ORIGINAL ARTICLE

Antibiotic Susceptibility Pattern of Uropathogens in a Tertiary Care Hospital

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ABSTRACT

Aim: To investigate the frequency of bacterial isolates in patients with UTI and their sensitivity to commonly used antibiotics in Sialkot, Pakistan.
Methods: A total of 695 samples were collected from suspected patients of UTI, referred to Khawaja M Safdar Medical College, and Abdul Sattar Lab, Sialkot during a period of 1 year from July 2017 to June 2018. The antimicrobial sensitivity was checked via Kirby-Bauer disc diffusion method for the cultured isolates.
Results: Out of 695 patients (232 males, 463 females), 321 (46.2%) yielded bacterial growth, while 15 (2.1%) had candida in urine. E. coli was most frequent isolate (79.1%), followed by Enterococcus (12.7%), and Enterobacter (3.1%). Most useful antibiotics were meropenem (96.6%), imipenem (96.2%), fosfomycin (93.8%), Piperacillin/Tazobactam (88.8%), and nitrofurantoin (87.8%).The most effective drugs against E. coli were Carbapenems (97.2%), fosfomycin (93.7%), Amikacin (92.9%), Piperacillin/Tazobactam (88.6%) and Nitrofurantoin (88.2%). E. coli had very high resistance against Quinolones (almost 70%) and Cephalosporin (almost 80%). Co-amoxiclauv was effective in 48% of bacteria. Fosfomycin and nitrofurantoin were the only oral options among most effective antibiotics. 3.4% (11/321) bacteria were resistant to Carbapenem.
Conclusion: Our results highlight alarming resistance to commonly used antibiotics, and highlight the sensitivity of broad spectrum drugs, like carbapenems, piperacillin/tazobactam, fosfomycin, and nitrofurantoin. Our results call for revision of current practices of treatment of urinary tract infection.
Key words: Antibiogram, Culture and sensitivity, Urinary tract infection

INTRODUCTION

Urinary tract infection is a common nosocomial infection as well as one of the most common community acquired diseases with a huge financial burden on health care systems.[1] A variety of organisms can be responsible for causing urinary tract infections (UTI), the vast majority of uncomplicated infections occur due to Escherichia coli, a common member of Enterobacteriaceae family.[2] Injudicious use of antibiotics has greatly enhanced the chances and risk of wide spread antibiotic resistance. There is alarmingly high prevalence of antibiotic resistance in bacteria causing urinary tract infection, both globally[3] as well as locally.[4] Rising resistance to beta-lactamase inhibitor combinations and carbapenems is a major concern.[5] Frequency of organisms causing UTI and their antibiotic susceptibility varies regionally, necessitating frequent testing of antibiotic sensitivity and resistance patterns. We planned this study to check antibiotic sensitivity patterns in uropathogens in patients referred to public sector hospital of Sialkot.

MATERIALS AND METHODS

This cross sectional descriptive study was carried out at microbiology department Khawaja Muhammad Safdar Medical College Sialkot from July 2017 to June 2018. A total of 695 patients with clinically suspected UTI, referred from private and public hospitals and clinics at Sialkot, Pakistan, were recruited in study. Following the standard procedures, patients were asked to collect midstream morning urine specimens using sterile wide mouth plastic containers. Using calibrated wire loops, 0.01 ml urine sample was inoculated on CLED agar. The plates were incubatedaerobically at 37°C for 24 hours. A semi-quantitative method was used to determine the colony counts to confirm the diagnosis of UTI and significant bacteriuria was defined as bacterial culture of $>10^5$colony forming units/ml of urine for a single bacterium. Colonial appearance and morphological characters of isolated bacteria were observed. Isolated colonies were subjected to preliminary tests like Gram staining, motility by hanging drop, catalase test and oxidase test. Biochemical reactions for identification of the isolated organism were used following preliminary tests. Isolated organisms were subjected to antibiotic susceptibility testing using the modified Kirby-Bauer disk diffusion method. Following drugs were used for antibiogram testing following the latest CLSI (Clinical and Laboratory Standards Institute) guidelines: Ampicillin (10µg), Co-amoxiclauv, 20/10µg), gentamycin (10µg), amikacin (30µg), ciprofloxacin (5µg), ofloxacin(5µg), levofloxacin (5µg), moxifloxacin (5µg), cefoperazone (30µg), ceftazidime (30µg), cefipime (30µg), tazobactam (10µg), meropenem (10µg), imipenem (10 µg), norfloxacin (10µg), nitrofurantoin (300µg), pipemidic acid (20µg), sulfamethoxazole-trimethoprim (25µg), aztreonam (30µg), cefotaxime (30µg), fosfomycin (50µg), linezolid (30µg), vancomycin (30µg). Data was entered in SPSS 20. Frequency of drug sensitivity for each bacterium was calculated.

