Original Article ISSN (O):2395-2822; ISSN (P):2395-2814

Study of Antibiotic Resistance Pattern in Uropathogens at a Tertiary Care Hospital.

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Received: June 2017
Accepted: June 2017

ABSTRACT

Background: Urinary tract infection (UTI) is common infection in the world caused by uropathogens, to make a proper treatment of UTI should be a proper diagnosis of the cause and therefore a proper application of drugs. Keeping in mind the causes of urinary tract infections and the sensitivity pattern of uropathogens towards the antibiotic, the present study was proposed to study the uropathogens. An empiric treatment of UTI is find out by the antibiotic sensitivity patterns of uropathogens in a population. There is an resistance increased to the first line empirical drugs used in the treatment of UTI. This study was conducted in Garhwal Uttrakhand (India) to determine the resistance patterns of amongst uropathogens, to help in the establishment of local guidelines on the treatment of UTI. **Methods:** This is a retrospective study on 338 urine cultures from July 2013 to June 2014. Antibiotic susceptibility test (AST) method was done by Kirby-Bauer disc diffusion method and compared. Data Analysis was done by using simple percentage method. **Results:** Out of the 338 samples subjected to culture, 166(49.11%) were positive for growth. Out of the 166 culture isolates, Escherichia coli was the most common 67 (19.8%) followed by CoNS 30(8.8%), Staphylococcus 14(4.1%), Enterococcus 11(3.3%), Acinetobacter spp. 10(2.9%), Klebsiella 8(2.4%), and Candida albicans 7(2.1%). The antibiotic sensitivity pattern was analyzed for all the bacterial isolates together and drugs are sort in order of their sensitivity. On the basis of antibiotic sensitivity pattern it is found that all bacterial isolates were 24.6 % sensitive to Amikacin, 23.1 % sensitive to Gentamicin, 18 % sensitive to Nitrofurantoin Acid, 15.1 % sensitive to Ciprofloxacin, 13.3 % sensitive to Meropenem and Cefoperazone- sulbactam, 13% sensitive to Piperacillin- tazobactam and Co-trimoxazole, 10.7 % sensitive to Amoxicillin-clavulanic acid, 10.4 % sensitive to Aztreonam and 10.1% sensitive to Chloramphenicol. All the isolates were 16.9% resistant to Ciprofloxacin and Co-trimoxazole, 12.7% resistant to Amoxicillin-clavulanic acid, 12.4% resistant to Ampicillin, 10.7% resistant to Cefotaxime, Cefazolin &Ticarcillin-Clavulanic acid and 10.4 % resistant to Cefuroxime. **Conclusion:** The alarming rate of resistance to Ciprofloxacin, Co-trimoxazole, Amoxicillin-clavulanic acid, Ampicillin, Cefotaxime, Cefazolin &Ticarcillin-Clavulanic acid of urinary isolates, precludes the use of these commonly used antibiotics for empiric treatment of urinary tract infections (UTI) in India. Therefore, urine culture is necessarily recommended for screening and diagnosis.

Keywords: Antibiotic susceptibility test(AST), CoNS coagulase negative staphylococcus , antibiotic susceptibility test (AST) ,Urinary tract infection(UTI).

INTRODUCTION

Urinary tract infection (UTI) is one of the most frequent conditions encountered by general practitioners.[7] An acute uncomplicated urinary tract infection (UTI) is one of the most common bacterial infections in women. It is estimated that as many as 60% of all women report having had an urinary tract infections(UTI) at least once in their lifetime. Worldwide, about 150 million people are diagnosed with urinary tract infections (UTI) each Year, costing in excess of 6 billion dollars. Among both outpatients(OPD) and inpatients, Escherichia coli is the most common isolate, accounting for 75% to 90% of uncomplicated urinary tract infections (UTI) isolates.[5,6] Staphylococcus saprophyticus, Klebsiella spp., Proteus spp., Enterococcus spp., and Enterobacter spp. are organisms less commonly isolated from outpatients. In the majority of cases, antibiotics are given empirically before the final bacteriology results are available. Therefore, area-specific monitoring studies to document the microorganisms causing urinary tract infections (UTI) and their antimicrobial susceptibility is mandatory for helping the selection of an effective empirical treatment.[20] Urinary Tract Infections (UTIs) are usually treated with different broad-spectrum antibiotics when one with a narrow spectrum of activity may be appropriate because of concerns about an infection with resistant organisms. Fluoroquinolones are preferred as an initial agents

