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ORIGINAL PAPER

Occurrence of Urinary Tract Infection in Patients after Kidney Transplantation

Elisa Camila de Souza e Silva[1], Sibely de Paula Guilherme[2], Cristina Nantes Miranda[2], André Luiz Silva Alvim[1], Gustavo Fernandes Ferreira[2], Thiago Cesar Nascimento[1], Ana Paula Machado da Rocha[3,*]

1.Universidade Federal de Juiz de Fora – Faculdade de Enfermagem – Juiz de Fora (MG) – Brazil.

2.Hospital Santa Casa de Misericórdia de Juiz de Fora – Serviço de Transplante – Juiz de Fora (MG) – Brazil.

3.Universidade Federal de Juiz de Fora – Departamento de Biofísica e Fisiologia – Juiz de Fora (MG) – Brazil.

*Corresponding author: rocha.ana@ufjf.br

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ABSTRACT

Introduction: The Brazilian Society of Nephrology estimates that approximately 10 million people in Brazil had chronic kidney disease in 2019. In 2022, 5,303 kidney transplants were performed in the country, with the city of Juiz de Fora standing out as one of the largest reference centers for kidney transplants. **Objectives:** The objective of this study is to evaluate the occurrence of urinary tract infections in post-transplant patients, as well as the type of infection. **Methods:** This is a retrospective quantitative cross-sectional study in which data from the medical records of patients who underwent kidney transplantation from 2019 to 2022 were analyzed. **Results:** Of a total of 537 kidney transplants performed during this period, 64 urinary tract infections associated with urinary catheters were observed in the first 30 days post-transplantation, with a higher incidence in the first 5 days. Most of the microorganisms observed belong to the human microbiota, indicating that the cause may be related to catheterization, the hospital environment, or the patient. The infections observed are caused by bacteria resistant to the antibiotics trimethoprim and sulfamethoxazole, such as *Escherichia coli*, *Klebsiella* sp., and *Serratia* sp. **Conclusion:** The study indicates that it is necessary to improve the handling of the patients and materials to reduce infections, mainly due to the high degree of antibiotic resistance of the microorganisms observed.

Descriptors: Urinary Tract Infection; Catheters, Kidney Transplant; Antimicrobial Resistance.

Ocorrência de Infecção do Trato Urinário em Pacientes após Transplante Renal

RESUMO

Introdução: A Sociedade Brasileira de Nefrologia estimou que cerca de 10 milhões de pessoas no Brasil tinham doença renal crônica em 2019. Em 2022, 5.303 transplantes renais foram realizados no país, destacando-se o município de Juiz de Fora como um dos maiores centros de referência em transplantes renais. **Objetivos:** O objetivo deste trabalho é avaliar a ocorrência de infecções no trato urinário de pacientes pós-transplante, bem como o tipo de infecção. **Métodos:** Trata-se de estudo transversal, quantitativo e retrospectivo, no qual dados dos prontuários dos pacientes que realizaram transplante renal de 2019 a 2022 foram analisados. **Resultados:** Do total de 537 transplantes renais realizados nesse período, foram observadas 64 infecções do trato urinário associadas ao cateter vesical nos primeiros 30 dias pós-transplante, com maior incidência nos primeiros 5 dias. A maior parte dos microrganismos observados pertence à microbiota humana, indicando que a causa pode estar relacionada ao cateterismo, ao ambiente hospitalar ou ao próprio paciente. As infecções são causadas por bactérias resistentes aos antibióticos trimetoprima e sulfametoxazol, como *Escherichia coli*, *Klebsiella* sp. e *Serratia* sp. **Conclusão:** O trabalho aponta que é necessário melhorar a manipulação dos pacientes e materiais, visando reduzir as infecções, principalmente em função do alto grau de resistência a antibióticos dos microrganismos observados.

Descritores: Infecção do Trato Urinário; Cateteres de Demora; Transplante Renal; Resistência a Antimicrobianos.

INTRODUCTION

In 2019, approximately 5.2 million people died from kidney disease in the Americas[1]. The Brazilian Society of Nephrology (Sociedade Brasileira de Nefrologia-SBN) estimates that more than 10 million people in Brazil had chronic kidney disease in 2019, considering that around 90 thousand were on dialysis[2,3].

Worldwide, the number of people undergoing renal replacement therapy in 2015 exceeded 2.5 million; by 2030, this total will double to around 5.4 million[4]. In 2017, around 700 million people had chronic kidney disease worldwide, while in Brazil, 16.7 million had chronic kidney disease, and 35.500 died as a result of this pathology[5].

