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ORIGINAL ARTICLE

PREVALENCE, DISTRIBUTION AND DETERMINANTS OF *ESCHERICHIA COLI* RESISTANCE TO CEFTRIAXONE IN ADULT INDOOR UTI POPULATION OF DISTRICT PESHAWAR, PAKISTAN

Ubed Ullah[1], Kiran Javed[2], Muhammad Asim Khan[3], Imran Ullah[4], Noor Ul Iman[1]

Departments of [1]Medicine & [3]Surgery, Khyber Teaching Hospital, Departments of [2]Gynaecology & Obstetrics and [4]Medicine, Lady Reading Hospital, Peshawar, Pakistan

ABSTRACT

Background: *Escherichia coli* resistance to ceftriaxone in UTIs is an emerging health problem. Our objectives were to determine prevalence, distribution and determinants of *E. coli* resistance to ceftriaxone in adult indoor UTI population of District Peshawar, Pakistan.

Materials & Methods: This cross-sectional study was conducted in Department of Medicine, Khyber Teaching Hospital, Peshawar, Pakistan from 1st January 2017 to 30th June 2017. 380 UTIs cases were selected from population at risk consecutively. Sex and age groups were demographic, while presence of *E. coli* resistance to ceftriaxone was research variable. All variables were nominal. Prevalence and distribution were analyzed by count, percentage and confidence intervals for proportion for population. Hypotheses for distribution were substantiated by chi-square goodness-of-fit and of association by chi-square test of association.

Results: Out of 380 patients with UTI, 136 (35.80%) were men, 244 (64.20%) women, 262 (68.95%) in age group 18-45 years and 118 (31.05%) in age group 46-65 years. Frequency/ prevalence of *E. coli* resistance was 287/380 (75.53%, 95%CI 71.20-79.85). Out of 287 patients with *E. coli* resistance to ceftriaxone, 101 (26.58%) were men and 186 (48.95%) women, 198 (52.11%) in age group 18-45 years and 89 (23.42%) in age group 46-65 years. Our prevalence of *E. coli* resistance to ceftriaxone was higher than expected ($p<.00001$), our distribution by sex ($p<.00125$) and age groups ($p<.00001$) were different than expected. Presence of *E. coli* resistance to ceftriaxone was not associated to sex ($p=.669333$) and age groups ($p=.975097$).

Conclusion: 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.

KEY WORDS: Urinary Tract Infections; *E. coli*; Ceftriaxone Resistance; Antibiotic Sensitivity; Anti-microbial Resistance; Adult; Chi-square Goodness of fit Test; Chi-square Test of Association; Peshawar; Pakistan.

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1. INTRODUCTION

1.1 Background: Urinary tract infections (UTIs) are common bacterial infections with significant morbidity and cost. About 150 million individuals are involved in UTI annually throughout the world, with approximate cost of more than six billion US dollars.[1]

Urinary tract infection is more prevalent in female than male with prevalence being highest in young adults.[2] About 40-50% females get infected with UTIs once throughout their life.[3] Increased women susceptibility to UTIs is due to two reasons. First, the urethral opening is near the anus and vagina and second the urethra is short which provides easy

Corresponding Author:

Dr. Imran Ullah
Registrar, Department of Medicine
Lady Reading Hospital, Peshawar, Pakistan
E-mail: drimranullah89@gmail.com

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access of bacteria to the urinary bladder.[4]

Globally, *Escherichia coli* is the most common organism (64.5%) causing UTI.[5] Also in Pakistan *E. coli* was the most common uropathogen isolated from urine cultures (73%) as compared to all others organisms (27%).[6] Two local studies showed *E. Coli* as one of the most common causative agent in UTIs (n=77, 68.1%)[7] and (n=75, 66.96%).[8]

Most clinicians treat UTI empirically, which may be a cause for increasing antibiotic resistance.[9] Studies have showed multiple and extensive drug resistant *E. coli*.[10] The emergence of extended-spectrum beta-lactamase has threatened the empirical use of cephalosporin and ciprofloxacin.[11] Ceftriaxone is a broad spectrum parenteral third generation cephalosporin. It is empirically used in multiple types of infections. But as the bacterial resistance to the common antibacterial drugs is increasing within *E. coli* causing UTIs, its empirical use must be reviewed at times at local levels.[12-14]

