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PREVALENCE OF UROPATHOGENS IN URINARY TRACT INFECTION AND THEIR ANTIMICROBIAL RESISTANCE PATTERN IN A NORTH DELHI HOSPITAL, INDIA: A NINE YEAR STUDY

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Abstract-

Background: Urinary tract infection is one of the most common infections seen in both community and hospital setting in developing countries. Area specific prevalence studies aimed to gain knowledge about the type of pathogens responsible for urinary tract infection and their resistance pattern may help the clinicians to choose the correct empirical treatment.

Objective: The aim of the study is to evaluate the prevalence of various uropathogens in suspected UTI patients and to find out their antimicrobial resistance pattern and long term trend.

Methods: A hospital based retrospective study conducted at Department of Microbiology, Hindu Rao Hospital, New Delhi. Urine samples, collected using mid stream clean catch method over a period of nine years from clinically suspected UTI patients, from various OPDs and wards of our hospital. The samples were tested for uropathogens using standard microbiological procedures. Antimicrobial susceptibility testing was performed on the bacterial isolates using Kirby-Bauer disk diffusion method as per Clinical and Laboratory standards institute guidelines.

Results: Of the 57255 samples evaluated, UTI was found in 15.6% (8921) of patients. *E.coli* (4838, 54.23%), and *Klebsiella spp*. (1905 21.35%), were the most common pathogens isolated followed by *Staphylococcus spp.* (746, 8.4%). A large proportion of uropathogens were resistant to common antimicrobial agents used for empirical treatment of UTI

Conclusion: *E.coli* remained as the most common pathogen causing UTI. Nine years trend shows an increase in antimicrobial resistance levels in uropathogens. Rising level of antimicrobial resistance leaves the clinicians with limited options for empirical treatment of UTI. Periodic surveillance monitoring studies are very important to know the changing pattern of antimicrobial resistance among uropathogens, helping physicians to formulate the most effective empirical treatment of UTIs.

Keywords- Urinary tract infection, Antimicrobial resistance, Uropathogens

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Introduction

Urinary tract infections (UTIs) are amongst the most common infections seen in both community and hospital setting in developing countries with an estimated annual global incidence of approx 250 million [1,2]. These infections pose major public health burden in terms of morbidity and financial cost. Urinary tract infection is defined as the microbial invasion of urinary tract. It can be divided into upper and lower tract infections based on anatomy, symptomatic and asymptomatic or complicated and uncomplicated, clinically [1,3].

UTI is more common in females as compared to males [2,4-6]. About 20-50% of adult women experience UTI in her lifetime [5-8]. Urinary tract is generally sterile but urinary tract infections can be caused by numerous conditions. Several antibacterial factors prevent colonization and infection of urinary tract but uropathogenic bacteria resist various host defense factors. These factors include pH, urea concentration, osmolarity urinary salt content, Tamm-Horsfall protein, secretory IgA, lactoferrin, various organic acids, low molecular weight oligosaccharides and bladder polysaccharides. In females risk factors include short urethra and short distance from anus, urethral meatus moisture content, low concentration of lactobacilli in elderly women, pregnancy and behavioral factors. In males it includes prostate fluid, anti bacterial activity, and genetic predisposition [8-10].

The incidence of predominant bacteria causing UTI varied over the years. Gram negative bacteria are most commonly implicated in the urinary tract infections. Enterobacteriaceae have several factors responsible for their attachment to the uroepithelium. These gram negative aerobic bacteria colonize the urogenital mucosa with adhesins, pili, fimbriae, and P_1-blood group phenotype receptor [6].

Generally the intestine is the main reservoir of micro-organisms causing UTI. *Escherichia coli* being a part of normal intestinal flora can easily colonise the lower urinary tract and therefore is the most common causative organism of UTI [4]. Other common microorganisms implicated are *Klebsiella spp., Proteus spp., Staphylococcus spp*. and *Enterococcus spp.* Highly resistant pathogens including *Pseudomonas aeruginosa* and *Enterococcus faecalis* are comparatively more encountered in UTI seen in hospital setting [1-6].

A large proportion of uncontrolled use of antibiotics for various therapeutic purposes is mainly responsible for the development and spread of antimicrobial resistance in the intestinal bacteria. In current scenario, antibiotic therapies are associated with rapid emergence of antimicrobial resistance in both, hospital and community setting. Treatment of UTI is mainly based on empirical therapy so it is important to know the locally prevalent pathogens along with their antibiogram pattern, but unfortunately the antibiogram patterns are becoming more unpredictable due to development of resistance to many commonly used antimicrobial agents.

Therefore, it is fundamental to investigate the epidemiology of UTI for health care providers and planners to formulate an effective empirical treatment regimen, based on the prevailing antibiogram patterns. Therefore, the present study was undertaken to evaluate the magnitude of infection, antimicrobial resistance pattern among uropathogens and plan strategies for implementation of effective prevention & control programmes. Routine surveillance and monitoring studies are very important to know the changing pattern of antimicrobial resistance of uropathogens helping physicians to formulate the most effective empirical treatment for UTIs.

Material and Methods

Type of Study

A Retrospective study done over 9 years period (January 2005 to December 2013). The study was approved from the institutional ethical review committee.

Study Population

Hospital based population. Urine samples received in Dept. of Microbiology from various indoor and outdoor clinics of Hindu Rao Hospital, a North Delhi tertiary care hospital. Relevant patient data i.e. collection date, OPD/ward, age, sex, culture results and antimicrobial susceptibility results were recorded and analysed. Patients are divided into 4 categories according to age groups [Table-1].

