CLINICAL AND MICROBIOLOGICAL PROFILE OF UTI (URINARY TRACT INFECTION) IN INDIAN SUBJECTS: A PROSPECTIVE CLINICAL STUDY

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Abstract

Background: The understanding of the antibiotic resistance pattern of organisms causing UTI and the etiological profile of UTI is vital for timely diagnosis and adequate management of the disease.

Aim: The present study aimed to assess the risk factors and clinical profile of community-acquired urinary tract infections in the Indian scenario. The study also assessed the distribution of bacterial strains in these subjects and the resistance pattern of these microorganisms.

Methods: The study included 255 subjects with confirmed community-acquired UTI (CA-UTI) on the positive urine culture were included and assessed for the clinical and microbiological profiles along with the risk factors and symptomatology of the disease. The study also assessed causative microorganisms and their resistance patterns.

Results: Among included 255 subjects, the majority of the subjects were from the age range of 50 to 79 years with 56.85% (n=145) subjects. The most common clinical features were dysuria and fever. However, these features were not specific to the prediction of community-acquired UTI. The most common organism causing UTI was E. coli with 66.6% (n=170) subjects two-thirds of cases reporting resistance to ESBL (extended-spectrum beta-lactamase) with 41.96% (n=107) subjects. High resistance was seen in fluoroquinolones in 74.11% (n=189) subjects and the lowest resistance was seen for carbapenems in 3.92% (n=10) subjects.

Conclusion: The present study concludes that in subjects with community-acquired UTI, a high rate of ESBL-positive microorganisms is seen with resistance to the commonly used antibiotics which can raise concern in the future treating subjects with community-acquired UTI.

Keywords: community-acquired urinary tract infections, antibiotic resistance, extended-spectrum beta-lactamase, UTI

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INTRODUCTION

Urinary tract infection (UTI) signifies infection in any part of the urinary system including the urethrae, bladder, ureter, and/or kidney. UTI depicts the microorganisms in the urine of the affected subjects. Urinary infections are divided into three classifications namely UTI-A, UTI-B, and UTI-C depicting symptomatic UTI with microbiologic confirmation, symptomatic UTI with no microbiologic confirmation, and asymptomatic bacteriuria UTI respectively.[1]

UTIs or urinary tract infections are one of the most common infectious diseases seen in the community at the level of community spread. In such cases, empirical antibiotic therapy is used for the management and to imply this therapy, it is vital to know the common uropathogens and their resistance pattern and susceptibility to the antibiotics that are commonly used for treatment of these community-acquired urinary tract infections.[2]

Treating these community-acquired urinary tract infections further becomes more challenging when different risk factors such as immunosuppression, comorbidity, and advanced age are present along with the infections in the affected subjects.[3] Further, various physicians sometimes prescribe broad-spectrum antibiotics to the affected subjects in place of specific antibiotics considering the resistance pattern in the causative organisms to the commonly prescribed antibiotics. In addition, the incomplete course of the antibiotics and poor compliance of the affected subjects further lead to emergence of the resistance to many antibiotics.[4]

Previous literature research conducted worldwide has depicted the change in the patterns of the etiologic profiles of urinary tract infections. However, the literature studies on the pattern of antibiotic resistance and UTI in the Indian scenario are scarce in the literature. It is vital to know the present trends of uropathogens and their susceptibility to different antibiotics to make the guidelines for the empirical therapy of urinary tract infections till the culture sensitivity is not known.[5]

The present clinical study aimed to assess the risk factors and the common clinical presentations for urinary tract infection (UTI). The study also assessed the distribution of various bacterial strains isolated from uncomplicated and complicated UTI cases seen in the community along with the resistance pattern against the antibiotics used commonly in the Indian scenario.

MATERIALS AND METHODS

The present prospective clinical study aimed to assess the risk factors and clinical profile of community-acquired urinary tract infections in the Indian scenario. The study also assessed the distribution of bacterial strains in these subjects and the resistance pattern of these microorganisms. The study was done at Department of General Surgery, Rama Medical College and Hospital and Research Centre, Kanpur, Uttar Pradesh, after the clearance was given by the concerned institutional ethical committee. Informed consent in both written and verbal format was taken from all the subjects before study participation.

The study included subjects that visited the institute with the symptoms suggestive of the UTI and the diagnosis was confirmed with the positive urine cultures. The exclusion criteria for the study were subjects having clinical symptoms of UTI but no growth of microorganisms on the culture and the subjects that were not willing to participate in the study along with the subjects with the contaminated samples. The study also excluded subjects that took any other antimicrobial within the past 48 hours or a single dose in the past 24 hours despite the positive urine culture, and subjects with vesicoureteral reflex and ileal loops.

