ANTIBIOTICS SUSCEPTIBILITY PATTERNS TO ESCHERICHIA COLI ISOLATES FROM UNIRARY TRACT INFECTION. A TERTIARY CARE HOSPITAL EXPERIENCE

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ABSTRACT

Objectives: To find the antibiotic sensitivity against Escherichia coli used in urinary tract infection.

Materials and Methods: It was a prospective study done at Department of Nephrology Khyber Teaching Hospital Peshawar, from May 2012 to December 2012. Inclusion criteria was patient having urinary tract infection caused by Escherichia Coli. We looked at the antibiotic sensitivity profile against E-Coli UTI.

Results: Hundred Patients were included in the study. Male to Female ratio was 1:2. Age range was 7-90 years. Tazobectum / Pipercillin and Carbapenem had 98% sensitivity while Nitrofurantoin and Nalidixic Acid showed least sensitivity of 2% and 1% respectively.

Conclusion: UTI is still more common in females. Sensitivity of Amikacin has reduced over the years. Quinolones are becoming resistant with increasing age.

Key Words: Antibiotic Sensitivity, Urinary Tract infection, Escherichia Coli.

INTRODUCTION

Urinary Tract Infection (UTI) is defined as a condition in which urinary tract gets infected with pathogens like bacteria, viruses and fungi. UTI is known to be the second most common cause of infection in USA, where about 8.1 million people seek treatment each year.[1] More than 150 million people are diagnosed with UTI annually and the treatment costs around 6 billion dollars.[2] The most prevalent bacteria that cause UTI include Escherichia coli (E.coli), Staphylococcus saprophyticus, Klebsiella, Enterococci and Proteus mirabilis. Patients attending OPD and admitted in hospitals, E.coli accounts for 75 – 90% of uncomplicated UTI.[3] Traditionally positive culture means urine containing more than 100,000 bacteria per ml, but now this has been modified and counts as low as 1000 per ml or even 100 per ml of bacteria such as E.coli with symptoms of UTI are considered as significant infection, especially if leukocytes are present in the urine.[4] The treatment of UTI is a challenge to physicians nowadays because of resistance to commonly used drugs like Cephalosporins and Fluoroquinolones. This is the reason that we should have studies that can tell us about the type of microorganisms and their susceptibility profile, so that we can empirically start effective treatment.[5] E. coli strain is showing increased resistance to the commonly used antibiotics therapy throughout the world. This may be attributed to the empiric treatment that is initiated before the culture sensitivity report is available.[6] With the use of antibiotics extensively without having known about the organisms involved and the susceptibility pattern, this leads to development of resistance, and now resistance is a global problem.[7] Sensitivity and resistance of antibiotics against different uropathogens is changing very fast over the years in all types of UTIs.[8] There is lot of difference according to geographical regions. Therefore, we conducted this study to know the current susceptibility of antibiotics to E.coli in UTI.

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MATERIALS AND METHODS

This prospective study was done in the Department of Nephrology of Khyber Teaching Hospital, Peshawar which is a 1300 bedded hospital, from May 2012 to December 2012. The patients included were between ages of 07 – 90 years, who attendant Out Patient Department of Nephrology and whose Urine Routine Examination showed more than10 WBC per high power field on microscopy. All types of UTI including relapse, recurrent, complicated, treatment naïve or treatment failures were included. Those patients who were still receiving treatment for UTI were excluded from the study.

Sampling technique used was convenience (Non Probability). Each patient was instructed to carefully collect mid-stream urine sample and then urine was sent for culture and sensitivity. For this study, positive culture

was defined as culture of a single bacterial species from the urine sample at a concentration of 105 CFU/ml. All patients whose Urine Culture and Sensitivity grew E. coli were included in the study. Positive urine culture was further processed for identification and antibacterial susceptibility of the uropathogens.

