Isolation of Organism and its Drug Sensitivity Pattern in Patients with Urinary Tract Infection at Kathmandu Model Hospital

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Aims: Lack of compliance and unjustified antibiotic prescriptions has resulted in increasing bacterial resistance and is proving as a major challenge in the management of infections. Knowing the commonly isolated uropathogens and their antimicrobial susceptibility is beneficial in planning treatment protocols.

Methods: A retrospective review of records of patients with urinary tract infection from January 2012 to December 2016 was conducted at Kathmandu Model Hospital. All patients who were diagnosed as having culture positive urinary tract infection in medical ward of Kathmandu Model Hospital during 5 years period were analyzed for demographic data, prevalence of organism and antibiotic susceptibility patterns.

Results: A total of 315 samples were culture positive. The majority of bugs were gram negative E.coli (48.57%) followed by multi-drug resistant E.coli (28.89%). The other major pathogens were *E. faecalis* (6.03%), *S. epidermidis* (4.44%), *K. pneumoniae* (4.13%), respectively. The highest level of sensitivity in first line antibiotics was seen in nitrofurantoin (84.9%), whereas least sensitivity was shown by amoxicillin/clavulanic acid (21%). Similarly, in second line antibiotics, highest sensitivity was seen in tetracycline (100%), imipenem (91.9%) and least to meropenem (49.2%). Ceftazidime is mostly (93.3%) resistant antibiotics among uropathogens. All the third line antibiotics such as polymyxin B, tigecycline and colistin were 100% sensitive to all our isolates.

Conclusions: Nitrofurantoin may be an appropriate choice for initial empirical therapy of urinary tract infection. Similarly, the multi-drug resistant *E.coli* is increasing but it can be tailored if antibiotics are used appropriately on the basis of susceptibility data.

Keywords: Colistin Sulphate; multi-drug resistant E.coli; Nitrofurantion

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INTRODUCTION

Urinary tract infection (UTI) presents with lower abdominal pain, increase in urinary frequency, dysuria, low backache and fever, including acute and chronic pyelonephritis, cystitis, urethritis, epididymitis and prostatitis. It is one of the commonest infections in clinical practice and the second most common infectious presentation in community. Worldwide, there is an estimated 150 million UTIs per year.[1, 2] Lack of compliance and unjustified antibiotic prescriptions has resulted in increasing bacterial resistance and is proving as a major challenge in the management of this infection.[3] Knowing the common isolated uropathogens and their antimicrobial susceptibility is beneficial in planning treatment protocols. Therefore, this study aimed to determine the bacteriological profile and antibiotic sensitivity patterns in UTI cases in our hospital over past five years.

METHODS

A retrospective review of records of patients with UTI from January 2012 to December 2016 was conducted at Kathmandu Model Hospital. All patients who were diagnosed as having culture positive UTI in medical ward of Kathmandu Model Hospital during 5 years period were analyzed for demographic data, prevalence of organism and antibiotic susceptibility patterns. Only the patients with urine cultures yielding significant growth of pathogens from a freshly voided midstream urine specimen were included in the study. Any patient records with incomplete information were excluded from this study. An antibiotic susceptibility pattern was further confirmed from the

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laboratory records. Antimicrobial susceptibility of the isolates was tested by the disc diffusion method. Due necessary permission from the concerned departments and Institutional Review Committee (IRC) of *phect*-NEPAL/ Kathmandu Model Hospital were obtained. Data were entered and analyzed using Excel and SPSS version 21. Data has been summarized using percentage, graph, bar diagram, and tables.

RESULTS

Table 1.Demographic and clinical variables of Urinary tract infection (n=315).