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RESULTS

There were 232 males and 463 females. Mean age of patients was 32.67 years, ranging from one week of age to 95 years. Out of total 695 patients, 321 patients had positive urine cultures for bacterial isolates (46.2%), while 15 were positive for Candida species (2.1%). Females had statistically insignificant higher percentage of positive urine culture 47.9% (222/463) as compared to males 43.1% (100/232). Out of bacterial uropathogens isolates, 87% were gram negative. Escherichia coliwere the most commonly encountered bacteria (79.1%), followed by Enterococcus faecalis (12.7%) and Enterobacter cloacae (3.1%). Antibiogram of bacterial isolates tested for different antibiotics is given in table 1. The most effective drugs against Escherichia coli were carbapenems (97.2%), fosfomycin (93.7%), Amikacin (92.9%), Piperacillin/Tazobactam (88.6%) and Nitrofurantoin (88.2%). Escherichia coli had very high resistance against fluoroquinolones and Cephalosporin antibiotics. The most effective antibiotics against Enterococcus faecalis were linezolid (100%), fosfomycin (97.6%), Vancomycin (95.1%), Carbapenems (95.1%), nitrofurantoin (92.7%), and Piperacillin/Tazobactam (90.2%). Enterobacter cloacae were 100% sensitive to fosfomycin, but showed 20% resistance to carbapenems and Piperacillin/Tazobactam, and 30% resistance to amikacin. Overall, most useful antibiotics were meropenem, imipenem, fosfomycin, Piperacillin/Tazobactam, and nitrofurantoin. Amikacin was more effective (85%) than gentamycin (58%). fluoroquinolones had almost 30% overall efficacy, while that of cephalosporins, it was around 20% only. Co-amoxiclav was effective in 48% of bacteria. Fosfomycin and nitrofurantoin were the only oral options among most effective antibiotics. In our study, 7/254 of the patients were infected with carbapenem resistant Escherichia coli, 2/41 people carbapenem resistant Enterobacter cloacae and 2/41 people were with carbapenem resistant Enterococcus faecalis. None of these carbapenem resistant bacteria were found to be resistant to all antibiotics tested. Most of them were sensitive to fosfomycin. One carbapenem resistant Escherichia coli resistant to even fosfomycin showed sensitivity to co-amoxiclav and amikacin out of the available and tested antibiotics.