Jamil, et al.[8]from Sawabi, Khyber Pukhtunkhwa, Pakistan for the period from Sep. 2016 to April 2017 reported 100% *E. coli* resistance to ceftriaxone in 75 adult UTI patients. Sohail, et al.[6] for the period from Dec. 2012 to Jan. 2014 and Sabir, et al.[10] published in 2014 showed prevalence of *E. coli* resistance to ceftriaxone in adult UTI cases as 71% and 43.3% from samples of 244 and 321 respectively from Lahore, Pakistan. A study by Dadi, et al.[15] from Ethiopia, published in 2018, reported prevalence of *E. coli* resistance to ceftriaxone in 200 adult UTI cases as 80.5%. Niranjan, et al.[16] from Aug 2011 to July 2012 and Prakash, et al.[17] from July 2011 to Jan. 2013 have given prevalence of *E. coli* resistance to ceftriaxone in adult UTI cases as 71.4% and 53.03% from samples of 119 and 66 respectively, from India. Alam, et al.[18]from Dhaka, Bangladesh for the period from Jan. 2016 to Dec. 2016 reported prevalence of *E. coli* resistance to ceftriaxone in adult UTI cases as 47.93% (497*100/1037=47.93%), with 12.83% in men and 35.10% in women from 497 positive cases of *E. coli* resistance out of 1037 adult UTI sample.

1.2 Research Problems, Knowledge Gaps, Research Questions& Rationale: We don't know the prevalence of *E. coli* resistance to ceftriaxone, its distribution by sex and age groups and its association to sex and age groups in adult indoor UTI population of District Peshawar, Pakistan. Unawareness of these five pieces of information were our five research problems. Relevant data regarding these research problems could not be retrieved through online search using different search engines and databases. These were our five knowledge gaps. What would be the prevalence of *E. coli* resistance to ceftriaxone, its distribution by sex and age groups and its association to sex and age groups would be our five research questions. To find answers to these questions would be the rationale of our study.

1.3 Research Objectives (ROs)

RO-1: To determine the prevalence of *E. coli* resistance to ceftriaxone in adult indoor UTI population of District Peshawar, Pakistan.

RO 2-3: To determine the distribution of *E. coli* resistance to ceftriaxone by sex and age groups respectively in adult indoor UTI population of District Peshawar, Pakistan.

RO 4-5: To determine the association between *E. coli* resistance to ceftriaxone and sex and age groups respectively in adult indoor UTI population of District Peshawar, Pakistan.

1.4 Research (Null) Hypotheses

H_{01}: The observed and expected prevalence of *E. coli* resistance to ceftriaxone was same in adult indoor UTI population of District Peshawar, Pakistan.

H_{02}: The distribution of *E. coli* resistance to ceftriaxone by sex was same in adult indoor UTI population of District Peshawar, Pakistan.

H_{03}: The distribution of *E. coli* resistance to ceftriaxone by age groups was same in adult indoor UTI population of District Peshawar, Pakistan.

H_{04}: The presence of *E. coli* resistance to ceftriaxone is independent of sex in adult indoor UTI population of District Peshawar, Pakistan.

H_{05}: The presence of *E. coli* resistance to ceftriaxone is independent of age groups in adult indoor UTI population of District Peshawar, Pakistan.

1.5 Significance: According to above studies resistance is increasing against ceftriaxone, therefore it is necessary to have local data on *E. coli* resistance to ceftriaxone in UTIs. This will provide local and current data on this subject which will guide physicians to do urine culture and sensitivity test before using ceftriaxone or any other antibiotic as empirical therapy in UTIs. This study will encourage hospitals to make antibiotic policy for them which will avoid irrational use of antibiotics and will help in prevention of increasing antibiotic resistance.

2. MATERIALS AND METHODS

2.1 Study Design, Settings & Duration: This cross-sectional study was done at the Department of Medicine, Khyber Medical College, Peshawar, Pakistan from 1st January 2017 to 30th June 2017. The data was collected from five medical, five surgical, three gynecology and one nephrology units of Khyber Teaching Hospital, Peshawar. Prior approval of the project was sought from the Hospital Ethical Review Committee. Patients' consent was also sought before inclusion in the study.