Sampling

Early morning urine samples were collected in sterile containers using mid stream clean catch method from clinically suspected UTI patients, attending OPDs and admitted to various wards of our Hospital. The patients were instructed on how to collect the sample aseptically prior to sample collection to avoid urethral contamination. A total 57255 consecutive urine samples were processed and evaluated. The urine samples were analysed within one hour after collection. When this was not possible, the samples were stored in the refrigerator at 4°C for a maximum period of 24 hours.

Culture

The samples were cultured on different media from time to time using CLED agar and HiChrome agar using standard microbiological procedures. Inoculation of urine sample was done by calibrated loop using streak plate method followed by incubation for 18-24 hours at 37°C under aerobic conditions. Based on growth, the cultures were classified as negative, insignificant, significant and contamination as per standard recommendations.

Bacterial Identification Antimicrobial Susceptibility Test

Appropriate biochemical tests were done on culture isolates based on colony morphology and results of Gram-stained smear. Antimicrobial susceptibility testing (AST) was performed using Kirby-Bauer disc diffusion method as per CLSI guidelines. A 0.5 McFarland physiological saline suspension prepared by picking up a single colony from pure culture was used. AST was done by placing standard antimicrobial impregnated disk (Himedia, India) on lawn cultured Mueller-Hinton agar followed by incubation for 18-24 hours at 37°C. Results were determined as sensitive or resistant based on the diameter of zone of inhibition. The control strains used were *E. coli* ATCC 25922, *Klebsiella pneumoniae* ATCC 700603, *Pseudomonas aeruginosa* ATCC27853 and *Staphylococcus aureus* ATCC 25923.

ESBL production was tested in isolates resistant to 3rd gen cephalosporins by disc synergy test using combined disc method. Ceftazidime (30 mcg), and ceftazidime plus clavulanic acid (30/10 mcg) were placed on Mueller-Hinton agar and incubated. Organism was considered as ESBL producer if there was a ≥5 mm increase in the zone diameter of ceftazidime/clavulanate disc when compared with ceftazidime disc alone.

Methicillin resistance testing in *Staphylococcus aureus* isolates was done by using cefoxitin disc (30 mcg) and the isolates were classified into MRSA and MSSA accordingly. Similarly Enterococcal isolates were screened for vancomycin resistance using vancomycin disc (30ug).

Statistical Analysis

After collection of data, it was verified twice in Microsoft excel sheet. Statistical analysis was performed using the SPSS statistical package (version 17.0). In analysis of antimicrobial resistance pattern, resistance to three or more antimicrobial agents in uropathogens was considered as multi-drug resistance (MDR). The data for each antibiotic and resistance in *E.coli*, *Klebsiella spp*., *S. aureus* and *Enterococcus spp.* was analysed individually for studying the trend over time using the function Y= aebt (b stands for the percentage growth rate per year). The growth rate is tested for its significance using t- test. P-values less than 0.05 were considered statistically significant.

Results

During the study period, a total of 57255 samples were analysed, 29710 (51.9 %) and 27545 (48.1%) from OPD and wards respectively. 32026 specimens (55.9%) were from female patients and 25229 (44.1%) from male patients. The age of patients ranged between 2 years to 80 years with the mean age of 42.03 years. Adult patients 19735 (34.5%) constituted the predominant group followed by young adults 18730 (32.7%), elderly 13103 (22.9%) and children and adolescents 5687 (9.9%) [Table-1].

Table 1- Distribution of patients in different age groups

Age Groups	Frequency	Percentage
A (<18 years): Children & Adolescents	5687	9.90%
B (18 to 30 years): Young Adults	18730	32.70%
C (31 to 60 years): Adults	19735	34.50%
D (> 60 years): Elderly	13103	22.90%
Total	57255	100%

Of the 57255 samples evaluated, urinary tract infection was found in 8921 (15.6%) patients [female 5553 (17.3%) and males 3368 (13.3%)]. Infection rate was found to be higher in the in-patients (17.7%) as compared to out-patients (13.6%) [Table-2].

Table 2- Distribution and Frequency of UTI in different patient categories

Groups	OPD	WARD	Total
Male	1519/13046 (11.6%)	1849/12183 (15.2%)	3368/25229 (13.3%)
Female	2537/16664 (15.2%)	3016/15362 (19.6%)	5553/32026 (17.3%)
Total	4056/ 29710 (13.6%)	4865 /27545 (17.7%)	8921/57255 (15.6%)

Out of 8921 significant positive cultures, Gram negative and positive isolates constituted 84.2% & 15.1% respectively and *Candida spp*. comprised 0.7% (63) of the isolates. *E.coli* was the predominant uropathogen throughout the study period accounting for 54.2% (4838) of the total urinary isolates. Other uropathogens were *Klebsiella spp.* 21.3% (1905), *Proteus spp., Pseudomonas aeruginosa, Acinetobacter spp., Citrobacter spp., Enterobacter spp., Providentia spp., Salmonella spp*. among gram negative isolates and *Staphylococcus aureus*, *Coagulase negative Staphylococci* and *Enterococcus spp*. among gram positive isolates [Table-3].

Table 3- Distribution of uropathogens in various patients groups

Organisms	Total (n)	Inpatient		Outpatient	
		Male	Female	Male	Female
E. coli	4838	789	1757	742	1550
Klebsiella spp.	1905	497	604	387	417
P. aruginosa	364	153	134	31	46
Acinetobacter spp.	142	42	56	25	19
Proteus spp.	127	22	31	34	40
Enterobacter spp.	46	9	21	4	12
Citrobacter spp.	79	25	23	12	19
Salmonella spp.	8	-	3	3	2
Providentia spp.	3	-	2	-	1
S. aureus	746	162	215	154	215
CoNS	176	26	43	42	65
Entrococcus spp.	424	99	101	81	143
Candida spp.	63	25	26	4	8
Total	8921	1849	3016	1519	2537

The antimicrobial resistance ranged anywhere from 0 to 80%. Bacterial uropathogens revealed high level of resistance for single and multiple antimicrobial agents. An increasing trend in antimicrobial resistance has been noted for most of the antimicrobials tested except co-trimoxazole during the study period which showing a decreasing trend over the years [Table-4], [Table-5], [Fig-1], [Fig-2], [Fig-3], [Fig-4], [Fig-5], [Fig-6], [Fig-7], [Fig-8], [Fig-9], [Fig-10], [Fig-11], [Fig-12].

