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Multi-Drug Resistance Pattern of Lactose Non-Fermenting *Escherichia coli* as Causative Agent of Urine Tract Infections in Luanda, Angola

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Abstract

This prospective study was carried out to assess the sensitivity and resistance pattern of lactose non-fermenting *Escherichia coli* from July 2018 to December 2018 in the Laboratory of Microbiology at Luanda Medical Center, Angola. Out of 1170 patient, a total of 120 urine specimens infected with *Escherichia coli* (>10^5 CFU/ml) were collected according to the routine protocol of urinalysis. Among these 120 isolates, 25 (21%) isolates were determined as "atypical", lactose non-fermenting *E. coli*s trains. The twenty-five lactose non-fermenting *Escherichia coli* strains isolated from urine samples in Luanda Medical Center were declared as Multiple Drugs-Resistant strains with high resistance to Cefalexine (100%), Cefuroxime (100%), Ceftriaxone (92%), Gentamycin (92%), Ciprofloxacin (72%) and Amoxiciclin/Clavulanic (80%). The alarming resistance level to the first-choice drugs for the treatment of urinary tract infections caused by non-fermentative lactose *E. coli* was observed.

Keywords

Escherichia coli, Multi-Drugs Resistance (MDR), Lactose Non-Fermenting, Urine Tract Infections, Colony Forming Unit (CFU)

1. Introduction

The Urinary tract infections (UTIs) are serious health affecting problems worldwide [1] [2]. The level of bacterial resistance to antibiotics is growing from year to year and is becoming one of the main problems in the world [3]. This is especially true for the developing countries including African continent where

self-medication, overuse and misuse of antibiotics leads to the emergence of multi drug resistant (MDR)bacteria [4] [5]. *E. coli* is the most common and predominated bacteria causing UTIs in human beings. *E. coli* is facultative anaerobic, Gram-negative bacilli ferments lactose to produce hydrogen sulphide. Historically been reported that up to 10% of *E. coli* can be "atypical" non-lactose fermenting. Lactose non-fermenting *E. coli* has a number of virulence factors and exhibit antibiotic resistance [6]. Now there is not a lot of data about lactose non-fermenting *E. coli* as the etiological agent of urinary tract infection, while the Gram-negative, non-fermenting multi-resistant bacilli make the treatment of these organisms very difficult and expensive [7]. According to the Antimicrobial Resistance Global Report of WHO, the data about antibiotic resistance obtained from the African countries is still not enough [1]. The aim of this study was conducted to determine the antibiotic resistance pattern of lactose non-fermenting *Escherichia coli*.

2. Subjects and Methods

2.1. Setting

This prospective study was carried out to assess the sensitivity and resistance pattern of lactose non-fermenting *Escherichia coli* from July 2018 to December 2018 in the Laboratory of Microbiology at Luanda Medical Center, Angola.

2.2. Sampling

Bacteria were isolated according to the routine protocol of urinalysis using MacConkey/CLED HY-Uritest and chromogenic media (Hy-Labs, Israel). The Uritest paddle was dipped into the aseptically collected urine sample and removed immediately. The paddle was transferred into the tube and cap was screwed back loosely, to allow for free transfer of atmosphere. The tube was incubated 18 - 24 hours at 37˚C. Test yielding $\geq 10^5$ CFU/ml are regarded as Positive. Additionally, the 0.01 mL of urine sample was inoculated on CHROME Orientation agar (HyLabs Ltd) by spread plate technique. The determination of lactose non-fermenter strains was using by observation colonies on MacConkey agar and Cystine Lactose Electrolyte Deficient (CLED) Agar. The lactose non-fermenting *E. coli* colonies were colorless on McConkey agar and colorless to blue on CLED agar. The isolated bacteria were then identified by using Gram Stain and their biochemical characteristics using Remelrap ID system kits.

2.3. Antimicrobial Susceptibility Testing

Antibiotic susceptibility was determined using the disc diffusion method on Mueller Hinton agar according to the Guidelines of the Clinical Laboratory Standards Institute (GCLSI). Different families of antibiotics (discs obtained from OXOID) were used in this study included Cephems; Beta-lactam + inhibitor, Cephalosporines (1st, 2nd and 3rd generations); Fluoquinolones; Tetracyclins; Folate pathway inhibitors; Nitrofurans; Aminoglycosides; Monobactams

and Carbapenemes. The diameter of the inhibition zone formed around the disc was measured and compared to the critical values of each antibiotic disc (according to CLSI) to qualify the target bacteria as sensitive or resistant. MDR bacteria are defined as resistant to at least three different classes of antibiotics. Multi Resistant strains were according to the Center for Disease prevention and Control [8] [9] [10].

