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ANTIMICROBIAL RESISTANCE OF *KLEBSIELLA PNEUMONIAE* STRAINS FROM PATIENTS WITH URINARY TRACT INFECTIONS IN SBMPMC HOSPITAL BIJAPUR, INDIA.

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ABSTRACT

The resistance profile of the *Klebsiella pneumoniae* were left undone despite the increasing prevalence rate of this organism in urinary tract infections (UTI) and its role in antibiotic resistance. The current study was undertaken to know the antibiotic sensitivity profile of *Klebsiella pneumoniae*, isolated from patients suffering from UTI in our medical college. The study was carried out over a period of 3 years from January 2010 to December 2012. Urine specimens from both outpatients and inpatients of our hospital were processed. Females were more frequently affected than males. ($P>0.05$) The most active antimicrobial agent against *K. pneumoniae* were piperacillin-tazobactum (72% sensitive), and amikacin (61%). One hundred and fifty two (97.4%) of all the isolates were multi-drug resistant. To conclude, this study stresses the importance of prior knowledge of the sensitivity pattern of the pathogen , before prescribing an antimicrobial agent for a meaningful therapy and to avoid fast emergence of resistant mutants.

KEY WORDS: Antimicrobial resistance*, Klebsiella pneumoniae*, urinary tract infections.

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INTRODUCTION

Urinary tract infections (UTI) are one of the most common bacterial infections in humans both in the community and hospital setting. [1] Urinary tract infections (UTI) are a serious health problem affecting 150 million people globally in each year. They are the second most common types of infection in humans accounting for 8.3 million doctor's visit annually in USA.[2] Malnutrition, poor hygiene, low socio-economic status is associated with UTI and these factors are usually found in rural settings. Although *Escherichia coli* has been reported as the commonest isolate causing UTI, few authors have reported changing patterns in the prevalence of uropathogens. [3-5] In 1883 Friedlander isolated a capsulated bacillus from the lungs of patient who died of pneumonia. This was named after him as Friedlander's bacillus. Later on this organism was given the generic name of *Klebsiella*, which is ubiquitously present and reported worldwide. Strains of *Klebsiella* are responsible for a wide variety of diseases in humans. In addition to being the primary cause of respiratory tract infections, it is also commonly involved in acute pyelonephritis in pregnant women with urinary tract abnormalities such as urolithiases, hydronephrosis or congenital deformities. [6] Extensive and often indiscriminate use of the extended-spectrum cephalosporins is associated with the emergence and spread of multi-drug resistant *K. pneumoniae*. Klebsiellae have a tendency to harbour antibiotic resistant plasmids; thus, infections with multiple antibiotic-resistant strains can be anticipated. Multidrug resistant bacteria cause serious nosocomial and community acquired infections that are hard to eradicate by using available antibiotics. Moreover, extensive use of broad-spectrum antibiotics in hospitalized patients has led to both increased carriage of *Klebsiella pneumoniae* and the development of multidrug-resistant strains infections have increased worldwide.[7,8] Most studies on UTIs have concentrated on the antimicrobial resistance profile of *E. coli* which is known to be the most prevalent UTIs causative organism while the resistance profile of the other Gram-negative organisms such as *Klebsiella pneumoniae* were left undone despite the increasing prevalence rate of this organism in UTIs and its role in antibiotic resistance. Thus, the current study was undertaken to know the antibiotic sensitivity profile of *Klebsiella pneumoniae*, isolated from patients suffering from UTI in our medical college.

MATERIALS AND METHODS

Study population, design, and setting

The study was carried out in the Department of Microbiology, Shri B M Patil Medical College, Bijapur, India over a period of 3 years from January 2010 to December 2012. Our hospital primarily caters to the semi urban population of southern India.

Ethical Clearance and Consent: As it was a retrospective study, ethical clearance and consent was not obtained.

Patient evaluation

Urine specimens from both outpatients and inpatients of our hospital having one or more urinary symptoms, like burning during micturition, fever, pyuria, frequency of urine, dysuria, hematuria, flank pain, suprapubic discomfort, etc., were processed.

