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PROFILE AND ANTIMICROBIAL SUSCEPTIBILITY PATTERN OF URINARY BACTERIAL ISOLATES AT A TERTIARY CARE HOSPITAL IN CENTRAL INDIA

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ABSTRACT
Aim: to study the antimicrobial susceptibility pattern in urinary bacterial isolates among patients admitted in a tertiary care hospital. **Methods**: A retrospective analysis was done for the susceptibility pattern of urinary bacterial isolates was done over a period of three years (April 2007 – March 2010) in a tertiary care hospital. **Results**: Among total 3759 urinary culture positive samples, commonest isolates were *E. coli* (61.59%) followed by *Klebsiella spp.* (25.46%), *Pseudomonas spp.* (3.72%), and *Proteus spp.* (0.85%) in gram negative whereas *Staphylococcus aureus* (5.69%) and *Enterococcus spp.* (1.33%) in gram positive organisms. Antibiotic susceptibility pattern of these isolates revealed that Amikacin susceptibility in gram negative isolates was more than 60% except for *Proteus spp*. Sensitivity to Imipenem was maximum (above 90%) while Co-trimoxazole, Norfloxacin, Cefotaxime and Nalidixic acid were not found to be effective. Among gram positive organisms, maximum susceptibility was seen to Nitrofurantoin and Vancomycin. **Conclusion**: Routine urine culture and susceptibility before therapy should be encouraged and periodic evaluation of predominant organisms and their antimicrobial susceptibility pattern should be studied for appropriate selection of antibiotic for effective management UTI cases.

KEYWORDS: *Acinetobacter spp*, *E.coli*, Imipenem, Indoor, Resistance Pattern.

INTRODUCTION
Urinary tract infection (UTI) remains the commonest bacterial infection. It is more common in females. *Enterobacteriaceae* is the commonest pathogen for UTI, which are well-known to get drug resistance easily. There has been an increasing trend in the drug resistance of urinary pathogens.[1-4] Distribution of urinary pathogens and their susceptibility to antibiotics varies regionally so it becomes essential to have knowledge of distribution of these pathogens and their susceptibility to antibiotics in a particular setting. This study is important for physicians to facilitate the effective empirical treatment and helpful management of patient with urinary tract infection.

MATERIALS AND METHODS
A retrospective analysis of 25,120 midstream urine specimens from inpatient departments of Government Medical College and Hospital, Nagpur, India, over a period of three years (April 2007 – March 2010) were processed for aerobic bacteriological examination. Urine specimens were processed within one hour of collection. Gram staining was done to find out pus cells and organisms. Bacterial culture was done by semi-quantitative method using calibrated loop delivering 0.001 ml of urine on MacConkey agar and blood agar. For gram negative bacilli more than 100 colonies corresponding to 10^5cfu/ml, whereas gram positive cocci irrespective of the colony count were considered as significant.[5] More than two growth and diphtheroids was considered as contamination. *Candida albicans* grown were reported separately. Colony count of less than 10^5cfu/ml for gram negative bacilli were considered as insignificant bacteriuria. Significant bacterial isolates were identified using standard bacteriological tests.[5]

Antimicrobial susceptibility pattern was studied on Mueller Hinton Agar plates (Hi Media India Ltd., Mumbai) by Kirby Bauer disc diffusion method recommended by Clinical and Laboratory Standards Institute (CLSI) guidelines.[6] Briefly, Petri dishes containing 14ml of Mueller-Hinton agar were seeded with a 24 hours old broth culture of the bacterial strains. Filter paper discs impregnated with the antimicrobial agent were applied to the seeded plates. After overnight incubation at 37^0C the zone of inhibition around the discs was measured and compared with the standard strains (ATCC *Staphylococcus aureus* 25923, ATCC *Escherichia coli* 25922, and ATCC *Pseudomonas aeruginosa* 27853) as per the CLSI guidelines.[6]

