RESEARCH

ANTIBACTERIAL SUSCEPTIBILITY PATTERN OF CLINICAL ISOLATES FROM PATIENTS OF COMPLICATED AND RECURRENT URINARY TRACT INFECTION PRESENTING IN TERTIARY CARE HOSPITAL OF NORTHERN INDIA

Waleem Ahmad[1], Naba Hasan[2], Saim Hasan[3]

[1]Assistant Professor, Department of Medicine, G.S. Medical College and Hospital, Hapur, UP, India
[2]Senior Resident, Department of Pathology, J.N. Medical College and Hospital, AMU, Aligarh, UP, India
[3]Professor, Department of Anatomy, SHKM Govt. Medical College, Nuh, Haryana, India

Received : 02/06/2022
Received in revised form : 16/09/2022
Accepted : 28/09/2022

Keywords:
Urinary Tract Infection, Antimicrobial Susceptibility, Uropathogen

Corresponding Author:
Dr. Saim Hasan,
Email: saimhasan99@gmail.com
ORCID: 0000-0002-1614-7491

DOI: 10.47009/jamp.2022.4.4.93

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2022; 4 (4); 475-479

Abstract

Background: Urinary Tract Infections (UTIs) are the leading cause of gram-negative bacteremia in patients of all ages and are associated with a high risk of morbidity and mortality, especially in the elderly and account for significant health care costs. Complicated UTI (cUTI) is one that occurs because of anatomic, functional or pharmacologic factors that predispose the patient to persistent infection, recurrent infection or treatment failure. The uropathogens causing cUTI and their antibiotic sensitivity pattern varies considerably not only from that in acute uncomplicated UTI but also with time. In the present scenario, the essence of antimicrobial drug resistance of major uropathogens has posed a global threat. The objective is to know the causative agents of complicated and recurrent UTIs and their antimicrobial susceptibility patterns, in a tertiary care hospital in northern India. **Materials and Methods:** This study of 102 patients with microbiologically confirmed complicated and recurrent UTIs was conducted between January 2013 and December 2014. Urine samples received by the laboratory for culture and susceptibility testing over a period of study were analyzed and included in this study. Antimicrobial susceptibility testing was done on cultured isolates. **Result:** Out of 102 isolates, the most commonly isolated organism was E.coli (72.54%) followed by Klebsiella species (14.70%), Staphylococcus aureus (4.90%), Enterococcus (4.90%) & Pseudomonas (2.94%) being the least common organism. E.coli was most susceptible to amikacin (86.48%) and nitrofurantoin (72.97%). Klebsiella species was most susceptible to amikacin (80%) and gentamicin (53.33%). Susceptibility of E. coli, Klebsiella species and staphylococcus aureus to Levofloxacin was 13.51%, 40% and 40% respectively. **Conclusion:** Treatment guidelines for UTIs should be based on the current local antimicrobial sensitivity pattern of uropathogen and should be revised periodically due to increasing resistance to commonly used antibiotics.

INTRODUCTION

Urinary Tract Infection (UTI) is one of the most common bacterial infections and the second most common infectious disease in community practice. UTI occurs in all populations, from the neonate to the geriatric patient, but it has a particular impact on females of all ages (especially during pregnancy), males at the two extremes of life, kidney transplant recipients, and those with functional or structural abnormalities of the urinary tract. In fact, UTIs are the leading cause of gram-negative bacteremia in patients of all age groups and are associated with a high risk of mortality and morbidity, especially in the elderly, and account for significant health care costs.[1] The most important issues regarding UTI are their long-term consequences rather than the direct infectious disease morbidity and mortality of these infections. Bacteriuria may have a significant impact on children, especially in the presence of an anatomic or functional abnormality, like Vasicoureteric reflux. UTI causes permanent renal damage in children. Chronic pyelonephritis is a frequent cause of hypertension in children and secondary hypertension in adults.[2,3] In case of pregnant women, untreated, asymptomatic bacteriuria is associated with a lot of adverse effects. Untreated bacteriuria in pregnancy either symptomatic or asymptomatic is associated with a 50% increase in the risk of low birth weight and a

ISSN (O): 2687-5365; ISSN (P): 2753-6556

significant increase in the risk of premature delivery, pre-eclampsia, anemia, hypertension and postpartum endometritis.[4,5] UTIs are classified into two groups: Uncomplicated UTI and complicated UTI.[6] Uncomplicated UTI refers to acute cystitis or pyelonephritis in non-pregnant outpatient women without anatomic abnormalities or instrumentation of the urinary tract.

