



Original Research Article

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COMPARATIVE STUDY OF ANTIMICROBIAL RESISTANCE OF *ESCHERICHIA COLI* ISOLATED FROM UTI PATIENTS IN SANA'A AND TIAZ CITIES, YEMEN

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ABSTRACT: One of the most pressing problems faced by healthcare services today is the increasing prevalence of inappropriate antibiotic prescription and rising resistance. Objective: The present study aimed to evaluate the levels of antibiotics resistance among pathogenic *Escherichia coli* isolated from patients diagnosed with urinary tract infection (UTI). Method: A total of 248 per diagnose of isolates pathogenic *E. coli* isolated from patients suffering from UTI were collected from different medical laboratories at Sana'a and Taiz cities. The strains of *E. coli* were reconfirmed again and tested the purity of each isolates by cultured it on Macconkey agar and then introduced to antibiotic susceptibility test using Mueller-Hinton agar. Results: In the this study, a total of 248 isolates of pathogenic *E. coli* were collected from different medical labs at Sana'a and Taiz cities. *E. coli* showed high resistance rate to co-trimoxazole (61.7 %), tetracycline (54.8%), cefuroxime (44.8%), ciprofloxacin (42.7%), whereas the isolates showed the lowest resistant with ceftriaxone (29.8 %). The isolates from infected males showed higher resistance rate to the tested antibiotics rather than the isolates of infected female. Conclusion: Susceptibility and resistance profile of all isolates in the current study have shown that co-trimoxazole and tetracycline possess the lower efficacy, while ciprofloxacin, cefuroxime and ceftriaxone possess the higher efficacy in treatment UTI at different levels.

KEYWORDS: Antibiotics, Resistance, *Escherichia coli*, UTI, Yemen.

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1. INTRODUCTION

Antibiotic resistance shows a great challenge to the treatment of infections, No doubt, the growing of this problem has developed and concerned a significant public health concern worldwide [1], as a result of many reasons such as random use of antibiotics or inappropriate prescription [2]. Accordingly, this phenomena increases drastically especially in developing countries. In the last few years, the emergence and wide dissemination of *E. coli* strains are representing resistance to broad-spectrum of antimicrobial agents has been reported [3,4,5]. Among the microbes causing urinary tract infection, *E. coli* alone are responsible for 85% of community acquired UTIs [6]. Furthermore, *E. coli* makes the empirical treatment of UTIs difficult and outcome unpredictable consequently its antibiotic resistance developed quickly [7]. In glebe's account, about 150 million people are diagnosed with UTI each year [8]. According to US healthcare system of UTIs, approximately 11.3 million office visits with an overall cost of 1.6 billion dollars annually [9]. In this sense, multidrug-resistant (MDR) is a serious problem that has been spreading quickly in clinical isolates and *E. coli* represents a major pathogen. Moreover, *E. coli* is well known with the healthcare problem with increased morbidity and mortality worldwide [10]. In fact, antimicrobial resistance has been occurred not only in pathogenic strains but also in non-pathogenic ones [11]. Yemen has insufficient medical research reports in this field among health care its cities. Therefore, the antibiotic resistance profiles at the local level must be known in order to support an empiric approach to help in the management of these infections. The present study was aimed to know the antimicrobial susceptibility for pathogenic *E. coli* and to provide comparison between the susceptibility of the isolates from two cities (Sana'a and Taiz) Yemen.

2. MATERIALS AND METHODS

Sample Collection

A total 248 isolates of *E. coli* were collected in two cities (Sana'a and Taiz) from different medical laboratories. In Sana'a city, the isolates were collected from Al-Thawra hospital laboratories (a government lab.) and Al-awlqi laboratories (a private lab.). In Taiz city, the isolates were collected from Al-Tadhamon international laboratories and Dar Alseha laboratories. The isolates of pathogenic *E. coli* were isolated from urine of UTI patients and the diagnostic tests were performed in medical laboratories and all information from patients were recording. The isolates were transported to the microbiology lab.in Faculty of Medicine and Health Sciences of Tamar University, under cool and sterile conditions and kept at 5°C till work. The revere, reconfirmed tests and the purity of all isolates were done using Macconkey agar (Hi media, India) in microbiology lab. Faculty of Medicine and Health Sciences, Tamar University. Antibacterial susceptibility tests for *E. coli* isolates were performed on Muller-Hinton agar (Hi media, India) plate, using the Kirby-Bauer disk diffusion method as per the Clinical and Laboratory Standards Institute-(CLSI,2007) [12].

