Common uropathogens and their antimicrobial susceptibility patterns at a tertiary care hospital in Pakistan

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Abstract

Introduction: Urinary tract infections (UTIs) are one of the most frequent infections encountered by doctors. It can be a significant source of morbidity for some patients. Microbes are growing resistant to commonly prescribed antimicrobials and UTIs are becoming more difficult to treat day by day. The study aimed to investigate the common uropathogens encountered in our geographical region and to study their antibacterial susceptibility patterns.

Material and Methods: It was a retrospective descriptive study carried out in the Armed Forces Institute of Urology, in collaboration with the Armed Forces Institute of Pathology, Rawalpindi, Pakistan, during the year 2019. Positive reports for urine culture and sensitivity performed during the last two years were studied to document various isolates and their antimicrobial sensitivity.

Results: A total of 3191 positive urine cultures in the last two years (2017-2019) were studied. Escherichia coli (66%), followed by Klebsiella Pneumonia (12%) were the most frequently encountered organisms. Overall resistance to Ciprofloxacin was 66%, Cotrimoxazole was 62%, Gentamycin was 40%, Fosfomycin (9.5%) followed by Meropenem (28%) and Nitrofurantoin (35%) were the most sensitive antibiotics.

Conclusion: Gram-negative bacilli are the predominant organisms responsible for urinary tract infections. These uropathogens show significant resistance to routinely used antibiotics. Fosfomycin and Nitrofurantoin are suitable oral anti-bacterials for patients with UTI, whereas Meropenem is suitable if an injectable therapy is required. Our study may act as a guide for the choice of empiric antibiotics based on local resistant patterns.

Keywords: Uropathogens; antibiotics; urine; culture; sensitivity.

Introduction

Urinary tract infection (UTI) is one of the most commonly found diseases in medical practice today, with a significant proportion of the patient population found in almost all age groups.[1] It is also emerging as one of the most common nosocomial infection, sharing a burden of up to 40% of all nosocomial infections.[2] It is also responsible for 1.2% and 0.6% of all office visits by females and males respectively.[3] UTI is an inflammatory process involving the urothelium due to bacterial invasion and usually comprises bacteriuria and pyuria.[4] The criteria to label urinary tract infection is the existence of >105 bacteria/ml of urine in a midstream 'clean catch' urine specimen or from urine directly collected from a catheter.[5] Bacteria may enter the urinary tract through the ascending, hematogenous, or lymphatic routes. The major reservoir for bacterial entry into the urinary tract is the bowel via passage through the urethra into the bladder.[6,7] On the other hand, the hematogenous pathway is an uncommon route of kidney infection in normal individuals. Some unusual cases like severe bowel infection or retroperitoneal abscesses may cause the direct spread of bacteria from adjacent organs via the lymphatic route.[8]

The best strategy to treat UTIs is by using empirical antibiotic therapy, the selection of antimicrobial agents should be based on the most likely pathogen involved, and its expected resistance pattern in a specific area.[9] Worldwide, many common bacteria including E.coli are becoming more prone to antimicrobial resistance.[10] Such resistance has also affected the sensitivity of uropathogens to antimicrobials owing to their excessive use. The knowledge and awareness of doctors regarding the prevalence and antimicrobial resistance of uropathogens is the need of the hour.[11] As common organisms are becoming more and more resistant to the routinely prescribed antibiotics, it is very important to address the prescribing habits of doctors of this era. It is becoming harder to treat infections with every passing day, and this may eventually lead to therapeutic dead ends.[12]

The purpose of this study is to register commonly encountered uropathogens along with their antimicrobial sensitivities. This information will not only help doctors understand the sensitivity pattern of common antimicrobials prescribed to treat urinary tract infections but also help improve the empirical treatment of patients.

Materials and Methods

All 3191, midstream 'clean catch' or catheter specimens with positive cultures during the study period were included in the study. The specimens were collected in sterilized wide mouth, leak-proof plastic containers of 20 ml capacity. Specimens were processed in the Microbiology Lab as soon as possible. The urine samples were inoculated on culture plates by a semi-quantitative method of urine analysis whereby, a fixed quantity of 0.2 microliters of urine from each specimen was applied on culture media. The culture media used were CLED agar (Cysteine, Lactose, Electrolyte Deficient) and Blood agar. The culture plates were incubated aerobically at 37°C for a minimum of 18 hours and a maximum of 48 hours. Culture plates were examined for growth after 18 hours of incubation. Positive cultures have proceeded for identification and negative cultures were re incubated to be examined again after 48 hours before reporting as No Growth. Those Cultures were taken positive which yielded growth equal to or greater than 20 CFU (Colony forming units) of a single isolate whereas, cultures yielding Mixed growth were disregarded. The isolates were identified using biochemical methods and API (analytical profile index) strips. Antibiotic Sensitivity was done by Disc Diffusion Method using Mueller Hinton agar supplemented with 5% sheep blood. Zone diameters were interpreted after 18 hours of incubation at 37*C according to CLSI (Clinical Laboratory Standard Institute) guidelines. Where necessary identification and sensitivity were confirmed by using an automated system VITEK 2 Version 8.101.

