Identification, Antimicrobial Resistance Patterns and Factors Associated With Urinary Tract Infections In A Tertiary Care Teaching Hospital of Rural Gujarat-India

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Abstracts: Background & objectives: Urinary tract infection is a common clinical condition affecting neonates to geriatric patients. Present study was undertaken to identify and characterize different uropathogens, to assess antimicrobial resistance pattern and, to find out factors associated with urinary tract infections. Methods: Observational study was carried out during February-2015 to January-2016 in a tertiary care teaching hospital. Relevant demographic and clinical details were collected. Identification and antimicrobial susceptibility testing of uropathogens was done by using VITEK®2-Compact microbiology systems. Results: From the 1,167 urine samples analyzed, 192 (16.5%) were positive for bacterial and fungal infections. UTIs were more frequent in males 109 (56.8%) and its incidence varied with age affecting the elderly patients more i.e. 57 (29.7%). E. coli was the most common pathogen implicated in UTI i.e. 82 (42.7%). Distribution of sample from intensive care units and various wards were similar i.e. 96 (50%) each. 112 (58.3%) patients had a urinary catheter; majority of the patients had 8-29 days of catheterization i.e. 46.4%. Resistance to antimicrobials was common but highly variable in our study. Predominant clinical conditions in the catheterized patients were cardio vascular failure followed by respiratory ailments. Interpretation & conclusion: E. coli was the most common etiological agent of UTI. Distribution of urine sample from intensive care units and various wards were similar. Majority of the patients were catheterized in ICU. [Disha S NJIRM 2017; 8(5):13-18]

Key Words: Urinary tract infection, Antimicrobial resistance, Prevalence

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Introduction: Urinary tract infection (UTI) is a common healthcare problem, both in community as well as hospital and is associated with significant morbidity. UTI occurs in all population, from neonates to elderly patients, but is seen more commonly in the females, males at extremes of ages, renal transplant recipients and patients with functional or structural abnormalities of the urinary tract.[1] Clinical spectrum of the disease is wide, and can range from asymptomatic bacteriuria to cystitis, pyelonephritis, or septic shock with multi organ failure.[1] Globally; 150 million people each year are diagnosed with UTI costing more than 6 billion dollars to the economy.[2] Gram negative bacteria particularly members of Enterobacteriaceae are the common etiological agents of both community and hospital acquired UTI, Escherichia coli being the most common.[3] Klebsiella spp., Proteus spp., Enterococcus spp., Staphylococcus spp. and Pseudomonas spp. account for most of the remaining infections.[4] The etiology of urinary tract infections and the antimicrobial resistance pattern of uropathogens have been changing over the past few years, both in the community and health care associated infections.[2] Present study was undertaken to identify and characterize different uropathogens, to assess antimicrobial resistance pattern and, to find out factors associated with urinary tract infections.
This work has generated epidemiological data for revision in antibiotic policy as well as for comparison of data from similar studies that might be undertaken in future.

Methods: This Observational study was conducted in a 610-beded tertiary care teaching hospital during the period of February 2015 to January 2016 after approval of the Institutional Ethics Committee (IEC). Samples were received from admitted patients with clinical symptoms of urinary tract infection. Relevant demographic and clinical data of each patient was collected in terms of type of infection, duration of hospital-stay, indwelling urinary catheter, associated factors and outcome till discharge in a predesigned proforma.

Sample collection and processing: Collected urine samples were received and accepted in the laboratory as per the laid down acceptance and rejection criteria. Patient's details were entered in to the hospital information system and sample was processed immediately once received at the Microbiology laboratory. In case of delay in the processing, urine

samples were refrigerated at 4ºC but not longer than 3 hours. Gram staining, wet film examination and culture of the urine sample was done as per the standard operating protocols. [5] The isolates were identified by VITEK®2 Compact fully automated microbiological system (bioMerieux, France) by using GN, GP, and YST cards.

