

Ciprofloxacin Susceptibility of *Proteus Mirabilis* Isolated From Sudanese Patients with Urinary Tract Infections

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Abstract : Urinary tract infections (UTIs) are major health problems affecting millions of people each year. A total of a three thousand and eight hundred and ninety five urine specimens (n =3895) were collected from patients with symptoms of UTIs from different hospitals in Khartoum State. The present study showed that the *P.mirabilis* 120 (3.1%) , the high number of UTIs bacteria was caused by *E. coli* 2185 (56.1%) followed by *K.pneumonia* 703 (18.0%) while less number was caused by *S.aureus* 14(0.4%), The frequent urinary bacteria isolated in our study were highly resistant to ciprofloxacin an (71.7%) *P.mirabilis* shown 36 (30%) resistant to ciprofloxacin, while the other bacteria 995 (26.36%) Sensitive, 23 (0.61%) Intermediate and 2757 (73.03%) resistant to ciprofloxacin.

Keywords – Ciprofloxacin, *Proteus mirabilis*, UTI, Khartoum, Sudan.

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I. Introduction

Urinary tract infections (UTIs) are major health problems affecting millions of people each year. They are considered as the second most frequent type of infection in the body¹¹. *Proteus mirabilis* is one of the frequently causes of urinary tract infections among Enterobacteriaceae¹⁵, As an opportunistic pathogen, *P. mirabilis* causes urinary tract infections, wounds, burns, the respiratory tract, and other sites¹⁸.

The treatment of UTIs differs according to the age of the patient, sex, underlying disease, infectious agent and whether there is lower or upper urinary tract involvement. Ciprofloxacin is a recommended drug for the treatment of UTIs⁷. Different strains of *P. mirabilis* are usually susceptible to fluoroquinolones^{7and 8}, but a progressive increase in fluoroquinolone resistance has been seen in clinical isolates of the bacterium^{8and 10}. Ciprofloxacin directly inhibits DNA synthesis. The inhibition appears to occur by interaction of the drug with complexes composed of DNA and either of the two target enzymes, DNA gyrase and topoisomerase IV⁹.

The mechanisms of fluoroquinolone resistance include one of main mechanistic categories, alterations in the drug target, and alterations in the infiltration of the drug to reach its target¹⁹. The primary mechanisms of resistance to fluoroquinolones are mutations that result in change of the target proteins, DNA gyrase (encoded by *gyrA* and *gyrB*) and topoisomerase IV (encoded by *parC* and *parE*), and decreased intracellular drug accumulation due to drug efflux or changes in outer membrane proteins in several species of Enterobacteriaceae¹⁸.

II. Materials and Method

The study was carried out using 3895 bacteria isolated from urine sample collected from different hospitals in Khartoum State. The isolates were collected from patients attending Military hospital , East Nile model , Soba university , Khartoum bahri teaching , Ahmed Gasim , Omdurman teaching and Ribat university Hospital. The isolates were collected during the period from June 2016 to May 2017. The Identification was based on colony characteristics and further identified by Gram staining and standard biochemical tests⁴.

Ciprofloxacin Susceptibility Test

All the isolates were tested against ciprofloxacin (CIP) (5 µg) *in vitro* by the Kirby-Baur disk diffusion method. Plates were incubated at 37°C overnight. After overnight incubation, the diameter of each zone of inhibition was measured in mm. The susceptibility testing results were recorded according to the Clinical and Laboratory Standards Institute (CLSI) guidelines⁵.

III. Results

A total of a three thousand and eight hundred and ninety five urine specimens (n =3895) were collected from patients with symptoms of UTIs from different hospitals in Khartoum State. Among the study Population 2085 patients(53.5%) were females while 1810(46.5%) were males , 120 (3.1%) were *P.mirabilis* 66 patents

(1.7%) were female and 54 (1.4%) were male . The present study showed that the *P.mirabilis* 120 (3.1%) , the high number of UTIs bacteria was caused by *E. coli* 2185 (56.1%) followed by *K.pneumonia* 703 (18.0%) while less number was caused by *S.aureus* 14(0.4%) as shown in Table 1.

Table 1. Frequency of isolates according to gender type

Isolate	Gender		Total
	Male	Female	
<i>P.mirabilis</i>	54 (1.4%)	66 (1.7%)	120 (3.1%)
<i>E.coli</i>	963 (24.7%)	1222 (31.4%)	2185 (56.1%)
<i>K.pneumonia</i>	212 (5.4%)	491 (12.6%)	703 (18.0%)
<i>P.vulgaris</i>	77 (2.0%)	8 (0.2%)	85 (2.2%)
<i>Ps.aeruginosa</i>	287 (7.4%)	61 (1.6%)	348 (8.9%)
<i>E.faecalis</i>	163(4.2%)	223 (5.7%)	386 (9.9%)
<i>S.epidermidis</i>	23 (0.6%)	0 (0.0%)	23 (0.6%)
<i>Citrobacterspp</i>	31 (0.8%)	0 (0.0%)	31 (0.8%)
<i>S.aureus</i>	0 (0.0%)	14 (0.4%)	14(0.4%)
Total	1810 (46.5%)	2085 (53.5%)	3895 (100.0%)

p-value=0.000

Patients in the study were divided into three age groups: less than 10 years old, 11- 49 years' old, and more than 50 years old. The highest frequency of isolates 2087 (53.6%) was in the age group 11-49 years, followed by the age group of more than 50 years 1663 (42.7%) while the lowest frequency of isolates 145 (3.7%) in the age group of less than 10 years as shown in Table 2.