3. Results

3.1. Samples

Between July 2018 and December 2018, 187 positive urine samples from 1170 out-patients were collected at Luanda Medical Center. Out of them, 120 (64%) urine specimens were infected with *E. coli* (>10^5 CFU/ml). 107 (89%) positive sample were belong to females and 13 (11%) were belong to males. Among these 120 isolates, 25 (21%) isolates were determined as atypical, lactose non-fermenting *E. coli*. The twenty two (88%) lactose non-fermenting *E. coli* we isolated from female urine samples and 3 (12%) strains were isolated from male samples. The average patient with UTI caused by lactose non-fermenting *E. coli* were 41 ± 14 years for males and 40 ± 14 for females.

3.2. Antibiotic Resistance

The comparison of antibiotic resistance rates was performed specifically for lactose non-fermenting *E. coli* (LNFEC) and lactose fermenting *E. coli* (LFEC) in (**Table 1** & **Table 2**). All of lactose non-fermenting *E. coli* isolates were Multiple Drug Resistant and exhibited the highest resistance to Cefalexine (100%), Cefuroxime (100%), Ceftriaxone (92%), Trimethoprim/Sulfamethoxazole (92%), Doxycycline (92%), Gentamicin (92%) followed by high level of resistance to Amoxicillin/Clavulanic acid (80%), Ciprofloxacin (72%) and low level of resistance to Nitrofurantoin (16%). It was not found lactose non-fermenting *E. coli* isolates resistant to Imipinem, Piperacilin/Tazobactam and Amikacin (**Table 1**).

While the lactose fermenting *E. coli* isolates exhibited the intermediate level of resistance to Trimethoprim/Sulfamethoxazole (55%), Doxycycline (78.4%) followed by low level of resistance to Ciprofloxacin (21%), Amoxicillin/Clavulanic acid (18%), Cefalexine (14%) Gentamicin (8%), Nitrofuratoin (5%), Cefuroxime (3%), Ceftriaxone (1%). It was not found lactose fermenting *E. coli* isolates resistant to Piperacilin/Tazobactam, Amikacin, Aztreonam and Imipinem (**Table 2**).

3.3. Multi-Drug Resistance

100% of the lactose non-fermenting *E. coli* isolates were found to be multidrug resistant while 21% lactose fermenting *E. coli* isolates were MDR.

4. Discussion

Urine tract infection is one of the most common infections in the world [1] [2].

Table 1. Antibiotic resistance rates for Lactose Non-fermenting *E. coli* (LNFEC) isolates.

Antibiotic subclass	Antibiotic	*Resistant*		*Intermediate*		*Sensitive*	
		n	%	n	%	n	%
Beta-lactam + inhibitor	Amoxicillin/clavulanic acid	20	80	0	0	5	20
	Piperacilin/tazobactam	0	0	0	0	25	100
Cephalosporin I	Cefalexine	25	100	0	0	0	0
Cephalosporin II	Cefuroxime	25	100	0	0	0	0
Cephalosporin III	Ceftriaxone	22	92	0	0	27	8
Fluoroquinolones	Ciprofloxacin	18	72	0	0	7	28
Tetracyclines	Doxycyline	22	92	0	0	3	8
Folate pathway inhibitors	Trimethoprim/sulfamethoxazole	22	92	0	0	3	8
Aminoglycosides	Gentamicin	22	92	0	0	3	8
	Amikacin	0	0	0	0	25	100
Nitrofurans	Nitrofurantoin	5	20	0	0	20	80
Monobactam	Aztreonam	12	48	5	20	8	32
Carbapenemes	Imipinem	0	0	0	0	25	100

Table 2. Antibiotic resistance rates for Lactose fermenting *E. coli* (LFEC) isolates.

Antibiotic subclass	Antibiotic	*Resistant*		*Intermediate*		*Sensitive*	
		n	%	n	%	n	%
Beta-lactam + inhibitor	Amoxicillin/clavulanic acid	18	18	9	9	73	73
	Piperacilin/tazobactam	0	0	0	0	95	100
Cephalosporin I	Cefalexine	14	15	65	68	15	17
Cephalosporin II	Cefuroxime	3	3	17	18	75	79
Cephalosporin III	Ceftriaxone	1	1	0	94	0	99
Fluoroquinolones	Ciprofloxacin	20	21	3	3	72	76
Tetracyclines	Doxycyline	43	45	1	1	51	54
Folate pathway inhibitors	Trimethoprim/sulfamethoxazole	52	55	1	1	42	44
Aminoglycosides	Gentamicin	8	8	0	0	87	92
	Amikacin	0	0	0	0	95	100
Nitrofurans	Nitrofurantoin	4	5	1	1	90	95
Monobactam	Aztreonam	0	0	0	0	95	100
Carbapenemes	Imipinem	0	0	0	0	95	100