Antimicrobial susceptibility testing (AST): Minimum inhibitory concentration (MIC) of the antimicrobials was done with VITEK®2-Compact fully automated microbiological system (bio Meriux, France), by using AST-N281, AST-N280, AST-P628, and YST-YS 07 cards. Manual AST using Kirby-Bauer disk diffusion method on Muller-Hinton agar medium (Hi-media Laboratories, Mumbai) was done for those agents not covered in AST cards of VITEK®2 system. The results were interpreted according to the clinical laboratory standards institute guidelines.[6]

Reference strains E. coli ATCC 25922, P. aeruginosa ATCC 27853, E. fecalis ATCC 29212, S. aureus ATCC 29123 and Candida krusei ATCC 6258 were used as a positive control. The results were analyzed using Statistical Package for Social Science (SPSS) version 14.0 for Windows.

Result: During the study period a total 1,167 urine samples were received for culture and AST; of these 192 (16.5%) were found to be culture positive for bacterial/fungal pathogens. Majority of the patients who had urinary tract infection were above 70 years of age i.e. 57 (29.7%) followed by 32 (16.7%) in age group of 51- 60 years and 31 (16.1%) in age group of 61-70 years. Majority of samples, 109 (56.8%) were from males. Among the 192 culture positive patients, the major leading uropathogens were E. coli 42.7% (n=82), P. aeruginosa 12.5% (n=24), K. pneumoniae 8.9% (n=17), E. faecium 6.8% (n=13), and C. tropicalis 6.2% (n=12), all accounting for around 77% (n=148) of total isolates. Gram negative organism represented 76% (n=146) of total urinary pathogens followed by Gram positive organisms and Candida species i.e. 11% (n=21) each. (Table: 1)

Majority of the samples were received from medical intensive unit (MICU) i.e. 57/192 (29.7%) followed by surgical intensive unit (SICU) 33/192 (17.2%), female medical ward (FMW) 24/192 (12.5%), and male medical ward (MMW) 24/192 (12.5%). Distribution of urine samples from intensive care units and various wards was similar i.e. 96 (50%) each. Majority of E. coli were isolated from urine samples received from FMW 18 (22%) followed by MICU 16 (19.5%) and MMW 12 (14.6%). Other leading organisms P. aeruginosa and K. pneumoniae were isolated predominantly from MICU i.e. 11 (45.8%) and 6 (35.3%) respectively. Majority (66.7%) of Candida tropicalis were isolated from SICU Among all UTI cases, 112 (58.3%) had a urinary catheter in place. Catheter days for majority of the patients (46.4%) were 8-29 days followed by 3-7 days (28.6%), while only 9.8% patients had catheter in situ for more than 30 days. Majority of the patients were catheterized in ICU (67%) followed by various wards (33%).

Table: 1 Distribution of bacterial and fungal isolates from urinary tract infection throughout the study period (n= 192)

Organism	Frequency (%)
E. coli	82 (42.7)
K. pneumoniae	17 (8.9)
K. oxytoca	1 (0.5)
E. cloacae	3 (1.5)
P. aeruginosa	24 (12.5)
P. putida	2 (1)
A. baumanii	6 (3.1)
P. rettgeri	6 (3.1)
P. mirabilis	1 (0.5)
P. stuartii	1 (0.5)
M. morganii	2 (1)
S. maltophilia	1 (0.5)
E. faecium	13 (6.8)
E. faecalis	4 (2)
S. aureus	4 (2)
C. tropicalis	12 (6.2)
C. albicans	6 (3.1)
C. famata	1 (0.5)
C. lucitaniae	1 (0.5)
C. freundii	1 (0.5)
Trichosporon spp.	3 (1.5)
Myroides spp.	1 (0.5)
Total	192(100)

Resistance of E. coli to ampicillin and cotrimoxazole was 81% and 69.1% respectively while quinolones ranged from 72.8% to 76.2%, and colistin, tigecycline, amikacin, carbapenems, and nitrofurantoin, showed low resistance in the range of 0% to 17%. K. pneumoniae showed 68.8% and 62.5% resistance to quinolones and cotrimoxazole respectively. Resistance

for P. aeruginosa ranged from 0% to 66.7%, and for A. baumanii from 0% to 100%. (Table: 2) P. rettgeri was found to be highly resistant organism. E. faecium demonstrated high resistance to quinolones, ampicillin and penicillin, while resistance rates for vancomycin and teicoplanin were 7.7% each.(Table: 3) 66% of the patients showed clinical improvement while 20.8% patients were discharged against medical advice with overall mortality of 13.5%.