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for empiric therapy of urinary tract infections (UTI) in the area where resistance is likely to be of concern.[3,19] This is because they have high bacteriological and clinical cure rates, as well as low rates of resistance, among most common uropathogens.[8] The resistance pattern of community-acquired urinary tract infections (UTI) pathogens has not been studied extensively.[8] The extensive use of antimicrobial agents has invariably resulted in the development of antibiotic resistance, which, in recent years, has become a major problem worldwide. The etiology of urinary tract infections (UTI) and the antibiotic resistance of uropathogens have been changing over the past years, both in the community and nosocomial infection.[11] However, there is not much information on etiology and resistance pattern of community acquired urinary tract infections (UTIs) in India. This retrospective study was done to compare the frequency and drug resistance pattern in uropathogens isolated from patients with urinary tract infections (UTIs) in IPD/OPD, Base Hospital Srikot and VCSG Medical College, Srinagar Garhwal, India.[17] Urinary Tract Infections (UTI) accounts for 25 to 40% of all nosocomial infections, making these infections an important medical and financial burden on health care systems. Urinary Tract Infections (UTI) usually starts as a bladder infection but can, depending on the bacterial strain, ascend to the kidneys and may ultimately be able to result in renal failure or dissemination to the blood. UTI is classified into disease categories according to the focal point and the severity of infection: bacteriuria (the urine), cystitis (the bladder), pyelonephritis (the kidneys). Growth in urine in the absence of symptoms is called asymptomatic bacteriuria (ABU). ABU resembles a commensal-like carrier state, which often goes unnoticed by the patient. UTIs primarily affect women and girls; 40 to 50% of adult women will experience at least one UTI episode during their lifetime.[5,6] Escherichia coli strains are generally commensal lifestyle in the gastrointestinal tract (GIT) flora. However, some strains have developed the ability to cause disease. Intestinal pathogenic Escherichia coli can cause a variety of intestinal disorders, while extra intestinal pathogenic Escherichia coli UPEC (Uropathogenic Escherichia Coli) causes a range of extra intestinal infections, such as urinary tract infections, septicemia, neonatal meningitis, and infections of the respiratory tract. Unlike diarrheagenic strains, UPEC strains do not cause disease in the intestinal tract. UPEC strains constitute about 20% of the Escherichia coli strains of the human fecal flora in healthy individuals. It is generally believed that strains infecting the urinary tract originate from the fecal flora. Escherichia coli is also found in the vagina in about 20% of healthy women.[22] Antibiotic resistance occurs when a microorganism has the competence to withstanding the effects of antibiotics. Antibiotic resistance that evolves by the way of the natural selection performing upon random mutation, but it can also be an engineered by applying an evolutionary stress on a population. The appearance of resistance of antibiotic in the management of UTIs is a serious public health issue, particularly in the developing world where apart from the high level of ignorance, poverty, and poor hygienic practices, there is also high prevalence of spurious and fake drugs of questionable quality in circulation. Studies aimed at gaining knowledge about the type of pathogens responsible for UTIs and their susceptibility patterns may help the clinicians to choose the right empirical treatment.[1,20]

MATERIALS AND METHODS

This study was designated as a retrospective survey of 338 urine culture specimens from July 2013 to June 2014. As we had no control over the collection of specimens, cultures which yielded more than one(not more than two) isolate was included in the study group. All the culture isolates were identified in the department of Microbiology, Base Hospital Srikot, and VCSG Medical College, Srinagar Garhwal, by standard laboratory techniques. Antimicrobial susceptibility testing was done by Kirby-Bauer disc diffusion method as per CLSI (clinical and laboratory standards institute) criteria.[2] ATCC control strains (Escherichia coli ATCC 25922, for Pseudomonas ATCC 27853 and for S. aureus ATCC 25923) were used as per CLSI guidelines. All the analysis was performed using simple percentage method.[2,4]

