), neonatal septicemia (3-20%) and infections in the intensive care units (4-17 %). It has been estimated that *K. pneumoniae* cause 5-7% of the total bacterial nosocomial infections [9].

To ensure appropriate therapy, current knowledge of the organisms that cause UTI and their antibiotic susceptibility testing is mandatory [10]. Due to rising antibiotic resistance among uropathogens, it is important to have local hospital based knowledge of the organisms causing UTI and their antibiotic sensitivity patterns [11].

Aim and objective of the present study is to find out the prevalence and antimicrobial susceptibility pattern of *K. pneumoniae* isolated from urine of UTI and preferred drug of choice for patients, attending People's Hospital of People's College of Medical Science & Research Centre, People's University, Bhanpur, Bhopal, M.P., India.

MATERIAL AND METHODS

In the present study, 1450 urine samples were collected for the antibiotic sensitivity testing in the Department of Microbiology from inpatient & outpatient department of People's College of Medical Science & Research Centre and hospital, Bhopal from the period January 2010 to December 2011.

First step done was to isolate the organisms from these urine samples and then to study the culture susceptibility in *Klebsiella pneumoniae*. Identification of bacteria was done by Gram staining. The samples were inoculated on MacConkey agar, nutrient agar and Cystine Lactose Electrolyte Deficient (CLED) agar medium plates by four flame method. Inoculated culture plates were kept in the incubator at 37°C for 24 hours. All the bacteria were identified using morphological, microscopy and biochemical tests following standard procedures described by Cowan and Steel (1974) and Cheesborough (2006) [12-13].

Antibiotic sensitivity test was performed by Kirby Bauer Disc Diffusion method [14]. A sterile cotton swab was used to streak the surface of Mueller Hinton agar plates. Filter paper disks containing designated amount of the antimicrobial drugs obtained from commercial supply firms (Himedia Labs, Mumbai, India) were used. The Mueller Hinton agar plates were allowed to dry before applying antibiotic disc. Then, some commercially available antibiotic discs were gently and firmly placed on the agar plates, which were then left at room temperature for 1 hour to allow diffusion of the antibiotics into the agar medium. The plates were then incubated at 37°C for 24 hours. If an antimicrobial activity was present on the plates, it was indicated by an inhibition zone. The diameter of the inhibition zones was measured in millimeter at 24 hours using a scale. An organism was interpreted as highly susceptible if the diameter of inhibition zone was more than 19 mm, intermediate if diameter was 15-18 mm and resistant if the diameter was less than 13 mm. The intermediate readings were considered as sensitive in the assessment of the data. AST of *K. pneumoniae* to different antibiotics is obtained. From AST antibiogram for *K. pneumoniae* is prepared and consequently probable drug of choice is selected for *K. pneumoniae c*onsidering the antibiotic susceptibility testing, cost, side effects and many other factors.

Table 1: Number and % of organisms isolated from urine

Sl. No.	Name of organism	Total number of organism (n = 421)	Percentage of organism
1	*Escherichia coli*	262	62.0 %
2	***K. pneumoniae***	**65**	**15.4 %**
3	*Enterococci*	28	6.9 %
4	*Pseudomonas*	24	5.7 %
5	*Staphylococcus aureus*	24	5.7 %
6	*Acinobactor*	07	1.7 %
7	*Citrobactor*	06	1.4 %
8	*Proteus* sp.	05	1.2 %
	Total	421	100 %

RESULTS

During the 24 month period, a total of 1450 urine samples were processed for culture and sensitivity testing. Urine samples of patients of all age groups (1day-85years) and both sexes were processed. A total 421different organisms were isolated from 1450 urine samples thus culture positivity was 29 % (421/1440) as shown in Table1.

Table 2: Antibiotic Sensitivity of *K. pneumonia* isolated from urine

Antibiotics used for AST	% Susceptibility
Imipenem	100
Gatifloxacin	87.5
Nitrofurantoin	84.5
Amikacin	74.6
Ampicillin/Sulbactam	64.8
Gentamicin	64.3
Levofloxacin	50
Amoxicillin/Clav. acid	50
Clindamycin	38.5
Netilmicin	37.5
Ceftazidime	26.3
Cotrimoxazole	22
Cephradine	17.2
Norfloxacin	15.7
Ceftriaxone	14.3
Cefoxitin	12.5
Ampicillin	10.5
Cefipime	0
Cefuroxime	0