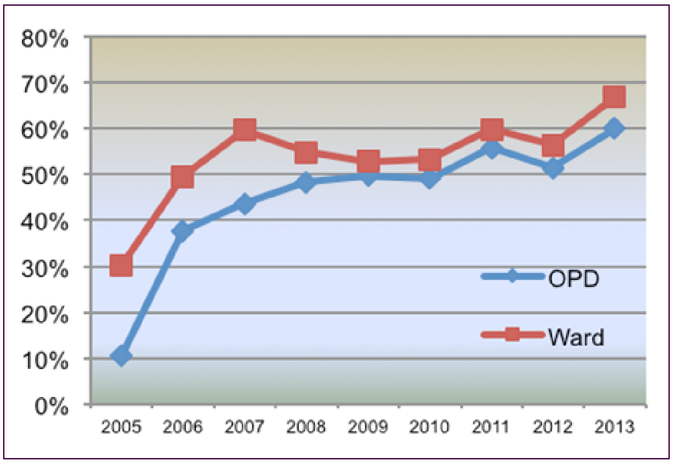

Fig. 1- Comparison of MDR uropathogens in *E.coli* among OPD and ward patients

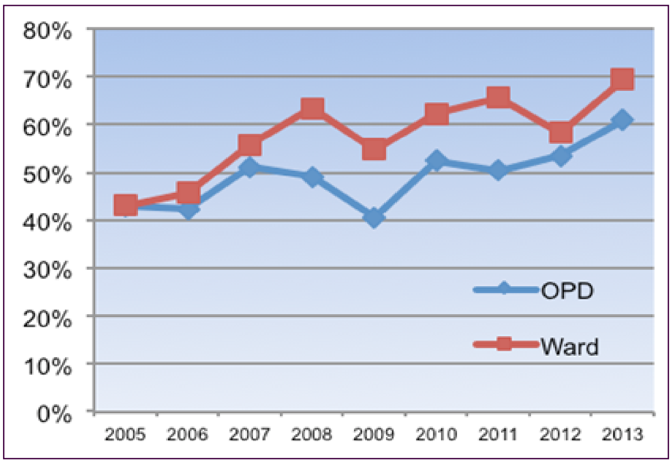

Fig. 2- Comparison of MDR uropathogens in *Klebsiella spp.* among OPD and ward patients

Table 4- Range (%) of antimicrobial resistance of the predominant gram negative isolates

Antibiotics	*E. coli* (n=4838)	Klebsiella spp. (n=1905)	*P. aruginosa* (n=364)	Acinetobacter spp. (n=142)	Proteus spp. (n=127)	Enterobacter spp. (n=46)	Citrobacter spp. (n=79)
Ceftriaxone	26.0-59.0	33.3-63.5	-	-	-	50-75	40-60
Ceftazidime	29.2-56.1	31.9-58.3	39.4-69	32-68	43-59	37.5-62.5	40-50
Amoxy-clav	11.4-31	11.1-33.3	-	-	-	-	-
Gentamicin	30.6-57.1	36.5-68.2	(41.3-76.8)	38-71	38-53	37.5-62.5	30-60
Amikacin	4.3-26.8	9.5-38.7	7.6-37.6	8.1-56	12.5-21	12.5-25	6.25-20
Meropenem	1.3-19.3	11.1-32.2	12.6-49	21-37	12.5-27	12.5-37.5	6.25-12.5
Imipenem	0-1.3	0.0-3.5	3.8-17	5.6-11	0	0	0
Ciprofloxacin	43.4-74.2	50-78.4	56- 83.4	43-76	37.5-74.5	50-62.5	37.5-66.7
Nitrofurantoin	0.5-6.4	1.1-9.6	-	-	-	0-6.25	0
Cotrimoxazole	48.7-69.6	46.1-73.0	-	-	37.5-50	62.5-37.5	50-33.3
Norfloxacin	36.3-63.0	39.7-68.3	42-81.2	40-67.3	37.5-62.5	50-62.5	33.3-50

Table 5- Range (%) of antimicrobial resistance of the gram positive isolates

Organism	Ciprofloxacin	Vancomycin	Penicillin	Cefoxitin	Linezolid	Amoxyclav	Gentamicin	Amikacin	Cotrimoxazole	Norflox	Nitrofurantoin
S. aureus (n= 714)	28.0-68.9	0	32.0-71.4	Oct-21	0	13.3-42.5	16.0-63.9	6.7-15.0	47-70.8	20.0-62.3	3.3-9.4
CoNS (n=74)	24.8-61.3	0	23-71.2	-	0	12.8-54.3	17.6-56.7	7.4-16.3	36.8-76.2	18.2-61.2	5.9-7.9
Entrococcus spp. (n=411)	35.3-80	0-12	15.8-66.7	-	0	-	17.6-56.7	5.9-33.3	-	35.3-70	0-12

