PREVALENCE AND ANTIBIOTIC SUSCEPTIBILITY OF COMMON URINARY BACTERIAL ISOLATES FROM OUT-PATIENTS IN MISRATA, LIBYA

By
Abdallah Abdallah Mahjoub, Aisha Mohammed Elshwehdi, Alaa Milad Bakeer
Department of Pharmaceutical care, Faculty of Pharmacy, Misurata University, Libya

ABSTRACT

Objective: To investigate the prevalence and antibiotic susceptibility of bacterial strains isolated from urine specimen of out-patients with UTI in Misrata region, Libya.
Method: A retrospective cross-sectional study was conducted by reviewing the results of microbiological culture and sensitivity tests performed in Alnoor Medical Laboratory in Misurata city from the first of January 2021 to 31th of December 2021. Data were processed and analyzed by IBM SPSS statistical version 25. A p value of less than 0.05 was considered as statistically significant. Results: Three hundred (300) urine samples of 300 UTI patients were positive for pathogenic bacteria. S. aureus was the predominate isolate, representing 49.33% of all bacterial isolates, followed by E. Coli (26.33%), Klebsiella Spp. (10.34%), Streptococcus Spp. (7.66%), Pseudomonas Spp. (2.66%), Proteus Spp. (2.34%), and Acinobacter Spp. (1.34%). The age of the patients has a significant effect on the distribution of uropathogens, since E. coli was the predominant bacteria in patients younger than 18 years. The isolated bacteria were most susceptible to imipenem, ciprofloxacin, and gentamicin. They were highly resistant to azithromycin, cefixime, and co-trimoxazole. Nitrofurantoin, ceftriaxone, and co-amoxiclav exhibit modest activity against most uropathogens. Conclusion: The obtained results indicate the high resistance against commonly used antibiotics, and emphasis the necessity of continuous evaluation of antibiogram of urinary isolates for proper use of antibiotics.

KEY WORDS: Urinary tract infection, Urinary pathogens, Antibiotic susceptibility test, Antibiotic resistance.

INTRODUCTION

Urinary tract infections (UTI) is a common medical problem affecting both males and females at different stages of life [1]. However, because of the difference in the anatomy of urinary tracts, UTI is more common in females [2,3]. UTI represented a group of diseases ranging from simple UTI such as cystitis to sever forms such acute pyelonephritis, which may further complicate to bacteremia, and septic shock [1]. Similar to many other infectious diseases, the treatment of UTI is usually initiated with empiric antibiotics. Guidelines are available to help clinician selecting the proper antibiotic therapy for specific type of UTI [4]. However, it is highly recommended for each institution or geographic region to have and update their local antibiogram [5,6]. Availability of local antibiogram will provide the prescriber with a recent and updated information regarding the causative organism and their susceptibility pattern. This will help the prescriber to direct the antibiotic therapy to the most expect pathogens and avoid the use of unnecessary broad-spectrum

Correspondence and reprint request: Abdallah Abdallah Mahjoub
E-mail:- aamahjoob@gmail.com

antibiotics [7]. Wide spread use and misuse of antibiotics, especially the broa-spectrum ones has led to increase the numbers and types of resistant bacteria causing UTI and other infectious disease [8,9]. Like many other counties in the world, Antibiotic resistant-uropathogens is a common and an increasing medical problem in Libya [10,11]. There are some studies characterizing the uropathogens and their antibiotic and their antibiotic susceptibility pattern in different regions in Libya; However, the results of these study are not consistent, regarding the prevalence and susceptibility of uropathogens [12–21]. To our knowledge, there is only one study conducted in Misrata, Libya to evaluate the prevalence and antibiotic susceptibility of uropathogens [21]. However, this study included diabetic patients only, therefore its results can't be generalized to all UTI patients. For this purpose, we aimed in this study to evaluate the prevalence and antibiotic susceptibility of uropathogens in the area of Misrata city.

METHODES

A retrospective cross-sectional study was conducted by reviewing the microbiological culture and sensitivity tests result records of 300 urine samples collected by the standard methods, of 300 patients with diagnosis of UTI. The study was conducted at Alnoor Medical Laboratory in Misurata city in the period from first of January 2021 to 31th of December 2021. Data collected included the following information; the patient's gender, age of the patient, type of the biological sample, name of the isolated bacteria, and the result of culture and sensitivity (C/S) test. Antibiotic susceptibility testing (AST) was done by disc diffusion method using commercially available antibiotic discs.

The AST results were recorded as sensitive, intermediate, or resistant according to the zone of inhibition of each antibiotic disc, according to standard conventional method.

