

Original Research**“Antibiotic Resistance Pattern Of The Hospital And Community Acquired Isolates Of Uropathogens In A Tertiary Care Centre at Kanpur”.**

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ABSTRACT

Background & Objectives: Urinary tract infections (UTIs) is among the most common health problems occurring both in the community and hospitalized patients. The resistance of bacteria causing UTI to commonly prescribed antibiotics is increasing both in developing as well as in developed countries. Resistance has emerged even to more potent antimicrobial agents. The current study was undertaken to report the current antibiotic resistance pattern among common bacterial uropathogens isolated from OPD and IPD patients in a tertiary care hospital in Kanpur. **Methods:** Midstream urine samples from (1857) patients were cultured and pathogens isolated were identified by standard methods. Antibiotic susceptibility was done by Kirby Bauer disk diffusion method (CLSI). **Results:** Out of 1857 urine samples received over a period of 1 yr, 30.69% (570) of the urine samples were culture positive. E.coli was the predominant isolate in both hospital acquired (75%) and community acquired (25%). UTI were more common in females (56.8%) in the age group of 20-40yrs than in males(43.19%) and in the age group of >60yrs. Most of the GNBs were susceptible to Imipenem, Amikacin, Cefeprozone sulbactam, piperacillin tazobactam, polymyxin B, Colistin and among the resistant strains are more in the IPD than OPD. Among the GPC Vancomycin, linezolid, teicoplanin are sensitive drugs. The prevalence of ESBL, MRSA, MRCONS in CAUTI are 45.22%, 38.46%, 40.05% and in HAUTI 54.77%, 61.53%, 40.0% respectively. **Conclusion:** Increasing antibiotic resistance trends indicate that it is imperative to rationalize the use of antimicrobials in the hospitals ,through proper antibiotic policies and in the community empirically and also use these conservatively.

Key words: Antibiotic Resistance Pattern, Uropathogens,E.coli,

INTRODUCTION

Urinary tract infection is a common disease, often contributes to a frequent cause of morbidity in out-patients as well as hospitalized patients, and people of all age groups and geographical locations are affected.[1] It is a serious ailment in human due to the frequency, recurrence and difficulty in eradication, poses stiff challenge because it may involve Kidney, ureters, bladder and urethra.[2] It has been estimated that 150 million people are infected with UTI per annum worldwide.[3] UTIs is describes as a bacteriuria with urinary symptom. UTI is more common in female than in male as female urethra structurally found more effective for bacterial entry, proximity of genital tract and urethra and adherence of urotheleal mucosa to the mucopolysaccharide lining.[4] Even though several different microorganisms can cause of UTI, including protozoan parasites, fungi and viruses, bacteria are the major causative organisms. They account for more than 95% of UTI cases.[5] Bacteria causing UTI are generally of faecal origin[6,7]. Among the bacteria, Escherichia coli (E.coli) are the most common etiological agent, accounting for 75-90% of UTI in both outpatients and inpatients. Complicated UTI exhibits a broader bacterial spectrum as the cause of infection [8]. The

etiology of UTI and the antibiotic resistance of uropathogens have been changing over the past

years, both in community and nosocomial infections[9]. In almost all cases of UTI, empirical antimicrobial treatment is initiated before the laboratory results of urine culture and sensitivity are available. Thus antibiotic resistance may increase in uropathogens due to frequent misuse of antibiotics.[8] The resistant bacterial strains are emerging and spreading throughout the world.[10] The increasing resistance trends are likely to have important clinical implication for the empirical use of antibiotics. In the present scenario, multidrug resistant uropathogens like Methicillin Resistant Staphylococcus aureus(MRSA), Extended Spectrum β -lactamases(ESBLs) producing organisms and High Level Aminoglycoside Resistant (HLAR) Enterococci have become common problem[11,12]. Resistance to newer and more potent antimicrobial agents like carbapenems, colistin and fosfomycin is also seen. The updated knowledge and situation of the prevailing bacterial uropathogens that are multidrug resistant (MDR) is of prime importance for the proper use of antimicrobial drugs and the policy making to combat multidrug resistance in UTIs. [13] The current study was undertaken to determine the bacteriological profile and antibiogram of uropathogens causing UTI in both hospital and

