UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL
INSTITUTO DE CIÊNCIAS BÁSICAS DA SAÚDE
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# INFECÇÃO DO TRATO URINÁRIO POR MICRORGANISMOS RESISTENTES A BETA-LACTÂMICOS EM TRANSPLANTADOS RENAIS DE UM HOSPITAL REFERÊNCIA EM PORTO ALEGRE: UMA ANÁLISE ATRAVÉS DE BANCO DE DADOS DOS ÚLTIMOS 10 ANOS

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## RESUMO

As infecções urinárias são ocasionadas principalmente por bactérias que ascendem do trato urinário inferior e quando não diagnosticadas e tratadas de forma adequada, podem evoluir para outras doenças mais graves. Os transplantes renais foram a modalidade pioneira no país e possuem o propósito de prolongar e melhorar a qualidade de vida dos pacientes. A infecção do trato urinário é de extrema relevância clínica devido ao risco de perda do transplante, uma vez que pode acelerar o processo de rejeição crônica do enxerto, além da alta mortalidade associada principalmente durante o primeiro ano. Este trabalho tem como objetivo avaliar por meio de banco de dados provenientes de um hospital referência em Porto Alegre/RS o número de casos de pacientes transplantados renais acometidos por infecções do trato urinário resistentes a beta-lactâmicos nos últimos 10 anos. Foram contabilizadas 13.310 uroculturas com bacteriúria significativa de pacientes submetidos a transplantes renais entre 2013 e 2023. Foi possível identificar que 83,53% das uroculturas foram positivas para bacilos gram negativos, 15,23% para cocos gram positivos e apenas 0,56% para candidemia. As bactérias mais prevalentes foram a *Escherichia coli* (38,12%), seguida por *Klebsiella* sp. (31,73%) e *Enterococcus* sp. (9,96%). Ao analisar o perfil dos antimicrobianos testados, 36% foram da classe dos beta-lactâmicos, sendo 36,96% com perfil de resistência para esses fármacos. Os resultados indicaram um maior índice de resistência para o grupo das cefalosporinas de 1ª geração (64,55%), precedido por monobactâmicos (45,59%), penicilinas (41,48%) e cafalosporinas de 2ª geração (41,99%). O crescente aumento das resistências em uroculturas tem motivado a contínua avaliação dos perfis de sensibilidade das bactérias isoladas na urina. O início precoce da terapia com antimicrobianos e o manejo adequado são de suma importância para evitar a mortalidade e perda do transplante renal. Entretanto, o uso inadequado e indiscriminado dos antibióticos contribuiu para as resistências bacterianas, que possuem cada vez mais novos desafios para o ambiente de saúde.



Palavras-chave: beta-lactâmicos; resistência; transplante; urocultura.

## ABSTRACT

Urinary tract infections are mainly caused by bacteria that travel up from the lower urinary tract and, if not diagnosed and treated properly, can develop into other more serious conditions. Kidney transplants were the pioneering modality in the country and their purpose is to prolong and improve patients' quality of life. Urinary tract infections are of great clinical relevance due to the risk of graft loss, as they can accelerate the process of chronic graft rejection, in addition to the high mortality associated with them, especially in the first year. This study aims to utilize a database from a referral hospital in Porto Alegre, RS, to evaluate the number of cases of urinary tract infections caused by beta-lactam-resistant bacteria in renal transplant patients during the last 10 years. A total of 13,310 urocultures with significant bacteriuria were counted in patients who underwent kidney transplantation between 2013 and 2023. It was found that 83.53% of urocultures were positive for gram-negative bacilli, 15.23% for gram-positive cocci and only 0.56% for candida. The most common bacteria were *Escherichia coli* (38.12%), followed by *Klebsiella* sp. (31.73%) and *Enterococcus* sp. (9.96%). When analysing the profile of the antimicrobials tested, 36% were from the beta-lactam class and 36.96% had a resistance profile to these drugs. The results showed a higher resistance rate for the group of 1st generation cephalosporins (64.55%), followed by monobactams (45.59%), penicillins (41.48%) and 2nd generation cafalosporins (41.99%). Increasing resistance in urocultures has prompted continuous evaluation of the susceptibility profiles of bacteria isolated from urine. Early initiation of antimicrobial therapy and appropriate management are of paramount importance to prevent mortality and loss of the kidney transplant. However, inappropriate and indiscriminate use of antibiotics has contributed to bacterial resistance, which poses an increasing challenge to healthcare.



Keywords: beta-lactams; resistance; transplantation; uroculture.

**SUMÁRIO**

# 1 INTRODUÇÃO

As infecções urinárias estão entre as causas mais comuns de busca por atendimento em serviços de saúde, independentemente da idade dos indivíduos[1]. São ocasionadas principalmente por bactérias que ascendem do trato urinário inferior e quando não diagnosticadas e tratadas de forma adequada, podem evoluir para outras doenças mais graves[2]. São classificadas em cistite, bacteriúria de baixa e alta contagem, síndrome uretral, contaminação urinária e pielonefrite não complicada ou complicada[3]. As causas e fatores de risco para as infecções do trato urinário (ITUs) são múltiplas e incluem higiene excessiva ou inadequada, uso de cateter, indivíduos diabéticos, gestantes e indivíduos imunossuprimidos[4].