Sample collection

Mid-stream urine sample in early morning was collected in wide mouth sterile container. Female patients were instructed to cleanse the area around the urethral opening with soap and water, dry the area, and collect the urine with the labia held apart. Male patients were instructed to cleanse the glans penis with soap and water, dry the area, and collect the urine with foreskin retracted. [9]

Isolation and identification

All urine samples were examined by a routine microscopic examination by wet mount of urine. Presence of pus cells, red blood cells (RBCs), epithelial cells, casts, and crystals were noted

as supportive findings of urinary infection. Simultaneously all urine samples were cultured over routine culture media; Cysteine lactose electrolyte deficient (CLED) agar with a sterile standard loop. These plates were incubated at 37°C for 24 hours.. Culture results were interpreted according to the standard criteria and a growth of $\geq 10^5$ colony forming units/ml was considered as significant bacteriuria. [10] To avoid duplication, repeated isolates of the same species from individual patients were excluded from the survey. Cultures with more than three colonies were discarded, as contaminants and their antibiotic susceptibility were not tested. *Klebsiella pneumoniae* was identified by conventional biochemical tests according to standard microbiological techniques. [9]

Antimicrobial susceptibility testing

All isolates of *Klebsiella pneumoniae* were tested for antimicrobial susceptibility on Mueller Hinton agar by the standard disc diffusion method recommended by the Clinical and Laboratory Standards Institute (CLSI). [11] Antimicrobial agents (disks) were obtained from HiMedia laboratories, Pvt Ltd, Mumbai. Appropriate quality control strains were used to validate the results of the antimicrobial disk. *E. coli,* ATCC 25922, and *Pseudomonas aeruginosa,* ATCC 27853, were used as quality control strains . [11]

Statistical analysis

Statistical analysis was performed with SPSS 14 software. Continuous data was summarized as mean and categorical data was summarized as percentage. Chi square test was applied for analysis of categorical data. *P* value < 0.05 was taken as significant for interpretation.

RESULTS

In all age groups,(Table 1) except those aged more than 50 years, females were more frequently affected than males. (P>0.05) Among females, frequency of UTI was more among 21-50 years age group and among males elderly patients were more commonly affected. The most active antimicrobial agent against *K. pneumoniae* isolates (Table 2)were piperacillin-tazobactum (72% sensitive), closely followed by amikacin (61%).Amikacin was more effective aminoglycoside than others. Least active antibiotics were ampicillin (5%). And cephalexin.(9%) One hundred and fifty two (97.4%) of all the isolates(Table 3) were multi-drug resistant. Multi-drug resistance in this study was defined as resistance of an isolate to at least one antimicrobial agent in at least three classes of antimicrobial agents tested.

Table 1

Age and sex wise distribution of K. pneumoniae isolates from UTI patients.

Age in years	Male (n=74)		Female (n=82)		Total (n=156)	
	Number	%	Number	%	Number	%
1-20	9	12.2	15	18.3	24	15.4
21-50	29	39.2	43	52.4	72	46.2
> 51	36	48.6	24	29.3	60	38.5

In all age groups, except those aged more than 50 years, females were more frequently affected than males. Among females, frequency of UTI was more among 21-50 years age group and among males elderly patients were more commonly affected

Table 2
Antimicrobial susceptibility of uropathogenic** K. pneumoniae. **isolates.

Antibiotics	Sensitive	Sensitive(%)
Ampicillin	8	5.26
Co -trimoxazole	36	23.7
Norfloxacin	41	27
Ciprofloxacin	63	41.4
Gentamicin	44	28.9
Nalidixic acid	35	23
Amoxyclav	20	13.2
Amikacin	95	60.1
Cephalexin	13	8.55
Cefoparazone –salbactam	54	35.5
Piperacillin-tazobactum	109	71.7
Ofloxacin	68	44.7
Nitrofurantoin	63	41.4

The most active antimicrobial agent against *K. pneumoniae* isolates were piperacillin-tazobactum (72% sensitive), closely followed by amikacin (61%).Amikacin was more effective aminoglycoside than others. Least active antibiotics were ampicillin (5%). And cephalexin.(9%)

Table 3
The prevalence of multi-resistance of K. pneumoniae. isolates from UTI patients

No. of classes of antibiotics resisted	No. of resistant *K. pneumoniae.* isolates
1	0
2	4
3	8
4	6
5	11
6	23
7	21
8	36
9	47
>3	152

One hundred and fifty two (97.4%) of all the isolates were multi-drug resistant . Multi-drug resistance in this study was defined as resistance of an isolate to at least one antimicrobial agent in at least three classes of antimicrobial agents tested.

