> ACESSE AOUI A REVISTA ONLINE

## SHORT COMMUNICATION

# Urinary microbiological profile from a referral hospital for the healthcare of women in Recife, Brazil

Perfil microbiológico urinário de um hospital referência para assistência à mulher em Recife, Brasil

Perfil microbiológico urinario de un hospital de referencia para la atención médica de mujeres en Recife, Brasil

Danylo César Correia Palmeira,¹ Amanda Vieira da Silva Melo,¹ Débora Ellen Pessôa Lima Serra,² Claudia Fernanda Azevedo Braga Albuquerque,¹ Thiago Augusto Maciel,³ Vinicius Vianney Feitosa Pereira,³ Claudia Fernanda de Lacerda Vidal.¹ Hospital das Clínicas, EBSERH, Universidade Federal de Pernambuco, Recife, PE, Brasil. ² Hospital Universitário Oswaldo Cruz- Universidade de Pernambuco, Recife, PE, Brasil. ³ Hospital Correia Picanço, Recife, PE, Brasil.

**Recebido em:** 22/09/2019 **Aceito em:** 02/10/2019 **Disponível online:** 30/12/2019

Autor correspondente: Danylo César Correia Palmeira dccpalm@gmail.com

### **ABSTRACT**

Urinary tract infections (UTIs) mainly affect women. We described microbial susceptibility of isolates from community urine samples of women aged between 18 and 60, treated at a hospital in Recife, Brazil, from May 2017 to May 2018. Isolates were tested by disk-diffusion. Of the 121 samples, Escherichia coli (40.5%), Klebsiella pneumoniae (19.0%) and Streptococcus agalactiae (17.3%) were isolated. Resistance in Gram-negative bacilli was observed to ampicillin, cephalexin, sulfamethoxazole-trimethoprim and nitrofurantoin (>30%); and ceftriaxone (7.7%). We identified 9.3% ESBL microorganisms and no ampicillin or vancomycin resistant Enterococcus sp. We recommend amoxicillin-clavulanate and ceftriaxone for the treatment of community-acquired UTIs in women.

**Keywords:** Urinary Tract Infections. Bacteriuria. Drug Resistance, Microbial.

## **RESUMO**

As infecções do trato urinário (ITU) afetam principalmente as mulheres. Descrevemos a suscetibilidade microbiana de isolados de amostras comunitárias de urina de mulheres

com idade entre 18 e 60 anos, atendidas em um hospital de Recife, Brasil, de maio de 2017 a maio de 2018. Os isolados foram testados por difusão de disco. Das 121 amostras, *Escherichia coli* (40,5%), *Klebsiella pneumoniae* (19,0%) e *Streptococcus agalactiae* (17,3%) foram isolados. Foi observada resistência em bacilos Gram-negativos à ampicilina, cefalexina, sulfametoxazol-trimetoprim e nitrofurantoína (> 30%); e ceftriaxona (7,7%). Identificamos 9,3% de microorganismos ESBL e *Enterococcus* sp resistente a ampicilina ou vancomicina. Recomendamos amoxicilina-clavulanato e ceftriaxona para o tratamento de ITUs adquiridas na comunidade em mulheres.

**Palavras-chave:** Infecções do trato urinário. Bacteriúria. Resistência Microbiana a Medicamentos.

## RESUMEN

Las infecciones del tracto urinario (ITU) afectan principalmente a las mujeres. Describimos la susceptibilidad microbiana de los aislamientos de muestras de orina comunitarias de mujeres de entre 18 y 60 años, tratadas en un hospital en Recife, Brasil, de mayo de 2017 a mayo de 2018. Los aislamientos se analizaron por difusión en disco. De las 121 muestras, se aisló *Escherichia coli* (40.5%), *Klebsiella pneu-*

moniae (19.0%) y Streptococcus agalactiae (17.3%). Se observó resistencia en bacilos gramnegativos a ampicilina, cefalexina, sulfametoxazol-trimetoprima y nitrofurantoína (> 30%); y ceftriaxona (7.7%). Identificamos 9.3% de microorganismos BLEE y ninguna ampicilina o Enterococcus sp resistente a vancomicina. Recomendamos amoxicilina-clavulanato y ceftriaxona para el tratamiento de infecciones urinarias adquiridas en la comunidad en mujeres.

