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STUDY OF PATTERNS OF ANTIBIOTIC SENSITIVITY OF URINARY TRACT INFECTIONS

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ABSTRACT

Background: Urinary tract infections (UTIs) are one of the most common bacterial infections in human. Catheter-associated UTIs are one of the most dangerous health risks contributing 34% of all health care associated infections. Extensive and inappropriate use of antimicrobial agents has resulted in the development of antibiotic resistance which has become a major problem worldwide. The objective of the present study was to highlight the bacterial etiology of UTIs and determination of resistance pattern of E. coli isolates. **Method:** A cross-sectional prospective study was carried out in the Department of Microbiology, Govt. Medical College, Jammu (J&K), India, over a period of 6 months, i.e. from April 2021 to September 2021, among the reported OPD and indoor patients of GMC Jammu, in the age group of 18 to 90 years. **Results:** Of the 894 urine samples processed 455 (50.89%) gave significant growth of pathogens. The patients were between 18 and 90 years of age. The prevalence of UTI was high among females (63.08%) than males (36.92%). Females of the reproductive age group (18-49 years) constituted 53.40% of the total patients with UTI. However, elderly (50-90 years) males had a higher incidence of UTI (10.11%) compared to the elderly females (9.67%). Rate of E. coli (264, 58.02%) isolation was highest followed by Staphylococcus aureus (51, 11.2%). E. coli was found sensitive to meropenem, imipenem and amikacin (almost 100%), with good susceptibility to Ciprofloxacin (88%). Overall, 97% of the isolates were sensitive to Imipenem, 98.1% to Meropenem, while 90.3% are sensitive to Amikacin, 81.1% to Nitrofurantoin and 70.4% to Gentamicin. **Conclusion**: Culture positive rate for uropathogens was high, majority coming from adult female patients. E.coli was the most common etiological agent but still susceptible to nitrofurantoin. Nitrofurantin, Imipenem and Amikacin are good choice to tackle the upcoming problems of ESBL producing E.coli.

KEYWORDS: Urinary Tract infection, Escherichia Coli, Prevalence, Antibiotic Sensitivity.

INTRODUCTION

Urinary tract infections (UTIs) are one of the most common bacterial infections in humans both in the community and hospital setting.[1] They are a major public health problem in terms of morbidity and financial cost, and incur the highest total health care cost among urological diseases, exceeding that of chronic renal failure even when renal dialysis and renal transplantation are included.[2] UTI represents one of the most common diseases encountered in medical practice today with an estimated 150 million UTIs per annum worldwide.[3] UTI is said to exist when pathogenic organisms are detected in the urine, urethra, bladder, kidney or prostate. Catheter-associated UTIs are one of the most dangerous health risks contributing 34% of all health care associated infections.[4] While up to 90% of the patients with UTIs complain of urinary tract symptoms, one third or more of the patients with these symptoms do not have bacteriuria.[5] E. coli, E. faecalis, K. pneumoniae, S. marcescens, P. aeruginosa, S. saprophyticus, S. aureus and Proteus mirabilis are most common bacteria causing UTIs in human beings. The E. coli accounts for approximately 85% of community acquired UTIs and 50% of hospital acquired UTIs.[6] The prevalence of antimicrobial resistance in patients with UTI is increasing and can vary according to geographical and regional location.[7,8]

ESBL or extended spectrum beta-lactamase, is an enzyme found in some strains of bacteria. ESBL-producing bacteria are harder to treat as they can't be killed by many of the antibiotics that doctors use to treat infections, like penicillins and some cephalosporins.[9]

Although UTIs occur in both men and women, clinical studies suggest that the overall prevalence of UTI is higher in women.[10] Microorganisms use various mechanisms to develop drug resistance, such as recombination of foreign DNA in bacterial chromosome; horizontal gene transfer and alteration in genetic material.[11] Resistance pattern of microorganisms vary from country to country, state to state, large hospital to

small hospital and hospital to community. There is no systematic national surveillance of antibiotic resistance and in- sufficient data is available to quantify the problem.[12] Detection of UTI causing pathogens and resistance of these pathogens to commonly prescribed antibiotics in clinical set ups is essential and helpful in improving the efficacy of empirical treatment.[13] Knowledge of the etiological agents of UTIs and their antimicrobial resistance patterns in specific geographical locations may aid clinicians in choosing the appropriate antimicrobial empirical treatments. At the same time, the extensive and inappropriate use of antimicrobial agents has invariably resulted in the development of antibiotic resistance which, in recent years, has become a major problem worldwide.[14] Therefore the objective of the present study was to highlight the bacterial etiology of UTIs and determination of resistance pattern of E. coli isolates.

