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RESEARCH ARTICLE
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FREQUENCY OF CEFTRIAXONE RESISTANCE IN PATIENTS WITH E. COLI-INDUCED UTI PRESENTING TO KHYBER TEACHING HOSPITAL PESHAWAR

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Abstract

UTIs are the second most common bacterial infection affecting individuals of different ages worldwide. Globally, an estimated 50% of women have UTIs at least once in their lifetime and UTIs are particularly more common in those aged 16–64 years. Since varying frequencies are determined by various available studies in different regions of the globe for prevalence of ceftriaxone resistance in E. Coli-induced UTIs, so I designed this study for determiningfrequency of ceftriaxone resistance in E. Coli-induced UTIs in patients admitted to our department.

OBJECTIVE: To determine the frequency of ceftriaxone resistance in patients with E. Coli-induced UTI presenting to Khyber Teaching Hospital Peshawar

Study Setting: Department of Medicine, Khyber Teaching Hospital, Peshawar.

Study Design: Descriptive study

Study Duration: 6 months 24/4/2022 to 24/10/2022.

MATERIAL AND METHOD: Mid-stream urine was taken in a sterile container. Urine routine examination to see for any pus cells and in case of urine positive for pus cells, it was sent for culture sensitivity.0.01 ml of urine sample was put on MacConkey and blood agar media through calibrated loop and incubated aerobically for 24 hours at 37°C. The plates showing significant growth as per Kass counts were processed further. Identification of isolated E. Coli was confirmed by colony characteristics, gram-staining andbio chemical analysis. E. coli growth detected was checked for ceftriaxone resistance and sensitivities. The treatment of all the patients were continued in the during culture and sensitivity results as per general ward guidelines. Ceftriaxone resistance was seen for in all included cases.

RESULTS: Our study shows that among 193 patients mean age was 35 years with SD ± 16.02. 69(36%) patients were male and 124(64%) patients were female. More over Ceftriaxone was resistant in 81(42%) patients and was not resistant in 112(58%) patients.
CONCLUSION: Our study concludes the frequency of ceftriaxone resistance was 42% in patients with E. Coli-induced UTI presenting to Khyber Teaching Hospital Peshawar

KEY WORDS: ceftriaxone resistance, E. Coli-induced, UTI.

INTRODUCTION

UTIs are the second most common bacterial infection affecting individuals of different ages worldwide. Globally, an estimated 50% of women have UTIs at least once in their lifetime and UTIs are particularly more common in those aged 16–64 years. Prevalence of UTIs is very low among boys but can be observed in the first year of life particularly in those with anatomical or functional abnormalities. Moreover, recurrence rates of UTIs are higher, mainly because of lapses in or cessation of treatment. Therefore, reinfection with the same or different microorganisms may occur.[1,2]

Several studies suggest that Gram-negative bacilli, including Enterobacteriaceae bacteria family, are the most common microorganisms in the appearance of UTIs. In the meantime, E. coli is causing more than 81% of cases of UTIs; afterward, Staphylococcus saprophyticus, Klebsiella, Enterobacter, Proteus, and Enterococci have identified as the causes of UTIs.[3]

One of the most important advances in modern medicine was the discovery of antibiotics, but their availability and expanded use slowly lead to microbial resistance for patients. From the literature, it appears that about 15% of all prescription antibiotics are used to treat UTI. Around 20–50% of all the antibiotic treatments are estimated to be inappropriately indicated, resulting in an increased risk of side effects, increased cost of treatment, and increased resistance.[4,5] Ceftriaxone is a third-generation cephalosporin antibiotic frequently used to treat invasive infections caused by Enterobacteriaceae such as Escherichia coli. The globally increasing prevalence of antimicrobial resistance (AMR) among Enterobacteriaceae is resulting in increased patient morbidity and mortality, increased healthcare costs, and increased use of last-line antibiotics.[6]

In a study 380 patients with UTI were studied. Among these 287 patients were having positive urine cultures for E. Coli. Ceftriaxone resistance to E. Coli- induced UTI in these was as high as 75.53%,[7] while other similar studies lower prevalence of E. coli resistance to ceftriaxone was shown by Prakash, et al.[8] from Meerut city, India as 53.03% in 66 patients with UTI and by Sabir, et al.[9] from Lahore, Pakistan published as 43.3% in 321 adult cases with UTI.

