Analysis of recurrent urinary tract infection (UTI) in University Hospital – approach of antibiotic resistance in clinical isolates

Análise da infecção recorrente do trato urinário (ITU) em Hospital Universitário – abordagem da resistência a antibióticos em isolados clínicos

Análisis de la infección del tracto urinario (ITU) recurrente en un Hospital Universitario – Aproximación a la resistencia antibiótica en aislados clínicos

Received: 06/08/2022 | Reviewed: 06/20/2022 | Accept: 07/12/2022 | Published: 07/19/2022

Danilo Antonini Alves
ORCID: https://orcid.org/0000-0002-0375-0400
University of Campinas, Brazil
E-mail: daniloantonini87@gmail.com

João Paulo de Oliveira Guarnieri
ORCID: https://orcid.org/0000-0003-3098-5851
University of Campinas, Brazil
E-mail: joaopauloguarnieri@gmail.com

Bruno Gaia Bernardes
ORCID: https://orcid.org/0000-0001-7631-3458
University of Campinas, Brazil
E-mail: brunogaiabernardes@gmail.com

Carlos Fernando Macedo da Silva
ORCID: https://orcid.org/0000-0003-2366-6748
University of Campinas, Brazil
E-mail: nandomacedo42@gmail.com

Marcelo Lancellotti
ORCID: https://orcid.org/0000-0002-4257-1034
University of Campinas, Brazil
E-mail: marcelo.lancellotti@fcf.unicamp.br

Abstract
The fifty-two bacteria were isolated from urinary tract infections in University Hospital in Sumaré, São Paulo State, Brazil. These isolates were analyzed about their antibiotic resistance and their bacterial characteristics. Around percentage from these isolates were identified as belonging to Escherichia coli strains, followed by Klebsiella pneumoniae and Pseudomonas aeruginosa. The multiresistance profile (resistance profile major than four 4 antibiotic classes) were viewed in thirteen (13) strains of Escherichia coli, sixteen (16) strains in Klebsiella pneumoniae (being two (2) carbapenem resistant suggesting an existence of KPC strain). The results had demonstrated an indiscriminate antibiotic use concentrated in the increase of quinolones resistance (principally in ciprofloxacin use), and also the rise of KPC super bacteria.

Keywords: Urinary tract infection; Antibiotic resistance; Multiresistant bacteria; UTI.

Resumo
As cinquenta e duas bactérias foram isoladas de infecções do trato urinário no Hospital Universitário de Sumaré, São Paulo, Brasil. Esses isolados foram analisados quanto a sua resistência a antibióticos e suas características bacterianas. Uma porcentagem desses isolados foram identificados como pertencentes a cepas de Escherichia coli, seguidas por Klebsiella pneumoniae e Pseudomonas aeruginosa. O perfil de multirresistência (perfil de resistência maior que quatro 4 classes de antibióticos) foi visualizado em treze (13) cepas de Escherichia coli, dezesseis (16) cepas de Klebsiella pneumoniae (sendo duas (2) resistentes a carbapenem sugerindo a existência de cepa KPC). Os resultados demonstraram um uso indiscriminado de antibióticos concentrado no aumento da resistência às quinolonas (principalmente no uso de ciprofloxacina), e também o surgimento de superbactérias KPC.

Palavras-chave: Infecção do trato urinário; Resistência a antibiótico; Bactéria multiresistente; ITU.

Resumen
Las cincuenta y dos bacterias fueron aisladas de infecciones del tracto urinario en el Hospital Universitario de Sumaré, Estado de São Paulo, Brasil. Esos fueron analizados por su resistencia a los antibióticos y características bacterianas. Un porcentaje de aislamientos se identificaron como de Escherichia coli, Klebsiella pneumoniae y Pseudomonas
aeruginosa. El perfil de resistencia a múltiples fármacos (perfil de resistencia superior a cuatro clases de antibióticos) se visualizó en trece (13) muestras de Escherichia coli, dieciséis (16) muestras de Klebsiella pneumoniae (dos (2) resistentes a carbapenem, lo que sugiere la existencia de una cepa KPC). Los resultados muestran uso indiscriminado de antibióticos enfocado a aumentar la resistencia a las quinolonas (principalmente en el uso de ciprofloxacino), y también la aparición de superbacterias KPC.

