MEDDOCS Open Access Publisher

ISSN: 2639-4391

Annals of Epidemiology and Public Health

Open Access | Research Article

Characteristics of Urinary Tract Infections Caused by *Escherichia Coli* Isolated from Community Patients in Londrina, Paraná, Brazil, From June 2016 to May 2019

Zuleica Naomi Tano[1]; Renato Rubia Garcia Junior[2]; Julia da Silva Pimenta[2]; Juliana Buck Dias[2]; Maria Julia Onça Moreira[2]; Sofia Rodrigues da Silva[2]; Ariane Tiemy Tizura[2]; Vanessa Koga[2]; João Gabriel Material Soncini[2]; Eliana Carolina Vespero[2]*

[1]Department of Internal Medicine - Health Sciences Center, State University of Londrina.

[2]Department of Pathology, Clinical Medicine and Toxicology - Center for Health Sciences, State University of Londrina.

***Corresponding Author(s): Eliana Carolina Vespero**

Department of Pathology, Clinical Medicine and Toxicology - Center for Health Sciences, State University of Londrina, Brazil.

Email: eliana.vespero@gmail.com

Received: Feb 04, 2023

Accepted: Feb 25, 2023

Published Online: Feb 28, 2023

Journal: Annals of Epidemiology and Public Health

Publisher: MedDocs Publishers LLC

Online edition: http://meddocsonline.org/

Keywords: Uropathogenic E. coli (UPEC), urinary tract infection s, extended-spectrum β-lactamases.

Abstract

Uropathogenic *E. coli* (UPEC) group, classified as Extraintestinal pathogenic *E. coli* (ExPEC), causes around 90% of community-acquired Urinary Tract Infections (UTIs). These strains have increased its level of antimicrobial resistance to frontline antibiotics due to the indiscriminate use of antimicrobials that exert a variety of selective pressure on pathogens, and because *Enterobacterales* can have plasmids capable of be transferred between strains - even between species - and these are able to carry genes that allows the resistance, which, in addiction, uses ESBLs as their most common mechanism of resistance. The aim of this study is to produce a survey that allows the trace of the epidemiological profile over the studied period in relation to the community UTI at Londrina city, Paraná, Brazil. A total of 22.810 samples from community patients in basic health units and emergency units, during June 2016 to May 2019, were analyzed. Although UTIs occur in both genders and in all age groups, its incidence is higher in women (91.9%) and increases with age, as noticed on the mean age among patients with ESBL-positive samples, 64 years old. These could possibly be factors for a higher rate of infections caused by resistant microorganisms and the worsening of the infection development, mainly due to the increased exposure to antibiotics, since ESBL producing *Enterobacterales* are frequently resistant to most of oral antibiotics used in the UTIs treatment, such trimethoprim, quinolones, cephalosporins and penicillins. Furthermore, there was a greater number of isolates resistant to both first and second choice drugs used in the treatments of UTIs among ESBL positive patients. By dint of that, it's necessary to know the profile of the main microorganisms and the local population, as different locations have unique characteristics that can directly influence

Cite this article: Zuleica NT, Garcia Junior RR, Julia da Silva P, Dias JB, Maria Julia OM, et al. Characteristics of Urinary Tract Infections Caused by *Escherichia Coli* Isolated from Community Patients in Londrina, Paraná, Brazil, From June 2016 to May 2019. A Epidemiol Public Health. 2023; 6(1): 1105.

the clinical and epidemiological conditions. Therefore, for that matter, the availability of comprehensive digital-data infrastructures can offer new opportunities to investigate the development of antimicrobial resistance spread. Antimicrobial resistance surveillance is necessary to determine the problem and to guide empirical selection of antimicrobial agents for UTIs treatment.

Introduction

Urinary Tract Infections (UTI) are the second most common bacterial infections, with the main etiological agent being Escherichia *coli (E. coli)*. That accounts for up to 80% of outpatient setting uncomplicated UTIs [1], generating a cost higher than 6 billion dollars worldwide [2].