0.5McFarland's standards. The plate was left for 15mins for drying and then a disc of 10µg meropenem was applied at the centre of plate. The isolates under study were streaked from the edge of the disk to the periphery of the plate. Four isolates were tested in each plate. After an overnight incubation at 37°C, the clover leaf like appearance between the test streaks near the disk was taken as positive for carbapenemase production.[14]

RESULTS:

Out of the 1857 urine samples processed, 570(30.69%) gave significant growth of pathogens. The prevalence of hospital acquired infection was (64.21%) and community acquired infections was (35.78%) respectively.(Figure-1). Significant Growth of Uropathogens was seen more in females (56.8%) when compared to males (43.2%). And female patients from IPD (59.6%) then OPD (40.4%) showed more growth.(Table.2).

Females of the age group(20-40yrs), showed a growth of 69.3%, and slightly more in OPD in comparison to IPD patients. Among the males growth was seen in age group of >60yrs(52.8%) respectively(Table.3) 86.49% isolates were gram negative bacteria, E.coli was the predominant isolate (45.61%) in both the groups. 12.63% were gram positive cocci, in which Enterococcus spp was seen in 6.66%, fungus were 0.89%, of which Candida species were isolated respectively.(Table:4)

Antimicrobial resistant pattern of gram negative bacilli showed lowest resistance to polymyxinB, colistin, imipenem, tigycycline, nitrofurantoin, piperacillin-tazobactam.(Table.5) Antimicrobial resistant pattern of gram positive cocci showed lowest resistance to vancomycin, linezolid, teicoplanin. (Table.6)

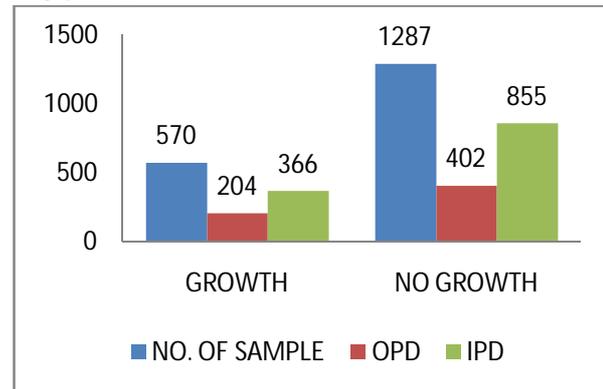
The prevalence of ESBL, MRSA, MRCONS and Carbapenem resistance in OPD was 45.22%, 38.46%, 40.0% and 20.0% respectively, and in IPD it was 54.77%, 61.53%, 60.0% and 80.0% respectively(Table:7).

11.5%[4], 11.1%[17], 10.86%[18] while some studies showed higher prevalence than present study which accounts for 53.82%[3]also it is seen, more in IPD than OPD patients. Rate of infection is more in IPD patients (366; 64.2%) than OPD patients (204; 35.8%) that may because of duration of hospitalization, per urethral catheterization and the duration of catheterization, other studies also found more culture positive results in IPDs.[19]

DISCUSSION

Urinary tract infection is most common infection, in both community and hospitalized patients, associated with significant mortality and morbidity. Current knowledge on antimicrobial resistant pattern is mandatory for appropriate therapy. In this study growth was seen in 30.69%, of the urine samples, was approximately similar to other studies 38.6%[15], 35.5%[16]. in comparison with other studies which showed low prevalence of

FIGURE 1



Female were mostly affected with UTIs in young age (21-40 years; 69.3%) of OPD patients that because of characteristic anatomical and physiological changes - short urethra, its proximity to the anus, urethral trauma during intercourse, dilatation of the urethra and the stasis of urine during pregnancy.[20] while in elderly male (>60 years) had a higher incidence of UTI (52.8%) as compared to the elderly females (47.2%) that due to prostate enlargement and neurogenic bladder. This result is similar to other findings. [3,21] .