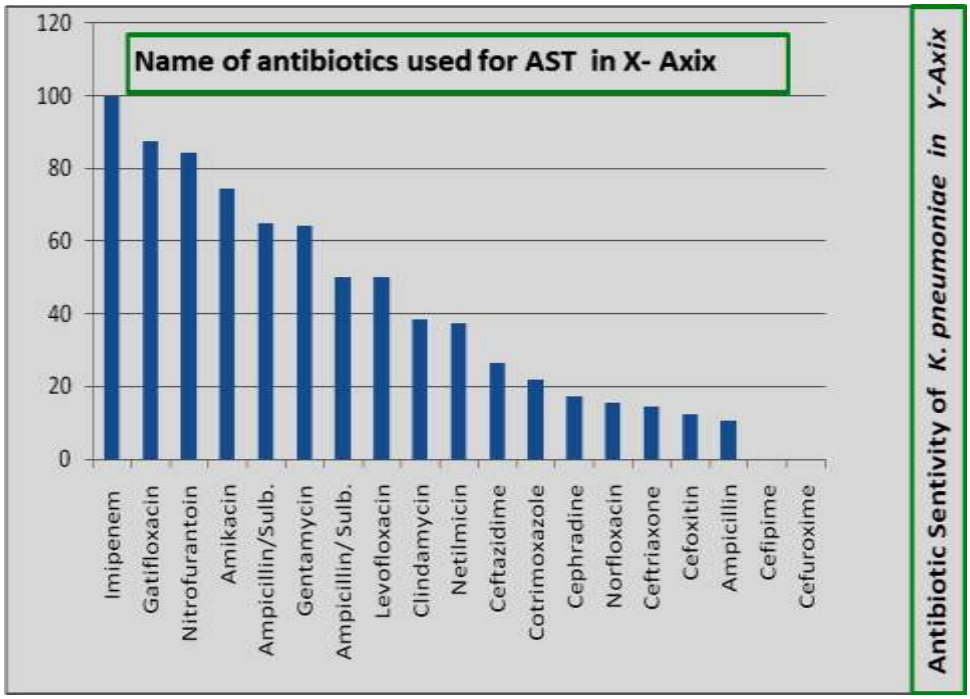

Fig. 1: Antibiotic Sensitivity of *K. pneumoniae* isolated from urine

Table 3: Preferred drug of choice for *K. pneumoniae* if isolated from urine

Sl. No.	Name of drug	% Sensi.	Route of Adm.	Price/10 tab/vial	Dose and total duration of treatment	Total cost of treatment	ADR/ Toxicity of drug
1	Imipenem	100	IV/IM	728 Rs/ vial	500 mg qid/ 7 days	20384 Rs	Mild
2	Nitrofurantoin	84.5	Oral	209 Rs / 10 tab	100 mg qid for 7 days	585 Rs	Mild to moderate
3	Gatifloxacin	75	Oral/IV	50 Rs /10 tab	500 mg OD/ 7 day	35 Rs	mild
4	Amikacin	74.6	IV/IM	10 Rs /500 mg vial	15 mg/kg in divided doses for 5 days	90-100 Rs	Mild to moderate
5	Ampicillin/Sulb.	64.8	Oral/ IV	89 Rs/ vial	1 gm qid for 7 days	2492Rs	Mild

Abbr.- IV- Intravenous, IM-Intramuscular, Adm.- Administration, Sensi.- Sensitivity, ADR- Adverse Drug Reaction

Result in table-1 shows that out of total 421 different organisms, *E.coli* was highest in number which accounted for 262 (62%). Second highest isolates was *K. pneumoniae* which accounted 65 (14.5%) followed by *Enterococci* (6.9%), *Pseudomonas* (5.7%), *Staphylococcus aureus* (5.7 %), *Acinobactor* (1.7%), *Citrobactor* (1.4 %) and *Proteus* spp.(1.2 %).

Out of 65 *K. pneumoniae* isolated, 43 (66%) was isolated from female and 22 (44%) was isolated from male. It showed the prevalence of *K. pneumoniae* infection is more in female than male. In this study it was found that the maximum isolates were isolated from age group of 61-70 years in male (27.3 %) and 21-30 in female and (44.1%).

Result in table 2 and fig.1 showed that *K. pneumoniae* was manifesting good antimicrobials susceptibility against imipenem (100%), gatifloxacin (87.5%), amikacin (74.6%), gentamicin (64.3%), ampicillin/Sulbactam (64.8%), levofloxacin (50 %) and amoxicillin/Clavulanic acid (50 %).