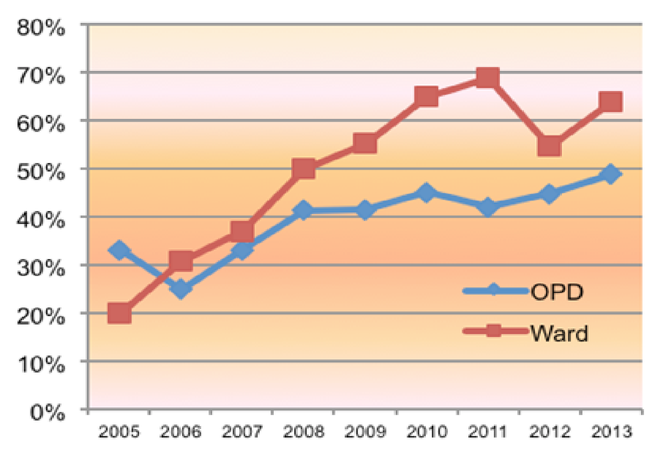

Fig. 3- Comparison of MDR uropathogens in *S.aureus* among OPD and ward patients

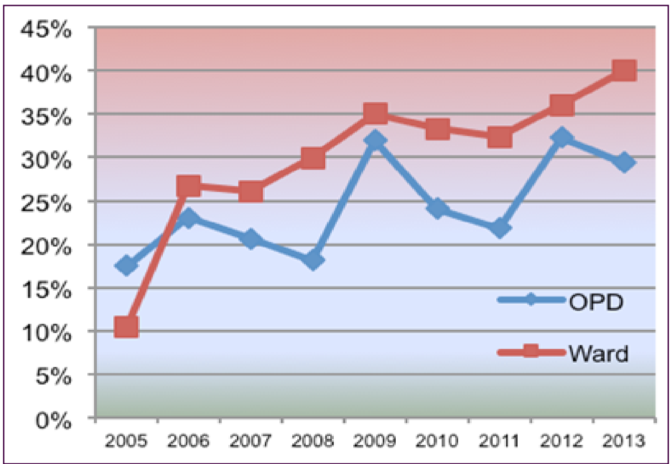

Fig. 4- Comparison of MDR uropathogens in *Enterococcus spp.* among OPD and ward patients

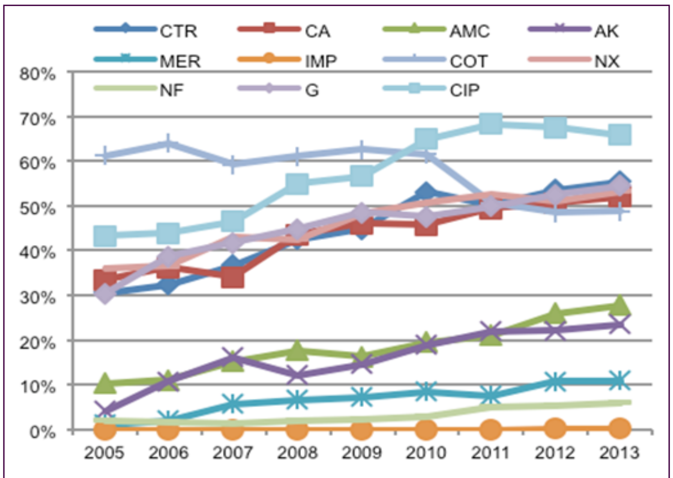

Fig. 5- Antimicrobial resistance trend for *E.coli* among OPD patients

Gram-negative uropathogens showed higher resistance to 3rd generation cephalosporins, fluoroquinolones, β-lactams, aminoglycosides and various other antimicrobials tested. *E.coli*, the predominant uropathogen showed high resistance towards fluoroquinolones (36.3 to 74.2%), β lactams (26.0 to 59.0%), aminoglycosides (4.3 to 57.1%) and lower resistance to nitrofurantoin (0.5 to 6.4%). The antimicrobial resistance levels of *E. coli*, to the carbapenems ranged from 1.3 to 19.3% and 0 to 1.3% towards meropenem and imipenem respectively. A high proportion of *E.coli* isolates were resistant to common orally administered drugs such as ciprofloxacin (43.4 to 74.2%), norfloxacin (36.3 to 63.0%), amoxyclav (11.4 to 31.0%) and co-trimoxazole (48.7 to 69.6%) [Fig-5], [Fig-6].