Table: 2 Antimicrobial drug resistance of Gram negative uropathogens (n=129)

Antimicrobial agent	E. coli n= 82 (%)	K. pneumoniae n= 17 (%)	P. aeruginosa n= 24 (%)	A. baumanii n= 6 (%)
Ampicillin-sulbactum	37/82 (45.1)	11/17 (64.7)	NA*	6/6 (100)
Aztreonam	38/82 (46.3)	11/17 (64.7)	14/24 (58.3)	NA*
Amikacin	13/82 (15.9)	9/17 (53)	14/24 (58.3)	5/6 (83.3)
Amoxicillin-clavulanic acid	32/81 (39.5)	9/15 (60)	NA*	NA*
Ampicillin	64/79 (81)	NA*	NA*	NA*
Cefepime	42/82 (51.2)	10/17 (58.8)	14/24 (58.3)	6/6 (100)
Cefepime/tazobactum	19/64 (29.7)	9/16 (56.2)	10/17 (58.8)	5/5 (100)
Cefotaxime	60/82 (73.1)	11/17 (64.7)	NA*	6/6 (100)
Ceftriaxone	58/81 (71.6)	11/15 (73.3)	NA*	5/6 (83.3)
Cefuroxime	61/82 (74.3)	11/16 (68.8)	NA*	NA*
Ceftazidime	55/81 (67.9)	11/17 (64.7)	15/24 (62.5)	5/5 (100)
Trimethoprim-sulfamethoxazole	56/81 (69.1)	10/16 (62.5)	NA*	6/6 (100)
Ciprofloxacin	59/81 (72.8)	11/17 (64.7)	14/24 (58.3)	6/6 (100)
Ertapenem	12/76 (15.8)	10/16 (62.5)	NA*	NA*
Imipenem	13/82 (15.9)	9/17 (52.9)	14/24 (58.3)	6/6 (100)
Meropenem	13/82 (15.9)	10/17 (58.8)	14/24 (58.3)	6/6 (100)
Doripenem	NA*	NA*	14/24 (58.3)	NA*
Levofloxacin	59/81 (72.8)	11/17 (64.7)	14/24 (58.3)	6/6 (100)
Norfloxacin	59/80 (73.8)	11/17 (64.7)	11/17 (64.7)	6/6 (100)
Ofloxacin	61/80 (76.2)	11/16 (68.8)	10/16 (62.5)	6/6 (100)
Gentamicin	37/81 (55.7)	10/17 (58.8)	14/24 (58.3)	4/6 (66.7)
Cefoperazone-sulbactum	13/70 (18.6)	6/12 (50)	13/22 (59.1)	3/5 (60)
Piperacillin	57/78 (73)	11/17 (64.7)	12/21 (57.1)	5/5 (100)
Piperacillin/tazobactum	27/82 (33)	9/16 (56.2)	15/24 (62.5)	6/6 (100)
Ticarcillin-clavulanic acid	49/81 (60.5)	10/16 (62.5)	14/24 (58.3)	5/5 (100)
Ticarcillin	NA*	NA*	16/24 (66.7)	NA*
Tetracycline	39/75 (52)	10/15 (66.7)	NA*	5/5 (100)
Tobramycin	34/80 (42.5)	9/16 (56.2)	14/23 (60.9)	5/6 (83.3)
Nitrofurantoin	14/82 (17)	9/16 (56.2)	NA*	NA*
Colistin	0/13 (0)	1/9 (11.1)	0/14 (0)	0/6 (0)
Tigecycline	0/13 (0)	3/6 (50)	NA*	0/6 (0)