A complicated UTI is one that occurs because of anatomic, functional or pharmacologic factors that predispose the patient to persistent infection, recurrent infection or treatment failure.[7] The definition is basically needed for the differing line of management of cUTI as against uncomplicated urinary tract infection. The uropathogens causing cUTI and their antibiotic sensitivity pattern varies considerably not only from that in acute uncomplicated UTI but also with time. Recurrent urinary tract infection is defined as three episodes of urinary tract infection with 3 positive urine cultures in the previous 12 months or two episodes in the last six months. In the present scenario, the essence of antimicrobial drug resistance of major uropathogens has posed a global threat.[8] Of the various uropathogens, the most common organisms are E.Coli, Enterococcus fecalis, Staphylococcus aureus, Enterococci spp and Klebsiella species.[9]

Taking all these into considerations we need a study to know the causative agents of complicated and recurrent UTIs and their antimicrobial susceptibility patterns, in a tertiary care hospital in northern India. This study can help us to take a step towards evidence-based medicine and help us to keep track of antimicrobial susceptibility trends.[10]

MATERIALS AND METHODS

The cross-sectional study was conducted among the patients who were attending the outpatient department or who were admitted with complicated and recurrent UTIs fulfilling inclusion criteria in the Department of Medicine and Department of Microbiology, J.N. Medical College and Hospital, AMU, Aligarh, a tertiary care hospital in Northern India. The study period was from January 2013 to December 2014. The study was approved by Institutional Ethics Committee.

Study Population

A total of 102 patients was enrolled in the study who were having clinical features and bacteriological evidence of urinary tract infection (i.e urinary tract infection confirmed by positive urine culture reports) and fulfilled inclusion and exclusion criteria after taking informed consent.

Inclusion Criteria

Age 13 years and above, Both sexes (i. e male and female), Patients with a diagnosis of UTI with at least one of the following features, Indwelling catheter, Diabetes mellitus, Functional/anatomical abnormality of the urinary tract, Immunosuppression, Male sex, Voiding dysfunction, Renal failure, Urolithiasis, History of urinary tract surgery, Polycystic kidney and Patients with a history of recurrent UTI (more than 2 episodes of UTI in previous 6 months or more than 3 episodes of UTI in previous 12 months).

Exclusion Criteria

HIV and immunocompromised patients, Advanced renal failure, Hepatic dysfunction, Multiorgan failure, uncontrolled diabetes mellitus, Patients with malignancy, critically ill patients, renal transplant and renal replacement therapy

Sample collection and processing

Clean catch mid-stream urine samples or those obtained by aspiration from catheter tube or suprapubic aspirate collected in sterile, wide mouth universal container, from all the suspected UTI patients (outdoor patients and indoor/ hospitalized patients) were received and processed by the Bacteriology Laboratory. Contaminated/ non-sterile samples were discarded and not processed.

Bacterial identification and susceptibility testing

Urine samples were inoculated on appropriate culture media by using semi-quantitative methods and inoculated media was incubated for 48 hours aerobically at 37°C. Cultures were then examined for growth and colonies were counted for the determination of significant or insignificant bacteriuria. A growth of ≥105 colony forming units/ml was considered assignificant bacteriuria, suggestive of UTI.[11] Identification was done based on standard biochemical and other laboratory tests.[12]

Standard methods for the isolation and identification of bacteria were used throughout the study. The identified bacteria were also confirmed by the selective media of the 'Hi-crome series' (Hi-media, Mumbai, India). Isolates in significant numbers were identified by using standard biochemical tests.[10] Antimicrobial susceptibility testing was done for all the isolates using Kirby Bauer disc diffusion method as recommended by the Clinical and Laboratory Standards Institute. The antibiotic panels for each group of isolates were selected according to the CLSI guidelines, M100-S22, 2012 were obtained from HiMedia, India.

