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Evaluation of the microbiological spectrum and antimicrobial profile of the pathogens associated with Urinary Tract Infection.

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ABSTRACT

Background: Empiric treatment of the urinary tract infections (UTI) is highly practiced throughout the world which should be actually based on the microbial spectrum and the antibiotic sensitivity profile of the uropathogens in the local population. This study was conducted in a newly started tertiary health care facility of north India to determine the resistance pattern of uropathogens in the hospital, and help in establishing local guidelines on treatment of UTI. **Methodology:** 346 consecutive non repetitive positive urine cultures between august 2016 and January 2017 were studied and were analyzed for the type of pathogens associated and there detailed antimicrobial sensitivity profile. Urine was primarily collected with midstream clean catch technique until otherwise indicated. **Results:** E. coli comprised 6.67%; Klebsiella 4.33%; Proteus 3.46%; pseudomonas 7.5% and staphylococcus 4.04% of the isolates. Furthermore, 23% of the gram negative isolates were ESBL producers. 51% of the gram negative isolates were sensitive to ciprofloxacin; 44% to SXT; 32% to amoxicillin. Sensitivity patterns at this institute were found to be better than others. **Conclusion:** High levels of ESBL producers among gram negative uropathogens was seen this study. High rates of resistance to ciprofloxacin, norfloxacin, cotrimoxazole and amoxicillin, precludes there use as the most commonly used antibiotics for empirical treatment of UTI. Instead Fosfomycin appears to be a more promising agent. More importantly, urine cultures should be made mandatory specially for all the indoor patients, patients with recurrent UTI, treatment failures or have complicated UTIs.

KEYWORDS : UTI, antibiotic susceptibility, urine culture.

INTRODUCTION:

Urinary tract infections (UTI) is one of the most prevalent bacterial infections found both in patients coming to hospital outdoor and indoor patients. It attributes to about 7 million visits to outpatient clinics and about 1 million emergency visits annually [1]. Accounting for almost 35% of nosocomial infections UTI has been found to be the most common hospital-acquired infection, and also the second most common cause of bacteremia [2, 3]. Since, some UTIs are asymptomatic or present with atypical signs and symptoms, it becomes challenging at times to establish an appropriate diagnosis. Large number of cases of UTI presents to the hospital everywhere annually therefore, laboratory examination and culture of urine samples constitute a major bulk of the workload in most laboratories and urine cultures being the most common type of culture.

Few studies suggested that the percentage of UTIs caused by E. coli is decreasing but still various studies have established that *Enterobacter*iaceae, especially Escherichia coli remains the most common cause of UTI [4, 5]. It has also been reported that, the percentage of UTIs caused by yeasts, group B streptococci, and Klebsiella pneumoniae increased in 1980s, whereas the percentage of UTIs caused by E. coli, Proteus species, and Pseudomonas species has decreased a little in previous years [6]. Few studies showed a decrease in the proportion of UTIs caused by Enterobacter species, and an increase in the proportion of UTIs caused by *Acinetobacter* species and *Pseudomonas aeruginosa* [4]. Amongst the candida species, *Candida albicans* was found as the most common cause of funguria [7]. In most Western countries, microbiological testing may be unnecessary in acute uncomplicated UTI, except for surveillance purposes [8], as culture is a more time consuming and expensive procedure than the antibiotic treatment itself. The Infectious Diseases Society of America (IDSA) guidelines currently recommend empirically treating acute, uncomplicated bacterial cystitis in healthy adults. However, these guidelines may not be applicable in other countries such as India. The resistance pattern of community acquired uropathogens has not been extensively studied in the Indian subcontinent [9]. This study was planned to identify the most common pathogens associated with UTI in this region of north India and to determine their antibiotic sensitivities. This epidemiological data might be a helpful guide for the choice of empirical antibiotic treatment of UTI at this tertiary care hospital.

MATERIALS AND METHOD:

This study is a retrospective observational study on the microbiological spectrum of the organisms obtained from all the urinary cultures in a teaching hospital of Rajasthan during the period of six months between august 2016 to January 2017. Both OPD and indoor patients with any clinical suspicion of UTI or any other indication of urine culture were included in the study. All the samples which had been submitted by patients other then pregnant females were taken into the study. Delayed samples or repetitive cultures from the same patient were excluded from the study. Data was collected from 346 consecutive non repetitive

positive cultures of urine which came to the department of microbiology between the period of Aug 2016 to Jan 2017. Only a single positive culture per patient was included in the analysis.