METHOD

A cross-sectional prospective study was carried out in the Department of Microbiology, Govt. Medical College, Jammu (J&K), India, over a period of 6 months, i.e. from April 2021 to September 2021, among the reported OPD and indoor patients of GMC Jammu. Urine samples of 894 patients were received during the above mentioned period. The age of patients included in the study ranged from 18 to 90 years. Ethical clearance for the study was duly obtained from Institutional Ethics Committee.

Clean catch midstream urine was collected from each patient into a 20mL calibrated sterile screw-capped universal container which was distributed to the patients. Patients were instructed about the method of collection of sample aseptically.

The specimens were labeled, transported to the laboratory, and analyzed within 6 hours. In each container boric acid (0.2mg) was added to prevent the growth of bacteria in urine samples. A calibrated loop method was used for the isolation of bacterial pathogens from urinary samples. A sterile 4.0mm platinum wired calibrated loop was used which delivered 0.001mL of urine. A loopful urine sample was plated on UTI Chrome agar and MacConkey agar. The inoculated plates were incubated at 37°C for 24h. The number of isolated bacterial colonies was multiplied by 1000 for the estimation of bacterial load/mL of the urine sample. Identification of bacterial isolates was done on the basis of their cultural and biochemical characteristics. Gram negative bacteria were identified by the standard biochemical tests.[15] and Gram positive microorganisms were identified with the corresponding laboratory tests: catalase, coagulase, and mannitol test for Staphylococcus aureus.[16] Antibiotic sensitivity pattern of E. coli isolates was determined on Muller Hinton agar plates by Kirby-Bauer disc diffusion. Isolates were declared as sensitive or resistant on the basis of zone of inhibition following the criteria of Clinical Laboratory standards Institute. After that antibiotic disks were placed on the surface of media and pressed gently. Mueller Hinton agar plates were then incubated at 37°C for 24h. After 24h the inhibition zones were measured and interpreted by the recommendations of clinical and laboratory standards. The following standard antibiotic discs were used for the isolates, ofloxacin (OFL), amikacin (AMK), gentamycin (GET), ceftazidime (CTZ), ceftriaxone (CFX), imipenem (IMP), nitrofurantoin (NTF), linezolid (LNZ). Standard strains of E. coli (ATCC 25922), S. aureus (ATCC 25923), and P. aeruginosa (ATCC 27853) were used routinely in this study as control.

Data was analyzed using MS Excel 2010 software.

RESULTS

Of the 894 urine samples processed 455 (50.89%) gave significant growth of pathogens. The patients were between 18 and 90 years of age. The prevalence of UTI was high among females (63.08%) than males (36.92%). Females of the reproductive age group (18-49 years) constituted 53.40% of the total patients with UTI. However, elderly (50-90 years) males had a higher incidence of UTI (10.11%) compared to the elderly females (9.67%). (Table 1)

Table 1: Demographic distribution of patients with urinary tract infections.

Age group (in years)	Females No (%)	Males No (%)	Total
18-29	104(22.85%)	53(11.65%)	157
30-49	139(30.55%)	69(15.16%)	208
50-90	44(9.67%)	46(10.11%)	90
Total:	287(63.08)	168(36.92)	455

The commonest isolates were Escherichia coli, Staphylococcus aureus, Enterococci, Klebsiella, Proteus, and Pseudomonas. Out of 455 bacterial isolates from patients, rate of E. coli (264, 58.02%) isolation was highest followed by Staphylococcus aureus (51, 11.2%).