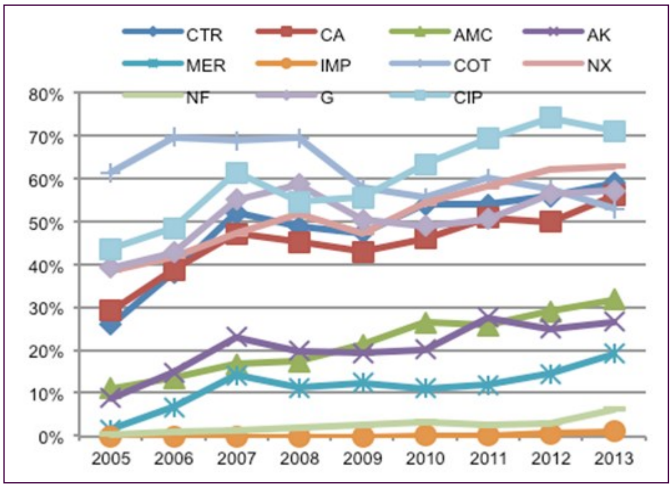

Fig. 6- Antimicrobial resistance trend for *E.coli* among ward patients

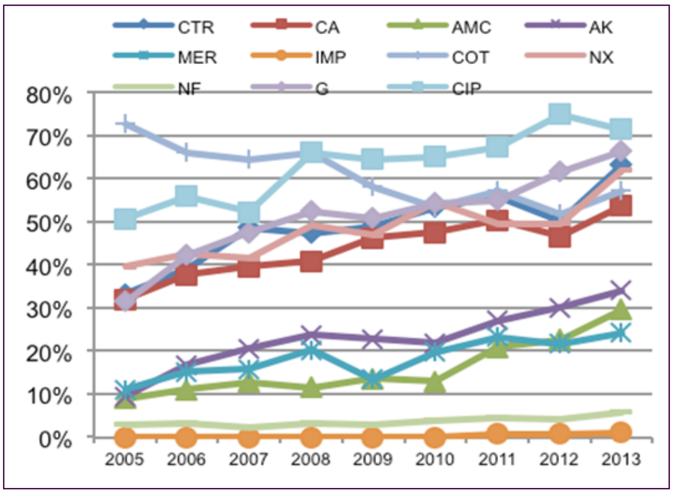

Fig. 7- Antimicrobial resistance trend for *Klebsiella spp*. among OPD patients

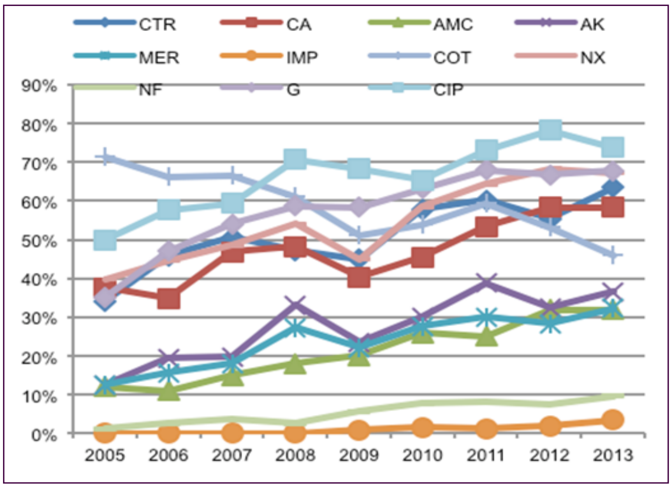

Fig. 8- Antimicrobial resistance trend for *Klebsiella spp*. among ward patients

Klebsiella spp. showed a comparatively higher resistance than *E.coli* for most of the antimicrobials tested. Resistance rates were as high as (39.7 to 78.4%) for fluoroquinolones (31.9 to 63.5%) for cephalosporins, (9.5 to 68.2%) for aminoglycosides (11.1 to 33.3%) for amoxyclav (11.1 to 32.2%) and (0 to 3.5%) for meropenem and imipenem respectively and (1.1 to 9.6%) for nitrofurantoin [Fig-7], [Fig-8].

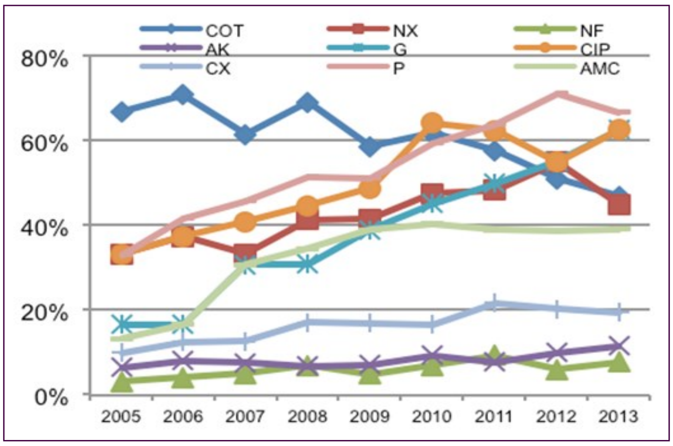

Fig. 9- Antimicrobial resistance trend for *S.aureus* among OPD patients

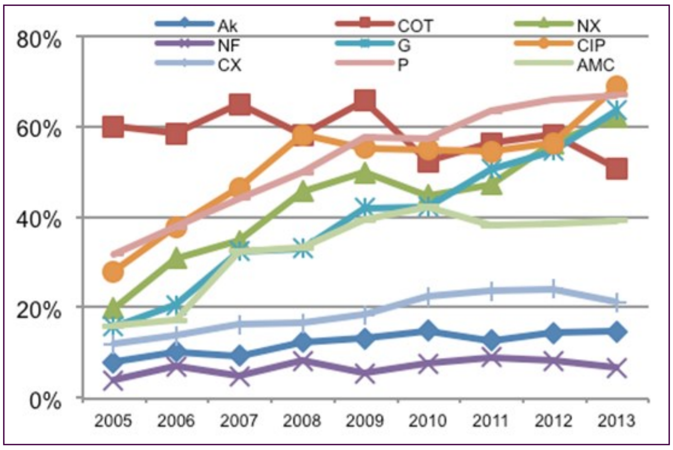

Fig. 10- Antimicrobial resistance trend for *S.aureus* among ward patients

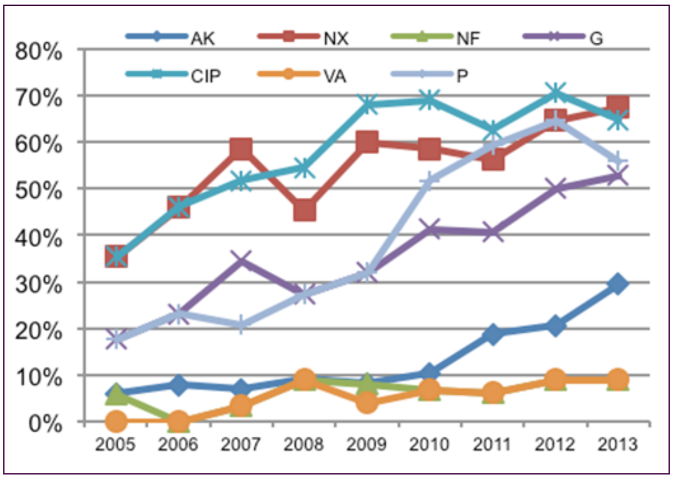

Fig. 11- Antimicrobial resistance trend for *Entrococcus spp*. among OPD patients