Uropathogenic *E. coli* (UPEC) group, classified as Extraintestinal pathogenic *E. coli* (ExPEC) and responsible for around 90% of community-acquired UTIs, have increased its level of antimicrobial resistance to frontline antibiotics such as trimethoprim-sulfamethoxazole and ciprofloxacin [3]. This happens because the indiscriminate use of antimicrobials exert a variety of selective pressure on pathogens (RAJA,2019). Moreover, *Enterobacterales* can have plasmids capable of being transferred between strains - even between species -, and these may carry genes that allow the resistance to most antibiotics [4].

The most common resistance mechanism among *Enterobacterales* is Extended-Spectrum B-Lactamases (ESBLs), a group of enzymes that hydrolyzes the β-lactam presented in the antibiotic compound, turning them ineffective and providing resistance against a several antibiotics from β-lactams-group [5]. The increasing of such isolates have serious consequences for patients outcome, associated with high rates of morbidity and mortality, longer hospitalization and chances of developing further health problems, besides the higher health care costs compared with infectious diseases caused by not ESBL-producing *E. coli* [6].

The awareness about the local prevalence of ESBL-producing *Enterobacterales*, such as *E. coli* - most common among them responsible mainly for causing UTIs - and their antibiotic susceptibility profile may help to select effective antimicrobial treatments [7].

The aim of this study is to produce a survey capable of tracing the epidemiological profile over the studied period in relation to the community UTI at Londrina city, Paraná, Brazil, once the possibility to view the epidemiological and sociodemographic data of community patients with urinary tract infection may aid to create and manage actions capable of controlling and reducing the spread of resistance mechanisms commonly found in Multidrug-Resistant Enterobacteria (MDR).

Materials and Methods

From June 2016 to May 2019, 195.080 urine cultures were performed by public health services, in a city in southern Brazil. Urocultures were performed at Central Laboratory of Londrina city (CentroLab), plating 10µL of urine samples into chromogenic agar, (chromID® CPS® agar, bioMérieux, Marcy-l'Étoile, France). *E. coli* strains were identified using Gram negative panels and their susceptibility was tested according to a breakpoint method using AST238 panel by Vitek® 2 automated system by Biomérieux (Marcyl'Etoile, France). Antimicrobial susceptibility profile was analyzed according to the Clinical and Laboratory Standards Institute (CLSI).

Patients with incomplete data about antibiogram or microorganism identification on the system and patients with repeated tests within six months, with the same susceptibility profile, were excluded from this study

This study was approved by the Ethics and Research Committee of the State University of Londrina CAAE 56869816.0.0000.5231 and authorized by the Health Department of Londrina city, Paraná.

Demographic data analysis

Demographic data including age, gender, pregnancy, and basic health units were collected from WebSaude system, a Londrina city hall interfacing system, which contains sociodemographic and epidemiological data from all basic health units in Londrina city.

Statistical analysis

Statistical analysis and graphical representation were performed using Statistical Package for Social Sciences (SPSS - IBM Corp., New York, USA), twentieth version for Windows. Categorical data were shown by frequency and percentage. The analysis was performed by Chi-square test or Fischer's exact test as needed. Alpha significance level was 0.05.

Results and discussion

A total of 34.293 samples were positive for gram-positive or gram-negative microorganisms; of these 22.810 (66,2%) were *E. coli* strains and a total of 2.033 (6,2%) were ESBL producing bacteria, being 1.480 (61,2%) ESBL production *E. coli*. Among the 22,810 samples analyzed, 91.9% (20.965) belong to women while 8.1% (1,845) to men. Of such, 6.5% (1,489) tested positive for the presence of ESBL, 85% (1,258) for females and 15% (222) for males, a significant statistical difference (p> 0.01).

Although it's a disease that affects both men and women, UTIs are traditionally more correlated to women, among whom 50% will be affected across their lives and around 25% of women presenting with a first episode of bacterial cystitis proceeds to suffer recurrent UTI within 6 months, contracting

until 6 or more infections in the year following the initial episode. This higher prevalence of UTI in females is attributed to anatomic factors, such as shorter urethral length and shorter distance from the anus to urethral meatus in women, additionally of the vaginal and perineal environments permissiveness to microbial colonization [8]. Besides that, as the most common therapeutic approach to UTI is the use of antibiotics and women with recurrent UTI often require multiple antibiotic regimens within short periods of time, this indiscriminate use of antibiotics increases women's risk of developing antibiotic resistance [9].