The data for the study were gathered using a performed structured questionnaire assessing the clinical and demographic data of the included study subjects. The study subjects were classified as having complicated UTIs following the criteria suggested by Rubenstein and Schaeffer in 2003.[6]

For identification and isolation of the uropathogens, a suprapubic aspirate or a clear midstream specimen was collected. The suprapubic aspirate was taken from the subjects where midstream urine specimens could not be collected. The sample was collected in a leak-proof container having a wide mouth that could hold nearly 50 ml of the sample. With a calibrated loop of 4 mm diameter, 10 µl of uncentrifuged specimen was kept on the agar plate followed by incubation for 24 hours at 35-37^{o} C. The specimen for UTI was taken positive when a single organism cultured >105 CFUs (colony forming units) per ml. The gram-negative and gram-positive organisms were culture isolates that were further identified using different biochemical reactions to the level of genus or species whichever was applicable.

For antibiotic sensitivity, with any potential growth, a modified Kirby-Bauer disc diffusion method was used following the guidelines of CLSI (Clinical and Laboratory Standards Institute). The antibiotics tested in the study were cotrimoxazole, nitrofurantoin, gentamicin, amikacin, norfloxacin, ofloxacin, ciprofloxacin, meropenem, and imipenem.

To detect the ESBL (extended spectrum beta-lactamase) ceftriaxone (≤25 mm), cefotaxime (≤27mm), aztreonam (≤27 mm), ceftazidime (≤22 mm), and cefpodoxime (≤17 mm) was used. When organisms presented a zone of inhibition lower compared to a minimum of any antibiotic disc, it was suspected to be ESBL positive. For phenotypic confirmation, the strain was tested against clavulanic acid/ceftazidime and ceftazidime. ESBL production was indicated and considered when a zone of inhibition with >5 mm diameter was seen for ceftazidime/clavulanic acid compared to ceftazidime. The reference strains for ESBL positive were taken as *Klebsiella pneumoniae* 700603 and ESBL negative as *Escherichia coli* ATCC 25922.[7]

To manage the subjects with UTI, in all subjects that were hemodynamically stable, oral cephalosporins and fluoroquinolones were started, whereas, in hemodynamically unstable subjects, parenteral third-generation cephalosporins were started. In subjects where symptoms did not subside within 72 hours of initiating the treatment with the culture depicting the ESBL-positive organisms, parenteral carbapenem therapy was initiated. All the subjects were started on antibiotics for seven days. In subjects with persistent fever even after 7 days, the antibiotics were further given for 48 hours after the fever subsided.

The data gathered were analyzed statistically using the SPSS software version 21.0 (IBM Corp., NY, USA). The various variables assessed were the risk factors for UTI, symptomatology of the affected subjects, antibiotic resistance, antibiotic sensitivity, organisms causing UTI, gender, and age of the affected subjects.

RESULTS

The present prospective clinical study aimed to assess the risk factors and clinical profile of community-acquired urinary tract infections in the Indian scenario. The study also assessed the distribution of bacterial strains in these subjects and the resistance pattern of these microorganisms.

For the gender and age distribution of the study subjects, it was seen that UTI was most prevalent in subjects of age 50-59 years with 19.60% (n=50) subjects followed by 18.03% (n=46) subjects from 70-79 years of age and 9.01% (n=23) subjects from 20-29 years of age range. Uncomplicated UTI was seen in 26 females with the majority of subjects from 20-29 years of age 38.46% (n=10) subjects followed by 23.07% (n=6) subjects from 40-49 years of age. Complicated UTI was seen in 143 males and 86 females where the majority of males were in the age range of 60-69 years with 22.37% (n=32) males and 22.09% (n=19) female subjects as shown in Table 1.

On assessing the risk factors associated with UTI, the most common factor was diabetes mellitus reported in 38.43% (n=98) subjects followed by the recurrent history of urogenital instrumentation in 14.50% (n=37) subjects, catheterization in 10.19% (n=26) subjects, recurrent UTI in 7.84% (n=20), congenital anomalies in 3.92% (n=10), renal stones in 1.96% (n=5), post-transplant cases in 1.56% (n=4) subjects, and immunosuppression in 0.78% (n=2) study subjects respectively as depicted in Table 2.

