

Fluoroquinolone Resistant *Escherichia Coli* and *Klebsiella Spp.* in Community-Acquired Urinary Tract Infections in Rural Kanpur, India

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ABSTRACT

Introduction: In the community, most of the patients are treated by the local physicians with empirically chosen antimicrobials, without any laboratory confirmation. The aim of the present study was to determine the aetiology and the antimicrobial susceptibility of the uropathogens in culture-positive, community-acquired urinary tract infections in the rural areas around Mandhana, Kanpur, over a period of 14 months.

Materials and Methods: The patients who presented with the symptoms of Urinary Tract Infection (UTI) were included in this study. The samples were inoculated in the camp on MacConkey's agar (MAC) and Sheep Blood Agar (SBA). The incubation, identification and the Antimicrobial Susceptibility Tests (AST) for the organisms which were done in the hospital laboratory.

Results: The most common bacteria which were isolated in all the age and gender groups were *Escherichia coli* (54%) and *Klebsiella spp* (11.3%). Among the oral antimicrobials which were usually prescribed by the local physicians in Kanpur, lomefloxacin, amoxicillin/sulbactam and nitrofurantoin were the ones to which the Enterobacteriaceae family was the most susceptible to. The resistance rate of *Klebsiella* to most of the antimicrobials was high (>20%). The resistance to the antimicrobials did not vary significantly with age, sex or any demographic factors.

Conclusion: The empirical treatment of the Community Acquired Urinary Tract Infections (CAUTIs) in the rural areas of Kanpur with co-trimoxazole, chloramphenicol, ciprofloxacin or norfloxacin is inadequate. Amoxicillin/sulbactam, nitrofurantoin or lomefloxacin should be the drugs of choice.

Key Words: Antimicrobial, Community, Infection, Urinary

INTRODUCTION

Community-Acquired Urinary Tract Infections (CAUTIs) are empirically treated in the rural areas of Kanpur (Population -4.5 million). However, the antibiotic resistance among the uropathogens that cause Urinary Tract Infections (UTIs) is increasing worldwide [1]. Most of the cases of UTIs are uncomplicated and the general practitioners in the rural areas usually prescribe antimicrobials to these patients without doing urine cultures. The guidelines for the management of UTIs and the appropriate empirical therapies rely on the knowledge of the prevailing bacteria which cause the infections and their antimicrobial susceptibility patterns [2]. No study has been done on the prevalence of the local uropathogens and their antibiograms in the rural population in Kanpur. A periodic surveillance is necessary as an increasing resistance to the antimicrobials among bacteria has been reported [3]. The ready availability of broad-spectrum antimicrobials, particularly quinolones, has changed the prescribing habits of the general practitioners in the treatment of community-acquired UTIs. Quinolones inhibit bacteria by interacting with the DNA topoisomerases (gyrases) thus, inhibiting the bacterial DNA synthesis. The aim of this study was to determine the aetiology and the antimicrobial susceptibility of the uropathogens in the culture-positive CAUTI cases which presented to us from August 2010 to October 2011.

MATERIALS AND METHODS

Samples were collected from the patients after taking an informed written consent from them. The subjects with one or more symptoms of UTIs (frequency, dysuria, urgency, haematuria, fever, suprapubic pain and flank pain), who attended the free health camps

which were organized by the Rama Medical College Hospital, Kanpur, India, in the adjoining villages which were included in the study. The subjects with a history of hospitalization or antibiotic therapy during the previous one year or those with indwelling catheterization were excluded from the study, to rule out the possibility of hospital acquired infections. The urine cultures which yielded $\geq 10^3$ colony forming units/ml of growth of a single bacterial species from freshly voided, mid-stream, clean catch urine specimens were considered to be culture positive. A contaminated sample was defined as a urine culture with $< 10^3$ cfu/ml or a yielding mixed growth of more than one bacterial species. MacConkey's agar and 7% sheep blood agar were streaked at the bedside of the patients with a 0.01 ml inoculation loop and they were brought to the laboratory for incubation at 37°C for 18hours. The isolates were processed and identified by the standard methods and Antimicrobial Susceptibility Tests (AST) were done according to the CSLI guidelines [4]. The results were analyzed by using descriptive statistics. The Chi-square and the Fisher's exact tests were applied for the categorical variables. All the statistical tests were two-tailed, and a p-value < 0.05 was considered to be statistically significant.