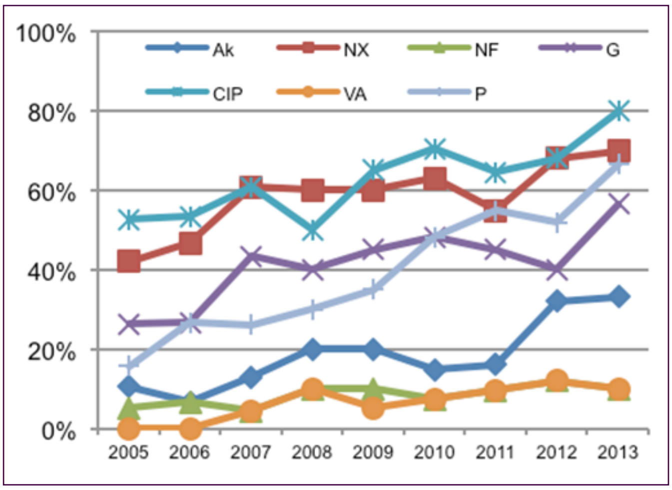

Fig. 12- Antimicrobial resistance trend for *Entrococcus spp.* among ward patients

The frequency of ESBL production in *E.coli* and *Klebsiella spp.* from year 2010 to 2013 revealed an increasing trend varying between 34 to 52%. ESBL production was comparatively higher in *Klebsiella spp.* (36.8 to 52%) than *E. coli* (34 to 48.6%) [Fig-13], [Fig-14].

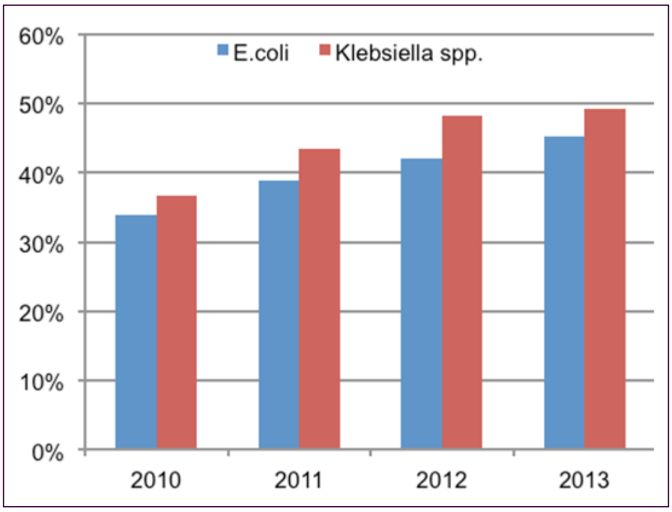

Fig. 13- Frequency of ESBL production (%) in *E.coli* and *Klebsiella spp.* over the study period in OPD patients

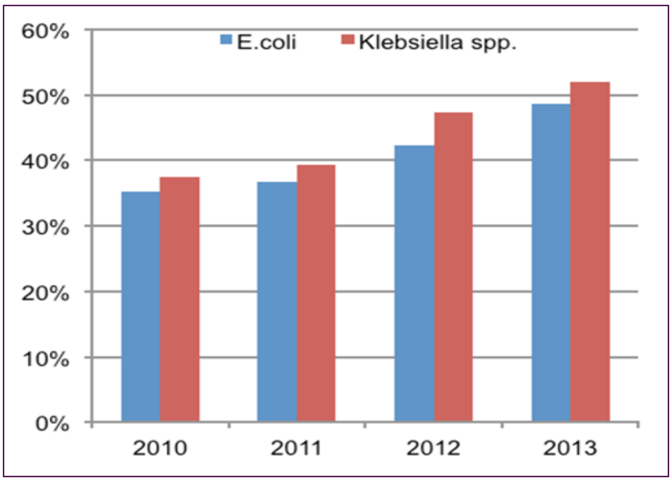

Fig. 14- Frequency of ESBL production (%) in *E.coli* and *Klebsiella spp.* over the study period in ward patients.

The isolates of *Pseudomonas spp*. and *Acinetobacter spp.* showed high resistance to several antimicrobial agents. Carbapenems had the least resistance (3.8 to 17.0% for imipenem and 12.6 to 49.0 % for meropenem), followed by amikacin (7.6 to 56%) [Table-4].

The gram positive bacteria also showed a higher resistance towards penicillins (15.8 to 71.4%), quinolones (24.8 to 80% for ciprofloxacin and 18.2 to 70% for norfloxacin), aminoglycosides (16.0 to 63.9% for gentamicin and 5.9 to 33.3% for amikacin) and other antimicrobials tested. Resistance towards nitrofurantoin was (0 to 12.0%) and (3.3 to 9.4%) for *Enterococcus spp.* and *S. aureus*. On average, 18.6% of the Staphylococcal isolates were found to be MRSA and 6.4% of Enterococcal isolates as VRE. However, the Staphylococcal isolates were fully susceptible to vancomycin and linezolid [Table-5], [Fig-9], [Fig-10], [Fig-11], [Fig-12].

The incidence of MDR isolates varied between 28.3 to 68.1% among bacterial uropathogens [Table-6]. A significant rise ($p>0.005$) has been noticed over the years in the incidence of MDR uropathogens during the study period in different patient groups [Fig -15], [Fig-16].