Table 1: Antibiogram of urinary pathogens

	Overall sensitivity	*Escherichia coli* (254)	*Enterococcus faecalis** (41)	*Pseudomonas aeruginosa* (4)	*Enterobacter cloacae* (10)	*Proteus mirabilis* (2)	*Klebsiella pneumoniae* (4)	*Providencia rettgeri* (4)	*Morganella morganii* (2)
Ampicillin	45 (14%)	23 (9.1%)	18 (43.9%)	NT	2 (20%)	0 (0%)	0 (0%)	1 (25%)	1(50%)
Augmentin	155 (48.3%)	126 (49.6%)	20 (48.8%)	NT	3 (30%)	1 (50%)	0 (0%)	4 (100%)	0 (0%)
Gentamycin	186 (57.9%)	152 (59.8%)	17 (41.5%)	2 (50%)	6 (60%)	2 (100%)	2 (50%)	3 (75%)	2(100%)
Amikacin	274 (85.3%)	236 (92.9%)	18 (43.9%)	3 (75%)	7 (70%)	2 (100%)	2 (50%)	4 (100%)	2 (100%)
Norfloxacin	79 (24.6%)	68 (26.8%)	6 (14.6%)	1 (25%)	2 (20%)	0 (0%)	1 (25%)	1 (25%)	0 (0%)
Ciprofloxacin	101 (31.5%)	81 (31.9%)	8 (19.5%)	1 (25%)	3 (30%)	1 (50%)	2 (50%)	3 (75%)	2 (100%)
Ofloxacin	99 (30.8%)	81 (31.9%)	7 (17.1%)	2 (50%)	3 (30%)	0 (0%)	2 (50%)	3 (75%)	1 (50%)
Levofloxacin	101 (31.5%)	85 (33.5%)	6 (14.6%)	1 (25%)	3 (30%)	0 (0%)	2 (50%)	3 (75%)	1 (50%)
Moxifloxacin	99 (30.8%)	83 (32.7%)	6 (14.6%)	2 (50%)	3 (30%)	0 (0%)	2 (50%)	3 (75%)	0 (0%)
Cefoperazone	61 (19%)	50 (19.7%)	2 (4.9%)	2 (50%)	3 (30%)	0 (0%)	1 (25%)	2 (50%)	1 (50%)
Ceftazidime	58 (18.1%)	50 (19.7%)	1 (2.4%)	1 (25%)	2 (20%)	0 (0%)	1 (25%)	2 (50%)	1 (50%)
Cefotaxime	53 (16.5%)	43 (16.9%)	2 (4.9%)	NT	3 (30%)	0 (0%)	1 (25%)	2 (50%)	1 (50%)
Cefipime	60 (18.7%)	51 (20.1%)	1 (2.4%)	2 (50%)	2 (20%)	0 (0%	1 (25%)	2 (50%)	1 (50%)
Pip/tazobactam	285 (88.8%)	225 (88.6%)	37 (90.2%)	4 (100%)	8 (80%)	2 (100%)	3 (75%)	4 (100%)	2 (100%)
Meropenem	312 (97.2%)	247 (97.2%)	39 (95.1%)	4 (100%)	8 (80%)	2 (100%)	4 (100%)	4 (100%)	2 (100%)
Imipenem	311 (96.8%)	247 (97.2%)	39 (95.1%)	4 (100%)	8 (80%)	2 (100%)	4 (100%)	4 (100%)	1(50%)
Nitrofurantoin	282 (87.8%)	224 (88.2%)	38 (92.7%)	NT	8 (80%)	NT	3 (75%)	4 (100%)	1 (50%)
Pipemidic acid	78 (24.3%)	63 (24.8%)	8 (19.5%)	1 (25%)	1 (10%)	0 (0%)	2 (50%)	1 (25%)	2 (100%)
TMP-SMX	43 (13.4%)	38 (15.0%)	1 (2.4%)	NT	1 (10%)	0 (0%)	1 (25%)	0 (0%)	2 (100%)
Fosfomycin	301 (93.8%)	238 (93.7%)	40 (97.6%)	NT	10 (100%)	2 (100%)	3 (75%)	4 (100%)	1(50%)

*Not tested (NT)

