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Antimicrobial Resistance of *Escherichia coli* Strains isolated from Community and Hospital-acquired Urinary Tract Infections in Khartoum (Sudan)

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Abstract

Background: Urinary tract infections (UTIs) are among the most common indications for antimicrobial use in both the community and in hospital care setting. An increase in resistance against many different drugs among UTI isolates has been observed in the last years.

Objective: To determine the trends of antimicrobial resistance of *Escherichia coli* strains isolated from community and hospital-acquired urinary tract infections in Khartoum (Sudan).

Materials and methods: The current study was a cross-sectional study, conducted in Khartoum, Sudan. Patients with clinical features suggestive of UTIs were investigated for the presence of significant pyuria and bacteriuria. Urine isolates were identified. Antimicrobial susceptibility was determined in accordance with standard bacteriological methods.

Results: Of 476 urine samples, 191 (40.1%) revealed significant pathogenic microbial growth, 64.9% were community acquired, while 35.1% were hospital acquired strains, including 85 (44.5%) *E. coli.* Resistance against ampicillin, amoxyclav, tetracycline, cefixime, ciprofloxacin, co-trimoxazole, nalidixic acid, gentamicin, and nitrofurantoin was found in 92.9%, 83.5%, 76.5, 72.9%, 61.2%, 85.9%, 89.4%, 69.4%, and 9.4% strains respectively. 55.3% of strains were multi-drugs resistant (MDR). 8.2% strains of *E. coli* produced extended-spectrums-β lactamases (ESBLs).

Conclusion: A high resistance rate of uro-pathogenic *Escherichia coli* strains was detectable in both community and hospital setting; together with an increase in MDR *E. coli* strains and ESBL producers.

Key words: Antimicrobial resistance, *E. coli,* Community and hospital-acquired UTIs, ESBLs

Introduction

Urinary tract infections (UTIs) are among the most common infections, both in the community and in hospital settings. *Escherichia coli (E. coli)* is the uro-pathogen with the highest prevalence rate among patients with UTIs. Unfortunately, broad-spectrum antibiotics are increasingly used for UTIs treatment, which is a risk factor for the development of strains resistant to most

commonly used antimicrobials. *E. coli* strains have the ability to change the susceptibility of different antimicrobial agents due to the continuous development of new resistance mechanisms, like the production of extended-spectrum beta-lactamases (ESBLs) or carbapenemases by bacteria and the spread of resistance genes on mobile elements[1].
Regarding community acquired UTIs (CA-UTIs), up to 95% of cases are treated without bacteriological investigations, with the empirically selected antimicrobials, varying according to the patient's age, gender, and symptoms. Over the last two decades, the proportion of community-acquired strains with resistance to first-line agents such as ampicillin, nitrofurantoin, and co-trimoxazole have been shown to be on the increase. More recently, resistance to fluoroquinolones such as ciprofloxacin and norfloxacin has been on the increase too. Recent studies indicate that UTIs caused by ESBLs-producing *E. coli* constitute an emerging problem in both hospital and community settings in various parts of the world. The knowledge of the resistance profiles of *E. coli* as uro-pathogen in community and hospital settings will improve the treatment and thus leads to the decrease of the costs of hospitalization, reduce the duration of treatment in community and limits antibiotic resistance in hospitals and in the community[2].
In the current study, we investigated the frequency rate of *E. coli* associated with community and hospital acquired UTIs and assessed the resistance pattern of this pathogen to commonly used antimicrobials.

Materials and methods

Between March and July 2017, 476 patients suffering from UTIs, 398 patients (83.6%) without past history of hospitalization or contact with hospitals during the past twelve months, and 78 hospitalized patients (16.4%) were enrolled in this study. This study was approved by the Ethical Review Board of Al-Neelain University. Informed consent was taken from each patient before collecting the demographic and clinical data. Permission to collect the specimens was taken from Khartoum State hospitals, and approval to conduct the study was granted by Al-Neelain University, Khartoum (Sudan). Data were analyzed using SPSS program.
Mid-stream urine specimens were collected from each patient into sterile containers and immediately processed. Strains were isolated by inoculation of the collected specimens on CLED media, and incubated overnight at 37°C. The isolates identification was based on colonial morphology, Gram's stain, biochemical tests, according to the standard microbiological procedures. The isolates were subcultured onto nutrient agar and incubated at 37°C for approximately 18 to 24 hours prior to antimicrobial susceptibility testing.
The antimicrobial resistance pattern of the *E. coli* strains was determined by the modified Kirby-Bauer disc diffusion method on Muller Hinton agar using the standard zone sizes of inhibition to determine the sensitivity or resistance to ampicillin (10mg), amoxyclav (10mg), tetracycline (30 µg), cefixime (5µg), ciprofloxacin (5µg), co-trimoxazole (25mg), nalidixic acid (30mg), and nitrofurantoin (100 µg) according to the CLSI guidelines[3].
Keyhole test): ESBLs-producing *E. coli* strains were detected by the double disk synergy test. This test was done by using a disc of amoxyclav (amoxicillin + clavulanic acid) and discs of cefpodoxime, ceftazidime, and cefotaxime; which were placed around the amoxyclav disc keeping a distance of 16 to 20 mm from it. *E. coli* strains were considered to be producing

ESBLs when the zone of inhibition around any of these cephalosporin discs showed a clear-cut increase towards the amoxyclav disc[4].