Os transplantes renais foram a modalidade pioneira no país e possuem o propósito de prolongar e melhorar a qualidade de vida dos pacientes[5]. A infecção do trato urinário é de extrema relevância clínica devido ao risco de perda do transplante, além da alta mortalidade associada principalmente durante o primeiro ano[6]. Os pacientes com enxerto renal apresentam imunossupressão, por conta do uso de medicações moduladoras da imunidade, o que os torna ainda mais susceptíveis a infecções[7]. Em conjunto, o risco é alto para aquisição de bactérias multirresistentes, uma vez que apresentam internações hospitalares prévias, assim como recorrentes consultas para as realizações das diálises[8].

Os beta-lactâmicos são uma classe de antibióticos utilizados para o tratamento das ITUs, agem na parede celular bacteriana como resultado de uma ligação covalente essencial à proteína ligadora de penicilina (PBPs), enzimas que estão envolvidas nas etapas terminais das ligações cruzadas do peptidioglicano tanto em bactérias gram negativas quanto em gram positivas[9]. Dentre os fármacos encontram-se a ampicilina, amoxicilina associada com clavulanato, aztreonam, cefazolina, cefepime, cefoxitina, cefuroxima, ceftazidima, ceftriaxona, imipenem e piperacilina associada ao tazobactam[10]. A resistência bacteriana, caracterizada pela capacidade das bactérias de sobreviverem e replicarem mesmo na presença de fármacos que atuam para inibi-las ou matá-las é um dos desafios encontrados para o tratamento das ITUs em pacientes transplantados renais, uma vez que pode acelerar o processo de rejeição crônica do enxerto[11].

O crescente aumento das resistências em uroculturas tem motivado a contínua avaliação dos perfis de sensibilidade das bactérias isoladas na urina. No Brasil, apesar de não existir uma sistematização de dados para monitoramento, estima-se que entre 5% e 15% de pacientes hospitalizados venham a adquirir alguma infecção decorrente da internação, um

número ainda mais crescente quando citadas as unidades de terapia intensivas (UTIs) saltando para 25% a 35% dos pacientes[12,13,14]. O início precoce da terapia com antimicrobianos é de suma importância, assim como o tratamento adequado da infecção[15]. Entretanto, o uso inadequado e indiscriminado dos antibióticos contribuiu para as resistências bacterianas encontradas na atualidade, que possuem cada vez mais novos desafios para o ambiente de saúde[16]. O Centro de Controle e Prevenção de Doenças (CDC), dos Estados Unidos, estima que no mundo, mais de dois milhões de pessoas anualmente são infectadas com bactérias multirresistentes e, destas, aproximadamente 23.000 morrerão devido ao processo infeccioso[17].

No Brasil, o Programa Nacional de Prevenção e Controle de Infecções Relacionadas à Assistência à Saúde estabelece metas e ações estratégicas a fim de reduzir a incidência dessas infecções, mas fatores como a desigualdade social e a inadequação do sistema de saúde como a falta de insumos para trocas constantes entre os atendimentos e a distância inadequada dos leitos, favorecem ainda mais as disseminações[18]. Além dessas preocupações relacionadas à saúde pública, outro fator impactante são os custos com drogas para o tratamento que podem compreender de 30% a 50% dos gastos hospitalares[19].

Por conta disso, dá-se a importância de avaliar a incidência de casos de pacientes transplantados renais com uroculturas resistentes a beta-lactâmicos nos últimos anos, assim como os principais germes envolvidos, consequências futuras e fatores de risco a essa exposição.

## 1.1 OBJETIVOS

### 1.1.1 Objetivo geral

Avaliar por meio de banco de dados provenientes de um hospital referência em Porto Alegre o número de casos de pacientes transplantados renais acometidos por infecções do trato urinário resistentes a beta-lactâmicos nos últimos 10 anos.

### 1.1.2 Objetivos específicos

a) Analisar a incidência dos pacientes submetidos a transplantes renais a adquirirem infecções do trato urinário;
b) Descrever os diferentes patógenos urinários, fenótipos resistentes e multirresistentes envolvidos;
c) Identificar os principais impactos da resistência bacteriana por beta-lactâmicos em pacientes submetidos a transplantes renais.

