



## Detection of Quinolones Resistance among Enterobacteriaceae Isolates from Urinary Tract Infections in Shendi

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### ABSTRACT

**Introduction:** Urinary tract infection is one of most prominent human microbial infections both in the community and hospital setting. Species of family *Enterobacteriaceae* represent the most frequent etiologic agents of Urinary tract infection. This study aimed to detect quinolones resistance among *Enterobacteriaceae* species isolated from outpatients and inpatients with urinary tract infection at Shendi Teaching Hospital and Almak Nimer University Hospital in Sudan.

**Methods:** A 100 mid-stream urine (MSU) specimens were collected during the study period (April to August 2018). The isolates were identified by Gram's staining and biochemical tests. Antibiotic susceptibility was done by modified Kirby-Bauer disc diffusion method and interpreted according to Clinical and Laboratory Standard Institute (CLSI) guidelines, 2018.

**Results:** The study revealed that 52% of urinary tract infections were due to members of family enterobacteriaceae, *E.coli* was the most predominant isolated species. The study also showed that 64% of isolated enterobacteriaceae species were resistant to nalidixic acid, 66.7 % to norfloxacin, and 56% to ciprofloxacin respectively.

**Conclusion:** High quinolones resistance rates were observed with urinary tract enterobacterial infections. These findings demonstrate the importance for detection of quinolones resistance among other bacterial families than enterobacteriaceae for improving quinolones prescription practices.

**KEY WORDS:** Quinolones resistance, Enterobacteriaceae, urinary tract infections, Shendi.

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### INTRODUCTION

Urinary tract infection is one of most common human bacterial infections both in the community and hospital setting, this disease affects people of all age group being more common in women, Because of the proximity to the anus, but also because their urethra is shorter than males, which allows an easier passage for bacteria to get up into the bladder (Inam *et al*; 2014). Yearly worldwide about (150) million urinary tract infections occur , leading to more than 6 billion dollar in direct healthcare cost , complicated urinary tract infections include patients with stones or obstructive uropathogens and those with catheter –related infections. <sup>[1]</sup>

Cystitis and pyelonephritis, are the most common infectious diseases in childhood, *Escherichia coli* is responsible for as much as 90% of the community-acquired and 50% of the hospital acquired urinary tract infection. <sup>[2]</sup>

The symptoms include painful urination and increasing frequency in case of cystitis as result of bladder infection whereas symptoms like high fever and flank pain are mainly detected in case of kidney infection which is referred to as pyelonephritis. <sup>[3]</sup>

Bacteria are the primary organisms that cause UTI among humans but the role of certain fungi and viruses cannot be passed. *Klebsiella*, *pseudomonas*, *proteus* and *enterococcus* species plays a minor role in causation of the infections (Nadia *et al.*, 2004), (Lina *et al.*, 2007). <sup>[4]</sup> <sup>[5]</sup>

*Escherichia coli* and *Klebsiella species* are the most frequent agents of UTI. In developing countries most of UTI are managed empirically in the absence of any laboratory tools of investigation. <sup>[6]</sup>

The patterns of antimicrobial resistance is not well defined among community-acquired organisms that circulate in developing countries where antimicrobials are applied without prior consultation with a physician. <sup>[7]</sup>

Fluoroquinolones (FQ) are broad spectrum antimicrobial agent applied widely. Among the FQs, Ciprofloxacin is the most frequently used FQ and has shown a brilliant activity against pathogens. <sup>[8]</sup>

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quinolones inhibit two enzymes (DNA gyrase and topoisomerase IV) essential for bacteria viability, the acquisition of quinolones resistance is mainly related to (i) chromosomal mutation either by a decreased uptake or by an increased efflux, and (ii) quinolone resistance genes associated with plasmids.<sup>[9]</sup>

Many studies revealed that resistance to the Fluoroquinolones among Enterobacteriaceae has increased dramatically worldwide especially during the last five years. However, *Escherichia coli* and other uropathogens are dramatically developing resistance to commonly prescribed antimicrobials leading to decreased activity of some standard regimes.<sup>[10]</sup>

globally, several studies documented an increase in ciprofloxacin resistance, by bacteria causing urinary UTI, The rate of resistance differ from place to place and also among organisms causing UTI.<sup>[11][12]</sup>

In Sudan there is no reported studies determined the occurrence of quinolones resistance among *Enterobacteriaceae* species isolated from urinary tract infection patients. This study is conducted to detect quinolones resistance among enterobacteriaceae species recovered from patients with Urinary tract infection.

Method:

Specimen and sample processing

A 100 urine specimens were gathered consecutively from in and out-patients at Shendi Teaching Hospital and Almak Nimer University Hospital in Sudan. The collection was achieved by trained personnel avoiding contamination. Mid-stream urine samples were collected from the target patients. The specimens were transported to the laboratory after collection and processed immediately. Participants with contaminated urine specimens and all those who refused to fill the consent form were excluded from the study.

Isolation and identification

A loop-full (0.001 ml) of uncentrifuged urine was plated out onto the surface of CLED agar. The plates were incubated at 37°C aerobically for 18-24 hours and counts were indicated in colony forming units (CFU) per milliliter (mL). A count of 100000 CFU/ML or more was considered significant bacteriuria. Organisms were identified based on colonial morphology, indirect gram staining reaction, and biochemical tests.