Whereas the lowest percentage of susceptibility was manifested by *K.pneumoniae*against cefipime and cefuroxime (not sensitive i.e. 100% resistant) followed by ampicillin (10.5%), ceftriaxone (14.3), norfloxacin, cephradine, cotrimoxazole (22%) and ceftazidime (26.3%).

Considering the antibiotic susceptibility testing, cost, side effects and many other factors, nitrofurantoin and gatifloxacin should be preferred. Imipenem and amikacin should be kept as reserved drugs.

DISCUSSION

This experiment was carried out to study the susceptibility of the bacterial isolates *Klebsiella pneumoniae* collected from urine specimens of UTI patients toward different 19 antibiotics. The percentages of susceptibility of *K. pneumoniae* isolates to the antibiotics which are commonly used to treat *K.pneumoniae* infections as shown in Table 2.

The most predictable and primary etiological bacteria involved in UTI are *Escherichia coli* followed by *K. pneumoniae* in both out and inpatient [15-18]. In the present study, *K. pneumoniae* was the 2nd most common bacteria isolated from urine samples and this finding is in agreement with others finding too.

The prevalence of UTI occurred more in females than in males secondary to shorter urethra, closer proximity to the perirectal area in females. Out of the 262 organisms, *K. pneumoniae* isolates were 65. Out of 65 *K. pneumoniae*, 43(66%) were from females while 22 (44%) were from males. UTIs are more frequent in females than males during adulthood [19-21]. A major age group in male was 61-70 years with positive urine culture in *K. pneumoniae*. In older men, the incidence of UTI may increase due to prostatic obstruction or subsequent instrumentation like folly's catheter [22]. In females, major age group was 21-30 years with positive urine cultures in *E. coli*. It seems that the incidence of UTI in females was more at an earlier age compared to that in males.

Antibiotic resistance is a major clinical problem in treating infections caused by *Klebsiella* spp. The resistance to the antimicrobials has increased over the years. Resistance rates vary from country to country [23].

K. pneumoniae is becoming resistant to co-trimoxazole and norfloxacin is very less. The possible explanation behind the resistance is shown to these antibiotics, may be because these antibiotics have been in use for a long period and must have been abused and as a result the organisms must have developed a different mode of action.

Overall resistance to various generations of cephalosporins and penicillins used alone was high on account of the production of extended spectrum β-lactamases (ESBLs) by the bacteria involved. Hence, based on the observations of the present study, we recommend use of ampicillin, amoxicillin or 3rd generation cephalosporins along with β-lactamase inhibitors (clavulanate or sulbactam) against infection caused by *K. pneumoniae*.The dose as well as the incidence of toxicity subsequently reduced if β-lactamase inhibitors are with piperacillin or cephalosporins.

The most useful antibiotics in this study were Imipenem (100 %). This drug is relatively expensive when compared to most antibiotics frequently used. This probably had restricted their procurement and indiscriminate use, therefore 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. pneumoniae*. In addition, regular antimicrobial susceptibility surveillance is essential for area-wise 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.

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.), sage (if the patient is neonate chloramphenicol is contraindicated) and pregnancy (tetracyclines are contraindicated). Other factors like allergic reactions to drugs like beta 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, ADR should also be considered.

CONCLUSION

The most of the isolates had a high level of resistance to examine antibiotics. 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.

Considering the antibiotic susceptibility testing, cost, side effects and many other factors, nitrofurantoin and

gatifloxacin should be preferred for *K. pneumoniae* infection for patients of UTI. Imipenem, amikacin, gentamicin should be kept as reserved drugs.