# 2 ARTIGO CIENTÍFICO

## URINARY TRACT INFECTIONS CAUSED BY BETA-LACTAM RESISTANT MICROORGANISMS IN KIDNEY TRANSPLANT PATIENTS OF A REFERENCE HOSPITAL IN PORTO ALEGRE: A DATABASE ANALYSIS OF THE LAST 10 YEARS

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**ABSTRACT**

Urinary tract infections are mainly caused by bacteria that travel up from the lower urinary tract and, if not diagnosed and treated properly, can develop into other more serious conditions. Kidney transplants were the pioneering technique in the country and their purpose is to prolong and improve patients' quality of life. Urinary tract infections are of great clinical relevance due to the risk of graft loss, as they can accelerate the process of chronic graft rejection, in addition to the high mortality associated with them, especially in the first year. This study aims to utilize a database from a referral hospital in Porto Alegre, RS, to evaluate the number of cases of urinary tract infections caused by beta-lactam-resistant bacteria in renal transplant patients during the last 10 years. A total of 13,310 urocultures with significant bacteriuria were counted in patients who underwent kidney transplantation between 2013 and 2023. It was found that 83.53% of urocultures were positive for gram-negative bacilli, 15.23% for gram-positive cocci and only 0.56% for candida. The most common bacteria were *Escherichia coli* (38.12%), followed by *Klebsiella* sp. (31.73%) and *Enterococcus* sp. (9.96%). When analysing the profile of the antimicrobials tested, 36% were from the beta-lactam class and 36.96% had a resistance profile to these drugs. The results showed a higher resistance rate for the group of 1st generation cephalosporins (64.55%), followed by monobactams (45.59%), penicillins (41.48%) and 2nd generation cafalosporins (41.99%). Increasing resistance in urocultures has prompted continuous evaluation of the susceptibility profiles of bacteria isolated from urine. Early initiation of antimicrobial therapy and appropriate management are of paramount importance to prevent mortality and loss of the kidney transplant. However, inappropriate and indiscriminate use of antibiotics has contributed to bacterial resistance, which poses an increasing challenge to healthcare.

Keywords: beta-lactams; resistance; transplantation; uroculture.

### INTRODUCTION

Urinary tract infections (UTIs) stand out as one of the primary reasons people seek medical care from an early age[1]. These infections primarily occur due to the ascent of bacteria from the lower urinary tract. If left undiagnosed and untreated, they can lead to more severe conditions[2]. Urinary tract infections comprise cystitis, low and high bacteriuria, urethral syndrome, urinary contamination, uncomplicated or complicated pyelonephritis[3]. Urinary tract infections result from a variety of causes and risk factors that include, but are not limited to, improper hygiene practices, catheter use, diabetes, pregnancy, and immunosuppression[4].

Kidney transplants were the pioneering technique in the country and their purpose is to prolong and improve patients' quality of life[5]. Urinary tract infections are highly relevant clinically because of the risk of

graft loss and high mortality, particularly during the first year[6]. Patients receiving a kidney transplant undergo immunosuppression due to immunomodulatory drug use, making them more susceptible to infection[7]. Together, they are at high risk of acquiring multidrug-resistant bacteria as a result of previous hospitalizations and repeated visits for dialysis[8].

Beta-lactams are antibiotics used to treat urinary tract infections that work on the bacterial cell wall by creating an essential covalent bond to penicillin-binding proteins (PBPs), which are enzymes involved in the final steps of peptidoglycan cross-linking in both gram-negative and gram-positive bacteria[9]. These antibiotics include ampicillin, amoxicillin combined with clavulanate, aztreonam, cefazolin, cefepime, cefoxitin, cefuroxime, ceftazidime, ceftriaxone, imipenem, and piperacillin combined with tazobactam[10.] Bacterial resistance is a challenge in treating UTIs in kidney transplant patients as it is characterized by the ability of bacteria to survive, multiply and cause infection despite the presence of drugs designed to inhibit or kill them, and it can accelerate the process of chronic graft rejection.[11]

Increasing resistance in urocultures has motivated the continuous evaluation of the susceptibility profiles of bacteria isolated from urine. In Brazil, although there is no systematization of data for surveillance, it is estimated that between 5% and 15% of hospitalized patients acquire an infection as a result of their hospital stay, and even more if intensive care units (ICUs) are included, with the figure rising to 25% to 35% of patients[12,13,14]. Early initiation of antimicrobial therapy is of paramount importance, as is appropriate treatment of the infection[15]. However, inappropriate and indiscriminate use of antibiotics has contributed to the emergence of bacterial resistance, which poses an increasing challenge to the healthcare environment[16]. The Centers for Disease Control and Prevention (CDC) in the United States estimates that more than two million people worldwide are infected with multidrug-resistant bacteria each year, and that approximately 23,000 of these people will die as a result of the infection[17].

In Brazil, the National Program for the Prevention and Control of Healthcare-Related Infections establishes objectives and strategic actions to reduce the incidence of these infections, but factors such as social inequality and the inadequacies of the health system, such as the lack of supplies for continuous exchange between care settings and the inadequate distance between beds, further favor the spread1[18]. In addition to these public health concerns, another influencing factor is the cost of medicines for treatment, which can represent 30% to 50% of hospital expenditure[19].