2.2 Population, Sample Size & Technique and Sample Selection: District Peshawar is the most populous district of Khyber Pakhtunkhwa; a northwest province of Pakistan. Its population was 2,026,851 in 1998 Census. For 2016, it was estimat-

ed to be around 4 million. Age group 18-65 years was assumed to contribute its 50%, hence 2 million population. With overall presumed prevalence rate of 5% of UTI in this age group,[19] the population with UTI will be around 100,000 (5*2,000,000/100). Out of this population with UTI, 73% are assumed to be caused by *E. coli*,[6] so73,000 (73*100,000/100) population with UTI caused by E. coli is our population at risk. With this much population, expected prevalence rate of 43.3% *E. coli* resistance to ceftriaxone in this population, margin of error 4.969% and confidence interval of 95%, sample size came to be 380 using online calculator Raosoft®.[20]

Consecutive non-probability sampling technique was used. All adults (18-65 years) indoor patients with UTI caused by *E. coli* were eligible for inclusion. All patients suffering from diabetes, HIV/AIDS or those on long term steroid therapy and patients who used antibiotics in the last 48 hours of presentation were excluded from the study.

2.3 Conduct of Procedure: Detailed history, examination and necessary investigations were done. Single sample of clean-catch mid-stream urine were taken from patients having clinical features of UTIs under strict aseptic conditions and were immediately sent to hospital laboratory for urine routine examination and inoculation on culture media for *E. coli*. 0.01 ml of urine sample were 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 and biochemical analysis.

E. coli growth detected was checked for ceftriaxone resistance and sensitivities. Susceptibility to ceftriaxone was determined by the minimum concentration of ceftriaxone needed to inhibit the growth of *E. Coli* on Mueller Hinton agar media by phenotypic method. This procedure was done under the supervision of one microbiologist.

2.4 Data Collection Plan: Sex (men/ women) and age groups (18-45 and 46-65 years) were demographic variables (attributes) while presence of *E. coli* resistance to ceftriaxone (yes/ no) was a research variable (attributes). The data type was nominal for all the variables. The presence of *E. coli* resistance was dependent variable, while sex and age groups were independent variables respectively for test of association.

2.5 Data Analysis Plan

2.5.1 Descriptive Statistics and Estimation of Parameters: All the three variables were analyzed by count and percentage for the sample. The estimated parameters for the population were stated as CI (confidence interval) for proportion at 95% CL through normal distribution approximation by proportion CI calculator.[21]

2.5.2 Hypotheses Testing: Observed and expected prevalence and observed and expected distribution of *E. coli* resistance to ceftriaxone by sex and age groups were substantiated by using chi-square goodness of fit test (H_{01-3}).[22-24] The association between the presences of *E .coli* resistance to ceftriaxone and sex and age groups was substantiated by using chi-square test of association/ independence (H_{04-5}).[22,23,25]

3. RESULTS

3.1 Descriptive Statistics & Estimation of Parameters

3.1.1 Sample Description & Prevalence of *E. coli* resistance to ceftriaxone in adult UTI population: Out of 380 patients with UTI, 136 (35.80%) were men and 244 (64.20%) women, 262 (68.95%) were in age group18-45 years and 118 (31.05%) in age group of 46-65 years.

Out of 380 patients with UTI, 287 (75.53%) had *E.coli* resistance to ceftriaxone, while 93 (24.47%) had no resistance to ceftriaxone. Estimated prevalence in population is shown below. (Table 3.1.1)

3.1.2 Distribution of positive cases of *E. coli* resistance to ceftriaxone in adult indoor UTI population by sex and age groups: The distribution of positive cases of *E. coli* resistance to ceftriaxone by sex and age groups in adult indoor UTI population of District Peshawar are shown in Table 3.1.2. Here the frequency of *E. coli* resistance to ceftriaxone in sample and its estimated prevalence in population was more in women 48.95%, than men 26.58%, and more in age group 18-45 years 52.11% than age group 46-65 years 23.42%.