In our study, Gram negative bacilli were more common (86.49%) uropathogen while gram positive cocci constitute 12.63%. Among gram negative bacilli most common organism was E.coli (45.61%) Other isolates were Klebsiella spp. (21.40%) followed by Proteus spp.(7.19%), Pseudomonas (6.49%), Enterobacter spp.(3.16%), Citrobacter spp (2.63%). E.coli was the most frequently reported isolate from patients with hospital and community acquired UTIs. This finding is in consistence with findings of other studies.[4,21,22,23] while in some studies Pseudomonas spp [24] and Klebsiella spp.[25] was the common pathogen. The present study results correlates with others in which Klebsiella spp. was reported as the second most frequently isolated

organism in UTI [21,22,23,28]. Among the gram positive cocci Enterococcus spp. (6.66%) followed

TABLE 1 SEX WISE DISTRIBUTION

SEX	TOTAL NO. OF SAMPLE	GROWTH	OPD	IPD
MALE	802(43.19%)	246(43.2%)	73(29.6%)	173(70.3%)
FEMALE	1055(56.81%)	324(56.8%)	131(40.4%)	193(59.6%)
TOTAL	1857	570	204	366

TABLE 2 AGE WISE DISTRIBUTION

AGE	MALE	FEMALE	OPD	IPD
<20	20(24.1%)	63(75.6%)	15(18.1%)	68(81.9%)
21-40	46(30.7%)	104(69.3%)	77(51.3%)	73(48.7%)
41-60	65(54.6%)	54(45.4%)	31(26.1%)	88(73.9%)
>60	115(52.8%)	103(47.2%)	81(37.1%)	137(62.8%)
TOTAL	246	324	204	366

TABLE 3 DISTRIBUTION OF ORGANISM

ORGANISM	GROWTH	OPD	IPD
GNB	493(86.49%)	156(31.64%)	337(68.35%)
E.coli	260(45.61%)	65(25%)	195(75%)
Klebsiella Spp.	122(21.40%)	37(30.32%)	85(69.67%)
Proteus Spp.	41(7.19%)	20(48.78%)	21(51.21%)
Pseudomonas	37(6.49%)	14(37.83%)	23(62.16%)
Enterobacter Spp.	18(3.16%)	11(61.11%)	7(38.89%)
Citrobacter Spp.	15(2.63%)	9(60.0%)	6(40.0%)
GPC	72(12.63%)	46(63.89%)	26(36.11%)
Enterococcus Spp.	38(6.66%)	22(57.89%)	16(42.10%)
S.aureus	23(4.03%)	16(69.56%)	7(30.43%)
Cons	11(1.92%)	8(72.72%)	3(27.27%)
Fungus	5(0.89%)	2(40.0%)	3(60.0%)
Candida albicans	4(0.70%)	2(50.0%)	2(50.0%)
Candida tropicalis	1(0.16%)	-	1(100%)
TOTAL	570	204	366

TABLE 4 Antibiotic Resistance Pattern of Gram negative bacilli

Anti biotic \ GNC	E.coli (%)	Klebsiella sp. (%)	Proteus spp. (%)	Pseudomonas Spp (%)	Enterobacter spp. (%)	Citrobacter spp.	OPD (%)	IPD (%)
AMP	74.3	R	R	54.0	R	R	35.5	64.5
AMC	44.2	75.4	60.9	67.5	R	R	23.2	76.8
A/S	44.2	63.9	60.9	59.4	44.4	53.3	60.8	39.2
CB	ND	ND	ND	75.6	ND	ND	21.4	78.6
TCC	ND	ND	ND	13.5	ND	ND	68.7	31.3
PIT	11.5	11.4	15.7	5.4	5.5	R	63.8	36.2
CX	65.4	57.4	56.1	51.4	R	53.3	32.7	67.3
CAZ	53.8	55.7	58.5	59.4	44.4	40.0	30.2	70.0
CTX	61.1	55.7	62.3	54.0	55.5	53.3	40.6	59.4
CTR	68.8	52.4	61.2	56.7	55.5	60.0	37.3	62.7
CPM	76.9	63.9	69.2	51.3	61.1	60.0	39.8	60.2
CFS	15.3	8.2	10.5	13.5	16.6	6.6	27.8	72.2
AK	12.3	10.4	15.7	18.9	5.5	6.6	66.5	33.5
GEN	31.5	40.2	30.1	32.4	R	38.0	29.0	71.0
NET	44.2	32.7	27.2	29.7	44.4	40.0	35.9	64.1
NX	56.1	65.7	65.3	64.8	61.1	60.0	67.1	32.9
LE	15.3	4.1	15.7	13.5	27.7	26.6	21.9	78.1
CIP	44.2	39.2	39.0	40.0	16.6	26.6	73.2	26.1
NIT	5.6	5.8	9.5	5.4	5.5	55.3	59.8	40.2
TE	64.3	31.5	34.1	54.0	55.5	55.3	38.7	61.3
IPM	2.3	4.1	4.8	5.4	5.55	S	67.4	32.6
MRP	15.8	21.3	9.7	5.4	5.55	6.6	59.2	40.8
AT	68.8	67.2	73.7	75.6	55.5	60.0	20.8	79.2
PB	S	S	R	S	S	S	-	-
CL	S	S	R	S	S	S	-	-
TGC	3.8	6.7	9.5	13.5	5.5	6.6	15.7	84.3