RESULTS

In the present study total, 338 samples were studied. Out of the 338 samples subjected to culture, 166(49.1%) were positive for growth (table1). Out of the 166 culture isolates [Table 2], Escherichia coli was the most common 67 (19.8%) followed by CoNS 30 (8.8%), Staphylococcus 14 (4.1%), Enterococcus 11 (3.3%), Acinetobacter spp. 10 (2.9%) and Klebsiella 8 (2.4%). The antibiotic sensitivity pattern was analyzed for all the bacterial isolates together and drugs are sorted within the table in order of their sensitivity [Table 3]. On the basis of antibiotic sensitivity pattern analysis, all bacterial isolates have shown their sensitivity and resistance towards specific antibiotics. The sensitivity was observed as - 24.6% to Amikacin, 23.1% to Gentamicin, 18% to Nitrofurantoin Acid, 15.1% to Ciprofloxacin, 13.3% to Meropenem and Cefoperazone- Sulbactam, 13% to Piperacillin-tazobactam and Co-trimoxazole, 10.7% to Amoxicillin-clavulanic acid, 10.4% to Aztreonam and 10.1% to Chloramphenicol. On the other hand, as far as the resistance of uropathogens towards antibiotics is concerned, it is found as - 16.9% to Ciprofloxacin and Co-trimoxazole, 12.7% to

Amoxicillin-clavulanic acid, 12.4% to Ampicillin, 10.7% to Cefotaxime, Cefazolin & Ticarcillin-Clavulanic acid and 10.4% to Cefuroxime.
The results obtained from data analysis are represented in following tables and further discussed.

Table 1: Sex Distribution of Study Group (N=338)

Age In Years	M	F	Total
21-30 Years	93 (27.5%)	245 (72.5%)	338 (100%)
Sterile	61 (18%)	88 (26%)	149 (44.1%)
Mixed Growth	1 (0.3%)	22 (6.5%)	23 (6.8%)
Positive for Uropathogens	31 (9.1%)	135 (39.9%)	166 (49.1%)
Total	93 (27.5)	245 (72.5%)	338 (100%)

[Table 1] shows the sex wise distribution of the sample, it shows that sample consists 27.5% male patients and 72.5% female patients. The sample in this age group is dominated by the female patients. It is evident from the table 3 that UTI is frequently found in females.

The sample distribution also shows that out of 338 urine samples, 149 samples (61 males, 88 females) are found sterile and 23 samples are found contaminated, there were 166 samples found positive for uropathogens.

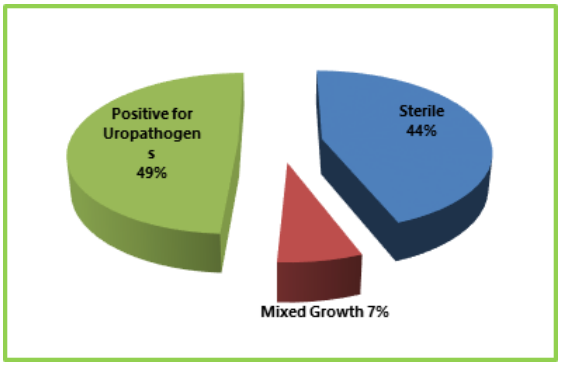

Figure 1: Sample Distribution

Table 2: Organism Isolated For Urinary Tract Infection (N =338)

Organism Isolated	(Count Value)			(% Value)		
	M	F	Total	M	F	Total
1. Sterile	61	88	149	18	26	44.1
2. Mixed Growth	1	22	23	0.3	6.5	6.8
3. Escherichia Coli	11	56	67	3.3	16.6	19.8
4. CoNS	6	24	30	1.8	7.1	8.8
5 Staphylococcus	2	12	14	0.6	3.6	4.1
6. Enterococcus	3	8	11	0.9	2.4	3.3
7. Acinetobacter Spp	3	7	10	0.8	2.1	2.9
8. Klebsiella Spp	1	7	8	0.3	2.1	2.4
9. Candida Albicans	0	7	7	0	2.1	2.1
10. Citrobacter	1	5	6	0.3	1.5	1.8
11. Methicilin Sensitive Cops	1	4	5	0.3	1.2	1.5
12. Candida Non Albicans	0	3	3	0	0.9	0.9
13. Proteus Mirabilis	0	2	2	0	0.6	0.6
14. Pseudomonas	2	0	2	0.6	0	0.6
15. Non Fermenter	0	1	1	0	0.3	0.3
16. Shigella	1	0	1	0.3	0	0.3
Total	93	245	338	27.5	72.5	100