Therefore, it is important to evaluate the incidence of cases of beta-lactam-resistant uropathies in renal transplant patients in recent years, as well as the main organisms involved, future consequences and risk factors for this exposure.

## MATERIALS AND METHODS

### Study population and location

Patients who underwent kidney transplant and presented urinary tract infections with antimicrobial susceptibility test (AST) results compatible with beta-lactam resistance in a reference hospital located in the city of Porto Alegre, RS, between January 2013 and February 2023.

**Research Methodology**

This research utilizes a descriptive, quantitative, and retrospective design, incorporating a documentary survey of medical records indexed in the databases of a public hospital. The database was consulted during May and July of 2023. Following the application of the analysis criteria, the data was quantified and filtered using spreadsheets based on the year, microorganisms, and resistance mechanisms found**.**

**Criteria for Inclusion and exclusion**

- Inclusion criteria: patients of legal age who have undergone renal transplantation, with a previous history of urinary tract infection and a beta-lactam resistance profile. Urocultures showing significant bacteriuria with counts greater than or equal to 105 CFU/mL (Colony Forming Units per milliliter of urine) are also included.

- Exclusion criteria: transplants that are not exclusively renal, re-transplants during the study period, and infections with antibiogram profiles other than beta-lactam resistance.

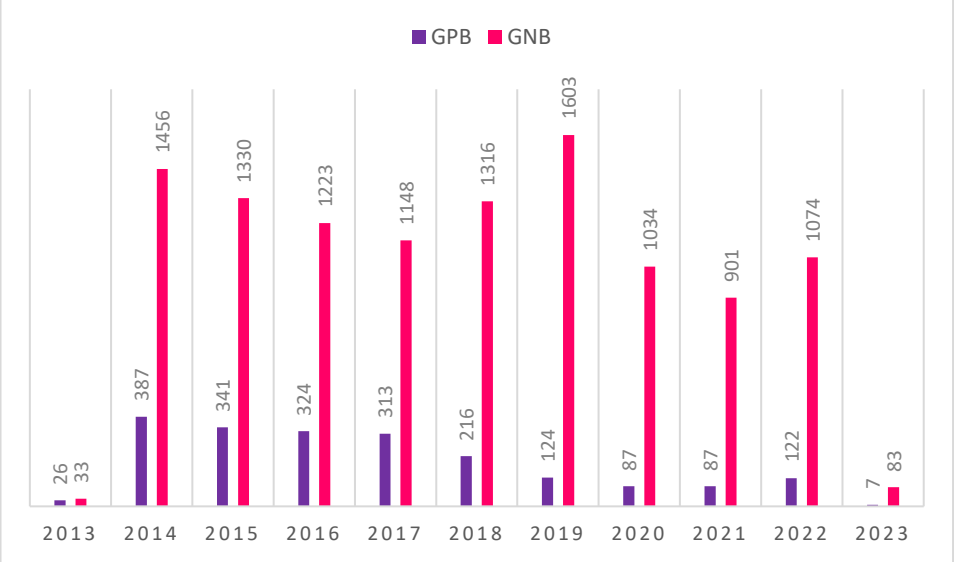
**Ethical considerations**

This study was approved with a Certificate of Presentation of Research Ethics Appreciation (CAAE) (appendix A). Data collection ensured confidentiality, anonymity of patients and report book data, and preserved the hospital institution's name.

## RESULTS

Data was collected from a transplant reference center in the city of Porto Alegre, which is the capital of Rio Grande do Sul. A total of 13,310 urocultures with significant bacteriuria were counted from patients who underwent kidney transplantation between 2013 and 2023. During the study, 83.53% of urocultures were positive for gram-negative bacteria, 15.23% for gram-positive bacteria, and only 0.56% were positive for candidemia (figure 1). In 2019, urocultures had the greatest increase compared to other years, totaling 1,730 and showing the highest number of cultures with growth of gram-negative bacteria (1,603). However, in 2014, there was the highest quantification of infection by gram-positive bacteria with 387 urocultures.

Figure 1. Prevalence of gram-positive and gram-negative bacteria in urine cultures of kidney transplant patients between 2013 and 2023.




A survey was conducted on urocultures with microbial growth to determine the most prevalent bacteria over the years. *Escherichia coli* was the most predominant pathogen, representing 38.12% (5,075) of the total bacteria isolated. It was followed by *Klebsiella* sp., which accounted for 31.73% (4,224), a percentage very similar to the most frequently identified pathogen. The species *Enterococcus* sp. was identified with a significantly lower percentage of 9.96% (1,327), followed by other microorganisms as listed in table 1.