For gram negative isolates antibiotic discs put up were Cefotaxime (30 µg), Cotrimoxazole (1.25 µg/23.75 µg), Gentamicin (10 µg), Nalidixic acid (30 µg), Norfloxacin (300µg), Ofloxacin (5 µg) as first line while Netilmicin (30 µg), Ceftazidime (30 µg), Amikacin (30 µg) and Meropenem (10µg) as second line. For pseudomonas, Ceprofloxacin (5 µg), Ceftazidime (30 µg), Gentamicin (10 µg) and Norfloxacin (300 µg) were put up. In strains resistant to first line of antibiotics Amikacin (30 µg), Piperacillin (100 µg) and Meropenem (10µg) were put up as a second line. For gram positive isolates Penicillin (10 IU), Cloxacillin (30 µg), Cefazolin (30 µg), Norfloxacin (300µg) and Gentamicin (10 µg) were added. For resistant strains of Staphylococcus Ofloxacin (5 µg), Vancomycin (30 µg) and Netilmicin (30 µg) were tested.

RESULTS

Out of 25,120 samples suspected of UTI, 17,219 (68.55%) were culture sterile. Significant bacteriuria was found in 3759 (14.96%), whereas 3517 (14%) showed non-significant growth. *Candida albicans* grown in 625 (2.49%). Out of the 3759 positive isolates, 3494 (92.95%) were gram negative and 265 (7.05%) were gram positive. Figure 1 shows the distribution of urinary bacterial isolates. Amongst gram negative isolates, *Escherichia coli* 2315 (61.59%) was the commonest organism followed by *Klebsiella spp.* 957 (25.46%) *Pseudomonas spp.* 140 (3.72%) and *Proteus spp.* 32 (0.85%). *Staphylococcus aureus* 214 (5.69%) and *Enterococcus spp. 50* (1.33%) were the predominant gram positive isolates.

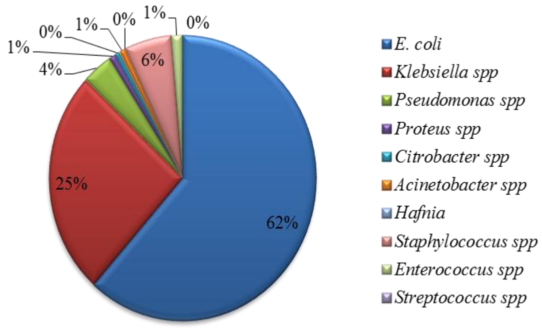

Figure: 1. Distribution of urinary bacterial isolates

Table 1 shows percentage of antimicrobial susceptibility pattern in urinary bacterial isolates. In gram negative isolates, Amikacin susceptibility was more than 60% except for *Proteus spp.* (42.86%) and for *Citrobacter spp.* (56.25%). Low antimicrobial susceptibility was seen to Ampicillin, cephalosporins (Cefotaxime and Ceftazidime), quinolones (Nalidixic acid), fluoroquinolones (ciprofloxacin, Norfloxacin and Ofloxacin), and Cotrimoxazole. In strains resistant to first line of antibiotics, Imipenem showed highest sensitivity followed by Amikacin. Most of the strains were resistant to Netilmicin. In *Pseudomonas spp.*, Piperacillin, Ceftazidime and fluoroquinolones were found to be highly resistant while Imipenem and Amikacin were found to be effective in strains resistant to first line of antibiotics.