[Table 2] is displaying the organism isolation in sampled units, responsible for causing the urinary tract infection among youth. The sampled units are of 21-30 years' age group and the most common causing bacteriuria responsible for urinary tract infection in youth is found Escherichia coli.
It is evident from above table that the organism highly responsible for urinary tract infections is Escherichia coli, meaning by that it is causing factor for UTI in 3.3% male and 16.6% female children, which is 20% approximate, so it is clearly said that Escherichia coli is responsible for causing UTI in 20% youth population. The other bacteria which were isolated in the sample but not highly responsible for causing urinary tract infections in the youth population, they are CoNS (8.8%),

Staphylococcus (4.1%), Enterococcus (3.3%), Acinetobacter spp. (2.9%), Klebsiella (2.4%).

The CoNS is responsible for 8.8% youth population (1.8% male and 7.1% female) for causing urinary tract infections. CoNS is responsible for causing urinary tract infection in 8.8% youth population which is highest after Escherichia coli, the next highest responsible uropathogen is found Staphylococcus (4.1%) followed by Enterococcus (3.3%), Acinetobacter spp. (2.9%) and Klebsiella (2.4%).

It is seen in table 2 that other different uropathogens are responsible for causing UTI only in 2.1%, 1.8%, 1.5%, 0.9%, 0.6%, 0.3% sample units which is negligible as compared to Escherichia coli, CoNS, Staphylococcus, Enterococcus, Acinetobacter spp. and Klebsiella.

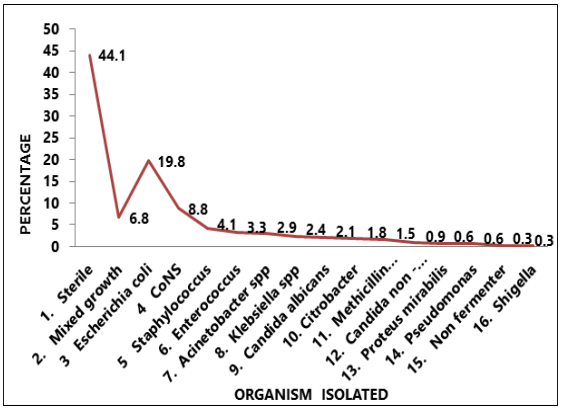

Figure 2: Organism Isolation In Urin Sample

Table 3:- Drug Sensitivity Pattern In Patients Of 21-30 Years Age Group (N = 338)