Antibiotics Susceptibility Tests

All *E. coli* isolates were tested against different antibiotics using disc diffusion method (Kirby-Bauer method) using Mueller-Hinton agar (Hi media, India) according to the guidelines of the Clinical and Laboratory Standards Institute, 2007. The antibiotics were including: ceftriaxone (FR) (30 μ g), cefuroxime (CR) (30 μ g), ciprofloxacin (CI) (5 μ g), tetracycline (TE) (30 μ g) and co-Trimoxazole (CT) (30 μ g). The antibiotics used were in the form of commercially available antimicrobial discs (SPAN, India). The susceptibility pattern of the tested isolates were determined according to the resulted zone of inhibition based on the standard database [12].

The Statistical Analysis

Documented data were analyzed using program of Statistical Package for Social Sciences SPSS (version 20) to calculate the frequencies cross tables and Pearson correlation.

3. RESULTS AND DISCUSSION

The results of all tests of the present study were observed, documented, analysis using program of Statistical Package for Social Sciences SPSS (version 20) and then the obtained data were presented in the figures and tables below. On Mullar Hinton's agar in (figure 1), the antibiotic appears different results in sensitive, intermediated and resistance degrees. Ciprofloxacin, ceftriaxone, and cefuroxime show sensitive, whereas co-trimoxazole and tetracycline represent high resistance.



Figure 1: Pathogenic *E. coli* showed the sensitivity for ciprofloxacin, ceftriaxone, and cefuroxime whereas for co-trimoxazole and tetracycline showed high resistance

Antibiotic susceptibility testing has done. Consequently, results have recorded. In Table 1 the distribution of *E. coli* isolates among area and gender between two cities showed no significant difference between sex and area. The antibiotic sensitivity test of all samples showed in Table 2 the highest rate resistance for co-trimoxazole. In contrast, ceftriaxone (3rd generation cephalosporin) showed the lowest rate of resistance. The results of the sensitivity of antibiotics against *E. coli* isolated from UTI is different in gender (male and female) showed co-trimoxazole and tetracycline are more resistance in infected females than infected males as illustrated in Table 3. The sensitivity of *E. coli* has been tested against using antibiotics depend on the geographical distributions the results showed that the isolates of Sana'a city stored a high resistances rate than the isolates of Taiz

city for all antibiotic used in this study expect cefuroxime and ceftriaxone in Table 4. The least effective agent with high resistance rate is co-trimoxazole (73.4%) in Sana'a city among infected males, whereas the infected males in Taiz city represent lower efficacy to tetracycline (50%) and co-trimoxazole (50%) among antibiotic of this study in Table 5. Infected female results are comparable in resistance rate between two cities. Tetracycline represented the least effective agent with high resistance rate in Sana'a isolates whereas co-trimoxazole in Taiz isolates as illustrated in Table 6.

DISCUSSION

E. coli was the most prevalent organisms causing UTI among patients studied [13]. Studies from India have reported *E. coli* as one of the most common organisms causing UTI.[14,15,16] The aim of this study was that provides useful information in bacteria *E. coli* to determine antibiotic resistance and provide information in rate of antibiotic resistance in two cities (Sana'a & Taiz) in Yemen. In two month, 248 of uropathogenic *E. coli* were collected, this indicated to increase of prevalence of urinary tract infection which caused by *E. coli*, a lot of factors contribute as many individuals do not access to a clean water supply and adequate sewage disposal or less personal hygiene. Increasing prevalence of the level of resistance commonly used antimicrobials, including trimethoprim-sulfamethoxazole (TMP-SMX, also known as Co-trimoxazole), ampicillin, and tetracycline has shown in the last 15 years in multiple studies [17]. In this study, the analyzed results of antibiotic susceptibility test to overall isolated of *E. coli* showed highly resistant to co-trimoxazole (61.7 %), followed tetracycline (54.8%), this consistently to other globe studies where shown high rate to co-trimoxazole (69.74%) [18]. And other showed tetracycline (52.4%) and co-trimoxazole (48.1%) [19]. That is consistently to locally studies showed tetracycline (50%) [20]. In this study, cefuroxime (44.8 %) and ciprofloxacin (42.7%) are shown closely related rates. In contract, the final agent used in this study was ceftriaxone (29.8%) represented low resistance rate and high efficacy in treatment of UTI. However, other studies reported from Turkey showed contrast results (cefuroxime 7%, ciprofloxacin 15%) [21]. And other reported in Iran (ciprofloxacin 26.32 %) [18]. A report from Eman explanted rate of ceftriaxone (10.11%), and ciprofloxacin (39.40%) [22], and this is consistent with our study. One of reasons of increasing in level of resistance is usage of antibiotics from unknown origin, i.e. from uncontrolled sources of production or the widespread and prolonged use of these antibacterial drugs in the world including Yemen. The prevalence and susceptibilities of antibiotic-resistant bacteria varies widely by geographic region, where antibiotic resistance in *E. coli* has increased worldwide and its susceptibility patterns show substantial geographic variation as well as differences in population and environment [23,24,25,26]. In City as Sana'a (capital of the country) where crowded area with population coming to treatment from many places in Yemen contains modern medical analytics techniques and qualified staff in health services compare to other cities. In our study, the useful information about uropathogenic *E. coli* from Sana'a