**Palabras clave:** Infección del tracto urinario; Resistencia antibiótica; Bacterias multirresistentes; ITU.

### 1. Introduction

In recent years, bacterial resistant infections have become a global health challenge and threaten the health of societies (Khameneh, et al., 2016; Riley, et al., 2012; Anes, et al., 2015; Nischal, 2014; Zhu, et al., 2022; Sakeena, et al., 2018). Due to emergence of resistant infections, existing antibacterial drugs have become less effective or even ineffective; this has led to development of new antibacterial drugs (Khameneh, et al., 2016). Also, quinolones are one of the most commonly prescribed classes of antibacterial in the world and are used to treat a variety of bacterial infections in humans (Aldred KJ, 2014). Ciprofloxacin was the first quinolone that displayed significant activity outside of the urinary tract (Aldred KJ, 2014; Emmerson & Jones, 2003; Mitscher, 2005; Andriole, 2005; Stein, 1988; Silva, et al., 2022; Li, et al., 2022).

The clinical success of ciprofloxacin spawned an array of newer-generation quinolones that displayed an even broader spectrum of activity, especially against Gram-positive species (Aldred KJ, 2014; Emmerson & Jones 2003; Mitscher, 2005; Andriole, 2005; Stein, 1988). Due to the development of antibiotic resistance and the outbreak of infectious diseases caused by resistant pathogenic bacteria, pharmaceutical companies and researchers are now searching for new unconventional antibacterial agents. The demand for individualized therapy and lower risks of adverse effects has always been a goal for health professionals. Besides, new pharmaceutical formulations seeking to increase efficiency and reduce drug toxicity are currently being researched (Nebert, et al., 2008; Audrey, 2014).

### 2. Methodology

The fifty-two (52) strains were isolated as described in the NCCSL protocols and growth in Brain Heart Infusion Agar (BHI Agar) in LABIOTEC (Alves, et al, 2016; Cavalieri, 2005; Santos, 2015; NCCLS, 2004; Baym, et al., 2016; Gajic, et al., 2022). The collection was identified as thirty-two (32) Escherichia coli strains, twenty-eight (28) Klebsiella pneumoniae strains and 1 Pseudomonas aeruginosa strain. The antibiotic resistance was tested in Mueller Hinton Agar, where it was purchased from AccuMedia (Neogen Corporation, Lansing, MI, USA), using the antibiotics disks. For the test were used AMI: Amikacin, APS: Ampicillin/Sublactam, AMP: Ampicillin, AZM: Aztreonam, CFL: Cephalothin, CPM: Cefepime, CXC: Cefotaxime/clavulanate, CFN: Cefotetan, CAZ: Ceftazidime CAC: Ceftazidime/ clavulanate, CFT: Ceftriaxone, CFR: Cefuroxime, CIP: Ciprofloxacin, ERT: Ertapenem, GEN: Gentamicin, IMP: Imipenem, LEV: Levofloxacin, MPM: Meropenem, NIT: Nitrofurantoin, PIT: Piperacillin/Tazobactam, PIP: Piperacillin, TET: Tetracycline, TGC: Tigecycline, TOB: Tobramycin, TRS: Trimethoprim/Sulfamethoxazole.

The protocol of inclusion of these strains in this study showed a recurrence of the UTI in one year. The strains were isolated of March 2013 to December of the same year.