Since varying frequencies are determined by various available studies in different regions of the globe for prevalence of ceftriaxone resistance in E. Coli-induced UTIs, so I designed this study for determiningfrequency of ceftriaxone resistance in E. Coli-induced UTIs in patients admitted to our department.

OBJECTIVE

To determine the frequency of ceftriaxone resistance in patients with E. Coli-induced UTI presenting to Khyber Teaching Hospital Peshawar

OPERATIONAL DEFINITIONS:

E .Coli-induced UTI: A urinary tract infection (UTI) was an infection in any part of urinary system —kidneys, ureters, bladder and urethra presented with pain or burning during urination, strong-smelling urine & urge to urinate. It was called E. Coli-induced if midstream urine culture having E. Coli count of $\geq 10^5$cfu/mL without the presence of any other organism.

Ceftriaxone resistance: If ceftriaxone disc produces an inhibitory zone of <14 mm on E. Coli growth media at 37^{o}C, then it was considered ceftriaxone-resistant.

MATERIAL AND METHOD

Study Setting: Department of Medicine, Khyber Teaching Hospital, Peshawar.
Study Design: Descriptive study
Study Duration: 6 months 24/4/2022 to 24/10/2022.
Sample Size: Sample size was 193, keeping 43.3% proportion of ceftriaxone resistance for E. Coli-UTI[9] keeping 95% confidence interval and 7% margin of error using sample size calculator.
Sampling Technique: Consecutive sampling (non probability)

SAMPLE SELECTION

Inclusion Criteria

1. Patients with culture positive E. Coli-induced UTI.
2. Age group 18 to 60 years.
3. Both genders

Exclusion Criteria

1. Patients who have taken antibiotics within the preceding 2 weeks.
2. Patients known to have anatomical urinary tract abnormalities.
3. Patients known to have neurologic urinary tract abnormalities.

The above mentioned conditions act as confounders and if included had introduce bias in the study results

DATA COLLECTION PROCEDURE:

The study was conducted after approval from hospitals ethical and research committee. All patients presenting to department of medicine with features of UTI were further investigated. Mid-stream urine was taken in a sterile container.Urine routine examination to see for any pus cells and in case of urine positive for pus cells, it was sent for culture sensitivity.0.01 ml of urine sample was put on MacConkey and blood agar mediathrough calibrated loop and incubated aerobicallyfor 24 hours at 37°C. The plates showing significant growth as per Kass counts were processed further. Identification of isolated E. Coli was confirmed by colony characteristics, gram-staining andbiochemical analysis. Those meeting urine sample positive for E. coli were included in the study. The purpose and benefits of the study was explained to the patient and a written informed consent was obtained. E. coli growth detected was checked for ceftriaxone resistance and sensitivities. All the culture and sensitivity procedures were done under supervision of same consultant microbiologist having minimum of five years of experience. The treatment of all the patients were continued in the during culture and sensitivity results as per general ward guidelines. Ceftriaxone resistance was seen for in all included cases. All the information including name, age, address, diabetic, non-diabetic was recorded in a pre-designed proforma (attached).

DATA ANALYSIS PROCEDURE:

Data collected on Proforma was analyzed in SPSS version 20.0. Mean $\pm$ SD were calculated for quantitative variables like age. Percentage and frequencies were computed for categorical variables like gender, diabetic, non-diabetic, married or unmarried and resistance of ceftriaxone for E. Coli. Ceftriaxone resistance for E. Coli were stratified among, age, gender, married, unmarried, diabetic and non-diabetic to see the effect modifications. Post stratification chi square test was applied keeping P value ≤ 0.05 as significant. All results were presented in the form of table and graphs.

RESULTS=

In this study age distribution was analyzed as 100(52%) patients were in age range 18-30 years and 93(48%) patients were in age range 31-60 years, Mean age was 35 years with SD ± 16.02.(table no 1)

Gender distribution was analyzed as 69(36%) patients were male and 124(64%) patients were female. (table no 2)
Marital status was analyzed as 141(73%) patients were married and 52(27%) patients were unmarried. (table no 3)

Status of diabetes mellitus was analyzed as 60(31%) patients were diabetic and 133(69%) patients were non diabetic. (table no 4)

Ceftriaxone resistance was analyzed as Ceftriaxone was resistant in 81(42%) patients and was not resistant in 112(58%) patients. (table no 5)

Stratification of Ceftriaxone resistance with respect to age, gender, marital status, diabetes mellitus is give in table no 6,7,8,9

TABLE NO 1: AGE DISTRIBUTION
(n=193)

AGE	FREQUENCY	PERCENTAGE
18-30 years	100	52%
31-60 years	93	48%
Total	**193**	**100%**

Mean age was 35 years with SD ± 16.