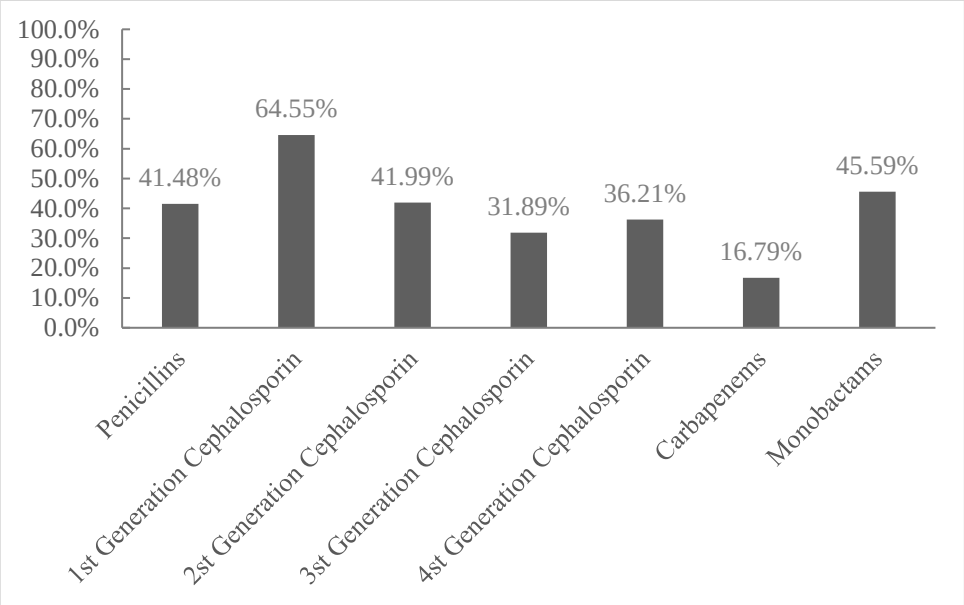
Table 1. Microorganism prevalence in urine cultures of kidney transplant patients, recorded from January 2013 to February 2023.

| **Microorganisms isolated** | **n total - %** |
|---|---|
| *Escherichia coli* | 5.075 (38,12) |
| *Klebsiella* sp | 4.224 (31,73) |
| *Enterococcus* spp | 1.327 (9,96) |
| *Streptococcus agalactiae* | 540 (4,05) |
| *Proteus* sp | 527 (3,95) |
| *Enterobacter* sp | 457 (3,43) |
| *Pseudomonas aeruginosa* | 433 (3,25) |
| *Morganella morganii* | 233 (1,75) |
| *Citrobacter* sp | 107 (0,80) |
| Candida sp | 75 (0,56) |
| *Serratia* sp | 61 (0,45) |
| *Burkholderia cepacia* | 41 (0,30) |
| *Staphylococcus aureus* | 37 (0,27) |
| *Stenotrophomonas maltophilia* | 12 (0,09) |
| *Acinetobacter* sp | 11 (0,08) |
| *Providencia* sp | 5 (0,03) |
| Outros microrganismos | 145 (1,08) |

Note - Table 1: Other microorganisms include: Non-fermenting Gram-negative bacilli, beta-hemolytic streptococci, alpha-hemolytic streptococci, coagulase-negative staphylococci, and Haemophilus species.

When analyzing the profile of the antimicrobials tested, 36% were from the beta-lactam class. Out of which, 36.96% demonstrated a resistance profile for these drugs. According to the results, 1st generation cephalosporins demonstrated the highest resistance rate (64.55%), followed by monobactams (45.59%), penicillins (41.48%), and 2nd generation cafalosporins (41.99%). The lowest resistance rates were observed for 4th generation caphalosporins (36.21%) and carbapenems (16.79%) (figure 2).

Figure 2. Percentage of resistance to beta-lactam antimicrobials.




**DISCUSSION**

Urinary tract infection is a common infectious disease affecting both adults and children. To ensure proper treatment, a uroculture examination is necessary. This examination allows visualization of the microorganism responsible for the infection and the sensitivity of the microorganism to drugs through antibiogram testing. Urinary tract infection in renal transplant patients leads to a higher incidence of transplant rejection and graft failure. This study analyzes the most common bacteria causing urinary tract infections in renal transplant patients, along with the drugs used most often and the percentage of resistance found within the analysis group.

In a study conducted by Campos et al. (2018) [20] with kidney transplant patients, the bacterium *Escherichia coli* was most prevalent with a result of 52.5%, a higher percentage compared to the 38.12% identified in this study. The bacterium under consideration is identified in the literature as the primary causative agent of urinary tract infections, found in 70% to 95% of cases, which confirms our findings regarding prevalence. The results also present an elevated number of infections caused by *Klebsiella* sp., responsible for 31.73% of all infections[21,22,23].

Beta-lactams, a class of broad-spectrum antibiotics, are frequently prescribed due to the variety of antibiotics included in this class and are recognized as one of the most extensive groups of antimicrobials[24]. The study results on the beta-lactam resistance profile align with those of Rocha et al. (2015) [25], indicating resistance to cephalosporins like ceftriaxone, ceftazidime, and cefepime, and penicillins like amoxicillin and ampicillin which were the third-most resistant class identified.