Characteristics	Total (n)=315	
	Number	Percentage (%)
Age		
≤ 20	20	6.3
21 to 40	62	19.7
41 to 60	79	25.1
61 to 80	114	36.2
≥ 81	40	12.7
History of UTI		
Yes	55	17.5
No	260	82.5
Risk Factors (Diabetes, renal calculus, history of cauterization ,VUR)		
Yes	113	35.9
No	202	64.1
Symptoms of UTI		
Yes	174	55.2
No	141	44.8
Pus cells in urine		
Yes	222	70.5
No	93	29.5

The mean age of study population is 56.1 years with a standard deviation of 21.19 (age distribution was 15 to 94). The data illustrates that the age group 61-80 years is highly vulnerable (over one third) to UTI followed by 41-60 years group (a fourth) with the least vulnerable (marginally over a twentieth) being the population under 20 years of age. Majority (82.5%) of patients did not have any history of UTI, lesser patients (35.9%) presented the risk factors and almost similar number (55.2%) of patients presented clinical symptoms. Lastly, while analyzing the presence of pus cells in the urine of culture positive patients, majority (70.5%) showed positive result. [Table-1]

Table 2: Organisms causing urinary tract infection (n=315).

Bacteria isolated	Number (n)	Percent (%)
E. coli	153	48.57%
MDR E. coli	91	28.89%
E. faecalis	19	6.03%
S. epidermidis	14	4.44%
K. pneumoniae	13	4.13%
Enterobacter Spp	6	1.9%
S. saprophyticus	3	1.0%
C. freundii	3	1.0%
P. vulgaris	3	1.0%
P. mirabilis	2	.6%
Acinetobacter spp	2	.6%
K. oxytoca	2	.6%
P. aeruginosa	2	.6%
C. koseri	1	.3%
Coagulase Negative Staphylococci	1	.3%
Total	315	100%

The majority of bugs were gram negative aerobic rods. Among the gram negative rods, *E.coli* was most frequently UTI causing uropathogens, which accounted for 48.57% followed by multi-drug resistant *E.Coli* (28.89%). The other major pathogens were *E. faecalis* (6.03%), *S. epidermidis* (4.44%), *K. pneumoniae* (4.13%), respectively. The prevalence of other uropathogens were almost similar in proportion. [Table-2]

Table 3 illustrates the sensitivity patterns of uropathogens to the first line, second line and third line antibiotics**.** The highest level of sensitivity in the first line antibiotics was seen in nitrofurantoin (84.9%), gentamycin (72.9%), levofloxacin (54.5%), cotrimoxazole (44.1%), norfloxacin (42.8%), ofloxacin (42.2%), and ciprofloxacin (41.8%), whereas least sensitivity was shown by amoxicillin/clavulanic acid (21%), amoxicillin (23.7%), ceftriaxone (29.7%), cefixime (37.4%) and cefotaxime (39.7%), respectively.

Similarly, the second line antibiotics also showed the mixed sensitivity patterns with highest sensitivity in tetracycline (100%), imipenem (91.9%), vancomycin (75%) and piperacillin/tazobactam (74.4%). Unfortunately, other carbapenen, mainly meropenem was sensitive in only 49.2% patients. Contrary to this, ceftazidime is mostly resistant antibiotics among uropathogens with 93.3% resistance. Fortunately, all the third line antibiotics polymyxin B, tigecycline and colistin were 100% sensitive to all our isolates.

Table 3: Overall sensitivity of uropathogens (n=315)