In 2022, 5.303 kidney transplants were performed in the country, of which 2.999 were in the Southeast Region, with São Paulo being the state with the highest absolute number of kidney transplants, followed by Minas Gerais, which, in 2022, performed 653 procedures[6].

When the kidney transplant is performed, an indwelling urinary catheter (IUC) is placed to drain urine. The IUC is maintained for 4-10 days, depending on the patient's condition. However, because it is an invasive procedure, the system connected to the IUC is susceptible to infections by microorganisms (bacteria and fungi) present in the hospital environment. Combined with the use of immunosuppressants, post-transplant infection in the hospital environment can favor graft loss, the development of sepsis and the death of the patient.

Preoperative, intraoperative, and postoperative risk factors may favor bacterial invasion and multiplication in any segment of the urinary tract, favoring urinary tract infection (UTI). Preoperative factors include being female, diabetes, advanced age, preoperative UTI, and having undergone dialysis for a prolonged period. Among postoperative factors, the use of immunosuppressants is one of the leading causes, as does rejection of the allograft. Regarding intraoperative risk, receiving an allograft from a deceased donor seems to increase the incidence of UTIs, as does the use of urethral stents, such as the urinary catheter[7].

Urinary catheter-associated UTI (UCUTI) is one of the main complications in the postoperative period of kidney transplant patients. This event is mainly facilitated by the immunosuppressive therapy patients must undergo after receiving the organ. In addition, there are other risk factors, such as handling the catheter during the sterile technique, length of stay in the intensive care unit (ICU), history of UCUTI, and prolonged dialysis time, among others[8,9]. UTI is associated with increased bacteremia, acute T-cell-mediated allograft rejection, impaired allograft function and allograft loss, with an increased risk of hospitalization and death (Pinchera et al., 2024). Morbidity and mortality in kidney transplant patients is most frequent in the first 3 months post-transplant[10].

Gram-negative and Gram-positive bacteria are on the list of priority bacterial pathogens released by the World Health Organization (WHO)[11], which aims to prioritize research, development and investment in tackling antimicrobial resistance.

During the first year after transplantation, the patient must receive continuous monitoring, a time when there is a greater chance of complications and graft loss. Risk factors such as infection, number of consultations, number of hospitalizations and length of hospital stay, among others, influence outcomes such as death and loss of the transplanted organ[12].

Thus, this study aims to evaluate the incidence and etiology of UTI in post-transplant patients in a tertiary hospital in Juiz de Fora, Minas Gerais state.

METHODS

This cross-sectional, retrospective, quantitative study used a cohort of kidney transplant recipients from 2019 to 2022 at a tertiary hospital in Juiz de Fora (HTJF). This hospital is a philanthropic institution with approximately 10 beds for transplant patients and 24 beds for multidisciplinary care, where an average of 134 kidney transplants are performed per year.

As a routine, HTJF performs immunosuppression immediately after hospitalization, following the Clinical Protocol and Therapeutic Guidelines for Immunosuppression in Kidney Transplantation (Joint Ordinance No. 1, of January 5, 2021, of the Ministry of Health), and provides preventive treatment with sulfamethoxazole/trimethoprim antibiotics after the transplant.

The following inclusion criteria were used for the study: patients who underwent kidney transplantation from 2019 to 2022 at the hospital, registered on the platforms used for medical record control, and presented with a positive urine culture up to 30 days after the date of transplantation. The clinical criteria for diagnosing clinical UTI were fever, dysuria, and low urinary flow, later confirmed with urine culture. As a routine, urine culture is performed in patients with more than 7 days of IUC use of double J or clinical symptoms. The exclusion criteria were participants not registered on either platform, incomplete medical records and transplants performed outside the determined period.

Data collection was carried out by the researchers themselves from January to August 2023 using data made available on the Magnus Portal and the hospital's Soul MV, which contain the medical records of transplant patients. The information was collected from tables generated by the Magnus system. It included full name, date of birth, date of transplant, type of donor (living/non-living), time of use of the indwelling urinary catheter, presence of UTI (after immediate removal of the catheter and/or 30 days after its removal), and adverse events. Thirty days after catheter removal was considered the time when patients had their first follow-up appointment at the transplant outpatient clinic. The hospital's Soul MV system stores patient examination records and is used to locate the antibiograms of transplant patients with infection and identify microorganisms in the urinary tract.