### 3. Results and Discussion

The Table 1(a and b) showed the resistance profile to Escherichia coli strains isolated in this work. And in Table 2(a and b), the aspects of Klebsiella pneumoniae resistance showed an important data: the occurrence of sixteen multiresistant strains (69,6%) and among these strains the presence of carbapenem resistant K. pneumoniae (KPC).
Table 1a. Resistance of *Escherichia coli* strains in this work. Where S is susceptible, R resistant and I are intermediary. In the first column we have the antibiotics tested in *E. coli* isolated from those patients mentioned in the other columns.

| E.c. | HES 1 | HES 2 | HES 3 | HES 4 | HES 5 | HES 6 | HES 7 | HES 8 | HES 9 | HES 10 | HES 11 | HES 12 | HES 13 | HES 14 |
|------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| AMI  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  |
| APS  | <16/8 | > 16/8| > 16/8| > 16/8| > 16/8| > 16/8| > 16/8| > 16/8| > 16/8| > 16/8| > 16/8| > 16/8| > 16/8| > 16/8|
| AMP  | > 16  | > 16  | > 16  | > 16  | > 16  | > 16  | > 16  | > 16  | > 16  | > 16  | > 16  | > 16  | > 16  | > 16  |
| CFL  | ≤ 8   | ≤ 8   | ≤ 8   | ≤ 8   | ≤ 8   | ≤ 8   | ≤ 8   | ≤ 8   | ≤ 8   | ≤ 8   | ≤ 8   | ≤ 8   | ≤ 8   | ≤ 8   |
| CPM  | ≤ 8   | ≤ 8   | ≤ 8   | ≤ 8   | ≤ 8   | ≤ 8   | ≤ 8   | ≤ 8   | ≤ 8   | ≤ 8   | ≤ 8   | ≤ 8   | ≤ 8   | ≤ 8   |
| CXC  | ≤ 0.5 | ≤ 0.5 | ≤ 0.5 | ≤ 0.5 | ≤ 0.5 | ≤ 0.5 | ≤ 0.5 | ≤ 0.5 | ≤ 0.5 | ≤ 0.5 | ≤ 0.5 | ≤ 0.5 | ≤ 0.5 | ≤ 0.5 |
| CFN  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  |
| CAZ  | ≤ 1   | ≤ 16  | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   |
| CAC  | ≤ 0.25| ≤ 0.25| ≤ 0.25| ≤ 0.25| ≤ 0.25| ≤ 0.25| ≤ 0.25| ≤ 0.25| ≤ 0.25| ≤ 0.25| ≤ 0.25| ≤ 0.25| ≤ 0.25| ≤ 0.25|
| CFR  | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   |
| CIP  | ≤ 1   | > 2   | > 2   | > 2   | > 2   | > 2   | > 2   | > 2   | > 2   | > 2   | > 2   | > 2   | > 2   | > 2   |
| ERT  | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   |
| GEN  | ≤ 4   | > 8   | > 8   | > 8   | > 8   | > 8   | > 8   | > 8   | > 8   | > 8   | > 8   | > 8   | > 8   | > 8   |
| IMP  | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   |
| LEV  | ≤ 2   | > 4   | > 4   | > 4   | > 4   | > 4   | > 4   | > 4   | > 4   | > 4   | > 4   | > 4   | > 4   | > 4   |
| MP   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   | ≤ 1   |
| NIT  | ≤ 32  | ≤ 32  | ≤ 32  | ≤ 32  | ≤ 32  | ≤ 32  | ≤ 32  | ≤ 32  | ≤ 32  | ≤ 32  | ≤ 32  | ≤ 32  | ≤ 32  | ≤ 32  |
| PIT  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  | ≤ 16  |
| PIP  | > 64  | > 64  | > 64  | > 64  | > 64  | > 64  | > 64  | > 64  | > 64  | > 64  | > 64  | > 64  | > 64  | > 64  |
| TET  | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   |
| TGC  | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   |
| TOB  | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   | ≤ 4   |
| TRS  | ≤ 2/38| ≤ 2/38| ≤ 2/38| ≤ 2/38| ≤ 2/38| ≤ 2/38| ≤ 2/38| ≤ 2/38| ≤ 2/38| ≤ 2/38| ≤ 2/38| ≤ 2/38| ≤ 2/38| ≤ 2/38|