Recent data have demonstrated sharped increases in bacterial resistance to first line antibiotics used to treat UTI in ambulatory settings. Resistance has been associated with increased microbiologic and clinical failure. Nonadherence to guidelines for UTI treatment can result in decreased effectiveness of antibiotics (due to development of resistance) and increased health care costs [10]. For treatment of acute patients, uncomplicated UTI, first-line antibiotics include nitrofurantoin, trimethoprim-sulfamethoxazole and fosfomycin trometamol. These have low collateral damage (selection for drug-resistant organisms), high efficacy, and good resistance profiles. Due to higher resistance in certain populations, trimethoprim-sulfamethoxazole is only

used as a first line drug if local resistance rates are not >20% [7,10]. In this study, cephalotin and trimethoprim-sulfamethoxazole, even in the non-ESBL group, showed more than 20% of resistant samples and is not advisable for empirical treatment of UTIs.

While ESBL producing *E. coli* infections in health care settings have been highlighted as an major issue for many years, the emergence of ESBL producing *E. coli* infections in the community has only recently been recognized. Since its initial description, the incidence of community-onset ESBL producing *E. coli* infections has increased significantly. A study performed in Switzerland reported an increase in ESBL producing *E. coli* prevalence among outpatients from 0.9% in 2004 to 5.3% in 2011.

In this study 20,965 female patients, 1,853 (8.8%) were pregnant and from these, 80 (4.3%) tested positive for the presence of ESBL, while among the 19,112 (91.2%) non-pregnant women, the number of positive ESBL was 1,178 (6.2%) samples, a statistically relevant result, with a p-value <0.01.

In pregnancy, bacteriuria can also lead to complications such as pyelonephritis, urosepsis, and increased risk of preterm birth [10]. A possible explanation for this is that, although it is less common, some UTIs can get worse when it's associated with a structural or functional abnormality (urinary obstruction, neurologic disease, immunosuppression, renal dysfunction, or catheterization), as well as those that occur in women during pregnancy [9].

The mean age among patients with ESBL-positive samples was 64,00 (40,00-76,00), higher than patients with ESBL-negative samples, which was 50,00 (29,00-68,00). Furthermore, 37,5% (8,553) of all patients were over 61 years old, and both groups in the range of 61-75 and >75 years old have greater positivity for ESBL, with 55,4% (820) of all positive patients samples. Additionally, it was possible to notice that the number of positive samples for ESBL in this study increased according to the age of the patients.

A possible relation between older women and the increase in cases of UTIs is that, in premenopausal women, vaginal flora is predominated by lactobacilli, responsible for the relatively acidic pH of the vagina. Otherwise, the acidic environment is lost in postmenopausal women, generating a loss of estrogen and enabling the increased colonization and infection by *E. coli* and enterococcus species [11].

In older men, a risk factor for UTIs is the benign prostatic hypertrophy [11]. This disease can cause urethral obstruction and turbulent urine flow, which facilitates ascension of organisms into the bladder, being a source for recurring cystitis or febrile urinary infection for some men. Among healthy men younger than 60 years old, asymptomatic bacteriuria is unusual, but between men older than 80 years, 5% to 10% have bacteriuria, evolving into complication in patients with functional or structural abnormalities of the genitourinary tract [12].

Elderly people with genitourinary abnormalities that impair voiding, which can even lead to urinary incontinence, have an increased frequency of UTIs and bacterial strains isolated from older subjects. In addition, those patients may have an increased frequency of resistance relative to younger populations because of repeated prior antimicrobial courses and health care exposures, including urologic interventions in subjects with complicated infection [12].

All the data above are shown in table 1.

Table 1: Sociodemographic data of patients with urinary E.coli isolates according to the presence of ESBL at Londrina city, Paraná, Brazil, from June 2016 to May 2019.