Table 2. Frequency of isolates according to age groups

Isolate	Age group Count (%)			Total
	Less than 10	From 11-49	More than 50	
<i>P.mirabilis</i>	7 (0.2%)	67 (1.7%)	46 (1.2%)	120(3.1%)
<i>E.coli</i>	79 (2.0%)	1294 (33.2%)	812 (20.8%)	2185(56.1%)
<i>K.pneumonia</i>	51 (1.3%)	354 (9.1%)	298 (7.7%)	703 (18.0%)
<i>P.vulgaris</i>	0 (0.0%)	35 (0.9%)	50 (1.3%)	85 (2.2%)
<i>Ps.aeruginosa</i>	8 (0.2%)	127 (3.3%)	213 (5.5%)	348 (8.9%)
<i>E.faecalis</i>	0 (0.0%)	179 (4.6%)	207 (5.3%)	386 (9.9%)
<i>S.epidermidis</i>	0 (0.0%)	0 (0.0%)	23 (0.6%)	23 (0.6%)
<i>Citrobacterspp</i>	0 (0.0%)	31 (0.8%)	0 (0.0%)	31 (0.8%)
<i>S.aureus</i>	0 (0.0%)	0 (0.0%)	14 (0.4%)	14 (0.4%)
Total	145 (3.7%)	2087 (53.6%)	1663 (42.7%)	389(100%)

p-value=0.000

Among the study population *P.mirabilis* shown 84 (70%) Sensitive to ciprofloxacin and 36 (30%) resistant to ciprofloxacin, while the other bacteria 995 (26.36%) Sensitive, 23 (0.61%) Intermediate and 2757 (73.03%) resistant to ciprofloxacin as shown in Table 3.

Table 3. Relation between *P.mirabilis* and Ciprofloxacin susceptibility compared to other isolates

Isolate	Ciprofloxacin susceptibility			Total
	Sensitive	Intermediate	Resistant	
<i>P.mirabilis</i>	84 (70%)	0 (0.0%)	36 (30%)	120 (100%)
Other bacteria	995 (26.36%)	23 (0.61%)	2757 (73.03%)	3775 (100%)
Total	1079 (27.7%)	23 (0.6%)	2793 (71.7%)	3895 (100%)

p-value=0.000

IV. Discussion

The present study showed that the *P.mirabilis* 120 (3.1%) ,the high number of UTIs bacteria was caused by *E. coli* 2185 (56.1%) followed by *K.pneumonia* 703 (18.0%) while less number was caused by *S.aureus* 14(0.4%). Among the study Population 2085 patients(53.5%) were females while 1810(46.5%) were males , 120 (3.1%) were *P.mirabilis* 66 patents (1.7%) were female and 54 (1.4%) were male as shown in (Table 1). That is agreement with the fact that UTIs are far more common among women than among men. This is mostly due to the anatomy shortness of the female urethra distance that bacteria must travel to reach the bladder. Bacteria from fecal matter at the anal opening can be easily transferred to the opening of the urethra ¹².

The high number of UTIs bacteria was caused by *E. coli* 2185 (56.1%) These results were agreement with those reported by Omar (2015) ¹², Murtada et al (2014) ¹¹, Othman (2007) ¹⁴, and Elder (2004), all agreed that *E.coli* was the most predominant causative organisms. The higher percentage of *E.coli* infection compared with the other organisms could be explained on the basis of their normal habitat in the intestinal tract that is why it is the most common organism founded.

Among the study population *P. mirabilis* shown 120 (3.1%) However, In Sudan it was increased from Murtada et al (2014)¹¹ who found that the *Proteus mirabilis* prevalence was (0.5%), and less than Amir et al (2017) (4%)² and Abd Elrahman et al (2018) (6%)¹. it was different than reported in the previous studies conducted in different countries, in Nigeria(9.5%) by Onoh et al (2013)¹³ and in India (4.54%) by Sujatha and Nawan, (2014)¹⁶, Our results are most similar to those of Yang et al (2017) in china (3.39 %)²⁰, De Francesco et al (2007) in Italy⁶, who found that the most common causative agents of UTIs were *E. coli*, *E. faecalis*, *K. pneumonia* and *P. mirabilis*.

The common urinary bacteria isolated in our study were highly resistant to ciprofloxacin an (71.7%) table (3) ,agreement with the study performed by Badri and Mohamed (2017) 79% of bacteria resistant to ciprofloxacin in Sudan³ and in agreement with the study performed By Abd Elrahman et al (2018) in Sudan (13.5%)¹, Onoh et al (2013)¹³ in Nigeria 35.3% resistance

P. mirabilis shown increase of ciprofloxacin resistance 36 (30%) table (3) this result agreement with the study performed by Wang et al (2014)¹⁷ who found that (68.7) ciprofloxacin resistant and in agreement with those reported by Amir et al (2017) who found that (0%) ciprofloxacin resistant², Generally, the possible reasons behind the resistance to ciprofloxacin in Sudan may be this antibiotic have been in use for a long period and must have been abused and as a result the organisms must have developed mechanisms of changing their mode of action.

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