Source: Prepared by the authors. Font
Table 1b. Resistance of *Escherichia coli* strains in this work. Where S is Susceptible, R resistant and I are intermediary. In the first column we have the antibiotics tested in *E. coli* isolated from those patients mentioned in the other columns.

| E.c | HES 15 | HES 16 | HES 17 | HES 18 | HES 19 | HES 20 | HES 21 | HES 22 | HES 23 | HES 24 | HES 25 | HES 26 | HES 27 | HES 28 |
|-----|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| AMP | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 |
| APS | ≤ 8/4 | ≤ 8/4 | ≤ 8/4 | > 8/4 | > 8/4 | > 8/4 | > 8/4 | > 8/4 | > 8/4 | > 8/4 | > 8/4 | > 8/4 | > 8/4 | > 8/4 |
| AMP | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 |
| CFL | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 |
| CM | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 | ≤ 8 |
| CXC | ≤ 0.5 | ≤ 0.5 | ≤ 0.5 | ≤ 0.5 | ≤ 0.5 | ≤ 0.5 | ≤ 0.5 | ≤ 0.5 | ≤ 0.5 | ≤ 0.5 | ≤ 0.5 | ≤ 0.5 | ≤ 0.5 | ≤ 0.5 |
| CFN | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 |
| CAZ | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 |
| CAC | ≤ 0.25 | ≤ 0.25 | ≤ 0.25 | ≤ 0.25 | ≤ 0.25 | ≤ 0.25 | ≤ 0.25 | ≤ 0.25 | ≤ 0.25 | ≤ 0.25 | ≤ 0.25 | ≤ 0.25 | ≤ 0.25 | ≤ 0.25 |
| CFR | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 |
| CIP | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 |
| ERT | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 |
| GEN | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 |
| IMP | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 |
| LEV | ≤ 2 | ≤ 2 | ≤ 2 | ≤ 2 | ≤ 2 | ≤ 2 | ≤ 2 | ≤ 2 | ≤ 2 | ≤ 2 | ≤ 2 | ≤ 2 | ≤ 2 | ≤ 2 |
| MP | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 |
| NIT | ≤ 32 | ≤ 32 | ≤ 32 | ≤ 32 | ≤ 32 | ≤ 32 | ≤ 32 | ≤ 32 | ≤ 32 | ≤ 32 | ≤ 32 | ≤ 32 | ≤ 32 | ≤ 32 |
| PIT | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 |
| PIN | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 | ≤ 16 |
| TET | > 8 | > 8 | > 8 | > 8 | > 8 | > 8 | > 8 | > 8 | > 8 | > 8 | > 8 | > 8 | > 8 | > 8 |
| TGC | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 |
| TOB | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 | ≤ 4 |
| TRS | ≤ 2/38 | ≤ 2/38 | ≤ 2/38 | ≤ 2/38 | ≤ 2/38 | ≤ 2/38 | ≤ 2/38 | ≤ 2/38 | ≤ 2/38 | ≤ 2/38 | ≤ 2/38 | ≤ 2/38 | ≤ 2/38 | ≤ 2/38 |

Source: Prepared by the authors.