TABLE NO 2: GENDER DISTRIBUTION
(n=193)

GENDER	FREQUENCY	PERCENTAGE
Male	69	36%
Female	124	64%
Total	**193**	**100%**

TABLE NO 3: MARITAL STATUS
(n=193)

MARITAL STATUS	FREQUENCY	PERCENTAGE
Married	141	73%
Unmarried	52	27%
Total	**193**	**100%**

TABLE NO 4: DIABETES MELLITUS
(n=193)

DIABETES MELLITUS	FREQUENCY	PERCENTAGE
Diabetic	60	31%
Non Diabetic	133	69%
Total	**193**	**100%**

TABLE NO 5: CEFTRIAXONE RESISTANCE
(n=193)

RESISTANCE	FREQUENCY	PERCENTAGE
Yes	81	42%
No	112	58%
Total	**193**	**100%**

TABLE NO 6: STRATIFICATION OF CEFTRIAXONE RESISTANCE WITH RESPECT TO AGE
(n=193)

RESISTANCE	18-30 years	31-60 years	Total	P value
Yes	44(44%)	37(39.78%)	81(41.96%)	0.5532
No	56(56%)	56(60.21%)	112(58.03%)	
Total	**100(100%)**	**93(100%)**	**193(100%)**	

Chi square test was applied

TABLE NO 7: STRATIFICATION OF CEFTRIAXONE RESISTANCE WITH RESPECT TO GENDER
(n=193)

RESISTANCE	Male	Female	Total	P value
Yes	33(47.82%)	48(38.70%)	81(41.96%)	0.2187
No	36(52.17%)	76(61.29%)	112(58.03%)	
Total	**69(100%)**	**124(100%)**	**193(100%)**	

Chi square test was applied

TABLE NO 8: STRATIFICATION OF CEFTRIAXONE RESISTANCE WITH RESPECT TO MARITAL STATUS
(n=193)

RESISTANCE	Married	Unmarried	Total	P value
Yes	62(43.97%)	19(36.53%)	81(41.96%)	0.3532
No	79(56.02%)	33(63.46%)	112(58.03%)	
Total	**141(100%)**	**52(100%)**	**193(100%)**	

Chi square test was applied

TABLE NO 9: STRATIFICATION OF CEFTRIAXONE RESISTANCE WITH RESPECT TO DIABETES MELLITUS
(n=193)

RESISTANCE	Diabetic	Non Diabetic	Total	P value
Yes	35(58.33%)	46(34.58%)	81(41.96%)	0.0019
No	25(41.66%)	87(65.41%)	112(58.03%)	
Total	**60(100%)**	**133(100%)**	**193(100%)**	

Chi square test was applied

DISCUSSION

UTIs are the second most common bacterial infection affecting individuals of different ages worldwide. Globally, an estimated 50% of women have UTIs at least once in their lifetime and UTIs are particularly more common in those aged 16–64 years. Prevalence of UTIs is very low among boys but can be observed in the first year of life particularly in those with anatomical or functional abnormalities. Moreover, recurrence rates of UTIs are higher, mainly because of lapses in or cessation of treatment. Therefore, reinfection with the same or different microorganisms may occur.[1,2]

Our study shows that among 193 patients mean age was 35 years with SD ± 16.02. 69(36%) patients were male and 124(64%) patients were female. 141(73%) patients were married and 52(27%) patients were unmarried. 60(31%) patients were diabetic and 133(69%) patients were non diabetic. More over Ceftriaxone was resistant in 81(42%) patients and was not resistant in 112(58%) patients.