Antimicrobial susceptibility testing

The Kirby Bauer Disc diffusion method with reference to the Clinical Laboratory Standard Institute (CLSI) performance guideline for antimicrobial susceptibility testing was applied. Quality was assured by testing the *E. coli* quality control strain. All inhibition zones were determined within the ranges provided by the CLSI. Three quinolones were used; Nalidixic acid (NA), Ciprofloxacin (CIP), and Norfloxacin.

## RESULTS

A total of (75) participants were included in this study, the majority of them (75%) were females and (25%) were males. Their age ranged from (10) to (95) years, more than one half were within the age group 30-60 years. In this study the species of family *Enterobacteriaceae* were responsible for 52% of UTI infections caused by bacterial pathogen, *E. coli* was the main detected *Enterobacteriaceae* species (52%), followed by *Klebsiella* species (41), *Proteus* species (5%) and *Providencia* species (2%) (Table 2). Out of the 75 isolates, 52 (69%) isolates were from in-patients and 23 (31%) from out patients. The prevalence of all Enterobacteriaceae in the in-patients was 26/52(56%) and in out-patients (OP) was 89/23(43%).

The resistance of each quinolone was Nalidixic acid 25 (64%); Norfloxacin 26 (66.7%); and Ciprofloxacin 22 (56%) (see Table 3). The resistance in *Escherichia* was 15/20(75%) for all the selected quinolones, for *Klebsiella* 8/16(50%) for Nalidixic acid and 9/16(56%) for Norfloxacin, and 5/16(31%) for Ciprofloxacin, for *proteus* 1/2(50%) for Nalidixic acid and 2/2 (100%) for Norfloxacin, and 1/26(50%) for Ciprofloxacin, for *Providencia* 1/1(100%) for Nalidixic acid and 0/2(0%) for Norfloxacin, and 1/1 (100%) for Ciprofloxacin. (Table 2).

**Table (1). Shows frequency of urinary tract infection caused by *Enterobacteriaceae* spp**

Isolates	No	Frequency
<i>Enterobacteriaceae</i>	39	52%
Others	36	48%
Total	75	100%

**Table (2).** Shows spectrum of isolated *Enterobacteriaceae* species.

Isolates	No	Frequency
<i>E. coli</i>	20	51%
<i>Klebsiella spp</i>	16	41%
<i>Proteus spp</i>	2	6%
<i>Providencia</i>	1	2%
<b>Total</b>	39	100%

**Table (3).** Shows the pattern of resistance among *Enterobacteriaceae* to the selected quinolones

Species	Nalidixic acid		Norfloxacin		Ciprofloxacin	
	No	%	No	%	No	%
<i>E. coli</i> (n=20)	15	75%	15	75%	15	75%
<i>Klebsiella</i> (n=16)	8	50%	9	56%	5	31%
<i>Proteus</i> (2)	1	50%	2	100%	1	50%
<i>Providencia</i> (1)	1	100%	0	0%	1	100%
<b>Total</b>	25	64%	26	66.7%	22	56%

## DISCUSSION

The species of enterobacteriaceae were responsible from 52% of urinary tract infections in this study. This finding is in agreement with results obtained by Gupta *et al*, (2016) who indicated that the species of family enterobacteriaceae were responsible for 55% of urinary tract infections.<sup>[13]</sup>

*E.coli* was the most frequent isolate 20 (51%), followed by *Klebsiella* species 16 (41%), *Proteus* species 2(6%), and *Providencia* species 1 (2%) this result is in accordance with that obtained by Emilia *et al*,(2015) who reported that the percentage of *enterobacteriaceae* isolates was: *Escherichia* 85 (41.1%); *Klebsiella* 64(30.9%); *Proteus* 17(8.2%); *Serratia* 16(7.7%); *Enterobacter* 13(6.3%); others (*Citrobacter*, *Kluyvera*, and *Morganella*) 12(5.9%) consecutively.<sup>[1]</sup>

In this study the resistance of enterobacteriaceae species to nalidixic acid was 64%, this finding is in difference with result obtained by Emilia *et al*; ( 2015) who reported that the resistance of enterobacteriaceae species to nalidixic acid were 35%.<sup>[1]</sup>

The resistance of Enterobacteriaceae to Norfloxacin 26(66.7%), this results were in difference with results revealed by Mahmood *et al*, (2016) who reported that the percentage of resistance among Enterobacteriaceae to Norfloxacin was 45(56.2%).<sup>[2]</sup>

The resistance of *Enterobacteriaceae* to the Ciprofloxacin were 22(56%), this finding is in agreement to the results obtained by Mahmood *et al* (2016) ciprofloxacin 45(56.2%).<sup>[2]</sup>

The current study revealed that *E.coli* isolates showed 75% resistance to all used quinolones, this finding is indifference to result obtained by Toukam *et el* (2010) who reported that only 60%of *E.coli* isolates were resistant to quinolones.<sup>[14]</sup>

This high resistance rates to quinolones may be attributed to many factors; misuse of antibiotics by health care workers, antibiotics purchased without a prescription, excessive antibiotic prescription, low drug quality.

Future studies should be directed to the genetic diversity and the characterization of such resistant strains. This will enable us determine the prevalence of plasmid-mediated resistance which is a common feature among quinolone resistant bacteria.

## CONCLUSION

High level of resistance to quinolones were detected for both in-patients and out-patients with urinary tract enterobacterial infections. The study highlights the importance of antibiotics susceptibility testing in quinolones prescription practices in Shendi town.

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