Antimicrobials tested for gram negative bacteria were Amikacin (30 µg), gentamicin (10 µg), Ofloxacin (5 µg), Cefoperazone(75 µg), Cefoperazone+ Sulbactam (75/75 µg), Cefepime (30 µg), Ceftriaxone (30 µg) and Nitrofurantoin (30µg). Antimicrobials tested for staphylococcus aureus bacteria were Amikacin (30 µg), Gentamicin(10µg), Ciprofloxacin (5 µg), Ofloxacin(5µg), Cefazolin (30µg), Vancomycin (30µg), Clindamycin(2µg), Azithromycin, Oxacillin (1µg) and Nitrofurantoin (30µg). Antimicrobials tested for streptococcus bacteria were Amoxycillin (30µg), Ciprofloxacin (5

ISSN (O): 2687-5365; ISSN (P): 2753-6556

µg), Gentamicin (10µg), Ofloxacin (5µg), Cefazolin (30 µg), Vancomycin (30 µg), Azithromycin, Nitrofurantoin (30µg), High Content Streptomycin (300 µg) and High Content Gentamycin (120 µg)

Statistical Analysis

All the data was tabulated in a Microsoft excel spreadsheet descriptive statistical analysis was done using SPSS Software version 16.

RESULTS

A total number of 102 (n=102) cases of complicated and recurrent urinary tract infections, who were either admitted to medicine, endocrinology or nephrology wards or attending medicine OPD, endocrinology OPD or nephrology OPD in the department of medicine, JNMCH, Aligarh, who met the inclusion criteria were included in the study.

[Table 1] shows the age distribution of all patients. The majority of patients were from the age group 41-50 years (27.45%) followed by the group 51-60 years (21.56%) and age group 31-40 years (18.62%). Out of 102 patients, males were 52 (50.98%), while the females were 50 (49.02%).

Out of 102 isolates, the most common organism was E.coli (72.54%) followed by Klebsiella species (14.70%), Staphylococcus aureus(4.90%), Enterococcus (4.90%) and Pseudomonas (2.94%) [Table 2]. [Table 3] shows the percentage of Antibiotic Sensitivity Pattern of amikacin and Gentamicin to uropathogens. It was seen that E. coli, Klebsiella species and staphylococcus aureus were highly sensitive to Amikacin 86.48%, 80% and 100% respectively but pseudomonas was mostly resistant to amikacin. [Table 3] also shows that E. coli, Klebsiella species and staphylococcus aureus were moderately sensitive to Gentamicin 50%, 53.33% and 100% respectively but Pseudomonas was mostly resistant to Gentamicin. [Table 4] shows the percentage of Antibiotic Sensitivity Pattern of Nitrofurantoin to uropathogens. It was seen that E. coli, staphylococcus aureus and Enterococcus were highly sensitive to Nitrofurantoin 72.97%, 100% and 60% respectively but Klebsiella species was mostly resistant to Nitrofurantoin. [Table 5] shows E. coli and Klebsiella species were mostly resistant to Ceftriaxone, Cefoparazone and Cefixime.

Table 1: Age distribution in the study group

Age	Number of Cases	% Total Case
15-20	8	7.84
21-30	10	9.80
31-40	19	18.62
41-50	28	27.45
51-60	22	21.56
61-70	11	10.78
71-80	24	3.92

Table 2: Organisms isolated from patients

Types of Organism	No. of Cases (N=102)	Percentage of Total cases (%)
E.coli	74	72.54
Klebsiella species	15	14.70
Staphylococcus aureus	5	4.90
Enterococcus	5	4.90
Pseudomonas	3	2.94

Table 3: Sensitivity and resistance pattern of various organisms to Amikacin and Gentamicin

Organisms	Amikacin		Gentamicin	
	Sensitive	Resistant	Sensitive	Resistant
E.Coli (74)	64 (86.48%)	10 (13.51)	37(50%)	37(50%)
Klebsiella (15)	12 (80%)	3(20%)	8(53.33%)	7(46.66%)
Staph. aureus (5)	5(100%)	0(0%)	5(100%)	0(0%)
Pseudomonas (3)	1(33.33%)	2(66.66%)	1(33.33%)	2(66.66%)

Table 4: Sensitivity and resistance pattern of various organisms to Nitrofurantoin

Organisms	Sensitive	Resistant
E.Coli (74)	54(72.97%)	20(27.02%)
Klebsiella (15)	5(33.33%)	10(66.66)
Staph. aureus (5)	5(100%)	0
Enterococcus(5)	3(60%)	2(40%)

Table 5: Sensitivity and resistance pattern of various organisms to Ceftriaxone, Cefoparazone and Cefixime

Organisms	Ceftriaxone		Cefoparazone		Cefixime	
	Sensitive	Resistant	Sensitive	Resistant	Sensitive	Resistant
E.Coli (74)	11(14.86%)	63(86.3%)	10(14.86%)	64(86.46%)	13(17.56%)	61(82.43%)