In these two tables above, we have the 28 patients in which we obtained the bacteria from the urinary tract, in addition to the antibiotics tested on each bacterium. From the results, it was possible to see a large number of resistant strains, in this case resistant to ciprofloxacin and levofloxacin (46.4%), which are the most used antibiotics for the treatment of UTI.
Table 2a. Resistance of *Klebsiella pneumoniae* strains in this work. Where S is Susceptible, R resistant. In the first column we have the antibiotics tested in *K. pneumoniae* isolated from those patients mentioned in the other columns.

| K.p. | HES 1 | HES 2 | HES 3 | HES 4 | HES 5 | HES 6 | HES 7 | HES 8 | HES 9 | HES 10 | HES 11 | HES 12 | HES 13 | HES 14 |
|------|-------|-------|-------|-------|-------|-------|-------|-------|-------|--------|--------|--------|--------|--------|
| AMI  | ≤ 16  | S     | ≤ 16  | S     | ≤ 16  | S     | > 16  | ≤ 16  | S     | ≤ 16   | S      | ≤ 16   | S      | ≤ 16   | > 16  |
| APS  | > 16/8| R     | > 16/8| R     | > 16/8| R     | > 16/8| R     | > 16/8| R     | > 16/8 | R      | > 16/8 | R      | > 16/8 |
| AMP  | > 16  | R     | > 16  | R     | > 16  | R     | > 16  | R     | > 16   | R      | > 16   | R      | > 16   | R      | > 16  |
| CFL  | > 16  | R     | ≤ 8   | S     | > 16  | R     | > 16  | R     | > 16   | R      | > 16   | R      | > 16   | R      | > 16  |
| CPM  | > 16  | R     | ≤ 8   | S     | ≤ 8   | S     | > 16  | R     | > 16   | R      | > 16   | R      | > 16   | R      | > 16  |
| CXC  | 4     | R     | ≤ 0.5 | S     | ≤ 0.5 | S     | ≤ 0.5 | S     | ≤ 0.5  | S      | ≤ 0.5  | S      | ≤ 0.5  | S      | ≤ 0.5 |
| CFN  | ≤ 16  | S     | ≤ 16  | S     | ≤ 16  | S     | ≤ 16  | S     | ≤ 16   | S      | ≤ 16   | S      | ≤ 16   | S      | ≤ 16  |
| CAZ  | > 16  | R     | ≤ 1   | S     | ≤ 1   | S     | ≤ 1   | S     | ≤ 1    | S      | ≤ 1    | S      | ≤ 1    | S      | ≤ 16  |
| CAC  | 2     | R     | ≤ 0.25| S     | ≤ 0.25| S     | ≤ 0.25| S     | 2      | R      | 2      | R      | ≤ 0.25 | S      | ≤ 0.25 |
| CFR  | > 16  | R     | ≤ 4   | S     | 8     | S     | 8     | S     | ≤ 16   | R      | > 16   | R      | > 16   | R      | ≤ 4    |
| CIP  | ≥ 2   | R     | ≤ 1   | S     | > 2   | R     | > 2   | R     | > 2    | R      | > 2    | R      | ≤ 1    | S      | ≤ 2    |
| ERT  | ≤ 1   | S     | ≤ 1   | S     | ≤ 1   | S     | ≤ 1   | S     | ≤ 1    | S      | ≤ 1    | S      | ≤ 1    | S      | ≤ 1    |
| GEN  | ≤ 4   | S     | > 8   | R     | ≤ 8   | R     | > 8   | R     | > 8    | R      | ≤ 8    | R      | ≤ 8    | R      | ≤ 4    |
| IMP  | ≤ 1   | S     | ≤ 1   | S     | ≤ 1   | S     | ≤ 1   | S     | ≤ 1    | S      | ≤ 1    | S      | ≤ 1    | S      | ≤ 1    |
| LEV  | > 4   | R     | ≤ 2   | S     | > 4   | R     | > 4   | R     | > 4    | R      | ≤ 4    | R      | ≤ 2    | S      | > 4    |
| MP  | ≤ 1   | S     | ≤ 1   | S     | ≤ 1   | S     | ≤ 1   | S     | ≤ 1    | S      | ≤ 1    | S      | ≤ 1    | S      | ≤ 1    |
| NIT  | > 64  | R     | ≤ 32  | R     | > 64  | R     | > 64  | R     | > 64   | R      | > 64   | R      | > 64   | R      | > 64   |
| PIT  | > 64  | R     | ≤ 16  | S     | > 64  | R     | > 64  | R     | > 64   | R      | > 64   | R      | > 64   | R      | > 16   |
| PIP  | > 64  | R     | ≤ 16  | S     | > 64  | R     | > 64  | R     | > 64   | R      | > 64   | R      | > 64   | R      | > 16   |
| TET  | ≤ 4   | S     | ≤ 4   | S     | ≤ 4   | S     | ≤ 4   | S     | ≤ 4    | S      | ≤ 4    | S      | ≤ 4    | S      | ≤ 4    |
| TGC  | ≤ 2   | S     | ≤ 2   | S     | ≤ 2   | S     | ≤ 2   | S     | ≤ 2    | S      | ≤ 2    | S      | ≤ 2    | S      | ≤ 2    |
| TOB  | > 8   | R     | ≤ 4   | S     | > 8   | R     | > 8   | R     | > 8    | R      | ≤ 4    | S      | ≤ 4    | S      | ≤ 8    |
| TRS  | > 2/38| R     | > 2/38| R     | > 2/38| R     | > 2/38| R     | > 2/38 | R      | > 2/38 | R      | > 2/38 | R      | > 2/38 |