The isolated microorganisms' identification and antimicrobial susceptibility profile were performed using an automated method (Vitek 2, bioMerieux), which provided the diagnosed microorganisms' minimum inhibitory concentration (MIC), according to the hospital's clinical analysis laboratory results.

For data analysis, information from the Magnus and Soul MV platforms was cross-referenced in the Microsoft Office Excel 2019 program (Microsoft® Corporation, USA), aiming to identify patterns concerning the percentage of infection and the time after kidney transplantation. The data were represented in absolute values or mean ± standard deviation (SD) of the mean. For continuous variables with normal distribution, a t-test was performed, while for those that did not follow a normal distribution, the Mann-Whitney U test was used, with $p < 0.05$ being considered significant. Pearson's correlation was used to assess whether the time spent with the urinary catheter correlates with the frequency of infections, adopting $p < 0.05$. For this purpose, the periods of stay of up to 5 days, from 5 to 7 days, and more than 7 days of stay were evaluated.

The Research Ethics Committee approved the study under opinion 5,575,996, dated August 11, 2022, and followed all the precepts of Resolution No. 466/2012.

RESULTS

From 2019 to 2022, 548 patients underwent kidney transplantation; 11 were not included in the study due to a lack of information on the HTJF platform. Of these 537 patients who underwent kidney transplantation at the hospital, 258 were white, 116 were black, and 163 were mixed race. Of this total, approximately 12% presented UTIs, of which 32 were white patients (50% of the total UTIs), 15 were mixed race (23% of the total UTIs), and 17 were black (26.5% of the total UTIs). Of the 64 cases of UTI, 11 were in patients who received living allografts, and 53 were in deceased patients. Graft loss among those with UTIs was observed in 12 patients, of which only two cases were of living allografts. Of this total number of patients with UTI, approximately 18.7% had allograft loss, which differs significantly from patients who did not have UTI (8.87%) (Table 1).

Table 1. Total number of transplants performed in a tertiary hospital in Juiz de Fora, state of Minas Gerais, and incidence of UTI in these patients from 2019 to 2022.

Year	Total number of transplant recipients (n)	Transplanted n (=%)		Graft loss (n)	
		No UTI	With UTI	No UTI	With UTI
2019	128	105	23 (17.0)	6	5
2020	106	98	8 (7.5)	6	1
2021	143	127	16 (11.0)	6	4
2022	160	143	17 (13.0)	24	2
Total	537	473	64 (12.0)	42	12

Source: Elaborated by the authors

Of the 64 patients who presented UTI between 2019 and 2022, 16 died: eight due to complications related to the infection, such as multiple infections, sepsis, hemodynamic instability due to infectious syndrome; four due to complications from coronavirus disease 2019 (COVID-19); and four due to other causes. Graft loss due to UTI was reported in only one case.

In 2020, due to COVID-19, there was a lower number of transplants than in other years. On the other hand, in 2022, the number of transplants increased by more than 50% compared to that year.

In all years, it is noted that the number of male patients who undergo kidney transplants is higher than that of female patients. Although in 2020 and 2022, the group of female patients had a higher rate of infections, there is no significant difference in UTI between the genders ($p > 0.05$) (Table 2).

Table 2. Incidence of UTI in patients who underwent kidney transplantation at a tertiary hospital in Juiz de Fora, state of Minas Gerais, from 2019 to 2022.

Year	Pacientes do sexo feminino			Pacientes do sexo masculino		
	Total transplants n	UTI n (%)	Mean age (± SD)	Total transplants n	UTI n (%)	Mean age (± SD)
2019	45	7 (15.5)	52.57 (14.94)	83	16 (19.3)	59.94 (8.54)
2020	30	4 (13.3)	34.75 (4.75)	76	4 (5.3)	53.00 (7.50)
2021	60	2 (3.3)	49.00 (3.00)	83	14 (16.9)	45.14 (12.59)
2022	65	9 (13.8)	52.78 (8.46)	95	8 (8.4)	52.33 (13.43)
Total	200	22 (11.0)	49.09 (11.09)	337	42 (12.5)	55.22 (11.09)

Source: Elaborated by the authors.

When analyzing kidney transplant patients who had positive urine cultures in the 30-day postoperative period, it was observed that the infection rate was higher in the first 5 days, both in men and women, gradually decreasing after this period. Thus, there was no positive linear correlation between the time spent with the urinary catheter and UTI ($r = -0.33$, $p < 0.05$) (Table 3).