RESULTS

A total of 500 patients showed the symptoms of UTIs. 230 (46%) of the 500 patients had culture-positive isolates. There was no growth in 47.4% samples. In 6.6% samples, there was a growth of contaminants. From these, 12 different types of bacteria were isolated. Among these 230 patients, 47 were males and 183 were females [Table/Fig -1]. A majority of the isolates (n=173) were from patients who were aged ≤ 60 years, while 57 isolates were from

Age (in years)	Gender		Total
	Male	Female	
11 – 20	2	7	9
21-30	9	51	60
31 – 40	2	37	39
41-50	12	31	43
51 – 60	3	19	22
Above 60	19	38	57
Total	47	183	230

[Table/Fig-1]: Distribution of people with positive growth in Urine Culture According to Age and Gender.

Bacteria	Number isolated from	
	Males	Females
<i>E. coli</i>	26	99
<i>Klebsiella spp</i>	5	21
<i>Staphylococcus saprophyticus</i>	2	12
<i>Citrobacter spp</i>	1	10
<i>Enterobacter spp</i>	1	9
<i>Staphylococcus aureus</i>	2	7
<i>Acinetobacter baumannii</i>	2	7
<i>Pseudomonas aeruginosa</i>	5	5
<i>Proteus mirabilis</i>	0	4
<i>Enterococcus spp</i>	2	4
<i>Streptococcus spp.</i>	1	4
<i>Morganella morganii</i>	0	1
Total	47	183

[Table/Fig-2]: Different uropathogens isolated from male and female patients in the community.

Antimicrobials	<i>E. coli</i>	<i>Klebsiella</i>	<i>Citrobacter</i>	<i>Enterobacter</i>	<i>Pseudomonas</i>	<i>Acinetobacter</i>
	N=124	N=26	N=11	N=10	N=10	N=9
Ampicillin salb	11.3	38.5	9.1	0	90.0	55.6
Co-trimoxazole	90.3	80.7	63.6	50	80	55.5
Ceftizoxime	50.8	76.9	54.6	0.0	90.0	55.6
Ciprofloxacin	92.7	92.3	81.8	80.0	100.0	100.0
Nitrofurantoin	11.3	26.9	0.0	0.0	60.0	66.7
Sparfloxacin	16.1	61.5	81.8	100.0	90.0	66.7
Amikacin	81.5	61.5	27.3	0.0	80.0	66.7
Lomefloxacin	4.0	57.7	0.0	0.0	50.0	0.0

[Table/Fig-3]: Resistance pattern (%) of Gram negative organisms to commonly used antimicrobials.

those who were aged >60 years. *Escherichia coli* was the most frequently isolated bacteria (n=125) from both the genders and age groups, followed by *Klebsiella spp.* (n=26). *E. coli*, *Klebsiella*, *Citrobacter*, *Enterobacter* or *Staphylococcus saprophyticus* were isolated from 82% of the female patients, while *E. coli*, *Klebsiella spp.* or *Pseudomonas aeruginosa* were isolated from 76.6% of the male patients. *E. coli*, *Klebsiella*, *S. saprophyticus* and *Citrobacter koseri* were isolated from 80% of the patients who were aged ≤ 60 years, whereas *E. coli* and *Klebsiella spp.* were isolated from 81% of those that were aged > 60 years. The organisms who belonged to the Enterobacteriaceae family accounted for 76.9% of the isolates, gram-positive organisms accounted for 14.8 % of the isolates and gram-negative non-fermenters accounted for 8.3% of all the isolates [Table/Fig-2].

There were no significant differences in the prevalence of the organisms between the male and the female groups, as well as between the two age groups (≤ 60 years and > 60 years) for all the organisms.

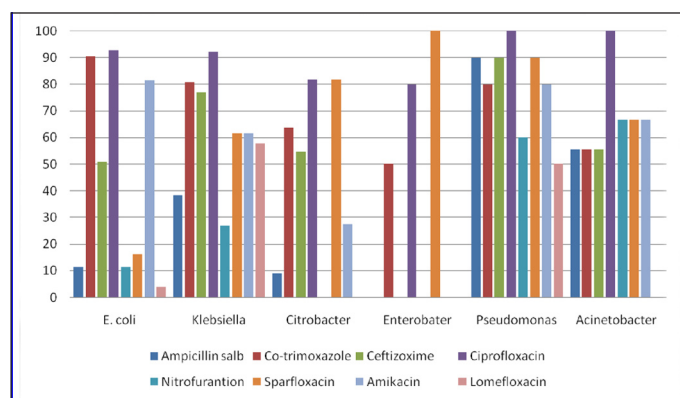
For the gram negative bacterial isolates, the antibiotic testing panels which were used were ampicillin-sulbactam, co-trimoxazole, ceftizoxime, ciprofloxacin, nitrofurantoin, sparfloxacin, amikacin and lomefloxacin. of the 125 *E. coli* isolates, 92% were resistant to ciprofloxacin.