Table: 1. Percentage of antimicrobial susceptibility pattern in urinary bacterial isolates

	E.coli	*Klebsiella spp*	*Pseudomonas spp*	*Proteus spp*	*Citrobacter spp*	*Acinetobacter spp*	*Staphylococcus spp*	*Enterococcus spp*
Ampicillin	14.28	00.00	ND	ND	ND	ND	ND	ND
Amikacin	66.16	64.49	65.55	42.86	56.25	63.16	30.43	45.24
Cefazolin	ND	ND	ND	ND	ND	ND	36.76	ND
Cefotaxime	23.68	19.58	ND	48.39	5.26	30.77	ND	ND
Cefoxitin	ND	ND	ND	ND	ND	ND	24.19	ND
Ceftazidime	27.23	23.12	35.00	40.74	15.79	22.73	ND	ND
Ciprofloxacin	38.63	18.75	20.56	ND	80	ND	ND	15.22
Cotrimoxazole	19.47	15.54	ND	28.13	23.53	40.00	ND	ND
Erythromycin	ND	ND	ND	ND	ND	ND	ND	31.58
Gentamicin	31.98	28.46	30.95	52.63	23.81	42.86	35.51	24.44
Imipenem	95.14	94.14	87.39	100	100	81.81	ND	ND
Nalidixic acid	05.87	12.11	ND	05.26	ND	ND	ND	ND
Netilmicin	41.55	40.34	ND	ND	ND	ND	64.00	ND
Nitrofurantoin	ND	ND	ND	ND	ND	ND	ND	68.29
Norfloxacin	15.27	16.33	21.14	28	11.76	29.17	17.19	12.82
Ofloxacin	17.83	22.27	ND	11.11	33.33	45.45	23.62	ND
Oxacillin	ND	ND	ND	ND	ND	ND	09.17	ND
Penicillin	ND	ND	ND	ND	ND	ND	18.59	ND
Piperacillin	ND	ND	25.71	ND	ND	ND	ND	ND
Tetracycline	ND	ND	ND	ND	ND	ND	ND	32.35
Vancomycin	ND	ND	ND	ND	ND	ND	82.35	ND

ND – not done

In gram positive isolates, Oxacillin sensitivity was reported in only 9.17% of *Staphylococcus* isolates. Maximum susceptibility was seen to Vancomycin (82.35%), Netilmicin (64%) and Cefazolin (36.76%). In *Enterococcus spp.*, Nitrofurantoin and Amikacin were found to be effective.

DISCUSSION

In present study out of 25,120 urinary samples received, only 18% had shown presence significant bacteriuria. This was probably due to being a tertiary care hospital the patients may have received previous antibacterial therapy, secondly the urine sample as obtained by non invasive method is one of the most frequently asked investigations in many non specific febrile illness or being non-bacterial samples (protozoal, viral or fungal origin) or being non-representative samples. Similar findings were reported by Veenakumari et al.[7] Our study showed that commonest isolates were *E. coli*, *Klebsiella spp.*, and *Psedomonas spp.* in gram negative isolates, whereas in gram positive isolates maximum were *Staphylococcus aureus* and *Enterococcus spp.* Similar findings were reported by several previous international[1-3,8-14] and Indian studies.[4,15-24] A study conducted by Koshariya et al[4] reported that *Pseudomonas spp.* was the second commonest organisms leading to UTI in catheterized patients. The diversity in the spectrum and frequency of occurrence can be due to the differences in the study plan and geographical location.

Among gram negative isolates, the susceptibility was highest for Imipenem (95%) which was comparable with other studies.[1-3,17,18,20,23] Although, 5% organisms showed the resistance to Imipenem, this may be due to New Delhi Metallo-β-lactamase-1 (NDM-1) producing organisms which were recently reported in India.[25] However, confirmatory identification by phenotypic and genotypic methods is recommended in our setting. Amikacin (43-66%) and Netilmicin (42%) were found to be effective in most of the cases. Nalidixic acid (5-12%) was having lowest sensitivity followed by Ampicillin, fluoroquinolones, Cotrimoxazole and cephalosporins. Similar findings were noted by many studies.[18,21,24]

