ORIGINAL ARTICLE

MULTIDRUG RESISTANT UROPATHOGENS IN URINARY TRACT INFECTIONS AND THEIR ANTIBIOTIC SUSCEPTIBILITY PATTERNS

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ABSTRACT

Objectives: To determine the frequency of multidrug resistant uropathogens and their antibiotic susceptibility patterns.

Material and Methods: This study was conducted in Medical B unit at Khyber Teaching Hospital, Peshawar, Pakistan from January 2015 to December 2015. A total of 539 cultures were processed and conventional microbiological techniques were used to isolate MDR and non MDR uropathogens. Antibiotic sensitivities were determined through Kirby Bauer disc diffusion methods. Data was analyzed through SPSS version 20.

Results: Out of 539 samples cultured, 375 grew significant growth. Mean age was 41.9 ± 18.9SD. UTI was more common in females (68.3% n=256) than males 31.7% (n=119). E. Coli was the most common organism isolated (78.1%). Out of 375 isolates, 221 (58.9%) were multidrug resistant. MDR strains were highly sensitive to imipenem (95.1%), meropenem (95%), tazobactum/piperacillin (92.9%), cefoperazonesulbactum (91.1%) and amikacin (90.1%) and least sensitive to ampicillin (2.8%) and nalidixic acid (3.5%).

Conclusion: Multidrug resistance in UTI is becoming a major health problem. Assessment of the risk factors, surveillance of resistance patterns and policies for proper antimicrobial use are urgently warranted.

Key Words: Urinary tract, Infection, Multidrug, Resistance, Antibiotic Susceptibility.

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INTRODUCTION

Urinary tract infection is the most common bacterial infection in Pakistan[1] and its more common in females than males.[2] Presentation of UTI varies from mild cystitis to pyelonephritis, septicemia.[3] The predominance of Gram-negative sepsis,usually Enterobacteriaceae and, particularly Escherichia coli remain the principal pathogens causing UTI, accounting for 75-90% of all urinary tract infections in both inpatients and outpatients settings.[4]

Resistance pattern of bacteria varies with time and environment[5]. They acquire resistance through different mechanisms for example horizontal gene transmission, recombination of extrinsic DNA and by changing genetic material[6]. Resistance to commonly used antibiotics has increased dramatically in recent past years. Over and misuse of antibiotics is one factor amongst others that has led to antibiotic resistance. It is the pressure of antibiotics used for the treatment that affects the resistance pattern of micro organisms.[7]

The emergence of multidrug resistant strains of uropathogens is on rise which has made the use of previously commonly used antibiotics inappropriate. A number of risk factors have been attributed to the development of MDR strains which include individual factors like older age, female gender or history of UTI, predisposing factors like prior exposure to antimicrobials, urinary catheterization, residence in the nursing home or previous hospitalization and bacterial factors.[8]

Cautious use of antibiotics, proper culture and drug susceptibility testing and modification of empiric antibiotics according to culture and sensitivity is warranted in order to prevent the development of drug resistance particularly multidrug resistance in order to decrease complications associated with MDR UTI also to decrease economic burden on health system.

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MATERIAL AND METHODS

This descriptive cross sectional study was conducted in Medical B unit, Khyber Teaching Hospital, Peshawar, Pakistan which is a 1300 bedded hospital from January 2015 to December 2015. Patients from outpatient or inpatient departments of any age having urinary symptoms and numerous pus cells on urine microscopy were included in the study. Non probability consecutive sampling technique was used. Midstream urine was aseptically collected and immediately processed for microscopy and subsequent culture on blood and MacConkey agar plates. A total of 539 cultures were performed out of which 375 grew microorganisms. Plates showing significant growth as per Kass count[9] were further processed. Identification of the uropathogens was done through gram staining and biochemical tests. Patients having no growth, mixed growth or preceding history of antibiotics use in last 48 hours were excluded from the study. After identification of the microorganism antimicrobial sensitivity testing was done through Kirby Bauer Disc diffusion method on Mueller Hinton agar. Multidrug resistant uropathogen was defined as resistance to at least one agent from three or more than three different antibiotic classes. Susceptibility patterns of MDR strains were determined and their susceptibility patterns were interpreted as described by Clinical laboratory standards Institute Guidelines 2014.[10]

RESULTS

Out of 539 samples 375 grew significant growth. Admitted patients provided 237 samples while 138 came from outpatient department. Mean age was 41.9 ± 18.9SD. Distribution of MDR among different age groups is shown in Table 1. UTI was more common in females (68.3% n=256) than males 31.7% (n=119) with a male to female ratio of 1:2.2. Similarly it was more common in sexually active age groups (age ranging from 18 years to 60 years). E. Coli was the most common organism isolated (78.1%) followed by citrobacter (10.4%), morganella (5.3%), pseudomonas 3.5% while klebsiella, proteus, streptococcus faecalis and staphylococcus aureus collectively comprised 2.6%. Out of 375 isolates 221 (58.9%) were multidrug resistant. MDR frequency and microorganisms is shown in Table 2. MDR isolates were slightly more common among female population (59.4% vs 58%), more common in sexually active age groups 18-40 years (62.6%) and 41-60 years (61.7%)

Table 1: Distribution of MDR among different age groups

Age group	MDR		Total
	No	Yes	
18 and below	22	27	49
19-40	52	87	139
41-60	51	82	133
>60	29	25	54
Total	154	221	375