**Palabras clave:** Infecciones del tracto urinario. Bacteriuria Resistencia a medicamentos, microbianos.

## COMMUNICATION

Urinary tract infections (UTIs) represent one of the principle community-acquired infections, and are a frequent cause for seeking emergency services and empiric antibiotic prescribing. Women are more prone to UTIs than men. The emergence of multidrug-resistant bacteria (MDR) has become a major public health problem worldwide. The phenomenon of antimicrobial resistance is not restricted to the hospital environment and health institutions. Surveillance of the local microbiota, sensitivity profiles and the dissemination of MDR isolates has become possible to adapt protocols for empirical therapy in UTIs in order to reduce morbimortality and prevent antimicrobial resistance. The aim of this study is to describe the microbiological profile and antimicrobial susceptibility of bacterial isolates in female urine samples from community.

We conducted a retrospective study with urine samples obtained from patients treated at the emergency department and clinics of a reference hospital for women in Recife-PE, from May, 2017 to May, 2018. Samples of patients outside the age range of the study (18 to 60 years) were excluded. The bacterial isolates were identified by manual biochemical tests and the antimicrobial susceptibility was conducted by disk-diffusion, according to EUCAST, 2017. We used broth microdilution to classify the Enterobacteriaceae isolates for susceptibility to polymyxin.

From the 157 urine cultures obtained, 121 samples were selected. The mean age was 40.90±10.99 years (median: 41.00). Eighty-six (71.1%) Gram-negative bacilli (GNB) were isolated, with a predominance of *Escherichia coli* 49 (40.5%) and *Klebsiella pneumoniae* 23 (19.0%); and 35 (28.9%) Gram-positive cocci, amongst which 21 (17.3%) were *Streptococcus agalactiae*. We identificated 8 (6.6%) non-fermenting Gram-negative bacilli (NFGNB). No species of *Candida sp* were isolated (Table 1).

Analysis of the overall antimicrobial resistance of Gram-negative uropathogens indicated a high level of

**Table 1.** Microbiological profile of bacterial isolates in community urine samples at a referral hospital for the healthcare of women in Recife, Brazil.

Microorganism	n (%)	
Enterobacteriaceae	78 (64.5)	
Escherichia coli	49 (40.5)	
Klebsiella pneumoniae	23 (19.0)	
Providencia rettgeri	6 (5.0)	
Gram-negative non-fermenters	8 (6.6)	
Acinetobacter baumannii	4 (3.3)	
Pseudomonas aeruginosa	4 (3.3)	
Gram-positives	35 (28.9)	
Streptococcus agalactiae	21 (17.3)	
Staphylococcus aureus	6 (5.0)	
Staphylococcus saprophyticus	3 (2.5)	
Enterococcus faecalis	5 (4.1)	

resistance (greater than 30%) to ampicillin, cephalexin, sulfamethoxazole/trimethoprim and nitrofurantoin. The rate of resistance to ceftriaxone in Enterobacteriaceae, excluding non-fermenting GNB, was 7.7% (6/78). We identified eight phenotypes of extended-spectrum beta-lactamases (ESBL) (8/86, 9.3%) and a *Providencia rettgeri* isolate producing AmpC beta-lactamase. No resistance was observed to carbapenems and polymyxins. All NFBGN were sensitive to ciprofloxacin (Table 2).

**Table 2.** Antimicrobial susceptibility profile of Gram-negative bacilli isolated from community urine samples in a reference hospital for the healthcare of women in Recife, Brazil.