SPECIMEN COLLECTION, TRANSPORTATION AND PROCESSING:
Urine samples were collected with cleancatch midstream technique after proper cleansing of the periurethral area. Only freshly voided urine was accepted for culture and samples coming after 2 hrs of collection were out rightly rejected. Semi quantitative urine cultures were inocculated on CLED (Cystein lactose electrolyte deficient) agar, using calibrated loops which provides us the approximate count of the bacteria in cfu/mL. Cultures were read after overnight incubation at 37°C. In general, significant bacteriuria was considered on isolation of a single bacterial species from the urine sample at a concentration of 105 cfu/mL or more in association with microscopy findings of >10 WBC per high power field [10]. But for patients already on antibiotics or in case of urine specimens obtained via suprapubic aspirate or catheterization, the bacterial count of 102 cfu/mL was also taken as significant[5, 11].

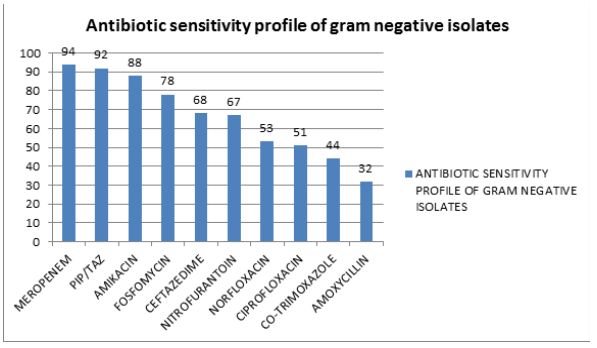
Conventional biochemical tests were put up to establish the correct identity of the isolate upto the species level. Simultaneously Antimicrobial susceptibility testing and interpretation for the isolated organism was performed using the standard disc diffusion method as described by the Clinical & Laboratory Standards Institute (CLSI 2016) criteria [12]. Sensitivity testing was done for amoxicillin, trimethoprim-sulfamethoxazole, ciprofloxacin, amikacin, nitrofurantoin, piperacillin-tazobactum, norfloxacin, ceftazidime, fosfomycin and meropenem for each isolate. Extended spectrum β-lactamase (ESBL) production was detected using ceftazidime and ceftazidime-clavulanic acid discs. A 5mm or greater increase in the zone of diameter around ceftazidime-clavulanic acid combination disc, as compared with the ceftazidime alone disc, was considered indicative of ESBL production [13, 14]. E. coli ATCC 25922, S. aureus ATCC 25923 and P. aeruginosa ATCC 27853 were used as quality control strains for antimicrobial discs. E. coli ATCC 25922 was used as ESBL negative and K. pneumoniae 700603 was used as ESBL positive reference strain to check the efficacy of ceftazidime and ceftazidime-clavulinic acid discs.

RESULTS:
This retrospective observational study of the duration of six months was done on total 346 consecutive, nonrepititive positive urine cultures which came out from total 733 urine samples sent for the culture to the department of microbiology. Out of these 733 samples 426 came from OPD patients and rest 307 samples came from indoor patients. Out of the 346 positive cultures 189(54.62%) samples came from female patients and remaining 157 (45.37%) were from male, clearly showing female preponderance of the infection in urinary tract.

The distribution of the isolates from the urinary culture is as shown in table 1. Only 8.86% of the isolates were found to of gram positive origin. 1.44% of isolates were found to be various candida species. Remaining about 90% of the isolates were of gram negative origin amongst which 66.47% was comprised of Escherichia coli. It was also noticed that maximum isolates of Staphylococcus aureus, Pseudomonas and Acinetobacter species were found to be associated with indoor patients clearly showing their preponderance in hospital acquired UTI.

The antimicrobial susceptibility pattern associated with Gram negative bacteria is shown in figure.1. It is well in line with the antibiogram of the most common urinary isolate ie; E.coli except for fosfomycin for which it showed almost 95% sensitivity. For rest of the antibiotics also it showed better sensitivity rates to various antibiotics as compared to the other isolates which were more associated with hospital acquired UTI ie; pseudomonas and acinetobacter species. 23% of all Gram negative organisms were found to be ESBL producers in this study.