DISCUSSION

UTI represent one of the most common diseases encountered in medical practice, causing significant associated morbidity and occurring from neonate to the elderly. Studies have demonstrated geographic variation in etiologic characteristics of UTI and their resistance patterns to antibiotics. Therefore to successfully eradicate UTI by empiric treatment, knowledge of local etiologic agents and their antibiotic susceptibility is of great value.[12,13][14] In the present study , UTI prevalence(Table 1) was higher in females (52.6%) than in males ,(47.4%) Which is in agreement earlier studies conducted across

India and other parts of the world.[5,14] Close proximity of the female urethral meatus to anus, short urethra, and sexual intercourse have been reported as factors which influence the higher prevalence in women. [5] Among females, frequency of UTI was more among 21-50 years age group. Among sexually active young women the incidence of symptomatic UTI is high, and the risk is strongly associated with recent sexual intercourse, recent use of diaphragm with spermicide, and a history of recurrent UTI. [14] Among males frequency of UTI was more in people of more than 50 years , elderly patients were more commonly affected This finding is similar to study conducted in Jaipur. [15] This is probably because with advancing age, the incidence of UTI increases among males due to prostate enlargement and neurogenic bladder. [16] Besides this a wide range of factors have been identified that can increase susceptibility to UTI. Among the specific genetic factors known to increase susceptibility are nonsecretor status or ABO blood-group antigens. Biologic factors that have been identified include congenital abnormalities, the presence of a urinary obstruction, and a prior history of UTI. Modifiable behavioral risk factors include the use of diaphragms, condoms and/or spermicides for contraception, and frequency of sexual intercourse among premenopausal women. [17] UTIs have been reported to be caused by Gram-negative bacilli with *E. coli* being the most prevalent. However, there is an increasing prevalence of *K. pneumoniae* as a UTIs' etiologic agent with an alarming rate of developing antimicrobial resistance. The development and spread of bacterial resistance to multiple antibiotics especially oral antibiotics due to the injudicious use of antimicrobial agents is recognized as a major problem globally. The clinicians are in a dilemma with limited treatment options available. [18] The present study demonstrates a high degree of resistance to ampicillin, cephalexin , co-trimoxazole and nalidixic acid.(Table 2) These antibiotics have been used for many years to treat UTI. the percentage resistance for ampicillin and co-trimoxazole, which are regarded as first line drugs for treatment of UTI ,are quite high and therefore cannot be used for empirical treatment in the current setting. The fluoroquinolones with their broad-spectrum activity are still being used as one of the best treatment options for UTI. In our study, the resistance to Norfloxacin ciprofloxacin and ofloxacin was quite high (27%-44%) which indicates that these drugs may no more be advocated for empirical therapy of UTI.[19] In the present study, comparatively, *K. pneumoniae* were less resistant to, piperacillin-tazobactam and amikacin , and therefore, can perhaps be used in the empiric treatment of UTIs. Other studies have also reported similar findings. [18,20] Standard antimicrobial regimens for empirical treatment of UTIs should be reassessed periodically in light of changing susceptibility patterns. Physician should be aware of current antimicrobial susceptibility patterns for *K. pneumoniae* and other uropathogens in their local communities as antimicrobial susceptibility changes over time.[21] Although, IDSA does address the areas of MDR isolates, however our study reports a very high (97.4%) multi-drug resistant *K. pneumoniae* (Table 3)among the UTIs patients in this environment. The isolates were commonly resistant to many classes of antimicrobial agents. The results of this study is only limited around one hundred and fifty samples in our hospital located in one of the southern states in the country therefore national antibiotic resistance surveillance of this organism is recommended for further study.

CONCLUSION

To conclude, this study stresses the importance of prior knowledge of the sensitivity pattern of the pathogen , before prescribing an antimicrobial agent for a meaningful therapy and to avoid fast emergence of resistant mutants. And also a good infection control and antibiotic policy will certainly help in delaying the era of unabated microorganisms for which no antibiotic is going to be effective.

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