city was co-trimoxazole (66.9%) appeared the least effective agent, following (63.7%), (46.0%), (42.7%) tetracycline, ciprofloxacin and cefuroxime respectively showed higher in resistance levels rather than isolates from Tiaz city indicated that the patients coming to Sana'a city have failure or recurrent in treatment. These results explain through study by Mabrook Mohanna [27] reported about (Sana'a city) showed that children had taken (60%) of an antibiotic without a medical prescription while (74%) obtained antibiotics from pharmacies and drug stores without any prescription. Amoxicillin, trimethoprim-sulfamethoxazole and amoxicillin-clavulanic acid accounted for (85%) of the prescribed antibiotics for children's in Sana'a [27]. Other explanation of this difference may be the extensive use of these antibiotics in the treatment. Ceftriaxone remains the most effective agent in treatment UTI by *E. coil* as study in both cities. However, the different in resistance rate between two cities to this agent was significant (30.6%) rate in isolates from patient in Tiaz city, whereas (29.0%) in Sana'a city. This can be explained may be due to over uses. The sex distribution of patient in our study is reverse with those in other studies showed females are more than males because anatomical structure of female urethra and vagina make them susceptible to trauma during sexual intercourse and bacterial passage through urethra up to the bladder during pregnancy and delivery [28]. Nevertheless, in our study consistently to local study in Yemen by Al-Haddad et al [20]. The number of infected males are more than infected females. In country as Yemen where socioeconomic conditions (majority of families are poor) do not allow many individuals (especially females) access to hospital for getting suitable treatment or correct follow up. The other social habits of most Yemeni males e.g. chewing Kat can be considered a contributing factor to increase rate of infected males, also. In general, the resistance rate to antibiotic used in this study indicated the female patient are higher than male patients in co-trimoxazole, ciprofloxacin and cefuroxime. Besides, indicated closed related rates between male and female in tetracycline, ceftriaxone. Ceftriaxone stills the most effective in treatment UTI, but in females more than males. While few other studies have explored the differences in antibiotic susceptibility of uropathogens isolated from male and female, as Canadian study [29] and other USA study [30], observed to be significantly higher to ciprofloxacin, and TMP/SMX in isolates collected from male patients versus female patients this is not consistently to our study. Furthermore, we indicated the antimicrobial susceptibility differed significantly for two cities between male patient from two cities or female patient .The higher resistance rate from male patients in cotrimoxazole (73.4%), tetracycline (59.4%), ciprofloxacin(40.6%) and cefuroxime (39.1%) in Sana'a city versus Taiz city where co-trimoxazole and tetracycline are both equally (50%),ciprofloxacin(39.4%) and cefuroxime (48.5%).Not only that but also *E. coil* isolated from female patients in Sana'a city versus female patients in Taiz city appear higher in resistance rate in tetracycline, ciprofloxacin and cefuroxime. This increase in rates to both sex in Sana'a patient's in our study consistent to other Yemeni study in Al-Thawra hospital in Sana'a city [31] showed the total resistance rate to both sex ciprofloxacin

(44.7%), and cotrimoxazole (66.2%). There is a correlation between antibiotic use and subsequent resistance. Finally, ceftriaxone appears the most effective agent as study in Eman [22] and Iran [19] indicated resistance rate (10.11%) and (10.6%) respectively. In this study indicated that in Taiz and Sana'a cities showed closed related in resistance rate in male patients, but female patients showed different rates between two cities. Consequently, this agent has randomly used in patient, especially in Sana'a city.