E.coli isolates were tested against following different antibiotics Tazobactam / Piperacillin (100/10μg), Cefoperazone sulbactam (75/30 μg), Imipenem Cilastatin (10μg), Amikacin (30μg), Ceftazidime (30μg), Ceftriaxone (30μg), Cefotaxime (30μg), Norfloxacin (10μg), Ciprofloxacin (5μg), Clavulanic acid / Amoxicillin (20/10μg), Enoxacin (5μg), Meropenem (10μg), Moxifloxacin (5μg), Nitrofurantoin (300μg), Ofloxacin (5μg) and Nalidixic acid (30μg). Data on age, sex, result of urine culture, etiological agent, and susceptibility pattern were recorded.

RESULTS

Out of 100 patients 67 (67 %) were female and 33 (33 %) were male patients with male to female ratio of 1:2(Table 1). Patient's age was in the range of 07 - 90 years with mean age of 47.15 ± years. Majority of patients that is 49 % were in age group 21 - 50 years (Table 2). Susceptibility patterns of different antibiotic groups showed that combination antibiotic Tazobactam / Piperacillin and Carbapenem showed sensitivity of 98 %, while the least susceptibility was shown by Nitrofurantoin (Table 3). Susceptibility pattern of different antibiotic in different age group showed highest susceptibility to tazobactum / piperacillin while least to Nalidixic acid (Table 4).

Table 1: Distribution of patients on sex

Characteristics	Number	% of total
All patients	100	100
Male	33	33
Female	67	67

Table 2: Distribution of patients in three main groups

No.	Age Group (years)	No. of Patients (%)
	0 – 20	12
	21 – 50	49
	51 – 90	39

Table 3: Susceptibility pattern of antibiotics against E.coli

No.	Antibiotic	(% susceptibility)
1.	Tazobactam / Piperacillin	98
2.	Cefoperazone sulbactam	96
3.	Imipenem Cilastatin	87
4.	Amikacin	84
5.	Ceftazidime	27
6.	Ceftriaxone	27
7.	Cefotaxime	27
8.	Norfloxacin	25
9.	Ciprofloxacin	23
10.	Clavulanic acid / Amoxicillin	16
11.	Enoxacin	14
12.	Meropenem	11
13.	Moxifloxacin	06
14.	Nitrofurantoin	02
15.	Ofloxacin	02
16.	Nalidixic acid	01

DISCUSSION

Antibiotic resistance is called emerging disease and challenge for world health organization (WHO). Once there is resistance then there is need and search for newer and stronger agents to overcome resistance. Drug resistance is acquired by different mechanisms like horizontal gene transfer, mutation in different chromosomal locus and incorporation of foreign DNA into the bacterial chromosomes.[9] The miss use and over use of antibiotics is increasing day by day and this is responsible for causing resistance to antibiotics. Ideally antibiotics prescription should depend on the type of organisms cultured and its susceptibility pattern. To treat UTI effectively one should know about the frequency of microorganisms with which it occurs and their sensitivity profiles. This should be checked from time to time as this may change and organisms develop resistance to commonly used antibiotics. In under develop and developing countries the substandard antibiotics used also results in developing drug resistance and contribute to mortality.[10]

In our study females (67 %) had more incidences of UTI then males (33 %). This is similar to the studies done by Manjunath and et al.[11] Sixty percent of females will report UTI once in their life time.[12] The reason for increased incidence of UTI in females can be either due to anatomical predisposition or some host factors.[13]

On dividing age group according to the important parts of human life i.e premarital, active sexual life and old age (0 – 20 years, 21 – 50 years and 51 – 90 years) we found that 49 % of patients had UTI during 21 – 50 years 39 % during 51 – 90 years and 12 % had UTI in age range of 0 – 20 years.