Table 3.1.1: Frequency of *E. coli* resistance to ceftriaxone in sample and prevalence in adult indoor UTI population of District Peshawar, Pakistan (n=380)

Variable	Attributes	Sample statistics		95%CI for proportion for population	
		Count	Percentage	Lower	Upper
Presence of *E. coli* resistance	Yes	287	75.53%	71.20	79.85
	No	93	24.47%	20.15	28.80
Total		380	100	Population parameters	

3.2 Hypotheses Testing

3.2.1 Observed vs. expected prevalence of *E. coli* resistance to ceftriaxone in adult indoor UTI population (H_{01}): Our observed counts for the presence of *E. coli* resistance (yes: no) were 287:93 from a sample of 380 against expected counts of 139:182 from a sample of 321 as reported by Sabir, et al.[10]With different sample sizes/ denominators, comparison was not possible. Hence the expected counts and expected percentages were adjusted for a sample of 380. The expected counts of 139:182 were replaced by 164.55:215.45. Adjusted Expected percentages came similar to expected percentages, so not changed. (Table 3.2.1.1)

Chi-square goodness-of-fit test showed p-value <alpha. H_{01} was declared as false and therefore rejected; showing that the observed prevalence is not similar to the expected prevalence. Simply, the prevalence of 75.53% of *E. coli* resistance to ceftriaxone in our population is significantly higher than what we were expecting from the prevalence of 43.30% from Sabir, et al.[10] (Table 3.2.1.2)

3.2.2 Observed vs. expected distribution of positive cases of *E. coli* resistance to ceftriaxone by sex in adult indoor UTI population (H_{02}): Our observed distribution for men versus women was 101:186 out of 287 positive cases from a sample of 380 adult indoor UTI patients against expected counts of 133:364 from 497 positive cases of *E. coli* resistance in 1037 adult UTI population as reported by Alam, et al.[18] from Dhaka, Bangladesh for the period from Jan. 2016 to Dec. 2016 (497*100/1037=47.93%). With different sample sizes/ denominators, comparison was not possible. Hence the expected counts and expected percentages were adjusted for a sample of 380. The expected counts of 133:364 were replaced by 76.80:210.20 and expected percentages of 12.83%:35.10% were replaced by 20.21%:55.32%. It is important to note

Table 3.1.2: Distribution of positive cases of *E. coli* resistance to ceftriaxone by sex and age groups in adult indoor UTI population of District Peshawar, Pakistan (n=287/380)

Variables	Attributes	Sample size	Sample statistics		95%CI for proportion	
			Count	Percentage	Lower	Upper
Sex	Men	136	101	101*100/380=26.58%	22.14	31.02
	Women	244	186	186*100/380=48.95%	43.92	53.97
Age groups	18-45years	262	198	198*100/380=52.11%	47.08	57.13
	46-60years	118	89	89*100/380=23.42%	19.16	27.68
	Total	380	287	287*100/380=75.53%	71.20	79.85

Table 3.2.1.1: Observed, expected and adjusted expected counts and percentages for prevalence of *E. coli* resistance to ceftriaxone in adult indoor UTI population of District Peshawar, Pakistan (n=380)

Presence of *E. Coli* resistance	Observed counts	Observed %ages	Expected counts	Expected %ages	Adjusted expected counts	Adjusted expected %ages
Yes	287	75.53%	139	43.30%	139*380/321=164.55	164.55*100/380 =43.30%
No	93	24.47%	182	56.70%	182*380/321=215.45	215.45*100/380 =56.70%
Total (n)	380	100%	321	100%	380	100%

Table 3.2.1.2: Observed vs. expected prevalence of *E. coli* resistance to ceftriaxone in adult indoor UTI population of District Peshawar, Pakistan (n=380)

Variable	Attributes	O	E	O-E	$(O-E)^2$	$(O-E)^2/E$	χ^2	d.f.	p-value
Presence of *E. coli* resistance	Yes	287	165	122	14884	90.21	159.434	1	<.00001
	No	93	215	-122	14884	69.23	H_{01} rejected at alpha .05		
	Total	380	380	Yates continuity correction applied					

O= Observed count, E= Expected count, χ^2= Chi-square statistics, d.f.= degree of freedom

that we are distributing only 287 positives (75.53%) and not the 93 (24.47%) negative cases out of 380 (100%) cases. (Table 3.2.2.1)

Chi-square goodness-of-fit test showed p-value <alpha. H_{02} was declared as false and therefore rejected, showing that the observations did not fit the statistical model of the population. In simple words, our observed prevalence of *E. coli* resistance to ceftriaxone in men 26.58% (101*100/380=26.58%) was statistically higher to what we expected (adjusted) for men 20.21% (76.80*100/380=20.21%) & our observed prevalence of *E. coli* resistance to ceftriaxone in women 48.95% (186*100/380=48.95%) was lower to what we expected (adjusted) for women 55.32% (210.20*100/380=55.32%) from Alam, et al.[18]. (Table 3.2.2.2)

3.2.3 Observed vs. expected distribution of 287 positive cases of *E. coli* resistance to ceftriaxone by age groups in adult indoor UTI population (H_{03}): Our observed distribution for age group 18-45 years versus 46-65 years was 198:89 out of 287 positive cases from a sample of 380 against hypothetical equal expected distribution of 143.5:143.5 (37.765%:37.765%) out of presumed 287 (75.53%) positive cases from a presumed sample of 380, as no studies could be found in different databases for distribution of *E. coli* resistance to ceftriaxone across the age groups.