Data were analyzed by IBM SPSS statistical version 25. a *p* value of less than 0.05 was considered as statistically significant. Descriptive analysis was used to find out the frequency of each bacteria according to the tested specimen. Cross tabulation analysis with Chi-square test, was used to find out the sensitivity of the isolated bacteria to different antibiotics.

RESULTS

During the year of 2021, 300 urine samples presented for culture and sensitive test at Alnoor Medical laboratory were positive for pathogenic bacterial growth. Patients were in the range of 1 year to 86 years, with a median (IQR) of 25 (29%) years. Most of the patients (199, 66.3%) were adults between 18 and 65 years. Most of the patients (88.7%) were females.

The frequency of isolated bacterial according to the patients' gender and age are shown in figures 1 and 2 respectively. S. aureus was the predominate isolate, representing 49.33% all bacterial isolates, followed by E. Coli, (26.33%), Klebsiella Spp., (10.34%) Streptococcus Spp., (7.66%), Pseudomonas Spp., (2.66%), Proteus Spp., (2.34%), and Acinobacter Spp., (1.34%). Bacterial isolates did not significantly differ between male and female. However, proteus species and Acinobacter species were not isolated from male patients. When the patients were divided into 2 groups according to their ages, the age has significant effect (P = 0.001, by Pearson Chi-Square test) on the distribution of isolated bacteria as shown in table 3. E.

Table 1: Bacterial isolates according the patients' gender (Pearson Chi-square = 2.311, df = 6, P = 0.889).

Isolated organism	No. M	No. F	Total
S. aureus	17 (50%)	131 (50%)	148 (50%)
E. Coli	8 (24%)	71 (27%)	79 (26%)
Klebsiella Spp.	5 (15%)	26 (10%)	*31 (10%)*
Streptococcus Spp.	3 (9%)	20 (8%)	23 (8%)
Pseudomonas Spp.	1 (3%)	7 (3%)	8 (3%)
Proteus Spp.	0 (0%)	7 (3%)	7 (2%)
Acinobacter Spp.	0 (0%)	4 (1.5%)	4 (1%)
Total	34 (11%)	266 *(89%)*	300

Table 2: Bacterial isolates according the patients' age (Pearson Chi-square = 22.779, df = 6, P = 0.001).

Isolated organism	<18	≥18	Total
S. aureus	31 (35%)	117 (55%)	148 (50%)
E. Coli	38 (43%)	41 (27%)	79 (26%)
Klebsiella Spp.	11 (12%)	20 (10%)	*31 (10%)*
Streptococcus Spp.	4 (0.5%)	19 (8%)	23 (8%)
Pseudomonas Spp.	2 (0.25%)	6 (3%)	8 (3%)
Proteus Spp.	3 (0.3%)	4 (3%)	7 (2%)
Acinobacter Spp.	0 (0%)	4 (1.5%)	4 (1%)
Total	89 (30%)	211 *(89%)*	300

E. Coli was the predominant isolates in patients less than 18 years' old (42.7%) followed by S. aureus (34.8%). However, S. aureus was the predominant isolates in older patients (55.5%) followed by E. Coli (19.4%). Eleven antibiotics from different classes were used in the C/S test (table 3). (84.1%), ciprofloxacin (79.8%), Gentamicin (72.2%), ceftriaxone (69.4%) and nitrofurantoin (68.9%). On the other hand, highest percentage of resistant isolates were found with; azithromycin (53%), cefixime (42%), co-trimoxazole (37.2%), and clindamycin (31.3%).

Table 4: summarize the sensitivity pattern each bacterial to different antibiotics less than the other 3 drugs, this is because considerably high percentage (25.6%) of tested S. aureus was intermediately sensitive to vancomycin. On the other hand, high percentage of resistance among S. aureus isolates was found against azithromycin, cefixime, and co-trimoxazole. E. coli was mostly sensitive to imipenem, ciprofloxacin, ceftriaxone, gentamicin.

Although sensitivity to vancomycin was less than the sensitivity to other 3 drugs, the resistance to vancomycin was also

The highest rate of resistance among E. Coli isolates was found with co-trimoxazole, amoxicillin/clavulanate, and azithromycin.

Isolates from Klebsiella Spp., were mostly sensitive to imipenem, and ciprofloxacin, and mostly resistant to amoxicillin/clavulanate, and ceftriaxone.

Isolates from Streptococcus Spp., were mostly sensitive to ceftriaxone, amoxicillin/clavulanate, and ciprofloxacin, and mostly resistant to co-trimoxazole, and gentamicin.