Our study correlated with another study carried out by Niu X et al[120] in which the total number of positive growth samples was 5378 (16.6%), including 3206 females (59.6%) and 2172 males (40.4%). The four most common urinary pathogens were *Escherichia coli* (39.2%), *Enterococcus faecalis* (12.4%), *Klebsiella pneumoniae* (7.6%), and *Enterococcus faecium* (7.6%). As far as antibiotic resistance was concerned, *Escherichia coli* had a greater than 50% resistance rate to ampicillin (76.1%), ciprofloxacin (58.6%), and levofloxacin (51.2%), ceftriaxone was 41%. The multidrug resistance rate was high (41.8%). Low levels of resistance were seen to ertapenem (0.1%), imipenem (0.7%), meropenem (0.7%), piperacillin/tazobactam (0.7%), and nitrofurantoin (1.8%). *Klebsiella pneumoniae* was highly sensitive to ertapenem (100%). The resistance rates to nitrofurantoin, ceftriaxone, and ciprofloxacin were 37.4%, 37.1%, and 35.1%, respectively. Up to 41% of *Escherichia coli* strains and 26% of *Klebsiella pneumoniae* strains produced extended-spectrum lactamases (ESBL). Two species of enterococci were highly sensitive to tigecycline and linezolid (100%), and a small number of norvancomycin-resistant strains (0.2%/two strains) were found.

Our study correlated with another study carried out by Abongomera G et al[121] in which Out of the 200 patients, 123 (62%) were female. The median age was 41.9 years (IQR 34.7–49.3). Only 32 (16%) urine cultures showed bacterial growth. *Escherichia coli* was the most commonly isolated uropathogen (72%), followed by *Klebsiella pneumonia*e (9%). *E. coli* was completely resistant to cotrimoxazole and ampicillin; resistance to ciprofloxacin and ceftriaxone was 44% and 35% respectively; 9% to gentamicin; no resistance detected to nitrofurantoin and imipenem.

Our study correlated with another study carried out by Ullah U et al[122] in which prevalence of E. coli resistance to ceftriaxone in adult UTI population of District Peshawar, Pakistan was alarmingly high 75.53%. Prevalence was more in women than men and more in younger age group (18-45 years) than older age group (46-60 years) population. Overall prevalence of E. coli resistance to ceftriaxone
was higher than expected. Distribution by sex showed higher prevalence than expected in men and lower than expected in women, and higher than expected in younger age group and lower than expected in older age group. Presence of E. coli resistance to ceftriaxone was not associated to sex and age groups respectively in adult UTI population of District Peshawar, Pakistan

Our study correlated with another study carried out by Prakash D et al[123] in which the UTI prevalence was 53.82% in patients; however, the prevalence was significantly higher in females than in males (females: 73.57%; males: 35.14%; P = 0.000). Females within the age group of 26-36 years and elderly males of ≥48 years showed higher prevalence of UTI. Gram negative bacteria (90.32%) were found in high prevalence than Gram positive (9.68%). Escherichia coli (42.58%) was the most prevalent gram negative isolate. Nitrofurantoin (78.71%) was found the most resistant drug among all uropathogens. Tested carbapenems were found the most susceptible drug against isolated uropathogens which showed 92.26% and 84.52% susceptibility, respectively

Our study correlated with another study carried out by Sabir S et al[124] in which Bacterial etiological agent was isolated from 402 samples with highest prevalence of E. coli (321, 80%) followed by Staphylococcus aureus (9.4%), Proteus species (5.4%) and Pseudomonas species (5.2%). The E. coli were highly resistant to penicillin (100%), amoxicillin (100%) and cefotaxime (89.7%), followed by intermediate level of resistance to ceftazidime (73.8%), cephradine (73.8%), tetracycline (69.4%), doxycycline (66.6%), augmentin (62.6%), gentamycin (59.8%), cefuroxime (58.2%), ciprofloxacin (54.2%), cefaclor (50%), aztreonam (44.8%), ceftriaxone (43.3%), imipenem (43.3%), and low level of resistance to streptomycin (30%), kanamycin (19.9%), tazocin (14%), amikacin (12.7%) and lowest to norfloxacin (11.2%). Out of 321 E. coli isolates, 261 (81%) were declared as multiple drug resistant and 5 (1.5%) were extensive drug resistant

CONCLUSION

Our study concludes the frequency of ceftriaxone resistance was 42% in patients with E. Coli-induced UTI presenting to Khyber Teaching Hospital Peshawar

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