Results

Positive urine culture and sensitivity reports of 3191 urine samples submitted to the laboratory of Armed Forces Institute of Pathology, Rawalpindi in two years (July 2017-June 2019) were studied retrospectively. Most common isolate was E.coli (66.3%) followed by Klebsiella (11.5%). Isolates are listed in Table 1. Currently, seven antibiotics are tested in routine use to determine the sensitivity of common uropathogens. Fosfomycin followed by Meropenem and Nitrofurantoin were the most effective antibiotics (Table 2).

Table 1: Microorganisms isolated from patients with UTI's

Organism	Positive Cultures	Percentage
Escherichia coli	2116	66
Klebsiella pneumonia	369	12
Enterococcus species	285	9
Pseudomonas aeruginosa	197	6
Enterobacter species	113	4
Proteus species	111	3

Table 2: Antibiotic resistance of microorganisms isolated (%)

Antibiotic	Escherichia coli	Klebsiella pneumoniae	Enterococcus	Pseudomonas aeruginosa	Enterobacter	Proteus
Ciprofloxacin	76	64	79	75	53	51
Nitrofurantoin	9	57	25	NT	50	NT
Fosfomycin	3	16	7	NT	12	NT
Ceftriaxone	69	63	NT	IR	57	53
Meropenem	12	33	NT	60	28	9
Gentamycin	34	36	NT	53	32	46
Cotrimoxazole	67	57	NT	IR	47	78

NT – Not tested   IR – Intrinsically resistant

Discussion

Our study aimed to determine the most commonly encountered uropathogens in clinical practice along with their antibiotic susceptibilities. To ensure early and effective treatment of the infection, recent updates on antibiotic resistance patterns is important for timely modification of drug of choice for empirical therapy.[13] Even though the uropathogens remain the same over time but they have developed increasing levels of resistance to easily available and less expensive antibiotics.

Gram-negative uropathogens have shown higher isolation rates (>90%) than gram-positive organisms (<10%) in many studies. E. coli is still considered the main uropathogen that causes UTIs while the prevalence of K. pneumonia and Enterococcus spp. has increased over the years.[14,15,16] Our data also revealed that gram-negative organisms like E. coli are still the most frequently isolated uropathogen (66%) followed by Klebsiella pneumoniae (12%). The high incidence of E. coli is mainly due to the fact that it is a part of the normal flora of the bowel and infection is mostly via fecal route accompanied by poor hygiene. A study conducted by Chiu et al[16] in Taiwan in 2016 showed Escherichia coli to be the most commonly isolated organism (54.5%), followed by Klebsiella pneumonia (13.1%), a finding concurrent with our study. The study showed the highest rate of antibiotic susceptibility with ceftriaxone (71.4%), cefepime (94.5%), amikacin (97.5%), and gentamycin (76.1%). On the other hand, our study showed the highest resistance rates to Ciprofloxacin (66%), Cotrimoxazole (62%), Ceftriaxone (61%), and Gentamycin (40%). The development of antibiotic resistance in a specific geographical area is highly dependent on antibiotic prescription habits. Another study conducted by Naz et al[17] in 2018 in Lahore, Pakistan showed the highest isolation rates of Escherichia coli (60.5%) and Klebsiella pneumonia (26.3%). This study was conducted in the paediatric population but still showed similar findings to our study which was conducted in the adult population.

Another study carried out by Setu et al[18] in Dhaka, Bangladesh in 2015 showed the highest isolation rates of Escherichia coli and Klebsiella pneumonia in gram-negative species and S. aureus in gram-positive species. The highest levels of antibiotic resistance were found to Amoxicillin (77%), Nalidixic acid (63%), and Ceftriaxone (56%). Our study also revealed similar findings for antibiotic resistance to ceftriaxone. In another study carried out in the southwest of Iran in 2012 by Valavi et al[19], similar findings were revealed as our study with Escherichia coli (84%) and Klebsiella pneumonia (10.1%) the most frequently isolated pathogens. Nitrofurantoin emerged as the most effective antibiotic in this study; a finding concurrent to our study. Nitrofurantoin has demonstrated

significant efficacy in many studies in the past. It has emerged as a good therapeutic option for uncomplicated cystitis in the United States and in some southern European countries, where fluoroquinolones and co-trimoxazole isolates from urine have shown high resistance rates.[20]