ND-Not Diagnose

R-All Resistance

S- All Sensitive

by *Staphylococcus aureus*(4.03%) and *CONS*(1.92%), similar to other studies[26,27,28]. In our study *Candida* species isolation was seen in 0.89% samples isolates with 60% in hospitalized patients. This shows a slightly lower isolation rate compared to other studies (10.3%, article a) but more in inpatients implies the presence of factors predisposing for fungal infections in IPDs patients, like long term antibiotic treatment, steroids, chronic illness, cancer patients or other immunocompromised conditions [29].

Most of the GNBs were susceptible to Imipenem (95%), Amikacin (85%), Cefeperazone sulbactam (80%), piperacillin tazobactam (80%), polymyxin B (100%), Colistin (100%) and nitrofurantoin (97%). Among the resistant strains are more in the IPD than OPD. Similar findings were reported in previous studies. [9,32]. However in the present study all the gram negative isolates showed high degree of resistance to β -lactam group of antibiotics like ampicillin, second and third generation cephalosporins and azetronam. Among β -lactam and β -lactamase inhibitor combinations, susceptibility of piperacillin-tazobactam was found to be much better than ampicillin sulbactam and amoxicillin-clavulanic acid. [30].

TABLE 5 Antibiotic Resistance Pattern of Gram positive cocci

GPC Anti biotic	Enterococ cus spp. (%)	S.aur eus (%)	CO NS (%)	OPD (%)	IPD (%)
AMP	65.7	34.7	54.5	32.3	67.7
AMC	ND	43.4	63.6	32.9	67.1
OX	ND	43.4	63.6	34.2	65.8
CX	ND	56.5	45.4	38.8	61.2
AK	ND	13.0	18.2	34.8	75.2
GEN	ND	17.3	27.3	30.8	69.2
NX	ND	43.4	54.5	32.8	67.2
CIP	ND	65.2	45.6	55.2	44.8
NIT	ND	13.4	18.2	26.3	73.7
TE	ND	17.3	18.2	38.8	61.2
CD	7.4	43.4	8.1	33.5	66.5
E	7.8	34.7	8.1	38.5	61.5
VA	S	34.7	18.2	44.9	55.1
LZ	S	S	S	30.6	69.4
TEI	5.2	13.0	8.1	29.6	70.4

ND-Not Diagnose R-All Resistance S- All Sensitive

The high susceptibility of *E.coli* to nitrofurantoin (86.6%) and ciprofloxacin (56.8%) correlated with

other studies [34] and showing contrast to our study. This finding emphasizes the geographical variation seen in the susceptibility patterns of uropathogens to different drugs. This is important in a vast country like ours.(5,29). factors predisposing for fungal infections in IPDs patients, like long term antibiotic treatment, steroids, chronic illness, cancer patients or other immunocompromised conditions[29].

TABLE 6 Resistance Pattern

Type a Resistance	NO. OF ORGANISM	OPD	IPD
ESBL	199(40.36.74%)	90(45.22%)	109(54.77%)
MRSA	13(56.52%)	5(38.46%)	8(61.53%)
MRCONS	5(45.45%)	2(40.0%)	3(60.0%)
CARBAPENEM RESISTANCE	10(2.0%)	2(20.0%)	8(80.0%)

The high resistance to fluoroquinolones and cephalosporins in the present study can be attributed to the easy access and indiscriminate use of these drugs of all types of infections and emphasizes the role of selective drug pressure in emergence of drug resistant mutants. Because a very high percentage of isolates in this study were sensitive to nitrofurantoin, this drug would be a better choice for the empiric treatment of UTI. Nitrofurantoin is a narrow – spectrum antimicrobial with no systemic activity. Early formulations were associated with substantial adverse effects of the gastrointestinal system, but the current macrocrystalline formulation is well tolerated. In cases with upper UTI or with systemic involvement, nitrofurantoin has a limited role and here aminoglycosides or the cefaperazone sulbactam combination would be more effective.