Table 6- Distribution of MDR isolates among various uropathogens

Organisms	Total	Multi Drug Resistant	Percentage
E. coli	4838	2479	51.20%
Klebsiella spp.	1905	1058	55.50%
P. aruginosa	364	248	68.10%
Acinetobacter spp.	142	93	65.50%
Proteus spp.	127	69	54.30%
Enterobacter spp.	46	17	37.00%
Citrobacter spp.	79	39	49.40%
Salmonella spp.	8	3	37.50%
Providentia spp.	3	2	66.70%
S. aureus	746	351	47.10%
Enterococcus spp.	424	120	28.30%
Coagulase Neg Staph.	176	77	43.80%

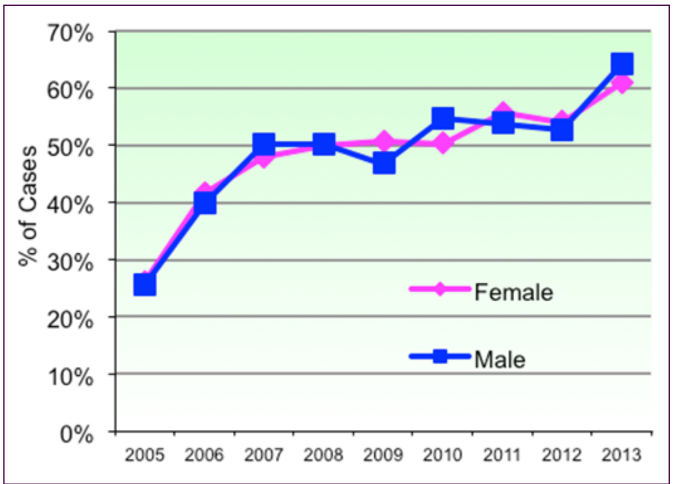

Fig. 15- Incidence of MDR uropathogens in male & female patients

Discussion

This retrospective study compiled valuable laboratory data regarding prevalence of various uropathogens implicated in causation of UTI and their nine year antimicrobial resistance trend from North India. A continuous surveillance of antimicrobial resistance is very important in the management of UTI. A little extra venture on antimicrobial resistance studies, in a health care setting facilitates the prediction of extremely practical information about the prevailing resistance pattern. In our study, UTI was found in 15.6% of the suspected patients by culture owing to the presence of nonspecific symptoms associated with UTI. The culture positivity in our study was comparable to the finding of Sood S from Jaipur [6]. A lower culture positivity was documented from Aligarh, Banglore, Ethiopia and Portugal [11,12,1,4], whereas a higher culture positivity rate was recorded from Odisha, Meerut and Puducherry [8,7,2].

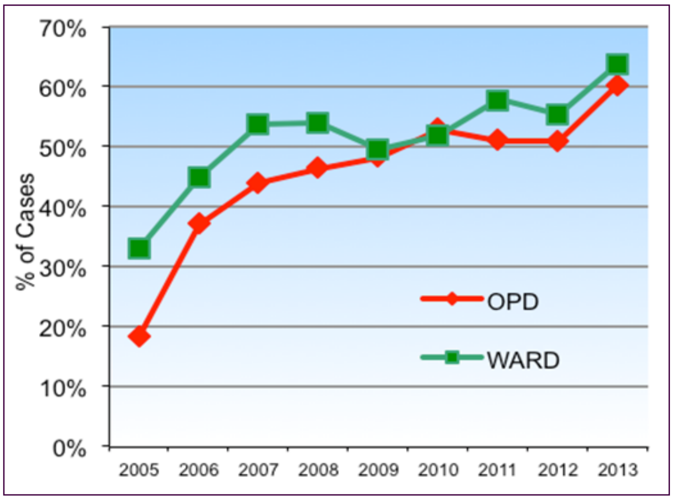

Fig. 16- Incidence of MDR uropathogens in OPD and ward patients

In our study UTI was found in 17.3% in females whereas 13.3% in males. In coherence with prior studies, a higher prevalence of UTI among female was noted owing to the presence of anatomical and physical factors showing their increased vulnerability towards UTI [2 -9]. The occurrence of UTI predominantly in patients with age ranging between 18-60 years in our study is similar to the findings of studies done in Kuwait and Nigeria [13,14].

In accord with the several global and regional reports, our study also revealed *E. coli* as the most predominant pathogen associated with UTI in both sexes throughout the entire study period.[2-11] In addition to *E. coli,* as also reported by previous studies *Klebsiella spp., Citrobacter* spp., *Proteus spp., P. aeruginosa, Acinetobacter spp, Staphylococcus spp.* and *Enterococcus spp.* were among other uropathogens implicated in the causation of UTI [1-11]. On contrary to the findings of various other previous studies which documented *Staphylococcus spp.* as the second most common isolate [15-17], our results showed it was Klebsiella spp. which is in agreement with the findings of Akram M, Kothari and Stratchounski LS [11,18,19]. Some authors documented *Enterococcus spp.* as second most common isolate [5,6,20,21]. Bacteria belonging to Enterobacteriaceae accounted for 78.5% of all the isolates followed by gram positive cocci (15.12%) and non-fermenter Gram negative bacteria (5.7%), which is again in coherence with other studies. [2-7]. Most of the *Candida spp*. isolated in our study were from in-patients implying that these patients are more vulnerable to fungal infections. During the study period, an increase has been noted for incidence of *Klebsiella spp., P. aeruginosa* and *Acinetobacter spp.* as well as for their resistance to different antimicrobials tested.

Emergence in antimicrobial resistance, documented increasingly worldwide is an important cause of concern [4-7,15-18]. Resistance among bacterial pathogens is more likely in case, there is a past infection history of patients and/or inpatient status [5,7]. Our study revealed a significant rise in bacterial resistance to commonly prescribed antimicrobials including various oral drugs for most of the isolates over the study period. Resistance rates were significantly higher (P <0.05) amongst the isolates from in-patients as compared to that from out-patients though insignificant when compared between males and females. High resistance among in-patients may be due to infection with the hospital acquired multidrug resistant strains or evolution of more drug resistance in uropathogens under selective drug pressure. The gram negative bacteria as well as the gram positive bacteria showed a steady rise in resistance rates to commonly used first line oral antimicrobial agents, however our results showed a decline for resistance rate towards co-trimoxazole. The prevalence of MDR uropathogens has increased over the years varying from place to place and time to time [1,4,11,17]. Complicated UTI caused by a MDR uropathogen leads to pyelonephritis and other significant co-morbidities as emphasized by Mishra MP [8]. Our study also revealed a significant rise in the incidence of MDR uropathogens over the study period. The incidence of MDR uropathogens were significantly higher in in-patients as compared to out- patients (p <0.001) whereas insignificant among males and females (p>0.05). Emergence in multi-drug resistance was seen among both, gram negative and positive isolates.