Antibiotics	Number (n)	Sensitivity (%)	Resistance (%)	Intermediate (%)
1st Line				
Amoxicillin	152	36 (23.7%)	115 (75.7%)	1 (0.6%)
Amoxicillin/Clavulanic Acid	38	8 (21%)	29 (76.3%)	1 (2.6%)
Cefixime	278	104 (37.4%)	168 (60.4%)	6 (2.2%)
Cefotaxime	295	117 (39.7%)	175 (59.3%)	3 (1%)
Ceftriaxone	229	68 (29.7%)	159 (69.4%)	2 (0.9%)
Ciprofloxacin	306	128 (41.8%)	167 (54.6%)	11 (3.9%)
Norfloxacin	306	131 (42.8%)	164 (53.6%)	11 (3.6%)
Ofloxacin	282	119 (42.2%)	155 (55%)	8 (2.8%)
Nitrofurantoin	312	265 (84.9%)	39 (12.5%)	8 (2.6%)
Cotrimoxazole	299	132 (44.1%)	165 (55.2%)	2 (0.7%)
Gentamycin	214	156 (72.9%)	52 (24.3%)	6 (2.8%)
Levofloxacin	145	79 (54.5%)	50 (34.5%)	16 (11%)
2nd line				
Amikacin	180	117 (37.1%)	6 (5.1%)	2 (.6%)
Cefoperazone/Salbactam	110	54 (49%)	50 (45.5%)	6 (5.5%)
Ceftazidime	132	5 (3.8%)	124 (93.9%)	3 (2.3%)
Doxycycline	46	24 (52.2%)	20 (43.5%)	(4).30%
Imipenem	99	91 (91.9%)	8 (8.1%)	—
Meropenem	130	64 (49.2%)	60 (52.2%)	6 (4.8%)
Piperacillin/Tazobactam	115	81 (74.4%)	30 (26%)	4 (3.5%)
Tetracycline	3	3 (100%)	—	—
Vancomycin	8	6 (75%)	2 (25%)	—
3rd Line				
Polymyxin B	5	5 (100%)	—	—
Tigecycline	9	9 (100%)	—	—
Colistin	10	10 (100%)	—	—

DISCUSSION

Urinary tract infections are the most frequent bacterial infection in women. In a study done in a rural area of India where the prevalence of UTI in female was 78.8%.[4] The close proximity of the female urethral meatus to anus, short urethra, altered vaginal biota and sexual intercourse influence the higher prevalence of UTI in female.[5] In addition, elderly populations have increased vulnerability towards UTI for various associated risk factors such as age-associated altered immunity, increased comorbid conditions and exposure to nosocomial pathogens.[6] Our study showed almost three-fourth of the UTI patients were over 40 years, indicating the higher prevalence of UTI in elderly people. A similar finding was demonstrated by the study done by Prakash and Saxena where the highest susceptible age group of patient to UTI was over 48 year with 63.51% prevalence.[7]

In our study, majority (82.5%) of the patients did not have any history of UTI which is similar to the study done by Derese et al where 73.1% patients had no history of UTI.[8] Similarly, we observed predisposing factors for UTI were present in 35.9% patient contrast to 64.1% with no risk factor. In this study, condition like diabetes, renal calculus, history of cauterization, VUR are considered as predisposing factor. Overall, these entire predisposing factors play role in causing UTI but the association with UTI is not very strong as shown in study done in Nepal by Subedi et al[9] and in study done by Holmgrem.[10] Over viewing the clinical symptoms, almost similar number of patient had clinical symptom (55.2 vs. 44.8%). Previous study also showed clinical symptoms were present in 47.3% which is nearly similar to our study.[8] When analyzing the presence of pus cells in culture growth patients, 70.5% patients showed positive result. In this study, pus cells more than 6/HPF is considered positive.[11] A cross sectional study from Bangladesh showed out of 100 urinary samples having pus cells >5/HPF, 93.3% culture positive patients showed significant pyuria.[12]

Increasing resistance in bacterial pathogens is of world-wide concern. In this study, the majority of