The overall sensitivity to Tazobactam / Piperacillin in our study is 98 %. The sensitivity is 100 % up to the age of 50 years and in 51 – 90 years it is 94.8 %. Mehr et al had 95.28 % sensitivity of E.coli against Tazobactam

Table 4: Susceptibility pattern of antibiotics against E. coli in different age groups

No.	Antibiotics	% susceptibility Age (0-20) years (n = 12)	% susceptibility Age (21-50) years (n =49)	% susceptibility Age (51-90) (n =39)
1	Tazobactam / Piperacillin	12 (100 %)	49 (100 %)	37 (94.8 %)
2	Cefoperazone sulbactam	12 (100%)	48 (97.9 %)	37 (94.8 %)
3	Imipenem Cilastatin	11 (91%)	43 (87.7 %)	33 (84.6 %)
4	Amikacin	11 (91%)	38 (77.5 %)	35 (89.7 %)
5	Ceftazidime	4 (33%)	18 (36.7 %)	6 (15.3 %)
6	Ceftriaxone	4 (33%)	18 (36.7 %)	6 (15.3 %)
7	Cefotaxime	4(33%)	17 (34.6 %)	6 (15.3 %)
8	Norfloxacin	6 (50%)	14 (28.5 %)	6 (15.3 %)
9	Ciprofloxacin	6 (50%)	12 (24.4 %)	6 (15.3 %)
10	Clavulanic acid / Amoxicillin	4 (33%)	8 (16.3 %)	4 (10.2 %)
11	Enoxacin	4 (33 %)	8 (16.3 %)	3 (7.9 %)
12	Meropenem	1 (8.3 %)	5 (10.2 %)	6 (15.3 %)
13	Moxifloxacin	0 (0 %)	5 (10.2 %)	1 (2.5 %)
14	Nitrofurantoin	1 (8.3 %)	1 (02 %)	0 (0 %)
15	Ofloxacin	0 (0 %)	2 (04 %)	0 (0 %)
16	Nalidixic acid	0 (0 %)	1 (02 %)	0 (0 %)

/ Piperacillin.[14] Ejaz et al had looked for resistance of E.coli against Tazobactam / Piperacillin in ESBL and non ESBL producing E.coli.[15] They found that resistance to Tazobactam / Piperacillin in ESBL producing E.coli was 10.3 % while it was 3.4% in non ESBL producing E.coli.

The sensitivity to Carbapenem group in our study was 98 % i.e 87 % to Imipenem and 11 % to Meropenem. In age wise distribution it was 99.3 % below the age of 20 years, 97.9 % for age range 21 – 50 years and 99.9 % for those patients who were more than 51 years old. Kiffer et al found that sensitivity to Meropenem and Imipenem was 99.90 % and 99.96 % respectively.[16] Ejaz et al had reported resistance of 0% and 13 % for non ESBL and ESBL producing E.coli against Carbapenem group, respectively.[15] Our results are also in concordance with this report. Recently Sumaira S et al has reported 43.3% resistance to imipenem.[17]

The cefoparazone sulbactum group showed that 96% of E. coli are sensitive to them. In age wise distribution it was 100%, 97.9% and 94.8% for the age range 0 - 20 years, 21 - 50 years and 51 - 90 years, respectively. Kiffer et al had also reported resistance to cefoparazone sulbactum around 5.4 %.[16] Mehr et al in their study reported that 93.49 % of E.coli are sensitive to cefoparazone sulbactum.[16] Our study has shown that cefoparazone / sulbactum is the second best combination after tazobactum/piperacillin as it showed 96 % sensitivity while tazobactum / piperacillin showed 98 % sensitivity against E.coli. This is different from the study done by Afridi and Farooq which showed sensitivity of cefoparazone / sulbactum to 96.17 % against 92.99 % of tazobactum / piperacillin.[18] The only difference in two studies is that we had looked for all E.coli and they had studied ESBL and non ESBL producing E.coli separately.

Amikacin showed 84% sensitivity to E.coli in overall group. Same level of sensitivity is shown by Niranjan V and Malini A in india recently. 1[9] It was 91%, 77.5% and 89.7% for different age groups i.e. 0 - 20 years, 21 - 50 years and 51 - 90 years respectively. Bano et al had reported 56% sensitivity to amikacin.[20] In a study done by Shigemura et al the susceptibility rate of E.coli to amikacin was 93%.[21] Another study done 4 years back in our own hospital showed sensitivity of E.coli to amikacin at 93.11%.[14] This is alarming because there is around 10% drop of sensitivity to amikacin in 4 years. We have observed that patients who come from periphery had used amikacin in sub-therapeutic doses for various types of infections. It is usually prescribed by general practitioners and paramedics because it is cheap in price and easy to administer as an injection due to small volume. This could be the reason for increase in resistance to amikacin in recent years.