Table 3. Length of stay with a urinary catheter and number of UTIs in kidney transplant patients in a tertiary hospital in Juiz de Fora, state of Minas Gerais, from 2019 to 2022.

Year	Interval of stay with the urinary catheter			
	Up to 5 days of probe	5 to 7 days of probe	More than 7 days	Total
2019	12	6	5	23
2020	4	4	0	8
2021	7	7	2	16
2022	10	3	4	17
Total	33	20	11	64

Source: Elaborated by the authors.

When analyzing the results of the urine culture, the microorganisms listed in Table 4 were observed, as well as the frequency of infections per patient, according to the year of analysis. Among the most frequent microorganisms, the following stand out: *Klebsiella pneumoniae* (32.8% of UTI cases), *Serratia marcescens* (30.3%) and *Escherichia coli* (26.5%).

Table 4. Total frequency of microorganisms isolated in patients after kidney transplantation in a tertiary hospital in Juiz de Fora, in the Brazilian state of Minas Gerais, from 2019 to 2022.

Microorganisms	Number of occurrences in patients with UCUTI n	Occurrences in patients with UCUTI %
Klebsiella pneumoniae	21	32.8
Serratia marcescens	17	30.3
Escherichia coli	13	26.5
Candida albicans	5	7.8

Source: Elaborated by the authors.

It was found that the frequency of these microorganisms tends to differ according to the patient's gender, with a greater variety and frequency of infecting microorganisms being observed in males from 2019 to 2021. Polymicrobial infections were also observed.

In the evaluation of the antimicrobial susceptibility profile by determining the MIC among isolated bacterial species, the highest resistance rates (adding the intermediate resistance rate to the resistance rate) for the Gram-negative group occurred against cefuroxime (68.7%) and cephalothin (62.5%). The Gram-positive group had the highest resistance rate against levofloxacin (75%). Regarding the antimicrobials sulfamethoxazole/trimethoprim, used by HTJF preventively before transplantation, considerable resistance was observed (33%), which may limit their prophylactic efficacy or their use in the treatment of urinary infections in transplant patients, considering the MIC90. In the Gram-negative group, there were resistance rates; in the Gram-positive group, there were no rates for gentamicin and linezolid. These results can be seen in Table 5, which shows the values of the sensitivity profile, intermediate resistance and resistance to each antimicrobial, and the other MIC_{50} and MIC_{90} values.

Table 5. Antimicrobial susceptibility profile of Gram-negative and Gram-positive bacterial species isolated from UTI in kidney transplant patients at a tertiary hospital in Juiz de Fora, state of Minas Gerais, from 2019 to 2022.