Chi-square goodness-of-fit test showed p-value <alpha. H_{02} was declared to be false and therefore rejected, showing that the observations did not fit the statistical model of the population. In simple words, our observed prevalence of *E. coli* resistance to ceftriaxone in age group 18-45 years 52.11% was statistically higher to what we expected hypothetically for age group 18-45 years 37.765% (percentage for expected count) & our observed prevalence of *E. coli* resistance to ceftriaxone in age group 46-65 years 23.42% was lower to what we expected hypothetically for age group 46-65 years 37.765% (percentage for expected count). (Table 3.2.3)

Table 3.2.2.1:Observed, expected and adjusted expected counts and percentages for distribution of 287 positive cases of *E. coli* resistance to ceftriaxone by sex in adult indoor UTI population of District Peshawar, Pakistan (n=380)

E. coli resistance	Observed counts	Observed %ages	Expected counts	Expected %ages	Adjusted expected counts	Adjusted expected %
Positive cases in men	101	101*100/380 =26.58%	133	133*100/1037 =12.83%	133*287/497 =76.80	76.80*100/380 =20.21%
Positive cases in Women	186	186*100/380 =48.95%	364	364*100/1037 =35.10%	364*287/497 =210.20	210.20*100/380 =55.32%
Total positive	287	287*100/380 =75.53%	497	497*100/1037 =47.93%	497*287/497 =287	287*100/380 =75.53%

Table 3.2.2.2: Observed vs. expected distribution of 287 positive cases of *E. coli* resistance to ceftriaxone by sex in adult indoor UTI population of District Peshawar, Pakistan (n=287/380)

Variable	Attributes	O	E	O-E	$(O-E)^2$	$(O-E)^2/E$	χ^2	d.f.	p-value
Sex	Men	101	76.80	24.20	585.64	7.63	10.412	1	.00125
	Women	186	210.20	-24.20	585.64	2.79	H_{02} rejected at alpha .05		
	Total	287	287.00	Yates continuity correction applied					

O= Observed count, E= Expected count, χ^2= Chi-square statistics, d.f.= degree of freedom

Table 3.2.3: Observed vs. expected distribution of 287 positive cases of *E. coli* resistance to ceftriaxone by age groups in adult indoor UTI population of District Peshawar, Pakistan

Variable	Attributes	O	E	O-E	(O-E)2	(O-E)2/E	χ^2	d.f.	p-value
Age group	18-45 years	198	143.5	54.50	2970.25	20.70	41.397	1	<.00001
	46-65 years	89	143.5	-54.50	2970.25	20.70	H_{03} rejected at alpha .05		
	Total	287	287	Yates continuity correction applied					

O= Observed count, E= Expected count, χ^2= Chi-square statistics, d.f.= degree of freedom

Table 3.2.4: Association of presence of *E. coli* resistance to ceftriaxone to sex in adult indoor UTI population of District Peshawar, Pakistan (n=380)

Variable/ Attributes	Presence of *E. coli* résistance		Rows Total	χ^2	d.f.	p-value
	Yes	No				
Sex	O (E) [χ^2]	O (E) [χ^2]		Chi-square test of association with Yates continuity correction applied		
Men	101 (102.72) [0.03]	35 (33.28) [0.09]	136	0.1824	1	0.669333
Women	186 (184.28) [0.02]	58 (59.72) [0.05]	244			
Columns Total	287	93	380	H_{04} accepted at alpha 0.05		

O= Observed count, E= Expected count, χ^2= Chi-square statistics, d.f.= degree of freedom

Table 3.2.5: Association of presence of *E. coli* resistance to ceftriaxone to age groups in adult indoor UTI population of District Peshawar, Pakistan (n=380)