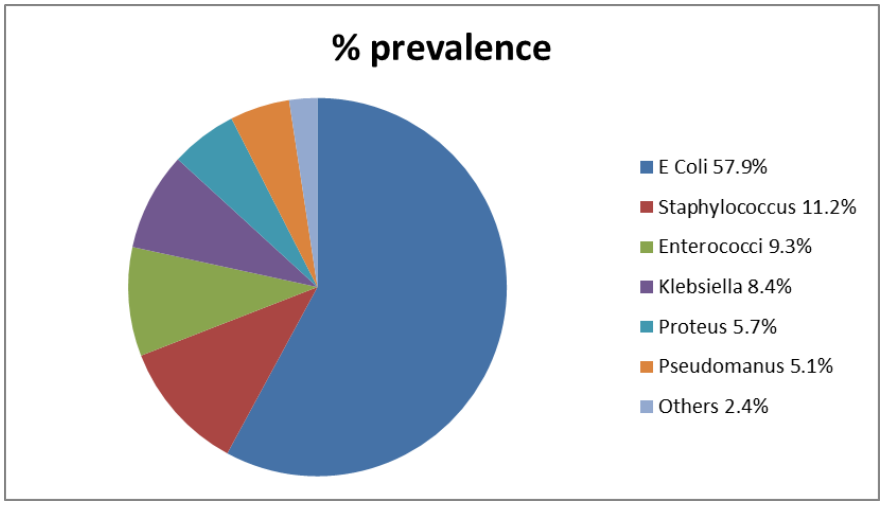

Figure 1: Common Isolates.

Since Escherichia coli, or E. coli was the most common isolate, its sensitivity could be established against each antimicrobial agent. E. coli was found sensitive to meropenem, imipenem and amikacin (almost 100%), with good susceptibility to Ciprofloxacin (88%). But ESBL E. coli also showed sensitivity to Imipenem (100%), Nitrofurantoin (90%) and Amikacin (83%).

Staphylococcus-aureus showed highest sensitivity to Nitrofurantoin (100%), Imipenem (100%), Meropenem (95%) and Amikacin (94%). Enterococci was sensitive to Imipenem (100%), Meropenem (100%), Nitrofurantoin (82%) and Gentamicin (56%). Pseudomonas showed highest sensitivity to Meropenem (90%) followed by Amikacin and Ciprofloxacin (46%). All the isolates showed low degree of susceptibility to Amoxycillin (15.4%), Ceftriaxone (39.3%) and Cefixime (39.5%). Sensitivity to Nitrofurantoin to pseudomonas was not tested as they have intrinsic resistance to that drug.

Overall, 97% of the isolates are sensitive to Imipenem, 98.1% to Meropenem, while 90.3% are sensitive to Amikacin, 81.1% to Nitrofurantoin and 70.4% to Gentamicin.

Out of 264 E. coli isolates, 208 (78.8%) were multiple drug resistant and 4 isolates were extensively drug resistant.

Table 2: Percentage of Uropathogens sensitivity to Antibiotics.

Antibiotic	Sensitivity (%)	Resistance (%)
Amoxycillin	15.4%	86.6%
Cefixime	39.5%	60.5%
Ceftriaxone	39.3%	60.7%
Ciprofloxacin	52.2%	47.8%
Gentamicin	70.4%	29.6%
Amikacin	90.3%	9.7%
Imipenem	97.0%	3.0%
Meropenem	98.1%	1.9%
Nitrofurantoin	81.1%	18.9%

DISCUSSION

UTIs are caused by microbial invasion and subsequent multiplication in urinary tract.[17] The present study conducted to study of patterns of antibiotic sensitivity of urinary tract infections, has generated a valuable amount of data to compare and monitor the status of antimicrobial resistance among uropathogens to improve efficient empirical treatment. Increasing antimicrobial resistance has been documented globally.[18] The prevalence of UTI accounted due to the significant growth of pathogens in the urine samples analyzed, was found to be 50.89% and this rate of prevalence is quite than in the other studies which account for 18% to 25.6%.[19] This was probably due to the fact that the urine samples of only those patients was analyzed, who otherwise showed other symptoms of UTI. E. coli was observed as the most common etiologic agent of UTI, which is also in accordance with previous studies.[20]

The study also observes that the prevalence of UTI is high among females (63.08%) than males (36.92%). Females of the reproductive age group (18-49years) constituted the majority among the studied group. It has been reported that adult women have a higher prevalence of UTI than men, principally due to anatomical and physical factors.[21] Among males an increased prevalence of UTI was recorded in elderly age group 50-90 (46/90, 51.1%) than young (53/157, 33.76%).This is probably because with advancing age, the incidence of UTI increases in men due to prostate enlargement and

neurogenic bladder.[22]