Distribution of urinary pathogens and their susceptibility to antibiotics varies regionally and periodically. The choice of antibiotics to be tested for antibiotic susceptibility testing is also changes regionally across the world and depends on the respective hospital policy. Thus, we purposefully compared our study findings with the recent Indian studies rather than the international studies (as shown in table 2). Our study observations were matching with Shah et al[21], Koshariya et al[4] and Rangari et al[23] with minimal differences. However, Shaifali et al[20] had reported higher sensitivity to Cotrimoxazole and quinolones antibiotics. These variations were probably due to less sample size (63) and samples restricted only from obstetrics and gynecology wards. Similarly, Shalini et al[22] had reported higher sensitivity to Norfloxacin and aminoglycosides, perhaps due to less sample size (143) and inclusion of only outdoor patients which most likely having community acquired UTI. Chatterjee et al[15] studied UTI in catheterized patients and showed good susceptibility to aminoglycosides but high resistance to imipenem. Similarly, Prakash et al[24] reported surprisingly very high resistance to Imipenem among the compared Indian studies.

Table: 2. Comparison of antimicrobial susceptibility pattern (%) of *E.coli* and *Klebsiella spp.* among the Indian studies.

Author, Sample size and Place of study	*E.coli*							*Klebsiella spp.*						
	Ce	Co	G	Na	Nx	Ip	Ak	Ce	Co	G	Na	Nx	Ip	Ak
Somaga et al (n=357), Karnataka[17]	61.5	28.8	75	-	80.7	100	86.5	41.6	25	25	-	58.3	83.3	66.7
Chattarjee et al (n=272), West Bengal[15]	10	15	72	-	5	33	74	25	50	75	-	25	52	72
Koshariya et al (n=44), Madhya Pradesh[4]	20.8	8.3	12.5	12.5	25	-	66.6	33.3	33.3	33.3	33.3	33.3	-	33.3
Shah et al (n=177), Gujarat[21]	-	25.9	32.4	5.6	10.2	-	74.0	-	16.7	12.5	16.7	29.2	-	41.7
Kazi et al (n=34), Maharashtra[18]	-	-	82	-	-	100	82	-	-	36	-	-	100	64
Rangari et al (n=300), Uttar Pradesh[23]	-	13.3	33.3	19.4	22.2	98.9	92.8	-	75	20	45.9	50	100	100
Prakash et al (n=155), Uttar Pradesh[24]	10.6	15.2	30.3	7.6	-	98.5	90.9	62.1	65.5	65.5	34.5	-	24.1	79.3
Shaifali et al (n=63), Uttar Pradesh[20]	4.3	60.9	45.7	65.2	50	-	4.3	9.1	81.9	45.5	72.7	72.7	-	9.1
Shalini et al (n=143), Uttar Pradesh[22]	-	19.7	66.3	-	73.9	-	98.9	-	10.3	62.1	-	72.4	-	89.7
Present study (n=3759), Maharashtra	23.7	19.5	31.9	5.9	19.3	95.1	66.2	19.6	15.5	28.5	12.1	16.3	94.1	64.5

Ak: Amikacin, Ce: Cefotaxime, Co: Cotrimoxazole, G: Gentamicin, Ip: Imipenem, Na: Nalidixic Acid, Nx: Norfloxacin

The present study was conducted in 1400 bedded, government run tertiary care hospital with occupancy index of 0.75, serving a large population of Central India. Accordingly, we had larger sample size from a wider geographical area, making our findings more reliable and can be generalized. Being a tertiary care hospital and a well established Microbiology laboratory, we had studied the sensitivity pattern of organism to most commonly prescribed antibiotics and to restrictive antibiotics as well.

Finally to conclude, *E. coli* was the commonest organism causing UTI at our hospital set up. Imipenem and Amikacin were highly effective against gram negative isolates while, Vancomycin and Netilmicin were highly effective against gram positive isolates. Periodic evaluation of micro-organisms and their antimicrobial susceptibility pattern should be studied for formulating the antibiotic policy. Earlier and timely administration of effective empirical therapy will be beneficial not only to the patient but also to the hospital and the community.

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