The excessive and inappropriate use of antibiotics to treat urinary tract infections can induce selective pressure, leading to the emergence of bacterial resistance to antibiotics[26,27]. In this context, considering the increasing number of deaths caused by antibiotic misuse and kidney transplant rejections, which pose a significant risk of a scarcity of treatments and the development of increasingly resistant bacteria, it is crucial to identify, monitor and constantly review the profile of infections found in healthcare treatment centers.

## CONCLUSION

Based on the evaluated data, *Escherichia coli* is still the primary microorganism causing urinary tract infections. In recent years, the incidence of UTIs caused by *Klebsiella* sp. has increased due to several modulations that help this bacterium evade drug actions, such as carbapenemase production.

As new antimicrobials emerged, bacteria began developing resistance to survive pharmacological attacks. These bacteria cause infections where the treatment becomes ineffective, leading to an inadequate response from clinical treatment, due to their cell wall composition, enzyme production, active transport proteins, or living in microbial communities. It was found that beta-lactam antibiotics, such as 1st generation cephalosporins, have a significant resistance, due to their long history of use. It should be noted though carbapenems had the lowest antimicrobial resistance rate in our study, since they are broad-spectrum and potent, which can cause both an indiscriminate use and a further increase in bacterial resistance rates.

Therefore, it is necessary to plan an effective therapeutic regimen, as it is not uncommon for patients who have recently undergone renal transplantation to return to health care services with UTIs, especially in the first two months. Also, essential mapping, monitoring, and guiding studies should be conducted in health centers as they help hospitals and regions to control and limit the spread of infections.

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## 3 CONCLUSÃO E PERSPECTIVAS

Com base nos dados avaliados, conclui-se que a *Escherichia coli* permanece como o principal microrganismo causador de infecções urinárias. Entretanto, a identificação de ITUs por *Klebsiella* sp. é crescente nos últimos anos, por diversas modulações que essa bactéria consegue realizar para driblar a ação dos fármacos, como a produção de carbapenemases.

Conforme foram surgindo novos antimicrobianos, as bactérias também começaram a expressar resistência, como forma de sobreviver aos ataques farmacológicos. Seja pela sua composição de parede celular, produção de alguma enzima, presença de proteínas de transporte ativo ou até mesmo vivendo em comunidades microbianas, estas bactérias causam infecções onde o tratamento se torna ineficaz, trazendo uma resposta clínica inadequada. Sendo assim, constatou-se que os fármacos já utilizados a mais tempo como as cefalosporinas de 1ª geração já possuem um número expressivo de resistência dentro dos antibióticos da classe dos beta-lactâmicos. Ainda que em nosso estudo os carbapenêmicos tenham sido o antimicrobiano com menor índice de resistência, deve-se ter alerta para essa classe de antibióticos, uma vez que são considerados drogas de última escolha, por serem mais fortes e de amplo espectro, o que pode acarretar no uso indiscriminado e elevar ainda mais os índices de resistência bacteriana.

Portanto, se faz necessário o planejamento de um esquema terapêutico eficaz, uma vez que não é incomum que pacientes que recém realizaram o enxerto renal retornem aos serviços de saúde com ITUs, principalmente nos dois primeiros meses. Além disso, são essenciais os estudos de mapeamento e monitoramento dentro de um centro de saúde, pois auxiliam e norteiam a criação e atualização tanto das comissões de controle de infecção hospitalar, quanto da região e segurança da comunidade.

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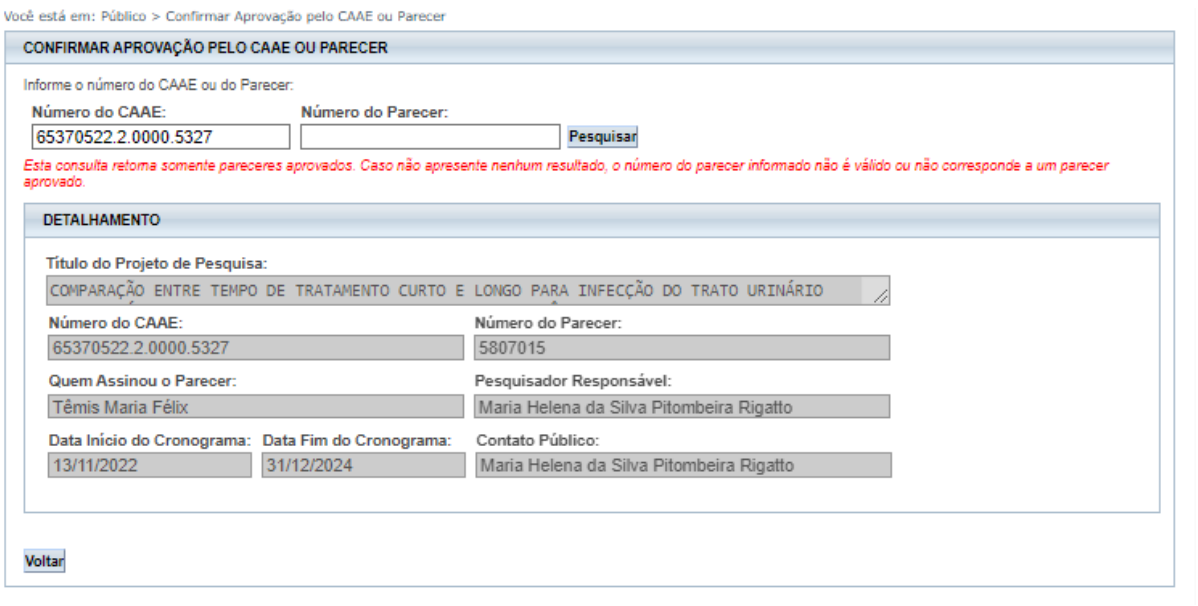
# APÊNDICE A – APROVAÇÃO DO COMITÊ DE ÉTICA EM PESQUISA