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Klebsiella (15)	2(13.33%)	13(86.66%)	2(13.33%)	13(86.66%)	2(13.33%)	13(86.66%)

Table 6: Sensitivity and resistance pattern of various organisms to Levofloxacin and Ofloxacin

Organisms	Levofloxacin		Ofloxacin	
	Sensitive	Resistant	Sensitive	Resistant
E.Coli (74)	10(13.51%)	64(86.46%)	6(8.10%)	68(91.84%)
Klebsiella (15)	6(40%)	9(60%)	5(33.33%)	10(66.66%)
Staph. aureus (5)	2(40%)	3(60%)	1(20%)	4(80%)

Susceptibility of E. coli, Klebsiella species and staphylococcus aureus to Levofloxacin was 13.51%, 40% and 40% respectively [Table 6]. Susceptibility of E. coli, Klebsiella species and staphylococcus aureus to Ofloxacin was 10%, 33.33% and 20% respectively [Table 6]. So [Table 6] shows that E. coli, Klebsiella species and staphylococcus aureus were highly resistant to Levofloxacin and Ofloxacin.

DISCUSSION

Urinary tract infections (UTIs) are among the most common bacterial infections both in the community and hospital setting. UTI is the most common hospital acquired infection, accounting for as many as 35 % of nosocomial infections. UTI is the second most common infectious presentation in the community practice.[13]

A complicated urinary tract infection is a urinary infection occurring in a patient with a structural or functional abnormality of the genitourinary tract. Gram negative bacteria are the most common organisms involved in the etiology of complicated UTI. Among the gram negative organisms, E.coli is the single most common organism involved in the complicated UTI. In the past few years the number of complicated UTIs due to resistant Gram-negative bacteria has increased.

Out of the 102 patients included in the study group the maximum age was 80 years and minimum age was 15 years with mean age of 45.83±14.54 yrs and Maximum number of cases were observed in 41-50yr age group. The majority of patients were males i.e 52 out of 102 (50.98 %) with females comprising 49.02 %. This observation is in concordance with Mahesh and associates' (Mahesh E et al., 2010) findings in their study on complicated urinary tract infection in a tertiary care center in south India.[14] They observed in their study that the majority of the patients come under the age 50-70 years. The mean age in their study was 55.47±21.51 years. And in that study, the majority of the patients were males i.e 62.45%. Most clinicians would suggest that male gender alone is criteria for being a complicated UTI.[15] Thus, even though the uncomplicated UTI more common in female and rare in male so any male urinary infection is usually considered complicated. Another reason for complicated UTI being more common in male is that the structural and genitourinary abnormalities are more common in male as compared to female. This substantiates the finding in our study, 50.98 % of males.

In our study, the major organism isolated was E.coli (72.54%) followed by Klebsiella species (14.70%). The results from worldwide review are similar to the present study.[16,17,18,19,20] HandeArslan et al, 2005, reported that E. coli was the causative agent in 78% of complicated UTI. E.coli (65.7%) topped the list of organisms causing complicated UTI. Peterson EA et al., 1976, in their study done in USA have reported E.coli as the most common organism causing complicated UTI. Chen SS et al., 1998, in their study done in Taiwan have reported E.coli, Proteus mirabilis and Pseudomonas aeruginosa as the most common uropathogens. A review by Lindsay Nicolle, 2001 on complicated UTI reported E.coli as the most common uropathogen with a worldwide prevalence rate of 21-54%.

CONCLUSION

The rising trend of antibiotic resistance amongst uropathogens, suggest the geographical location-based information about uropathogens and its antimicrobial susceptibility patterns. This study provides important data to monitor and compare with other studies, the trend of antimicrobial susceptibility of uropathogens and helps us towards deciding empirical treatment of UTIs at this tertiary care hospital. Furthermore studies should be done on a larger scale periodically in different regions, so that empirical antibiotic therapy guidelines can be framed according to local antimicrobial susceptibility trends improving patient outcomes and minimizing anitbiotic misuse.