The study demonstrates that E.coli remain the leading uropathogen being responsible for UTI. This is in consistence with findings of other studies.[23] Our study reveals that 40% of E.coli isolates and 45% of Klebsialla species to be ESBL producers. Aggarwal et al. reported similar results with 40% of E.coli and 54.54% of Klebsialla species reported were ESBL producers.[24] E. coli was found sensitive to meropenem, imipenem and amikacin (almost 100%), with good susceptibility to Ciprofloxacin (88%). But ESBL E. coli also showed sensitivity to Imipenem (100%), Nitrofurantoin (90%) and Amikacin (83%).

Our study confirms the global trend towards increased resistance to beta lactum antibiotics. ESBL producing bacteria may not be detectable by routine disk diffusion susceptibility test, leading to inappropriate use of antibiotics and treatment failure. It is emphasized that institutions should avoid and discourage indiscriminate use of third generation cephalosporins. From this study, it can be seen that antibiotics like amoxicillin are virtually useless against uropathogens as they were poorly effective against almost all isolated organisms respectively.

Nitrofurantoin however showed strong activity against 70.4% of isolated organisms and was very active against E.coli and Staphylococcus aureus. It was weak against Proteus spp and Pseudomonas spp. It has also been shown to be very safe in pregnancy.[25] The consistent and high level susceptibility of E.coli to Nitrofurantoin may be influencd by nitrofurantoin's narrow spectrum of activity, limited indication, narrow tissue distribution and limited contact with bacteria outside the urinary tract.[26] From our study, it can be seen that more than 97% of the isolates are sensitive to Imipenem, Meropenem and most of them are sensitive to Amikacin, 90% and Nitrofurantoin, 81%.

Complications in UTIs have increased because of the prevalence of extended spectrum beta-lactamases (ESBL) producing bacterial patho-gens which are also causing many management and epidemiological issues. Quinolones, especially ciprofloxacin have been used for E. coli infections in recent past. In the present study however E. coli were highly resistant to ciprofloaxacin (54.2%), which is consistent with the previous reports.[27] To treat the UTIs caused by E. coli combination therapy especially amikacin and ciprofloaxacin may provide better results. Antibiotic resistance in E. coli isolated from UTIs insinuates for its close monitoring and prescription of antibiotics after the culture sensitivity tests.

The factors of this increasing incidence of UTI in young age females are associated with high sexual activity, recent use of a diaphragm with spermicide, and a history of recurrent UTIs. In this study, the Gram negative bacilli constituted 90.32% of the total bacterial isolates while Gram positive cocci constituted 9.3%. This result is consistent with reports from other studies.[28] Higher incidence of gram negative bacteria, related to Enterobacteriaceae, in causing UTI has many factors which are responsible for their attachment to the uroepithelium. The antimicrobial susceptibility pattern of E. coli varies widely by region. High efficacy of Nitrofurantoin was observed against Klebsiella in this study. Similar trends were reported by Kothari et al.[29]

The alarming finding in this study is the resistance to third-generation antibiotics; The possible explanation behind this situation is that the III generation antibiotics has been in use for a long period and must have been abused and over time organisms have developed resistant mechanisms due to changing their mode of action. The inappropriate usage of wide spectrum antibiotics, insufficient hygiene, immune-suppression, and a prolonged stay in the hospital are some other major etiological factors that elevate the chances of multi-drug resistant infections.[30] The emergence and spread of resistance can be reduced through appropriate or careful use of antimicrobial drugs and increasing awareness among the population to the hazards of inappropriate antimicrobial use through public health education campaign.[31]

The limitations of the present study were however the selection of a limited range of isolates and antibiotics, and more of such studies with other variants of isolates and drugs could be done.

CONCLUSION

This study provides valuable laboratory data to monitor the status of antimicrobial resistance among uropathogens and to improve treatment recommendations in a specific geographical region. Culture positive rate for uropathogens was high, with the majority coming from adult female patients. E.coli was the most common etiological agent and remains susceptible to nitrofurantoin. This drug should be the ideal antibiotic to use for uncomplicated UTI. To tackle the upcoming problems of ESBL producing E.coli, Imipenem and Amikacin are good choice along with nitrofurantin.

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Declarations

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