Amikacin resistance is high in inpatients, because amikacin and cefaperazone sulbactam are injectable drugs and therefore, their use is more common in a hospital setup than in community, thereby increasing the chance of development of resistant strains in the hospital surroundings.

Among the GPC vancomycin, linezolid, teicoplanin were found to be sensitive drugs, which is in contrast with a study conducted at Tamilnadu [12], in which significant vancomycin resistance was reported among *Staphylococcus* spp and *Enterococcus* spp indicating geographical differences. Nitrofurantoin, is (85%) sensitive to the isolates correlates with other studies. Also gram

positive uropathogen showed good sensitivity to amikacin(86%) and gentamycin(80%). Norfloxacin and ciprofloxacin are more resistant, suggesting that these oral drugs no more effective for treatment of UTIs, correlates with other studies. Resistance of Amoxicillin-clavulinic acid was tested for CONS and staphylococcus species.

The resistance rate was reported more in uropathogens isolated from hospital acquired UTIs than community acquired UTIs, similarly also seen with other studies[1]. The infectious disease society of America (IDSA) recommends a bench mark of 10-20% resistance at which first line empiric therapy should be modified [30].

Considering these guidelines imipenem, piperacillin-tazobactam, amikacin, vancomycin, and linezolid with overall susceptibility of > 80% can be considered as empiric therapy for community acquired UTIs, but since these drugs are available in injectable formulations which may limit their use in OPD patients. For hospital acquired UTIs, imipenem, vancomycin and linezolid can be used as first line-empiric therapy. But the inappropriate and empirical usage of these wide spectrum antimicrobial agents may increase the chances of drug resistance. These antibiotics should be reserved for complicated UTIs.

From this present study we suggest urine culture and antimicrobial susceptibility testing for all UTI patients before start of antibiotics.

The prevalence of ESBL, MRSA, MRCONS in CAUTI are 45.22%, 38.46%, 40.05% and in HAUTI(54.77%, 61.53%, 40.0%) respectively was seen in our study, in both OPD and IPD patients suggests that the threat of multidrug resistance among uropathogens is limited not only to the ICUs or the tertiary care hospital but also they are found in OPD patients. ESBLs producers were 45.22% & 54.77% in OPD & IPD, which correlated with other studies showing a prevalence rate of 42%, 48.9% [17,31]. MRSA were seen in 38.46% & 61.53% in OPD & IPD, which correlated with other studies showing a prevalence rate of 41.4%, 48.9% [11]. MRCONS were 40.05% & 40.0% in OPD & IPD, which correlated with other studies showing a prevalence rate of 42%, 48.9% by (11). Carbapenem resistance was detected in 2.0% isolates while other study found 5.4% [33]. This variability could be due to difference in geographical distribution and different patterns of antibiotic use.

CONCLUSION

From our study we infer that Gram negative bacteria among which E.coli was the most common uropathogen both in community and hospitals. Nitrofurantoin can be used for empirical treatment both for gram positive and gram negative organisms in Uncomplicated UTIs.

For complicated UTIs parenteral broad spectrum antimicrobial drugs are given, for Gram negative bacteria are susceptible to imipenem, meropenem, piperacillin-tazobactam, amikacin and gentamycin, and for Gram positive bacteria are susceptible to vancomycin, linezolid and teicoplanin. Also the presence of multi-drug resistant uropathogens like ESBLs, MRSA, MRCONS and Carbapenems are isolated not only from hospitalized patients but also from community indicating the spread in the community as well. Hence it is essential to report these isolates along with routine susceptibility testing. In view of emerging antimicrobial resistance, therapy should be started, as far as possible, after urine culture and sensitivity has to been done. At the end, it is felt that international guidelines are no longer applicable for treatment of UTIs in India and developments of specific guidelines based on local susceptibility patterns are necessary.

RECOMMENDATION: The increasing rate of uropathogens resistance to traditional empiric agents has also had an important effect on the empiric selection of antimicrobials. We recommend that constant evaluation of the antibiotic sensitivity pattern of UTI pathogens for commonly used antimicrobial agents in a particular environment should be carried out.

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