REFERENCES

1. Stamm WE, Norrby SR. Urinary tract infections: disease panorama and challenges. J Infect Dis. 2001;183: S1-S4.
2. Hansson S, Martinell J, Stokland E, Jodal U. The natural history of bacteriuria in childhood. Infect Dis Clin North Am. 1997;11(3):499-512. doi: 10.1016/s0891-5520(05)70370-6.
3. Nebigil I, Tümer N. Asymptomatic urinary tract infection in childhood. Eur J Pediatr. 1992;151(4):308-9. doi: 10.1007/BF02072236.
4. Mittendorf R, Lain KY, Williams MA, Walker CK. Preeclampsia: A nested, case-control study of risk factors and their interactions. J Reprod Med. 1996;41:491-494.
5. Rizvi M, Khan F, Shukla I, Malik A, Shaheen. Rising prevalence of antimicrobial resistance in urinary tract infections during pregnancy: Necessity for exploring newer treatment options. J Lab Physicians. 2011;3:98-103.
6. Johansen TE, Botto H, Cek M, Grabe M, Tenke P, Wagenlehner FM et al. Critical review of current definitions of urinary tract infections and proposal of an EAU/ESIU classification system. Int J Antimicrob Agents. 2011;38:64–70.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

7. LE Nicolle, AMMI Canada Guidelines Committee. Complicated urinary tract infection in adults. Can J Infect Dis Med Microbiol. 2005;16:349-360.
8. Akram M, Shahid M, Khan AU. Etiology and antibiotic resistance patterns of community-acquired urinary tract infections in J N M C Hospital Aligarh, India. Ann Clin Microbiol Antimicrob. 2007;6:4. doi: 10.1186/1476-0711-6-4.
9. Otajevwo FD. Urinary tract infection among symptomatic outpatients visiting a tertiary hospital based in midwestern Nigeria. Glob J Health Sci. 2013;5(2):187-99. doi: 10.5539/gjhs.v5n2p187.
10. Jellheden B, Norrby RS, Sandberg T. Symptomatic urinary tract infection in women in primary health care. Bacteriological, clinical and diagnostic aspects in relation to host response to infection. Scand J Prim Health Care. 1996;14(2):122-8. doi: 10.3109/02813439608997082.
11. KASS EH. Bacteriuria and the diagnosis of infections of the urinary tract; with observations on the use of methionine as a urinary antiseptic. AMA Arch Intern Med. 1957;100(5):709-14. doi: 10.1001/archinte.1957.00260110025004.
12. Duffy HR, Godfrey RW, Williams DL, Ashton NN. A Porcine Model for the Development and Testing of Preoperative Skin Preparations. Microorganisms. 2022;10(5):837. doi: 10.3390/microorganisms10050837.
13. Kolawole AS, Kolawole OM, Kandaki-Olukemi YT, Babatunde SK, Durowade KA, Kolawole CF. Prevalence of urinary tract infections (UTI) among patients attending DalhatuAraf Specialist Hospital, Lafia, Nasarawa state, Nigeria. Int J Med Med Sci. 2009;1:163-167.
14. Mahesh E, Ramesh D, Indumathi VA, Punith K, Kirthi R, Anupama HA. Complicated urinary tract infection in a tertiary care center in South India. Al Ameen J Med Sci. 2010;3:120-127.
15. Foxman B: Epidemiology of urinary tract infections—incidence, morbidity, and economic costs. Am J Med. 2002;113:55-58.
16. Arslan H, Azap OK, Ergönül O, Timurkaynak F; Urinary Tract Infection Study Group. Risk factors for ciprofloxacin resistance among Escherichia coli strains isolated from community-acquired urinary tract infections in Turkey. J Antimicrob Chemother. 2005;56(5):914-8. doi: 10.1093/jac/dki344.
17. Petersen EA, Friedman BA, Crowder ED, Rifkind D. Coccidoidouria: clinical significance. Ann Intern Med. 1976;85(1):34-8. doi: 10.7326/0003-4819-85-1-34.
18. Chen SS, Chen KK, Lin AT, Chang YH, Wu HH, Hsu TH, et al. Complicated urinary tract infection: analysis of 179 patients. Zhonghua Yi Xue Za Zhi (Taipei). 1998;61(11):651-6.
19. Jump RLP, Crnich CJ, Mody L, Bradley SF, Nicolle LE, Yoshikawa TT. Infectious Diseases in Older Adults of Long-Term Care Facilities: Update on Approach to Diagnosis and Management. J Am Geriatr Soc. 2018;66(4):789-803. doi: 10.1111/jgs.15248.
20. Prakash D, Saxena RS. Distribution and antimicrobial susceptibility pattern of bacterial pathogens causing urinary tract infection in urban community of meerut city, India. ISRN Microbiol. 2013;2013:749629. doi: 10.1155/2013/749629.

ISSN (O): 2687-5365; ISSN (P): 2753-6556