Table 3: The overall sensitivity of all isolates to different antibiotics

Antibiotic	Sensitive		Intermediate		Resistance		Total	Missing
	F	%	F	%	F	%		
Co-trimoxazole	149	51.4	33	11.4	108	37.2%	290	10
Gentamicin	235	72.2	35	11.2	45	15.6%	288	12
Amoxicillin/clavula-nate	156	54.6	65	22.7	65	22.7%	286	14
Azithromycin	71	24.9	63	22.1	151	53%	285	15
Ciprofloxacin	209	79.8	19	7.2	34	13%	262	38
Ceftriaxone	172	69.4	21	8.5	55	22.2	248	52
Cefixime	107	43.7	35	14.3	103	42	245	55
Nitrofurantoin	156	68.7	35	15.4	36	15.9	227	73
Clindamycin	74	64.4	5	4.3	36	31.3	115	185
Vancomycin	56	68.3	22	26.3	4	4.9	82	218
Imipenem	37	84.1	3	6.8	4	9.1	44	256

Table 4: Sensitivity of common uropathogens to different antibiotics

Antibiotics	***S. aureus No., %***			***E.coli No, , %***			***Klebsiella No, %.,***			***Streptococcus No, %***		
	S	**I**	**R**	**S**	**I**	**R**	**S**	**I**	**R**	**S**	**I**	**R**
Co-tri-moxazole	70 48	22 15.2	53 36.6	52 69.3	3 4	20 26.7	17 56.7	3 10	10 33.3	6 26.1	5 21.7	12 52.2
Gentami-cin	111 77.6	15 10.5	17 11.9	58 79.5	9 12.3	6 8.2	16 51.6	8 25.8	7 22.6	10 43.5	2 8.7	11 47.8
Amoxi-cil/clavula	95 68.8	26 18.8	17 16.3	34 44.2	24 31.2	19 24.7	5 16.7	8 26.7	17 56.6	18 81.8	3 13.6	1 4.5
Azithro-mycin	17 11.8	20 13.9	107 74.3	36 48	21 28	18 24	5 18.5	13 48.1	9 33.3	9 45	6 30	5 25
Ciproflox-acin	104 77.6	10 7.5	20 14.9	57 85.1	3 4.5	7 10.4	22 81.5	2 7.4	3 11.1	16 80	2 10	2 10
Ceftriax-one	70 59.8	15 12.8	32 27.4	58 84.1	1 1.4	10 14.5	14 56	1 4	10 40	20 95.2	1 4.8	0 0
Cefixime	25 21.6	18 15.5	73 62.9	52 78.8	3 4.5	11 16.7	14 56	4 14	7 25.8	10 47.6	8 38.1	3 14.3
Nitrofu-rantoin	92 75.4	12 9.8	18 14.8	40 78.4	10 19.6	1 2	11 45.8	7 29.2	6 25	8 53.3	4 26.7	3 20
Clindamy-cin	61 63.5	2 2.1	33 34.4	--	--	--	--	--	--	12 75	2 12.5	2 12.5
Vancomy-cin	55 70.6	20 25.6	3 3.8	--	--	--	--	--	--	0 0	2 100	0 0
Imipenem	2 100	0 0	0 0	21 87.5	1 4.2	2 8.3	10 90.9	1 9.1	0 0	--	--	--

DISCUSSION

In both in-patients, and out-patients setting, treatment of UTI is usually initiated with empiric antibiotic therapy [22, 23]. Acute uncomplicated cystitis [AUC], is the most common form of UTI in out-patient setting.

It is widely acceptable that, E. Coli is the most common bacteria causing AUC. Furthermore, there is a wide believe, that

the E. Coli causing UTI is sensitive to most antibiotics [23]. Therefore, most guidelines recommend a 3-day course of co-trimoxazole, or 5-day course of nitrofurantoin or a single dose of fosfomycin as the first choice for management of AUC [22,23]. Nevertheless, the emergence of bacterial resistance among urinary pathogens including E. coli is increasing world-wild [10,11,24,25]. For these reasons, availability of local data describing the uropathogens and their antibiotic susceptibility to different antibiotics is crucial for proper patients' management, and limiting the emergence of bacteria resistance [6].

Our study shows that S. aureus is the most common bacteria isolated from urine specimens obtained from out-patients in Misrata city. While most studies in Libya have shown that E. coli was the most prevalent isolates [11-17]. Our finding is in agreement with other studies conducted in Tripoli, Derna, and Benghazi [18-20]. Similarly, S. aureus was the predominant uropathogens in a study conducted by Ekwealor et al., in Nigeria [26]. Nevertheless, E. coli remains an important cause of UTI.