Antimicrobials	No. of susceptible isolates, n (%) N= 86
Colistin	86 (100)
Meropenem	86 (100)
Ertapenem	86 (100)
Amikacin	85 (98.8)
Piperacillin-Tazobactam	85 (98.8)
Cefepime	78 (90.7)
Gentamicin	77 (89.5)
Ceftazidime	76 (88.4)
Aztreonam	74 (86.0)
Ceftriaxone	72 (83.7)
Ciprofloxacin	71 (82.6)
Amoxicillin-Clavulanate	71 (82.6)
Nitrofurantoin	60 (69.8)
Sulfamethoxazole-Trimethoprim	52 (60.5)
Cefalexin	44 (51.2)
Ampicillin	28 (32.6)

Only one isolate of *S. agalactiae* was resistant to ampicillin, but was sensitive to cephalosporins and quinolones. All six isolates of *Staphylococcus aureus* were sensitive to oxacillin and one isolate of *Staphylococcus saprophyticus* was resistant to oxacillin. The overall rate of oxacillin resistance was 11.1% (1/9). All staphylococci were susceptible to clindamycin, levofloxacin and nitrofurantoin. The five isolates of *Enterococcus faecalis* were sensitive to ampicillin. No vancomycin-resistant enterococci (VRE) were identified (Table 3).

**Table 3.** Antimicrobial susceptibility profile of Gram-positive cocci isolated from community urine samples at a reference hospital for the healthcare of women Recife, Brazil.

Antimicrobials	No. of susceptible isolates, n (%)
Streptococcus agalactiae	
Penicillin	21 (100)
Erythromycin	21 (100)
Levofloxacin	21 (100)
Ampicillin	20 (95.2)
Clindamycin	19 (90.5)
Ceftriaxone	19 (90.5)
Staphylococcus aureus	
Oxacillin	6 (100)
Clindamycin	6 (100)
Levofloxacin	6 (100)
Nitrofurantoin	6 (100)
Vancomycin	6 (100)

Sulfamethoxazole-Trimethoprim	4 (66.7)	
Staphylococcus saprophyticus		
Clindamycin	3 (100)	
Levofloxacin	3 (100)	
Nitrofurantoin	3 (100)	
Vancomycin	3 (100)	
Oxacillin	2 (66.7)	
Sulfamethoxazole-Trimethoprim	2 (66.7)	
Enterococcus faecalis		
Ampicillin	5 (100)	
Gentamicin	5 (100)	
Nitrofurantoin	5 (100)	
Vancomycin	5 (100)	
Levofloxacin	4 (80.0)	

UTIs are generally caused by Gram-negative bacteria, mainly Enterobacteriaceae, and also by Gram-positive bacteria, such as S. saprophyticus, E. faecalis and S. agalactiae. According to the literature, E. coli is responsible for around 75 to 90% of UTIs, which are higher rates than observed in this study (40.5%). On the other hand, infections caused by K. pneumoniae, around 10%, are lower than the 19% observed. UTIs by Gram-positive bacteria are more frequent in specific demographic groups, such as pregnant women and older people. The studied hospital is referral for the healthcare of women, especially prenatal and senescent follow-up, which may explain the 28.9% isolated Gram-positive cocci. S. aureus bacteriuria is also associated with pregnancy. It is estimated that rates of oxacillin-resistant Staphylococcus spp. are between 1-8% in urinary isolates.<sup>5</sup> Our analyzes revealed an overall rate of 11.1%.

The high prevalence of GNB producing beta-lactamases in the community confirms the progressive increase of levels of resistance to ampicillin over the years. The rates of ESBL-producing Enterobacteriaceae in the community range from 1.7-16.3%. Our results are in line with this data with a frequency of 9.3%. In 2009 in Curitiba, Brazil, low susceptibility to ampicillin (56%) and sulfamethoxazole (66%) were identified and endorsed rates of susceptibility to ceftriaxone (97%), gentamicin (93%) and fluoroquinolones (82%).