E. coli is the most common and predominated causative bacteria in urine tract infections. The level of bacterial resistance to antibiotics is growing from year to year and is becoming one of the main problems in the world [3] [11]. Particularly concerned about the increase multidrug resistance level of lactose non-fermenting gram negative rods. The lactose non-fermenting bacilli possess several different

mechanisms of resistance that makes treatment of these organisms difficult and expensive [6] [7]. This is especially true for the developing countries including African continent where improper medication, self-medication, overuse and misuse of antibiotics leads to the emergence of MDR bacteria [4].

Our study has showed that *E. coli* were implicated in 64% of all Urine Tract Infection pathogens. This rate is similar to results reported from Maroco (63%) [12], Ethiopia (60%) [13], but higher from studies in Equatorial Guinea (55%) [14], Nigeria (37%) [15] and Ghana (37%) [16]. The rate of lactose non fermenting *E. coli* urinary isolates from this study was 21%, which is similar to the study authored by Chang (about 20%) [17] and more higher than studies of Bhat (about 13%) [18], Bajapai (4%) [19].

Our study revealed 72% lactose non-fermenting *E. coli* isolates resistant to Ciprofloxacin. This result agreed with study of Chang [17] who recorded 66.7% resistance to Ciprofloxacin and was higher than results published by Yaratha (30% resistance to Ciprofloxacin) [20]. Our study has showed that "atypical" lactose non-fermenting *E. coli* isolated were highly resistant to a broad spectrum of antibiotics: Cefalexine (100%), Cefuroxime (100%), Ceftriaxone (92%), Trimethoprim/Sulfamethoxazole (92%), Doxycycline (92%), Gentamicin (92%), Amoxicillin/Clavulanic acid (80%), Ciprofloxacin (72%). These results demonstrate the highest level resistance of lactose non-fermenting bacteria in comparison with the resistant pattern of "common" lactose fermenting *E. coli* isolates as observed in this study (**Figure 1**). Our date is partially agrees with some studies in Nigeria [21], Maroco [12] and Kenya [22] were the similar results were received.

5. Conclusion

Our study has shown the high percentage (21%) presence of the "atypical" lactose

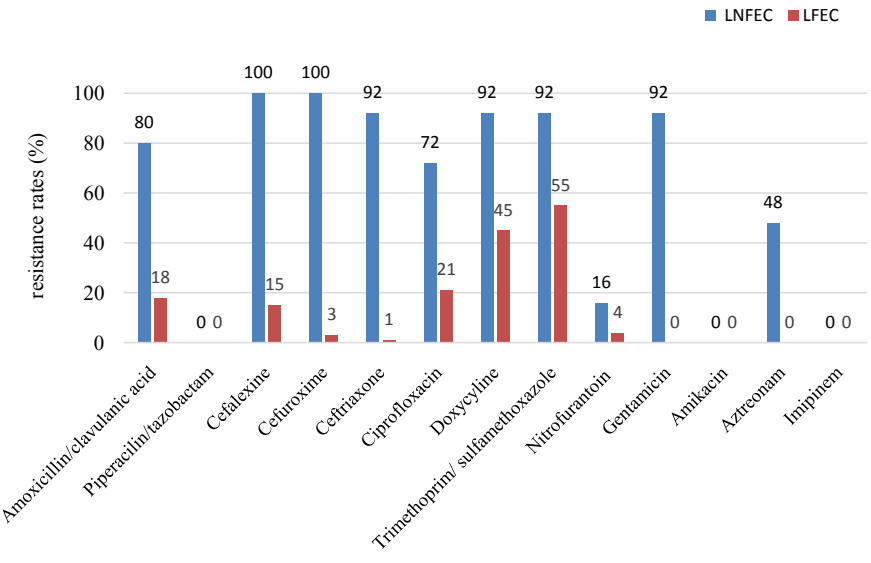

Figure 1. Antibiotic resistance rates (%) for Lactose Non-Fermenting *E. coli* (LNFEC) and Lactose Fermenting *E. coli* (LFEC) isolates.

non-fermenting *E. coli* causing urinary tract infections. The alarming level of multi-drug resistance to the first-choice drugs for the treatment of UTIs caused by lactose non-fermenting *E. coli* was detected. To our knowledge, this is the first study determined the antibiotic resistance pattern of in UTIs in Angola.

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Conflicts of Interest

The author declares that he has no competing interests.

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