Our study documented an emergence in fluoroquinolone resistance among gram positive and negative urinary isolates especially for ciprofloxacin which is in accordance with previous studies [2,6,12,24]. Emergence in fluoroquinolone resistance is multifactorial and is usually related to the intensity of antibiotic usage [2]. An association has been reported between the increased quinolone use and bacterial resistances with from several countries [2,5,22]. In our study this may, probably have resulted as a consequence of frequent exposure to fluoroquinolones for the treatment of repeated infections. Similarly most of the isolates showed reduced susceptibility to aminoglycosides (6.25 to 76.8%). Resistance rates towards amikacin were significantly lesser than that of gentamicin [Table-4] & [Table-5].

In agreement with the studies of several investigators, isolates of *Klebsiella spp.* offered high resistance towards various antimicrobial agents tested except nitrofurantoin and carbapenems [1,5,7,17,19]. Isolates of *E.coli* were comparatively less resistant to these antimicrobials. A few studies from India quoted high resistance against nitrofurantoin (>75%) in *E.coli* and *Klebsiella* isolates [8,11].

Confirming the global trend towards increased β-lactam resistance, in our study, ESBL producers were seen to the extent of 48.6% in *E. coli* and 52% in *Klebsiella spp.,* which is quoted in the range of 9.52 to 55% by previous studies [6,11,18,23]. The prevalence of MDR gram negative bacilli, especially ESBL producers, has increased worldwide with marked regional variations of their distribution as also mentioned by Pitout et al [24]. Plasmids responsible for ESBL production carrying genes encoding resistance to several other structural drug classes especially aminoglycosides and fluoroquinolones have been identified making treatment options of such infections difficult and limited.

P. aeruginosa and *Acinetobacter spp.* are amongst major pathogens with remarkable properties of exhibiting resistance to many antibiotics; therefore, their isolation is an important cause of concern [5-7]. These strains revealed high resistance towards cephalosporins, aminoglycosides and fluoroquinolones. In coherence with various previous studies [5-7,19], nitrofurantoin and carbapenems were the most active agents against resistant Gram-negative organisms. There are recent reports of emergence of resistance against these antimicrobials too making situation worse [7,8,11,12].

In Staphylococci, emergence of *Methicillin-resistant Staphylococcus aureus* (MRSA) and therapeutic challenges it poses are well recognized, narrowing down the therapeutic options to treat these infections. A rising trend has been noted for the incidence of MRSA in both hospital as well as community setting, supporting the findings of other regional and global studies [15-17].

Vancomycin and linezolid remained as the drugs with least resistance for gram positive cocci with an efficacy of more than 90%. However, an emergence in vancomycin resistance was noted in *Enterococcus spp.* during the study period as also mentioned by other authors [6,20,21]. In our study, vancomycin, linezolid, nitrofurantoin and imipenem were among the least resistant drugs tested, probably due to their lower usage.

Generally, UTIs are mainly treated empirically with short course antibiotics. Empirical treatments mainly based on broad spectrum antibiotics are not adequately effective in controlling the growth of predominant uropathogens resulting in evolution of more resistant bacterial strains with time. Emergence of antimicrobial resistance and MDR among urinary isolates is a matter of grave concern warning judicious use of antimicrobials. We found nitrofurantoin as a good alternative in the treatment of UTI with an efficacy as high as 90%. Vancomycin and linezolid are the drugs with least resistance to gram positive cocci. The increasing resistance against fluoroquinolones earlier considered a drug with good coverage and readily prescribed to patients rules out its prescription for empirical treatment of UTI, mandating its rational and conservative use. Our study emphasizes to avoid indiscriminate use of cephalosporins which are extensively used in healthcare settings for treatment of a variety of infections as most of β-lactams are no longer active along with associated co-resistance, limiting therapeutic options further.

Limitations

There may be over estimation of true resistance rate as in many cases urine samples may have been sent following treatment failure or recurrent infection. The clinical and outcome data co-relating isolate with type and severity of urinary tract infection were not taken. The incidence of ESBL producing organisms may be underreported in the present study as the phenotypic confirmation of ESBL-positive organisms was done using ceftazidime/clavulanic acid only and not cefotaxime/clavulanic acid as per the latest CLSI recommendation. Another limitation of our study was not including screening of Amp C beta lactamases and metallo-beta lactamases (MBLs) production and also lack of genomic analysis.

Conclusion

UTI is one of the most common infectious disease clinicians are dealing with. Increasing antimicrobial resistance among uropathogens implicated in UTI is a matter of concern. Alarming rate of resistance to fluoroquinolone, aminoglycoside and beta-lactam antibiotics precludes use of these commonly used antimicrobials for empirical treatment of UTI and leaves the clinicians with limited options along with significant increase in patient morbidity, cost of treatment, rates and duration of hospitalization and use of broad spectrum agents. Routine urine cultures and antimicrobial susceptibility testing of clinically significant isolates may be necessary especially in our Indian setting where no definitive resistance or susceptibility patterns are available in a given geographic location for common urinary pathogens. A strong commitment has to be established regarding the good antibiotic practices and policies for UTI to ensure rational and controlled use of available antimicrobial agents for better tomorrow options.

Conflicts of Interest: None declared.

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