Most of the *E. coli* isolates were moderately resistant to ampicillin-sulbactam, nitrofurantoin and sparfloxacin (r=11.2%,11.2% and 16% respectively) but those which were highly resistant to other antimicrobials were also detected (co-trimoxazole- 89.6%, amikacin- 80.8% and ceftizoxime 50.4%). Most of the *E. coli* (96%) isolates were sensitive to lomefloxacin. Of the 26 *Klebsiella* isolates, 92.3% were resistant to ciprofloxacin, 80.7% to co-trimoxazole, 76.9% to ceftizoxime, 61.8% to sparfloxacin and amikacin, 57.7% to lomefloxacin, 38.5% to ampicillin-sulbactam and 26.9% to nitrofurantoin [Table/Fig-3].

Fifty percent or more of the *P. aeruginosa* (n=10) and the *Acinetobacter baumannii* (n=9) isolates were resistant to all the antimicrobials except lomefloxacin, to which all the *Acinetobacter* isolates were sensitive. The resistance to the antimicrobials did not vary significantly with the age, sex or any demographic factors (p > 0.05) [Table/Fig-4].

DISCUSSION

The present study analyzed the aetiological agents, the distribution of the patients and the antibiotic susceptibility patterns of the bacterial species which were isolated from patients with CAUTIs from the rural areas of Kanpur during August 2010 to October



[Table/Fig-4]: Resistance pattern (%) of Gram negative organisms to commonly used antimicrobials.

2011. Many of the patients are treated by quacks/unqualified practitioners who indiscriminately prescribe a wide range of oral and injectable antimicrobials.

The patients in the present study were symptomatic for UTIs and therefore the samples of the patients with asymptomatic bacteriuria were missed. The samples were not screened for pus cells due to practical constraints. The complicated, recurrent and relapsed UTIs were excluded from this study to avoid a bias in favour of the resistant strains. In the present study, the urine cultures confirmed that UTIs were present in 46% of the patients with CAUTIs.

If the empiric treatment was based on the symptoms alone, then one would be giving the treatment for UTIs to at least 40% patients who didn't have UTIs [5]. The culture plates were inoculated at the bedside of the patients to avoid delays in their transport and bacterial overgrowth [6]. About 42.6% of the samples did not yield any growth and 6.6% were contaminated, which was less than that reported by Cheong et al., (19%) [7] but similar to that reported by Keah et al., (3%) [6]. *E. coli* was the commonest uropathogen which was responsible for CAUTIs (54.3%), followed by *Klebsiella spp.* (11.3%).

The prevalence of *E. coli* and *Klebsiella spp.* were reported to be 77% and 8.5% respectively by Keah et al., [6], and to be 24.7% and 6.5% respectively by Garcia Moure et al., [8]. In the present study, 89.6% of the *E. coli* strains which were isolated were resistant to co-trimoxazole, which was higher than that which was reported from Japan 3.4% (2002) [9], Canada, Finland, Germany, Portugal, Ireland and United Kingdom 4.9-26.7% (2003) [10], Korea 32% (2011) [11], Nicaragua 64% (2004) [12] and Aligarh, India 76% (2007) [13].

Similarly, 92% of the *E. coli* isolates in the present study were resistant to ciprofloxacin. The prevalence of ciprofloxacin resistance among the *E. coli* strains which were isolated from CAUTIs was reported to be 18% in Philippines (1997) [14], 22% in Granada, Spain (2000) [15], 24% in Singapore (2009) [16], 72.5% in Chandigarh, India (2009) [17] and 73% in Monterrey NL, Mexico (2008) [8]. In the present study, *E. coli* was susceptible to lomefloxacin (96%), ampicillin-sulbactam, nitrofurantoin and sparfloxacin ($r=11.2\%$, 11.2% and 16% respectively). The resistance rate of the *Klebsiella spp.* was high.

The *Klebsiella spp.* were most sensitive to ampicillin-sulbactam and nitrofurantoin ($r=38.5\%$ and 26.9% respectively) but not to lomefloxacin ($r=57.7\%$) although only 10.3% of all the gram negative bacteria which were tested were resistant to it. Since the overall resistance rate of the gram negative bacteria ($n=196$) to ampicillin-sulbactam ($r=20.4\%$), nitrofurantoin ($r=20.9\%$) and lomefloxacin ($r=10.3\%$) is not high, these antimicrobials should be considered for the empirical treatment of the CAUTIs among the rural population of Kanpur. The indiscriminate use of antimicrobials increases the risk of the increasing resistance rate to that particular drug [18]. In conclusion, the common uropathogens which are present in CAUTIs have a high resistance rate to the commonly used antimicrobials in the rural setting. Ampicillin-sulbactam, nitrofurantoin and lomefloxacin could be the empirical drugs of choice for the treatment of CAUTIs in the rural areas of Kanpur. In view of a high prevalence of the resistance rate, a molecular epidemiological study is mandated.

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