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REFERENCES

1. Messele G; Urinary Tract infections; Etiologic patterns and resistance. Ethiop.Med. J., 1983; 21: 3-13.
2. Dawit W, Worku E; Increased incidence of resistance to Antimicrobial by urinary pathogens isolated at Tikur Anbessa hospital. Ethiop. Med. J., 1997; 35(2): 127-135.
3. Lindtjorn B, Setegne D, Niemi M; Sensitivity pattern of bacterial isolates from patients at Sidamo Reginal Hospital. Ethiop. Med. J., 1989; 27(1): 27-31.
4. Schappert SM; Ambulatory care visits to physician offices, hospital outpatient departments, and emergency departments: United States, 1997. Vital Health Stat. 13, 1999; 143(i-iv): 1-39.
5. Karlowsky JA, Kelly LJ, Thornsberry C, Jones ME, Sahm DF; Trends in antimicrobial resistance among urinary tract infection isolates of *Escherichia coli* from female outpatients in the United States. Antimicrobial Agents Chemother., 2002; 46 (8): 2540-2545.
6. Nakhjavani FA, Mirsalehian A, Hamidian M, Kazemi B, Mirafshar M, Jabalameti F; Antimicrobial susceptibility testing for *Escherichia coli* strains to fluoroquinolones, in urinary tract infections. Iran. J. Public Health, 2007, 36(1): 89-92.
7. Omigie O, Okoror L, Umolu P, Ikuuh G; Increasing resistance to Quinolones: A four year prospective study of urinary infection pathogens. IInt. J. Gen. Med., 2009; 2: 171-175.
8. Shankel S; Urinary tract infections. Genitourinary disorders, The Merck Manuals Online Medical Library, 2007.
9. Podschun R, Ullmann U; *Klebsiella* spp. as nosocomial pathogens: epidemiology, taxonomy, typing methods, and pathogenicity factors. Clin.Microbiol. Rev., 1998; 11(4): 589-603.
10. Tankhiwale SS, Jalgaonkar SV, Ahamad S, Hassani U; Evaluation of extended spectrum beta lactamase in urinary isolates. Indian J Med Res., 2004; 120(6): 553-556.
11. Kahlmeter G, ECO.SENS; An international survey of the antimicrobial susceptibility of pathogens from uncomplicated urinary tract infections: the ECO.SENS Project. J Antimicrobial Chemother., 2003; 51(1): 69-76.
12. Cheesborough M; Medical Laboratory Manual for Tropical Countries, 2nd edition. Microbiology (ELBS), New York, 2009: 62-70.
13. Cowan SJ, Steel KJ; Cowan and Steel manual for identification of medical bacteria, 2nd edition, Cambridge University Press, London, 1974.
14. Bauer AW, Kirby WMM, Sherris JC, Tuck M; Antibiotics susceptibility testing by a standardized single disc method. Am J Clin Pathol., 1966; 45(4): 493-496.
15. Hooton TM, Stamm WE; Diagnosis and treatment of uncomplicated urinary tract infection. Infect Dis Clin North Am., 1997; 11(3): 551-581.
16. Gupta K, Hooton TM, Wobbe CL, Stamm WE; The prevalence of antimicrobial resistance amonguropathogens causing uncomplicated cystitisin young women. International Journal of Antimicrobial agents, 1999; 11(3-4): 305-308.
17. Jones RN, Kugler KC, Pfaller MA, Winokur PL; Characteristics of pathogens causing urinary tract infections in hospitals in North America: Results from the SENTRY Antimicrobial Surveillance Program, Diagnostic Microbiology and Infectious Disease, 1999; 35(1): 55–63.
18. Gales CA, Jones R, Gordon KA, Sader SH, Wilke WW, Beach ML, Pfaller MA, Doern GV; Activity and spectrum of 22 antimicrobial agents tested against urinary tract infections pathogens in hospitalized patients in Latin America: Report from the second year of the SENTRY Antimicrobial Surveillance Programme (1998). J. Antimicrob. Chemother., 2000; 45: 295-303.
19. Akinyemi KO, Alabi SA, Taiwo NA, Omonighehin EA; Antimicrobial susceptibility pattern and plasmid profile of pathogenic bacteria isolated from subjects with urinary tract infections in Lagos, Nigeria. Nig. Qt J Hosp Med., 1997; 1: 7-11.
20. Burbige KA, Retik AB, Colony A, Bauer SB, Lebowitz R; Urinary tract infection in boys. J Urol., 1984; 132: 541-542.
21. Ibeawuchi R, Mbata TI; Rational and irrational use of antibiotics. Afri Health, 2002; 24(2): 16-18.
22. Jung-Sheng Y, Kun-Hung S, Wen-Chi C, Jiann-Shyan H, Ching-Liang H; Effects of Electro-acupuncture on Benign Prostate Hyperplasia Patients with Lower Urinary Tract Symptoms: A Single-Blinded, Randomized Controlled Trial. Evidence-Based Complementary and Alternative Medicine, 2011; Article ID 303198, 8 pages.
23. Kahan NR, Chinitz DP, Waitman DA, Dushnitzky D, Kahan E, Shapiro M; Empiric treatment of uncomplicated urinary tract infection with fluoroquinolones in older women in Israel: another lost treatment option. Ann. Pharmacother., 2006; 40(12): 2223-27.