Variable/ Attributes	Presence of *E. coli resistance*		Rows Total	χ^2	d.f.	p-value
	Yes	No				
Age groups	O (E) [χ^2]	O (E) [χ^2]		Chi-square test of association with Yates continuity correction applied		
18-45 years	198 (197.88) [0.00]	64 (64.12) [0.00]	262	0.001	1	0.975097
46-65 years	89 (89.12) [0.00]	29 (28.88) [0.00]	118			
Columns Total	287	93	380	H_{05} accepted at alpha 0.05		

O= Observed count, E= Expected count, χ^2= Chi-square statistics, d.f.= degree of freedom

3.2.4 Association of presence of *E. coli* resistance to ceftriaxone to sex in adult indoor UTI population (H_{04}): Presence of *E. coli* resistance to ceftriaxone being a dependent variable was cross-tabulated by sex as an independent variable. With p-value greater than alpha, H_{04} was declared as true and therefore accepted, showing that the presence of *E. coli* resistance to ceftriaxone is independent of sex i.e. there is no association between the presence of *E. coli* resistance to ceftriaxone and sex. (Table 3.2.4)

3.2.5 Association of presence of *E. coli* resistance to ceftriaxone to age groups in adult indoor UTI population (H_{05}): Presence of *E. coli* resistance to ceftriaxone being a dependent variable was cross-tabulated by age groups as an independent variable. With p-value greater than alpha, H_{05} was declared as true and therefore accepted, showing that the presence of *E. coli* resistance to ceftriaxone is independent of age groups i.e. there is no association between the presence of *E. coli* resistance to ceftriaxone and age groups. (Table 3.2.5)

4. DISCUSSION

4.1 Prevalence of *E. coli* resistance to ceftriaxone in adult indoor UTI population (H_{01}): The frequency of *E. coli* resistance to ceftriaxone in our sample was 75.53% with estimated prevalence in adult indoor UTI population of District Peshawar as 71.20%-79.85% at 95% CL. Similar prevalence to our study was noted by Sohail, et al.[6] from Lahore, Pakistan for the period from Dec. 2012 to Jan. 2014 as 71% from a sample of 244 adult cases with UTI and by Niranjan, et al.[16] from Puduchery, South India for the period from August 2011 to July 2012 as 71.4% from 119 indoor cases with UTI.

Lower prevalence of *E. coli* resistance to ceftriaxone than our study was shown by Prakash, et al.[17] from Meerut city, India for the period from July 2011 to January 2013 as 53.03% in 66 patients with UTI and by Sabir, et al.[10] from Lahore, Pakistan published in 2014 as 43.3% in 321 adult cases with UTI.

Higher prevalence to our study was shown by Jamil, et al.[8] from Sawabi, Khyber Pukhtunkhwa, Pakistan for the period from September 2016 to April 2017 as 100% from 75 patients with UTI and by Dadi, et al.[15] from Addis Abeba, Ethiopia published in 2018 as 80.5% from a sample of 200 patients with UTI. Our observed prevalence of *E. coli* resistance in UTI 75.53% from a sample of 380 was significantly higher (p=<.00001) than what we expected as 43.3% from a study by Sabir, et al.[10]from a sample of 321.

4.2 Distribution of 287 positive cases of *E. coli* resistance to ceftriaxone in adult indoor UTI population by sex (H_{02}): The prevalence of *E. coli* resistance to ceftriaxone in adult indoor UTI population was higher in women 48.95% (95% CI 43.92-53.97) than men 26.58% (22.14-31.02) in our population.

Similarly higher prevalence in women 35.10% (364*100/1037=35.10) than men as 12.83%

(133*100/1037=12.83%) [total ceftriaxone resistance=497*100/1037=47.93%] was shown by Alam, et al.[18] from Dhaka, Bangladesh for the period from January 2016 to December 2016.

Our observed prevalence of *E.coli* resistance to ceftriaxone in adult indoor UTI population from a sample of 380 in men 26.58% was statistically higher to what we expected for men 20.21% & our observed prevalence of *E. coli* resistance to ceftriaxone in women 48.95% was statistically lower to what we expected for women 55.32% from a study by Alam, et al.[18] from Dhaka, Bangladesh (adjusted expected %). (Table 3.2.2.2)

4.3 Distribution of 287 positive cases of *E. coli* resistance to ceftriaxone in adult indoor UTI population by age groups (H_{03}): The prevalence of *E. coli* resistance to ceftriaxone in adult indoor UTI population was higher in age group 18-45 years 52.11% (95% CI 47.08-57.13) than in age group 46-65 years 23.42% (95% CI 19.16-27.68) in our population.