In our study it ranks the second after S. aureus as the main isolated bacteria. Furthermore, in young patients less 18-year old, the

percentage of E. coli was slightly higher than S. aureus (42.7% vs 34.8%).

In the current study, imipenem showed the highest sensitivity (84.1%) against the overall uropathogens. This finding is in agreement with other Libyan studies [11,14]. However, in our study imipenem was used in 44 samples (14.66%) only which may make this result is not comprehensive.

When imipenem is excluded, our results indicated that, ciprofloxacin was the most sensitive antibiotics against overall uropathogens. It has similar sensitivity pattern with gentamicin against S. aureus. Furthermore, ciprofloxacin was the most active against E. coli, Klebsiella Spp., and ranks as the third most sensitive antibiotics against Streptococcus Spp., after ceftriaxone, and amoxicillin/ clavulanate. In our study, 14.9 % of S. aureus isolates was resistant to ciprofloxacin. This rate of ciprofloxacin-resistant S. aureus, is slightly higher than what have reported in Benghazi [9%], and in Zliten (12.2%) [13,17]. However, the rate of resistance to ciprofloxacin among S. aureus isolates was extremely higher in other Libyan studies, ranging from 39% in Sirte to 70% in Tripoli [12, 15,16,19]. Similarly, 14.5% of E. coli isolates in our study was resistance to ciprofloxacin. This rate was much lower comparing with other studies conducted in Libya [14-17].

Our results indicated only 11.9% and 8.2% of S. aureus, and E. coli respectively was resistant to gentamicin. However, the resistance of Klebsiella Spp. and Streptococcus Spp., was considerably higher. Yet, because Klebsiella Spp. and Streptococcus Spp., were not abundant in our study, the resistance of overall uropathogens to gentamicin [15.9%] is not high. Sensitivity of uropathogens to gentamicin is considerably variable across the Libyan studies. For instance, the rate of gentamicin-resistance E. coli in Messelata (12.4%) was comparable to our study [14]. However, other local studies have reported a higher rate of gentamicin- resistance among E. coli isolates, ranging from 19.2% 60% [16-18].

Similarly, rate of gentamicin-resistance among S. aureus bacteria in our study (11.9%) was similar to the rate found in Tripoli (13.3%) [18]. However, this rate was much lower than the rate found in Sirte (56%), and in Tobruk (69%) [12,16].

Although, imipenem, ciprofloxacin, and gentamicin were the most effective antibiotics in our study, they are unlikely to be used as first line antibiotics for treatment of out-patients with UTI [22,23]. Imipenem is a very broad-spectrum antibiotic, it ranks by some authors as rank 6 [the broadest spectrum antibiotics], therefore it's high sensitivity against most gram positive and gram-negative bacteria is highly expected [27,28]. However, because of the its high rank, imipenem should not be used for empiric treatment of UTI especially for uncomplicated cases [4,22,23]. Similarly, Ciprofloxacin is a very broad-spectrum antibiotic, that ranks as rank 4, therefore, it usually reserved for more complicated cases such acute pyelonephritis [22,23, 27,28]. Furthermore, ciprofloxacin is not safe for pregnant ladies, and children [29,30]. The disadvantageous of gentamicin include; the parenteral administration, and possible harmful effects on pregnant ladies [29,30].

In the current study, ceftriaxone, and nitrofurantoin showed a similar rate of sensitivity against the overall uropathogens (69.4% vs 68.7%). Our results show that a considerable high percentage (27.4%) of S. aureus was resistant to ceftriaxone. A similar rate of resistance rate was found in Sirte city, where only 72% of S. aureus isolates was sensitive to ceftriaxone [16]. Moreover, in Tripoli, 2 previous studies have documented a higher rate of resistance (60 % and 40%) among S. aureus isolates [15,18]. Resistance of E. coli to ceftriaxone in our study (14.5%) is comparable with other studies in Libya [14,18]. However, the rate of ceftriaxone-resistant E. coli was much higher in other studies [15,17]. Although the resistance of Klebsiella Spp., to ceftriaxone in our study appears to be high [(%), it in fact is in agreement with other local studies [14,16,17].