Table 1: Distribution of isolates among area and gender

City	Male 130 (52.4%)	Female 118 (47.6%)	Total 248 (100%)
Sana'a	64 (51.6%)	60 (48.4%)	124 (50%)
Taiz	66 (53.2%)	58 (46.8%)	124 (50%)

Table 2: Overall rates (percentages) of sensitivity, intermediary and resistance among *E. coil* isolates against different kinds of antibiotics

Antibiotic	Sensitive *N=248 (100%)	Intermediate N=248 (100%)	Resistance N=248 (100%)
Co-trimoxazole (CT)	92 (37.1%)	3 (1.2%)	153 (61.7 %)
Tetracycline (TE)	100 (40.3%)	12 (4.8%)	136 (54.8%)
Ciprofloxacin (CI)	131 (52.8%)	11 (4.4%)	106 (42.7%)
Cefuroxime (CR)	128 (51.6%)	9 (3.6%)	111 (44.8 %)
Ceftriaxone (FR)	152 (61.3%)	22 (8.9%)	74 (29.8%)

* N: number of isolator

Table 3: Frequency resistant of *E. coli* isolates to different antibiotics among gender

Gender	*CT	*TE	*CI	*CR	*FR
Male N=130	80 (61.5%)	71 (54.6%)	52 (40%)	57 (43.8%)	41 (31.5%)
Female N=118	73 (61.9%)	65 (55.1%)	54 (45.8%)	54 (45.8%)	33 (28%)

*CT :Co-trimoxazole, TE: Tetracycline, CI: Ciprofloxacin, CR: Cefuroxime, FR Ceftriaxone

Table 4: Resistance rate to *E. coil* among two cities

Area	CT	TE	CI	CR	FR
Sana'a	83 (66.9%)	79 (63.7%)	57 (46.0%)	53 (42.7%)	36 (29.0%)
Taiz	70 (56.5%)	57 (46.0%)	49 (39.5%)	58 (46.8%)	38 (30.6%)

*CT: Co-Trimoxazole, TE: Tetracycline, CI: Ciprofloxacin, CR: Cefuroxime, FR: Ceftriaxone.

Table 5: Resistance rate (percentage) between male patients from two cities among *E. coil* isolate

Area	CT	TE	CI	CR	FR
Sana'a N=64	47 (73.4%)	38 (59.4%)	26 (40.6%)	25 (39.1%)	21 (32.8%)
Taiz N=66	33 (50%)	33 (50%)	26 (39.4%)	32 (48.5%)	20 (30.3%)

*CT: Co-Trimoxazole, TE: Tetracycline, CI: Ciprofloxacin, CR: Cefuroxime, FR: Ceftriaxone.

Table 6: Resistance rate(percentage) between female patients from two cities among *E. coil* isolate

Area	CT	TE	CI	CR	FR
Sana'a N=60	36 (60%)	41 (68.3%)	31 (51.7%)	28 (46.7%)	15 (25%)
Taiz N=58	37 (63.8%)	24 (41.4%)	23 (39.7%)	26 (44.8%)	18 (31%)

*CT: Co-Trimoxazole, TE: Tetracycline, CI: Ciprofloxacin, CR: Cefuroxime, FR: Ceftriaxone.

4. CONCLUSION

The resistance rate for one of the majority cause UTI bacteria *E. coli* has increased quickly between two city (Sana'a, Taiz). In general, this study all agents used showed critical rates due to over, uncontrolled prescriptions by prescribers or misuse by patient. In this case, the antibiotic sensitivity test must be done, so that will be increased in cost in treatment. Moreover, the increasing chooses of expensive agents that employed in life-threatening situations rather than substituted for cheaper agents. The problem not only increases cost of treatment, but when resistance spreads the cost of resistance is difficult to compute and generally underestimated. This leads to patients from Sana'a city represented *E. coli* become more resistance due to many factors as failure in treatment (recurrent infection), lower education and not complete course of treatment or increase prescription of combination drugs rather than one drug in treatment.

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CONFLICT OF INTEREST

Authors have no conflict of interest.

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