Sr. No.	Drugs	Count Value			Total	Percentage (%) Value			Total
		NR	R	S		NR	R	S	
1.	Amikacin	238	17	83	338	(70.4)	(5.0)	(24.6)	(100)
2.	Gentamicin	227	33	78	338	(67.2)	(9.8)	(23.1)	(100)
3.	Nitrofurantoin	262	15	61	338	(77.5)	(4.4)	(18)	(100)
4.	Ciprofloxacin	230	57	51	338	(68)	(16.9)	(15.1)	(100)
5.	Meropenem	285	8	45	338	(84.3)	(2.4)	(13.3)	(100)
6.	Cefoperazone- Sulbactam	284	9	45	338	(84)	(2.7)	(13.3)	(100)
7.	Piperacillin- Tazobactam	282	12	44	338	(83.4)	(3.6)	(13)	(100)
8.	Co-Trimoxazole	237	57	44	338	(70.1)	(16.9)	(13)	(100)
9.	Amoxicillin-Clavulanic Acid	258	43	36	338	(76.3)	(12.7)	(10.7)	(100)
10.	Aztreonam	281	22	35	338	(83.1)	(6.5)	(10.4)	(100)
11.	Chloramphenicol	294	10	34	338	(87)	(3)	(10.1)	(100)
12.	Cefotaxime	271	36	31	338	(80.2)	(10.7)	(9.2)	(100)
13.	Linezolid	304	4	30	338	(89.9)	(1.2)	(8.9)	(100)
14.	Cefazolin	272	36	30	338	(80.5)	(10.7)	(8.9)	(100)
15.	Cefuroxime	275	35	28	338	(81.4)	(10.4)	(8.3)	(100)
16.	Rifampicin	305	9	24	338	(90.2)	(2.7)	(7.1)	(100)
17.	Vancomycin	312	3	23	338	(92.3)	(0.9)	(6.8)	(100)
18.	Teicoplanin	311	7	20	338	(92)	(2.1)	(5.9)	(100)
19.	Clindamycin	299	20	19	338	(88.5)	(5.9)	(5.6)	(100)
20.	Erythromycin	295	24	19	338	(87.3)	(7.1)	(5.6)	(100)
21.	Cefipime	297	23	18	338	(87.9)	(6.8)	(5.3)	(100)
22.	Ampicillin	281	42	15	338	(83.1)	(12.4)	(4.4)	(100)
23.	Ticarcillin-Clavulanic Acid	288	36	14	338	(85.2)	(10.7)	(4.1)	(100)
24.	Ceftazidime	323	7	8	338	(95.6)	(2.1)	(2.4)	(100)
25.	Oxacillin/Cephoxitin	329	1	8	338	(97.3)	(0.3)	(2.4)	(100)
26.	Penicillin	313	18	7	338	(92.6)	(5.3)	(2.1)	(100)
27.	Netilmicin	333	0	5	338	(98.5)	(0)	(1.5)	(100)
28.	Nalidixic Acid	331	2	5	338	(97.9)	(0.6)	(1.5)	(100)
29.	Tobramycin	336	0	2	338	(99.4)	(0)	(0.6)	(100)
30.	Piperacillin	336	1	1	338	(99.4)	(0.3)	(0.3[8[8[)	(100)
31.	Colistin	337	0	1	338	(99.7)	(0)	(0.3)	(100)
32.	Polymixin B	338	0	0	338	(100)	(0)	(0)	(100)
33.	Tetracycline	337	1	0	338	(99.7)	(0.3)	(0)	(100)

[Table 3] is showing the antibiotic sensitivity pattern in the studied sample. By observing drug sensitivity pattern in sampled units, it is found that all bacterial isolates have shown their sensitivity and resistance towards specific antibiotics, as far as sensitivity is concerned it was observed as - 24.6% to Amikacin, 23.1% to Gentamicin, 18% to Nitrofurantoin, 15.1% to Ciprofloxacin, 13.3% to Meropenem and

Cefoperazone- sulbactam, 13% to Piperacillin-tazobactam and Co-trimoxazole, 10.7% to Amoxicillin-clavulanic acid, 10.4% to Aztreonam and 10.1% to Chloramphenicol. On the other hand, as far as the resistance of uropathogens towards antibiotics is concerned, it is found as - 16.9% to Ciprofloxacin and Co-trimoxazole, 12.7% to Amoxicillin-clavulanic acid, 12.4% to Ampicillin, 10.7% to Cefotaxime, Cefazolin & Ticarcillin-Clavulanic acid and 10.4% to Cefuroxime.

These antibiotics—Amikacin (24.6%), Gentamicin (23.1%), Nitrofurantoin (18%), Ciprofloxacin (15.1%), Meropenem (13.3%), Cefoperazone-sulbactam (13.3%), Piperacillin-tazobactam (13%), Co-trimoxazole (13%), Amoxicillin-clavulanic acid (10.7%), Aztreonam (10.4%%) and Chloramphenicol (10.1%) are found highly sensitive in studied sample, who are of 21-30 years age group. On the other hand the high resistance for the applied drugs shown by the youth group was for Ciprofloxacin (16.9%), Co-trimoxazole (16.9%), Amoxicillin-clavulanic acid (12.7%), Ampicillin (12.4%), Cefotaxime (10.7%), Cefazolin (10.7%), Ticarcillin-Clavulanic acid (10.7%) and Cefuroxime (10.4%).

DISCUSSION

The study was undertaken to determine the incidence of urinary tract infection in youth as well as to evaluate the bacterial agents involved in this UTI. Out of the 338 patients in youth group that participated in this study, only 166 (31 males (9.1%) and 135 females (39.9%), 49.0%) had urine samples with significant infection of urinary tract while 172 (62 male (18.3%) and 110(32.5%) females, 50.8%) were asymptomatic. A large number of microorganisms were isolated from female patients with the high bacteria count. This study shows a higher incidence of urinary tract infection in females than males.