bugs were gram negative aerobic rods. Among the gram negative rods, *E.coli* was most frequently UTI causing uropathogens, which accounted for 48.57%. Frequency of pathogens causing urinary tract infection in a tertiary care hospital in Western Nepal was studied, where the most common pathogens isolated were *E. coli* (59.4 %).[13] Similarly, the study done in india showed *E. coli* was found positive in 61.02% samples. The second frequently occurred organism in our study is multi-drug resistant *E.coli* (28.89%). In most of the study done in Nepal, other organisms like *E. faecalis, S. epidermidis, K. pneumoniae* are the second most causatives of UTI,[14] but in our study MDR *E. coli* is the second most frequently occuring organism which is similar to the study done in Thailand where MDR *E. coli* is higher.[15] The other major pathogens were *E. faecalis* (6.03%), *S. epidermidis* (4.44%), and *K. Pneumoniae* (4.13%), respectively. Antibiotic susceptibility pattern of urinary isolates from Manipur showed *Klebsiella* species (14.4%) is the second most common after *E. coli*.[16] In a prospective study undertaken over a 14-month period in Iran, *E. coli* was the most common etiological agent of UTI (74.6%), followed by *Klebsiella* spp (11.7%), *S. saprophyticus* (6.4%), and *P. aeruginosa* (2.2%).[17] In another study, *Klebsiella* species caused urinary tract infection in maximum number of cases (124, 37.35%) followed by *E. coli* (114, 34.4%).[18] The prevalence of antimicrobial resistance in both out and hospital patients with UTI is increasing and can vary according to geographical and regional location, but in overall, *E. coli* is causing UTI in most of the people worldwide.

Regarding the sensitivity patterns of uropathogens to first line antibiotics**,** the highest level of sensitivity was seen with nitrofurantion (84.9%), gentamycin (72.9%), levofloxacin (54.5%) , cotrimoxazole (44.1%), norfloxacin (42.8%), ofloxacin (42.2%), and ciprofloxacin (41.8%), whereas the least sensitivity was shown by amoxicillin/clavulanic acid (21%), amoxicillin 36 (23.7%), ceftriaxone (29.7%), cefixime (37.4%) and cefotaxime (39.7%). Considering antibiotic sensitivity, our results were different from a year-long study conducted in Shankarapur Hospital in Kathmandu valley in 2015 where the sensitivity rates of nitrofurantion (59.4%), gentamycin (56.4%) were lesser than our findings. Whereas similar comparable sensitivity was seen with cotrimoxazole (47.3%), ofloxacin (50%), ciprofloxacin (49.7%), and cefixime (48.5%). In addition, a higher antibiotic sensitivity to ceftriaxone (73.3%%) and amoxicillin/clavulanic acid (60.6%%) was seen which is contrary with our finding.[9] Other study done at Bangladesh showed cotrimoxazole and amoxicillin are virtually useless against uropathogens as they were effective against 31.81%and 11.81% of all isolated organisms respectively. This study also showed gentamycin is sensitive in 74.54% which is almost similar to our study but amikacin sensitivity is much higher than our study (86.3%).[19] Reduced susceptibility to amoxicillin in our study may indicate patients presenting to primary care which may have less severe symptoms and likely to present earlier or may reflect changes in antibiotic susceptibilities due to physicians' prescribing behavior.[20]

Similarly, second line antibiotics also showed the mixed sensitivity patterns with highest sensitivity with tetracycline (100%), imipenem (91.9%), vancomycin (75%) and piperacillin/tazobactam (74.4%). The study done by Subedi et al showed similar sensitivity to tazobactam (73.3%).[9] Similarly, study from Bangladesh showed imipenem and meropenem is 98.18% sensitive to uropathogens whereas our study shows similar result with imipenem (91.9%) but, unfortunately meropenem was sensitive in only 49.2% patients. According to our results, ceftazidime was 3.6% sensitive which differ from a Pakistani study done by Tabish and Iqbal where ceftazidime sensitivity was 46.66%.[20]

In our study, overall the third line antibiotics polymyxin B, tigecycline and colistin were 100% sensitive to all our isolates. Identical results are reported in a study from USA where tigecycline were found to be most efficacious.[21]

CONCLUSIONS

In conclusion, nitrofurantion may be an appropriate choice for initial empirical therapy of UTI though the uropathogens showed high levels of resistance to multiple urinary antimicrobial agents. Similarly, the multi-drug resistant *E.coli* is increasing but it can be tailored if antibiotics are used appropriately on the basis of susceptibility data. The third line antibiotics polymyxin B, tigecycline and colistin could be used only if needed to preserve it for future for MDR uropathogens.

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