* Not applicable[6]

Table: 3 Antimicrobial drug resistance of Gram positive uropathogens (n=21)

Antimicrobial agent	E. faecium n= 13 (%)	E. faecalis n= 04 (%)	S. aureus n= 04 (%)
Penicillin	12/13 (92.3)	2/4 (50)	3/4 (75)
Ampicillin	13/13 (100)	3/4 (75)	NA*
Erythromycin	NA*	NA*	1/4 (25)
Clindamycin	NA*	NA*	1/4 (25)
Linezolid	0/13 (0)	0/4 (0)	0/4 (0)
Vancomycin	1/13 (7.7)	0/4 (0)	0/4 (0)

Teicoplanin	1/13 (7.7)	0/4 (0)	0/4 (0)
Oxacillin	NA*	NA*	1/4 (25)
Cefoxitin	NA*	NA*	1/4 (25)
HL Streptomycin	10/13 (76.9)	1/4 (25)	NA*
HL Gentamicin	10/13 (76.9)	1/4 (25)	NA*
Ciprofloxacin	13/13 (100)	2/4 (50)	4/4 (100)
Levofloxacin	12/13 (92.3)	2/4 (50)	3/4 (75)
Norfloxacin	12/13 (92.3)	NA*	4/4 (100)
Tetracycline	9/13 (69.2)	3/4 (75)	1/3 (33.3)
Nitrofurantoin	8/13 (61.5)	0/4 (0)	0/4 (0)
Cotrimoxazole	NA*	NA*	2/4 (50)
Gentamicin	NA*	NA*	1/4 (25)

* Not applicable[6]

Discussion: The present study describes the distribution and antimicrobial resistance of bacterial/fungal species isolated, age and gender of the patients, location in the hospital, characteristics of patients with urinary catheterization, antimicrobial resistance, associated clinical conditions and outcome of the patient from a large number of urine samples collected over a one year period, from hospitalized patients. Culture positivity rate in UTI has been reported to range from 9 to 31.6% in various studies.[7-10] We had positivity rate of 16.5%. UTI is known to be a disease of females and has been reported in literature where 80% of the isolates were from female patient[4] but in our study, males predominance (56.8%) was seen which is similar to findings by Chatterjee et. al.(2009)[11] in our study higher prevalence was seen among the young females in the age group of 21-40 years who represented 23.9% of the total cases.

Frequency of UTIs has been reported to be 22.7% in females with mean age of >60 yrs by Ghadiri et. al.(2012).[12] 29.7% patients in our study were above 70 years of age followed by 16.7% in the age group 51-60 and 16.1% were 61-70 years of age. The results were in concordance with the fact that, elderly are more susceptible to infections.[11]

Enrico Magliano et.al. (2012) has also reported 58% of patients in the age group of 60 years or more[4] while Ghadiri et. al.,(2012) has reported 33% of patients belonging to age above 60 years, followed by 26.9% in age group 40-60 years and 25% belonging to age group of 20-40 years.[12] 22.2% infection were seen in patients above 50 years of age by Tiruneh et. al., (2014).[13]

In our study E. coli (42.7%) was the most prevalent gram negative bacteria followed by P. aeruginosa (12.5%), K. pneumoniae (8.9%), E. faecium (6.8%), Proteus spp. (4.2%), A. baumanii (3.1%), S. aureus (2%), and Enterobacter spp. (1.5%). The major fungal isolates were C. tropicalis (6.2%) followed by C. albicans (3.1%). Ines Linhares et. al., (2013) in their ten years surveillance study has reported the predominant agents of UTI as E. coli (64.5%), S. aureus (6.0%), P. mirabilis (4.7%), Klebsiella spp. (4.3%), E. faecalis (3.6%), P. vulgaris (2.7%), P. aeruginosa (2.4%), Enterobacter spp. (1.9%), S. epidermidis (1.8%), and Providencia spp. (1.7 %).[14] Ghadiri et. al.,(2012) has also found E. coli (66.7%) as the most common gram-negative bacilli isolated from UTI patients followed by CoNS (11.7%), S. aureus (6.7%), Proteusvulgaris (6.7%), Enterococcus spp. (5%), P. aeruginosa (1.7%), and Enterobacter spp. (1.7%).[12] Tasbakan MI et. al.,(2013) has reported five leading microorganism as E. coli (45.5%), Candida spp. (15.9%), Klebsiella spp. (13.3%) Enterococcus spp. (10.2%) and Pseudomonas spp. (10%).[15]