Our observed prevalence of *E. coli* resistance to ceftriaxone in adult UTI population from a sample of 380 in age group of 18-45 years 52.11% was significantly higher to what we expected for age group 18-45 years 37.765% & our observed prevalence of *E. coli* resistance to ceftriaxone in age group 46-65 years 23.42% was significantly lower to what we expected for age group 46-65 years 37.765%, assuming equal expected counts and percentages for *E. coli* resistance to ceftriaxone for age groups in adult UTI population, as no similar studies were found for comparison.

4.4 Association of presence of *E. coli* resistance to ceftriaxone to sex in adult indoor UTI population (H_{04}):

In our study there was no association between the presence of *E. coli* resistance to ceftriaxone and sex in adult indoor UTI population of District Peshawar (H_{04}) (Table 3.2.4, p=0.669333). No similar studies were found for comparison.

4.5 Association of presence of *E. coli* resistance to ceftriaxone to age groups in adult indoor UTI population (H_{05}): In our study there was no association between the presence of *E. coli* resistance to ceftriaxone and age groups in adult indoor UTI population of District Peshawar (H_{05}) (Table 3.2.5, p=0.975097). No similar studies were found for comparison.

4.6 Strengths/ weaknesses of the study

4.6.1 Marwat Logical Trajectory of Research Process: We have employed this logical flow of activities, including; identifying the research problems for our population of interest, isolating the knowledge gaps, putting problems into categorical questions, narrating them in measurable objectives and collecting probable answers for our questions from the observed answers for other similar populations (research hypotheses). Next is the verification of our hypotheses; our probable answers. It is a three steps activity, including; data collection, data analysis and data interpretation. This activity will provide us observed answers regarding our population. If any of these observed answers is similar to its relevant probable answer, we say that the hypothesis is true and hence accepted. Otherwise it is rejected. This way our objectives are met, questions are answered, knowledge gaps are filled and our research problems are solved; the ultimate justification and significance of our research process.[26-30]

4.6.2 Population-Sample-Population flow: Research is a never ending activity to identify and solve problems for a specified/ defined population. But many studies are started from a sample and ended with a sample. We have specified our population and then the sample is drawn. Variables of interest are identified with their attributes and data types. Data is collected by observation/ questionnaire/ interview from that sample. Data is analyzed to describe the sample (descriptive statistics), then it is inferred to the population from which it was drawn to describe that population (estimation of parameter- inferential statistics) and lastly the data from the samples is compared to tell us the differences between the populations or relationships between the variables (hypothesis testing-inferential statistics).[26-30]

4.6.3 Cause-n-effect analysis: The best evidence to identify determinants (causes/ risk factors) of a disease/ health related event is an experiment, which is un-ethical in humans. Then is the cohort and then is the case-control study. The minimum evidence is from cross-sectional study, which we have employed. This cannot tell which variable is cause/ exposure/ risk factor and which one is the effect/ disease. The only evidence it can give is that the two variables are seen together more often than by chance.

5. CONCLUSIONS & RECOMMENDATIONS

1. Prevalence of *E. coli* resistance to ceftriaxone in adult UTI population of District Peshawar, Pakistan was alarmingly high 75.53%.

2. The prevalence was more in women than men and more in younger age group (18-45 years) than older age group (46-60 years) population.

3. Our overall prevalence of *E. coli* resistance to ceftriaxone was higher than expected.

4. The 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.

5. The presence of *E. coli* resistance to ceftriaxone was not associated to sex and age groups respectively in adult UTI population of District Peshawar, Pakistan.

A trend of decrease in bacterial susceptibility to ceftriaxone indicates that the clinicians should be careful in rational use of antimicrobial agents for their patients. They should go for individual culture and sensitivity testing, and where it is not practicable, should use these conservatively relying on susceptibility data in local context.

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CONFLICT OF INTEREST
Authors declare no conflict of interest.
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AUTHORS' CONTRIBUTION

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Conception or Design:	UU, NUI
Acquisition, Analysis or Interpretation of Data:	UU, KJ, MAK, IU, NUI
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All the 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.