The highest sensitivity rates of oral antibiotics for UTIs were observed in amoxicillin-clavulanate (82.6%) and ciprofloxacin (82.6%). Fluoroquinolones are recommended for the treatment of UTIs. However, they should be avoided as a first choice for cystitis, since they are parenteral alternatives for pyelonephritis.<sup>3,4</sup> In 2018, an alert regarding the risks of irreversible adverse effects and induction of antimicrobial resistance have been raised concerning the use of quinolones.<sup>8</sup>

A limit resistance rate for empirical use of an antimicrobial is up to 10%. Thus, our study corroborates with the indication of ceftriaxone as the first option for parenteral treatment of complicated community-acquired ITUs, since the resistance rate was 7.7%. The low level of resistance to aminoglycosides makes this class a therapeutic alternative. However, because of its adverse effects and it is active against isolates resistant to carbapenems, it should be used judiciously. The carbapenems resistance levels found are similar to those found in the US and Europe. 6,10

Amongst the limitations of this study, we emphasize the insufficiency of data to classify the bacteriuria in colonization or infection, the lack of analysis on the clinical outcomes obtained with the antimicrobial regimens used and the unavailability of a sensitivity test for fosfomycin.

According to our study, we recommend amoxicillin-clavulanate and ceftriaxone as empirical therapeutic

options for the treatment of community-acquired UTIs in women aged between 18 and 60. Although they are still options, we recommend a restricted use of fluoroquinolones. The observed changes in the sensitivity profiles and the presence of ESBL-producing isolates in the community reinforce the need to continuously monitor the microbiota in order to develop protocols consistent with the local reality and the rational use of antimicrobials.

## CONFLICT OF INTERESTS

No conflicts of interests.

#### FINANCIAL SUPPORT

This study received no external funding.

#### REFERENCES

- 1. Flores-Mireles AL, Walker JN, Caparon M, et al. Urinary tract infections: epidemiology, mechanisms of infection and treatment options. Nat Rev Microbiol 2015;13(5):269–84. doi: 10.1038/nrmicro3432
- 2. Ben Ayed H, Koubaa M, Hammami F, et al. Performance of an easy and simple new scoring model in predicting multidrug-resistant Enterobacteriaceae in community-acquired urinary tract infections. Open Forum Infect Dis 2019;6(4):ofz103. doi: 10.1093/ofid/ofz103
- 3. Bader MS, Loeb M, Brooks AA. An update on the management of urinary tract infections in the era of antimicrobial resistance. Postgrad Med. 2017;129(2):242–58. doi: 10.1080/00325481.2017.1246055
- 4. Nicolle LE. Urinary tract infection. Crit Care Clin 2013;29(3):699-715. doi: 10.1016/j.ccc.2013.03.014
- 5. Kline KA, Lewis AL. Gram-positive uropathogens, polymicrobial urinary tract infection, and the emerging microbiota of the urinary tract. Microbiol Spectr 2016;4(2). doi: 10.1128/microbiolspec.UTI-0012-2012
- Sader HS, Flamm RK, Jones RN. Frequency of occurrence and antimicrobial susceptibility of Gram-negative bacteremia isolates in patients with urinary tract infection: results from United States and European hospitals (2009–2011). J Chemother 2014;26(3):133–8. doi: 10.1179/1973947813Y. 0000000121
- 7. Salles MJC, Zurita J, Mejía C, et al. Latin America Working Group on Bacterial Resistance. Resistant Gramnegative infections in the outpatient setting in Latin America. Epidemiol Infect 2013;141(12):2459–72. doi: 10.1017/S095026881300191X
- 8. Disabling and potentially permanent side effects lead to suspension or restrictions of quinolone and fluoroquinolone antibiotics [Internet]. Europe: European Medicines Agency. Inc.; EMA/175398/2019 [updated 2019 Mar 19; cited 2018 Nov 16]. Available from: https://www.ema.europa.eu/en/news/disabling-potentially-permanent-side-effects-lead-suspension-restrictions-quinolone-fluoroquinolone
- 9. Rank EL, Lodise T, Avery L, et al. Antimicrobial susceptibility trends observed in urinary pathogens obtained from New York State. Open forum Infect Dis 2018;5(11):ofy297. doi: 10.1093/ofid/ofy297
- 10. Cantón R, Loza E, Aznar J, et al. Monitoring the antimicrobial susceptibility of Gram-negative organisms involved in intraabdominal and urinary tract infections recovered during the SMART study (Spain, 2016 and 2017). Rev Esp Quimioter 2019;32(2):145-55.