Table 2: Microorganisms and their MDR frequency

Microorganism	MDR		Total
	No	Yes	
E.coli	111	182	293
Morganella	14	6	20
Pseudomonas	3	10	13
Citrobacter	19	20	39
Klebsiella	4	1	5
Proteus	2	0	2
Streptococcus faecalis	0	1	1
Staph aureus	1	1	2
Total	154	221	375

Table 3: Antibiotic sensitivities of uropathogens

Antibiotic	Sensitivity (%) of	
	MDR	Non MDR
Imipenem	95.1	100
Tazobactum	92.9	99
Ceftriaxone	10.3	46.1
augmentin	27.2	90.9
Naladixic acid	3.5	32.2
Amikacin	90.1	99.3
Cefixime	11.8	46.9
Cefepime	42.1	83.8
Enoxacin	10.1	44
Meropenem	95	100
ciprofloxacin	11.9	45.9
Gentamicin	52.7	95.1
Cefotaxime	15.9	54.8
moxifloxacin	13.7	48
Sparfloxacin	12.6	45.3
Cefoperazonesulbactum	91.1	100
Ofloxacin	11.8	43.8
Ceftazidime	39.1	78.9
Co trimoxazole	10.9	63.2
Norfloxacin	10.9	45.7
Cefoperazone	19.2	59.8
Ampicillin	2.8	35.3

than patients having age less than 18 years (55.1%) or more than 60 years (46.3%). Multidrug resistance was more common in hospitalized patients as compared to OPD patients (61.6% vs 54.4%). Frequency of MDR E. Coli was (82.4%), citrobacter (9%), morganella (2.7%), pseudomonas (4.5%) and 1.4% among all other isolates. MDR strains were highly sensitive to imipenem (95.1%), meropenem (95%), tazobactum/piperacillin (92.9%), cefoperazonesulbactum (91.1%) and amikacin (90.1%). MDR uropathogens were least sensitive to ampicillin (2.8%) and nalidixic acid (3.5%). Sensitivity pattern to other fluoroquinolones ranged from 10.1% to 13.7%. Sensitivity pattern to cephalosporins was: ceftriaxone (10.3%), cefixime (11.8%), cefotaxime (15.9%), cefoperazone (19.2%), ceftazidime (39.1%) and cefepime (42.1%). Sensitivity to Gentamicin was 52.7% and 10.9% to co-trimoxazole shown in Table 3.

DISCUSSION

Urinary tract infection is most common[11] and serious[12] health problem worldwide. Antimicrobial resistance is growing throughout the world and is becoming a matter of great clinical concern both in the community and healthcare associated settings. Resistance patterns of uropathogens and frequency of their MDR strains vary according to region from time to time.[13] Our study was aimed to determine frequency of MDR bacteria causing urinary tract infection and local antibiotic sensitivity patterns as guiding principles in selecting empirical treatment options in UTI.

UTI was more common in females than males in our study and this data agrees to the results reported in a local study by Mehr et al.[14] E Coli was the most common organism isolated followed by Citrobacter, morganella, pseudomonas and others. Similar prevalence of microorganisms has been reported by Shabbir et al in urinary tract infections.[15]

Frequency of MDR uropathogens was 58.9%. Similar prevalence of MDR has been reported by Jafri et al. Sabir et al reported much higher prevalence (82%) compared to our studies. This different results can be explained on different study settings and study population. MDR were slightly more common in female population and more common in hospitalized patients. Though these differences were statistically not significant in our study, Ikram et al[16] reported female gender to be a risk factor for multidrug resistance and Santo et al[17] reported much higher percentage of MDR from hospitalized patients vs community. Some studies reported high resistance in male vs female patients, different results from our study.[18,19,20]

The production of beta-lactamase enzymes by microorganisms that destroy penicillins and cephalosporins byhydrolyzing their b-lactam nucleus, is the most common mechanism of resistance. Antimicrobial agents which resist the hydrolyzing effects of beta lactamases prove first line antibacterial agents. MDR strains in our study were highly sensitive to carbapenems, cefoperazonesulbactum, tazobactampepiracillin and amikacin and they were highly resistant to ampicillin, Co-trimoxazole, fluoroquinolones, augmentin and some of the cephalosporins. Similar antibiotic sensitivities has been reported in a number of studies but distribution between MDR and non MDR strains has not been made. Sensitivity patterns of non MDR uropathogens to amoxicillin clavulanic acid was 90.9% suggesting it as empirical treatment when MDR infection is unlikely.

An exponential rise in multidrug resistance in expected and is becoming a major health problem mostly because of the quackery, use of the over the counter and self medication, inappropriate and over or under dosing of antibiotics for infrequent durations,[20] lack of hospital prescription policies and lack antibiograms are some out of many factors contributing to this problem. Antimicrobial stewardship programs have linked antimicrobial resistance development with antimicrobial use. Reduction in antibiotics use can directly decrease resistance. Similarly front end intervention (restricting the availability of selected antibiotics) and back end interventions (reviewing broad spectrum antimicrobial therapy and streamlining it according to sensitivity testing) are required in order to decrease resistance.[20]

LIMITATION

The major limitation of the study is that it didn't assess the risk factors contributing to the development of multidrug resistance as a result association or recommendation on risk factors can't be drawn. Also the lack generalizability of our findings to other populations with different local MDR frequency and antibiotics sensitivities is another limitation of the study.

CONCLUSION

Multidrug resistance in UTI is becoming a major health problem. Assessment of the risk factors, surveillance of resistance patterns and policies for proper antimicrobial use are urgently warranted.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

Shabbir M: Data collection , analysis interpretation ,statistical expertise.

Iman NU: Concept ,design, critical, revision, final approval.

Shah MZ: Drafting Referencing.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.