Overall sensitivity of 3rd generation cephalosporins against E.coli was 27 %. This was as low as 15.3 % in patients between 51 - 90 years age. It was double i. e more than 30 % for patients in age range 0 - 20 and 21 - 50 years. Ijaz et al has shown that there is 100 % and 99.4 % resistance to cefotaxime and ceftazidime in ESBL producing E.Coli and it was 35.3% and 13.8% in non ESBL producing E.Coli.[15] According to surveillance network USA nations of southern Europe had highest

rate of resistance that is around 42 % while in USA it was around 3 % which is equal to Scandinavian countries. The resistance to fourth generation cephalosporin is also increasing suggesting cross resistance with third generation.

Overall sensitivity of Quinolones against E.coli was 26 %, the individual sensitivity of different Quinolones is shown in the table 4. Manikandan et al reported 46 % resistance to ciprofloxacin.[22] Ciprofloxacin was reported to have resistance rate of more than 15% in Madagascar.[23] Worldwide resistance to fluoroquinolones is increasing and sensitivity is decreasing. It has been found that the resistance to quinolones is higher in developing than in developed nations due to use of less potent quinolones for example nalidixic acid, and even when potent compound like ciprofloxacin is used it is used in sub-therapeutic doses, this results in the mutant isolates.[24] Presence of complicated UTI, use of ciprofloxacin more than once in the last year and age over 50 years is associated with ciprofloxacin resistance.[25] Astals study done in China also confirms that the resistance against ciprofloxacin has increased from 46.6 to 59.4 % during the years 1998 – 2000.[26] The high resistance of quinolone against E.coli in our region can be due to increased use of fluoroquinolones in the last two decades.

Our study showed 16 % sensitivity of Amoxicillin / Clavulanic acid against E.coli, which is 33 %, 16.3 % and 10.2 % for the age range 0 – 20 years, 21 – 50 years and 51 – 90 years respectively. Mehr et al and Bano et al in their studies had reported sensitivity of E.coliagainst Co-amoxiclave at 22.4% and 38% respectively.[14,18] ECO. SENS II project data from Austria has also reported higher resistant rate for Amoxicillin / Clavulanic acid. Only two patients that is 2% in our study were sensitivity to Nitrofurantoin. One of them was in age group 0 – 20 years and the other one was in the age group 21 – 50 years. In a study conducted by Akram et al in India Aligarh on community acquired UTI, the resistance to Nitrofurantoin was as high as 80 %.[10] There are other studies which have shown, contrary to our results that the resistance to Nitrofurantoin was as low as 5 %.[18] Similar results were demonstrated by Rani et al.[27] The persistent and increased susceptibility level of E.coli against nitrofurantoin may be caused by its narrow spectrum of activity, narrow tissue distribution, limited contact of the blood with bacteria outside with urinary tract and its limited indications.[28] None of our patients showed sensitivity to Fosfomycin where as Sohail M et al have shown 90% sensitivity in Punjab Pakistan.[29] Recently Yaddav K and Prakash S have emphasized the need for periodic monitoring of drugs sensitivity pattern to prevent resistance.[30]

CONCLUSION

We conclude that UTI is still more common in females, majority of patients belong to age group of 41 - 50 years. Tazobactum /Piperacillin followed by carbapenem group and cefoparazone sulbactum having highest rate of susceptibility against *E.coli* in all age groups. Sensitivity of Amikacin has reduced over the years. Third generation cephalosporins are sensitive in one third of the patients, The worldwide guidelines for empirically treating UTI may not be applicable for our region, as there are decrease rate of susceptibility to commonly used antibiotics. It is for more important to develop local guidelines based on antibiotic susceptibility patterns that can be done from time to time, to prevent treatment failure and decrease chances of resistance.

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