Source: Prepared by the authors.
In these two tables above, we have the 23 patients in which we obtained the urinary tract bacteria, in addition to the antibiotics tested on each bacterium. From the results, it was possible to observe a large number of resistant strains, totaling 69.6% of resistance to antibiotics in general. We also highlight the case of two patients, HES12 and HES19, in which they have *K. pneumoniae* with multi-resistance to many antibiotics.

Further this analysis, the occurrence of these bacterial resistance could be an indicative of the non-employed of good pharmaceutical practices for antibiotic use and consequent antibiotic resistance acquisition for bacteria. Also, the use of quinolones, principally ciprofloxacin, showed the involvement of the wrong medical protocols, performed before an easy microbiological resistance analysis of the bacteria causing UTI.

### 4. Conclusion

In conclusion, the incorrect use of the antibiotic therapy in the UTI treatment is a principal cause of the bacterial
resistance in recurrent infection presented in this clinical etiology. The knowledge around the multiresistant bacteria, their genes and genomic structure is an aim of our group to elucidate the new resistance mechanisms for bacteria causing UTI. Based on the knowledge obtained in this article, the group intends to continue monitoring antibiotic resistance linked to the UTI.

Acknowledgments

The authors would like to thank FAPESP (2011/21822-3, 2011/21685-6) for the financial support. Also, thanks to Dr. Ana Lúcia da Costa Darini from FCFRP-USP, for giving us the reference resistant strains for this study.

References

Aldred, K. J., Kerns, R. J., & Osheroff, N. Mechanism of Quinolone Action and Resistance. Biochemistry. 2014 Mar 18;53(10):1565-74. PubMed PMID: WOS:000333235600004. English.

Alves, D. A., Machado, D., Melo, A., Pereira, R. F. C., Severino, P., Hollanda, L. M., Araújo, D. R., & Lancellotti, M. (2016) Preparation of Thermosensitive Gel for Controlled Release of Levofloxacin and Their Application in the Treatment of Multidrug-Resistant Bacteria. BioMed Research International, 1-10

Andriole, V. T. The quinolones: past, present, and future. Clinical infectious disease: an official publication of the Infectious Diseases Society of America. 2005 41(2), S113-9.

Anes, J., McCusker, M. P., Fanning, S., & Martins, M. (2015) The ins and outs of RND efflux pumps in Escherichia coli. Frontiers in microbiology. 6. WOS:000356351200001. English.

Audrey, N. S. (2014) Antimicrobial Resistance and Susceptibility Testing of Anaerobic Bacteria, Clinical Infectious Diseases, 59(5), 1 698–705, https://doi.org/10.1093/cid/ciu395

Baym, M., Stone, L. K., & Kishony, R., “Multidrug evolutionary strategies to reverse antibiotic resistance,” Science, 351(6268), 2016.