		ESBL				
		Susceptible (n=21330)		Resistant (n=1480)		p
Age (average in years)		50,00 (29,00-68,00)		64,00 (40,00-76,00)		<0.001
Age (age range)	0-15	1677	7,9%	70	4,7%	<0.001
	16-30	4003	18,8%	178	12,0%	
	31-45	3652	17,1%	190	12,8%	
	46-60	4265	20,0%	222	15,0%	
	61-75	4774	22,4%	442	29,9%	
	>75	2959	13,9%	378	25,5%	
Gender	Female	19707	92,4%	1258	85,0%	<0.001
	Male	1623	7,6%	222	15,0%	
Pregnancy	Non pregnant	17934	91,0%	1178	93,6%	<0.001
	Pregnant	1773	9,0%	80	6,4%	

Categorical data were shown in absolute number (n) and percentage (%) and continuous data in mean and. standard deviation.

Table 2: Antimicrobial resistance profile of patients with urinary *E.coli* isolates in the city of Londrina, from June 2016 to May 2019.

		ESBL				
		Susceptible (n=21330)		Resistant (n=1480)		p
First choice antibiotic						
Nalidixic Acid	Susceptible	15005	70,4%	370	25,0%	<0.001
	Resistant	6315	29,6%	1109	75,0%	
Ampicillin	Susceptible	11395	53,4%	0	0,0%	<0.001
	Resistant	9930	46,6%	1477	100,0%	
Cephalotin	Susceptible	10699	50,2%	0	0,0%	<0.001
	Resistant	10624	49,8%	1479	100,0%	
Ciprofloxacin	Susceptible	17546	82,3%	518	35,0%	<0.001
	Resistant	3764	17,7%	961	65,0%	
Nitrofurantoin	Susceptible	20373	95,6%	1277	86,3%	<0.001
	Resistant	944	4,4%	202	13,7%	
Norfloxacin	Susceptible	17568	82,4%	519	35,1%	<0.001
	Resistant	3758	17,6%	960	64,9%	
Sulfamethoxazole/Trimetropim	Susceptible	15037	70,7%	654	44,4%	<0.001
	Resistant	6245	29,3%	818	55,6%	
Second choice antibiotic						
Amikacin	Susceptible	21273	99,8%	1452	98,1%	<0.001
	Resistant	53	0,2%	28	1,9%	
Amoxicillin Clavulanic Acid	Susceptible	18601	87,2%	831	56,1%	<0.001
	Resistant	2726	12,8%	649	43,9%	
Cefepime	Susceptible	21249	99,6%	15	1,0%	<0.001
	Resistant	79	0,4%	1465	99,0%	
Ceftriaxone	Susceptible	21159	99,2%	0	0,0%	<0.001
	Resistant	166	0,8%	1480	100,0%	
Cefuroxime	Susceptible	19904	93,4%	0	0,0%	<0.001
	Resistant	1417	6,6%	1479	100,0%	
Ertapenem	Susceptible	21285	99,8%	1444	97,6%	<0.001
	Resistant	36	0,2%	36	2,4%	
Gentamycin	Susceptible	20105	94,3%	1098	74,2%	<0.001
	Resistant	1224	5,7%	381	25,8%	
Piperacycline Tazobactam	Susceptible	20565	97,5%	1193	83,1%	<0.001
	Resistant	520	2,5%	242	16,9%	
Meropenem	Susceptible	21274	99,8%	1448	98,0%	<0.001
	Resistant	35	0,2%	30	2,0%	

Table 2 shows that there was a greater number of resistance isolates to both first and second choice drugs used in the treatments of UTIs among ESBLpositive patients. These samples could hydrolyze the rings present in β-lactam drugs, thus conferring resistance to antimicrobials such as penicillins, cephalosporins and aztreonam. ESBL producing Enterobacterales are frequently resistant to most of the oral antibiotics used in the UTIs treatment, such as trimethoprim, quinolones, cephalosporins and penicillins. Thereafter there's an urgent need for Discovery of new antimicrobials and as a consequence of that, the rediscovery of forgotten antibiotics such as fosfomycin a bactericidal antimicrobial agent which has a good activity against Gram positive and negative organisms - and nitrofurantoin which has been used for the last 50 years to treat UTIs- are being helpful until the emergence of new antimicrobial agents [2].

The enhanced resistance of prompter of UTIs microorganisms isassociated with increased mortality, morbidity, health costs, and, subsequently,there is often a need for the introduction of broad-spectrum antimicrobials [13].