SR. NO.	ISOLATES	PERCENTAGE
1.	E.coli species	66.47%
2.	Pseudomonas species	7.5%
3.	Klebsiella species	4.33%
4.	Proteus species	3.46%
5.	Enrerobacter species	3.46%
6.	Citrobacter species	2.89%
7.	Acinetobacter species	2.31%
8.	Morganella species	0.86%
9.	Staphylococcus aureus	4.04%
10.	Enterococcus species	2.20%
11.	Staphylococcus saprophyticus	1.155
12.	Candida species	3.46%



DISCUSSION:
In this study of positive urinary cultures the most commonly isolated organism was E. coli. The proportion of different bacterial species isolated in this study correlates well with few other studies done previously[15,16]. Most of the isolates of Staphylococcus, pseudomonas and Acinetibacter found in this study were associated with hospitalized patients, clearly indicating there absence in the causation of community acquired UTI. This study demonstrated greater resistance in gram negative organisms to amoxicillin, ciprofloxacin, norfloxacin and cotrimoxazole. 23% of all Gram negative organisms were found to be ESBL producers in this study. The percentage of ESBLs producers is lesser than that reported by few other studies in India [17,18,19]. Higher resistance rates to the oral antibiotics may be attributed to the indiscriminated consumption of these antibiotics in the community [20,21]. On the other hand restricted usage of antibiotics like meropenem, piperacillin-tazobactum and amikacin has contributed to a better sensitivity of these drugs. Sensitivity patterns at this institute were found to be better than others. It may be attributed to the better control of by the hospital infection control program and better infrastructural facility as it is a newly started health care facility. Fosfomycin is an oral antibiotic which has been found to be very effective in community acquired UTI, specially in E. coli. Nitrofurantoin which was initially thought to be an appropriate agent for CA-UTI also showed an increased resistance of about 33%. It is much higher than that shown by few previous Indian studies [22,23]. Earlier, flouroquinolones and cotrimoxazole were considered for the empirical therapy in the cases of uncomplicated UTI. But looking at the increasing level of drug resistance, local antimicrobial susceptibility patterns must always be taken into account before choosing the appropriate antimicrobial agent.

The urine samples in this study were obtained primarily by the midstream clean-catch technique. This was chosen as the standard method for collection because it is a simple, inexpensive, non invasive and comfortable technique of urine collection and carries no associated risk of introducing new infection into the bladder. Colony counts from this method have been found to be correlating well with those of specimens collected via catheterization or suprapubic aspiration[5]. But this method of collection is known to be associated with high rate of contamination with commensal flora of distal urethra. So to avoid this contamination it was preceeded

with proper cleansing of skin and mucous membranes adjacent to the urethral orifice before micturition, and collecting middle part of the urinary stream for culture [24]. Contrastingly, few other studies suggested that the cleansing procedures may not significantly decrease the contamination rates so may be unnecessary as a routine [25,26].

Collection of urine by inserting a urinary catheter, though associated with minimal contamination, was practically chosen only for the patients who were already catherized. Apart from being technically demanding it is also associated with inherent risk of introducing pathogenic bacteria into the urinary tract. Suprapubic aspiration is known to be the best method to avoid urinary contamination but has been rarely used in the study population as it is an invasive, uncomfortable and a time consuming procedure.

On the basis of the results obtained on the comparative studies, It has been observed that delay in transportation or processing of urine specimens exert an adverse effect on the quality of the result [27,28]. So in this study it was ensured that all the samples were processed within 2 hrs of collection or were refrigerated if any delay was expected. It is well established that correct interpretation of test results, is largely dependent on the proper collection of specimen, timely and correct processing and handling of the urine. Therefore it is important for clinicians to specify all the relevant details such as method of collection, date and time of specimen collection, patient demographic information, antimicrobial usage and clinical history with the test requisition slip.

CONCLUSION:

Though routine urine cultures might not appear necessary for the evaluation of outpatients with uncomplicated UTI[55, 56]. But looking at the ever-changing spectrum of the organisms isolated from urine cultures and continuously escalating antimicrobial resistance amongst the pathogens, it is strongly recommended that urine cultures should be sent necessarily in all the indoor patients, patients with recurrent UTI, treatment failures or have complicated UTIs. The bacterial culture remains an important test for the diagnosis of UTI, because it helps to document infection, determine the identity of the infecting microorganisms and also provide the true antimicrobial susceptibility pattern. For the accurate interpretation of culture results, clinical information is required which is usually available only to the clinician so to get the best results, proper communication between the treating clinician and the laboratory should be established through various means along with the adequately filled requisition forms..

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