DISCUSSION

Our study is the one to represent antibiogram in UTI from a district level hospital. The study represents higher number of female subjects referred for urine culture and higher percentage of growth isolated in female subjects' urine is consistent with international literature[6] as well as one reported recently from Karachi.[7] Our study represents the high antimicrobial resistance of urinary pathogens in a city where use of higher generation antibiotics is not thought of, and UTI is still preferred to be treated with lower generation antibiotics. The results of our study may reflect that most UTIs may have been poorly treated with primitive antibiotics. A similar study from CMH Sialkot done during same duration[8] reported almost similar antibiogram results, showing highest frequency of Escherichia coli (66%), followed by Klebsiella pneumoniae (12%). Reported susceptibility of Escherichia coli was highest to Fosfomycin, Nitrofurantoin and carbapenems. Escherichia coli isolates in their study were13% resistant to carbapenem, while in our study, it was <2%. The reason for the difference could lie in population under study, because the other study also included hospitalized patients who might have taken multiple antibiotics before their urine was cultured for antibiotic susceptibility. Their study alarmingly shows almost 14% frequency of carbapenem resistant Klebsiella pneumoniae, while it was none in our study.

Escherichia coli were most prevalent urinary pathogen isolated in our study. There was almost complete resistance of Escherichia coli to ampicillin, and high resistance to flouroquinolones, cephalosporins and trimethoprim-sulfamethoxazole in our study. Most sensitive oral antibiotics for Escherichia coliwere fosfomycin and nitrofurantoin, and rests are injectables. A study from Abbottabad showed 60.2% urinary isolates of Escherichia coliwere sensitive to ciprofloxacin.[9] A study from Karachi also reported 43% sensitivity of uropathic gram negative

rods to ciprofloxacin.[10] Another study from Rawalpindi reported 21.5% sensitivity of Escherichia coli to ciprofloxacin.[11] Our study showed that only 32% of Escherichia coli were sensitive to ciprofloxacin. Sensitivity rates to other flouroquinolones (ofloxacin, levofloxacin, moxifloxacin) were also around 30%, depicting universally high resistance of uropathogens, especially Escherichia coli, to flouroquinolones. A study from King Edward Medical University Lahore in 2014 reported that 81% of Escherichia coliisolates from infected urine were multidrug resistant.[12] Carbapnem resistance in our study was 2.7%, which was comparable to other studies locally[13] as well as internationally[14]. In our study, treatment options in these bacteria were fosfomycin, aminoglycosides and co-amoxiclav. A review from Germany looking into carbapenem resistant gram negative bacteria showed that colistin, aminoglycosides, tigecycline, fosfomycin, ceftazidime/avibactam, and ceftolozan/tazobactam may be available treatment options[15]. We however, didn't check with colistin. Antibiogram of these highly resistant bacteria need further evaluation in our community.

Carbapenem resistance in Klebsiella pneumoniae is also an emerging global threat.[16] Fortunately, no Klebsiella pneumoniae in our study was carbapenem resistant. The difference in sensitivity patterns observed in different regions and this research is observed mainly because of the difference in patterns of usage of antibiotics in different regions. These findings suggest a heterogeneous regional clustering of individual and combined resistance phenotypes, probably via mutually shared resistance elements (plasmids, integrons, etc.), which might include different combinations of resistant clones of uropathogenic E. coli in varied areas of the country and even in different countries.

Infectious diseases society of Pakistan, in its document produced in 2012, recommended ciprofloxacin, and trimethoprim-sulfamethoxazole[15] as first line treatment of UTI in different patients. In view of present antibiogram, this recommendation needs extensive revision.

The research was carried out regionally at microbiology lab of a tertiary care hospital, the homogenous and consistent pattern in the collection of samples, testing for antibiogram and patient information provision eliminates a number of errors. But as the data was collected from referred patients only, actual drug sensitivity patterns of uropathogns may differ in community. We suggest studies in specific groups of community subjects, and in hospitals, to further elucidate the factors associated with drug resistance in uropathogens in our community. Moreover, molecular and genetic factors causing critical drug resistance needs urgent research.

CONCLUSION

Our study showed a high prevalence of resistance to commonly used antibiotics including significant resistance to higher generation antibiotics, in urinary pathogens isolated at public sector hospital in Sialkot, Pakistan. The results emphasize revision of treatment recommendations for UTI in our community and hospitals. Further research is required to elucidate important genetic and molecular mechanisms contributing to increased drug resistance.

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