Conclusions

UTIs occur in both genders and in all age groups, however, as noticed in the study, its incidence is higher in women and increases with age. These factors are also possible predisposing agents for a higher rate of infections caused by resistant microorganisms and the worsening of the development of the infection, mainly due to the increased exposure to the use of antibiotics.

Thus, resistance to antibiotics previously presented exclusively in the hospital environment, is now also found in community patients, which makes it increasingly difficult to manage and treat these infections, since pharmacological options are scarce.

In order to deal with this situation, it's necessary to be aware of the profile of the main microorganisms and local population, considering that different locations have particular characteristics, which can directly influence the clinical and epidemiological conditions. For this, the availability of comprehensive digital-data infrastructures can offer new opportunities to investigate the development of antimicrobial resistance spread.

Antimicrobial resistance surveillance is necessary to determine the problem and, therefore, to guide empirical selection of antimicrobial agents for UTIs.

Acknowledgment

This work was completely supported by the Bill & Melinda Gates Foundation (number OPP1193112). Under the grant conditions of the Foundation, a Creative Commons Attribution 4.0 Generic License has already been assigned to the Author Accepted Manuscript version that might arise from this submission. The Grant is part of Grand Challenges Explorations Brazil—New Approaches to Characterize the Global Burden of Antimicrobial Resistance (OPP1193112).

References

1. Kang CI, Kim J, Park DW, Kim BN, Ha US, et al. Clinical practice guidelines for the antibiotic treatment of community-acquired urinary tract infections. Infection and Chemotherapy. 2018; 50: 67-100.

2. RAJA NS. Oral treatment options for patients with urinary tract infections caused by extended spectrum βeta-lactamase (ESBL) producing Enterobacteriaceae. Journal of Infection and Public Health. 2019; 12: 843-846.

3. ALQASIM A, ABU JAFFAL A, ALYOUSEF AA. Prevalence of multidrug resistance and extended-spectrum β -Lactamase carriage of clinical uropathogenic Escherichia coli isolates in Riyadh, Saudi Arabia. International Journal of Microbiology. 2018; 2018.

4. Lee DS, Lee SJ, Choe HS. Community-Acquired Urinary Tract Infection by Escherichia coli in the Era of Antibiotic Resistance. BioMed Research International. 2018; 2018.

5. Kuster SP, Hasse B, Huebner V, Bansal V, Zbinden R, et al. Risks factors for infections with extended-spectrum beta-lactamase-producing escherichia coli and klebsiella pneumoniae at a tertiary care university hospital in Switzerland. Infection. 2010; 38: 33-40.

6. ROTTIER WC, AMMERLAAN HSM, BONTEN MJM. Effects of confounders and intermediates on the association of bacteraemia caused by extended-spectrum b -lactamase-producing Enterobacteriaceae and patient outcome: a meta-analysis. 2012; 131-1320.

7. Gupta K, Hooton TM, Naber KG, Wullt B, Colgan R, et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. Clinical Infectious Diseases. 2011; 52: 103-120.

8. MCLELLAN LK, HUNSTAD DA. Urinary Tract Infection: Pathogenesis and Outlook. Trends in Molecular Medicine. 2016; 22: 946-957.

9. Fu Z, Liska D, Talan D, Chung M, et al. Cranberry Reduces the Risk of Urinary Tract Infection Recurrence in Otherwise Healthy Women: A Systematic Review and and Meta-Analysis. J Nutr. 2017; 147: 2282-2288.

10. CHU CM, LOWDER JL. Diagnosis and treatment of urinary tract infections across age groups. American Journal of Obstetrics and Gynecology. 2018; 219: 40-51.

11. DETWEILER K, MAYERS D, FLETCHER SG. Bacteruria and Urinary Tract Infections in the Elderly. Urologic Clinics of North America. 2015; 42: 561-568.

12. NICOLLE LE. Urinary Tract Infections in the Older Adult. Clinics in Geriatric Medicine. 2016; 32: 523-538.

13. Koksal E, Tulek N, Sonmezer MC, Temocin F, Bulut C, et al. Investigation of risk factors for community-acquired urinary tract infections caused by extended-spectrum beta-lactamase Escherichia coli and Klebsiella species. Investigative and Clinical Urology. 2019; 60: 46- 53.