Results

The median age of community-acquired UTIs (CA-UTIs) patients was 41 years; with 24.1% males and 75.9% females. While the median age of hospital-acquired UTIs (HA-UTIs) patients was 63 years; with 53.8% males and 46.2% females.
E. coli was found to cause UTIs among 29 (34.1%) HA patients; and to cause UTIs among 56 (65.9%) CA patients.
A total of 476 urine samples were investigated for the presence of significant pyuria (using microscopy) and for presence of bacteriuria (by culture). 285 (59.9%) of the specimens showed no or insignificant pathogenic microbial growth; while 191 (40.1%) revealed significant pathogenic microbial growth (i.e. UTIs). Out of the 191 patients, 64.9% were with CA-UTIs and 35.1% were with HA-UTIs. Regarding their gender two thirds of the 191 patients (66%) were females and one third 34% was males.
Of the 191isolates, *E. coli* was the most commonly (85/44.5%) isolated organism. Other associated organisms isolated were *Klebsiella* spp (29/15.1%), *Proteus* spp (18/9.4%), *Pseudomonas* spp (15/7.9%), and other Gram negative bacilli (9/4.7%). *Staphylococcus aureus* being the most commonly (15/7.9%) isolated Gram positive bacteria. While *Staphylococcus saprophyticus*, *Enterococcus* spp and *Candida albicans* were 3 (1.6%), 5 (2.6%), and 12 (6.3%) respectively.
Resistance pattern to the antibiotics tested is shown in Table (1). 55.3% of *E. coli* strains were multi-drugs resistance (MDR), i.e. resists to 4 antimicrobial agents or more. While 8.2% *E. coli* strains produced ESBLs.

Discussion

Urinary tract infection ranks one of most common medical diseases encountered in medical practice with significant morbidity and health costs, occurring from neonate to elderly. Due to the overuse and abuse of antibiotics, the bacterial resistance rates were increased.
This study aimed to evaluate the pattern of antimicrobial resistance of *E. coli* isolated from patients with community and hospital-acquired UTIs.
A trend towards younger age in the CA-UTIs patients compared with patients with HA-UTIs was found; whereas older patients were more common in the HA-UTIs, (median age, 41 years vs. 63 years). UTIs were more frequent in females than males (2:1) and it had been shown that most of UTIs (90%) were caused by microorganisms of an intestinal origin. This may explain the high frequency rate of UTIs observed in females when compared to males, which was often attributed to a shorter urethra, that facilitates colonization by these microorganisms[5].
Antimicrobial resistance was known to be an increasing global problem. The increasing rate of UTIs caused by *E. coli* that resists antimicrobials makes empirical treatment of infections more difficult. In the current study, a high resistance rate to ampicillin, amoxyclav, co-trimoxazole,

Table (1): Resistance pattern, MDR and ESPL production of *E. coli* isolates

Antimicrobial agents	CA- *E. coli* No. (%)	HA- *E. coli* No. (%)	Total No. (%)
Ampicillin	50 (89.3)	29 (100)	79 (92.9)
Amoxyclav	42 (75.0)	29 (100)	71 (83.5)
Tetracycline	40 (71.4)	25 (86.2)	65 (76.5)
Cefixime	36 (64.3)	26 (89.7)	62 (72.9)
Ciprofloxacin	29 (51.8)	23 (79.3)	52 (61.2)
Co-trimoxazole	46 (82.1)	27 (93.1)	73 (85.9)
Nalidixic acid	48 (85.7)	28 (96.6)	76 (89.4)
Gentamicin	36 (64.3)	23 (79.3)	59 (69.4)
Nitrofurantoin	03 (05.4)	05 (17.2)	08 (09.4)
MDR	28 (50.0)	19 (65.5)	47 (55.3)
ESPL	03 (05.4)	04 (13.8)	07 (08.2)
Total	56 (65.9)	29 (34.1)	85 (100)

and nalidixic acid was observed. This study revealed that more than 55% of *E. coli* isolates were multi-drug resistant (i.e. resistant to 4 or more antimicrobials). Similar findings were reported in India, Iran, and other countries[6].

CA- *E. coli* isolates were more likely to be susceptible to multiple antimicrobials; while the majority of HA- *E. coli* isolates were multi-resistant. This may be due to exposure of *E. coli* strains to a high antimicrobial selection pressure. Similar findings were reported in other studies[7]

In the current study, more than half of the isolated strains were resistant to ciprofloxacin. This was of great concern since fluoroquinolones were used as reasonable empirical agents for both hospital and community-acquired UTIs due to the low cost of these antibiotics along with the possibility of oral administration. Resistance to co-trimoxazole was over 85%. It does not seem to be appropriate for the empirical treatment UTI. All recent studies reported high resistance rate among these antimicrobials[6].

In the current study, 8.2% (7/85) *E. coli* strains were found to be ESBL-producing. From these, 5.4% (3/65) were community-acquired and13.8% (4/29 were hospital-acquired strains. Higher frequency rates of ESBL-producing uro-pathogens were reported in other studies[8].

All ESBL-producing *E. coli* strains in the current study were multi-drug resistant. This finding will underscore the therapeutic challenge of UTIs. Urine culture and antimicrobial susceptibility testing seem to be essential in order to face this challenge for both community and hospital-acquired UTIs.

From this study, it may be recommended that co-trimoxazole and the fluoroquinolones-sparing agents such as nitrofurantoin should be used as alternative therapies for hospital and community-acquired uro-pathogens.

Conclusion: A high resistance rate of UTI *E. coli* strains was detectable in both community and hospital setting; together with an increase in MDR *E. coli* strains and ESBL producers.

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