Concerning the distribution pattern of the pathogens and ESBL production, the most common pathogen was ESBL-negative E. coli seen in 24.70% (n=63) complicated and 46.15% (n=12) uncomplicated cases of UTI followed by pseudomonas in 21.83% (n=50) and 3.84% (n=1) cases of complicated and uncomplicated UTI cases, ESBL-positive *Klebsiella* in 20.52% (n=47) and 7.69% (n=49) complicated and uncomplicated UTI cases, ESBL-negative *Klebsiella* in 12.66% (n=29) and 3.84% (n=1) subjects with complicated and uncomplicated UTI cases. ESBL-positive E. coli were cultured in 7.84% (n=20) and 26.92% (n=7) complicated and uncomplicated UTI cases, Citrobacter freundii was seen in 3.13% (n=8) subjects with complicated UTI, Enterobacter spp. was seen in 2.35% (n=6) and 3.84% (n=1) complicated and uncomplicated UTI cases, Enterococcus faecalis was reported in 1.17% (n=3) and 3.84% (n=1) complicated and uncomplicated UTI cases, Providencia alkalifaciens was seen in 0.39% (n=1) and 3.84% (n=1) subjects from complicated and uncomplicated UTI cases, and proteus vulgaris and Morganelle were seen in 0.39% (n=1) subject each from the complicated UTI cases (Table 3).

For the assessment of the resistant pattern in uropathogens to different antibiotics, resistance to ofloxacin and norfloxacin was seen in 76.85% (n=176) subjects from complicated UTI and 50% (n=13) and 46.15% (n=12) subjects from uncomplicated UTI respectively. Resistance to nitrofurantoin was seen in 31% (n=71) and 7.69% (n=2) subjects with complicated and uncomplicated UTI respectively, to meropenem and imipenem in 3.93% (n=9) subjects with complicated UTI and 3.84% (n=1) subjects with uncomplicated UTI respectively. The resistance to gentamicin was seen in 51.09% (n=117) subjects and 30.76% (n=8) subjects respectively with complicated and uncomplicated UTI, to cotrimoxazole in 34.06% (n=78) and 3.84% (n=1)

subject respectively with complicated and uncomplicated UTI cases, to ciprofloxacin in 55.02% (n=126) and 50% (n=13) subjects respectively from complicated and uncomplicated UTI cases to amikacin in 26.63% (n=61) and 19.23% (n=5) subjects with complicated and uncomplicated UTI respectively as shown in Table 4.

DISCUSSION

For the gender and age distribution of the study subjects, it was seen that UTI was most prevalent in subjects of age 50-59 years with 19.60% (n=50) subjects followed by 18.03% (n=46) subjects from 70-79 years of age and 9.01% (n=23) subjects from 20-29 years of age range. Uncomplicated UTI was seen in 26 females with the majority of subjects from 20-29 years of age 38.46% (n=10) subjects followed by 23.07% (n=6) subjects from 40-49 years of age. Complicated UTI was seen in 143 males and 86 females where the majority of males were in the age range of 60-69 years with 22.37% (n=32) males and 22.09% (n=19) female subjects. These results were similar to the studies of Micek St et al[8] in 2010 and Prais D et al[9] in 2003 where authors assessed UTI subjects with demographic data comparable to the present study.

The study results showed that for the risk factors associated with UTI, the most common factor was diabetes mellitus reported in 38.43% (n=98) subjects followed by recurrent history of urogenital instrumentation in 14.50% (n=37) subjects, catheterization in 10.19% (n=26) subjects, recurrent UTI in 7.84% (n=20), congenital anomalies in 3.92% (n=10), renal stones in 1.96% (n=5), post-transplant cases in 1.56% (n=4) subjects, and immunosuppression in 0.78% (n=2) study subjects respectively. These results were consistent with the studies of D Francesco MA et al[10] in 2007 and Al-Sweih N et al[11] in 2005 where risk factors described as associated with UTI were similar to the present study.

It was seen that for the distribution pattern of the pathogens and ESBL production, the most common pathogen was ESBL-negative E. coli seen in 24.70% (n=63) complicated and 46.15% (n=12) uncomplicated cases of UTI followed by pseudomonas in 21.83% (n=50) and 3.84% (n=1) cases of complicated and uncomplicated UTI cases, ESBL-positive *Klebsiella* in 20.52% (n=47) and 7.69% (n=49) complicated and uncomplicated UTI cases, ESBL-negative *Klebsiella* in 12.66% (n=29) and 3.84% (n=1) subjects with complicated and uncomplicated UTI cases. ESBL-positive E. coli were cultured in 7.84% (n=20) and 26.92% (n=7) complicated and uncomplicated UTI cases, Citrobacter freundii was seen in 3.13% (n=8) subjects with complicated UTI, Enterobacter spp. was seen in 2.35% (n=6) and 3.84% (n=1) complicated and uncomplicated UTI cases, Enterococcus faecalis was reported in 1.17% (n=3) and 3.84% (n=1) complicated and uncomplicated UTI cases, Providencia alkalifaciens was seen in 0.39% (n=1) and 3.84% (n=1) subjects from complicated and uncomplicated UTI cases, and proteus vulgaris and Morganelle were seen in 0.39% (n=1) subject each from the complicated UTI cases. These findings were in agreement with the findings of Das RN et al[12] in 2006 and Colonder R et al[13] in 2001 where the distribution pattern of the pathogens and ESBL production was reported by the authors as in the present study.