Cavaliere, S. J. Manual of Antimicrobial Susceptibility Testing, National Committee for Clinical Laboratory (NCCL), 2005.

Emmerson, A. M., & Jones, A. M. The quinolones: decades of development and use. The Journal of antimicrobial chemotherapy. 2003 May;51 Suppl 1:13-20. PubMed PMID: 12702699.

Gajic, I., Kabic, J., Kekic, D., Jovicic, M., Milenkovic, M., Mitic Culafic, D., Trudic, A., Ranin, L., & Opavski, N. Antimicrobial Susceptibility Testing: A Comprehensive Review of Currently Used Methods. Antibiotics. 2022; 11(4):427. https://doi.org/10.3390/antibiotics11040427

Khameneh, B., Dib, R., Ghazvini, K., & Fazly Bazzaz, B. S. Breakthroughs in bacterial resistance mechanisms and the potential ways to combat them. Microbial pathogenesis. 2016 Feb 18. PubMed PMID: 26911646.

Li, X., Fan, H., ZI, H., Hu, H., Li, B., Huang, J., Luo, P., & Zeng, X. Global and Regional Burden of Bacterial Antimicrobial Resistance in Urinary Tract Infections in 2019. Journal of Clinical Microbiology. 2022; 11(10):2817. https://doi.org/10.1128/jcm.0112817

Mitscher, L. A. Bacterial topoisomerase inhibitors: quinolone and pyridone antibacterial agents. Chem Rev. 2005 Feb;105(2):559-92. PubMed PMID: 15700957.

NCCLS, M11-A6 Methods for Antimicrobial Susceptibility Testing of Anaerobic Bacteria; Approved Standard, NCCLS, Philadelphia, Pa, USA, 6th edition, 2004.

Nebert, D. W., Zhang, G., & Vesell, E. S. From human genetics and genomics to pharmacogenetics and pharmacogenomics: past lessons, future directions. Drug metabolism reviews. 2008;40(2):187-224. PubMed PMID: 1846403. PubMed Central PMCID: 2752627.

Nischal, P. M. First global report on antimicrobial resistance released by the WHO. NAtl Med J India. 2014 Jul-Aug;27(4):241-. PubMed PMID: WOS:000350087400016. English.

Riley, M. A., Robinson, S. M., Roy, C. M., Dennis, M., Liu, V., & Dorit, R. L. Resistance is futile: the bacteriocin model for addressing the antibiotic resistance challenge. Biochem Soc T. 2012 Dec; 40:1438–42. PubMed PMID: WOS:000312096800048. English.

Sakeena, M. H. F., Bennett, A. A., & McLachlan, A. J. Enhancing pharmacists' role in developing countries to overcome the challenge of antimicrobial resistance: a narrative review. Antimicrob Resist Infect Control, 2018;7:63.

Santos, A. C. M., Akkari, A. C. S., & Ferreira, I. R. S. “Poloxamer-based binary hydrogels for delivering tramadol hydrochloride: sol-gel transition studies, dissolution-release kinetics, in vitro toxicity, and pharmacological evaluation,” International Journal of Nanomedicine, 10, 2391–2401, 2015.

Silva, A., Costa, E., Freitas, A., & Almeida, A. Revisiting the Frequency and Antimicrobial Resistance Patterns of Bacteria Implicated in Community Urinary Tract Infections. Antibiotics. 2022; 11(6):768. https://doi.org/10.3390/antibiotics11060768

Stein, G. E. The 4-quinolone antibiotics: past, present, and future. Pharmacotherapy. 1998;8(6):301-14. PubMed PMID: 2851772.

Zhu, Y., Huang, W. E., & Yang, Q. Clinical Perspective of Antimicrobial Resistance in Bacteria. Infect Drug Resist. 2022; 15:735-746. Published 2022 Mar 2.10.2147/IDR.S345574