Ceftriaxone is a third generation, broad-spectrum antibiotic with excellent activity against many gram-negative and gram positive bacteria. However, our study, and other previous studies in Libya showed a high percentage of resistance to this antibiotic among uropathogens especially, Klebsiella Spp., and S. aureus. In a systemic review about the bacterial resistance in Libya, only 3.13% of Klebsiella Spp., was resistance to ceftriaxone, and the fraction of resistance strains of E. coli and S. aureus was less than 0.1%. This increase in the fraction of resistance in Klebsiella Spp., and other bacteria against ceftriaxone, reflecting the growing of resistance against this antibiotic, which should be considered as warning sign to limit the overuse of such broad-spectrum antibiotic.

Nitrofurantoin is among the first line antibiotic recommended for treatment of uncomplicated cystitis, because of its presumed high activity against most uropathogens [22,23,29]. Furthermore, nitrofurantoin is known to be highly concentrated in the urinary tract which further improve it activity against uropathogens, and limit its systemic adverse effects [29]. Our study showed that, 15.9% of all uropathogens was resistant to nitrofurantoin. Klebsiella Spp., was the most

resistant bacterial (25%) to nitrofurantoin. However, the rate of nitrofurantoin-resistant Klebsiella Spp., in other local studies was extremely higher than our studies [13-15]. In our study, only 2% of E. coli and 14.8 % of S. aureus isolates was resistance to nitrofurantoin. This percentage appears to less than what have reported in other studies in Libya [12,13,15,19].

Our results showed that 22.7% of all isolates was resistant to amoxicillin-clavulanate or Co-amoxiclav. The highest rate of resistance was found in Klebsiella Spp., [56.6%], however, similar rate of resistance was found in other Libyan studies [15-17]. Our results showed that 224.7% of E. coli and 16.7% of S. aureus was resistance to amoxicillin/clavulanate, this rate appears to be lower than what has been reported in other Libyan studies [13,14,16,17,18].

Co-trimoxazole is one of the antibiotics recommended for treatment of AUC, because of its expected good antibacterial effects against most uropathogens [22,23]. Furthermore, co-trimoxazole, is among the low-rank antibiotics, which are not associated with increase in the emergence of multidrug resistance bacteria [27,28,32]. Moreover, co-trimoxazole is available in solid and liquid dosage form, which make it suitable for outpatients treatment for both children and adults. However, resistance to co-trimoxazole among uropathogens is increasing in Libya [10].

The rate of co-trimoxazole-resistant E. coli in our study (26.7%) was in agreement with the rate found in Benghazi (24%) and in Messelata (29.2%) [13, 14]. However, the rate of co-trimoxazole- resistant E. coli was about 40 % in other Libyan studies [15,17,18]. In the current study 36.6% of S. aureus was resistance to co-trimoxazole, which is higher than what was found in Zliten (24.2%) [17]. However, the rate of co-trimoxazole-resistant among S. aureus isolates was in the range of 64% in Benghazi, to 77.6% in Derna [12,13,19].

our study shows a high resistance of uropathogens against cefixime (42%) and azithromycin (53%). The highest rate of resistance against these antibiotics was found in the S. aureus isolates. There was a 62.9% of S. aureus resistant to cefixime in our study, which is in agreement with the rate found in Sirte [16]. Nevertheless, in our study, resistance to cefixime among E. coli and Klebsiella Spp., was much lower than what was found in Sirte [16]. Our results indicated a high resistance against azithromycin especially among S. aureus, this finding, is in agreement with the result of Elmanefi et al., [13]. Surprisingly, in a systemic review of antimicrobial resistance in Libya, azithromycin was among most effective antibiotic against S. aureus with a sensitivity rate of about 99.9% [11]. However, this review, included old studies, therefore, changing in the pattern bacterial sensitivity is expected especially against the widely used antibiotic such azithromycin. High resistance of uropathogens against azithromycin is found in other country, for instance, one study in India, showed a 100 % of E. coli was azithromycin-resistant [33].

CONCLUSION

In conclusion, our study indicated that S. aureus is the predominant urinary isolates, followed by E. coli. The urinary isolates in our study were mostly sensitive to imipenem, ciprofloxacin, and gentamicin. However, because of the

high broa-spectrum of activity of theses antibiotics and unavailability of some of them in oral dosage form, they may be not recommended for initial empiric therapy for outpatients with uncomplicated forms of UTI. Nitrofurantoin, showed a good activity against E. coli and S. aureus, therefore it may be the suitable antibiotics for empiric therapy, providing its low rank and its availability in oral dosage form. There was a high rate of resistance against azithromycin, cefixime, co-trimoxazole and co-amoxiclav which may be due its wide use in our society.

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