Antimicrobials	MIC (µg/Ml)			Susceptibility profile (%)			
	CIM_{50}	CIM_{90}	Variação	S	RI	R	NT
Gram-negative bacteria							
Amikacin	≤ 2.0	32.0	≤ 2.0 - ≥ 64.0	85.4	2.1	10.4	2.1
Amoxicillin/clavulanate	≥ 32.0	≥ 32.0	≤ 2.0 - ≥ 32.0	12.5	12.5	47.9	27.1
Nalidixic acid	8.0	≥ 32.0	≤ 2.0 - ≥ 32.0	45.8	-	37.5	16.7
Cephalothin	≥ 64.0	≥ 64.0	≤ 2.0 - ≥ 64.0	8.3	2.1	60.4	29.2
Cefepime	8.0	≥ 64.0	≤ 1.0 - ≥ 64.0	50.0	2.0	48.0	-
Ceftriaxone	8.0	≥ 64.0	≤ 1.0 - ≥ 64.0	39.6	-	50.0	10.4
Cefuroxime	≥ 64.0	≥ 64.0	≤ 1.0 - ≥ 64.0	10.5	-	68.7	20.8
Ciprofloxacin	0.5	≥ 4.0	≤ 0.25 - ≥ 4.0	60.4	-	39.6	-
Ertapenem	≤ -0.5	≤ -0.5	≤ 0.5 - ≥ 8.0	60.4	-	6.3	33.3
Gentamicin	≤ 1.0	≥ 16.0	≤ 1.0 - ≥ 16.0	62.5	8.4	29.1	-
Meropenem	≤ -0.25	≥ 16.0	≤ 0.25 - ≥ 16.0	66.6	-	31.2	2.2
Nitrofurantoin	128.0	≥ 512.0	≤ 16.0 - ≥ 512.0	25.0	12.5	43.8	18.7
Norfloxacin	≤ -0.5	≥ 16.0	≤ 0.5 - ≥ 16.0	56.2	-	27.1	16.7
Piperacillin/tazobactam	32.0	≥ 128.0	≤ 4.0 - ≥ 128.0	33.3	8.4	27.1	31.2
Sulfamethoxazole/ trimethoprim	≤ -20.0	≥ 320.0	≤ 0.5 - ≥ 320.0	54.2	-	33.3	12.5
Gram-positive bacteria							
Ampicillin	≤ 2.0	≥ 32.0	≤ 2.0 - ≥ 32.0	25.0	-	25.0	50.0
Gentamicin	≤ 0.5	≤ 0.5	-	100.0	-	-	-
Levofloxacin	≥ 8.0	≥ 8.0	2.0 - ≥ 8.0	25.0	-	75.0	-
Linezolid	1.0	2.0	1.0 - 2.0	100.0	-	-	-
Nitrofurantoin	≤ 16.0	≥ 128	≤ 16.0 - ≥ 128.0	75.0	-	25.0	-
Oxacillin	≥ 4.0	≥ 4.0	-	-	-	50.0	50.0
Penicillin G	≥ 0.5	≥ 0.5	-	-	-	50.0	50.0
Sulfamethoxazole/ trimethoprim	40.0	160.0	40.0 - 160.0	25.0	-	25.0	50.0
Teicoplanin	2.0	≥ 32.0	≤ 0.5 - ≥ 32.0	75.0	-	25.0	-
Vancomycin	1.0	≥ 32.0	1.0 - ≥ 32.0	75.0	-	25.0	-

Source: Elaborated by the authors. NT = not tested; R = resistance; IR = intermediate resistance; S = sensibility.

DISCUSSION

Immunosuppression, which must be administered to all patients who undergo transplants, makes them more susceptible to infectious conditions, which is one of the leading causes of death in transplant recipients, especially in the first year after the transplant[13]. The hospital where the study was carried out adopts in its routine the infection prevention measures recommended by Anvisa[14], proving to be relatively effective, with an infection rate of approximately 12% in the years evaluated, with the lowest percentage of cases of urinary tract infection in 2020. This fact can be related to the COVID-19 pandemic; due to the lethality of the virus, the main transplant centers suffered from the impact of the situation, resulting in a reduction in the number of transplants due to changes in the eligibility criteria for organ donors and recipients and the diversion of resources to centrally combat the pandemic[15], which may have reduced the eligibility criteria, as well as additional care with aseptic conditions.

The IUC is an invasive device that becomes a gateway for infectious conditions, mainly due to the time it is in place. Thus, during catheterization, lack of care in the urinary meatus, inadequate use of sterile collection and poor use of sterile insertion techniques favor the installation of infectious microorganisms[16]. According to Kumar et al.[17], the rate of UTI in transplant patients ranges from 35 to 80% in the first months after transplantation. Sousa et al.[18] observed a similar rate at the Kidney and Hypertension Hospital and the Hospital de São Paulo (31.3%) in the 1st year after transplantation. The exact rate was observed in children who underwent kidney transplants (32%) at the Federal University of São Carlos[19]. Although this study was only evaluated in the first 30 days, the average infection rate was only 12% (64 patients out of 537

transplant recipients) from 2019 to 2022, since 18.75% lost the graft. Female patients are more susceptible to urinary tract infections due to the reduced size of the urethra and its proximity to the anus and vagina, which facilitates the migration of microorganisms that do not belong to the urinary tract microbiota[20]. Men, on the other hand, have a longer urethra, which makes infection more difficult. However, male transplant patients in the hospital are immunosuppressed, which may explain the higher frequency of infections in this group. In addition, inadequate catheter insertion management, poor hygiene at the site, and the length of stay may have contributed to the higher frequency of UTIs in this group[21]. In the case of HTJF, the higher rate of infections in the first 5 days appears to be related to intraoperative risks, such as allografts from deceased individuals and/or the use of urethral catheters. Reduced UTI cases since 2020 may be associated with using more rigorous protocols and excellent care with asepsis, highlighting the possibility that infections are related to intraoperative risks.