The study results showed that concerning the assessment of the resistant pattern in uropathogens to different antibiotics, resistance to ofloxacin and norfloxacin was seen in 76.85% (n=176) subjects from complicated UTI and 50% (n=13) and 46.15% (n=12) subjects from uncomplicated UTI respectively. Resistance to nitrofurantoin was seen in 31% (n=71) and 7.69% (n=2) subjects with complicated and uncomplicated UTI respectively, to meropenem and imipenem in 3.93% (n=9) subjects with complicated UTI and 3.84% (n=1) subjects with uncomplicated UTI respectively. The resistance to gentamicin was seen in 51.09% (n=117) subjects and 30.76% (n=8) subjects respectively with complicated and uncomplicated UTI, to cotrimoxazole in 34.06% (n=78) and 3.84% (n=1) subject respectively with complicated and uncomplicated UTI cases, to ciprofloxacin in 55.02% (n=126) and 50% (n=13) subjects respectively from complicated and uncomplicated UTI cases to amikacin in 26.63% (n=61) and 19.23% (n=5) subjects with complicated and uncomplicated UTI respectively. These results were in line with the findings of Prakash V et al[14] in 2009 and Taneja N et al[15] in 2008 where the resistant pattern to uropathogens to various antibiotics was as seen in the results of the present study.

CONCLUSION

Considering its limitations, the present study concludes that in subjects with community-acquired UTI, a high rate of ESBL-positive microorganisms is seen with resistance to the commonly used antibiotics which can raise concern in the future treating subjects with community-acquired UTI.

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TABLES

Age range	Uncomplicated UTI (females)		Complicated UTI				Total	
	n	%	Male (n=143)	%	Females (n=86)	%	N=255	%
0-9	2	7.69	11	7.69	2	2.32	15	5.88
10-19	2	7.69	4	2.79	4	4.65	10	3.92
20-29	10	38.46	8	5.59	5	5.81	23	9.01
30-39	4	15.38	9	6.29	4	4.65	17	6.66
40-49	6	23.07	12	8.39	5	5.81	23	9.01
50-59	2	7.69	29	20.27	19	22.09	50	19.60
60-69			32	22.37	19	22.09	51	20
70-79			27	18.88	19	22.09	46	18.03
80-89			9	6.29	7	8.13	16	6.27
90-99			2	1.39	2	2.32	3	1.17
Total	26	100	143	100	86	100	255	100

Table 1: Gender and age-wise distribution of uncomplicated and complicated UTIs in study subjects

Risk factors	**N=255**	**%**
Renal stones	5	1.96
Recurrent UTI	20	7.84
Recurrent history of urogenital instrumentation	37	14.50
Post-transplant	4	1.56
Immunosuppression	2	0.78
Diabetes mellitus	98	38.43
Congenital anomalies	10	3.92
Catheterization	26	10.19

Table 2: Risk factors in study subjects with UTI

Organisms	**Complicated**		**Uncomplicated**		**Total**	
	N=229	**%**	**N=26**	**%**	**N=255**	**%**
Pseudomonas	50	21.83	1	3.84	51	20
Providencia alkalifaciens	1	0.39	1	3.84	2	0.78
Proteus vulgaris	1	0.39	0	-	1	0.39
Morganelle	1	0.39	0	-	1	0.39
ESBL-negative *Klebsiella*	29	12.66	1	3.84	30	11.76
ESBL-positive *Klebsiella*	47	20.52	2	7.69	49	19.21
ESBL-negative E. coli	63	24.70	12	46.15	75	29.41
ESBL-positive E. coli	20	7.84	7	26.92	27	10.58
Enterococcus faecalis	3	1.17	1	3.84	4	1.56
Enterobacter spp.	6	2.35	1	3.84	7	2.74
Citrobacter freundii	8	3.13	0	-	8	3.13
Total	229	100	26	100	255	100

Table 3: Distribution pattern of the pathogens and ESBL production

Organisms	**Complicated**		**Uncomplicated**		**Total**	
	N=229	**%**	**N=26**	**%**	**N=255**	**%**
Ofloxacin	176	76.85	13	50	189	74.11
Norfloxacin	176	76.85	12	46.15	188	73.72
Nitrofurantoin	71	31	2	7.69	79	30.98
Meropenem	9	3.93	1	3.84	10	3.92
Imepenem	9	3.93	1	3.84	10	3.92
Gentamicin	117	51.09	8	30.76	125	49.01
Cotrimoxazole	78	34.06	1	3.84	79	30.98
Ciprofloxacin	126	55.02	13	50	139	54.50
Amikacin	61	26.63	5	19.23	66	25.88

Table 4: Resistance pattern in uropathogens to different antibiotics