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CONFIRMAR APROVAÇÃO PELO CAAE OU PARECER

Informe o número do CAAE ou do Parecer:

Número do CAAE: 65370522.2.0000.5327

Número do Parecer:

Pesquisar

*Esta consulta retorna somente pareceres aprovados. Caso não apresente nenhum resultado, o número do parecer informado não é válido ou não corresponde a um parecer aprovado.*

DETALHAMENTO

Título do Projeto de Pesquisa: COMPARAÇÃO ENTRE TEMPO DE TRATAMENTO CURTO E LONGO PARA INFECÇÃO DO TRATO URINÁRIO

Número do CAAE: 65370522.2.0000.5327

Número do Parecer: 5807015

Quem Assinou o Parecer: Têmis Maria Félix

Pesquisador Responsável: Maria Helena da Silva Pitombeira Rigatto

Data Início do Cronograma: 13/11/2022

Data Fim do Cronograma: 31/12/2024

Contato Público: Maria Helena da Silva Pitombeira Rigatto

Voltar

# ANEXO A – NORMAS DE PUBLICAÇÃO DA REVISTA BRAZILIAN JOURNAL OF MICROBIOLOGY

Article types and sections

ARTICLE TYPES

**Research article:** report results of original research, which has not been published elsewhere.
**Short communication:** a short communication is new and significant findings. Submit form is the same way as research paper. They receive the same review, they are not published more rapidly than research papers.
**Review:** Review articles should deal with microbiological subjects of broad interest.
**Letters to the editor:** letters to the editor are intended only for comments on Published in the journal and must cite published references to support the writer's argument.

SECTIONS

**Biotechnology and Industrial Microbiology:** biosynthesis and bioconversion of natural products, including antibiotics, xenobiotics, and macromolecules produced by bacteria. Biosynthesis and bioconversion of natural products, including antibiotics, xenobiotics, and macromolecules produced by fungi. Molecular aspects of fungal biotechnology. Molecular aspects of bacterial biotechnology.
**Food Microbiology:** applications of microorganisms (bacteria and fungi) for food production. Food borne diseases, food spoilage, and microbial ecology in foods.
**Bacterial and Fungal Pathogenesis:** genetic, biochemical, and structural basis of bacterial pathogenesis.
**Clinical Microbiology:** studies of medically-important bacteria, fungi and virus.
**Environmental Microbiology:** ecology of natural microbial assemblages, microbial diversity of natural environments such as water, soil, sediments and higher organisms. Microbial interactions. Biodegradation, Bioremediation, and Environmental considerations for genetically engineered microorganisms.
**Veterinary Microbiology:** diseases of animals, Control and/or treatment of animals, Animal pathogen diagnostics, and Veterinary or zoonotic pathogens.
**Fungal and Bacterial Physiology:** biochemistry, biophysics, metabolism, cell structure, stress response, growth, differentiation and other related process.
**Human Microbiome:** studies on human microbiota, its association with physiological or pathological processes.
**Bacterial, Fungal and Virus Molecular Biology:** fungal and bacterial genetics, molecular biology, gene regulation, DNA replication and repair, genomics, proteomics, transcriptomics.

Scientific style

- Please always use internationally accepted signs and symbols for units (SI units).
- Genus and species names should be in italics.
- Generic names of drugs and pesticides are preferred; if trade names are used, the generic name should be given at first mention.

## Manuscript Submission

### Manuscript Submission

Submission of a manuscript implies: that the work described has not been published before; that it is not under consideration for publication anywhere else; that its publication has been approved by all co-authors, if any, as well as by the responsible authorities – tacitly or explicitly – at the institute where the work has been carried out. The publisher will not be held legally responsible should there be any claims for compensation.

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Please follow the hyperlink "Submit manuscript" on the right and upload all of your manuscript files following the instructions given on the screen.

Please ensure you provide all relevant editable source files. Failing to submit these source files might cause unnecessary delays in the review and production process.

### Title page

Please make sure your title page contains the following information.

### Title

The title should be concise and informative.