UTIs are frequently caused by Gram-negative agents, such as *Escherichia coli, Klebsiella* sp., *Proteus* sp., *Enterobacter* sp. and *Citrobacter* spp., observed in about 80% of cases. In about 10%, Gram-positive agents are observed, such as *Staphylococcus saprophyticus, Enterococcus faecalis* and *Staphylococcus aureus*[21-25]. However, in our finding, we verified a high frequency of *Serratia marcescens*, a Gram-negative bacterium of the Enterobacteriaceae family, with a high potential for dissemination, resistant to several antimicrobials and many antiseptics used in the hospital environment[26-28]. Currently, the genus *Serratia* spp. is considered an emerging bacterium.

Although different transplant centers use antibiotics prophylactically in kidney transplantation, the effectiveness of this method is questionable since it has little impact on preventing infections and may induce resistance to routinely used antibiotics[29]. As the first days after surgery are crucial for the body to recover homeostasis, it can be inferred that there is a greater risk of infections due to the probe[30]. Therefore, HTJF also provides preventive treatment with sulfamethoxazole/trimethoprim antibiotics after transplantation; however, a higher frequency of infections is observed up to the first 5 days after surgery. The susceptibility profile evaluated with sulfamethoxazole/trimethoprim antibiotics shows a relatively high degree of resistance (33%), demonstrating its limited efficacy as prophylaxis or treatment of urinary infections in kidney transplant patients. Several bacteria resist sulfamethoxazole/trimethoprim antimicrobials, such as *Escherichia coli, Klebsiella* sp., *Proteus* sp., *Morganella* sp. and *Serratia* sp.[31]; many occur frequently in cases of UCUTI in transplant patients in the hospital. Given this, reviewing the antimicrobial used as pre-treatment may be essential.

During the microbiological analysis of the research results, polymicrobial infections were identified in the patients – around 5%. The contamination may have been caused by various factors related to the host, such as immunosuppression and urological disorders, together with external factors, such as injury, use of a urinary catheter or even the hospital environment itself[32].

During the Groupe Transplantation and Infection (GTI) meeting in Paris, France, in 2023, new approaches to managing complications from infections in transplant recipients were discussed. Among the group's concerns is the increase in multidrug-resistant bacteria. The group suggests optimizing the available antimicrobial drugs, rapid resistance diagnosis, and determining the MIC for the different molecules for solid organ transplants, such as kidneys. Combinations between different antimicrobials, as well as optimizing dosages with the use of high doses and prolonged infusions, are also alternatives to contain infections. Furthermore, they emphasize that a more significant multidisciplinary discussion between microbiologists and clinicians is extremely important[33].

Due to all these factors, UTI in kidney transplant patients requires attention from the healthcare team, as it can trigger serious complications in the transplanted organ systemically, directly influencing the functioning and vitality of the graft[34].

CONCLUSION

Our study, which analyzed the medical records of patients who underwent kidney transplantation at the hospital and presented UTI from 2019 to 2022, showed a relatively low rate in the first 30 days after surgery compared to the average of other hospitals in the country. Although low, it was possible to observe that the most frequent bacteria observed in the UCUTI are resistant to the antimicrobials sulfamethoxazole/trimethoprim, which is used preventively before hospital transplantation.

The frequency of these infections is higher in the first 5 days after surgery, which may be related to handling and asepsis during bladder catheterization in the hospital environment, which may favor infection.

Evaluating the antimicrobial susceptibility profile by determining the MIC revealed significant resistance rates for the group of Gram-negative bacteria. The group of Gram-positive bacteria had the highest resistance rate against levofloxacin. The study corroborates the importance of patient management during urinary catheter placement and daily care since a significant

part of infections originates from the human microbiota. This care should be emphasized mainly due to the high degree of resistance of the microorganisms observed to antibiotics.

CONFLICT OF INTEREST

Nothing to declare.

AUTHOR'S CONTRIBUTION

Substantive scientific and intellectual contributions to the study: Silva ECS, Guilherme SP, Ferreira GF, Nascimento TC, Miranda CN; **Conception and design:** Silva ECS, Ferreira GF, Rocha APM; **Data analysis and interpretation:** Silva ECS, Nascimento TC, Miranda CN, Rocha APM; **Article writing:** Silva ECS, Nascimento TC, Alvim ALS, Rocha APM; **Critical revision:** Silva ECS, Nascimento TC, Alvim ALS, Rocha APM; **Final approval:** Rocha APM

DATA AVAILABILITY STATEMENT

All dataset were generated or analyzed in the current study.

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