We received samples equally from ICU and wards accounting to 50% each. Among the ICU, prevalence of UTI was found higher in medical ICU i.e. 59.3% followed by surgical ICU 34.4%. Medical wards, both male and female had 25% samples followed by male and female surgical wards i.e. 12.5% and 11.5% respectively. Tasbakan MI et. al., (2013) has reported majority of samples from intensive care units, [15] in contrast to our findings. Cairns S. et. al., (2010) has also found a significantly higher prevalence in intensive care units i.e. 27.1% than wards i.e. 9.3%.[16] In our study 58.3% patients were catheterized. Duration of catheter was 8-29 days in 46.4%, 3-7 days in 28.6% patients, and only 9.8% for more than 30

days. This tallies with findings by Tasbakan MI et. al., (2013) where the majority of the patients (46.3%) had catheter for a period of 8-29 days, followed by 28.2% for 3-7 days, and 19.4% for more than 30 days.[15]

We found Carbapenems i.e. ertapenem (84.2%), imipenem (84.1%) and meropenem (84.1%) to be the most effective drugs against E. coli. Joly-Guillou ML et. al., (2010) has shown 100% E. coli and more than 98% of other Enterobacteriaceae to be susceptible to carbapenems. Against non fermeters, meropenem was active on 84-94% of the strains and imipenem on 84-98% of the strains. [17] Fluoroquinolones resistance was high in our study, i.e. E. coli; 72.8% to 73.8%; K. pneumonia; 64.7% to 68.8%; P. aeruginosa; 58.3% to 64.7% similar to findings by Kothari A et. al., (2008),[18] Rashedmarandi F. et. al., (2008)[19] and Gobernado M et. al., (2007).[20] Resistance rates to third generation cephalosporins in our study were highly variable, i.e. E. coli; 67.9% to 73.1%; K. pneumonia; 64.7% to 73.3%; P. aeruginosa; 62.5%; A. baumanni; 83.3% to 100% in contrast to findings by Enrico Magliano et.al.(2012). [4]

Clinical conditions of catheterized patients in our study were cardio vascular failure (14.3%) followed by aspiration pneumonia/COPD/respiratory failure (13.4%). Other conditions like road traffic accident, seizure/unresponsiveness/drug induced drowsiness/diabetic ketoacidosis, urinary retention/neurogenic bladder, malignancy of solid organ, and septic shock were almost equally distributed. In non-catheterized patients, major clinical condition were cardio vascular failure i.e. (15%) followed by gastrointestinal dysfunction and aspiration pneumonia/COPD/respiratory failure. Hazelett SE et. al. (2006) has reported various co-morbid conditions which were similar to our findings.[21]

66% patients in our study improved clinically while 20.8% (40) patients were discharged against medical advice with overall mortality of 13.5% (26). Bouza E et. al. (2006) has reported 11.7% mortality rate in their study group.[22] However the mortality was due to multi factorial clinical conditions associated with urinary tract infection.

Conclusion: E. coli remains the most common etiological agent of UTI. Old age, catheterization, prolonged duration of catheterization and admission in critical care units are important contributors in urinary tract infection. Drug resistance is a evolving threat and thus after identification of clinical conditions, more aggressive measures must be employed to prevent infection in these patients, including early removal of catheters, reduce patient hospital stay and rational use of antimicrobials.

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