### Author information

- The name(s) of the author(s)
- A concise and informative title
- The affiliation(s) of the author(s), i.e. institution, (department), city, (state), country
- A clear indication and an active e-mail address of the corresponding author
- If available, the 16-digit ORCID of the author(s)

If address information is provided with the affiliation(s) it will also be published.

For authors that are (temporarily) unaffiliated we will only capture their city and country of residence, not their e-mail address unless specifically requested.

Large Language Models (LLMs), such as ChatGPT, do not currently satisfy our authorship criteria. Notably an attribution of authorship carries with it accountability for the work, which cannot be effectively applied to LLMs. Use of an LLM should be properly documented in the Methods section (and if a Methods section is not available, in a suitable alternative part) of the manuscript.

Abstract

Please provide an abstract of 150 to 250 words. The abstract should not contain any undefined abbreviations or unspecified references.

Please note: For some articles (particularly, systematic reviews and original research articles), 250 words may not be sufficient to provide all necessary information in the abstract. Therefore, the abstract length can be increased from the 250-word limit (to up to 450 words) if the topic dictates, and to allow full compliance with the relevant reporting guidelines.

Keywords

Please provide 4 to 6 keywords which can be used for indexing purposes.

Statements and Declarations

The following statements should be included under the heading "Statements and Declarations" for inclusion in the published paper. Please note that submissions that do not include relevant declarations will be returned as incomplete.

- **Competing Interests:** Authors are required to disclose financial or non-financial interests that are directly or indirectly related to the work submitted for publication. Please refer to "Competing Interests and Funding" below for more information on how to complete this section.

Text

Text Formatting

Manuscripts should be submitted in Word.

- Use a normal, plain font (e.g., 10-point Times Roman) for text.
- Use italics for emphasis.
- Use the automatic page numbering function to number the pages.
- Do not use field functions.
- Use tab stops or other commands for indents, not the space bar.
- Use the table function, not spreadsheets, to make tables.
- Use the equation editor or MathType for equations.
- Save your file in docx format (Word 2007 or higher) or doc format (older Word versions).

Manuscripts with mathematical content can also be submitted in LaTeX. We recommend using Springer Nature's LaTeX template.

Headings

Please use no more than three levels of displayed headings.

Abbreviations

Abbreviations should be defined at first mention and used consistently thereafter.

Footnotes

Footnotes can be used to give additional information, which may include the citation of a reference included in the reference list. They should not consist solely of a reference citation,

and they should never include the bibliographic details of a reference. They should also not contain any figures or tables.

Footnotes to the text are numbered consecutively; those to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data). Footnotes to the title or the authors of the article are not given reference symbols.

Always use footnotes instead of endnotes.

## Acknowledgments

Acknowledgments of people, grants, funds, etc. should be placed in a separate section on the title page. The names of funding organizations should be written in full.

## References

### Citation

Reference citations in the text should be identified by numbers in square brackets. Some examples:

1. Negotiation research spans many disciplines.

2. This result was later contradicted by Becker and Seligman.

3. This effect has been widely studied.

### Reference list

The list of references should only include works that are cited in the text and that have been published or accepted for publication. Personal communications and unpublished works should only be mentioned in the text.

The entries in the list should be numbered consecutively.

If available, please always include DOIs as full DOI links in your reference list (e.g. “https://doi.org/abc”).

- Journal article
  Gamelin FX, Baquet G, Berthoin S, Thevenet D, Nourry C, Nottin S, Bosquet L (2009) Effect of high intensity intermittent training on heart rate variability in prepubescent children. Eur J Appl Physiol 105:731-738. https://doi.org/10.1007/s00421-008-0955-8

  Ideally, the names of all authors should be provided, but the usage of “et al” in long author lists will also be accepted:

  Smith J, Jones M Jr, Houghton L et al (1999) Future of health insurance. N Engl J Med 965:325–329

- Article by DOI
  Slifka MK, Whitton JL (2000) Clinical implications of dysregulated cytokine production. J Mol Med. https://doi.org/10.1007/s001090000086

- Book
  South J, Blass B (2001) The future of modern genomics. Blackwell, London

- Book chapter
  Brown B, Aaron M (2001) The politics of nature. In: Smith J (ed) The rise of modern genomics, 3rd edn. Wiley, New York, pp 230-257

- Online document
  Cartwright J (2007) Big stars have weather too. IOP Publishing PhysicsWeb. http://physicsweb.org/articles/news/11/6/16/1. Accessed 26 June 2007

- Dissertation
  Trent JW (1975) Experimental acute renal failure. Dissertation, University of California

Authors preparing their manuscript in LaTeX can use the bibliography style file sn-basic.bst which is included in the Springer Nature Article Template.

Tables

- All tables are to be numbered using Arabic numerals.
- Tables should always be cited in text in consecutive numerical order.
- For each table, please supply a table caption (title) explaining the components of the table.
- Identify any previously published material by giving the original source in the form of a reference at the end of the table caption.
- Footnotes to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data) and included beneath the table body.