The most commonly isolated organism found in our study was Escherichia coli [Table 2]. The proportion of bacterial species isolated in the present study was similar to those described in several previous studies.[5,21] This study shows the distribution and antibiotic susceptibility pattern of microbial species isolated from patients with UTIs in HNB Base Hospital Srikot, Srinagar Garhwal. These isolated organisms cause a variety of infections including UTIs.[23] The study was taken with the age group 21-30 years which is the most common affected group. Females (39.9%) were more frequently affected than males (9.1%). The age and sex distribution of the study group are shown in [Table 1]. The UTIs are more frequent in women than in men, which corresponds to our findings because 39.9% of our patients were females as compared to 9.1% male patients.[9] The high resistance rates [Table 3] shown to the oral antibiotics (Ciprofloxacin, Co-trimoxazole, Amoxicillin-clavulanic acid, Ampicillin, Cefotaxime, Cefazolin, Ticarcillin-Clavulanic acid, Cefuroxime) in the present study may be due to the uncontrolled consumption of these antibiotics in the community in the past decade in Garhwal region.[16] On the other hand, resistance to Ceftazidime, Oxacillin/Cefoxitin, Penicillin, Netilmicin, Nalidixic acid, Tobramycin, Piperacillin, and Colistin are low, meaning by that lower usage of these drugs by the community. Our study demonstrates high sensitivity of isolated organisms to Amikacin, Gentamicin, Nitrofurantoin, Ciprofloxacin, Meropenem, Cefoperazone-sulbactam, Piperacillin-tazobactam, Co-trimoxazole, Amoxicillin-clavulanic acid, Aztreonam and Chloramphenicol in the youth population.

The international trend of empirically treating UTI may not apply for specific geographical regions such as India, where decreased susceptibility rates are documented for common urinary pathogens. In the Indian setting, routine urine cultures may be necessary, since treatment failure with empirical therapy is likely to occur and in India, we need specific guidelines based on local susceptibility patterns. Development of regional surveillance programs is necessary to provide information which would then enable the development of Indian UTI guidelines.[19]

CONCLUSION

In conclusion, this study determined the incidence of urinary tract infection in youth population and highlighted the major bacterial agent involved in this condition. The pattern of isolates and antibiotics reported in this study is consistent with the usually reported pattern, with Escherichia coli being the most common organism isolated in cases of urinary tract infection. The high rate of resistance to Ciprofloxacin, Co-trimoxazole, Amoxicillin-clavulanic acid, Ampicillin, Cefotaxime, Cefazolin, Ticarcillin-Clavulanic acid, Cefuroxime of urinary isolates, precludes the use of these commonly used antibiotics for empiric treatment of UTI in India. Therefore, urine culture is necessarily recommended for screening and diagnosis.

In conclusion, this study determined the incidence of urinary tract infection in youth population of Garhwal region in India and highlighted the major bacterial agent involved in this condition.

Since urinary tract infection may be asymptomatic in most cases (as this study has shown), it is therefore suggested that routine screening of patients of PUO (Pyrexia of unknown origin) should be done for urinary tract infection and the appropriate antimicrobials administered after antibiotic sensitivity tests have been carried out in order to prevent the cases becoming symptomatic later with resultant renal damage.

Abbreviations

N- No response, R- Resistance, S- Sensitivity, ABST - Antibiotic sensitivity testing

Ethical Clearance

Ethical clearance not required as study was on routine laboratory isolates.

Patient Consent

From each patient, patients inform consent to participate in the study was obtained for study purpose.

Acknowledgement

The study was carried out without any funding and did not require any ethical approval. I would like to express my sincere thanks to Dr. Rohit Sachdeva, Assistant Professor, Dept. of Microbiology, VCSG Medical College Srinagar Garhwal for his contribution during the preparation of this manuscript.

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How to cite this article: Semwal AC, Mathuria YP, Saklani P. Study of Antibiotic Resistance Pattern in Uropathogens at a Tertiary Care Hospital. Ann. Int. Med. Den. Res. 2017; 3(5): MB01-MB06.

Source of Support: Nil, **Conflict of Interest:** None declared