Another study carried out by Obiofu et al[21] in Nigeria in 2018, differed from our study as Staphylococcus aureus (47.2%) was the predominant isolate, followed by E.coli (20.2%) and Klebsiella (15.7%). The study showed the highest susceptibility rate of gram-negative organisms to Nitrofurantoin. Variation in isolated organisms might be due to the difference in the geographical distribution of the pathogens. Our results were further supported by a study carried out by Mitiku et al[22] in Ethiopia in 2017 where E.coli emerged as the predominant gram-negative uropathogen (55%), followed by Klebsiella spp (16.3%) and Proteus species (12.2%). This study showed Nitrofurantoin (100%) and Ciprofloxacin (92%) as the most effective antibiotics for E.coli. Nitrofurantoin also proved to be effective for E.coli in our study (91%). On the contrary, Ciprofloxacin did not show considerable efficacy (24%) in our study. In another study conducted by Lakshminarayana et al[23] in India in 2015, the most common isolate was E.coli (66.5%) followed by Klebsiella Pneumoniae (14.3%). Similar to our study, Meropenem and Nitrofurantoin were amongst the most sensitive antibiotics in this study.

Other antibiotics did not show significant sensitivity rates thus limiting their use as empirical therapy. It was interesting to note that the once frequently prescribed Quinolones and Ceftriaxone have now developed a significant level of resistance. Increasing levels of resistance can be due to poor sterilization techniques and disinfection practices and not following appropriate WHO guidelines for implementation of the antibiotic remedy. The similarities and differences in the distribution of uropathogens may exist due to difference in environmental conditions and host factors, healthcare awareness, socioeconomic standards, and hygiene practices in each country.[24] Recently, fosfomycin has also proven to be beneficial for the treatment of infections with multidrug-resistant uropathogens; a finding also supported by our study.[25]

Our study has certain limitations. Firstly, it was a single centre study, further multi-centric studies are required to assess the resistance patterns of various antibiotics in our setup. Secondly, we did not perform phenotypic testing nor genotypic testing of bacterial enzymes as a cause of antibiotic resistance. Thirdly, we did not include the distribution of patients based on the source of infection like nosocomial, community-acquired, or catheter-associated to further categorize the uropathogens involved.

Conclusion

Urinary tract infections are considered to be one of the most common infections encountered by humans. The most frequent uropathogens are gram-negative bacilli which demonstrate significant resistance to routinely prescribed antibiotics. The choice of antimicrobial therapy is directed by the knowledge of antibiotic sensitivity till the arrival of culture and sensitivity reports. Fosfomycin, Nitrofurantoin, and Meropenem are suitable options for empirical therapy as they have the least resistance.

Management of urinary tract infections may improve by continued surveillance of antibiotic resistance and antibiotic prescription patterns of doctors and evolving antibiotic guidelines for urinary tract infections to slow down the fast-developing resistant patterns in our geographical area.

References

1. A Singhal, R Sharma, M Jain, and L Vyas. Hospital and Community Isolates of Uropathogens and their Antibiotic Sensitivity Pattern from a Tertiary Care Hospital in North West India. Ann Med Health Sci Res. 2014 Jan-Feb; 4(1): 51–56. DOI: 10.4103/2141-9248.126611

2. Szasz M, Lehotkai N, Kristóf K, Szabó D, Nagy K. Prevalence and antimicrobial resistance of uropathogens in different inpatient wards. Acta Microbiol Immunol Hung. 2009;56:375–87. DOI: 10.1556/amicr.56.2009.4.7

3. Hansel DE, McKenney JK, Stephenson AJ, Chang SS. The Urinary Tract: A Comprehensive Guide to Patient Diagnosis and Management, New York: Springer; 2012. 64 p DOI: 10.1007/978-1-4614-5320-8

4. Mittal S, Kumar A, Govil N, Urinary tract infections: General considerations. SM Journals, Dec 2015. DOI: 10.5005/jp/books/18034_9

5. Stark RP, Maki DG. Bacteriuria in a catheterized patient. N Eng J Med 1984; 311:560–4. DOI: 10.1056/NEJM198408303110903

6. Hickling DR, SUN TT and WU XR. Anatomy and Physiology of the Urinary Tract: Relation to Host Defense and Microbial Infection. Microbiol Spectr. 2015 Aug; 3(4): 10.1128/microbiolspec.UTI-0016-2012. DOI: 10.1128/9781555817404.ch1

7. Kucheria R, Dasgupta P, Sacks SH, et al Urinary tract infections: new insights into a common problem Postgraduate Medical Journal 2005;81:83-86. DOI: 10.1136/pgmj.2004.023036

8. Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA. Infections of the urinary tract. In: Wein AJ, editor. Campbell-Walsh Urology. 10th edition. Philadelphia: Elsevier; 2012. 261 p DOI: 10.1111/j.1749-771X.2007.00017.x

9.   Alabi AS, Frielinghaus L, Kaba H, Koster K, Huson MA, Kahl BC, et al. Retrospective analysis of antimicrobial resistance and bacterial spectrum of infectionin Gabon, Central Africa. BMC Infect Dis. 2013;13:455. DOI:10.1186/1471-2334-13-455

10. Tahir Hameed, Abdullah Al Nafeesah, Syed Chishti, Mohammed Al Shaalan, and Khaled Al Fakeeh. Community-acquired urinary tract infections in children: Resistance patterns of uropathogens in a tertiary care center in Saudi Arabia. Int J Pediatr Adolesc Med. 2019 Jun; 6(2): 51–54. DOI: 10.1016/j.ijpam.2019.02.010

11. Khan S, Ahmed A. Uropathogens and their susceptibility patterns; A retrospective analysis. J Pak Med Assoc 2005;51(2):98–100.

12. Moroh JLA, Fleury Y, Tia H, et al. Diversity and antibiotic resistance of uropathogenic bacteria from Abidjan. Afr J Urol. 2014;20:18–24. DOI: 10.1016/j.afju.2013.11.005

13. Niranjan V, Malini A. Antimicrobial resistance pattern in Escherichia coli causing urinary tract infection among inpatients. Indian J Med Res. 2014;139:945–8. DOI: 2014/139/6/945/138080

14. Farrell DJ, Morrissey I, De Rubies D, Robbins M, Felmingham D. A UK Multicentre study of the antimicrobial susceptibility of bacterial pathogens causing urinary tract infection. J Infect 2003;46(2):94–100. DOI: 10.1053/jinf.2002.1091

15. Ahmed NH, Raghuraman K, Baruah FK, Grover RK. Antibiotic Resistance Pattern of Uropathogens: An Experience from North Indian Cancer Patient. J Glob Infect Dis. 2015;7(3):113–115. DOI: 10.4103/0974-777x.161742

16. Chiu CC, Lin TC, Wu RX, Yang YS, Hsiao PJ, Lee Y, Lin JC, Chang FY. Etiologies of community-onset urinary tract infections requiring hospitalization and antimicrobial susceptibilities of causative microorganisms. Journal of Microbiology, Immunology and Infection. 2017 Dec 1;50(6):879-85. DOI: 10.1016/j.jmii.2016.08.008

17. Naz Z, Batool A, Rauf A. High resistance in uropathogens isolated from children at Pakistani hospital. Journal of University Medical & Dental College. 2018 Apr 3;9(1):26-32.

18. Setu SK, Sattar AN, Saleh AA, Roy CK, Ahmed M, Muhammadullah S, Kabir MH. Study of Bacterial pathogens in Urinary Tract Infection and their antibiotic resistance profile in a tertiary care hospital of Bangladesh. Bangladesh Journal of Medical Microbiology. 2016;10(1):22-6. DOI: 10.3329/bjmm.v10i1.31449

19. Valavi E, Nikfar R, Ahmadzadeh A, Kompani F, Najafi R, Hoseini R. The last three years antibiotic susceptibility patterns of uropathogens in southwest of Iran. DOI: 10.5812/jjm.4958.

20. Duława J. Urinary tract infection-2003. Rocz Akad Med Bialymst. 2004;49:182-4.

21. Obiofu EN, Ige OH, Iroro O. Antimicrobial susceptibility pattern of urinary isolates from outpatients suspected for urinary tract infection. GSC Biological and Pharmaceutical Sciences. 2018;5(3):001-11.DOI: 10.30574/gscbps.2018.5.3.0124

22. Mitiku SY. Bacterial uropathogens and their antibiotic susceptibility pattern at Dessie regional health laboratory. J Microbiol Biotechnol Res. 2017;3:1-9. DOI: 10.3390/molecules22081255

23. Lakshminarayana SA, Chavan SK, Prakash R, Sangeetha S. Bacterial pathogens in urinary tract infection and antibiotic susceptibility pattern from a Teaching Hospital, Bengaluru, India. Int J Curr Microbiol Appl Sci. 2015;4(11):731-6.

24. Shaifali I, Gupta U, Mahmood SE, Ahmed J. Antibiotic susceptibility patterns of urinary pathogens in female outpatients. North American journal of medical sciences. 2012 Apr;4(4):163. DOI: 10.4103/1947-2714.94940

25. Michalopoulos AS, Livaditis IG, Gougoutas V. The revival of fosfomycin. International journal of infectious diseases. 2011 Nov 1;15(11):e732-9. DOI: 10.1016/j.ijid.2011.07.007